Modular $Pd^{(I)}$ Cross-Coupling Strategies and Original $Ni^{(I)}$ Metalloradical Catalysis

Von der Fakultät für Mathematik, Informatik und Naturwissenschaften der RWTH Aachen University zur Erlangung des akademischen Grades eines Doktors der Naturwissenschaften genehmigte Dissertation

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Für meine Eltern in größter Dankbarkeit

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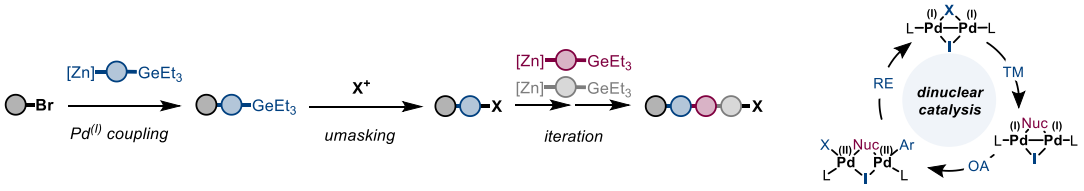
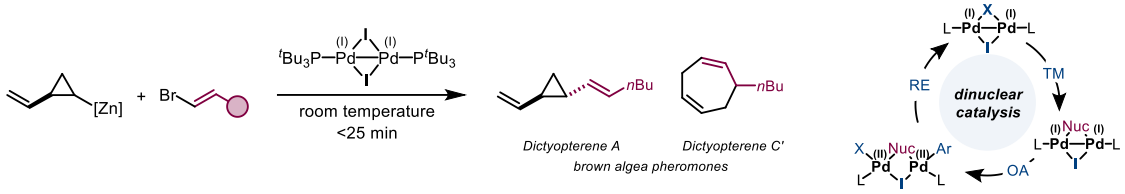
Abstract

Homogeneous metal catalysis has revolutionized modern organic synthesis. Traditionally, most reported methods have focused on closed-shell two-electron processes involving mononuclear species, *e.g.* $Pd^{(0)}/Pd^{(II)}$ cycles. In contrast, processes involving dimeric metal complexes in rather unusual oxidation states like $Pd^{(I)}$ have – by comparison – received much less attention. In the context of this thesis, dinuclear palladium$^{(I)}$ and nickel$^{(I)}$ complexes were studied. Traditionally, such dinuclear scaffolds were utilized as precursors for highly reactive, low-valent mononuclear species. However, our group found strong evidence for dinuclear $Pd^{(I)}$ reactivity and mononuclear $Ni^{(I)}$ metalloradical catalysis.

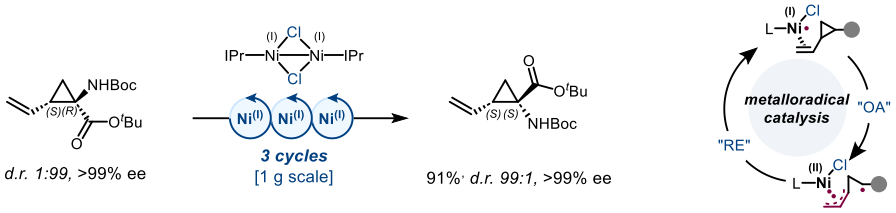
The modular assembly of standardized building blocks is a powerful way to generate diverse molecules quickly. However, to make this approach more widely applicable, the generality of the coupling methodology is critical. The first chapter of this thesis discusses a new modular coupling method that complements the existing strategy of boron-containing precursors. Our approach uses polyfunctionalized organogermane-containing building blocks that display orthogonal reactivity towards $Pd^{(I)}$-catalyzed cross-coupling conditions. The organogermane moiety itself is unreactive towards $Pd^{(I)}$ dimer bond construction but can act as a masked halide functionality that can be revealed in an electrophilic unmasking event. This method significantly shortens reaction times for iterative coupling steps and allows for the creation of linear iodinated polyarenes, which were previously inaccessible via modular cross-coupling. Furthermore, the recycling of the germanium handle was showcased, improving the methodology's sustainability.



Vinylcyclopropanes are functional handles with significant value in mechanistic studies, drugs, and natural products. They are also used as precursors for various synthetic transformations. However, their reactive nature makes their installation through catalytic approaches challenging. In this context, chapter two highlights the development of a modular and stereoretentive method for installing (di)vinylcyclopropanes under mild conditions. This method enables access to *cis* or *trans* cyclopropane and *E* or *Z* vinyl-stereochemical relationships. The process relies on air-stable dinuclear $Pd^{(I)}$ catalysis, allowing rapid and highly selective access to a diverse range of vinylcyclopropane motifs at room temperature within 30 minutes. The efficiency has been showcased in the synthesis of the naturally occurring *Dictyopterenes* found in brown algae.



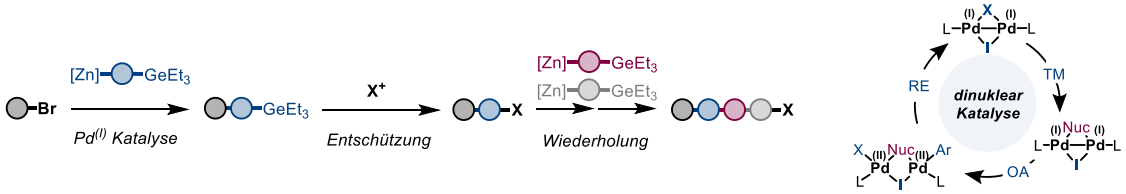
Traditionally, organic free radicals, upon addition to a vinylcyclopropane, lead to rapid ring-opening under strain release. This transformation is widely used as a mechanistic probe for the intermediacy of radicals. However, the last chapter of my thesis has revealed a new perspective. A $Ni^{(I)}$ metalloradical triggers reversible *cis/trans*-isomerization instead of opening towards the thermodynamic equilibrium. This isomerization proceeds under chiral inversion and is remarkably rapid and mild. The extensive mechanistic studies support novel metalloradical reactivity, and key mechanistic features were revealed, such as the reversibility of the process. The new approach has been applied in two protocols: a dynamic thermodynamic resolution strategy of a valuable pharmaceutical building block and a *trans*-to-*cis* isomerization-tandem Cope rearrangement strategy.



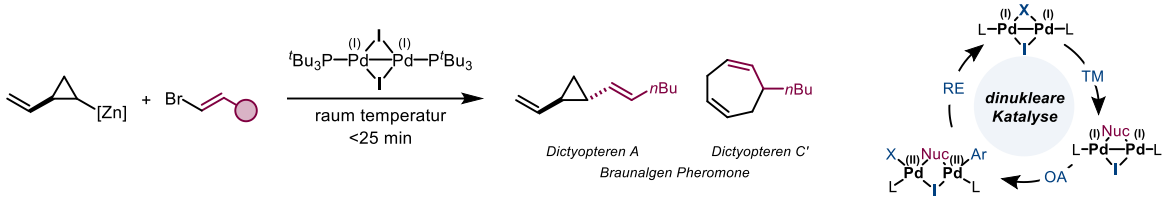
Zusammenfassung

Die homogene Metallkatalyse hat die moderne organische Synthese revolutioniert. Traditionell lag der Fokus auf zwei-Elektronen-Prozesse und einkernige Spezies, wie zum Beispiel in $Pd^{(0)}/Pd^{(II)}$ Systemen. Im Gegensatz dazu erhielten Prozesse, die mehrkernige Metallkomplexe in unkonventionellen Oxidationsstufen wie $Pd^{(I)}$ einbeziehen, wesentlich weniger Aufmerksamkeit. Im Rahmen dieser Arbeit wurden zweikernige bzw. dinukleare Palladium$^{(I)}$ und Nickel$^{(I)}$ Komplexe untersucht. Solche Dimere galten lange als sehr effektive Vorstufen für hochreaktive, niedrigvalente Katalysator-Spezies. Darüber hinaus hat unsere Arbeitsgruppe Bedingungen für dinukleare $Pd^{(I)}$ Reaktivität wie auch einkernige $Ni^{(I)}$ Metalloradikalkatalyse entdeckt.

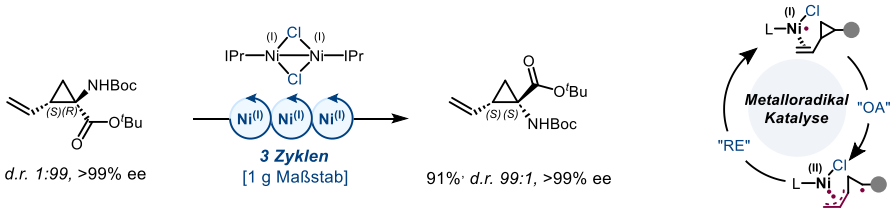
Auch in der organischen Synthese ist das modulare Zusammenbauen von Standardbausteinen eine äußerst effiziente Methode, um eine Vielzahl verschiedener Moleküle schnell herzustellen. Damit dieser Ansatz jedoch universell anwendbar ist, ist die Flexibilität der Kopplungsmethode von entscheidender Bedeutung. Im ersten Kapitel dieser Arbeit wird eine neue modulare Kopplungsmethode diskutiert, die die bestehenden Strategien erweitert. Unser Ansatz nutzt innovative Organogermanium-Bausteine, die eine orthogonale Reaktivität gegenüber $Pd^{(I)}$ katalysierten Kreuzkupplungsreaktionen aufweisen. Die Organogermanium-Einheit selbst reagiert nicht unter $Pd^{(I)}$-Katalyse, kann jedoch selektiv elektrophil halogeniert werden und somit als maskiertes Halogenid dienen. Diese Methode verkürzt erheblich die Reaktionszeiten für wiederholte Kopplungsschritte und ermöglicht die Herstellung von linear iodierten Polyarenen, die zuvor nicht durch modulare Kreuzkupplungen erreichbar waren. Darüber hinaus ermöglicht die Wiederverwendung der Germanium-Einheit eine Verbesserung der Nachhaltigkeit dieser Methodik.



Vinylcyclopropane sind von erheblichem Wert für mechanistische Studien, Medikamentenentwicklung und die Herstellung von Naturprodukten. Sie dienen auch als Vorläufer für verschiedene synthetische Transformationen. Aufgrund ihrer reaktiven Natur gestaltet sich jedoch ihre Installation durch katalytische Ansätze oft herausfordernd. In diesem Kontext präsentiert Kapitel Zwei die Entwicklung einer modularen und stereoselektiven Methode zur Einführung von (Di)vinylcyclopropanen unter milden Bedingungen. Diese Methode ermöglicht den Zugang zu *cis*- oder *trans*-Cyclopropanen sowie zu *E*- oder *Z*-Vinyl-Stereochemie. Unser Prozess beruht auf der Verwendung luftstabiler dinuklearer $Pd^{(I)}$-Katalyse, die in weniger als 30 Minuten bei Raumtemperatur einen hochselektiven Zugang zu einer Vielzahl von Vinylcyclopropan-Motiven ermöglicht. Die Effizienz dieses Ansatzes wurde unter anderem anhand der Synthese der natürlich vorkommenden *Dictyopterene* demonstriert, die in Braunalgen zu finden sind.



Traditionell führt die Zugabe von organischen Radikalen zu einem Vinylcyclopropan oft zu einer schnellen Ringöffnung unter Freisetzung der Ringspannung. Diese Reaktion wird unter anderem zur Detektion von freien Radikalen eingesetzt. Im letzten Kapitel meiner Dissertation präsentiere ich jedoch eine neue Perspektive. Wir haben ein $Ni^{(I)}$-Metalloradikal entdeckt welches eine reversible *cis/trans*-Isomerisierung auslöst, anstatt, der erwarteten, thermodynamisch Begünstigten Ringöffnung. Diese Isomerisierung erfolgt unter chiraler Inversion und verläuft bemerkenswert schnell unter milden Reaktionsbedingungen. Umfangreiche mechanistische Studien unterstützen einen völlig neuartigen Metalloradikal-Mechanismus, wobei wichtige mechanistische Merkmale, wie die Reversibilität des Prozesses, aufgedeckt wurden. Die neue Methode wurde in zwei Anwendungsfällen erfolgreich eingesetzt: erstens in einer dynamisch thermodynamischen Resolution eines wertvollen pharmazeutischen Bausteins und zweitens in einer *trans-zu-cis*-Isomerisierung-Tandem-Cope-Umlagerungsstrategie.



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Parts of the work described in this thesis have already been published in the following publications:

M. Mendel, T. Karl, J. Hamm, S. J. Kaldas, T. Sperger, B. Mondal, F. Schoenebeck 'Dynamic Stereomutation of Vinylcyclopropanes with Metalloradicals', *Nature* **2024**, DOI 10.1038/s41586-024-07555-1.

M. Mendel, L. Gnagi, U. Dabranskaya, F. Schoenebeck, 'Rapid and Modular Access to Vinylcyclopropanes Enabled by Air-stable Palladium$^{(I)}$ Dimer Catalysis', *Angew. Chem. Int. Ed.* **2023**, *62*, e202211167.

T. Kreisel, M. Mendel, A. E. Queen, K. Deckers, D. Hupperich, J. Riegger, C. Fricke, F. Schoenebeck, 'Modular Generation of (Iodinated) Polyarenes Using Triethylgermane as Orthogonal Masking Group', *Angew. Chem. Int. Ed.* **2022**, *61*, e202201475.

C. Fricke, T. Sperger, M. Mendel, F. Schoenebeck, 'Catalysis with Palladium$^{(I)}$ Dimers', *Angew. Chem. Int. Ed.* **2021**, *60*, 3355-3366.

Further publications that have not been featured in this thesis:

M. Mendel, I. Kalvet, D. Hupperich, G. Magnin, F. Schoenebeck, 'Site-Selective, Modular Diversification of Polyhalogenated Aryl Fluorosulfates ($ArOSO_2F$) Enabled by an Air-Stable Pd$^{(I)}$ Dimer', *Angew. Chem. Int. Ed.* **2020**, *59*, 2115-2119.

Conference presentations:

3rd Winter in Person Organic Symposium (WIPOS), **2023**, Honolulu, Hawaii, 'Exploration of the reactivity of dinuclear metal complexes' (poster presentation).

Dream Reactions with (or without) Hydrogen, **2023**, Münster, Germany 'Exploration of the reactivity of dinuclear metal complexes' (poster presentation).

21st International Symposium on Organometallic Chemistry Directed Towards Organic Synthesis (OMCOS XXI), **2023**, Vancouver, Canada 'Exploration of the reactivity of dinuclear metal complexes' (poster presentation).

15th New Year Symposium (NYS), 2023, Aachen, Germany, 'Molecular Complexity from Simple Building Blocks Enabled by $Pd^{(I)}$ Catalysis' (poster presentation).

22nd Lecturer Conference on Organic Chemistry (ORCHEM), 2022, Münster, Germany, 'Molecular Complexity from Simple Building Blocks Enabled by $Pd^{(I)}$ Catalysis' (poster presentation).

Frontiers of Organometallic Chemistry, 2020, Kühtai, Austria, 'Site-Selective, Modular Diversification of Polyhalogenated Aryl Fluorosulfates (ArOFs) enabled by an Air-Stable $Pd^{(I)}$ Dimer' (oral presentation).

13th New Year Symposium (NYS), 2020, Aachen, Germany, 'Site-Selective, Modular Diversification of Polyhalogenated Aryl Fluorosulfates (ArOFs) enabled by an Air-Stable $Pd^{(I)}$ Dimer' (flash talk and poster presentation).

Å	Ångström (1 Å = 0.1 nm)
AIBN	azobisisobutyronitrile (2,2′-Azobis(2-methylpropionitrile))
Ar	aryl
BDE	bond dissociation enthalpy
Bn	benzyl
cod	1,5-cyclooctadiene
Cp	cyclopentadienyl ligand
CI_4	*tetra*-iodomethane
CPCM	conductor polarizable continuum model (solvation model)
CPhos	2-dicyclohexylphosphino-2′,6′-bis(*N*,*N*-dimethylamino)biphenyl
*c*Pr	cyclopropyl
Cy	cyclohexyl
DABCO	1,4-diazabicyclo[2.2.2]octane
dba	dibenzylideneacetone (*trans*,*trans*-1,5-diphenyl-1,4-pentadien-3-one)
def2-TZVP	Ahlrichs basis set; split-valence triple-zeta
DFT	density functional theory
DIPEA	di-*iso*-propylethylamine
DMAc	*N,N*-Dimethylacetamide
dmbyp	dimethoxybipyridine
DMF	*N*,*N*-dimethylformamide
DMI	1,3-Dimethyl-2-imidazolidinone
DMSO	dimethylsulfoxide
dppf	1,1′-ferrocenediyl-bis(diphenylphosphine)
ECP	effective core potential
HAT	hydrogen atom transfer
IPent	1,3-bis(2,6-di-3-pentylphenyl)imidazol-2-ylidene
*i*Pr	*iso*-propyl (2-propyl)
IPr	1,3-bis(2,6-di-*iso*-propylphenyl)imidazol-2-ylidene
Isom	isomerization
JohnPhos	2-(di-*tert*-butylphosphino)biphenyl
L	general abbrevation for ligands
LANL2DZ	Los Alamos ECP
LiHMDS	lithium hexamethyldisilazane (lithium bis(trimethylsilyl)amide)
LiTMP	lithium 2,2,6,6-tetramethylpiperidide
M	general abbrevation for metals
M06	DFT method (hybrid metaGGA, Minnesota suite)
M06L	DFT method (metaGGA, Minnesota suite)
Me	methyl
MeCN	acetonitrile
Mes	mesityl (2,4,6-trimethylphenyl)
MeTAA	tetramethyltetraaza[14]annulene
MIDA	N-methyliminodiacetic acid

MOM	Methoxymethyl ether
MN15	DFT method (meta-NGA)
NBS	N-bromosuccinimide
*n*Bu	*n*-butyl (1-butyl)
n.d.	not determined
NIS	N-iodosuccinimide
NHC	*N*-heterocyclic carbene
NMP	*N*-Methylpyrrolidone
NMR	nuclear magnetic resonance spectroscopy
*n*Oct	*n*-octyl (1-octyl)
*n*Pr	*n*-propyl (1-propyl)
Nuc	nucleophile
OA	oxidative addition
OAc	acetate
OTf	triflate (trifluoromethanesulfonate, $^{-}OSO_2CF_3$)
OFs	fluorosulfate ($^{-}OSO_2F$)
*o*Tol	*ortho*-tolyl (2-methylphenyl)
Pd-PEPPSI	[NHC](3-chloropyridyl)palladium(II) dichloride
Ph	Phenyl
PMB	*para*-methoxybenzyl
Py	Pyridine
QPhos	1,2,3,4,5-Pentaphenyl-1′-(di-*tert*-butylphosphino)ferrocene
RE	reductive elimination
R/A	rearrangement
r.t.	room temperature
SDD	Stuttgart/Dresden ECP
SIPr	1,3-bis(2,6-di-*iso*-propylphenyl)imidazolidene
SMD	continuum solvation model by Cramer and Truhlar (based on charge density employing full solute electron density)
spl	square planar
*t*Bu	*tert*-butyl
$P(tBu)_3$	*tri(tert*-butyl)phosphine
TEMPO	2,2,6,6-tetramethylpiperidine-1-oxyl radical
tfp	*tris-o*-furylphosphane
THF	Tetrahydrofuran
TS	transition state
tet	tetrahedral
VCP	vinylcyclopropane
X	general abbrevation for halides
Xphos	2-dicyclohexylphosphino-2′,4′,6′-tri-*iso*-propylbiphenyl
xs	Excess
ωB97XD	hybrid DFT method (long-range and dispersion-corrected)
6-31G(d)	Pople basis set; split-valence double-zeta with added polarization functions on heavy atoms

Table of Contents

1

Introduction to Dinuclear Metal Complexes in Catalysis

Parts of this chapter were published in Angewandte Chemie International Edition.[1]

1 Introduction

1.1 Preamble

Chemical synthesis is the application of fundamental principles of reactivity and selectivity to obtain molecules with desired properties.[2] For this purpose, a broad toolbox of different reaction types exists, and one of the most powerful tools that has emerged over the last decades is homogeneous metal catalysis. Numerous metal complexes have successfully been used as catalysts for synthetic applications in areas such as fine chemistry and natural product synthesis, creating access to novel molecular structures. Consequently, four Nobel Prizes were awarded for significant contributions to this field in the early 21st century confirming its outstanding relevance (Knowles, Noyori, and Sharpless for catalytic hydrogenation and oxidation in 2001; Chauvin, Grubbs, and Schrock for metathesis in organic synthesis in 2005; Heck, Negishi, and Suzuki for palladium-catalyzed cross-coupling in 2010; Sharpless, Meldal and Bertozzi for the development of copper-catalyzed click chemistry and biorthogonal reactions in 2022). Furthermore, homogeneous metal catalysis is also expected to be vital in tackling major future challenges, such as sustainability, energy, and environmentally related questions. In this context, the fundamental understanding of reaction mechanisms and rational reaction design is a powerful driving force for further discoveries in homogeneous transition metal catalysis.

1.2 Dinuclear Palladium$^{(I)}$ and Nickel$^{(I)}$ complexes

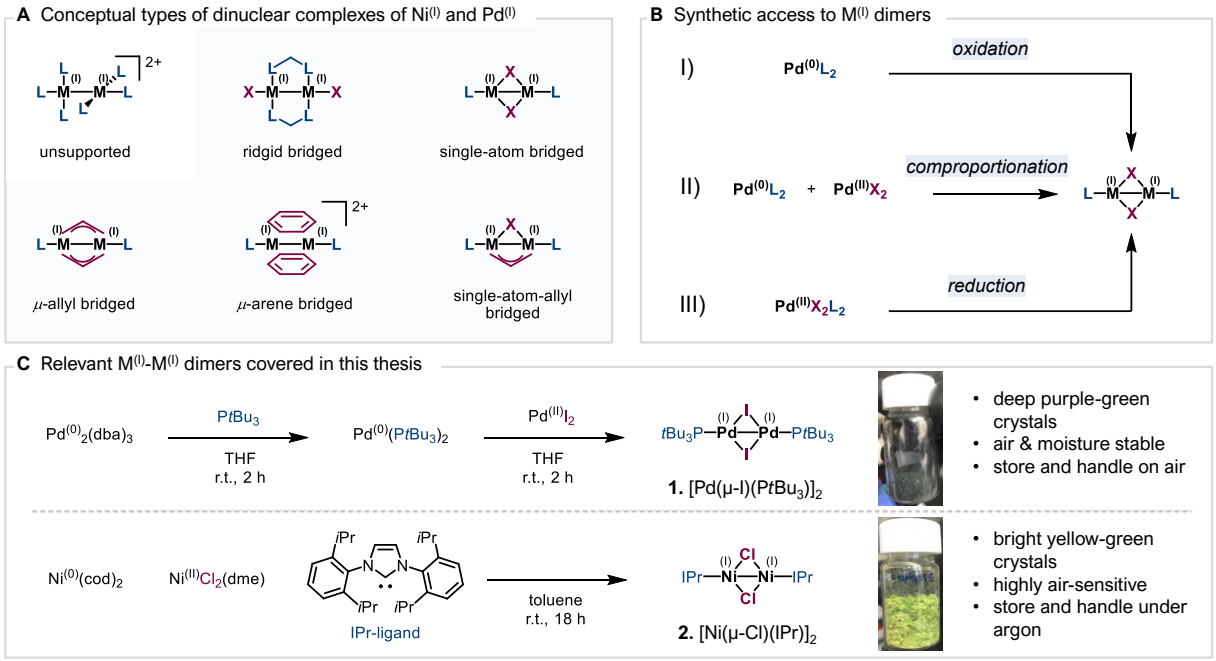
In homogeneous metal catalysis, transition metals are typically present in their most stable valence states, such as $Pd^{(0)}$ and $Pd^{(II)}$. Although mononuclear $Pd^{(I)}$ is less common, the paramagnetic d^9 $M^{(I)}$ species can be stabilized with auxiliary ligands and form diamagnetic, dinuclear $Pd^{(I)}$-$Pd^{(I)}$ species.[3-5] Dinuclear metal$^{(I)}$ complexes can be classified into unsupported or supported dimers (**Scheme 1A**). In unsupported dimers, both metal centers form a single $M^{(I)}$-$M^{(I)}$ σ-bond without any additional bridging ligands. In supported dimers, the bonding between the two $M^{(I)}$ centers is more developed due to the influence of additional bridging ligands. Supported dimers can be ridged-, single atom-, allyl- or arene-bridged, and hybrids between those conceptual types are viable.[3] Transition metal dimers can be synthesized from their precursors by various methods, including (i) oxidation of $M^{(0)}$, (ii) comproportionation of $M^{(0)}$ and $M^{(II)}$, or (iii) reduction of $M^{(II)}$ (**Scheme 1B**). Those strategies were also applied in the synthesis of $Pd^{(I)}$ dimer $[Pd(\mu\text{-}I)(P\textit{t}Bu_3)]_2$ **1** and $Ni^{(I)}$ dimer $[Ni(\mu\text{-}Cl)(IPr)]_2$ **2** (where IPr is 1,3-*bis*(2,6-diisopropylphenyl)imidazol-2-yli-dene) which are of particular interest in this thesis (**Scheme 1C**).

$[Pd(\mu\text{-}I)(P\textit{t}Bu_3)]_2$ (1): The physical appearance is deep purple crystals that are air- and moisture-stable and can be stored on the bench. The first synthesis of **1** was achieved by Mingos via oxidation of $Pd^{(0)}(P\textit{t}Bu_3)_2$ using different halogen-containing compounds (*e.g.,* N-iodosuccinimide, CI_4) with a maximum yield of 23%.[6] An improved synthesis of the related bromide-bridged $[Pd(\mu\text{-}Br)(P\textit{t}Bu_3)]_2$ with 89% yield was developed by the group of Colacot via the alkoxide-mediated reduction of the corresponding $Pd^{(II)}Br_2$(cod) precursor in the presence of 1.0 equivalent of $P\textit{t}Bu_3$ ligand.[7, 8] In contrast, our group accessed $Pd^{(I)}$ dimer

1 via the direct comproportionation of 1:1 molar ratio of $Pd^{(II)}I_2$ and $Pd^{(0)}(PtBu_3)_2$ in quantitative yield, while the latter can also be prepared in situ from $Pd_2(dba)_3$ (**Scheme 1C**).[9]

[Ni(μ-Cl)(IPr)]$_2$ (2): The physical appearance is yellow-greenish crystals that are remarkably air sensitive and oxidize within seconds once exposed to air.[10] The first preparation of **2** was achieved by Sigman in 10-20% yield via oxidation addition of bulky allylic chlorides to $Ni(cod)_2$ in the presence of IPr-ligand. Most likely, $Ni^{(I)}$ is formed after homolytic cleavage of the carbon-$Ni^{(II)}$ bond promoted by the size of both, the IPr-ligand and the bulky allyl group. Subsequently, Sigman improved the preparation by the direct comproportionation of $Ni^{(II)}Cl_2(dme)$, $Ni^{(0)}(cod)_2$ and IPr-ligand (1:1:2 molar ratio) in toluene, yielding **2** in 68% (**Scheme 1C**).[10]

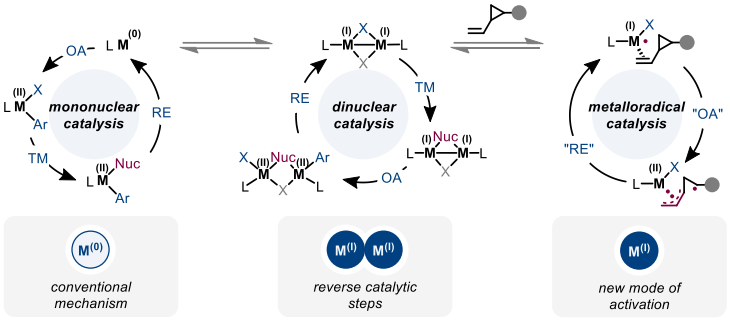
Scheme 1 | Introduction to dinuclear $M^{(I)}$-$M^{(I)}$ species: A) conceptual types; B) common synthetic strategies; and C) preparation of relevant dimers covered in this thesis.



1.3 Catalysis with Palladium$^{(I)}$ and Nickel$^{(I)}$ dimers

In transition metal catalysis, the right choice of precatalyst is crucial for desired reactivity because reaction parameters, including oxidation state, nuclearity, or ligation state, can be defined and controlled to a high degree of precision.[11] In this context, dinuclear $M^{(I)}$-$M^{(I)}$ systems can serve as unique precatalysts for the formation of monomeric species such as $M^{(0)}$, $M^{(I)}$ or $M^{(II)}$ (**Scheme 2**).[1, 3] Possible mechanistic scenarios could be the heterolytic cleavage or disproportionation of the $M^{(I)}$-$M^{(I)}$ bond into $M^{(0)}$ and $M^{(II)}$ or its homolytic cleavage into paramagnetic $M^{(I)}$ species accompanied by reduction or oxidation processes.[12] Similarly, in situ formation of dimeric $M^{(I)}$-$M^{(I)}$ species can occur,[13-16] which can function as a stable resting state or, moreover, under specific conditions, dinuclear reactivity can be feasible.[1, 3] In the following, chosen examples for mononuclear, dinuclear, and metalloradical catalysis with $Pd^{(I)}$ and $Ni^{(I)}$ dimers will be discussed.

Scheme 2 | Application of dinuclear $M^{(I)}$-$M^{(I)}$ scaffolds as diverse (pre)catalysts in mononuclear, dinuclear, and metalloradical catalysis.

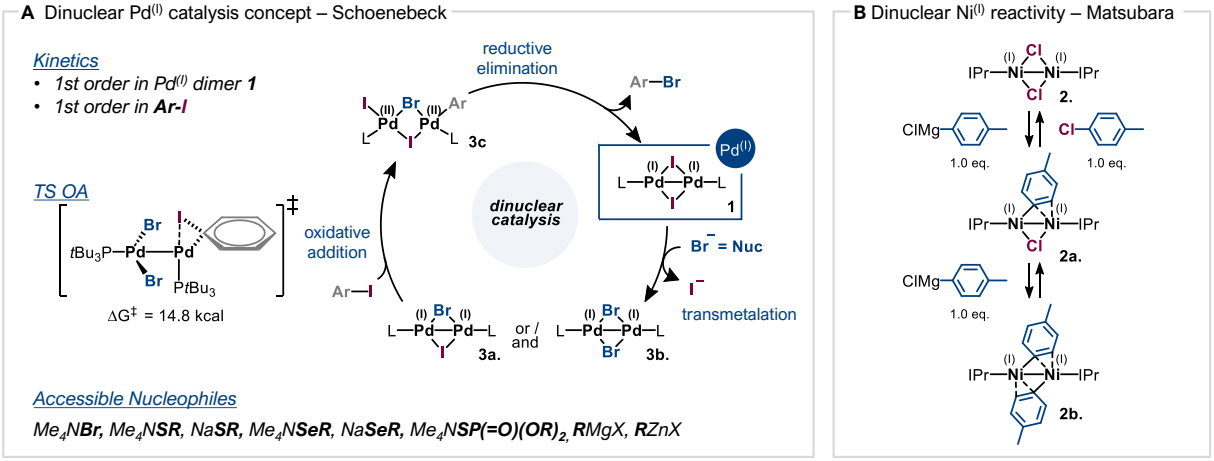


In the context of classical mononuclear $Pd^{(0)}/Pd^{(II)}$ catalysis, suitable nucleophiles can activate and destabilize the dinuclear framework.[8, 17] Consequently, $Pd^{(I)}$ dimers can function as a reservoir for highly reactive, monoligated 12-valence electron $Pd^{(0)}L$ species, resulting in increased activity, better product yields, and higher selectivities in various $Pd^{(0)}/Pd^{(II)}$ bond formation processes.[18] Comparison with correlated precatalysts such as $Pd^{(0)}L_2$ has shown that while ligand decoordination is already disfavored, its re-coordination is in direct competition with the desired substrate coordination, leading to decreased reactivity.

Determining whether the active compound is mononuclear or dinuclear can be challenging. However, our group found strong evidence for dinuclear $Pd^{(I)}$ reactivity.[1, 19, 20] The dinuclear $Pd^{(I)}$ catalysis concept relies on suitable nucleophiles as coupling partners that stabilize the dinuclear $Pd^{(I)}$ framework as bridging-unit (**Scheme 3**): Starting from $Pd^{(I)}$ dimer **1**, an initial one- or two-fold nucleophile replacement of the μ-bridging-unit takes place forming **3a** and/or **3b**. Then, the oxidative addition of aryl iodide at one single Pd center and subsequent ligand displacement leads to the semi-stable $Pd^{(II)}$ dimer **3c** that eliminates the product and regenerates $Pd^{(I)}$ dimer **1**. Noteworthy, the reversal of elementary steps (compared to mononuclear $Pd^{(0)}/Pd^{(II)}$ catalysis) enabled privilege reactivity: lack of catalyst deactivation,[21, 22] different driving force in transmetallation[23] as well as unique site-selectivity in oxidative addition have been discovered.[16, 24-26] Impressive examples include the dinuclear iodide-bromide halide exchange (Nuc = Me_4NBr),[19, 20] thiolation (Nuc = Me_4NSCF_3, NaSR)[21, 22] and selenolation reactions (Nuc = Me_4NSeCF_3, NaSeR).[9, 27] Furthermore, the site-selective functionalization of poly(pseudo)halogenated arenes with organomagnesium or organozinc as suitable nucleophiles have been achieved using dinuclear $Pd^{(I)}$ catalysis. Under standard $Pd^{(0)}/Pd^{(II)}$ conditions, site-selectivity depends on various factors, *e.g.*, steric and electronics of the substrate, ligation state, bond strength, additive effects, or solvent polarity can influence the outcome.[28-30] By employing $Pd^{(I)}$ dimer **1**, the fully site-selective functionalization of aryl bromides (Ar–Br) in the presence of aryl triflates (Ar–OTf), aryl fluorosulfates (Ar–OFs)[31] and aryl chlorides (Ar–Cl) was achieved within minutes at room temperature and in air.[16, 24-26] The selectivity was completely substrate-independent, and even sterically hindered C–Br sites were selectively functionalized while leaving other reactive sites untouched.[32] However, by increasing solvent polarity (NMP, DMI, or DMAc), the same $Pd^{(I)}$ dimer enabled the functionalization of aryl triflates, fluorosulfates, and chlorides.[25, 26] Most likely cleavage of the $Pd^{(I)}$ dimer into monomeric palladate species occurs under those conditions featuring $Pd^{(0)}/Pd^{(II)}$ catalysis. The protocol

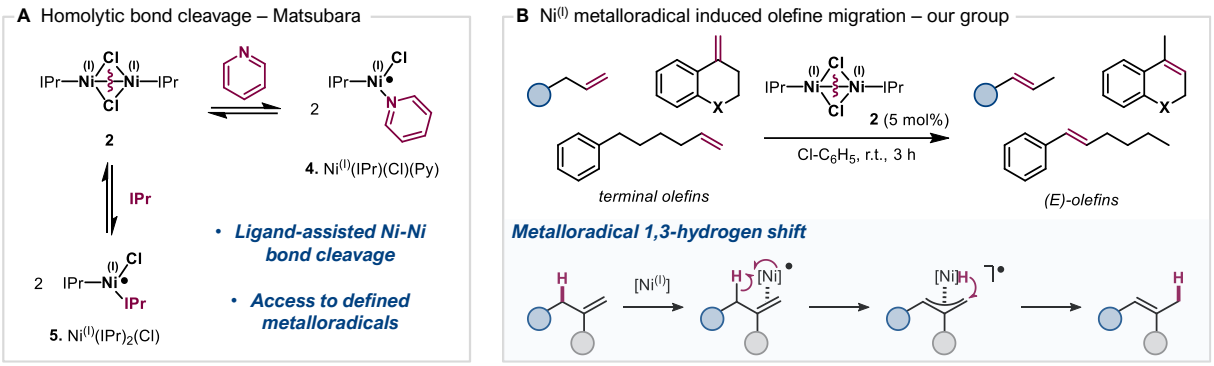
culminated in the triple sequential functionalization of polyhalogenated arenes in a one-pot fashion in less than one hour (reactivity order: Br > OTf / OFs > Cl).

Scheme 3 | Examples of dinuclear catalysis: A) $Pd^{(I)}$ catalysis concept by our group[1] and B) stoichiometric $Ni^{(I)}$ dimer reactivity by Matsubara and co-workers.[33]



As long as the dinuclear framework stays intact during catalysis, dinuclear reactivity using $Ni^{(I)}$ dimers can proceed similarly to $Pd^{(I)}$ dimers.[3] In this context, Matsubara and co-workers have found inevitable evidence for the direct involvement of $Ni^{(I)}$ dimer **2** in the Kumada-Tamao-Corriu cross-coupling of aryl halides (**Scheme 3B**).[33] Interestingly, the authors isolated and characterized the one- (**2a**) and two-fold (**2b**) aryl-bridged $Ni^{(I)}$ dimers obtained from stoichiometric reactions between $Ni^{(I)}$ dimer **2** and *para*-tolyl magnesium chloride, similar to $Pd^{(I)}$ dimers **3a** and **3b** (**Scheme 3B**). Further stoichiometric reactions with aryl chlorides lead to the biphenyl cross-coupling products and the regeneration of $Ni^{(I)}$ dimer **2**, clearly indicating their involvement in the catalytic cycle. It is noteworthy that the aryl-bridged $Ni^{(I)}$ dimer **2a** was also obtained from a stoichiometric reaction of $Ni(cod)_2$, IPr-ligand and chlorobenzene, indicating the complex speciation in $Ni^{(0)}$ catalysis. Although the authors proposed an alternative mechanism for the catalytic reaction in which the OA at $Ni^{(I)}$ dimer **2** first takes place, the findings strongly support the existence of dinuclear systems in nickel catalysis. On the other hand, the most significant differences between $nickel^{(I)}$ and $palladium^{(I)}$ dimers are that the $Ni^{(I)}$-$Ni^{(I)}$ bond is more labile and that the monomeric $Ni^{(I)}$ species are significantly more stable (**Scheme 4A**). For instance, Matsubara has demonstrated that $Ni^{(I)}$ dimer **2** can easily be cleaved into monomeric $Ni^{(I)}$ species in the presence of an appropriate ligand such as pyridine **4** or IPr **5**.[34, 35] Moreover, the monomeric and dimeric species were found in equilibrium with each other. Similarly, our group discovered that $Ni^{(I)}$ dimer **2** can act as a precursor for defined $Ni^{(I)}$ metalloradicals *via* homolytic scission of the $Ni^{(I)}$-$Ni^{(I)}$ bond when exposed to an olefin (**Scheme 4B**).[36] The olefin-bound monomeric unit (olefine)(IPr)$Ni^{(I)}$-Cl subsequently underwent H-atom abstraction from the olefin, and consecutive relocation of the H-atom (HAT) resulted in double-bond migration, which was the first ever reported metalloradical induced 1,3-hydrogen atom shift in olefin migration. The computational and experimental mechanistic studies suggested that a $Ni^{(I)}$ controlled reactivity of the olefinic double-bond via radical pathway is operative. Noteworthy, radical probe experiments using a vinylcyclopropane did not show the expected opening, and instead, partial isomerization was observed, which built the foundation of one subchapter discussed in this thesis.

Scheme 4 | Application of $Ni^{(I)}$ dimer **2** in: A) Nucleophile-induced homolytic Ni-Ni bond cleavage observed by Matsubara and co-workers[34, 35] and B) our group showed the first $Ni^{(I)}$ metalloradical 1,3-hydrogen atom shift.[36]



1.4 Thesis outline

This thesis explores the potential of dinuclear $Pd^{(I)}$-$Pd^{(I)}$ and $Ni^{(I)}$-$Ni^{(I)}$ metal complexes as unique (pre)catalysts to tackle extensive synthetic challenges and unlock novel possibilities.

- Chapter 2 describes the development of a modular iterative cross-coupling protocol that complements the state-of-the-art strategies. It demonstrates the synthesis of the *bis*-functional organogermane-zinc building blocks and their compatibility with $Pd^{(I)}$ catalysis towards the synthesis of iodinated polyarenes.
- Chapter 3 showcases the extension of $Pd^{(I)}$ catalysis towards the formation of (di)vinylcyclopropanes. This includes the Negishi cross-coupling towards vinylcyclopropanes and the direct late-stage installation of the vinylcyclopropyl functionality in a stereocontrolled fashion.
- Chapter 4 discloses the results of a $Ni^{(I)}$ metalloradical induced vinylcyclopropane stereomutation study. Fundamental mechanistic investigations are discussed, and the value of the new methodology is highlighted in a dynamic thermodynamic resolution and a tandem Cope-isomerization strategy.

2

Modular Generation of (Iodinated) Polyarenes Using Triethylgermane as Orthogonal Masking Group

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The results described in this chapter were published in Angewandte Chemie International Edition.[37] Experimental work has partially been carried out in collaboration with other members of the Schoenebeck group, whose contributions are stated in detail in the respective subchapters.

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2 Modular Generation of (Iodinated) Polyarenes Using Triethylgermane as Orthogonal Masking Group

2.1 Introduction

The advantage of a general synthesis methodology involving the sequential or iterative assembly of interchangeable building blocks has been demonstrated in the development of automated peptide and oligonucleotide synthesizers that have improved access to those compound types and accelerated further discoveries in several research areas.[38, 39] Similarly, small molecules have significant untapped potential to benefit society, but individual customized syntheses limit the current accessible chemical space.[40] Although some modular approaches to access specific oligomeric structures have been developed, there needs to be a more general, non-customized synthesis of small molecular structures such as polyarenes.[41] A modular assembly of diverse building blocks that is general, entirely predictable, and selective for a wide range of bond-forming processes offers the possibility of reaching molecular diversity faster and most likely accelerates the discovery of new functional molecules.[40] Metal-mediated cross-coupling has been identified as an exceptional methodology for the modular construction of small molecules: cross-coupling reactions are very general yet very efficient, a wide variety of bond types can be formed, and the building blocks used are versatile and readily available.[42]

2.1.1 Sequential cross-coupling

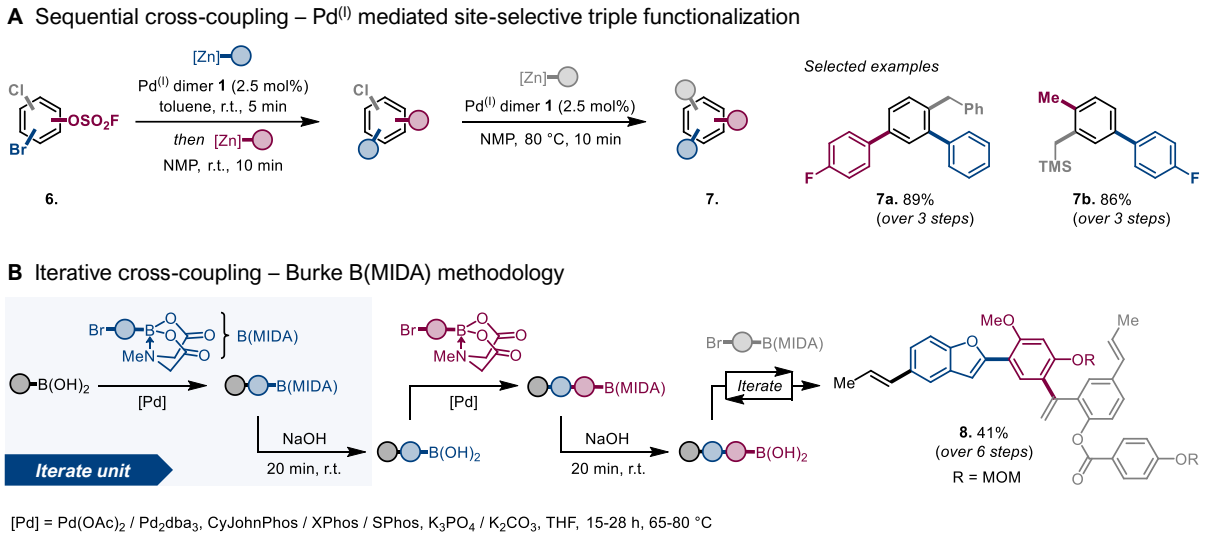
In sequential cross-coupling reactions, a pre-functionalized building block is functionalized at one reactive handle over another in a subsequent fashion (Scheme 5A). A powerful example is the site-selective functionalization of poly(pseudo)halogenated arenes (**6**) enabled by $Pd^{(I)}$ catalysis. Starting from simple building blocks, various polysubstituted arenes (**7**) can be accessed in an entirely predictable (Br > OTf/OFs > Cl), general, and substate-independent manner.[25, 26] The methodology is characterized by its simplicity and robustness, and triple sequential functionalization (**7a**, **7b**) can be performed in a one-pot manner within short reaction times and under mild conditions while a wide range of bonds can be formed.

2.1.2 Iterative cross-coupling

Iterative cross-coupling is the linear assembly of bifunctional building blocks in a repetitive manner. Superior examples involve bromoaryl N-methyliminodiacetic acid (MIDA)-protected boronate esters (Br-Ar-B(MIDA)) as bifunctional building blocks (Scheme 5B).[43] The B(MIDA) group is easily handled, bench-top stable, compatible with silica gel chromatography, and most importantly, unreactive under anhydrous Suzuki-Miyaura cross-coupling conditions. However, the B(MIDA) group can be deprotected under mild aqueous basic conditions to give the free boronic acid. The iterative cross-coupling methodology developed by Burke and co-workers involves the $Pd^{(0)}$ catalyzed cross-coupling of aryl boronic acids (Ar–$B(OH_2)$) and bifunctional bromo/B(MIDA) arenes (Br–Ar–B(MIDA)).[43] Subsequently, the B(MIDA) group is deprotected to release the free boronic acid (Ar–$B(OH)_2$) ready for the next iteration (*coupling & deprotection*). This powerful strategy has even been developed into a fully automated process.[44] However, drawbacks such

as the long reaction times (16-28 hours), elevated temperatures (65-80 °C), and the instability of electron-deficient boronic acids restrict the accessible chemical space. In addition, heteroatom bond formations such as the Buchwald-Hartwig amination often require strong basic conditions that can lead to deprotection of the B(MIDA) handle. Clearly, iterative cross-coupling could benefit from additional functional handles that complement the limitations of the existing BMIDA-strategy, such as organogermanes.

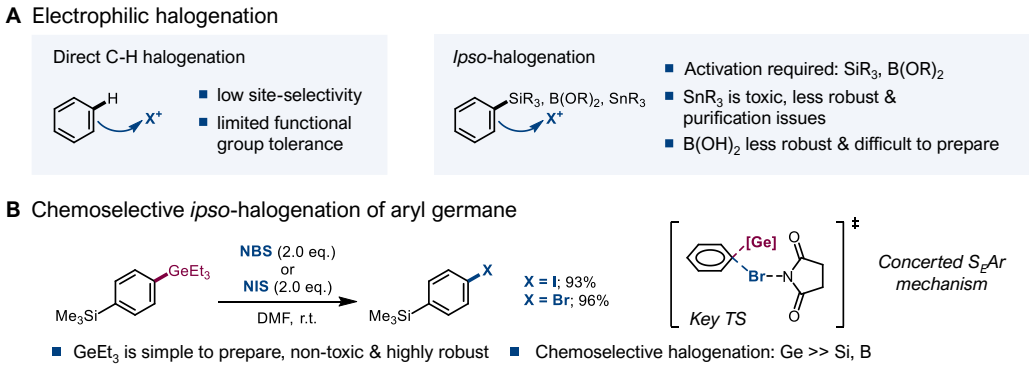
Scheme 5 | Modular building block assembly *via* sequential (A) and iterative cross-coupling (B).



2.1.3 Triethylgermane as orthogonal halide masking group

Our group's ongoing research program on organogermanes (*e.g.*, Ar–$GeEt_3$) has revealed their high value as functional handles in synthetic organic chemistry.[45, 46] These compounds exhibit significant chemical properties, including low toxicity, high stability towards acids and bases, and facile synthetic accessibility. Moreover, C–GEt_3 is a privileged orthogonal functional handle in a multitude of bond formations.[46] For example, in metal-catalyzed cross-coupling reactions, organogermanes were found inert under conventional conditions but highly reactive in electrophilic bond activation, tolerating functional groups such as boronates, silanes, or aryl halides.[47-49]

Scheme 6 | Orthogonal *ipso*-halogenation of C–$GeEt_3$ sites by our group.



Aryl halides are key functional handles in carbon-carbon and carbon-heteroatom bond formations, and consequently, transformations that tolerate these are vital for subsequent derivatizations. Alternatively,

halogens can be introduced later in synthesis for example via direct aromatic halogenation of C–H sites (**Scheme 6A**) or by the *ipso*-halogenation of suitable precursors such as stannanes (C–SnR_4),[50] silanes (C–SiR_4)[51, 52] or boronates (C–$B(OR)_2$).[53] In addition, the selective halogenation of C_{sp2}–$GeEt_3$ sites has also been accomplished (**Scheme 6B**).[54, 55] Our group found that Ar–$GeEt_3$ reacts efficiently with electrophilic halogenation reagents, such as *N*-bromosuccinimide (NBS) and *N*-iodosuccinimide (NIS), resulting in chemoselective halogenation of the C–$GeEt_3$ site via a concerted electrophilic aromatic substitution (S_EAr).[55] The methodology is mild, air- and moisture-stable, operationally simple, and showcases a superior functional group tolerance. In contrast, the direct C–H halogenation lacks selectivity, and alternative halogenations at the corresponding C–SnR_4, C–SiR_4, or C–$B(OR)_2$ sites are less efficient and generate toxic waste or require harsh conditions.

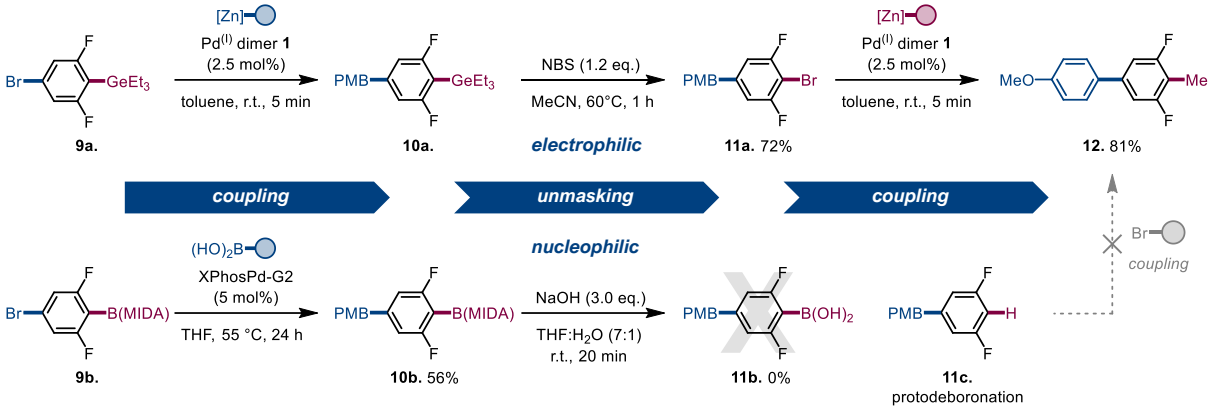
Based on the superior orthogonality of the $GeEt_3$ handle, the following chapter discusses our efforts in developing new bifunctional building blocks that can be integrated into $Pd^{(I)}$ catalysis and additionally utilize the $GeEt_3$ handle as a halide masking group. The new protocol successfully complements the existing nucleophilic BMIDA unmasking strategy for modular, sequential, and iterative cross-coupling reactions.

2.2 Sequential cross-coupling with Et_3Ge as orthogonal masking group

Experimental data presented within this subchapter were obtained in collaboration with other members of the Schoenebeck group: Dr. Christoph Fricke (initial findings), Tatiana Kreisel (general method development), Dr. Adele E. Queen (method comparison), Kirstina Deckers (experimental assistance), Daniel Hupperich (experimental assistance) and Julian Rieger (amination method development).

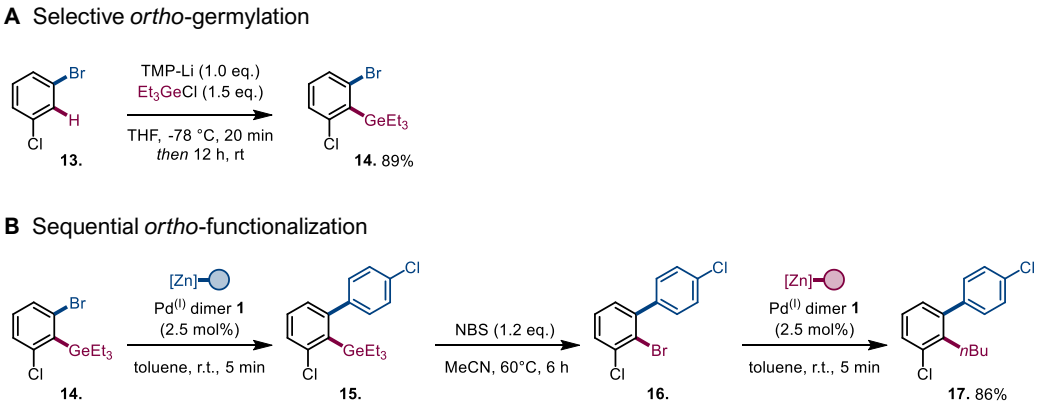
In the context of sequential cross-coupling reactions, Dr. Christoph Fricke and Tatiana Kreisel successfully developed a protocol for the sequential cross-coupling of bromoaryl germanes (*such as* **9a**) enabled by $Pd^{(I)}$ catalysis. The protocol is based on a coupling-unmasking-coupling strategy (**Scheme 7**): First, **9a** is selectively functionalized at the C–Br site to give **10a** (while the $GeEt_3$-handle remains untouched) using $Pd^{(I)}$ dimer **1** within 5 minutes at room temperature. Next, in a subsequent electrophilic unmasking step, the $GeEt_3$ functionality is converted to another reactive bromide site within 1 hour at 60 °C using NBS as a bromination reagent. Lastly, cross-coupling at the new bromide leads to the final polysubstituted arene **12** in less than 90 minutes total reaction time. Consequently, Dr. Adele E. Queen compared the new electrophilic coupling sequence with the established nucleophilic B(MIDA) approach (**Scheme 7**).[44] Therefore, a similar bifunctional bromoaryl boronate **9b** was functionalized at the C–Br site using $Pd^{(0)}$ based Suzuki coupling within 24 hours at 55 °C. The resulting biaryl **10b** was then deprotected from B(MIDA) using NaOH (3.0 eq.) in THF/H2O (7:1) for 20 min at room temperature. The desired free boronic acid **11b** was not obtained, and protodeboronation to **11c** occurred due to the low stability of such fluorinated boronic acids. The investigations mentioned above clearly highlight the value of a complementary electrophilic unmasking approach and, moreover, the broader potential of $GeEt_3$ as a halogen masking group in organic synthesis.

Scheme 7 | Sequential cross-coupling using aryl germane (electrophilic unmasking) and aryl boronate (nucleophilic unmasking).[i]



Since the $GeEt_3$-handle is highly sterically demanding, the possibility of *ortho*-functionalization needed to be clarified and investigated next. Therefore, following a modified literature procedure of our group,[56] (2-bromo-6-chlorophenyl)triethylgermane **14** was synthesized in 89% yield by selective *ortho*-metalation of 1-bromo-3-chlorobenzene **13** using LiTMP as a metalating agent and quenching with Et_3GeCl. Noteworthy, no benzyne formation was observed, a common side-reaction of 2-(bromophenyl)lithium species. This could be due to the one-pot procedure, the unique properties of LiTMP base, or the nature of the substrate, and it was not further investigated. The obtained (2-bromo-6-chlorophenyl)triethylgermane **14** was then subjected to sequential cross-coupling. The highly sterically demanding $GeEt_3$ group had no influence in the $Pd^{(I)}$ mediated cross coupling, but the reaction time of the subsequent unmasking step was elongated to 6 hours at 60 °C. The resulting bromide was further alkylated, affording the final bis-functionalized product **17** in 86% yield. The ability to also manipulate in *ortho*-position demonstrates the generality of the new *$Pd^{(I)}$/Ge-coupling&unmasking&coupling* strategy.

Scheme 8 | Synthesis of sterically demanding bromoaryl germane (A) and sequential cross-coupling (B).



Conditions: A) **13** (10 mmol), TMP-Li (1.0 eq.), THF (0.2 M), -78 °C, 20 min then Et_3Ge-Cl (1.5 eq.), r.t., 12 h; B) *C-C coupling*: **14** (1.0 mmol), $Pd^{(I)}$ dimer **1** (2.5 mol%), toluene (0.2 M), slow addition of organozinc (1.5 eq.) over 10 min, r.t., 5 min; *Bromination*: NBS (1.2 eq.), MeCN (0.2 M), 60 °C, 6 h; Isolated yields are reported based on the initial aryl bromide overall steps.

[i] T. Kreisel and Dr. A. Queen have carried out the experimental work presented within **scheme 7**; more precisely, the accomplishments starting from **9a** and **9b** towards **12**.

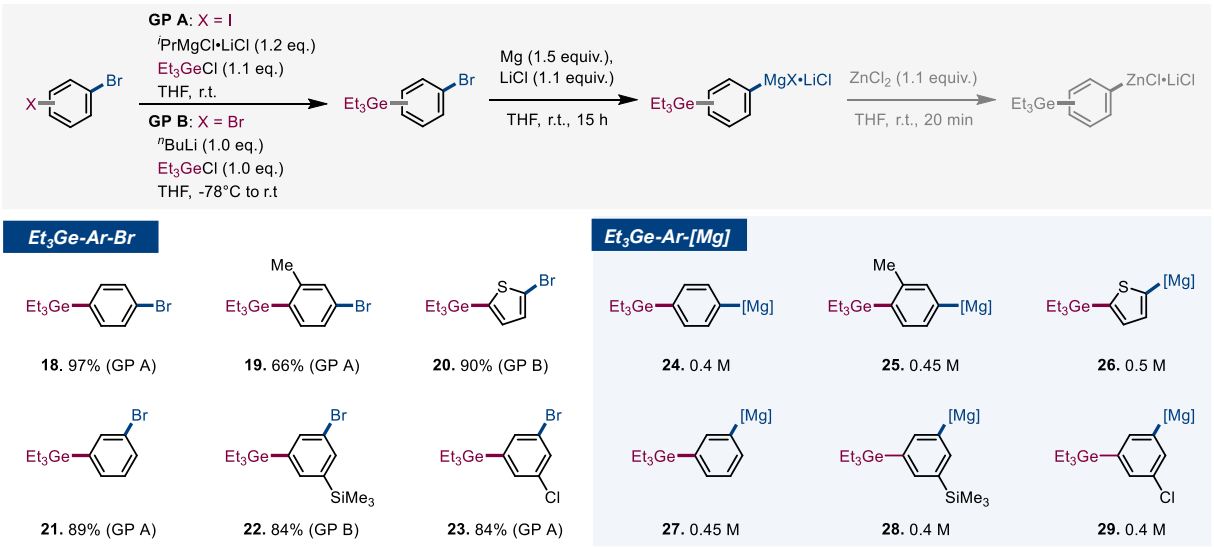
2.3 Iterative cross-coupling with bifunctional germane building blocks

2.3.1 Building block design

The successful use of $GeEt_3$ as a robust halide masking group in sequential cross-coupling reactions encourages the exploration of iterative cross-couplings. The possibility of cross-coupling organometallic species that additionally contain the $GeEt_3$ moiety would significantly impact the number of iterations and, thus, the accessible chemical space.

Therefore, several bifunctional building blocks were synthesized from commercially available halogenated arenes. Following a modified literature procedure developed by our group,[57] the $GeEt_3$ moiety was introduced by selective metal-halogen exchange of one halide and subsequent quenching with $GeEt_3Cl$. In the case of bromo-iodo arenes, selective functionalization at the iodide site was performed using Knochel´s turbo Grignard (*i*PrMgCl•LiCl) at ambient temperature (**Scheme 9**, **GP A**).[58] For dibromo arenes, lithium-halogen exchange using stoichiometric *n*BuLi at low temperatures was sufficient for selective mono functionalization (**Scheme 9**, **GP B**). The bromoaryl germanes **18**-**23** were all obtained in good to excellent yields; even the sterically demanding *ortho*-substituted example **19** was isolated in 66% yield. The bromoaryl germanes were further exposed to organomagnesium formation in the presence of magnesium tunings and LiCl.[59] The presence of LiCl is reported to accelerate the insertion of Mg into aryl bromides, and no heating or other additives were required. The aryl Grignard reagents were obtained quantitatively and stored inside an argon-filled Glovebox for several months without any sign of decomposition. Since organozinc are of high functional group tolerance, the organomagnesium reagents were further transformed into their corresponding zinc species by transmetallation with $ZnCl_2$ and used as received without further purification and analysis.

Scheme 9 | Synthesis of bifunctional bromoaryl germanes ([Ge]–Ar–Br) and Grignard reagents ([Ge]–Ar–[Mg]).

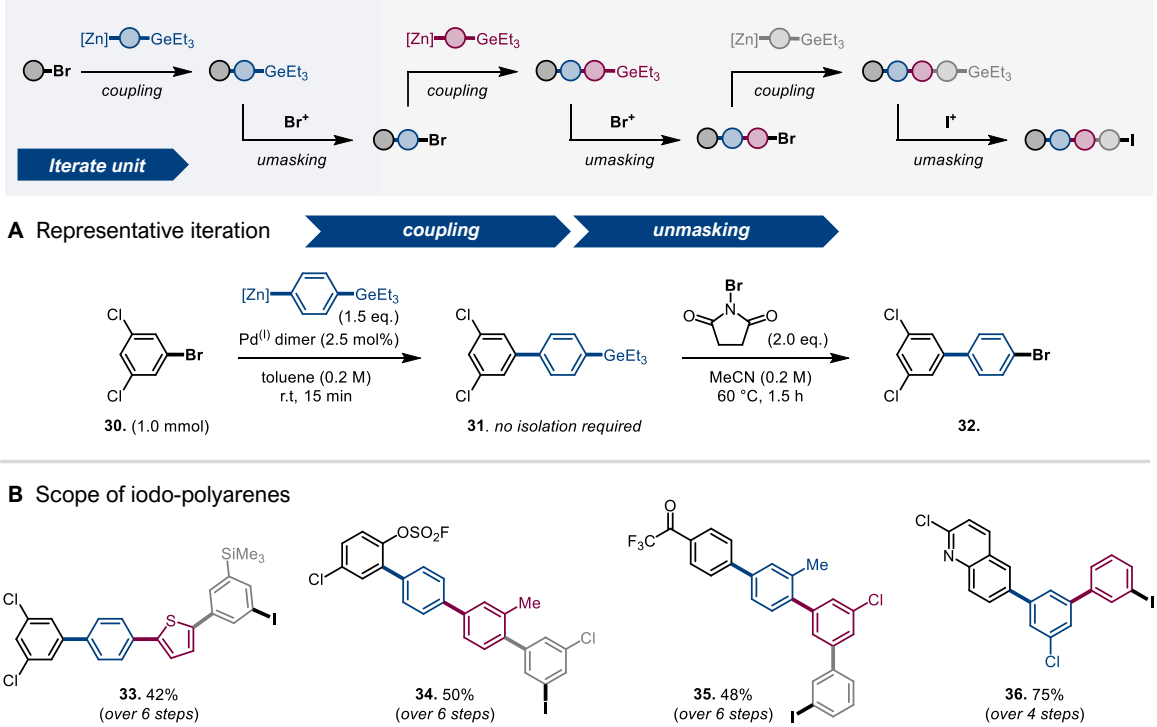


Conditions: *GP A*: aryl iodide (1.0 eq.), THF (0.2 M), *slow addition of* *i*PrMgCl-LiCl (1.2 eq.), Et_3GeCl (1.1 eq.), 0 °C to r.t., 16 h. *GP B*: Aryl bromide (1.0 eq.), THF (0.2 M), *slow addition of* *n*BuLi (1.0 eq.), Et_3GeCl (1.1 eq.), -78 °C to r.t. 16 h. *Grignard formation:* Ar-$GeEt_3$ (1.0 eq.), Mg (1.5 eq.), LiCl (1.1 eq.), r.t., 16 h.

2.3.2 Iterative cross-coupling protocol

The novel building blocks were then tested for compatibility with $Pd^{(I)}$ catalysis to develop an iterative cross-coupling methodology combining two highly efficient protocols ($Pd^{(I)}$ mediated cross-coupling and electrophilic unmasking). We started our investigations with the $Pd^{(I)}$ mediated cross-coupling of 1-bromo-3,5-dichlorobenzene **30** and (4-(triethylgermyl)phenyl)zinc (**Scheme 10**). Therefore, the organozinc (1.5 eq.) was added slowly over 10 minutes to a solution of aryl bromide (1.0 mmol, 1.0 eq.) and $Pd^{(I)}$ dimer **1** (2.5 mol%) in toluene (0.2 M) and it was stirred for 5 minutes at room temperature. According to previous reports, slow addition reduced the amount of organozinc homo-coupling.[26] Palladium was precipitated by adding a spatula tip of pyrrolidine-1-dithiocarboxylic acid ammonium salt, and the mixture was filtered through a silica plug and concentrated under reduced pressure.[60] Reaction control showed complete consumption of aryl bromide **30** and selective formation of the corresponding biaryl germane product **31**. Other detected species were 4,4'-bis(triethylgermyl)-1,1'-biphenyl (homo-coupling) and triethyl(phenyl)germane (quenched organozinc). Driven by the successful cross-coupling, a one-pot unmasking step was envisioned in which the cross-coupling crude was used as received to save resources and time. Since the crude contained several triethylgermane species, the unmasking was performed with an excess of NBS (2.0 eq.) at 60 °C for 1.5 hours. Pleasingly, excellent bromination of each available triethylgermane handle was observed, and the final aryl bromide **32** was purified using column chromatography. This first coupling-unmasking iteration showcased the fully compatible bifunctional building block with the existing $Pd^{(I)}$ cross-coupling protocol and the electrophilic unmasking of triethylgermane in a subsequent one-pot fashion. Next, the broad, accessible chemical space of this novel methodology was demonstrated with several examples and an increased number of iterations (**33-36**). The method enables access to various poly(hetero)arenes very efficiently and high yielding (42-75%), especially considering that three subsequent iterations involve six reactions and three purification steps. In addition, reactive functional groups such as aryl fluorosulfates **34**, chlorides (**33-34, 36)**, an electron deficient CF_3-substituted ketone **35**, or 2-chloro-quinoline **36** were well tolerated. Moreover, the polyarenes were successfully iodinated in the final unmasking step, highlighting the versatility of the protocol. Noteworthy, electron-deficient or sterically demanding aryl germanes showed decreased reactivity in the corresponding electrophilic unmasking step under standard conditions in MeCN. Still, efficient halogenation was obtained in hexafluoroisopropanol (HFIP) under identical conditions. It has been proposed that HFIP's strong H-bond donation ability activates N-halosuccinimides in electrophilic halogenations.[61]

Scheme 10 | Iterative cross-coupling protocol: Representative coupling/unmasking sequence (A) and scope of iodo-polyarenes (B).



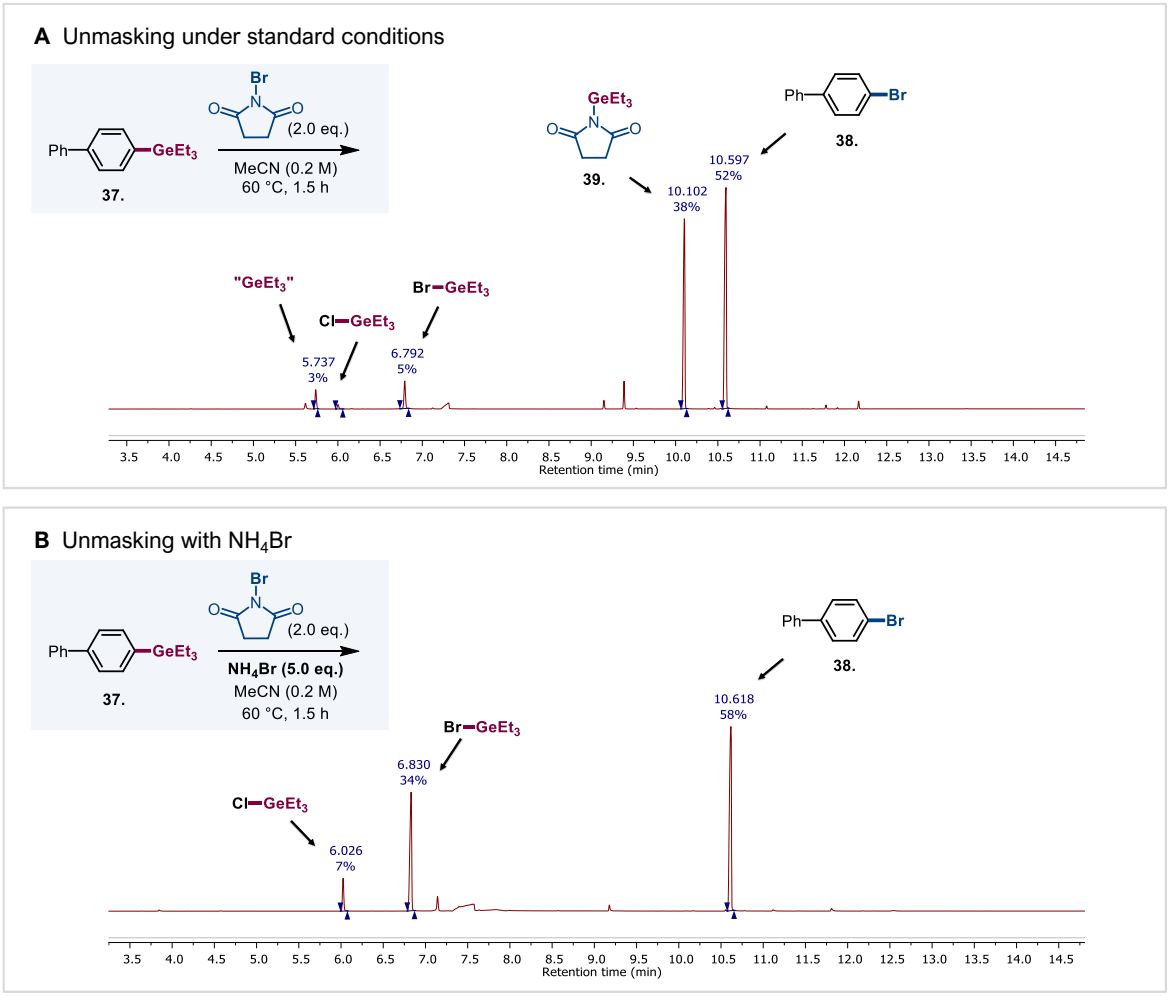
Conditions: *C-C coupling*: arylbromide (1.0 mmol), Pd(I) dimer **1** (2.5 mol%), toluene (0.2 M), *slow addition of* [Zn]-Ar-$GeEt_3$ (1.5 eq.) over 10 min, r.t., 5 min; *Bromination*: NBS (2.0 eq.), MeCN (0.2 M) or HFIP (0.2 M, in case of electron-deficient or sterically hindered arenes), 60 °C, 1.5 h; *Iodination*: NIS (2.0 eq.), HFIP (0.2 M), 60 °C, 24 h. Isolated yields are reported based on the overall steps of the initial aryl bromide.

2.3.3 Recycling of germanium

Besides all the highlighted advantages of this novel iterative cross-coupling protocol, one drawback is the low atom economy of the unmasking step. This section will discuss my efforts toward the recycling of germanium.

During the investigation on the halogenation of **37** with NBS as a halogenating reagent, the formation of **38** but also **39**, a succinimide–$GeEt_3$ species, followed by low amounts of Br–$GeEt_3$ and Cl–$GeEt_3$ has been observed (**Scheme 11A**). Presumably, the succinimide-$GeEt_3$ species **39** results from NBS; we assumed that the formation of the latter two germanium halides occurs due to the presence of the corresponding anions in solution, derived from $ZnCl_2$, organomagnesium bromide, or aryl bromide. Since our attempts to isolate **39** failed, we next wanted to increase the formation of Br–$GeEt_3$ by adding an excess of NH_4Br to the reaction mixture, and indeed, the formation of **39** was fully suppressed, and increased amounts of Br–$GeEt_3$ (and Cl–$GeEt_3$) were observed in GCMS analysis (**Scheme 11B**).

Scheme 11 | GCMS analysis after bromination: Under standard conditions (A) and with excess H_4NBr (B).

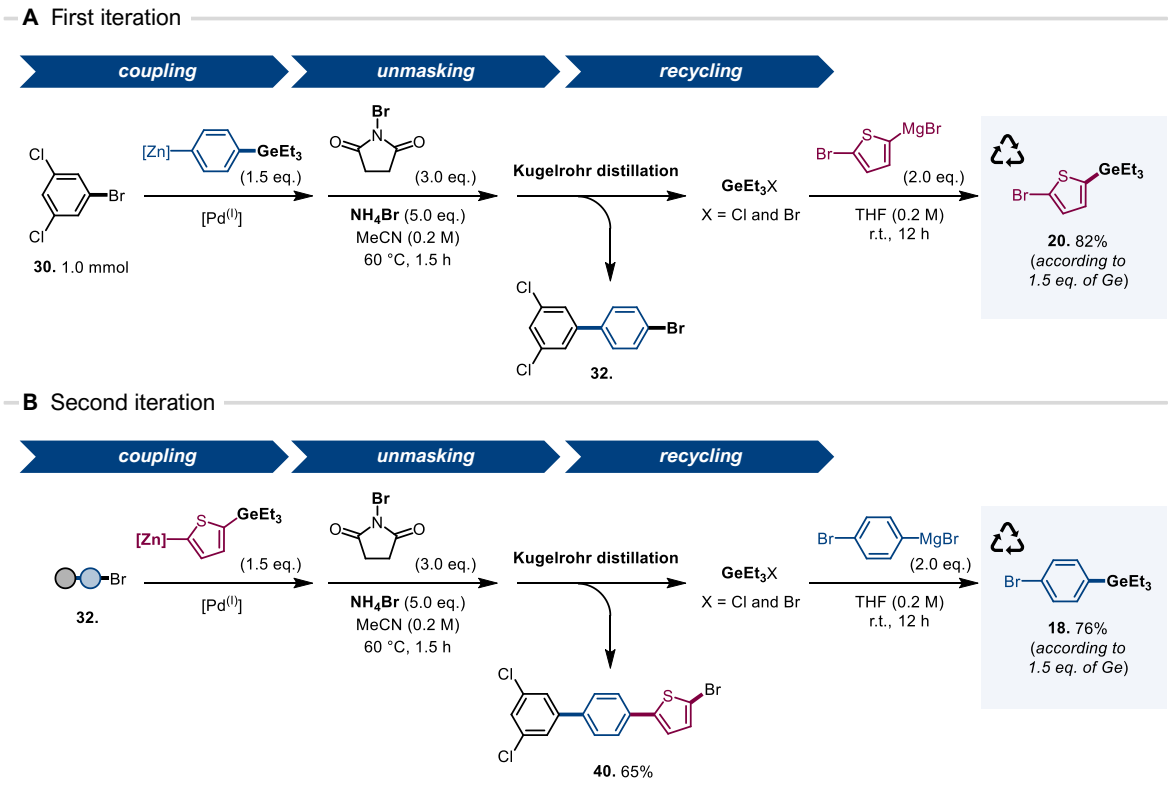


Conditions: A) **37** (1.0 eq.), NBS (2.0 eq.), MeCN (0.2 M), 60 °C, 1.5 h; B) with NH_4Br (5.0 eq.).

The recovery of germanium as the Et_3Ge-halide species offers the possibility of directly reusing it to synthesize organogermanium building blocks (**Scheme 12**). Ideally, this would allow a single Ge-unit to be used for the entire iteration sequence. Therefore, 1-bromo-3,5-dichlorobenzene **30** and (4-

(triethylgermyl)phenyl)zinc (from **24**) were coupled, and subsequent unmasking to **32** was performed using NBS (3.0 eq.) in the presence of NH_4Br (5.0 eq.). Following the initial experiments, the formation of germanium halides (Br–$GeEt_3$ and Cl–$GeEt_3$) was observed, but not the germanium-succinimide **39** species. The mixture of germanium halides (Br–$GeEt_3$ and Cl–$GeEt_3$) was then isolated by Kugelrohr distillation (70 °C, 10 mbar, 2 h) using ice bath cooling. The obtained distillate was then reacted with (5-bromothiophen-2-yl)magnesium bromide to form (5-bromothiophen-2-yl)triethylgermane **20** in 82% yield (**Scheme 12A**). Next, using the organozinc obtained from (5-bromothiophen-2-yl)triethylgermane **20**, another coupling-unmasking-recycling iteration was performed to afford **40** in 65% yield and the previous building block (4-bromophenyl)triethylgermane **18** in 76% yield (**Scheme 12B**). As such, the recycling of triethylgermanium and its usage as a single unit throughout two iterations has been demonstrated.

Scheme 12 | Recycling of triethylgermanium-halide and reuse in iterative cross-coupling.



Conditions: *C-C coupling:* aryl bromide **30** (1.0 mmol), $Pd^{(I)}$ dimer **1** (2.5 mol%), toluene (0.2 M), *slow addition of* [Zn]-Ar-$GeEt_3$ (1.5 eq.) over 10 min, r.t., 5 min; *Bromination:* NBS (3.0 eq.), NH_4Br (5.0 eq.), MeCN (0.2 M), 60 °C, 1.5 h; *Kugelrohr-distillation:* 10 mbar, 70 °C, 2 h, ice-bath cooling; *Germylation*: $GeEt_3X$ (1.5 eq.), RMgBr (2.0 eq.), THF (0.2 M), r.t., 12 h. Isolated yields of polyarenes are reported based on the initial aryl bromide **30** overall steps. Isolated yields of recycled bromoaryl germanes are reported based on the initial [Zn]-Ar-$GeEt_3$ (1.5 mmol).

In conclusion, two highly efficient protocols were combined to a superior iterative cross-coupling methodology. This was achieved by using the rapid, mild, and site-selective $Pd^{(I)}$ cross-coupling protocol together with the orthogonal and fully predictable reactivity of $GeEt_3$ as a unique electrophilic masking group. The new methodology supplements existing protocols and extends the available chemical space for cross-coupling.

3

Rapid and modular access to (di)vinylcyclopropanes enabled by $Pd^{(I)}$ catalysis

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The results described in this chapter were published in Angewandte Chemie International Edition[62] and have been highlighted in Synfacts.[63] Experimental work has partially been carried out in collaboration with other members of the Schoenebeck group, whose contributions are stated in detail in the respective subchapters.

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3 Rapid and modular access to (di)vinylcyclopropanes enabled by $Pd^{(I)}$ catalysis

3.1 Introduction

Vinylcyclopropanes are key structural motifs in pharmaceuticals, agrochemicals, and natural products (**Figure 1**). Drugs such as *Simeprevir* and *Danoprevir* are used to treat hepatitis C infections, and the latter has also shown potency for the treatment of COVID-19.[64, 65] Notable natural products that consist of the vinylcyclopropyl group are *Pyrethrins*, naturally occurring esters, and derivatives of *trans*-chrysanthemic acid with potent insecticidal activity.[66] *Pyrethroids*, a collective term for synthetic versions of *Pyrethrins*, are widely used as commercial and household insecticides such as *Resmethrin* or *Allethrin* due to their high insecticidal activity and low mammalian toxicity. Another distinctly different class of natural products is the *Dictyopterenes*.[67, 68] These are pheromones found in several species of brown algae and consist of a divinylcyclopropane skeleton.

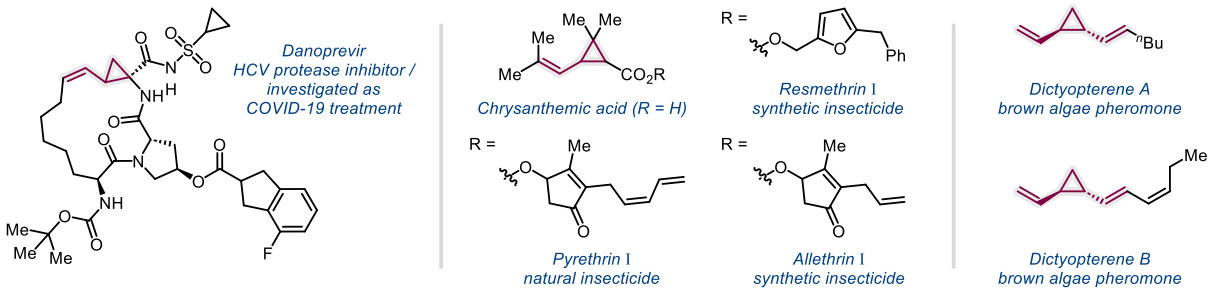
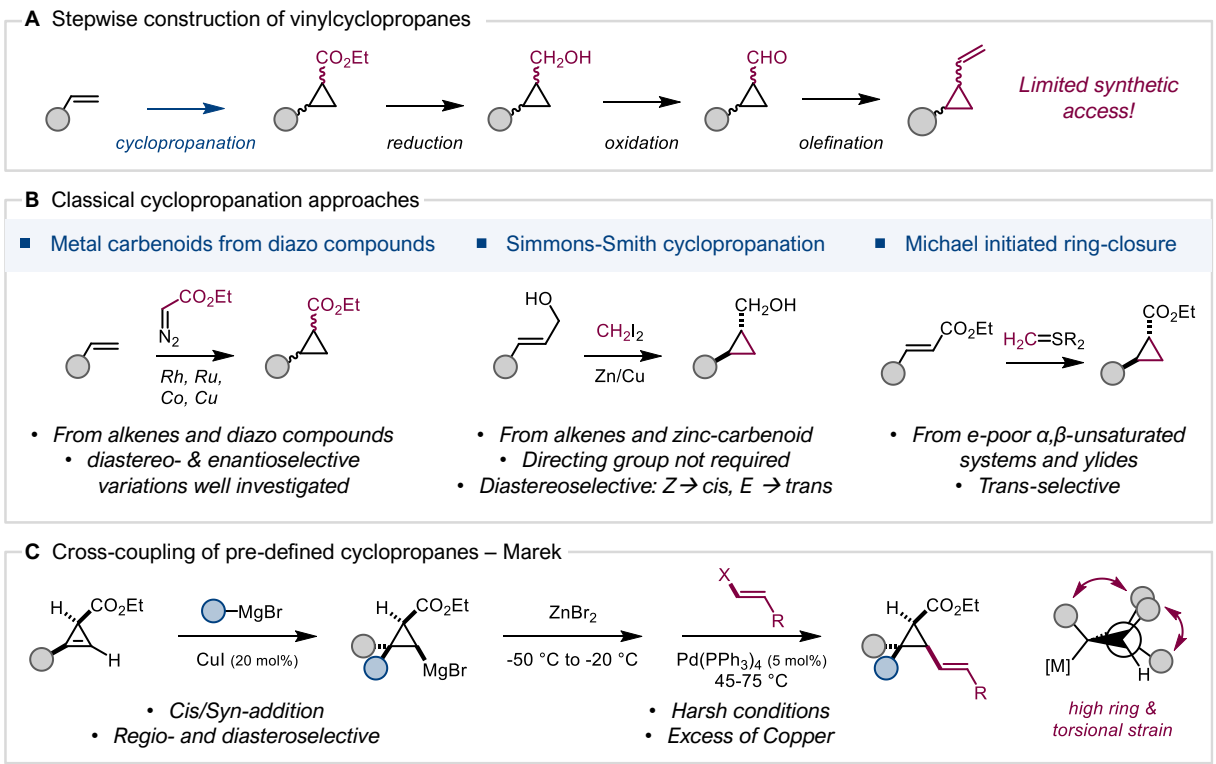


Figure 1 | Examples of bioactive vinylcyclopropanes: present in pharmaceuticals, insecticides, and pheromones.

The unique bonding properties of vinylcyclopropanes make them valuable intermediates in synthetic organic chemistry. Vinylcyclopropanes find application in a wide range of reactions, such as ring-opening reactions, cycloadditions, and rearrangements, for the synthesis of complex molecular structures.[69-72] However, synthesizing certain reactive vinylcyclopropanes can be challenging. Preparing the *cis*/*trans* cyclopropane geometry with multiple substituents in a stereoselective manner while considering the possible *E*/*Z* geometry of the alkene can also be particularly difficult. Most common strategies involve the stepwise synthesis of the cyclopropane fragment followed by functional group interconversions to introduce the vinyl moiety later (**Scheme 13A**). Representative cyclopropanation methodologies are the Simmons-Smith cyclopropanation, the transition metal-mediated decomposition of diazo compounds (*e.g.*, diazoacetate), or the addition of ylides to *α,β*-unsaturated Michael acceptors (*e.g.*, Corey-Chaykovsky cyclopropanation) (**Scheme 13B**). Moreover, cyclopropanation methodologies for direct access to vinylcyclopropanes have been developed.[70] While preparing vinylcyclopropanes is a well-investigated topic, there is one intrinsic problem: the methods tend to be substrate-specific, and structural diversification can be of immoderate synthetic effort. Especially enantio- and diastereoselective methods do lack generality. In contrast, directly modifying a readily prepared three-membered carbon ring by metal catalysis can increase the accessibility of vinylcyclopropanes and, ideally, introduce the desired stereochemistry (*cis*/*trans*-cyclopropane, *E*/*Z*-alkene)

from pre-defined building blocks. The power of such modular construction has been showcased in the carbometallation of cyclopropenes.[73, 74] Copper-mediated carbometallation especially gives access to various poly-substituted cyclopropanes, including vinylcyclopropanes, in a diverse and stereoselective fashion.[75] The success of this methodology is based on the *syn*-addition of an organometallic species to the cyclopropene double bond, resulting in a cyclopropyl metal intermediate that is subsequently functionalized, either by quenching with various electrophiles[76] or by metal-catalyzed cross-coupling.[74] The latter has been demonstrated by Marek and co-workers in the stereoselective synthesis of poly-substituted vinylcyclopropanes (**Scheme 13C**).[77] The protocol is based on a Cu-catalyzed *syn*-carbomagnesiation of cyclopropenes to afford cyclopropyl magnesium halides, which were further subjected to $Pd^{(0)}$-catalyzed cross-coupling with alkenyl halides at 45–75 °C over 18 hours. Other cross-coupling protocols that couple a cyclopropyl fragment to a vinyl moiety typically showcase *trans*-diastereomers with *E*-alkene geometry under harsh conditions and with few substituents on the cyclopropane.[78-83]

Scheme 13 | Synthesis of vinylcyclopropanes: A) Step-by-step access; B) Classical cyclopropanation approaches used in the stepwise synthesis and C) Metal catalyzed cross-coupling of a pre-defined cyclopropane ring.



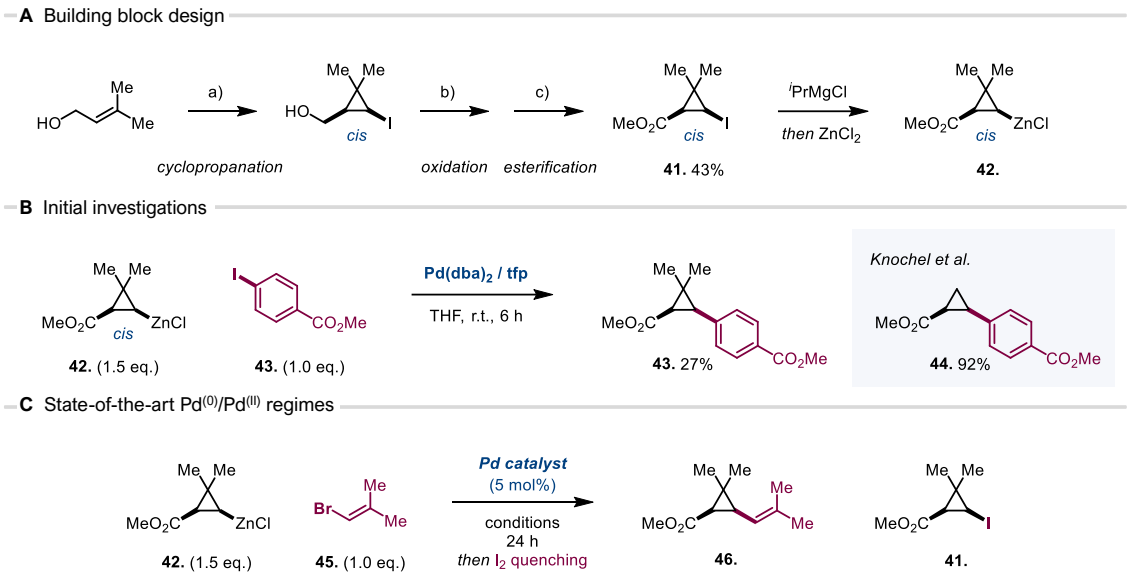
$Pd^{(I)}$ catalysis has emerged as a mild, rapid, and versatile cross-coupling methodology for a broad range of molecules (see chapter 1.2 ff.). We envisioned that a $Pd^{(I)}$-catalyzed protocol could be very beneficial for the construction of vinylcyclopropanes, particularly for sensitive compounds or those with sterically demanding substituents. The following subchapters will discuss the expansion of $Pd^{(I)}$ catalysis towards vinylcyclopropanes.

3.2 Initial investigations

Experimental data presented within this subchapter were obtained in collaboration with Dr. Lars Gnägi (method comparison and synthesis of chrysanthemic acid derivatives).

We started our investigation by choosing *cis*-chrysanthemic acid methyl ester as our model substrate. The cross-coupling of this compound class combines several challenges we liked to encounter with $Pd^{(I)}$ catalysis, such as a richly substituted and sterically demanding cyclopropane motif, the stereochemical information in the cis-cyclopropane or the alkene, and a sensitive ester functionality. Although Marek demonstrated the cross-coupling of similar compounds employing $Pd(PPh_3)_4$/CuI catalysis,[77] to the best of our knowledge, no modular cross-coupling approach for the direct synthesis of chrysanthemic acid derivatives does exist. However, the modular assembly of various alkenes with a dimethylcyclopropyl methyl ester fragment would enable rapid access to previously unknown derivatives of this valuable compound class. Therefore, in cooperation with Dr. Lars Gnägi (former Postdoc of the Schoenebeck Group), the corresponding *cis*-dimethylcyclopropyl zinc **42** was synthesized (**Scheme 14A**) and, to examine whether the cross-coupling to chrysanthemic acid derivatives is simply something that has not been tried before, we tested **42** in $Pd^{(0)}$ catalyzed cross-coupling reactions (**Scheme 14B**). Knochel and Marek demonstrated that *bis*(dibenzylideneacetone)palladium $Pd^{(0)}(dba)_2$ and *tris*-*o*-furylphosphane (tfp) mediates efficient cross-coupling between an unsubstituted *cis*-ethoxycarbonylcyclopropane zinc and aryl iodide at r.t. within 6 hours to give the coupling product **44** in 92% yield.[84] The same conditions were applied to the sterically more demanding dimethyl cyclopropyl zinc **42**, and interestingly, only 27% of the arylated product **44** was obtained (**Scheme 14B**). The subsequent quenching with iodine revealed that 64% of the *cis*-dimethylcyclopropyl zinc remained untouched and was recovered as the corresponding *cis*-dimethylcyclopropyl iodide **41**. Moreover, when the aryl iodide **43** was replaced with dimethylvinyl bromide **45**, no product formation to **24** was observed and 80% of the quenched cyclopropyl iodide **41** was recovered instead (**Scheme 14C, entry 1**).

Scheme 14 | Modular access to chrysanthemic acid derivatives: A) Building block design. B) Initial investigations on building blocks. C) Cross-coupling methodology comparison.[ii]



entry	conditions	solvent	temperature	Yield 46[d]	Recovered 41[d]
1	$Pd(dba)_2$ / tfp	THF	r.t.	0%	80%
2	$Pd(dba)_2$ / XPhos	THF	r.t.	0%	76%
3	$Pd(dba)_2$ / CPhos	THF	r.t.	0%	<5%
4	$Pd(PPh_3)_4$ (10 mol%)	THF	60 °C	traces	<5%
5	$Pd(PPh_3)_4$ (1.0 equiv.)	THF	60 °C	18%	<5%
6	Pd-PEPPSI-*IPent*	PhMe	r.t.	0%	<5%
7	Only **42**	THF	r.t.	0%	76%
8	Only **42**	THF	60 °C	0%	<5%

Conditions: a) *cyclopropanation*: $ZnEt_2$ (2.2 eq.), CHI_3 (4.4 eq.), DCM (0.1 M); b) *oxidation*: Jones reagent (2.75 eq.), acetone (0.06 M); c) *esterification*: $SOCl_2$ (3.0 eq.), MeOH (1 M), reflux; d) Quantitative GC-MS yield using mesitylene as internal standard.

Dr. L. Gnägi further examined alternative cross-coupling methodologies that find either usage in cross-coupling of cyclopropanes or represent highly efficient alkylation methodologies such as Buchwalds XPhos or CPhos Pd-ligand systems or Organs Pd-PEPPSI-*IPent* precatalyst (**Scheme 14C**).[78, 80-83, 85] However, no product formation was observed, and iodine quenching experiments revealed that *cis*-dimethylcyclopropyl zinc **42** was largely untouched (**Scheme 14C, entries 1–2**, up to 80% of **41** recovered) or fully consumed resulting in complex reaction mixtures (**Scheme 14C, entries 3–8**, with <5% of **41** recovered). During $Pd^{(0)}/Pd^{(II)}$ cross-coupling, there may be difficulties with a challenging transmetallation that is sterically too demanding or an unfavored reductive elimination. This could lead to decreased reactivity and result in unwanted side reactions, such as metal-halogen exchange between the two coupling partners. Furthermore, successful cross-coupling can only occur if the used building blocks are compatible with the applied reaction conditions, such as elevated temperature or prolonged reaction time. In this context, the organozinc species **42** decomposed slowly at room temperature and relatively fast at elevated temperatures

[ii] Dr. Gnägi has carried out the experimental work presented within **Scheme 14**, more precisely, the synthesis of **42** and the following investigations towards **43** and **46**.

(Scheme 14C, entry 7–8). This could also explain the low reactivity of the $Pd(PPh_3)_4$ system, which Marek has previously applied for similar sterically demanding cyclopropyl couplings.[77] Interestingly, when the catalyst loading increased from 10% to 100%, product formation increased significantly to 18% (Scheme 14C, entries 4–5). Noteworthy, the reaction conditions of Marek and co-workers involve 20 mol% CuI, which is proposed to accelerate transmetallation as a co-catalyst in Pd catalysis and is not present in the shown comparison experiment.[86] In summary, our initial investigations have not only revealed that the cross-coupling of sterically hindered cyclopropanes with alkene bromides is a challenging reaction but also that $Pd^{(0)}$ methodologies have reached their limitations of what is currently achievable.

3.3 Modular access to vinylcyclopropanes enabled by dinuclear $Pd^{(I)}$ catalysis

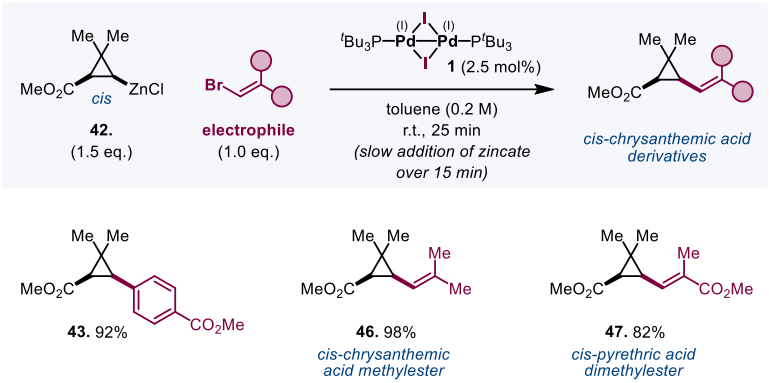
The experimental data presented in this subchapter were obtained in collaboration with Dr. Lars Gnägi (method comparison and synthesis of chrysanthemic acid derivatives) and Uladzislava Dabranskaya (stereospecific cross-coupling).

3.3.1 Synthesis of chrysanthemic acid derivatives

With the discovery of $Pd^{(I)}$ catalysis, our group has successfully addressed some of the challenges that can arise in cross-coupling reactions with $Pd^{(0)}/Pd^{(II)}$ regimes.[1] These challenges include air stability, site-selective functionalization, unfavored steric bulkiness, β-hydride elimination in alkylations, and more.[1] Moreover, Knochel and his team demonstrated the stereoselective cross-coupling of chiral secondary dialkylzinc reagents with very high configuration retention by employing the $Pd^{(I)}$ dimer **1**.[87] The success of dinuclear $Pd^{(I)}$ catalysis is based on the opposite of elementary steps compared to $Pd^{(0)}/Pd^{(II)}$ regimes. Changing the elementary steps alters the driving forces, which leads to exceptional reactivity. Previous studies of our group have demonstrated the extraordinary reactivity of $Pd^{(I)}$ catalysis in the rapid coupling of aryl halides with alkyl zinc species, even successfully with sterically demanding ortho-adamantly arenes.[24] However, highly substituted cyclopropyl zinc compounds have not been showcased so far. We, therefore, set out to cross-couple *cis*-dimethylcyclopropyl methyl ester zinc **42** with the corresponding aryl bromide (**43-Br**) by using $Pd^{(I)}$ dimer **1**, and to our delight, the cross-coupling was catalyzed in an extraordinarily rapid and efficient manner (Scheme 15). The arylated product **43** was afforded 92% yield in 25 minutes at room temperature (for comparison, see Scheme 14B). The original coupling protocol was modified as follows: aryl bromide (1.0 eq.) and $Pd^{(I)}$ dimer (2.5 mol%) were dissolved in dry toluene (0.2 M), and the cyclopropyl zinc **42** was added slowly over 15 minutes to minimized potential metal-halogen exchange and then stirred for additional 10 minutes at room temperature. We next envisioned the $Pd^{(I)}$ coupling with alkenyl bromides. Although dinuclear $Pd^{(I)}$ catalysis with alkenyl halides has not yet been demonstrated, our initial mechanistic studies are consistent with the dinuclear catalysis concept: No reactivity between $Pd^{(I)}$ dimer **1** and vinyl bromide is observed, however, addition of organozinc leads to the instantaneous activation and consumption of **1** (see supporting information for details, chapter 5.3.5, p. 93 ff.). In addition, my own computational study for the oxidative addition between a mixed iodo-propyl-bridged $Pd^{(I)}$ dimer and vinyl

bromide (16.6 kcal mol^{-1}) suggested a similar activation barrier as for phenyl bromide (18.2 kcal mol^{-1}) (see supporting information for details, chapter 5.3.6, p. 95 ff.). Indeed, Dr. Lars Gnägi could demonstrate that numerous alkenyl bromides succeeded in the Pd$^{(I)}$ mediated cross-coupling. The modular protocol enables the fast assembly of *cis*-chrysanthemic acid derivatives, for example, chrysanthemic acid methyl ester **46** (98%) or pyrethric acid dimethyl ester **47** (82%), in high yields. In contrast, literature routes to access modification of the vinyl moiety in chrysanthemic acid derivatives often involve several steps of functional group interconversion.[88]

Scheme 15 | Modular access to chrysanthemic acid derivatives.[iii]



Conditions: vinyl or aryl bromide (0.5 mmol) and Pd$^{(I)}$ dimer **1** (2.5 mol%) in toluene (0.2 M), *slow addition of organozinc* (1.5 eq.) over 15 min, 10 min at r.t.; Slow additions were performed using a syringe pump.

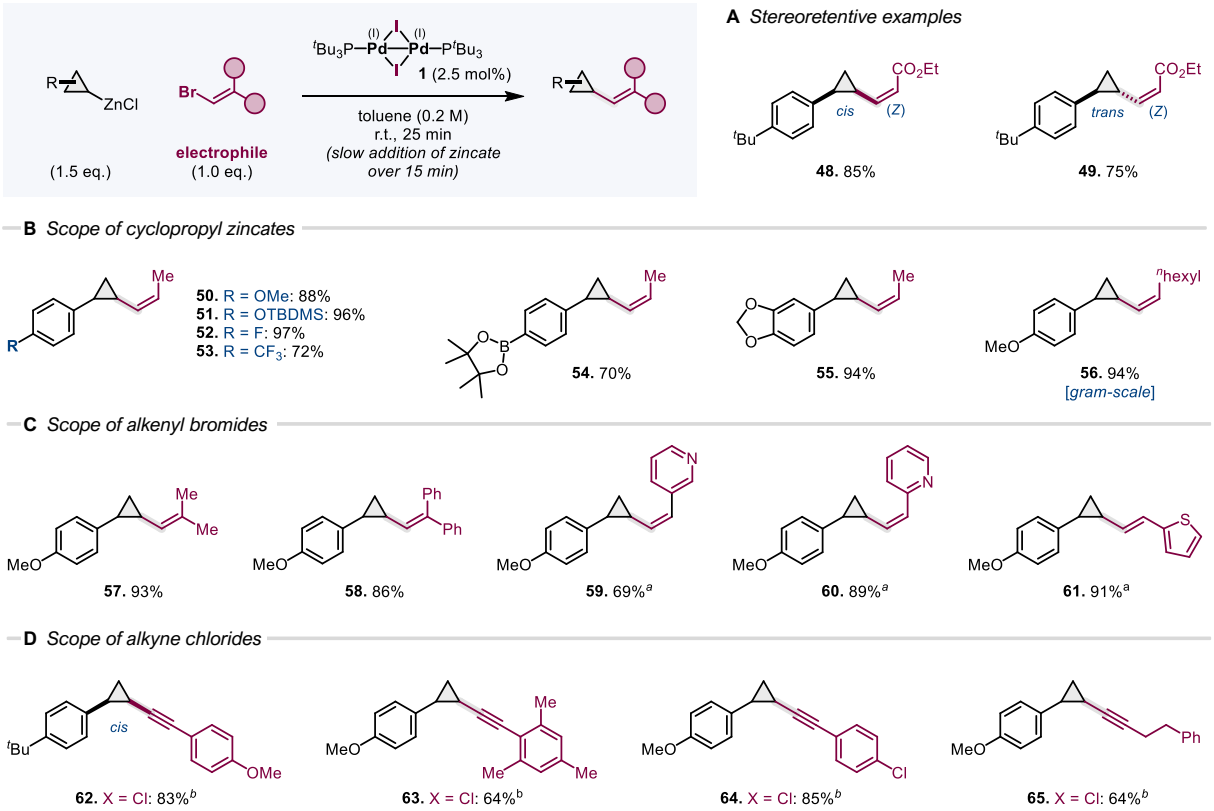
3.3.2 Scope of the Pd$^{(I)}$ catalyzed cross-coupling

We further explored the scope of this protocol in the synthesis of various vinylcyclopropanes. Therefore, numerous alkenyl bromides and cyclopropyl zinc were synthesized and cross-coupled using the Pd$^{(I)}$ protocol (**Scheme 16**). Uladzislava Dabranskaya (current PhD student of the Schoenebeck group) could demonstrate that the coupling was fully stereoretentive regarding the cyclopropyl- (*cis*/*trans*) or the alkenyl-fragment (*Z*) and no isomerization was observed for either of the moieties (**Scheme 16A**). The coupling of the pure *cis*- and *trans*-cyclopropyl zinc leads solely to the desired diastereomerically pure products (**48–49**) in excellent yields. Similarly, when cis/trans mixtures of the cyclopropyl zinc were employed, the diastereomeric ratio was fully preserved, and no change in the stereochemical information was observed. In addition, numerous cyclopropyl zinc compounds were tolerated, and no significant influences on the reaction outcome of the electronic nature of the cyclopropyl zinc building blocks were observed (**Scheme 16B**). Electron-donating substituents at the arene ring such as methoxy- (**50**), *tert*-butyl- (**48–49**) or *tert*-butyldimethylsilyl ether- (**51**) as well as electron-withdrawing substituents like fluoride- (**52**), trifluoromethyl- (**53**), pinacol boronate- (**54**) or 1,3-benzodioxole (**55**) were all coupled efficiently in moderate to high yields (70-97%). Variation of the electrophilic coupling partner further increased the accessible chemical space of this transformation and was found to be feasible (**Scheme 16C**). Linear alkenes (**50–56**), branched alkenes (**57–58**), conjugated alkenes (**58–61**), or heterocyclic styrene derivatives (**59–61**) were all well tolerated. To further assess the functional group tolerance of the Pd$^{(I)}$ coupling strategy, a compatibility screen was

[iii] Dr. Gnägi has partially carried out the experimental work presented within **Scheme 15**, more precisely, the synthesis of **46** and **47**.

performed.[89] Therefore, the cross coupling was demonstrated in presence of various additives (arenes containing amine, nitro, aldehyde, nitrile, OH, Bpin functionalities and heterocycles) and analyzed for product formation and recovered additive. The screen indicated a broad functional group tolerance (see supporting information for details, chapter 5.3.4, p. 92 f.). Furthermore, this highly general transformation is not restricted to alkenyl bromides; alternative electrophiles such as alkyne chlorides can also be utilized to give valuable alkyne cyclopropanes in good yields (**Scheme 16D**). Aromatic (**62–64**) and alkyl substituted (**65**) alkyne chlorides were successfully employed by a slightly modified protocol and using the electrophile in excess.

Scheme 16 | Scope of $Pd^{(I)}$ mediated vinylcyclopropane cross-coupling: A) Coupling with stereoretention. B) Variation of cyclopropyl zinc. C) Variation of alkenyl bromides. D) Coupling with alkyne chlorides.[iv]



Conditions: vinyl bromide (0.5 mmol), $Pd^{(I)}$ dimer **1** (2.5 mol%), toluene (0.2 M), *slow addition of organozinc* (1.5 eq.) over 15 min, 10 min at r.t.; a) *reverse addition over 15 min to organozinc*; b) alkyne chloride (2.0 eq.) and **1** (2.5 mol%) in toluene (0.2 M), *slow addition of organozinc* (0.5 mmol) over 15 min, 10 min at r.t; Slow additions were performed using a syringe pump.

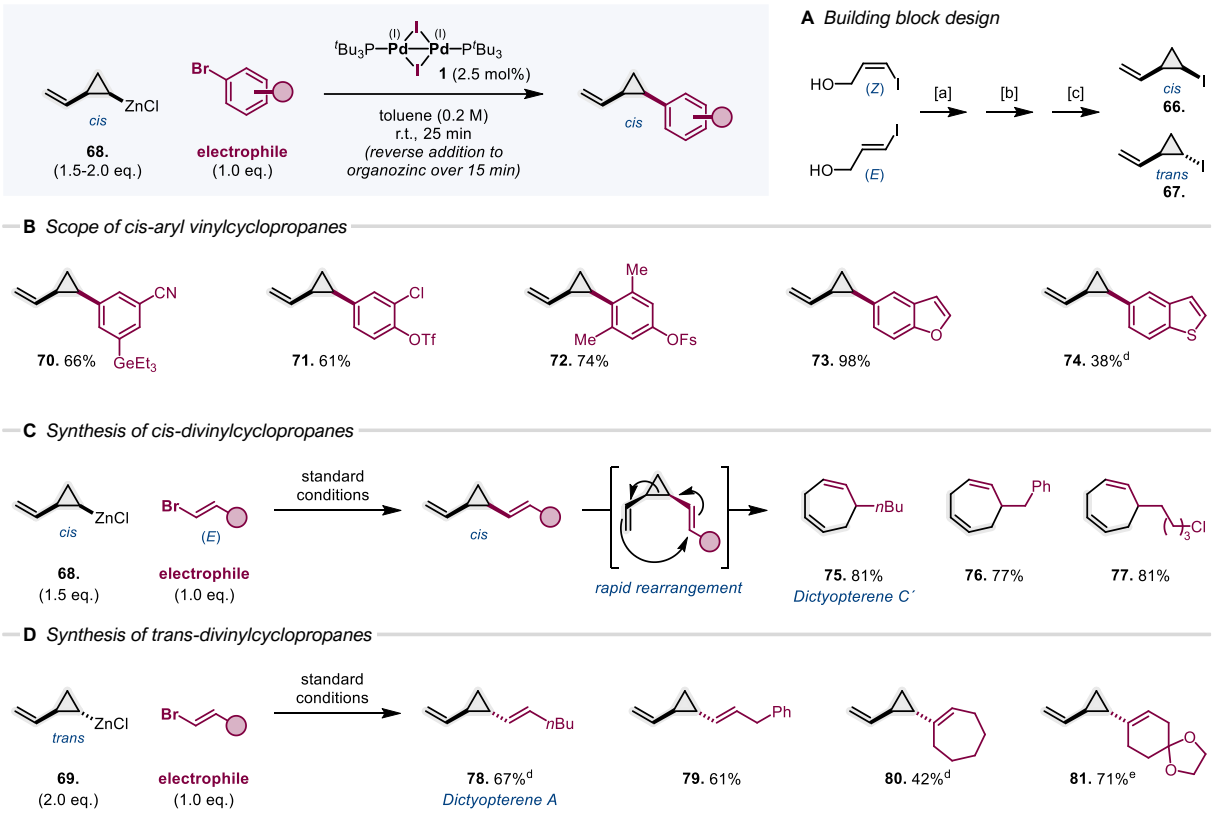
3.3.3 Application of vinylcyclopropane zinc building blocks

For wider modularity and to access vinylcyclopropanes in an even more practical fashion, a complementary approach was next investigated that enables the direct coupling of a readily prepared vinylcyclopropane zinc building block and aryl bromides to access (di)vinylcyclopropanes in a late-stage manner. Therefore, the diastereomerically pure *cis*-vinylcyclopropyl zinc **68** was synthesized starting from (*Z*)-iodo allyl alcohol (**Scheme 17A**). Simmons-Smith cyclopropanation, Dess-Martin oxidation, and Wittig olefination gave the corresponding *cis*-iodo-vinylcyclopropane **66**. Lithium-halogen exchange and subsequent transmetallation

[iv] U. Dabranskaya has carried out the experimental work presented within **Scheme 16A**, more precisely, the synthesis of **48** and **49**.

with $ZnCl_2$ afforded **68** as a single diastereomer. Similarly, the *trans*-vinylcyclopropyl zinc **69** was synthesized starting from (*E*)-iodo allyl alcohol following the same reaction sequence (**Scheme 17A**). The practical application of related vinylcyclopropyl organozinc[79] and cuprate[90, 91] building blocks has been demonstrated by Piers and co-workers and, as such, is expected to be likely feasible employing mild and efficient $Pd^{(I)}$ catalysis methodology. Indeed, $Pd^{(I)}$ mediated cross-coupling of *cis*-vinylcyclopropyl zinc **68** with various aryl bromides succeeded highly efficiently (**Scheme 17B**). However, the previous procedure was slightly modified by adding a solution of $Pd^{(I)}$ dimer **1** and aryl bromide to the organozinc (*reverse addition*). This approach enables the late-stage introduction of the valuable *cis*-vinylcyclopropyl functionality to arenes in a fully predictable and site-selective manner. Aryl bromides bearing additional functional groups such as $GeEt_3$ and nitrile **70**, chloride and triflate **71,** or fluorosulfate **72** were exclusively functionalized at the bromide within 25 min at room temperature. In accordance with previous reports of our group on dinuclear $Pd^{(I)}$ couplings, the bromide selectivity was fully independent of the sterically (ortho-dimethyl in **72**) or electronic (**71**) nature of the substrate. Also, benzofuran **73** and benzothiophene **74** were efficiently decorated with a *cis*-vinylcyclopropane group. Moreover, the stereochemical information of the *cis*-cyclopropane moiety was preserved in all examples, and no isomerization or opening was observed. With the knowledge acquired from the previous studies, it was only natural to extend the $Pd^{(I)}$ mediated cross-coupling of vinylcyclopropane building blocks to the challenging synthesis of divinylcyclopropanes (**Scheme 17C**). Although this cross-coupling protocol is remarkably mild, the reaction of *cis*-vinylcyclopropyl zinc **68** with (*E*)-1-bromo-hex-1-ene yielded exclusively *Dictyopterene C´* **75**. This compound arises from a divinylcyclopropane-cycloheptadiene rearrangement, a unique type of the Cope rearrangement.[92-94] The rearrangement of the corresponding *cis*-divinylcyclopropane intermediate (termed *Dictyopterene C*), which is most likely formed in cross-coupling, is reported to occur within seconds at room temperature.[93, 95] The rearrangement was also observed in the cross-coupling with other alkenyl bromides, resulting in cycloheptadienes **76** and **77** with similar yields. However, given that this rearrangement goes through an *endo-boat-like* transition state and thus is exclusively described for *cis*-divinylcyclopropanes the cross-coupling of *trans*-vinylcyclopropyl zinc **69** with (*E*)-1-bromo-hex-1-ene allowed the selective preparation of *trans*-divinylcyclopropane *Dictyopterene A* **78** (**Scheme 17D**). This highlights the stereoretentive nature of the $Pd^{(I)}$ mediated coupling protocol and several *trans*-divinylcyclopropanes were obtained in moderate to good yields (**78–81**). In addition, by changing the solvent to NMP as a more polar and coordinative solvent, alternative electrophiles such as vinyl triflates can be used in this transformation (**81**), most likely due to a change in speciation.[25]

Scheme 17 | Use of vinylcyclopropane zinc building blocks: A) Synthesis of building blocks. B) Cross-coupling of *cis*-vinylcyclopropyl zinc with aryl bromides. C) Cross-coupling of *cis*-vinylcyclopropyl zinc with alkenyl bromides and subsequent Cope rearrangement. D) Cross-coupling of *trans*-vinylcyclopropyl zinc with alkenyl bromides.



Conditions: Electrophile (0.5 mmol) and Pd$^{(I)}$ dimer **1** (2.5 mol%) in toluene (0.2 M); *reverse addition to organozinc over 15 min*, 10 min at r.t.; a) *Simmons-Smith cyclopropanation*: $ClCH_2I$ (4.0 eq.) and $ZnEt_2$ (2.0 eq.) in DCM (0.25 M); addition of iodo-allyl alcohol (1.0 eq.) in DCM (1 M), 2 h at 0 °C; b) *Dess-Martin oxidation*: cyclopropylmethanol (1.0 eq.) and DMP (1.4 eq.) in DCM, 1h at 0°C, 2 h at r.t.; c) *Wittig olefination*: NaH (1.05 eq.) and Ph_3PCH_3Br (1.05 eq.) in DMSO (0.8 M); addition of cyclopropyl aldehyde (1.0 eq.), overnight at r.t.; d) compound is volatile; e) NMP was used as solvent.

In conclusion, dinuclear Pd$^{(I)}$ mediated cross-coupling methodology has been extended by a new protocol for the modular access of (di)vinylcyclopropanes. The practical method is characterized by its efficiency and generality. Coupling reactions proceed at room temperature within a total reaction time of 25 minutes, and a diverse range of cyclopropyl zinc, as well as numerous aryl, alkenyl, or alkyne electrophiles, were demonstrated to couple to the corresponding products in a fully stereoretentive and site-selective manner. The protocol allowed access to valuable natural products such as *Chrysanthemic methyl ester*, *Dictyopterene A*, or *Dictyopterene C´* that arise from a subsequent Cope-type rearrangement.

4

Dynamic Stereomutation of Vinylcyclopropanes with $Ni^{(I)}$ Metalloradicals

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The results described in this chapter were published in Nature.[96] Experimental and computational work has partially been carried out in collaboration with other members of the Schoenebeck group, whose contributions are stated in detail in the respective subchapters.

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4 Dynamic stereomutation of vinylcyclopropanes with $Ni^{(I)}$ metalloradicals

4.1 Metalloradical catalysis

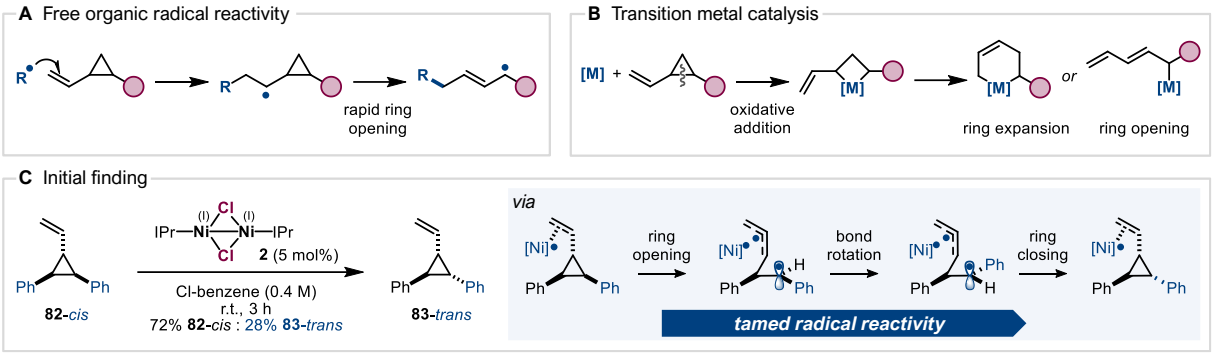
Metalloradicals are metal complexes with one unpaired electron at the metal center. Metalloradical catalysis (MRC) refers to using metalloradicals to catalyze organic transformations.[97] In metalloradical catalysis, the unpaired spin is preserved throughout the entire catalytic cycle based on one-electron radical-type elementary steps. Metal-stabilized organic radicals are generated as key intermediates of discrete radical-type reactivity, resulting in controlled reactivity and selectivity in radical reactions, which is in strong contrast to free radical reactivity.[98-100] It is noteworthy that tamed radical reactivity is a key feature in catalytic units of various metalloenzymes.[101] However, the exact features required for metalloradicals to unfold their full potential and why their reactivities differ from organic free radicals are yet to be fully understood. Obtaining a complete understanding of the reactivities of metalloradicals and the factors necessary to selectively generate and tame them in a catalytic context will undoubtedly open many powerful applications. The following chapter will discuss our attempts to understand novel $Ni^{(I)}$ metalloradical reactivity and its application in the stereomutation of vinylcyclopropanes.

4.2 Initial investigations

Experimental data presented within this subchapter were obtained in collaboration with other members of the Schoenebeck group: Dr. Bashkar Mondal (initial computational predictions), Dr. Theresa Sperger (initial computational predictions), Dr. Sherif J. Kaldas and Dr. Ajoy Kapat (initial findings).

Vinylcyclopropanes have demonstrated unparalleled synthetic value associated with their ring-opening reactivity initiated by organic free radicals.[102] The radical-mediated ring-opening process follows a common mechanism: the radical initiator species (R•) adds to the double bond, forming a cyclopropylcarbinyl radical that rapidly fragmentates to the corresponding homoallyl radical via ring opening (Scheme 18A). The ring-opening process is thermodynamically favored as it releases the strain energy of the cyclopropane ring. Such reactivity makes vinylcyclopropane derivatives a suitable radical clock substrate for mechanistic investigations involving radicals.[103] Besides the thermodynamically driven olefine addition & ring-opening reactivity, the release of the ring strain of vinylcyclopropanes also facilitates the oxidative addition to transition metal complexes by C–C cyclopropyl bond cleavage (Scheme 18B). This property makes vinylcyclopropanes valuable building blocks for various downstream functionalizations such as allylic substitutions, cycloadditions and rearrangements.[104]

Scheme 18 | Versatile reactivity of vinylcyclopropanes: A) Organic radical initiated ring-opening. B) Established transition metal catalysis. C) Initial finding on metalloradical induced isomerization and mechanistic proposal.[5]



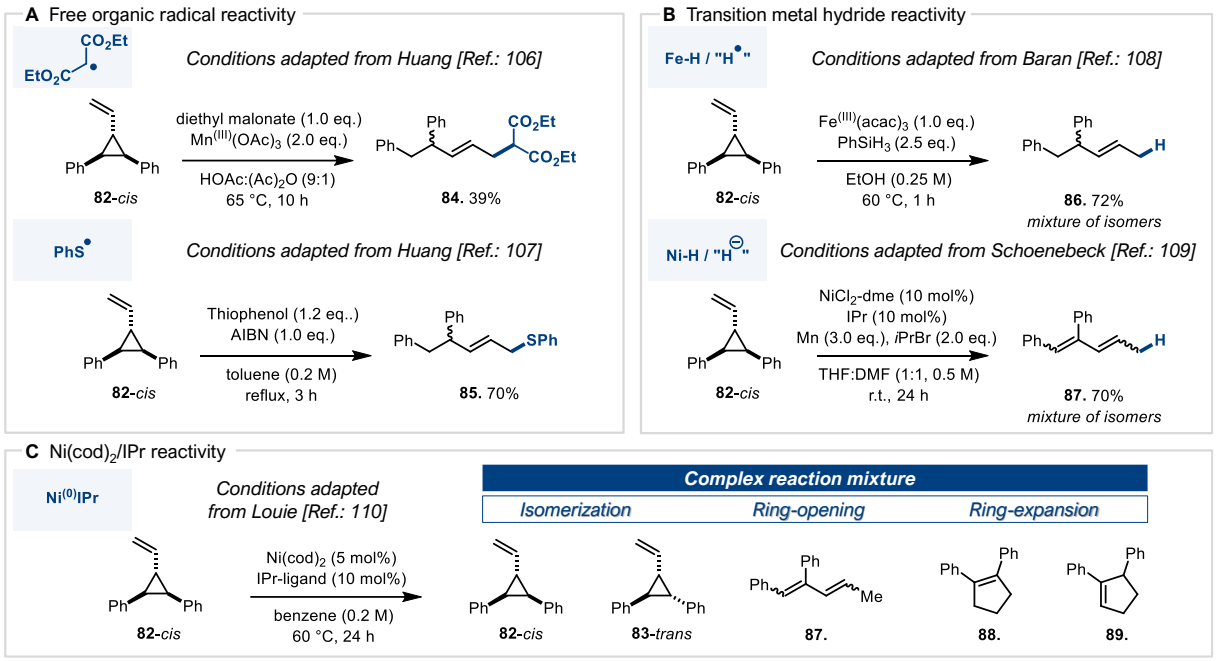
In the context of the mechanistic investigation of the $Ni^{(I)}$ metalloradical induced double bond migration discovered by our group (see chapter 1.3 Catalysis with Palladium$^{(I)}$ and Nickel$^{(I)}$ dimers), Dr. Ajoy Kapat (former postdoc in the Schoenebeck group) performed radical probe experiments by exposing the $Ni^{(I)}$ dimer **2**, $[Ni^{(I)}(\mu\text{-Cl})IPr]_2$, to *cis*-diphenyl vinylcyclopropane **82** (**Scheme 18C**). Because the $Ni^{(I)}$ dimer **2** acts as precursor for defined $Ni^{(I)}$ metalloradicals, rapid ring-opening of the vinylcyclopropane was expected. However, instead partial isomerization to *trans*-diastereomer **83** occurred; more precisely, 72:28 *cis/trans* after 3 hours and 60:40 *cis/trans* after 6 hours were detected (**Scheme 18C**).[36] The mechanistic investigation into the $Ni^{(I)}$ metalloradical triggered vinylcyclopropane isomerization without uncontrolled ring-opening has not been done yet and is a crucial aspect of the following chapter. We envisioned that a mechanistic understanding could have far-reaching implications for metalloradicals and their application in organic synthesis.

We started our investigation on the $Ni^{(I)}$ metalloradical reactivity by comparing the reactivity with selected control experiments. Therefore, *cis*-diphenyl-vinylcyclopropane **82** was exposed to free organic radicals, Iron hydride and Nickel hydride species (**Scheme 19**). The reaction of **82** with free organic radicals has not been reported but Huang and co-workers reported a radical ring-opening of related substrates with malonic acid diethyl ester under the action of $Mn^{(III)}(OAc)_3$,[105] or alternatively, with benzenethiol in the presence of azobisisobutyronitrile (AIBN) as a radical initiator.[106] As part of my thesis, both methodologies were applied to *cis*-diphenyl-vinylcyclopropane **82**, and indeed, the ring-opening was observed (**Scheme 19A**). The opening is expected to occur by selective addition of the free radical to the C=C vinyl double bond, forming a cyclopropylcarbinyl radical, which undergoes a rapid cyclopropyl-allyl radical rearrangement. Subsequent hydrogen atom transfer gives the final products **84** in 39% and **85** in 70% yield, respectively. In this context, it can be stated that the isomerization of **82** is no result of free organic radical reactivity and moreover, the presence of free organic radicals can be excluded. We next investigated the reactivity of **82** with transition metal hydrides. Therefore, **82** was exposed to hydrogen atom transfer (HAT) conditions adapted from Baran and co-workers, and similarly to the above-discussed free organic radical reactivity, the ring-opening process was observed (**Scheme 19B**).[107] The reaction is assumed to proceed via an in situ generated dimeric iron hydride species ("$[Fe\text{-}H]_2$"), which transfers a hydrogen atom to the vinyl moiety, generating a

[5] The partial isomerization of **82** presented in **Scheme 18C** has been discovered by Dr. A. Kapat.

cyclopropylcarbinyl radical that undergoes spontaneous ring-opening. The ring-opened alkene **86** was isolated as a mixture of isomers in 72% yield indicating that the isomerization of **82** is no result of hydrogen atom transfer. In order to investigate the potential involvement of Nickel hydride species in the observed isomerization, we conducted an experiment using *cis*-diphenyl-vinylcyclopropane **82** and (IPr)Ni$^{(II)}$-H, which was formed in situ using a literature procedure from our group.[108] The resulting reaction produced a mixture of dienes **87** in a yield of 70% (**Scheme 19B**). The formation of the dienes is likely due to an allylic substitution and β-hydride elimination type mechanism. Overall, irreversible ring-opening was observed for both, free organic radicals and metal hydrides, indicating a fundamentally different reactivity between the control experiments and the Ni$^{(I)}$ isomerization.

Scheme 19 | Investigation on the reactivity of vinylcyclopropane **82**-*cis*: A) Free organic radical induced ring-opening. B) Iron hydride (HAT) and nickel hydride-induced ring-opening. C) Partial isomerization, ring-opening, and ring-expansion with established Ni$^{(0)}$IPr system.

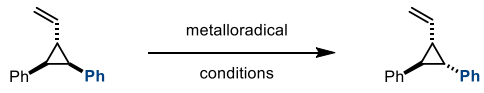


Next, Ni$^{(0)}$ reactivity was investigated: Louie and co-workers reported the ring expansion of vinylcyclopropanes to cyclopentenes (solely with substrates bearing alkene substituents and no substituents at the cyclopropane ring).[109] The reaction is catalyzed by Ni$^{(0)}$(IPr) via oxidative addition into the cyclopropane ring to form a four-membered metallacycle (**Scheme 18B**). Subsequent rearrangement to the corresponding six-membered metallacycle is assumed, and final reductive elimination leads to cyclopentene.[110] Although in the initial mechanistic investigations of our group, pre-synthesized Ni$^{(0)}$(IPr)$_2$ remained reactivity-silent, Louie reported cyclooctadiene (cod) as a crucial additive. Therefore, the conditions were applied to our substate and *cis*-diphenyl-vinylcyclopropane **82**, Ni(cod)$_2$ (5 mol%) and IPr-ligand (10 mol%) were dissolved in benzene (0.2 M) and stirred for 24 hours at 60 °C (**Scheme 18C**). Interestingly, while most of the starting vinylcyclopropane **82** was recovered, complex reactivity was observed: Besides partial isomerization towards **82** and **83** as major components, cyclopropane opening to the corresponding diene diastereomers **87** (*e.g.* Ni-H reactivity) and rearrangement of cyclopentene isomers **88–89** was detected. Clearly, different mechanistic scenarios under Ni$^{(0)}$ catalysis can take place,

such as Louie´s $Ni^{(0)}/Ni^{(II)}$ reactivity, but the generation of Ni-H species or comproportionation to $Ni^{(I)}$ metalloradical might also be feasible.[111] If the vinylcyclopropane isomerization activity originates from metalloradical reactivity, then other metalloradicals should exhibit similar isomerization activity. Therefore, pre-defined metalloradicals were synthesized and tested in vinylcyclopropane isomerization (**Table 1**). Complexes of interest were $Ni^{(I)}$(IPr)(Cl)(Py) **4** (Py = Pyridine)[34] and $Ni^{(I)}$(IPr)(OR) **90** (OR = 2,4,6-*t*Bu-phenolate)[112] because of their close relationship to the low valent $Ni^{(I)}$(IPr)(Cl)(alkene) metalloradical **94** that is assumed to form via homolytic cleavage of $Ni^{(I)}$ dimer **2** (**Table 1B**). Similarly, $Ni^{(I)}$(IPr)(Cl)(Py) **4** is synthesized via homolytic cleavage of the Ni-Ni bond by the addition of pyridine to $Ni^{(I)}$ dimer **2** and ligand exchange could lead to the same species **94**.[34] Noteworthy, $Ni^{(I)}$ metalloradicals **4** and **90** showed related isomerization potential compared to **2** as a precursor (**Table 1A, entry 1–3**). This evidence supports that isomerization activity results from the $Ni^{(I)}$(IPr)(Cl)(alkene) **94** metalloradical. To further investigate the influence of the geometry and electronic nature of the metal complex, we synthesized additional metalloradicals (**Table 1C**), including $Ni^{(I)}$(dmbyp)(Cl) **91** (dmbyp = dimethoxybipyridine), $Ni^{(I)}$(dppf)Cl **92** (dppf = 1,1′-bis (diphenylphosphino)ferrocene) and $Co^{(II)}$(MeTAA) **93** (MeTAA = tetramethyltetraaza[14]annulene). Interestingly, none of these complexes showed isomerization potential (**Table 1A, entry 4–6**) and, overall, the experiments indicate that vacant coordination sites are required for successful isomerization.

Table 1 | Vinylcyclopropane isomerization study using pre-defined metalloradicals. A) experimental comparison. B) Olefine-mediated homolytic bond cleavage in $Ni^{(I)}$ dimer **2**. C) Structures of pre-defined metalloradicals.

A Metalloradical reactivity comparison



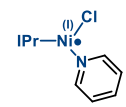
82-*cis* **83**-*trans* **88**-*opening*

entry	catalyst	conditions	cis:trans:opening
1	$[Ni^{(I)}(\mu\text{-Cl})(IPr)]_2$ **2**	Cl-benzene (0.4 M), 6 h, r.t.	60:40:nd
2	$Ni^{(I)}$(IPr)(Cl)(Py) **4**	Cl-benzene (0.4 M), 24 h, r.t.	55:35:10
3	$Ni^{(I)}$(IPr)(OR) **90**	Cl-benzene (0.4 M), 24 h, r.t.	45:41:14
4	$Ni^{(I)}$(dmbpy)(Cl) **91**	toluene (0.4 M), 24 h, r.t.	100:0:0
5	$Ni^{(I)}$(dppf)(Cl) **92**	toluene (0.4 M), 48 h, r.t.	100:0:0
6	$Co^{(II)}$(MeTAA) **93**	toluene (0.4 M), 24 h, r.t. / 60 °C / 100 °C	100:0:0

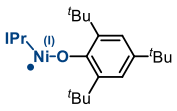
B Homolytic Ni-Ni bond scission

2 **94** $Ni^{(I)}$(IPr)(Cl)(alkene)

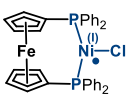
C Pre-defined metalloradicals



4 $Ni^{(I)}$(IPr)(Cl)(Py)

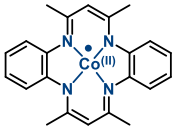


90 $Ni^{(I)}$(IPr)(OR)



92 $Ni^{(I)}$(dppf)(Cl)

91 $Ni^{(I)}$(dmbyp)(Cl)



93 $Co^{(II)}$MeTAA

The initial investigation described above clearly questions the usages of vinylcyclopropanes as mechanistic probes for metal-based radical reactivity and as such, control experiments should be performed and interpreted carefully. However, a fundamental difference in reactivity was observed, and the following chapter will discuss our efforts in understanding the reactivity and developing a synthetic relevant metalloradical-based methodology.

4.3 Stereomutation of vinylcyclopropanes

Experimental data presented within this subchapter were obtained in collaboration with Dr. Sherif J. Kaldas (reaction optimization and development). Computational studies presented in this subchapter were initiated by Dr. Bashkar Mondal (initial computational investigation), partially continued by me, and finalized by Dr. Theresa Sperger (method assessment and final predictions).

4.3.1 Introduction

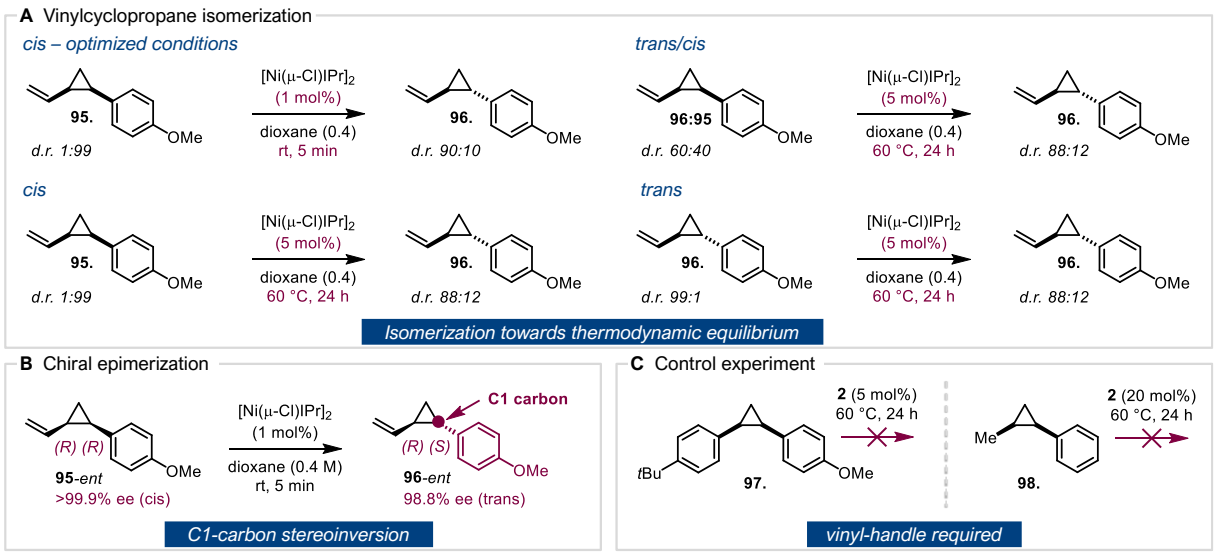
The importance of the vinylcyclopropane motif as a valuable functional group has been highlighted in previous sections (for synthesis of VCP, see section 3.1; for reactivity of VCP, see section 4.2). Briefly summarized: Vinylcyclopropanes are key functional motifs in numerous bioactive molecules and find widespread application in organic synthesis as versatile building blocks.[70] The function of any vinylcyclopropane is ultimately defined by its substitution geometry as, for example, *cis*- and *trans*-vinylcyclopropane diastereomers can be of discrete reactivity.[94] Consequently, the diastereo- and enantioselective preparation of (vinyl)cyclopropanes is a well-investigated area, and impressive achievements have been developed. However, methods tend to be substrate-specific (see section 3.2). In this context, a complementary approach is the unselective preparation of cyclopropane diastereomer mixtures followed by selective stereomutation towards one diastereomer. Such cyclopropane isomerization involves reversible homolytic or heterolytic cyclopropane bond cleavage via 1,3-diradical or zwitterionic intermediates.[113] The reversible cyclopropyl ring-closing process is thermodynamically unfavored and harsh conditions are usually required. For example, more than 400 °C is necessary to isomerize *cis*-1,2-dideuteriocyclopropane to the *trans*-isomer.[114] However, the barriers can be lowered with specific substitution patterns (donor/acceptor substituents),[115, 116] catalyzed by lewis acids,[117] and also the effect of light and photosensitizers have been studied.[118, 119] In addition, the stereomutation of vinylcyclopropanes has been demonstrated applying high temperature,[120] stochiometric oxidant,[121] or transition metal catalysis as $Rh^{(I)}$,[122] $Rh^{(II)}$,[123] $Au^{(I)}$,[124] or $Au^{(III)}$.[125] This is particularly impressive since the isomerization of vinylcyclopropanes is in direct competition with rapid opening[69, 102] and rearrangement reactivity.[72, 94] Although certain efforts have been made, to the best of our knowledge, a universal *cis*-to-*trans* vinylcyclopropane isomerization protocol does not exist. Isomerization strategies seem limited to specific substrate classes, and challenges such as the general chiral epimerization of enantiopure vinylcyclopropanes have yet to be solved.[113, 126] In this context, we envisioned that a novel $Ni^{(I)}$ metalloradical isomerization strategy could be of additional value to the design of vinylcyclopropanes and lay the foundation for further applications and developments.

4.3.2 Thermodynamically driven and chiral epimerization

We started our investigation by evaluating the reaction parameters and in collaboration with Dr. Sherif J. Kaldas (former postdoc in the Schoenbeck group) it has been discovered that when *cis*-1-methoxy-4-(2-vinylcyclopropyl)benzene **95** and 1.0 mol% $Ni^{(I)}$-dimer **2** were dissolved in dry dioxane (0.4 M) and stirred for 5 minutes at room temperature, efficient isomerization to a 90:10 **96**-*trans*/**95**-*cis* mixture took place

(**Scheme 20A**). The **96**-*trans* enriched mixture was isolated by simple filtration with high purity in 98% yield. Interestingly, longer reaction time or increased temperature did not affect the diastereomeric ratio and, moreover, the same diastereomeric ratio was obtained no matter if the pure **95**-*cis* isomer, a **96**-*trans*/**95**-*cis* mixture or the pure **96**-*trans* isomer was used as the starting point (**Scheme 20A**). This clearly indicates the thermodynamic equilibrium as the driving force of the process. Noteworthy, the thermal isomerization of the similar 1-phenyl-2-vinylcyclopropane requires heating at over 200 °C for 90 minutes and results in roughly 80:20 *trans*:*cis*-selectivity accompanied by cyclopentene formation.[127] The thermolytic isomerization is assumed to proceed through homolytic cyclopropane bond cleavage resulting in diradical intermediates.[113] Both radicals then undergo bond rotation, and ring-closure results in isomerization towards a thermodynamic equilibrium but loss of chiral information if a chiral starting material is applied.[127] Consequently the single enantiomer 1-methoxy-4-((1*R*,2*R*)-2-vinylcyclopropyl)benzene **95**-*ent* was prepared in >99.9% *ee* and was then subjected to $Ni^{(I)}$ isomerization (**Scheme 20B**). Interestingly, selective epimerization at the aryl substituted C1-carbon took place leading to 1-methoxy-4-((1*S*,2*R*)-2-vinylcyclopropyl)benzene **96**-*ent* in >98.8% *ee* and 90:10 d.r. (*trans*/*cis*). Additional control experiments with the *non*-vinylcyclopropanes, *cis*-biaryl cyclopropane **97** and *cis*-1-methyl-2-phenylcyclopropane **98**, highlighted that the vinyl handle is required since no isomerization was observed (**Scheme 20C**). To the best of our knowledge, such a rapid, mild, and chiral epimerization of vinylcyclopropanes is, to date, unprecedented.

Scheme 20 | Rapid and mild vinylcyclopropane isomerization. A) Optimized conditions and study on driving force. B) Selective stereomutation of the C1-stereocenter. C) Control experiment with *non*-vinylcyclopropanes.[6]



4.3.3 Investigation on the reaction pathway

Next, DFT studies were performed to shine light on the mechanistic scenario, and, to explain the unique role of the vinyl handle. We started the investigation with the assumption that the vinyl group mediates a homolytic cleavage of the $Ni^{(I)}$–$Ni^{(I)}$ bond, similarly to previous observations made by Matsubara[34] (*e.g.*

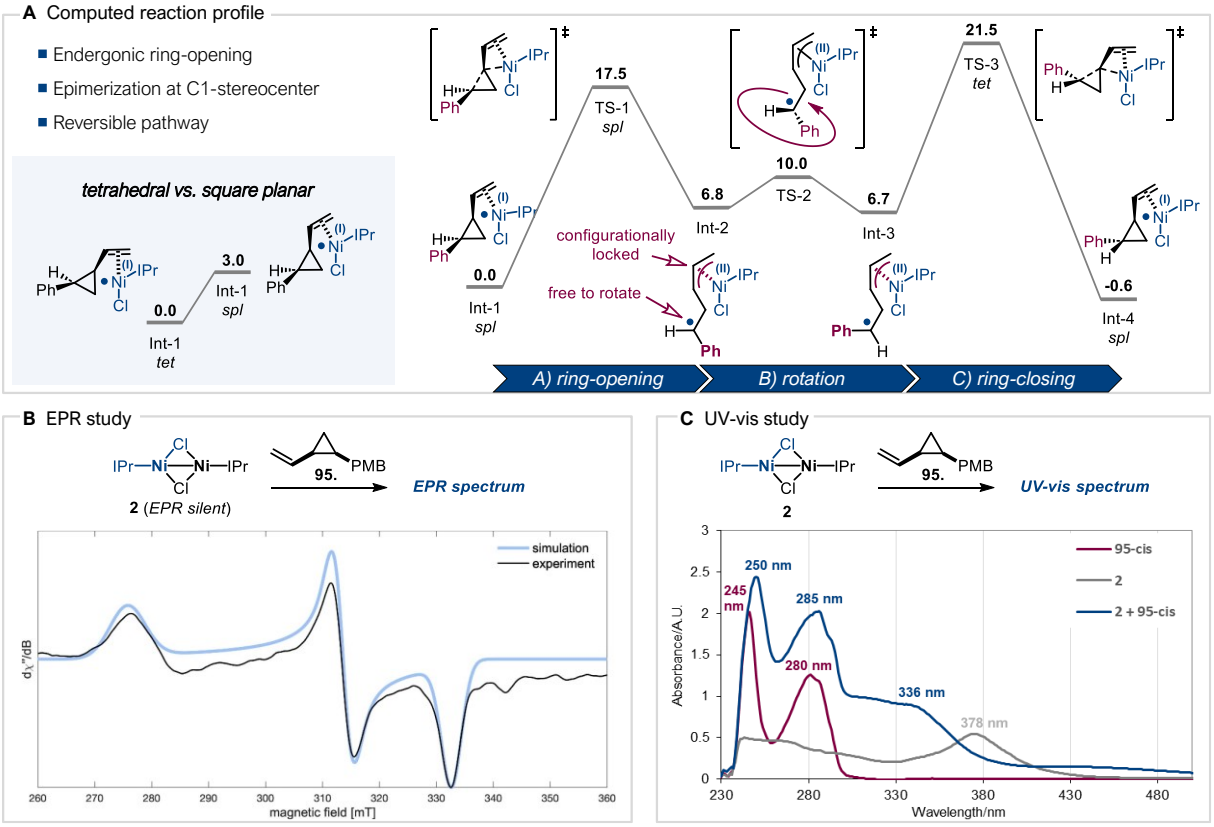
[6] Dr. S. J. Kaldas discovered 1,4-dioxane as a suitable solvent for vinylcyclopropane isomerization.

pyridine coordination) and our group (olefin coordination).[36] This would result in the low valent (IPr)(Cl)Ni$^{(I)}$-vinyl coordinated intermediate (**Int-1**) with the vinylcyclopropane solely as π-coordinating ligand. Through computations, two plausible conformers were identified that differ in vinyl group coordination to the Ni center (**Scheme 21A**): a square planar (**Int-1** *spl*) and a tetrahedral geometry (**Int-1** *tet*) with the latter being 3.0 kcal/mol higher in energy, calculated at the CPCM(1,4-dioxane) M06L/def2-TZVP//ωB97XD/6-31G(d)(SDD) level of theory. The presence of such a monomeric Ni$^{(I)}$ intermediate **Int-1**, is additionally supported by EPR (**Scheme 21B**) and UV-vis spectroscopic studies (**Scheme 21C**). While the sole Ni$^{(I)}$ dimer **2** is diamagnetic and EPR silent, after addition of *cis*-1-methoxy-4-(2-vinylcyclopropyl)benzene **95**, a distinct signal was observed indicating the presence of metalloradical species (such as **Int-1**). The signal is of rhombic symmetry having distinct g-values greater than the one of a free electron (2.4526 $g_x \neq$ 2.1560 $g_y \neq$ 2.0323 g_z), which is characteristic of unpaired electrons in a transition metal environment like **Int-1**. Moreover, control experiments using the defined Ni$^{(I)}$ metalloradical Ni$^{(I)}$(IPr)(Cl)(Py) **4** showed both efficient isomerization of **95** and EPR signals comparable to the one obtained with the Ni$^{(I)}$ dimer **2** (for details, see supporting information p. 150 f. and p. 156 ff.). Noteworthy, the spectra differentiate between the Ni$^{(I)}$ complexes in the presence and in the absence of **95**, which would be in line with the formation of π-olefin coordinated Ni$^{(I)}$ metalloradicals **Int-1**. The formation of **Int-1** is also supported by UV-vis absorption spectroscopy. The individual absorption spectra of vinylcyclopropane **95** and Ni$^{(I)}$ dimer **2** are distinct from the absorption acquired after mixing the two components, which displays a new absorption peak at 336 nm (**Scheme 21C**). Next, starting from the square planar Ni$^{(I)}$ olefine complex **Int-1** the reaction profile was investigated computationally at the CPCM(1,4-dioxane) M06L/def2-TZVP//wB97XD/6-31G(d)(SDD) level of theory. The computational data suggests the following:

- ***Ring-opening:*** Homolytic C1–C2 bond cleavage takes place via **TS-1** by partial induction of radical character onto the vinylcyclopropane from Ni$^{(I)}$ metalloradical with an overall activation free energy barrier of 17.5 kcal/mol leading to ring-opened **Int-2**. The Ni$^{(I)}$ mediated opening was found to be endergonic by 6.8 kcal/mol indicating that the resulting benzylic radical in **Int-2** is less stable than the Ni-centered radical in **Int-1**. This is in contrast with organic free radical reactivity where ring-opening is exergonic, driven by strain release and the formation of a stabilized open shell intermediate (for free organic radical reactivity, see section 4.2).
- ***Bond-rotation:*** A dynamic bond rotation between **Int-2** and **Int-3** can take place with a free energy barrier of 3.2 kcal/mol (**TS-2**). It is noteworthy, that in **Int-2** and **Int-3** only the C1-benzyl radical is free to rotate and, on the other hand, the C2-allyl ligated Ni$^{(II)}$ species is conformationally locked. This finding is supported by the exclusive epimerization at the C1-center (**Scheme 20B**). In contrast, if the C1-benzyl radical and the C2-allyl radical are free to rotate racemization occurs, which is the case for thermal isomerization.[127]
- ***Ring-closing***: Final ring-closing via **TS-3** gives rise to the π-coordinated *trans*-vinylcyclopropane Ni$^{(I)}$ metalloradical **Int-4**. The barrier is with 21.5 kcal/mol significantly higher than the one for the opening but still feasible at room temperature. It is noteworthy that only the tetrahedral conformation of **TS-3** could be located, and possible lower energy conformers were not identified at this time. According to the computational data the Ni$^{(I)}$ *cis*- **Int-1** and Ni$^{(I)}$ *trans*-vinylcyclopropane **Int-4** have a small difference in energy

(-0.6 kcal/mol) and the whole pathway should be fully reversible at room temperature. In this context, the diastereomeric ratio is expected to be solely determined by the thermodynamics of the substrate. This is supported by the experimental observations discussed above (**Scheme 20A**).

Scheme 21 | A) Computed DFT reaction profile calculated by myself at the CPCM(1,4-dioxane) M06L/def2-TZVP//wB97XD/6-31G(d)(SDD) level of theory; All values are given in Gibbs free energies (in kcal/mol); Abbreviations *"tet"* and *"spl"* refer to tetrahedral and square planar Ni conformers, respectively. B) EPR spectroscopic investigation on $Ni^{(I)}$ olefine complex;[7] C) UV-vis spectroscopic investigation on $Ni^{(I)}$ olefine complex.

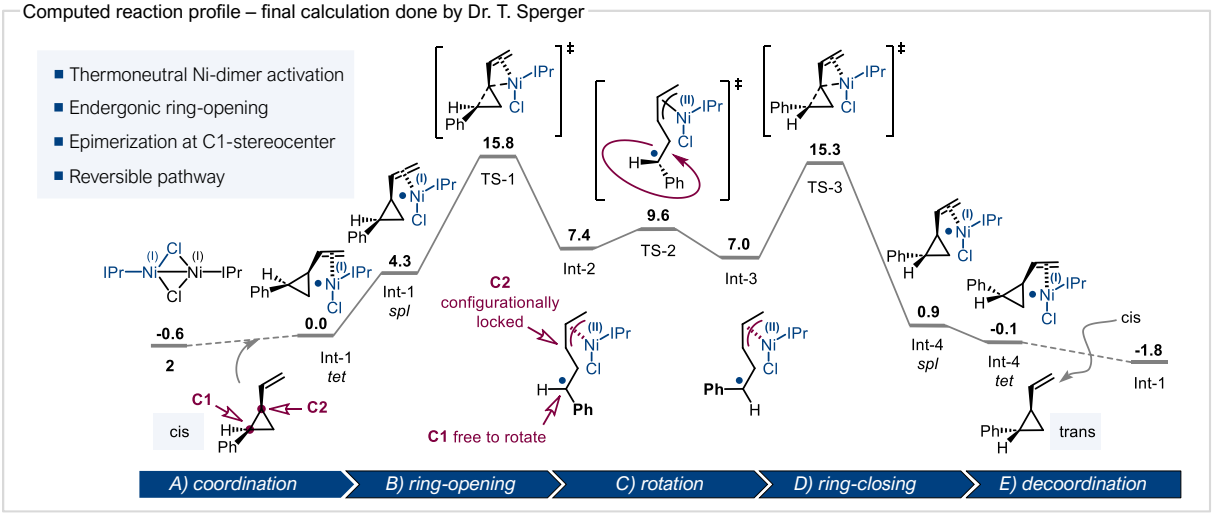


While the computed reaction profile complements the experimental trends, Dr. Theresa Sperger (senior scientist of the Schoenebeck group) performed an extensive method evaluation and observed a significant method dependence for the relative stability of open and closed-shell species. Dr. Sperger optimized and evaluated the geometries on the basis of known crystal structures and identified the MN15 functional as the most reasonable functional for geometry optimization, while the M06L functional was identified as the most reasonable method for single point energy calculations. Finally, she calculated the reaction profile in more detail using the CPCM (1,4-dioxane) M06L/def2-TZVP//MN15/6-31G(d)(SDD) level of theory (**Scheme 22**). The detailed computational profile complements my own in the following: The Ni-Ni bond in the $Ni^{(I)}$ dimer **2** is, in the presence of the vinylcyclopropane, homolytic cleaved. The bond scission was found to be roughly thermoneutral (0.6 kcal/mol) towards the VCP-coordinated $Ni^{(I)}$ monomer **Int-1**. Next, reorganization from square planar (**Int-1** *spl*) to tetrahedral (**Int-1** *tet*) conformation takes place with a free energy barrier of 4.3 kcal/mol followed by the ring opening step. Similarly, reorganization from tetrahedral back to square planar

[7] EPR spectra simulation and plotting shown in **Scheme 21** was conducted by Dr. T. Sperger.

occurs after ring-closing in **Int-4**. Furthermore, Dr. Sperger identified that the pathway is fully reversible and that the main driving force stems from the thermodynamic preference of the substrate, in this case from a -1.8 kcal/mol free energy difference between the two diastereomers.

Scheme 22 | Detailed DFT reaction pathway calculated by Dr. T. Sperger; All values are given in Gibbs free energies (in kcal/mol) calculated at the CPCM (1,4-dioxane) M06L/def2-TZVP//MN15/6-31G(d)(SDD) level of theory. The descriptions *"tet"* and *"spl"* refer to tetrahedral and square-planar Ni conformers. Both transition states also have square-planar geometry around Ni.



In summary, the computational and experimental data strongly support the mechanistic scenario of a $Ni^{(I)}$ metalloradical that mediates the observed isomerization and valuable insights into the stereoretentive nature of the reaction were obtained. On the other hand, an alternative $Ni^{(0)}$ / $Ni^{(II)}$ reaction pathway seems unlikely since control experiments using the $Ni(cod)_2$/IPr system mediates the isomerization of **95** less efficiently, elongated reaction times and increased temperatures are necessary (for details, see supporting information p. 137 ff.). In addition, the isomerization using $Ni(cod)_2$/IPr is significantly affected by the applied solvent and, moreover, in dioxane an EPR signal was detected that indicates the in situ formation of $Ni^{(I)}$ species. Furthermore, $Ni(cod)_2$/IPr showed a significant substrate dependency and product mixtures including ring-opening and cyclopentene formation where observed (see Supporting Information p. 152 ff.). Clearly, a different mechanistic scenario under $Ni^{(0)}$ catalysis has to be considered that includes the formation of various Ni-species including $Ni^{(I)}$ metalloradicals.

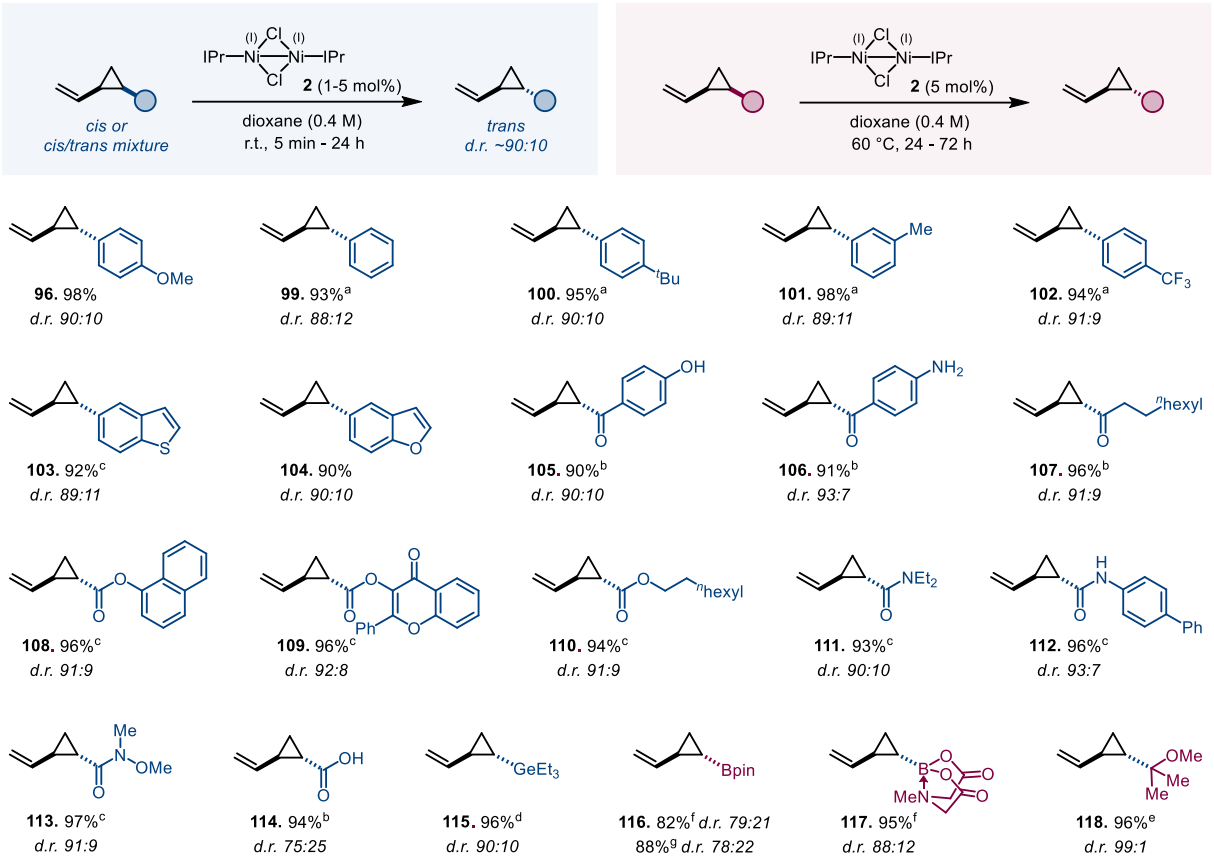
4.3.4 Scope of isomerization

We next explored the broader scope of the isomerization methodology (**Scheme 23**). Variation of the aryl moiety had no remarkable impact and efficient isomerization towards the thermodynamically favored *trans*-diastereomers occurred in dioxane and 1.0 mol% $Ni^{(I)}$ dimer **2** within 5 min at room temperature. Electron-donating substituents at the arene ring such as methoxy- (**96**), *tert*-butyl- (**100**) or *meta-methyl*- (**101**), an electron-withdrawing trifluoromethyl group (**102**), as well as benzothiophene (**103**) or benzofuran (**104**) substituted vinylcyclopropanes, were all well tolerated leading to equally *trans*-enriched mixtures (*~90:10 d.r.*) in high yields (82-98%). In line with the proposed pathway above other radical stabilizing group at the

C1-center should have a profound effect on the bond cleavage event and the ring-opened intermediates. Therefore, we shifted our attention to the isomerization of carbonyl-substituted vinylcyclopropanes. Isomerization of aromatic (substituted with unprotected OH **105**, substituted with unprotected NH_2 **106**) as well as aliphatic (**107**) vinylcyclopropyl ketones was effective using 5 mol% $Ni^{(I)}$ dimer within 15 minutes at room temperature. The isomerization of vinylcyclopropyl esters (**108-110**) as well as aromatic and aliphatic amides (**111-112**), including a Weinreb amide (**113**), was accomplished with good *trans*-selectivity using 5 mol% $Ni^{(I)}$ dimer within 60 minutes at room temperature. Even the free vinylcyclopropyl carboxylic acid (**114**) was efficiently isomerized within 15 minutes, although with a decreased *trans*-selectivity of 75:25 (*trans*/*cis*). Noteworthy, in most cases, no by-product formation is observed, and purification was straightforwardly achieved by precipitation of Nickel using pyrrolidine-1-dithiocarboxylic acid[60] and subsequent filtration. Noteworthy, radical stabilization group variation results in reaction time and temperature variation. In this context, isomerization to *trans*-vinylcyclopropyl-GeEt3 *(***115***)* was also successful, but the elongation of the reaction time to 24 hours at room temperature was necessary. Furthermore, isomerization towards vinylcyclopropyl-Bpin (**116**) and vinylcyclopropyl-BMIDA (**117**) was achieved at 60 °C within 72 hours. The isomerization of these building blocks is very pleasing due to the vast application of germanes and boronates in organic synthesis. Interestingly, *α*-metallated radicals, especially *α*-boryl radicals, are well known for their good stability due to hyperconjugation-like structures between the radical and the metal center.[128] In contrast, alkyl radicals are less stabilized, but effective isomerization (*99:1 d.r.*) of vinylcyclopropane (**118**) was observed within 24 hours at 60 °C.

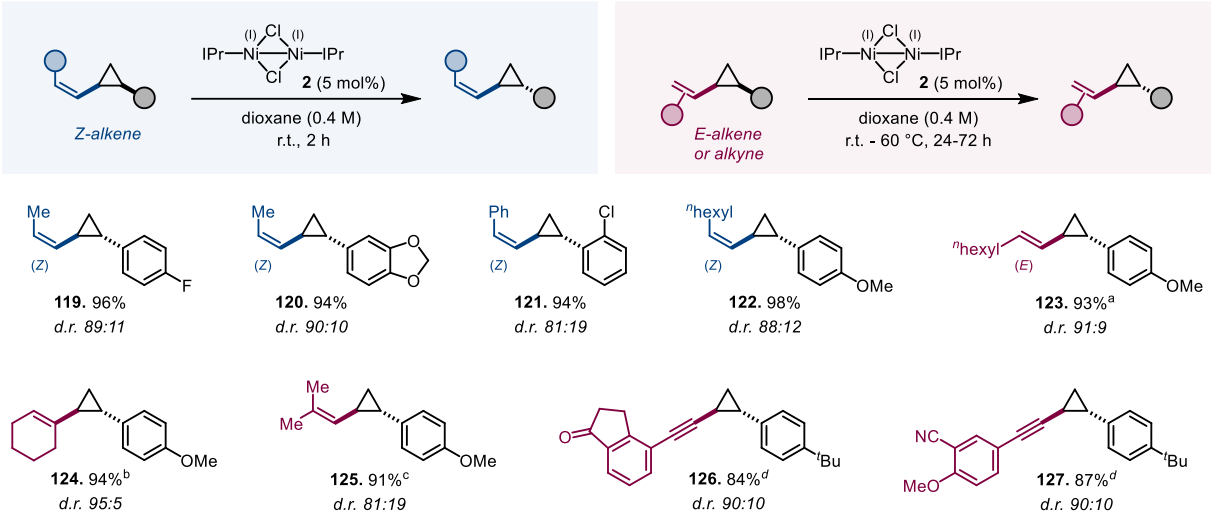
Next, the effect of substitution on the vinyl handle was investigated (**Scheme 24**). Therefore, we synthesized cis/trans mixtures of aryl-substituted *Z*-alkenyl cyclopropanes and exposed them to isomerization. Interestingly, the thermodynamic equilibrium (*90:10 d.r.*) was reached using 5 mol% $Ni^{(I)}$ dimer **2** after 2 hours at room temperature and aliphatic (**119**, **120**, **122**) as well as aromatic (**121**) substituted *Z*-alkenes were well tolerated and isolated in high yields and good diastereomeric ratios. Impressively, no isomerization of the *Z*-alkene handle was observed, although the same catalyst is known for *Z*/*E*-alkene isomerization.[36] Perhaps this results from the locked alkene in the ring-opened allyl-Ni intermediated (see **Scheme 22**, **Int-2**). Likely, the elongated reaction times are based on the increased sterically hindrance at the alkene handle since isomerization of the analogous terminal vinylcyclopropanes is completed within 5 minutes using 1 mol% $Ni^{(I)}$ dimer **2**. Indeed, comparison with the *Z*-alkene (**122**) showed that isomerization of the bulky (*E*)-1-methoxy-4-(2-(oct-1-en-1-yl)cyclopropyl)benzene (**123**) was accomplished within 48 hours at 60 °C instead. In addition, higher substituted alkenylcyclopropanes (**124**, **125**) can also be isomerized in good yields by applying elongated reaction time and heating. To our delight, the isomerization of aryl cyclopropanes having an alkyne handle (**126**, **127**) was also accomplished by applying elongated reaction time. It becomes clear that the electronic and steric nature of the alkenyl unit determines the reaction rate, and with decreased coordination affinity, the rate significantly slows down.

Scheme 23 | Scope of vinylcyclopropane isomerization under mild (blue) and more demanding conditions (red).



Conditions: vinylcyclopropane (0.1-0.2 mmol) and $Ni^{(I)}$ dimer **2** (1 mol%) in dioxane (0.4 M), 5 min at r.t.; a) Yield determined by quantitative ^1H NMR; b) $Ni^{(I)}$ dimer **2** (5 mol%), reaction time 15 min at r.t.; c) $Ni^{(I)}$ dimer **2** (5 mol%), reaction time 60 min at r.t.; d) $Ni^{(I)}$ dimer **2** (5 mol%), reaction time 24 h at r.t.; e) $Ni^{(I)}$ dimer **2** (5 mol%), reaction time 24 h at 60 °C; f) $Ni^{(I)}$ dimer **2** (5 mol%), reaction time 72 h at 60 °C; g) $Ni^{(I)}$ dimer **2** (5 mol%), pyridine (10 mol%), reaction time 72 h at 60 °C.

Scheme 24 | Scope of alkenyl- and alkynylcyclopropane isomerization.



Conditions: cyclopropane (0.1-0.2 mmol) and $Ni^{(I)}$ dimer **2** (5 mol%) in dioxane (0.4 M), 2 h at r.t.; a) Reaction time 48 h at 60 °C; b) Reaction time 24 h at 60 °C; c) $Ni^{(I)}$ dimer **2** (10 mol%), reaction time 72 h at 60 °C; d) $Ni^{(I)}$ dimer **2** (5 mol%), reaction time 24 h at r.t.

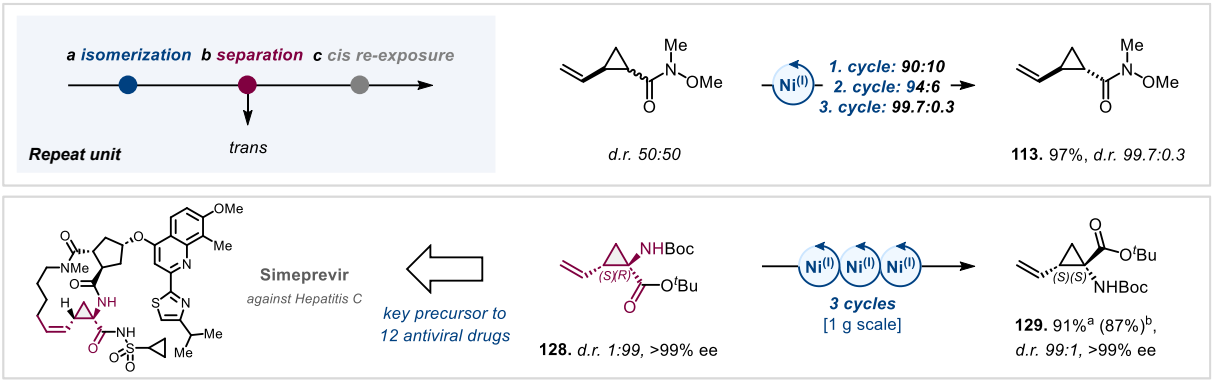
4.4 Application of vinylcyclopropane isomerization

In the previous sections, a novel metalloradical mediated vinylcyclopropane isomerization methodology has been developed that is of metalloradical nature and enables the stereomutation of chiral substrates without loss of chiral information. The rapid and mild isomerization methodology has been tested with numerous substrates, demonstrating a broad functional group tolerance. In addition, it has been showcased that the isomerization is reversible, and the final *cis/trans* ratio solely depends on the thermodynamic equilibrium between the two diastereomers. In the following, two applications are discussed that make use of the dynamic nature of the process by removing either one diastereomer from the equilibrium and shifting the latter accordingly.

4.4.1 Dynamic thermodynamic resolution

The first approach is based on manipulating the equilibrium between *cis* and *trans* diastereomers by manually removing *trans* after $Ni^{(I)}$ isomerization. The remaining *cis* isomer is then exposed to additional $Ni^{(I)}$ isomerization, resulting in the dynamic formation of more *trans* isomer (Scheme 25). We started our investigation on such *'dynamic thermodynamic resolution'* with a *50:50 trans/cis* mixture of Weinreb amide **113** and subjecting it to $Ni^{(I)}$ isomerization. The resulting mixture (*90:10 d.r.*) was then purified by silica gel column chromatography, leading to pure **113**-*trans* (125 mg, 81%) and a *trans/cis* mixture (28 mg, *52:48 d.r.*). The remaining mixture was then re-exposed to another round of $Ni^{(I)}$ isomerization and diastereomer separation, and the pure **113**-*trans* (20 mg, 13%) and a *trans/cis* mixture (6 mg, *53:47 d.r.*) were obtained. Three rounds of this isomerization/separation sequence were performed, and **113** were obtained in 97% yield with *99.7:0.3 d.r. (trans/cis*). The dynamic thermodynamic resolution is a powerful strategy for diastereomer enrichment, complementary to existing diastereoselective preparation methodologies. In ideal circumstances, the dynamic thermodynamic resolution could be applied if a certain diastereomer is available, but the opposite diastereomer is wanted. For example, this could be the case for the highly valuable building block **128** vinyl-ACCA (vinyl-**a**mino **c**yclopropyl **c**arboxylic **a**cid). Vinyl-ACCA is found in numerous anti-viral drugs (*e.g., Simeprevir) and is* even called an *essential pharmacophore*.[129] In this context, large-scale industrial processes have been developed, and the (1*R*,2*S*)-**128** diastereomer is easily accessible; in contrast, the opposite (1*S*,2*S*)-diastereomer **129** is not. However, the direct access of the *trans*-isomer **129** from the well-established *cis*-isomer **128** could greatly impact the preparation and discovery of new antiviral drugs. Therefore, (1*R*,2*S*)-**128** was prepared in enantiomerically pure form and exposed to dynamic thermodynamic resolution. As a result, 1 g (1*R*,2*S*)-**128** was converted to (1*S*,2*S*)-**129** in a highly diastereo- and enantioselective fashion (99:1 d.r., >99% ee). Hereby, the diastereomeric separation between the isomerization rounds can be performed using silica gel column chromatography (86% yield) or crystallization (91% yield).

Scheme 25 | Dynamic thermodynamic resolution of vinylcyclopropanes.

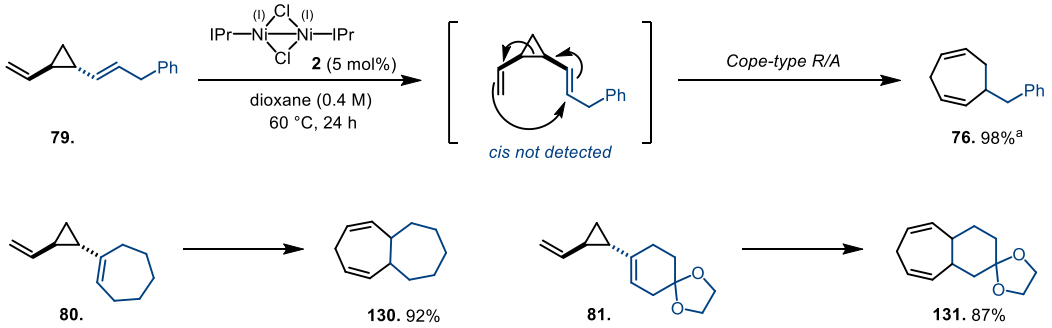


Conditions: a) separation by crystallization; b) separation by chromatography.

4.4.2 Tandem isomerization and Cope rearrangement

The second approach involves selectively removing the *cis*-diastereomer to shift the equilibrium towards it. Therefore, $Ni^{(I)}$ isomerization is combined with a reaction that is specific for *cis*-diastereomers, the divinylcyclopropane-cycloheptadiene rearrangement. The divinylcyclopropane-cycloheptadiene rearrangement is a powerful tool for the construction of various cycloheptane-1,4-dienes from *cis*-divinylcyclopropanes.[92-94, 130] Being a special type of the Cope rearrangement, it offers unique characteristics and can occur spontaneously at room temperature due to the strong thermodynamic driving force based on the release of cyclopropane ring strain. The rearrangement is proposed to occur via a boat-like transition state, requiring *cis*-configuration of the divinylcyclopropane.[94] In this context, synthetic strategies usually involve the direct and selective generation of the *cis*-diastereomer.[93, 131] However, *trans*-divinylcyclopropanes are easier to access but can only be employed by thermal isomerization at around 200 °C. This leads to the partial formation of *cis*-divinylcyclopropane, which is subsequently removed from the equilibrium as a consequence of the Cope rearrangement, shifting the whole equilibrium towards the *cis*-diastereomer. We envisioned to apply the novel $Ni^{(I)}$ metalloradical mediated vinylcyclopropane isomerization in a similar tandem isomerization-Cope rearrangement (**Scheme 26**). Indeed, subjecting *trans*-divinylcyclopropane **79** to 5 mol% $Ni^{(I)}$ dimer **2** at 60 °C for 24 hours led to an impressively clean formation of the cycloheptadiene **76** in 98% yield. Moreover, the same conditions were also suitable for accessing bicyclic cycloheptadiene (**130**, **131**) starting from cyclic *trans*-divinylcyclopropanes. This highly atom-economical process is the first example of a general and mild tandem isomerization-Cope sequence. The process is based on the dynamic formation of the *cis*-diastereomer and its subsequent consumption via the Cope reaction, ultimately shifting the equilibrium towards the *cis*-diastereomer.

Scheme 26 | *Trans*-to-*Cis* isomerization and Cope rearrangement towards selected cycloheptadienes.



Conditions: Divinylcyclopropane (0.1-0.2 mmol) and $Ni^{(I)}$ dimer **2** (5 mol%) in dioxane (0.4 M), 24 h at 60 °C. a) Pyridine (10 mol%).

5

Supporting Information

5 Supporting Information

5.1 General experimental details

Techniques

All reactions were performed utilizing standard Schlenk techniques unless otherwise stated. The synthesis of Ni-complexes and isomerization reactions have been performed under an Argon atmosphere inside a Glovebox. Glassware and magnetic stir bars were dried in an oven (130 °C) for at least 24 hours prior to use and allowed to cool under vacuum at 0.2 mmHg (oil pump). Liquid reagents, solutions or solvents were added via syringe or cannula through rubber septa. Unless otherwise stated, experiments were carried out at room temperature (25 ± 2 °C). The removal of solvents in vacuo was achieved using a rotary evaporator (bath temperatures up to 40 °C) at a pressure of 20 mmHg (diaphragm pump), or at 0.1 mmHg (oil pump) on a vacuum line at room temperature.

Solvents, reagents and starting materials

Unless otherwise stated, all anhydrous solvents were purchased from Sigma Aldrich. Hexane, THF, Et_2O, DCM and toluene were dried using a PS-MD-5 solvent purification system from Innovative Technology. Technical grade solvents were distilled prior to use for chromatography and extraction. Unless otherwise stated, all commercially available reagents and starting materials were used as received.

Purification

Thin layer chromatography (TLC) was performed on Macherey Nagel ALUGRAM Xtra SIL G UV254 aluminum plates with unmodified silica and visualized either under UV light or stained with iodine, $KMnO_4$ or PMA. Flash silica gel column chromatography was performed with silica gel (0.04 – 0.063 mm particle size) purchased from Macherey Nagel. Preparative HPLC was performed on a Knauer Azura HPLC (employing UV detector 2600, at 254 and 230 nm) using a LiChrosorb Si60 column (Merck, 250 x 25 mm, 7 µm silica porosity). For chiral separation, a Chiralpak IA column (Daicel, 250 x 20 mm, 5 µm silica porosity) was employed.

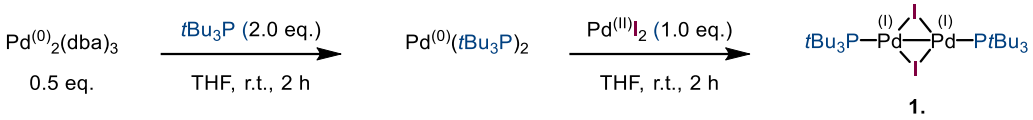
Characterization

All ^{1}H, ^{11}B, ^{13}C, ^{19}F and ^{31}P NMR spectra were recorded on Bruker Avance Neo 600, Varian VNMRS 600 or Varian VNMRS 400 or Bruker Avance Neo 400 spectrometers at ambient temperature (unless otherwise specified). Chemical shifts (δ) are reported in parts per million (ppm) and were referenced either to residual solvent peak ($CDCl_3$, CD_2Cl_2, C_6D_6, CD_3CN for ^{1}H and ^{13}C spectra) or internally by the instrument after locking and shimming to the deuterated solvent (for ^{11}B and ^{19}F). Coupling constants (*J*) are given in Hertz (Hz). Multiplicities of signals in ^{1}H, ^{19}F, and ^{13}C NMR were designated as s (singlet), d (doublet), dd (doublet of doublet), dt (doublet of triplets), ddd (doublet of doublets), t (triplet), td (triplet of doublets), q (quartet), p (quintet), h (sextet), hept (septet), and m (multiplet). For general and accurate prediction of the diastereomeric ratio of the corresponding *cis* and *trans* vinylcyclopropanes, a relaxation delay of 10 seconds was applied.

Gas chromatography coupled with mass spectrometry (**GC-MS**) was performed on an Agilent Technologies 5975 series MSD mass spectrometer under electrospray ionization (EI) mode coupled with an Agilent Technologies 7820A gas chromatograph employing an Agilent 19091s-433 HP-5MS column (30 m x 0.250 µm x 0.250 µm). High-resolution mass spectrometry (**HRMS**) was performed using a Thermo Scientific LTQ Orbitrap XL spectrometer (ESI), Finnigan MAT 95 (EI) or Bruker Maxis II LC-MS-System (APCI). Low-resolution masses of known compounds were extracted from their GC-MS chromatograms. **CW-EPR** spectra were recorded on a Freiberg Instruments MS5000 spectrometer with a FC 400 frequency generator and a low-temperature Dewar filled with liquid nitrogen for sample cooling. All spectra were recorded with the same microwave power of 50 mW, modulation amplitude of 0.2 mT and sweep time constant of 60 s. **Melting points** were measured with a Melting Point Meter MPM-H2 with visual detection and temperature increase of 1 °C/min. **IR** spectra were recorded on a Spectrum 100 spectrometer with a UATR Diamond/KRS-5 crystal with attenuated total reflectance (ATR). **Analytical HPLC** of chiral compounds was performed on a Hewlett-Packard 1100 Series instrument using chiral stationary phases. Analytical GC of chiral compounds was performed on an Agilent GC 8890 instrument using chiral stationary phases. **Optical rotations** were measured on a Perkin Elmer 241 Polarimeter at the Sodium D line (589 nm) at 25 °C. Specific rotation $[\alpha]_D^{25}$ was calculated as $[\alpha]_D^{25} = (100 \cdot \alpha)/(l \cdot c)$ with l = 10 cm. Concentration and solvent are provided in g/100 mL.

5.1.1 Synthesis of Pd$^{(I)}$ and Ni$^{(I)}$ catalysts

Synthesis of Pd$^{(I)}$ dimer [Pd(μ-I)(PtBu$_3$)]$_2$ (1)

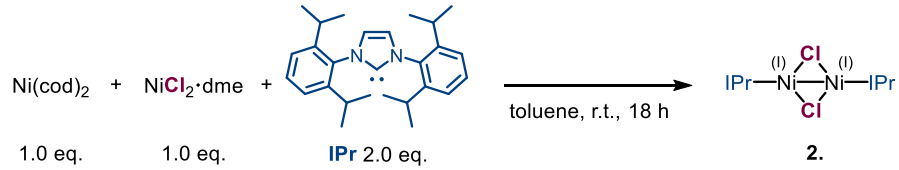


Synthesized following the procedure of Schoenebeck and co-workers.[9] Inside the *t*Bu$_3$P (510 mg, 2.52 mmol, 2.0 eq.) and Pd$_2$dba$_3$ (577 mg, 0.63 mmol, 0.5 eq.) were suspended in dry THF (15 mL) and it was stirred at room temperature for 2 h. Next, Pd$^{(II)}$iodide (454 mg, 1.26 mmol, 1.0 eq.) was added in one portion and the mixture was stirred for further 2 h. Then, dry acetone (~200 mL) was added and the resulting mixture was left to crystallize in the freezer (-30°C) overnight. Dark purple-green crystals of [Pd(μ-I)(P*t*Bu$_3$)]$_2$ **1** (0.78 g, 0.895 mmol, 71%) were collected by filtration inside the fume hood and washed with ice-cold acetone (~50 mL). **^{1}H NMR** (600 MHz, C_6D_5-CD_3) δ 1.31 (dd, *J* = 6.0, 6.0 Hz, 54H). **^{31}P NMR** (243 MHz, C_6D_5-CD_3) δ 102.2. Spectroscopic data match with those reported previously in the literature.[9]

Synthesis of IPr ligand

1,3-Bis-(2,6-di-isopropylphenyl)imidazolium tetrafluoroborate (IPrH·BF$_4$) was synthesized following the reported procedure by Briggs.[132] The free carbene 1,3-bis(2,6-di-isopropylphenyl)-1,3-dihydro-2*H*-imidazol-2-ylidene (IPr) was prepared according to the protocol developed by Nolan and co-workers.[133]

Synthesis of Ni$^{(I)}$ dimer [Ni(μ-Cl)(IPr)]2 (2)

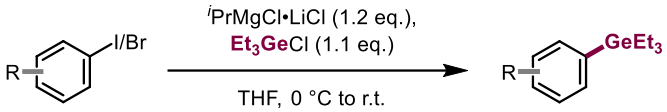


Synthesized following the procedure of Sigman and co-workers.[10] The following experimental procedure was carried out inside an Argon-filled glovebox. Air and moisture exclusion must be ensured at all times. Ni(dme)Cl$_2$ (279 mg, 1.27 mmol, 1.0 eq.), Ni(cod)$_2$ (349 mg, 1.27 mmol, 1.0 eq.) and IPr (987 mg, 2.54 mmol, 2.0 eq.) were suspended in toluene (20 mL). The resulting mixture was stirred at room temperature for exactly 18 h. The obtained red mixture was filtered through a small pad of dry Celite in a fritted funnel and the filtrate concentrated to 8 mL under reduced pressure. Pentane (32 mL) was added and the mixture was placed to the freezer at -30 °C overnight. The formed crystals were collected by filtration and washed with cold pentane (3 x 2 mL) to afford [Ni(μ-Cl)(IPr)]$_2$ **2** as greenish yellow crystals in 66% yield (807mg, 0.84 mmol). The crystals were stored inside the Glovebox in the freezer (-30 °C). **^{1}H NMR** (400 MHz, C_6D_6): δ 7.08-7.14 (m, 12H), 6.67 (s, 4H), 3.07-3.13 (sept, *J* = 6.6 Hz, 8H), 2.51 (d, *J* = 6.6 Hz, 24H), 1.16 (d, *J* = 6.6 Hz, 24H). Spectroscopic data match with those reported previously in the literature.[10] *Note: If the crystals contained red impurities a recrystallization was performed: The solid was dissolved in a minimum amount of dry toluene and four times the volume of pentane was added. The mixture was then cooled at -30 °C overnight and crystals were collected by filtration and washed with cold pentane (3 x 2 mL).*

5.2 Supporting information for chapter 2

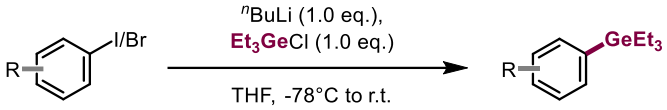
5.2.1 General experimental procedures

General procedure A (GP A): Synthesis of aryl germanes with *i*PrMgCl·LiCl



According to Fricke *et al.*[57] the appropriate aryl halide was weighed into an oven dried Schlenk flask and dissolved in dry THF (0.2 M). The solution was cooled to 0 °C and a solution of *i*PrMgCl·LiCl (1.0 eq., 1.3 M in THF) was added dropwise to the stirred solution. After the addition was complete, $GeEt_3Cl$ (1.0 eq.) was added and the reaction mixture stirred at ambient temperature. After full conversion was observed (monitored *via* GC-MS), saturated aq. NH_4Cl was added and the aqueous layer was extracted with DCM (3x). The combined organic layers were dried over Na_2SO_4 and evaporated under reduced pressure. The product was purified by column chromatography on silica gel.

General procedure B (GP B): Synthesis of aryl germanes with *n*BuLi



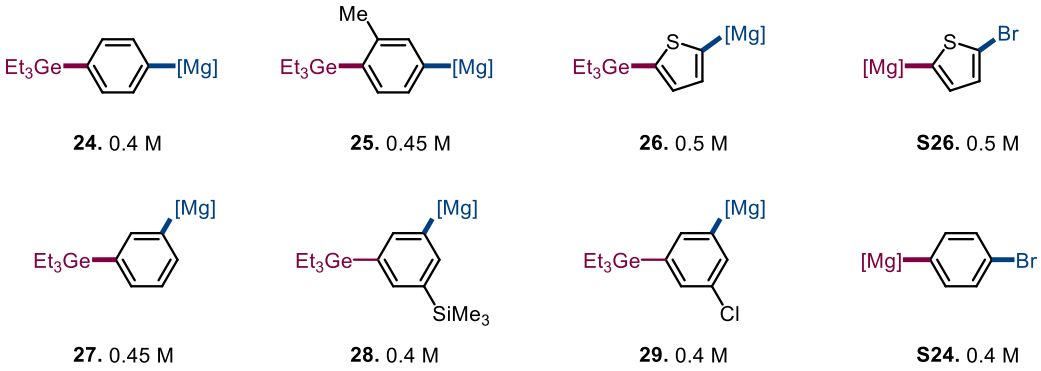
According to Fricke *et al.*[57] the appropriate aryl halide (1.0 eq.) was placed to an oven dried Schlenk flask and dissolved in THF (0.25 M). The solution was then cooled to -78 °C and *n*Buli (2.5 M in hexane, 1.0 eq.) was added dropwise stirred for 30 min at the same temperature. Et_3GeCl (1.0 eq.) was added and the reaction was stirred overnight, while warming up to ambient temperature. The reaction was quenched with saturated aq. NH_4Cl and the aqueous layer was extracted with DCM (3x). The combined organic layers were dried over Na_2SO_4 and concentrated under reduced pressure. The product was purified by column chromatography on silica gel.

General procedure C: Preparation of organomagnesium and -zinc reagents

- ***Organomagnesium Reagents***: In an oven dried flask magnesium powder (1.5 eq.) and dry LiCl (1.1 eq.; previously dried under high vacuum using a Bunsen burner and allowing to cool under high vacuum) were suspended in dry THF (1 M). A solution of aryl bromide or iodide in THF (1 M) was added and the mixture was stirred overnight. The obtained mixture was filtered through a syringe filter and stored at ambient temperature in the glovebox (no decomposition was observed for months). The organomagnesium reagents were titrated following Knochel's protocol.[134]
- ***Organozinc Reagents***: Solutions of $ZnCl_2$ (1M in THF, 1.1 eq.) and LiCl (0.5M in THF, 1.1 eq.; only added if a commercial organomagnesium reagent was employed) were added to a solution of aryl

magnesium halide (in THF, 1.0 eq.) in a 16 mL vial under argon atmosphere and stirred for 10 min. The organometallic species was then used without further analysis.

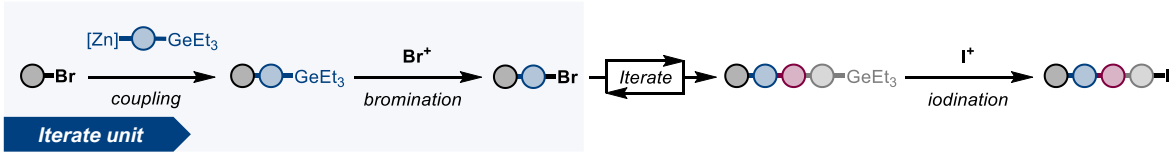
- ***$ZnCl_2$ solution***:[135] To an oven dried Schlenk tube equipped with a stir-bar was added anhydrous $ZnCl_2$ (1.36 g, 10 mmol) under argon atmosphere. Upon melting under high vacuum using a Bunsen burner, the tube was allowed to cool to room temperature and was then refilled with argon. Subsequently, anhydrous THF (10 mL) was added and the mixture was stirred vigorously until a clear solution resulted.



24. 0.4 M **25.** 0.45 M **26.** 0.5 M **S26.** 0.5 M

27. 0.45 M **28.** 0.4 M **29.** 0.4 M **S24.** 0.4 M

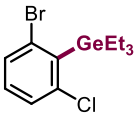
General Procedure D: Iterative cross-coupling



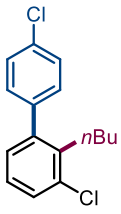
- ***Coupling***: The appropriate aryl bromide (1.0 eq., 1 mmol) and $[Pd(\mu\text{-}I)(P^tBu_3)]_2$ **1** (2.5 mol%) were placed into 25 mL round bottom flask. The flask was evacuated and backfilled with argon three times before dry toluene (0.2 M, 5 mL) was added. A freshly prepared solution of organozinc reagent (1.5 eq.) was added slowly to the reaction mixture via syringe pump over 15 min while the mixture was stirred gently. The reaction mixture was stirred for additional 5 min before the reaction was quenched with pentane or hexane and a spatula tip ammonium pyrrolidine-1-dithiocarboxilic acid was added to precipitate palladium.[60] The mixture was filtered through a plug of silica eluting with Et_2O, the filtrate was concentrated under reduced pressure.
- ***Bromination***: The crude aryl germane was dissolved in MeCN (0.2 M) or HFIP (0.2 M, for electron deficient or sterically hindered aryl germanes) and NBS (2.0 eq.) was added. The reaction was stirred at 60 °C for 1.5 hours. After that time, the mixture was allowed to cool to room temperature, filtered through a plug of silica gel, eluting with Et_2O. Volatiles were removed under reduced pressure and the crude material was purified by column chromatography on silica gel. *Note: For sequential coupling the C-C coupling and bromination steps were repeated, followed by a final iodination.*
- ***Iodination***: The crude obtained from cross-coupling was dissolved in HFIP (0.2 M) and NIS (2.0 eq.) was added. The reaction was stirred at 60 °C for 24 hours. After that time, the mixture was allowed to cool to room temperature, filtered through a plug of silica, concentrated under reduced pressure and the crude material was purified by column chromatography on silica gel.

5.2.2 Compound characterization data

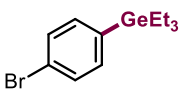
(2-bromo-6-chlorophenyl)triethylgermane (14): An oven dried round bottom flask equipped with a magnetic stirrer was evacuated and refilled with argon three times. Then, 2,2,6,6-tetramethylpiperidine (1.2 eq., 12 mmol, 2.05 mL) was added and it was dissolved in dry THF (0.2 M, 50 mL). The solution was cooled to 0 °C and a hexane solution of *n*butyllithium (1.0 eq., 2.4 M, 4.2 mL) was added dropwise. After 15 minutes of stirring the solution was cooled to -78 °C and a solution of 1-bromo-3-chlorobenzene (1.0 eq., 10 mmol, 1.2 mL) in THF (5 mL) was added dropwise. It was stirred for additional 20 minutes before Et_3GeCl (1.5 eq., 15 mmol, 2.5 mL) was added and the reaction mixture was allowed to warm up to room temperature overnight. The reaction was quenched with an excess of sat. aqueous NH_4Cl solution. The phases were separated and the aqueous phase was washed with DCM (2 x 50 mL). The combined organic phases were dried over Na2SO4 and concentrated under reduced pressure. The title product was obtained after purification by column chromatography (Pentane) as a colorless oil (3.10 g, 8.85 mmol, 89%). R_f (Hexane): 0.8. **^{1}H NMR** (600 MHz, CDCl3): δ 7.43 (dd, *J* = 7.9, 1.2 Hz, 1H), 7.27 (d, *J* = 7.9 Hz, 1H), 7.04 (dd, *J* = 7.9 Hz, 1H), 1.30 (q, *J* = 7.9 Hz, 6H), 1.08 (t, *J* = 7.9 Hz, 9H). **^{13}C NMR** (151 MHz, CDCl3): δ 142.4, 140.9, 132.0, 131.5, 130.5, 128.9, 9.3, 8.8. **HRMS** (APCI): m/z $[M-Et]^+$ calculated for $C_{10}H_{13}{}^{79}Br^{35}Cl$ 74Ge: 320.9096; found: 320.9089.



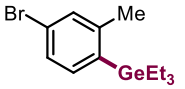
2-butyl-3,4'-dichloro-1,1'-biphenyl (17): Prepared, following coupling/bromination/coupling sequence according to general procedure D from (2-bromo-6-chlorophenyl)triethylgermane (**14**), 4-chlorophenylzinc chloride and *n*butylzinc chloride. Bromination of germanium was performed at 60 °C for 6 h. The title product was obtained after purification by column chromatography (hexane) as a colorless oil (96.0 mg, 0.344 mmol, 86%). R_f (Hexane): 0.5. **^{1}H NMR** (600 MHz, $CDCl_3$): δ 7.41 – 7.34 (m, 3H), 7.21 (d, *J* = 8.3 Hz, 2H), 7.14 (dd, *J* = 7.8 Hz, 1H), 7.05 (dd, J = 7.6, 1.3 Hz, 1H), 2.63 (m, 2H), 1.43 (tt, *J* = 7.9, 6.3 Hz, 2H), 1.22 (h, *J* = 7.4 Hz, 2H), 0.80 (t, *J* = 7.4 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$): δ 142.8, 140.0, 138.6, 135.0, 133.3, 130.5, 129.2, 128.6, 128.3, 126.5, 31.8, 30.6, 22.8, 13.8. **HRMS** (APCI): *m/z* $[M+H]^+$ calculated for $C_{16}H_{17}{}^{35}Cl_2$: 279.0702; found: 279.0691.



(4-Bromophenyl)triethylgermane (18): Prepared, following the general procedure A from 1-bromo-4-iodobenzene. The title product was obtained after purification by column chromatography (hexane) as a colorless oil (872.0 mg, 2.76 mmol, 97%). **^{1}H NMR** (600 MHz, $CDCl_3$): δ 7.47 (d, *J* = 8.1 Hz, 2H), 7.30 (d, *J* = 8.1 Hz, 2H), 1.07 – 1.02 (m, 9H), 1.01 – 0.95 (m, 6H). **^{13}C NMR** (151 MHz, $CDCl_3$): δ 138.7, 135.7, 131.1, 123.0, 9.0, 4.3. **HRMS** (EI): *m/z* $[M]^+$ calculated for $C_{12}H_{19}{}^{79}Br^{74}Ge$: 315.9876; found: 315.9882. The data are in agreement with those previously reported.[57]



(4-Bromo-2-methylphenyl)triethylgermane (19): Prepared, following the general procedure A from 5-bromo-2-iodotoluene. The title product was obtained after purification by column chromatography (hexane) as a colorless oil (1.09 g, 3.30 mmol, 66%). **^{1}H NMR** (600 MHz, $CDCl_3$): δ 7.32 (d, *J* = 1.9 Hz, 1H), 7.28 – 7.26 (m, 1H), 7.19 (d, *J* = 7.9 Hz, 1H), 2.37 (d, *J* = 0.6 Hz, 3H),



1.03 (s, 15H). **^{13}C NMR** (151 MHz, $CDCl_3$): δ 145.7, 137.2, 136.2, 132.5, 128.0, 123.1, 22.9, 9.1, 5.1. **HRMS** (APCI): *m/z* $[M\text{-}Et]^+$ calculated for $C_{11}H_{16}{}^{79}Br^{74}Ge$: 300.9642; found: 300.9641.

(5-Bromothiophen-2-yl)triethylgermane (20): Prepared, following the general procedure B from 2,5-dibromothiophene. The title product was obtained after purification by column chromatography (hexane) as a colorless oil (1.45 g, 4.51 mmol, 90%). **^{1}H NMR** (600 MHz, $CDCl_3$): δ 7.10 (d, *J* = 3.5 Hz, 1H), 6.90 (d, *J* = 3.5 Hz, 1H), 1.10 – 1.06 (m, 9H), 1.03 – 0.98 (m, 6H). **^{13}C NMR** (151 MHz, $CDCl_3$): δ 140.8, 134.0, 131.0, 115.6, 8.9, 5.6. **HRMS** (APCI): *m/z* $[M+H]^+$ calculated for $C_{10}H_{18}{}^{79}Br^{74}GeS$: 322.9519; found: 322.9517.

(3-Bromophenyl)triethylgermane (21): Prepared, following the general procedure A from 1-bromo-3-iodobenzene. The title product was obtained after purification by column chromatography (pentane) as a colorless oil (4.23 g, 13.4 mmol, 89%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.53 (dd, *J* = 2.2, 1.0 Hz, 1H), 7.44 (ddd, *J* = 7.9, 2.1, 1.2 Hz, 1H), 7.34 (ddd, *J* = 7.2, 1.1 Hz, 1H), 7.20 (dd, *J* = 7.6 Hz, 1H), 1.08 – 1.04 (m, 9H), 1.02 – 0.98 (m, 6H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 143.3, 136.5, 132.4, 132.2, 129.7, 123.1, 9.0, 4.3. The data are in agreement with those previously reported.[57]

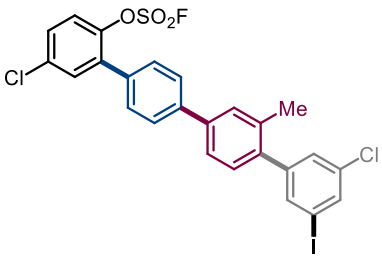
(3-Bromo-5-(triethylgermyl)phenyl)trimethylsilane (22): Prepared, following the general procedure B from 3,5-dibromo-1-trimethylsilylbenzene. The title product was obtained after purification by column chromatography (hexane) as a colorless oil (163.0 mg, 0.42 mmol, 84%). **^{1}H NMR** (600 MHz, $CDCl_3$): δ 7.55 – 7.54 (m, 1H), 7.51 – 7.50 (m, 1H), 7.44 – 7.43 (m, 1H), 1.07 – 1.05 (m, 9H), 1.02 – 0.96 (m, 6H), 0.26 (s, 9H). **^{13}C NMR** (151 MHz, $CDCl_3$): δ 143.1, 142.6, 137.1, 136.8, 135.7, 123.6, 9.0, 4.4, -1.1. **HRMS** (EI): *m/z* $[M]^+$ calcd for $C_{15}H_{27}{}^{79}Br^{74}GeSi$: 388.0272; found: 388.0261. The data are in agreement with those previously reported.[47]

(3-Bromo-5-chlorophenyl)triethylgermane (23): Prepared, following the general procedure A from 1-bromo-3-chloro-5-iodobenzene. The title product was obtained after purification by column chromatography (pentane) as a colorless oil (4.41 g, 12.6 mmol, 84%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.46 (dd, *J* = 1.9, 1.9 Hz, 1H), 7.39 (dd, *J* = 1.8, 0.8 Hz, 1H), 7.29 (dd, *J* = 2.0, 0.8 Hz, 1H), 1.08 – 0.96 (m, 15H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 145.2, 135.0, 134.6, 132.3, 131.0, 123.1, 8.9, 4.4. **HRMS** (APCI): *m/z* $[M\text{-}Et]^+$ calculated for $C_{10}H_{13}{}^{35}Cl^{79}Br^{74}Ge$: 320.9095, found 320.9093.

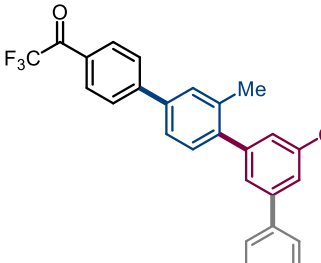
(3-(5-(3',5'-dichloro-[1,1'-biphenyl]-4-yl)thiophen-2-yl)-5-iodophenyl)trimethylsilane (33): Prepared, following the general procedure D. The title product was obtained after purification by column chromatography (20:1 pentane:DCM) as a white solid (244 mg, 0.421 mmol, 42%). **R_f** = 0.2 (20:1 pentane:DCM). **M.p.**: 55–64 °C. **^{1}H NMR** (600 MHz, $CDCl_3$): δ 7.96 (dd, *J* = 1.7 Hz, 1H), 7.74 – 7.70 (m, 3H), 7.68 (dd, *J* = 1.7, 0.9 Hz, 1H), 7.57 (d, *J* = 8.4 Hz, 2H), 7.49 (d, *J* = 1.8 Hz, 2H), 7.37 – 7.34 (m, 2H), 7.30 (d, *J* = 3.8 Hz, 1H), 0.32 (s, 9H). **^{13}C NMR** (151 MHz, $CDCl_3$): δ 144.8, 143.5, 142.6,

141.1, 137.7, 135.7, 135.5, 134.8, 134.4, 129.6, 127.7, 127.4, 126.3, 125.5, 125.0, 124.6, 96.0, -1.1. **HRMS** (APCI): *m/z* $[M+H]^+$ calculated for $C_{25}H_{22}{}^{35}Cl_2SSiI$: 578.9628, found 578.9629.

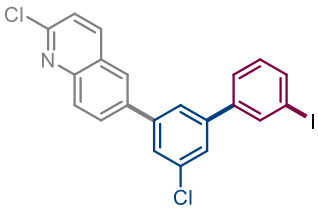
3‴,5-dichloro-5‴-iodo-3″-methyl-[1,1′:4′,1″:4″,1‴-quaterphenyl]-2-yl fluorosulfate (34): Prepared, following the general procedure D. The title product was obtained after purification by column chromatography (10:1 hexane:EtOAc) and precipitation as a white solid (324 mg, 0.501 mmol, 50%). R_f = 0.5 (10:1 hexane:EtOAc). **M.p.**: 55–59 °C. **^{1}H NMR** (600 MHz, $CDCl_3$): δ 7.75 – 7.72 (m, 3H), 7.62 (d, *J* = 1.6 Hz, 1H), 7.57 – 7.54 (m, 4H), 7.52 (dd, *J* = 7.7, 1.8 Hz, 1H), 7.44 (d, *J* = 2.4 Hz, 2H), 7.34 (dd, *J* = 1.7 Hz, 1H), 7.28 (d, *J* = 7.8 Hz, 1H), 2.36 (s, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$): δ 145.5, 144.8, 141.0, 140.0, 138.5, 136.4, 136.4, 135.8, 135.5, 134.7, 134.6, 133.4, 131.8, 130.1, 129.4, 129.3, 129.1, 128.8, 127.5, 124.7, 123.0, 93.8, 20.5. **^{19}F NMR** (564 MHz, $CDCl_3$): δ 40.64 (s, 3F). **HRMS** (ACPI): *m/z* $[M+H]^+$ calculated for $C_{25}H_{18}O_3{}^{35}ClFSI$: 612.9299, found 612.9301.



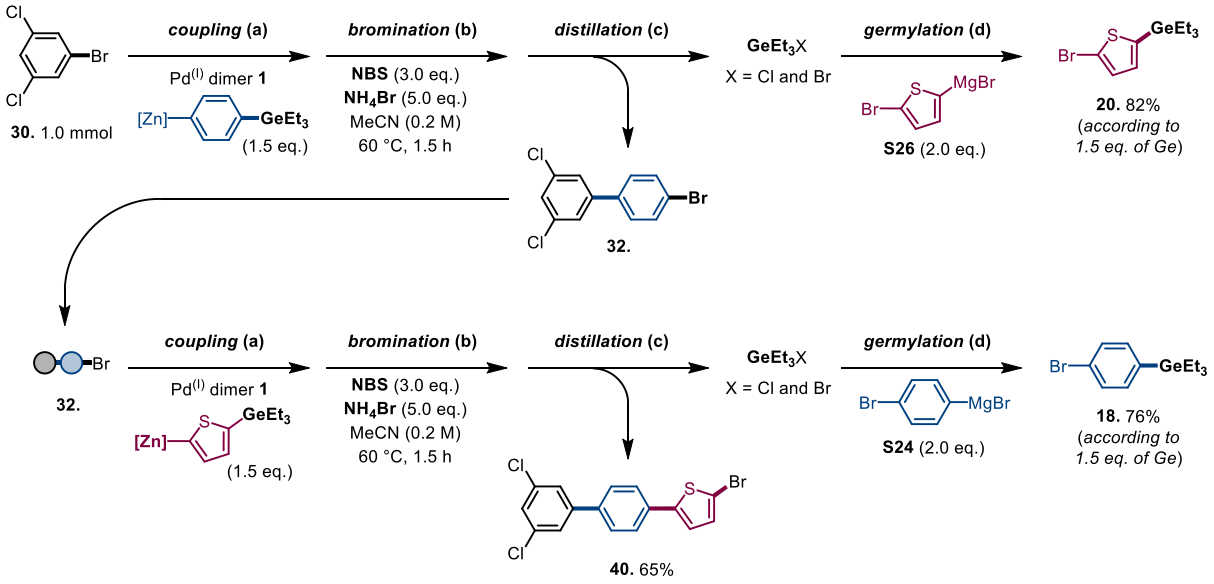
1-(5′-chloro-3-iodo-2″-methyl-[1,1′:3′,1″:4″,1‴-quaterphenyl]-4‴-yl)-2,2,2-trifluoroethan-1-one (35): Prepared, following the general procedure D. The title product was obtained after purification by column chromatography (4:1 pentane:DCM) and precipitation (dropwise addition of MeOH to a DCM solution of the product) as a white solid (277 mg, 0.480 mmol, 48%). R_f = 0.6 (4:1 pentane:DCM). **M.p.**: 92–96 °C. **^{1}H NMR** (600 MHz, $CDCl_3$): δ 8.18 (d, *J* = 8.0 Hz, 2H), 7.95 (s, 1H), 7.82 (d, *J* = 8.4 Hz, 2H), 7.73 (d, *J* = 7.8 Hz, 1H), 7.59 – 7.55 (m, 4H), 7.41 (d, *J* = 1.7 Hz, 1H), 7.38 (d, *J* = 7.9 Hz, 1H), 7.36 (d, *J* = 1.8 Hz, 1H), 7.20 (dd, *J* = 7.8 Hz, 1H), 2.40 (s, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$): δ 180.22 (q, *J* = 35.0 Hz), 147.8, 143.6, 141.9, 141.5, 141.1, 138.9, 137.1, 136.4, 136.3, 134.8, 130.9 (d, *J* = 1.9 Hz), 130.7, 130.6, 129.6, 128.8, 128.5, 127.7, 126.6, 126.3, 126.1, 125.1, 116.9 (q, *J* = 291.8, 291.4 Hz), 95.0, 20.8. **^{19}F NMR** (565 MHz, $CDCl_3$): δ -71.30 (s, 3F). **HRMS** (APCI): *m/z* $[M+H]^+$ calculated for $C_{27}H_{18}O^{35}ClF_3I$: 577.0038, found 577.0041.



2-chloro-6-(5-chloro-3′-iodo-[1,1′-biphenyl]-3-yl)quinoline (36): Prepared, following the general procedure D. The title product was obtained after purification by column chromatography (1:2 pentane:DCM) as a white solid (178 mg, 0.374 mmol, 75%). R_f = 0.3 (1:2 pentane:DCM). **M.p.**: 155–160 °C. **^{1}H NMR** (600 MHz, $CDCl_3$): δ 8.13 (d, *J* = 8.5 Hz, 1H), 8.09 (d, *J* = 8.7 Hz, 1H), 7.95 (m, 3H), 7.72 (ddd, *J* = 7.9, 1.7, 1.0 Hz, 1H), 7.65 (dd, *J* = 1.6, 1.6 Hz, 1H), 7.62 (dd, *J* = 1.8, 1.8 Hz, 1H), 7.55 (ddd, *J* = 7.8, 1.8, 1.0 Hz, 1H), 7.51 (dd, *J* = 1.8, 1.8 Hz, 1H), 7.41 (d, *J* = 8.5 Hz, 1H), 7.19 (dd, *J* = 7.8, 7.8 Hz, 1H). **^{13}C NMR** (151 MHz, $CDCl_3$): 151.1, 147.5, 142.2, 142.1, 141.7, 139.1, 138.1, 137.1, 136.1, 135.5, 130.7, 129.9, 129.4, 127.0, 126.8, 126.6, 126.5, 125.7, 124.5, 123.1, 95.0. **HRMS** (ESI): *m/z* $[M+H]^+$ calculated for $C_{21}H_{13}N^{35}Cl_2I$: 475.9464; found: 475.9458.



5.2.3 Recycling of germanium masking group



- *Coupling* (a): The coupling was performed according to general procedure D.
- *Bromination* (b): The aryl germane obtained after cross-coupling was dissolved in MeCN (0.2 M). Subsequently, NBS (3.0 eq.) and NH_4Br (5.0 eq.) were added. The reaction was stirred at 60 °C for 1.5 hours. After that time, the mixture was allowed to cool to room temperature, filtered through a plug of silica gel, washed with Et_2O and concentrated under reduced pressure.

Note: During the reaction Et_3GeCl and Et_3GeBr are formed, both are volatile, and one must make sure that the pressure is higher than 200 mbar and that the temperature remains below 40 °C.

- *Distillation* (c)*:* The obtained crude mixture was subjected to Kugelrohr distillation (70 °C, 10 mbar, 2 hours, ice bath cooling). The distilled fractions were combined yielding a mixture of Et_3GeCl and Et_3GeBr, while the remainder of the distillation (*i.e.* the halogenated arene) was purified by column chromatography (pentane) and directly used for further coupling.
- *Germylation* (d)*:* The obtained distillate (mixture of Et_3GeCl and Et_3GeBr) was placed into a 25 mL round bottom flask equipped with a magnetic stir bar. The flask was closed with a septum and gently purged with argon for 2 min. Subsequently, THF (1 M) was added followed by the appropriate organomagnesium reagent (**S26** or **S24**, 2.0 eq. with regard to [Ge]). After stirring overnight saturated aq. NH_4Cl (5 mL) was added and the aqueous phase was washed with DCM (3x 10 mL). The combined organic phases were dried over Na_2SO_4 and concentrated under reduced pressure. The aryl germanes (5-bromothiophen-2-yl)triethylgermane (**20**) and (4-bromophenyl)triethylgermane (**18**) were obtained after purification by column chromatography (pentane) as colorless oils in 82% (**20**) and 76% (**18**) yield (based on employed [Ge]), respectively. Characterization data match those of the independently synthesized compounds.

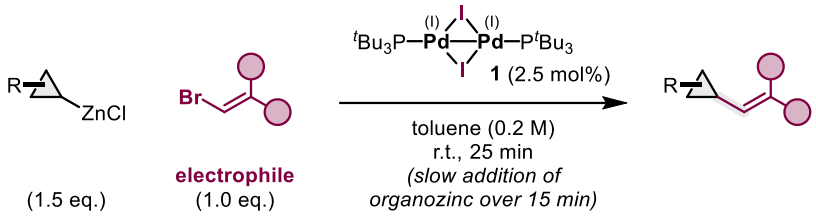
2-bromo-5-(3',5'-dichloro-[1,1'-biphenyl]-4-yl)thiophene (40): The title product was obtained after purification by column chromatography (hexane) as a pale yellow solid (248 mg, 0.645 mmol, 65%). **M.p.**: 128–131 °C. **^{1}H NMR** (600 MHz, $CDCl_3$): δ 7.62 – 7.56 (m, 2H), 7.56 – 7.53 (m, 2H), 7.47 (d, *J* = 1.8 Hz, 2H), 7.35 (dd, *J* = 1.9, 1.9 Hz, 1H), 7.11 (d, *J* = 3.8 Hz, 1H), 7.06 (d, *J* = 3.9 Hz, 1H). **^{13}C NMR** (151 MHz, $CDCl_3$): δ 145.0, 143.4,

137.9, 135.5, 133.9, 131.1, 127.7, 127.5, 126.2, 125.5, 123.8, 112.2. **HRMS** (APCI): *m/z* $[M+H]^+$ calculated for $C_{16}H_{10}{}^{35}Cl_2SBr$: 383.8956, found: 383.8956.

5.3 Supporting information for chapter 3

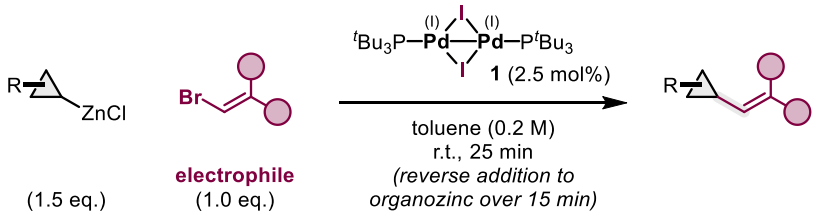
5.3.1 $Pd^{(I)}$ cross coupling

General procedure A (standard conditions)



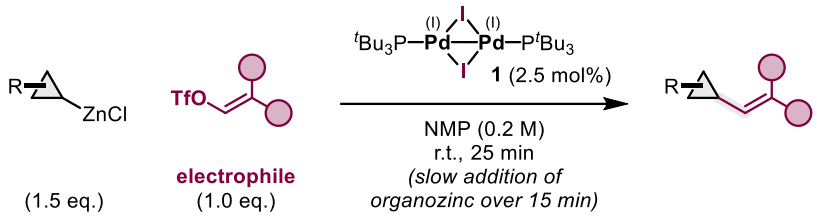
In an argon filled glovebox, vinyl halide (1.0 eq.) was placed into an oven dried 20 mL screw top vial (or an oven dried round bottom flask in case of scale up) equipped with a magnetic stir bar. It was dissolved in dry toluene (0.2 M) and $Pd^{(I)}$-iodo-dimer **1** (2.5 mol%) was added. The vial was sealed with a rubber septum, brought outside and connected to a Schlenk line. Then, a previously prepared solution of cyclopropyl organozincate (1.2–2.0 eq.) was added slowly to the reaction mixture via syringe pump (over 15 min). The reaction mixture was stirred for additional 10 min, before it was quenched by the addition of wet pentane or hexane. A spatula tip of ammonium pyrrolidine-1-dithiocarboxilic acid was added and the mixture stirred for additional 5 min to precipitate palladium.[60] The mixture was filtered through a plug of silica, washing with Et_2O and the filtrate was concentrated under reduced pressure. The crude material was further purified by silica gel column chromatography.

General procedure B (reverse addition)



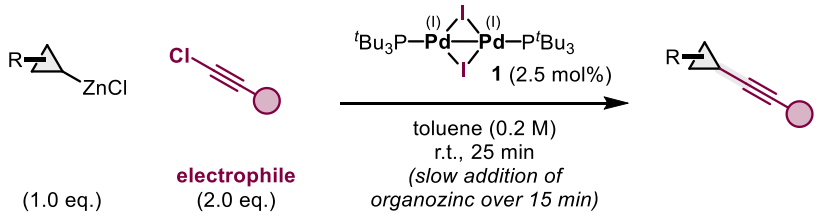
In an argon filled glovebox, a previously prepared solution of organozinc (1.2–2.0 eq.) was placed into an oven dried 20 mL screw top vial (or an oven dried round bottom flask in case of scale up) equipped with a magnetic stir bar. The vial was sealed with a rubber septum, brought outside and connected to a Schlenk line. Then, vinyl halide (1.0 eq.) was dissolved in dry toluene (0.2 M) and $Pd^{(I)}$-iodo-dimer **1** (2.5 mol%) was added. The obtained mixture was added slowly to the cyclopropyl organozincate solution via syringe pump (over 15 min). The reaction mixture was stirred for additional 10 min, before it was quenched by the addition of wet pentane or hexane. A spatula tip of ammonium pyrrolidine-1-dithiocarboxilic acid was added and the mixture stirred for additional 5 min to precipitate palladium.[60] The mixture was filtered through a plug of silica, washing with Et_2O and the filtrate was concentrated under reduced pressure. The crude material was further purified by silica gel column chromatography.

General procedure C (for vinyl pseudohalides)



In an argon filled glovebox, vinyl pseudohalide (1.0 eq.) was placed into an oven dried 20 mL screw top vial (or an oven dried round bottom flask in case of scale up) equipped with a magnetic stir bar. It was dissolved in dry NMP (0.2 M) and $Pd^{(I)}$-iodo-dimer **1** (2.5 mol%) was added. The vial was sealed with a rubber septum, brought outside and connected to a Schlenk line. Then, a previously prepared solution of cyclopropyl organozincate (1.2–2.0 eq.) was added slowly to the reaction mixture via syringe pump (over 15 min). The reaction mixture was stirred for additional 10 min, before it was quenched by the addition of wet pentane or hexane. A spatula tip of ammonium pyrrolidine-1-dithiocarboxilic acid was added and the mixture stirred for additional 5 min to precipitate palladium.[60] The mixture was filtered through a plug of silica, washing with Et_2O and the filtrate was concentrated under reduced pressure. The crude material was further purified by silica gel column chromatography.

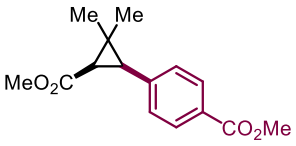
General procedure D (for alkynyl chlorides)



In an argon filled glovebox, alkynyl chloride (2.0 eq.) was placed into an oven dried 20 mL screw top vial equipped with a magnetic stir bar. It was dissolved in dry toluene (0.2 M) and $Pd^{(I)}$-iodo-dimer **1** (2.5 mol%) was added. The vial was sealed with a rubber septum, brought outside and connected to a Schlenk line. Then, a previously prepared solution of cyclopropyl organozincate (1.0 eq.) was added slowly to the reaction mixture via syringe pump (over 15 min). The reaction mixture was stirred for additional 10 min, before it was quenched by the addition of wet pentane or hexane. A spatula tip of ammonium pyrrolidine-1-dithiocarboxilic acid was added and the mixture stirred for additional 5 min to precipitate palladium.[60] The mixture was filtered through a plug of silica, washing with Et_2O and the filtrate was concentrated under reduced pressure. The crude material was further purified by silica gel column chromatography.

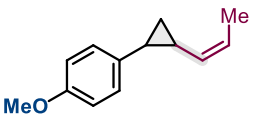
Compound characterization data

Methyl 4-(*cis*-3-(methoxycarbonyl)-2,2-dimethylcyclopropyl)benzoate (43): Following general procedure A using methyl 4-bromobenzoate (86 mg, 0.4 mmol, 1.0 eq.) and a suspension of freshly prepared **2** (0.6 mmol, 1.5 eq.). Flash column chromatography (20:1 hexane:Et_2O) afforded **3** as a colorless oil (97 mg, 0.37 mmol, 92%). R_f = 0.41



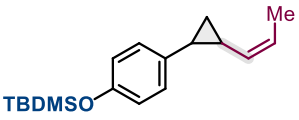
(8:2 pentane:Et_2O). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.95 (d, *J* = 8.0 Hz, 2H), 7.19 (d, *J* = 8.2 Hz, 2H), 3.89 (s, 3H), 3.60 (s, 3H), 2.46 (d, *J* = 9.1 Hz, 1H), 1.93 (d, *J* = 9.1 Hz, 1H), 1.36 (s, 3H), 1.27 (s, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 171.0, 167.2, 141.4, 130.4, 129.3, 128.4, 52.1, 51.4, 36.7, 30.7, 29.2, 26.6, 16.5. **MS** (70eV, EI): *m/z* (%): 262 (5) [M^+], 231 (16), 203 (100), 187 (13), 171 (28), 143 (37), 129 (47). **MS** (70eV, EI): *m/z* (%): 262 (5) [M^+], 231 (17), 203 (100), 202 (14), 143 (35), 129 (44), 128 (43), 115 (15), 105 (10), 91 (9), 59 (18).

(*Z*)-1-methoxy-4-(2-(prop-1-en-1-yl)cyclopropyl)benzene (50): Following general procedure A using (*Z*)-1-



bromoprop-1-ene (122 mg, 1.0 mmol, 1.0 eq.) and a suspension of freshly prepared (2-(4-methoxyphenyl)cyclopropyl)zinc(II) chloride (1.2 mmol, 1.2 eq.). Flash column chromatography (50:1 hexane:EtOAc) afforded the title product as a diastereomeric mixture as a colorless oil (163 mg, 0.87 mmol, 87%, 65:35 *cis*/*trans* (^{1}H NMR)). **R_f** = 0.18 (50:1 hexane:EtOAc). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.12 – 7.10 (m, 2H, *cis-isomer*), 7.05 – 7.00 (m, 2H, *trans-isomer*), 6.85 – 6.79 (m, 4H, *cis*+*trans-isomer*), 5.44 (dqd, *J* = 10.7, 6.7, 0.9 Hz, 1H, *trans-isomer*), 5.37 (dqd, *J* = 10.8, 6.8, 1.1 Hz, 1H, *cis-isomer*), 4.95 (ddq, *J* = 11.0, 9.4, 1.7 Hz, 1H, *trans-isomer*), 4.66 (ddq, *J* = 11.2, 9.6, 1.8 Hz, 1H, *cis-isomer*), 3.79 (s, 6H, *cis*+*trans-isomer*), 2.28 (td, *J* = 8.6, 6.2 Hz, 1H, *cis-isomer*), 2.00 – 1.89 (m, 1H, *cis-isomer*), 1.84 (dt, *J* = 9.3, 5.0 Hz, 1H, *trans-isomer*), 1.76 (dddd, *J* = 9.6, 8.6, 5.4, 1.1 Hz, 1H, *trans-isomer*), 1.73 – 1.71 (m, 6H, *cis*+*trans-isomer*), 1.26 (td, *J* = 8.4, 4.9 Hz, 1H, *cis-isomer*), 1.15 (ddd, *J* = 8.5, 5.6, 4.8 Hz, 1H, *trans-isomer*), 0.95 (dt, *J* = 8.6, 5.1 Hz, 1H, *trans-isomer*), 0.86 (q, *J* = 5.5 Hz, 1H, *cis-isomer*). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 157.9, 157.9, 134.8, 133.4, 131.2, 130.2, 123.0, 127.0, 124.1, 123.1, 114.0, 113.6, 55.5, 55.4, 24.5, 22.3, 22.0, 17.0, 16.8, 13.4, 13.3, 12.5. **HRMS** (ESI): *m/z* $[M]^+$ calculated for $C_{13}H_{17}O$: 189.1274, found 189.1269.

(*Z*)-*tert*-butyldimethyl(4-(2-(prop-1-en-1-yl)cyclopropyl)phenoxy)silane (51): Following general procedure A



using (*Z*)-1-bromoprop-1-ene (48 mg, 0.4 mmol) and a suspension of freshly prepared (2-(4-((tert-butyldimethylsilyl)oxy)phenyl)cyclopropyl)zinc(II) chloride (0.6 mmol). Flash column chromatography (pentane) afforded the title product as a diastereomeric mixture as colorless oil (111 mg, 0.38 mmol, 96%, 58:42 *cis*/*trans* (^{1}H NMR)). **R_f** = 0.24 (pentane). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.04 (d, *J* = 8.3 Hz, 2H, *cis-isomer*), 6.94 (dd, *J* = 8.0 Hz, 2H, *trans-isomer*), 6.77 – 6.70 (m, 4H, *cis-* + *trans-isomer*), 5.43 (dq, *J* = 10.6, 6.8 Hz, 1H, *trans-isomer*), 5.36 (dq, J = 10.6, 6.5 Hz, 1H, *cis-isomer*), 4.95 (ddd, *J* = 10.9, 9.2, 1.9 Hz, 1H, *trans-isomer*), 4.66 (ddd, *J* = 11.1, 9.4, 1.8 Hz, 1H, *cis-isomer*), 2.27 (td, *J* = 8.5, 6.3 Hz, 1H, *cis-isomer*), 1.93 (qd, *J* = 8.9, 5.5 Hz, 1H, *trans-isomer*), 1.83 (td, *J* = 10.0, 8.8, 6.7 Hz, 1H, *trans-isomer*), 1.77 (td, *J* = 9.0, 4.6 Hz, 1H, *cis-isomer*), 1.75 – 1.69 (m, 6H, *cis-* + *trans-isomer*), 1.24 (td, *J* = 8.5, 4.9 Hz, 1H, *cis-isomer*), 1.14 (dt, *J* = 8.6, 5.2 Hz, 1H, *trans-isomer*), 0.98 (s, 18H, *cis-* + *trans-isomer*), 0.91 – 0.87 (m, 1H, *trans-isomer*), 0.85 (q, *J* = 5.6 Hz, 1H, *cis-isomer*), 0.18 (s, 12H, *cis-* + *trans-isomer*). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 153.8, 153.7, 135.3, 133.4, 131.8, 130.2, 130.1, 130.0, 126.8, 124.1, 123.0, 120.0, 119.7, 25.9, 25.9, 24.6, 22.4, 22.0, 18.4, 18.3, 17.0, 17.0, 13.4, 13.3, 12.5, -4.3. **HRMS** (EI): *m/z* $[M]^+$ calculated for $C_{18}H_{28}OSi$: 288.1904, found 288.1903.

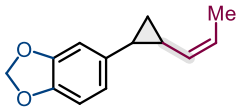
(*Z*)-1-fluoro-4-(2-(prop-1-en-1-yl)cyclopropyl)benzene (52): Following general procedure A using (*Z*)-1-bromoprop-1-ene (363 mg, 3.0 mmol) and a suspension of freshly prepared (2-(4-fluorophenyl)cyclopropyl)zinc(II) chloride (3.6 mmol). Flash column chromatography (pentane) afforded the title product as a diastereomeric mixture as colorless oil (514 mg, 2.92 mmol, 97%, 65:35 *cis*/*trans* (^{19}F NMR)). **R_f** = 0.88 (pentane). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.18 – 7.12 (m, 2H, *cis-isomer*), 7.07 – 7.02 (m, 2H, *trans-isomer*), 6.99 – 6.93 (m, 2H, , *cis-* + *trans-isomer*), 5.51 – 5.42 (m, 1H, *trans-isomer*), 5.44 – 5.35 (m, 1H, *cis-isomer*), 4.96 (ddt, *J* = 10.9, 9.2, 1.7 Hz, 1H, *trans-isomer*), 4.64 (ddt, *J* = 11.1, 9.4, 1.8 Hz, 1H, *cis-isomer*), 2.30 (q, *J* = 8.1 Hz, 1H, *cis-isomer*), 2.03 – 1.93 (m, 1H, *cis-isomer*), 1.87 (dt, *J* = 9.2, 4.8 Hz, 1H, *trans-isomer*), 1.79 (tt, *J* = 9.4, 5.1 Hz, 1H, *trans-isomer*), 1.73 (d, *J* = 6.8 Hz, 3H, *cis-* + *trans-isomer*), 1.30 (tdd, *J* = 8.5, 5.1, 1.2 Hz, 1H, *cis-isomer*), 1.24 – 1.14 (m, 1H, *trans-isomer*), 1.07 – 0.97 (m, 1H, *trans-isomer*), 0.89 (q, *J* = 5.6, 5.1 Hz, 1H, *cis-isomer*). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 161.4 (d, *J* = 243.6 Hz, *cis*), 161.3 (d, *J* = 243.0 Hz, *trans*), 138.4 (d, *J* = 3.1 Hz, *trans*), 134.8 (d, *J* = 3.1 Hz, *cis*), 133.0 (*trans*), 130.7 (d, *J* = 7.9 Hz, *cis*), 129.5 (*cis*), 127.3 (d, *J* = 7.8 Hz, *trans*), 124.7 (*cis*), 123.5 (*trans*), 115.2 (d, *J* = 21.2 Hz, *trans*), 114.9 (d, *J* = 21.2 Hz, *cis*), 24.5 (*trans*), 22.3 (*cis* + *trans*), 17.1 (*trans*), 17.1 (*cis*), 13.4 (*trans*), 13.3 (*cis*), 12.7 (*cis*). **^{19}F NMR** (565 MHz, $CDCl_3$) δ -117.52 (m, 1F, *cis-isomer*), -117.99 (m, 1F, *trans-isomer*). **HRMS** (EI): *m/z* $[M]^+$ calculated for $C_{12}H_{13}F$: 176.0996, found 176.0987.

1-(*cis*-2-((*Z*)-prop-1-en-1-yl)cyclopropyl)-4-(trifluoromethyl)benzene (53): Following general procedure A using (*Z*)-1-bromoprop-1-ene (24 mg, 0.2 mmol) and a suspension of freshly prepared (*cis*-2-(4-(trifluoromethyl)phenyl)cyclopropyl)zinc(II) chloride (0.38 mmol). Flash column chromatography (hexane) afforded the title product as a colorless oil (44 mg, 0.14 mmol, 72%). **R_f** = 0.57 (hexane). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.51 (d, *J* = 8.1 Hz, 2H), 7.28 (d, *J* = 8.5 Hz, 2H), 5.41 (dqd, *J* = 10.8, 6.8, 1.2 Hz, 1H), 4.66 (ddd, *J* = 11.0, 9.3, 1.8 Hz, 1H), 2.37 (td, *J* = 8.6, 6.4 Hz, 1H), 2.06 (qdd, *J* = 9.1, 5.8, 1.2 Hz, 1H), 1.71 (dd, *J* = 6.8, 1.8 Hz, 3H), 1.36 (td, *J* = 8.4, 5.2 Hz, 1H), 0.99 (q, *J* = 5.8 Hz, 1H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 143.7 (m), 129.3, 128.7, 128.1 (q, *J* = 32.2 Hz), 125.5, 125.0 (q, *J* = 3.9 Hz), 124.7 (q, *J* = 271.7 Hz), 23.0, 17.9, 13.4, 12.9. **^{19}F NMR** (564 MHz, $CDCl_3$) δ -62.29. **HRMS** (EI): *m/z* $[M]^+$ calculated for $C_{13}H_{13}F_3$: 226.0964, found 226.0967.

4,4,5,5-tetramethyl-2-(4-(*cis*-2-((*Z*)-prop-1-en-1-yl)cyclopropyl)phenyl)-1,3,2-dioxaborolane (54): Following general procedure A using (*Z*)-1-bromoprop-1-ene (25 mg, 0.2 mmol) and a suspension of freshly prepared (*cis*-2-(4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)cyclopropyl)zinc(II) chloride (0.3 mmol, *3.0 eq. ^{t}BuLi were used for the preparation of organozincate due to formation of the corresponding boronate complex, no subsequent titration was performed*). Flash column chromatography (30:1 pentane:Et_2O) afforded the title product as a colorless oil (40 mg, 0.14 mmol, 70%). **R_f** = 0.25 (30:1 pentane:Et_2O). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.24 (d, *J* = 8.2 Hz, 2H), 7.15 (d, *J* = 8.2 Hz, 2H), 6.39 (dq, *J* = 11.6, 2.0 Hz, 1H), 5.72 (dq, *J* = 11.5, 7.2 Hz, 1H), 2.34 (ddd, *J* = 10.3, 7.9, 6.0 Hz, 1H), 1.86 (dd, *J* = 7.1, 1.9 Hz, 3H), 1.28 (ddd, *J* = 7.2, 6.0, 4.2 Hz, 1H), 1.10 (ddd, *J* = 9.2, 7.9, 4.2 Hz, 1H), 1.02 (s, 6H),

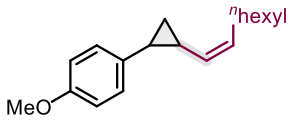
0.90 (s, 6H), 0.44 (ddd, *J* = 10.2, 9.3, 7.2 Hz, 1H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 139.2, 135.2, 130.0, 128.6, 128.3, 126.0, 83.1, 25.0, 24.5, 21.7, 14.7, 9.1. **^{11}B NMR** (192 MHz, $CDCl_3$) δ 32.00 (bs, 1B). **HRMS** (EI): *m/z* $[M]^+$ calculated for $C_{18}H_{25}O_2B$: 284.1942, found 284.1941.

(*Z*)-5-(2-(prop-1-en-1-yl)cyclopropyl)benzo[d][1,3]dioxole (55): Following general procedure A using (*Z*)-1-



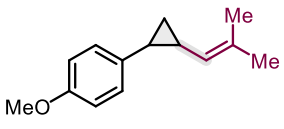
bromoprop-1-ene (605 mg, 5.0 mmol, 1.0 eq.) and a suspension of freshly prepared (2-(benzo[*d*][1,3]dioxol-5-yl)cyclopropyl)zinc(II) chloride (6.0 mmol, 1.2 eq.). Flash column chromatography (heptane) afforded the title product as a diastereomeric mixture as a colorless oil (950 mg, 4.70 mmol, 94%, 52:48 *cis*/*trans* (^{1}H NMR)). **R_f** = 0.19 (heptane). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 6.72 (dd, *J* = 8.0, 2.6 Hz, 1H, *cis*- + *trans-isomer*), 6.71 – 6.65 (m, 1H, *cis*- + *trans-isomer*), 6.60 (dd, *J* = 8.0, 1.7 Hz, 1H, *cis*- or *trans-isomer*), 6.57 (d, *J* = 1.8 Hz, 1H, *trans*- or *cis-isomer*), 5.92 (d, *J* = 3.0 Hz, 2H, *cis*- + *trans-isomer*), 5.45 (dq, *J* = 10.7, 7.0 Hz, 1H, *trans-isomer*), 5.39 (dq, *J* = 10.5, 6.9 Hz, 1H, *cis-isomer*), 4.98 – 4.91 (m, 1H, *trans-isomer*), 4.72 – 4.65 (m, 1H, *cis-isomer*), 2.31 – 2.23 (m, 1H, *cis-isomer*), 1.94 (qd, *J* = 8.9, 5.5 Hz, 1H, *cis-isomer*), 1.83 (dt, *J* = 9.3, 5.0 Hz, 1H, *trans-isomer*), 1.76 (dt, *J* = 9.4, 4.9 Hz, 1H, *trans-isomer*), 1.73 (d, *J* = 6.8 Hz, 3H, *cis*- + *trans-isomer*), 1.25 (td, *J* = 8.4, 4.9 Hz, 1H, *cis-isomer*), 1.14 (dt, *J* = 8.5, 5.2 Hz, 1H, *trans-isomer*), 0.95 (dt, *J* = 8.6, 5.2 Hz, 1H, *trans-isomer*), 0.85 (q, *J* = 5.6 Hz, 1H, *cis-isomer*). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 147.8, 147.4, 145.8, 145.6, 136.7, 133.1, 133.0, 129.8, 124.3, 123.2, 122.2, 119.1, 109.8, 108.2, 107.9, 106.4, 100.9, 100.9, 25.0, 22.8, 22.1, 17.1, 16.9, 13.4, 13.3, 12.6. **HRMS** (ESI): *m/z* $[M]^+$ calculated for $C_{13}H_{14}O_2$: 202.0988, found 202.0979.

(*Z*)-1-methoxy-4-(2-(oct-1-en-1-yl)cyclopropyl)benzene (56): Following general procedure A using (*Z*)-1-



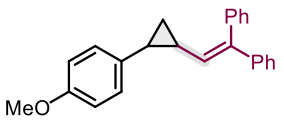
bromooct-1-ene (765 mg, 4.0 mmol, 1.0 eq.) and a suspension of freshly prepared (2-(4-methoxyphenyl)cyclopropyl)zinc(II) chloride (4.8 mmol, 1.2 eq.). Flash column chromatography (50:1 hexane:EtOAc) afforded the title product as a diastereomeric mixture as a colorless oil (969 mg, 3.75 mmol, 94%, 71:29 *cis*/*trans* (^{1}H NMR)). **R_f** = 0.42 (50:1 hexane:EtOAc). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.11 (d, *J* = 8.5 Hz, 2H, *cis-isomer*), 7.03 (d, *J* = 8.6 Hz, 2H, *trans-isomer*), 6.85 – 6.80 (m, 2H, *cis*+*trans-isomer*), 5.37 (dt, *J* = 10.7, 7.4 Hz, 1H, *trans-isomer*), 5.30 (dt, *J* = 10.8, 7.3 Hz, 1H, *cis-isomer*), 4.93 (t, *J* = 10.1 Hz, 1H, *trans-isomer*), 4.63 (t, *J* = 10.3 Hz, 1H, *cis-isomer*), 3.79 (s, 3H, *cis*+*trans-isomer*), 2.27 (td, *J* = 8.5, 6.2 Hz, 1H, *cis-isomer*), 2.15 (p, *J* = 7.0 Hz, 2H, *cis*+*trans-isomer*), 1.93 (qd, *J* = 9.1, 7.0 Hz, 1H, *cis-isomer*), 1.89 – 1.81 (m, 1H, *trans-isomer*), 1.78 – 1.70 (m, 1H, *trans-isomer*), 1.40 – 1.21 (m, 9H *cis* + 8H *trans-isomer*), 1.15 (dt, *J* = 8.7, 5.4 Hz, 1H, *trans-isomer*), 0.95 (dt, *J* = 8.8, 5.1 Hz, 1H, *trans-isomer*), 0.93 – 0.83 (m, 4H *cis*+ 3H *trans-isomer*). **^{13}C NMR** (151 MHz, Chloroform-*d*) δ 157.9 (*cis*), 157.9 (*trans*), 134.8 (*trans*), 132.5 (*trans*), 131.2 (*cis*), 130.4 (*cis*), 130.3 (*cis*), 129.3 (*trans*), 129.1 (*cis*), 127.0 (*trans*), 113.9 (*trans*), 113.6 (*cis*), 55.5 (*trans*), 55.4 (*cis*), 32.0 (*cis*), 31.9 (*trans*), 29.9 (*trans*), 29.9 (*cis*), 29.1 (*cis*), 29.1 (*trans*), 27.9 (*trans*), 27.8 (*cis*), 24.6, 22.8 (*cis*), 22.8 (*trans*), 22.4 (*cis*), 22.2 (*trans*), 17.2 (*cis*), 16.8 (*trans*), 14.3 (*cis*), 14.2 (*trans*), 12.6 (*cis*). **HRMS** (APCI): *m/z* $[M+H]^+$ calculated for $C_{18}H_{27}O$: 259.2056, found 259.2063.

1-methoxy-4-(2-(2-methylprop-1-en-1-yl)cyclopropyl)benzene (57): Following general procedure A using 1-



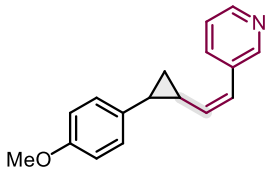
bromo-2-methylprop-1-ene (67.5 mg, 0.5 mmol, 1.0 eq.) and a suspension of freshly prepared (2-(4-methoxyphenyl)cyclopropyl)zinc(II) chloride (0.6 mmol, 1.2 eq.). Flash column chromatography (50:1 hexane:EtOAc) afforded the title product as a diastereomeric mixture as a colourless liquid (94 mg, 0.46 mmol, 93%, 57:43 *cis*/*trans* (^{1}H NMR)). R_f = 0.42 (50:1 hexane:EtOAc). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.09 (d, *J* = 8.4 Hz, 2H, *cis-isomer*), 7.02 (d, *J* = 8.2 Hz, 2H, *trans-isomer*), 6.84 – 6.80 (m, 4H, *cis*+*trans-isomer*), 4.73 (d, *J* = 8.9 Hz, 1H, *trans-isomer*), 4.46 (d, *J* = 8.7 Hz, 1H, *cis-isomer*), 3.80 (s, 3H, *trans-isomer*), 3.78 (s, 3H, *cis-isomer*), 2.21 (td, *J* = 8.5, 6.2 Hz, 1H, *cis-isomer*), 1.88 – 1.77 (m, 2H, *cis*+*trans-isomer*), 1.74 – 1.70 (m, 6H *trans-isomer* + 3H *cis-isomer*), 1.64 (tt, *J* = 9.3, 5.1 Hz, 1H, *trans-isomer*), 1.57 (s, 3H, *cis-isomer*), 1.21 (td, *J* = 8.5, 4.8 Hz, 1H, *cis-isomer*), 1.10 (dt, *J* = 8.5, 5.2 Hz, 1H, *trans-isomer*), 0.77 (q, *J* = 5.6 Hz, 1H, *cis-isomer*), 0.64 – 0.59 (m, 1H, *trans-isomer*). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 157.8, 157.8, 135.1, 132.5, 131.6, 131.5, 130.1, 127.5, 126.9, 123.5, 113.9, 113.5, 55.5, 55.4, 25.8, 25.7, 24.3, 22.9, 22.1, 18.5, 18.4, 18.0, 16.7, 12.5. **HRMS** (ESI): *m/z* $[M]^+$ calculated for $C_{14}H_{19}O$: 203.1430, found 203.1428.

(2-(2-(4-methoxyphenyl)cyclopropyl)ethene-1,1-diyl)dibenzene (58): Following general procedure A using



(2-bromoethene-1,1-diyl)dibenzene (130 mg, 0.5 mmol, 1.0 eq.) and a suspension of freshly prepared (2-(4-methoxyphenyl)cyclopropyl)zinc(II) chloride (0.6 mmol, 1.2 eq.). Flash column chromatography (20:1 hexane:Et_2O) afforded the title product as diastereomeric mixture as opaque white oil (142 mg, 0.43 mmol, 87%, 70:30 *cis*/*trans* (^{1}H NMR)). R_f = 0.38 (20:1 hexane:Et_2O). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.41 (dd, *J* = 7.5 Hz, 2H, *cis-isomer*), 7.36 – 7.30 (m, 2H *cis-isomer* + 4H *trans-isomer*), 7.30 – 7.25 (m, 2H *cis-isomer* + 1H *trans-isomer*), 7.23 (d, *J* = 8.7 Hz, 2H *cis-isomer* + 3H *trans-isomer*), 7.20 – 7.12 (m, 2H *cis-isomer* + 2H *trans-isomer*), 7.00 (d, *J* = 7.9 Hz, 2H, *cis-isomer*), 6.97 (d, *J* = 8.3 Hz, 2H, *trans-isomer*), 6.88 (d, *J* = 8.2 Hz, 2H, *cis-isomer*), 6.80 (d, *J* = 8.3 Hz, 2H, *trans-isomer*), 5.60 (d, *J* = 9.7 Hz, 1H, *trans-isomer*), 5.33 (d, *J* = 10.1 Hz, 1H, *cis-isomer*), 3.82 (s, 3H, *cis-isomer*), 3.78 (s, 3H, *trans-isomer*), 2.32 (q, *J* = 8.2 Hz, 1H, *cis-isomer*), 2.08 (dt, *J* = 9.3, 5.2 Hz, 1H, *trans-isomer*), 1.90 (qd, *J* = 9.0, 5.9 Hz, 1H, *cis-isomer*), 1.77 (tt, *J* = 9.3, 4.9 Hz, 1H, *trans-isomer*), 1.30 (td, *J* = 8.3, 5.2 Hz, 1H, *cis-isomer*), 1.18 (tt, *J* = 10.3, 5.1 Hz, 2H, *trans-isomer*), 1.09 (q, *J* = 5.6 Hz, 1H, *cis-isomer*). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 158.1, 157.9, 142.9, 142.9, 141.4, 140.7, 140.6, 140.2, 133.9, 133.0, 131.0, 130.5, 130.5, 130.4, 130.2, 128.3, 128.2, 128.2, 128.1, 127.4, 127.3, 127.2, 127.1, 127.0, 126.9, 126.7, 113.9, 113.8, 55.4, 55.4, 25.8, 24.7, 24.0, 20.2, 17.9, 13.9. **HRMS** (ESI): *m/z* $[M+H]^+$ calculated for $C_{24}H_{23}O$: 327.1743, found 327.1737.

(*Z*)-3-(2-(2-(4-methoxyphenyl)cyclopropyl)vinyl)pyridine (59): Following general procedure B using (*Z*)-3-



(2-bromovinyl)pyridine (92 mg, 0.5 mmol, 1.0 eq.) and a suspension of freshly prepared (2-(4-methoxyphenyl)cyclopropyl)zinc(II) chloride (0.6 mmol, 1.2 eq.). Flash column chromatography (1:1 hexane:EtOAc) afforded the title product as a diastereomeric mixture as a colorless oil (87 mg, 0.35 mmol, 69%, 69:31 *cis*/*trans* (^{1}H NMR)). R_f = 0.5 (1:1 hexane:EtOAc). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 8.78 (s, 1H, *cis-isomer*),

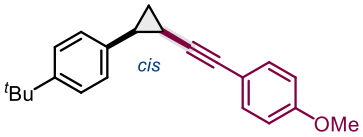
8.68 (s, 1H, *trans-isomer*), 8.51 (dd, *J* = 5.0, 1.4 Hz, 1H, *cis-isomer*), 8.46 (dd, *J* = 5.0, 1.4 Hz, 1H, *trans-isomer*), 7.76 (d, *J* = 7.9 Hz, 1H, *cis-isomer*), 7.69 (d, *J* = 7.9 Hz, 1H, *trans-isomer*), 7.32 (dd, *J* = 7.8, 5.0 Hz, 1H, *cis-isomer*), 7.24 (dd, *J* = 7.9, 5.0 Hz, 1H, *trans-isomer*), 7.16 (d, *J* = 8.3 Hz, 2H, *cis-isomer*), 7.01 (d, *J* = 8.2 Hz, 2H, *trans-isomer*), 6.86 – 6.79 (m, 2H, *cis-* + *trans-isomer*), 6.34 (d, *J* = 11.5 Hz, 1H, *trans-isomer*), 6.24 (d, *J* = 11.6 Hz, 1H, *cis-isomer*), 5.40 (t, *J* = 10.6 Hz, 1H, *trans-isomer*), 5.13 (t, *J* = 10.7 Hz, 1H, *cis-isomer*), 3.79 (s, 3H, *cis-isomer*), 3.77 (s, 3H, *trans-isomer*), 2.49 – 2.41 (m, 1H, *cis-isomer*), 2.16 – 2.09 (m, 1H, *cis-isomer*), 2.06 – 2.02 (m, 1H, *trans-isomer*), 1.99 – 1.92 (m, 1H, *trans-isomer*), 1.41 (ddd, *J* = 8.5, 5.7 Hz, 1H, *cis-isomer*), 1.33 – 1.29 (m, 1H, *trans-isomer*), 1.15 – 1.11 (m, 1H, *trans-isomer*), 1.08 (q, *J* = 5.7 Hz, 1H, *cis-isomer*). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 158.2, 158.1, 149.7, 147.3, 147.1, 138.0, 136.7, 136.4, 135.5, 134.2, 133.9, 133.2, 130.3, 130.1, 130.1, 127.0, 124.9, 123.8, 123.7, 123.6, 114.1, 113.7, 55.4, 55.3, 25.9, 24.0, 23.4, 18.9, 17.7, 13.9. **HRMS** (ESI): *m/z* $[M+H]^+$ calculated for $C_{17}H_{18}ON$: 252.1383, found 252.1384.

(*Z*)-2-(2-(2-(4-methoxyphenyl)cyclopropyl)vinyl)pyridine (60): Following general procedure B using (*Z*)-2-(2-bromovinyl)pyridine (61 mg, 0.33 mmol, 1.0 eq.) and a suspension of freshly prepared (2-(4-methoxyphenyl)cyclopropyl)zinc(II) chloride (0.39 mmol, 1.2 eq.). Flash column chromatography (5:1 hexane:Et_2O) afforded the title product as a diastereomeric mixture as a yellowish oil (74 mg, 0.29 mmol, 89%, 69:31 *cis*/*trans* (^{1}H NMR)). **R_f** = 0.46 (5:1 hexane:Et_2O). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 8.61 (d, *J* = 3.9 Hz, 1H, *cis-isomer*), 8.57 (d, *J* = 4.5 Hz, 1H, *trans-isomer*), 7.63 (t, *J* = 7.6 Hz, 1H, *cis-isomer*), 7.57 (t, *J* = 7.5 Hz, 1H, *trans-isomer*), 7.32 (d, *J* = 7.9 Hz, 1H, *cis-isomer*), 7.26 (d, *J* = 8.5 Hz, 1H, *trans-isomer*), 7.19 (d, *J* = 8.5 Hz, 2H, *cis-isomer*), 7.12 – 7.07 (m, 1H, *cis-isomer*), 7.06 (dd, *J* = 7.7, 5.2 Hz, 3H, *trans-isomer*), 6.83 (dd, *J* = 12.6, 8.5 Hz, 2H, *cis-* + *trans-isomer*), 6.42 (d, *J* = 11.6 Hz, 1H, *trans-isomer*), 6.32 (d, *J* = 11.8 Hz, 1H, *cis-isomer*), 5.38 (t, *J* = 10.9 Hz, 1H, *trans-isomer*), 5.11 (t, *J* = 11.2 Hz, 1H, *cis-isomer*), 3.80 (s, 3H, *cis-isomer*), 3.78 (s, 3H, *trans-isomer*), 3.06 (dt, *J* = 14.6, 7.2 Hz, 1H, *cis-isomer*), 2.90 (tt, *J* = 9.6, 5.0 Hz, 1H, *trans-isomer*), 2.47 (q, *J* = 8.0 Hz, 1H, *cis-isomer*), 2.03 (dt, *J* = 9.7, 5.0 Hz, 1H, *trans-isomer*), 1.47 – 1.40 (m, 1H, *cis-isomer*), 1.32 (dt, *J* = 8.6, 5.4 Hz, 1H, *trans-isomer*), 1.14 (dt, *J* = 9.5, 5.2 Hz, 1H, *trans-isomer*), 1.09 (q, *J* = 5.6 Hz, 1H, *cis-isomer*). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 158.1, 157.9, 157.2, 156.9, 149.3, 149.3, 139.8, 137.3, 136.1, 133.9, 130.6, 130.4, 128.0, 127.2, 127.2, 127.2, 123.9, 123.7, 121.1, 121.1, 113.9, 113.6, 55.4, 55.3, 26.0, 24.1, 23.3, 18.8, 17.9, 13.9. **HRMS** (ESI): *m/z* $[M+H]^+$ calculated for $C_{17}H_{18}ON$: 252.1383, found 252.1384.

(*E*)-2-(2-(2-(4-methoxyphenyl)cyclopropyl)vinyl)thiophene (61): Following general procedure B using (*E*)-2-(2-bromovinyl)thiophene (50 mg, 0.26 mmol, 1.0 eq.) and a suspension of freshly prepared (2-(4-methoxyphenyl)cyclopropyl)zinc(II) chloride (0.317 mmol, 1.2 eq.). Flash column chromatography (50:1 hexane:Et_2O) afforded the title product as a diastereomeric mixture as a yellowish liquid (62 mg, 0.24 mmol, 91%, 78:22 *cis*/*trans* (^{1}H NMR)). **R_f** = 0.31 (50:1 hexane:Et_2O). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.25 (d, *J* = 4.9 Hz, 2H, *cis-isomer*), 7.18 (d, *J* = 5.1 Hz, 1H, *trans-isomer*), 7.15 (d, *J* = 8.5 Hz, 2H, *cis-isomer*), 7.08 (d, *J* = 8.5 Hz, 2H, *trans-*

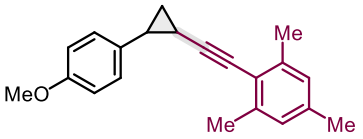
isomer), 7.04 – 7.00 (m, 2H, *cis-isomer*), 7.01 – 6.97 (m, 1H, *trans-isomer*), 6.99 – 6.94 (m, 1H, *trans-isomer*), 6.87 – 6.80 (m, 2H, *cis-* + *trans-isomer*), 6.52 (d, *J* = 11.4 Hz, 1H, *trans-isomer*), 6.47 (d, *J* = 11.4 Hz, 1H, *cis-isomer*), 5.20 (dd, *J* = 11.3, 9.5 Hz, 1H, *trans-isomer*), 4.92 (dd, *J* = 11.2, 9.5 Hz, 1H, *cis-isomer*), 3.80 (s, 3H, *trans-isomer*), 3.79 (s, 3H, *cis-isomer*), 2.52 – 2.45 (m, 1H, *cis-isomer*), 2.37 – 2.29 (m, 1H, *cis-isomer*), 2.28 – 2.20 (m, 1H, *trans-isomer*), 2.03 (ddd, *J* = 9.6, 5.0 Hz, 1H, *trans-isomer*), 1.47 (ddd, *J* = 8.4, 5.0 Hz, 1H, *cis-isomer*), 1.32 (ddd, *J* = 8.3, 5.3 Hz, 1H, *trans-isomer*), 1.12 (ddd, *J* = 8.4, 5.2 Hz, 1H, *trans-isomer*), 1.05 (q, *J* = 5.6 Hz, 1H, *cis-isomer*). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 158.1, 158.0, 141.1, 140.8, 134.0, 133.3, 130.6, 130.3, 130.2, 127.2, 127.1, 127.1, 126.9, 126.9, 124.7, 124.6, 122.6, 121.3, 114.0, 113.7, 55.5, 55.4, 25.8, 23.7, 23.7, 19.4, 18.0, 14.0. **HRMS** (ESI): *m/z* $[M+Na]^+$ calculated for $C_{16}H_{16}ONaS$: 279.0814, found 279.0814.

1-(*tert*-butyl)-4-(*cis*-2-((4-methoxyphenyl)ethynyl)cyclopropyl)benzene (62): Following general procedure D



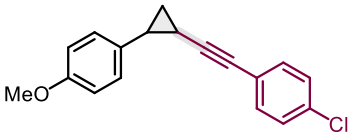
using 1-(chloroethynyl)-4-methoxybenzene (133 mg, 1 mmol, 2.0 eq.) and a suspension of freshly prepared *cis*-2-(4-(tert-butyl)phenyl)cyclopropyl)zinc(II) chloride (0.5 mmol, 1.0 eq.). Flash column chromatography (50:1 hexane:EtOAc) afforded the title product as a colorless oil (101 mg, 0.33 mmol, 66%). **R_f** = 0.14 (50:1 hexane:EtOAc). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.34 (d, *J* = 8.4 Hz, 2H), 7.28 – 7.23 (m, 2H), 7.06 – 7.00 (m, 2H), 6.73 – 6.67 (m, 2H), 3.76 (s, 3H), 2.36 (td, *J* = 8.4, 6.6 Hz, 1H), 1.93 (td, *J* = 8.5, 5.7 Hz, 1H), 1.40 (td, *J* = 8.6, 4.9 Hz, 1H), 1.33 (s, 9H), 1.24 (dd, *J* = 11.8, 5.6 Hz, 1H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 159.0, 149.1, 135.3, 132.9, 128.2, 124.8, 116.2, 113.7, 88.6, 79.9, 55.3, 34.5, 31.5, 23.6, 15.1, 10.1. **HRMS** (ESI): *m/z* $[M+Na]^+$ calculated for $C_{22}H_{24}ONa$: 327.1719, found 327.1718.

2-((2-(4-methoxyphenyl)cyclopropyl)ethynyl)-1,3,5-trimethylbenzene (63): Following general procedure D



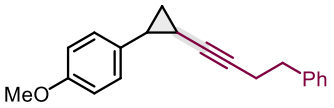
using 2-(chloroethynyl)-1,3,5-trimethylbenzene (179 mg, 1 mmol, 2.0 eq.) and a suspension of freshly prepared (2-(4-methoxyphenyl)cyclopropyl)zinc(II) chloride (0.5 mmol, 1.0 eq.). Flash column chromatography (2:1 hexane:toluene) afforded the title product as a diastereomeric mixture as a colorless oil (93 mg, 0.32 mmol, 64%, 73:27 *cis*/*trans* (^{1}H NMR)). **R_f** = 0.38 (2:1 hexane:toluene). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.24 (d, *J* = 8.6 Hz, 2H, *cis-isomer*), 7.07 (d, *J* = 8.6 Hz, 2H, *trans-isomer*), 6.86 – 6.80 (m, 2H *cis-isomer* + 4H *trans-isomer*), 6.73 (s, 2H, *cis-isomer*), 3.80 (s, 3H, *trans-isomer*), 3.78 (s, 3H, *cis-isomer*), 2.37 (s, 1H *cis-isomer* + 6H *trans-isomer*), 2.30 (dd, *J* = 8.2, 4.8 Hz, 1H, *trans-isomer*), 2.26 (s, 3H, *trans-isomer*), 2.21 (s, 3H, *cis-isomer*), 2.08 (s, 6H, *cis-isomer*), 2.02 (td, *J* = 8.5, 5.6 Hz, 1H, *cis-isomer*), 1.71 (dt, *J* = 8.6, 5.0 Hz, 1H, *trans-isomer*), 1.42 (td, *J* = 8.6, 4.9 Hz, 1H, *cis-isomer*), 1.36 (dt, *J* = 8.6, 5.1 Hz, 1H, *trans-isomer*), 1.30 (ddd, *J* = 8.5, 6.1, 4.7 Hz, 1H, *trans-isomer*), 1.26 – 1.19 (m, 1H, *cis-isomer*). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 158.4 (*cis*), 158.3 (*trans*), 140.2 (*cis*), 140.1 (*trans*), 136.9 (*trans*), 136.6 (*cis*), 133.1 (*trans*), 130.4 (*cis*), 129.9 (*cis*), 127.6 (*trans*), 127.4 (*cis*), 127.3 (*trans*), 120.7 (*cis*), 120.6 (*trans*), 114.1 (*trans*), 113.6 (*cis*), 100.0 (*trans*), 97.4 (*cis*), 77.7 (*cis*), 74.7 (*trans*), 55.5 (*trans*), 55.5 (*cis*), 26.6 (*trans*), 23.5 (*cis*), 21.4 (*trans*), 21.3 (*cis*), 21.1 (*trans*), 20.8 (*cis*), 18.4 (*trans*), 14.8 (*cis*), 12.2 (*trans*), 10.3(*cis*). **HRMS** (ESI): *m/z* $[M+Na]^+$ calculated for $C_{21}H_{22}ONa$: 313.1563, found 313.1560.

1-chloro-4-((2-(4-methoxyphenyl)cyclopropyl)ethynyl)benzene (64): Following general procedure D using



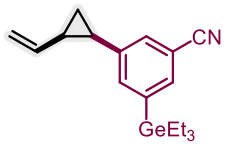
1-chloro-4-(chloroethynyl)benzene (137 mg, 1 mmol, 2.0 eq.) and a suspension of freshly prepared (2-(4-methoxyphenyl)cyclopropyl)zinc(II) chloride (0.5 mmol, 1.0 eq.). Flash column chromatography (2:1 hexane:toluene) afforded the title product as a diastereomeric mixture as a colorless oil (105 mg, 0.37 mmol, 74%, 75:25 *cis*/*trans* (^{1}H NMR)). R_f = 0.38 (2:1 hexane:toluene). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.32 (d, *J* = 8.5 Hz, 2H, *trans-isomer*), 7.28 – 7.21 (m, 2H, *cis-* + *trans-isomer*), 7.16 (d, *J* = 8.5 Hz, 2H, *cis-isomer*), 7.06 (d, *J* = 8.5 Hz, 2H, *cis-* + *trans-isomer*), 6.87 (d, *J* = 8.6 Hz, 2H, *cis-isomer*), 6.84 (d, *J* = 8.6 Hz, 2H, *trans-isomer*), 3.81 (s, 3H, *cis-isomer*), 3.79 (s, 3H, *trans-isomer*), 2.36 (td, *J* = 8.4, 6.7 Hz, 1H, *cis-isomer*), 2.34 – 2.30 (m, 1H, *trans-isomer*), 1.92 (ddd, *J* = 8.5, 5.7 Hz, 1H, *cis-isomer*), 1.61 (dt, *J* = 8.8, 5.1 Hz, 1H, *trans-isomer*), 1.42 (td, *J* = 8.6, 5.0 Hz, 1H, *cis-isomer*), 1.37 (dt, *J* = 8.9, 5.2 Hz, 1H, *trans-isomer*), 1.29 (ddd, *J* = 8.6, 6.1, 4.7 Hz, 1H, *trans-isomer*), 1.22 (q, *J* = 5.9 Hz, 1H, *cis-isomer*). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 158.4 (*cis* + *trans*), 133.6 (*trans*), 133.4 (*cis*), 133.0 (*trans*), 132.7 (*cis*), 132.7 (*trans*), 130.1 (*cis*), 129.5 (*cis*), 128.7 (*trans*), 128.5 (*cis*), 127.4 (*trans*), 122.5 (*cis*), 122.4 (*trans*), 114.1 (*trans*), 113.4 (*cis*), 93.4 (*trans*), 91.4 (*cis*), 79.1 (*cis*), 76.0 (*trans*), 55.5 (*cis* + *trans*), 26.1 (*trans*), 23.5 (*cis*), 17.7 (*trans*), 15.1 (*cis*), 11.6 (*trans*), 9.9 (*cis*). **HRMS** (ESI): *m/z* $[M+Na]^+$ calculated for $C_{18}H_{16}ONa$: 305.0704, found 305.0703.

1-methoxy-4-(2-(4-phenylbut-1-yn-1-yl)cyclopropyl)benzene (65): Following general procedure D using (4-

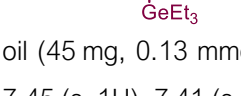


chlorobut-3-yn-1-yl)benzene (165 mg, 1 mmol, 2.0 eq.) and a suspension of freshly prepared (2-(4-methoxyphenyl)cyclopropyl)zinc(II) chloride (0.5 mmol, 1.0 eq.). Flash column chromatography (2:1 hexane:toluene) afforded the title product as a diastereomeric mixture as a colorless oil (89 mg, 0.32 mmol, 64%, 75:25 *cis*/*trans* (^{1}H NMR)). R_f = 0.22 (2:1 hexane:toluene). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.33 (t, *J* = 7.5 Hz, 2H, *trans-isomer*), 7.31 – 7.18 (m, 2H, *cis-* + *trans-isomer*), 7.16 (d, *J* = 8.5 Hz, 2H, *cis-isomer*), 7.10 (d, *J* = 7.6 Hz, 2H, *cis-isomer*), 7.03 (d, *J* = 8.1 Hz, 2H, *trans-isomer*), 6.84 (d, *J* = 8.5 Hz, 2H, *cis-* + *trans-isomer*), 3.82 (s, 3H, *cis-isomer*), 3.81 (s, 3H, *trans-isomer*), 2.84 (t, *J* = 7.6 Hz, 2H, *trans-isomer*), 2.70 – 2.59 (m, 2H, *cis-isomer*), 2.48 (t, *J* = 7.6 Hz, 2H, *trans-isomer*), 2.40 – 2.27 (m, 2H, *cis-isomer*), 2.19 (q, *J* = 8.0 Hz, 1H, *cis-isomer*), 2.14 (dt, *J* = 9.4, 5.2 Hz, 1H, *trans-isomer*), 1.72 (q, *J* = 8.2 Hz, 1H, *cis-isomer*), 1.43 – 1.37 (m, 1H, *trans-isomer*), 1.29 (td, *J* = 8.7, 5.0 Hz, 1H, *cis-isomer*), 1.19 (dt, *J* = 10.0, 5.2 Hz, 1H, *trans-isomer*), 1.14 (dt, *J* = 8.4, 5.5 Hz, 1H, *trans-isomer*), 1.01 (q, *J* = 5.7 Hz, 1H, *cis-isomer*). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 158.2 (*trans*), 158.2 (*cis*), 141.1 (*cis*), 141.1 (*trans*), 133.3 (*trans*), 130.5 (*cis*), 129.5 (*cis*), 128.6 (*trans*), 128.5 (*cis*), 128.4 (*trans*), 128.4 (*cis*), 127.3 (*trans*), 126.3 (*trans*), 126.2 (*cis*), 114.0 (*trans*), 113.3 (*cis*), 83.1 (*trans*), 80.4 (*cis*), 79.7 (*cis*), 76.3 (*trans*), 55.5 (*trans*), 55.4 (*cis*), 35.7 (*trans*), 35.4 (*cis*), 25.5 (*trans*), 22.6 (*cis*), 21.3 (*trans*), 21.1 (*cis*), 17.3 (*trans*), 14.7 (*cis*), 11.2 (*trans*), 9.5 (*cis*). **HRMS** (ESI): *m/z* $[M+Na]^+$ calculated for $C_{20}H_{20}ONa$: 299.1406, found 299.1406.

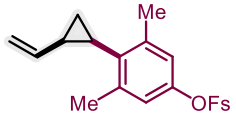
3-(triethylgermyl)-5-(*cis*-2-vinylcyclopropyl)benzonitrile (70): Following general procedure B using 3-bromo-5-(triethylgermyl)benzonitrile (69 mg, 0.2 mmol, 1.0 eq.) and a suspension of freshly prepared (*cis*-2-vinylcyclopropyl)zinc(II) chloride (0.4 mmol, 2.0 eq.). Flash column chromatography (30:1 pentane:Et_2O) afforded the title product as a colorless oil (45 mg, 0.13 mmol, 66%). R_f = 0.31 (30:1 pentane:Et_2O). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.50 (s, 1H), 7.45 (s, 1H), 7.41 (s, 1H), 5.14 (dd, *J* = 17.0, 1.9 Hz, 1H), 5.02 (ddd, *J* = 16.9, 10.2, 8.7 Hz, 1H), 4.89 (dd, *J* = 10.2, 1.9 Hz, 1H), 2.33 (td, *J* = 8.6, 6.3 Hz, 1H), 1.93 (qd, *J* = 8.7, 5.6 Hz, 1H), 1.32 (td, *J* = 8.4, 5.4 Hz, 1H), 1.06 – 0.98 (m, 16H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 141.6, 139.5, 139.4, 137.1, 135.1, 132.4, 119.7, 115.4, 111.9, 23.0, 22.9, 12.0, 9.0, 4.3. **HRMS** (APCI): *m/z* $[M - C_2H_5]^+$ calculated for $C_{16}H_{20}GeN$: 300.0802, found 300.0800.



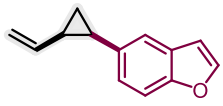
***cis*-2-chloro-4-(*cis*)-2-vinylcyclopropyl)phenyl trifluoromethanesulfonate (71):** Following general procedure B using 4-bromo-2-chlorophenyl trifluoromethanesulfonate (68 mg, 0.2 mmol, 1.0 eq.) and a suspension of freshly prepared (*cis*-2-vinylcyclopropyl)zinc(II) chloride (0.4 mmol, 2.0 eq.). Flash column chromatography (50:1 hexane:EtOAc) afforded the title product as a colorless oil (40 mg, 0.12 mmol, 61%). R_f = 0.43 (20:1 hexane:EtOAc). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.35 (d, *J* = 2.1 Hz, 1H), 7.24 (d, *J* = 8.5 Hz, 1H), 7.15 (dd, *J* = 8.6, 2.1 Hz, 1H), 5.16 (dd, *J* = 16.9, 1.9 Hz, 1H), 5.06 (ddd, *J* = 16.9, 10.2, 8.7 Hz, 1H), 4.94 (dd, *J* = 10.2, 1.9 Hz, 1H), 2.31 (td, *J* = 8.6, 6.4 Hz, 1H), 1.94 (qd, *J* = 8.7, 5.7 Hz, 1H), 1.33 (td, *J* = 8.4, 5.5 Hz, 1H), 1.01 (q, *J* = 5.8 Hz, 1H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 143.9, 141.2, 136.7, 131.8, 129.1, 126.8, 122.5, 115.8, 23.4, 22.6, 12.3. <u>*Note*</u>: The CF_3 carbon was not observed in ^{13}C NMR. **HRMS** (EI): *m/z* $[M]^+$ calculated for $C_{12}H_{10}O_3{}^{35}Cl^{79}F_3S$: 325.9986, found 325.9970.



***cis*-3,5-dimethyl-4-(*cis*-2-vinylcyclopropyl)phenyl fluorosulfate (72):** Following general procedure B using 4-bromo-3,5-dimethylphenyl fluorosulfate (57 mg, 0.2 mmol, 1.0 eq.) and a suspension of freshly prepared (*cis*-2-vinylcyclopropyl)zinc(II) chloride (0.4 mmol, 2.0 eq.). Flash column chromatography (50:1 hexane:EtOAc) afforded the title product as a colorless oil (41 mg, 0.15 mmol, 76%). R_f = 0.2 (50:1 hexane:EtOAc). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 6.94 (s, 1H), 5.14 (dd, *J* = 16.4, 2.3 Hz, 1H), 4.94 – 4.82 (m, 2H), 2.42 (s, 6H), 2.09 – 2.01 (m, 1H), 1.98 (dddd, *J* = 8.6, 5.2 Hz, 1H), 1.52 (ddd, *J* = 8.5, 5.2 Hz, 1H), 0.83 (ddd, *J* = 7.1, 5.3 Hz, 1H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 148.1, 138.5, 136.4, 119.6, 114.3, 22.7, 21.2, 20.1, 15.8. **^{19}F NMR** (565 MHz, $CDCl_3$) δ 37.45. **HRMS** (EI): *m/z* $[M]^+$ calculated for $C_{13}H_{15}O_3FS$: 270.0720, found 270.0708.

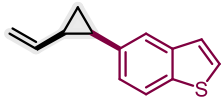


5-(*cis*-2-vinylcyclopropyl)benzofuran (73): Synthesized following the General Procedure F using 5-bromobenzofuran (197 mg, 1 mmol, 1.0 eq.) and a suspension of freshly prepared (*cis*-2-vinylcyclopropyl)zinc(II) chloride[62] (4.9 mL, 2.0 eq.). Flash column chromatography (pentane/Et_2O 100:1) afforded the title product as a colorless oil (180 mg, 0.98 mmol, 98%). R_f = 0.2 (100:1 pentane:Et_2O, PMA). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.59 (d, *J* = 2.2 Hz, 1H), 7.45 – 7.42 (m, 1H), 7.41 (d, *J* = 8.5 Hz, 1H), 7.18 (dd, *J* = 8.5, 1.8 Hz, 1H), 6.72 (dd, *J* = 2.2,

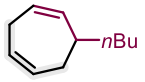


1.0 Hz, 1H), 5.17 – 5.03 (m, 2H), 4.83 (dd, *J* = 10.0, 2.3 Hz, 1H), 2.45 (td, *J* = 8.6, 6.3 Hz, 1H), 1.88 (qd, *J* = 8.7, 5.4 Hz, 1H), 1.30 (td, *J* = 8.4, 5.2 Hz, 1H), 1.06 (dt, *J* = 6.3, 5.3 Hz, 1H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 153.8, 145.2, 138.6, 133.3, 127.4, 126.2, 121.4, 113.9, 110.9, 106.6, 23.3, 22.9, 12.2. **HRMS** (ESI): *m/z* $[M]^+$ calculated for $C_{13}H_{12}O$: 184.0882, found 184.0883.

5-(*cis*-2-vinylcyclopropyl)benzo[*b*]thiophene (74): Synthesized following the General Procedure F using 5-bromobenzo[*b*]thiophene (213 mg, 1 mmol, 1.0 eq.) and a suspension of freshly prepared (*cis*-2-vinylcyclopropyl)zinc(II) chloride[62] (4.9 mL, 2.0 eq.). Flash column chromatography (100:1 pentane:Et_2O, PMA) afforded the title product as a colorless oil (77 mg, 0.38 mmol, 38%). **R_f** = 0.42 (100:1 pentane:Et_2O). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.78 (d, *J* = 8.3 Hz, 1H), 7.66 (s, 1H), 7.42 (d, *J* = 5.4 Hz, 1H), 7.29 (dd, *J* = 5.4, 0.8 Hz, 1H), 7.24 (dd, *J* = 8.3, 1.7 Hz, 1H), 5.18 – 5.06 (m, 2H), 4.85 – 4.83 (m, 1H), 2.48 (td, *J* = 8.6, 6.4 Hz, 1H), 1.92 (qd, *J* = 8.6, 5.4 Hz, 1H), 1.32 (td, *J* = 8.4, 5.2 Hz, 1H), 1.12 (dt, *J* = 6.4, 5.4 Hz, 1H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 139.9, 138.4, 137.7, 135.1, 126.6, 126.4, 123.8 (2C), 122.1, 114.1, 23.4, 23.1, 12.1. **HRMS** (ESI): *m/z* $[M]^+$ calculated for $C_{13}H_{12}S$: 200.0654, found 200.0656.

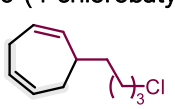


(±) Dictyopterene C´ (75): General procedure A was followed using (*E*)-1-bromohex-1-ene (82 mg, 0.5 mmol, 1.0 eq.) and a suspension of freshly prepared (*cis*-2-vinylcyclopropyl)zinc(II) chloride (1 mmol, 2.0 eq.). Flash column chromatography (pentane) afforded the title product as a colorless oil (61 mg, 0.41 mmol, 81%). **R_f** = 0.70 (pentane). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 5.75 – 5.67 (m, 1H), 5.65 – 5.59 (m, 3H), 2.95 (ddq, *J* = 19.7, 4.4, 2.1 Hz, 1H), 2.70 (dt, *J* = 19.8, 5.7 Hz, 1H), 2.48 – 2.43 (m, 1H), 2.22 (ddt, *J* = 15.8, 6.3, 3.0 Hz, 1H), 2.15 – 2.06 (m, 1H), 1.42 – 1.26 (m, 7H), 0.92 – 0.88 (m, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 137.0, 130.0, 128.2, 127.4, 37.3, 36.2, 33.0, 29.6, 28.5, 23.0, 14.2. **HRMS** (EI): *m/z* $[M]^+$ calculated for $C_{11}H_{18}$: 150.1403, found 150.1396. The data are in agreement with those previously reported in the literature.[136]



6-benzylcyclohepta-1,4-diene (76): General procedure A was followed using (*E*)-(3-bromoallyl)benzene (99 mg, 0.5 mmol, 1.0 eq.). and a suspension of freshly prepared (*cis*-2-vinylcyclopropyl)zinc(II) chloride (1 mmol, 2.0 eq.). Flash column chromatography (pentane) afforded the title product as a colorless oil (71 mg, 0.39 mmol, 77%). **R_f** = 0.37 (hexane). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.29 (dd, *J* = 15.2 Hz, 2H), 7.20 (dd, *J* = 8.0 Hz, 3H), 5.74 – 5.64 (m, 2H), 5.66 – 5.58 (m, 2H), 2.94 (d, *J* = 19.8 Hz, 1H), 2.80 – 2.70 (m, 3H), 2.62 (dd, *J* = 13.1, 7.8 Hz, 1H), 2.26 (dt, *J* = 15.6, 2.8 Hz, 1H), 2.14 – 2.08 (m, 1H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 140.9, 135.7, 129.7, 129.2, 128.9, 128.3, 127.6, 126.0, 42.4, 39.2, 32.2, 28.6. **HRMS** (EI): *m/z* $[M]^+$ calculated for $C_{14}H_{16}$: 184.1247, found 184.1238.

6-(4-chlorobutyl)cyclohepta-1,4-diene (77): General procedure A was followed using (*E*)-1-bromo-6-chlorohex-1-ene (92 mg, 0.5 mmol, 1.0 eq.). and a suspension of freshly prepared (*cis*-2-vinylcyclopropyl)zinc(II) chloride (1 mmol, 2.0 eq.). Flash column chromatography (pentane) afforded the title product as a colorless oil (69 mg, 0.37 mmol, 75%). **R_f** = 0.35 (hexane). **^{1}H NMR**



(600 MHz, $CDCl_3$) δ 5.70 (dddt, *J* = 9.3, 6.0, 4.4, 1.5 Hz, 1H), 5.68 – 5.60 (m, 2H), 5.58 (ddd, *J* = 11.2, 4.7, 2.1 Hz, 1H), 3.54 (t, *J* = 6.7 Hz, 2H), 3.01 – 2.90 (m, 1H), 2.71 (dt, *J* = 19.7, 6.0 Hz, 1H), 2.55 – 2.43 (m, 1H), 2.28 – 2.19 (m, 1H), 2.16 – 2.07 (m, 1H), 1.78 (p, *J* = 7.0 Hz, 2H), 1.51 – 1.44 (m, 2H), 1.44 – 1.32 (m, 2H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 136.2, 129.6, 128.2, 127.6, 45.0, 37.0, 35.4, 32.7, 32.7, 28.4, 24.5. **MS** (70eV, EI): *m/z* (%): 184 (10) [M^+], 107 (23), 93 (69), 79 (100), 77 (46), 66 (13). **HRMS** (EI): *m/z* [$M-^{35}Cl]^+$ calculated for $C_{11}H_{17}$: 149.1325, found 149.1318.

(±)-Dictyopterene A (78): Following general procedure A using (*E*)-1-bromohex-1-ene (82 mg, 0.5 mmol, 1.0 eq.) and freshly prepared (*trans*-2-vinylcyclopropyl)zinc(II) chloride (1.0 mmol, 2.0 eq.). Flash column chromatography (pentane) afforded the title product as a colorless liquid (50 mg, 0.34 mmol, 67%). **R_f** = 0.79 (pentane). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 5.50 (dt, *J* = 15.1, 6.8 Hz, 1H), 5.40 (ddd, *J* = 18.3, 10.2, 8.2 Hz, 1H), 5.09 – 4.96 (m, 2H), 4.86 (dd, *J* = 10.3, 1.6 Hz, 1H), 1.98 (qd, *J* = 7.1, 1.5 Hz, 2H), 1.43 – 1.25 (m, 8H, overlap with pentane), 0.95 – 0.88 (m, 1H, overlap with pentane), 0.84 – 0.74 (m, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 141.0, 131.7, 129.3, 112.0, 32.3, 31.9, 24.4, 23.7, 22.4, 14.9, 14.1. **MS** (70eV, EI): *m/z* (%): 150 (1) [M^+], 122 (1), 108 (3), 91 (34), 79 (100), 66 (15). *Note: Residual solvent could not be completely removed due to the volatility of the product.* The data are in agreement with those previously reported in the literature.[137]

((*E*)-3-(*trans*-2-vinylcyclopropyl)allyl)benzene (79): Prepared following general procedure G using (*E*)-(3-bromoallyl)benzene[62] (492.0 mg, 2.5 mmol, 1.0 eq.), freshly prepared (*trans*-2-vinylcyclopropyl)zinc(II) chloride (5.0 mmol, 2.0 eq.) and dry toluene (12.5 mL, 0.2 M). Flash column chromatography (pentane → 100:1 pentane:Et_2O) afforded the title product **41** as a colorless liquid (281.0 mg, 1.525 mmol, 61%). **R_f** = 0.5 (100:1 pentane:Et_2O, PMA). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.32 – 7.26 (m, 2H), 7.22 – 7.16 (m, 3H), 5.66 (dt, *J* = 15.2, 6.9 Hz, 1H), 5.40 (ddd, *J* = 16.9, 10.3, 8.3 Hz, 1H), 5.12 (ddt, *J* = 15.2, 8.2, 1.5 Hz, 1H), 5.05 (dd, *J* = 17.1, 1.6 Hz, 1H), 4.87 (dd, *J* = 10.2, 1.7 Hz, 1H), 3.33 (d, *J* = 6.8 Hz, 2H), 1.45 – 1.39 (m, 2H), 0.84 – 0.80 (m, 2H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 140.9, 140.8, 133.4, 128.6, 128.5, 127.6, 126.1, 112.2, 39.0, 24.5, 23.7, 15.0. **HRMS** (EI): *m/z*: calculated for $[M]^+$ $C_{14}H_{16}$: 184.1247, found: 184.1247.

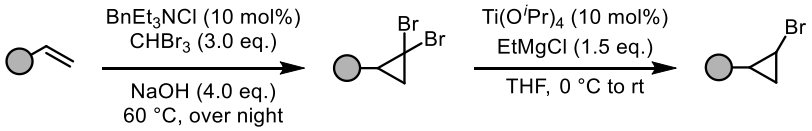
1-((*cis*)-2-vinylcyclopropyl)cyclohept-1-ene (80): Prepared following general procedure G using 1-bromocyclohept-1-ene (87.5 mg, 0.500 mmol, 1.0 eq.), freshly prepared (*trans*-2-vinylcyclopropyl)zinc(II) chloride (1.0 mmol, 2.0 eq.) and dry THF (2.5 mL, 0.2 M). Flash column chromatography (pentane) afforded the title product **S47** as a colorless liquid (34.0 mg, 0.210 mmol, 42%). **R_f** = 0.7 (hexane, PMA). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 5.59 (t, *J* = 6.6 Hz, 1H), 5.50 – 5.39 (m, 1H), 5.04 (dd, *J* = 17.1, 1.7 Hz, 1H), 4.85 (dd, *J* = 10.3, 1.7 Hz, 1H), 2.08 (td, *J* = 7.0, 3.5 Hz, 2H), 1.99 – 1.95 (m, 2H), 1.72 (p, *J* = 5.9 Hz, 2H), 1.49 – 1.36 (m, 6H), 0.87 (ddd, *J* = 8.0, 6.4, 4.7 Hz, 1H), 0.68 (dt, *J* = 7.9, 5.1 Hz, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 143.8, 141.6, 125.5, 111.8, 32.8, 30.7, 28.9, 28.3, 27.4, 27.0, 22.4, 12.7. **IR** (neat, cm^{-1}): 3078, 3000, 2920, 2849, 2690, 2489, 2330, 2156, 2107, 2001, 1966, 1725, 1634, 1446, 1351, 1274, 1220, 1073, 1016, 984, 892, 838, 793, 764, 723, 666.

HRMS (EI): *m/z*: calculated for $[M]^+$ $C_{12}H_{18}$: 162.1403, found: 162.1405. *Note: Caution, compound is volatile.*

8-((*trans*)-2-vinylcyclopropyl)-1,4-dioxaspiro[4.5]dec-7-ene (81): Prepared following general procedure G using 1,4-dioxaspiro[4.5]dec-7-en-8-yl trifluoromethanesulfonate[138] (144.1 mg, 0.500 mmol, 1.0 eq.), freshly prepared (*trans*-2-vinylcyclopropyl)zinc(II) chloride (1.0 mmol, 2.0 eq.) and dry NMP (2.5 mL, 0.2 M). NMP was removed by flash column chromatography (10:1 pentane:Et_2O). Final flash column chromatography (10:1 pentane:Et_2O) afforded the title product **S50** as a colorless liquid (58.0 mg, 0.357 mmol, 71%). R_f = 0.4 (10:1 pentane:Et_2O, PMA). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 5.42 (ddd, *J* = 17.0, 10.3, 8.5 Hz, 1H), 5.34 (ddt, *J* = 3.9, 2.4, 1.3 Hz, 1H), 5.03 (dd, *J* = 17.1, 1.6 Hz, 1H), 4.85 (dd, *J* = 10.2, 1.7 Hz, 1H), 3.97 (s, 4H), 2.28 – 2.22 (m, 2H), 2.10 (tt, *J* = 6.4, 1.9 Hz, 2H), 1.75 (t, *J* = 6.5 Hz, 2H), 1.48 (ddt, *J* = 13.5, 8.7, 4.3 Hz, 1H), 1.38 (dt, *J* = 9.9, 5.3 Hz, 1H), 0.94 (ddd, *J* = 8.4, 6.1, 4.9 Hz, 1H), 0.71 (dt, *J* = 8.6, 5.0 Hz, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 141.4, 136.7, 117.4, 112.1, 108.3, 64.5, 35.7, 31.2, 26.9, 26.0, 22.8, 13.0. **IR** (neat, cm^{-1}): 3077, 2882, 2673, 2331, 2236, 2211, 2087, 1997, 1923, 1800, 1634, 1550, 1474, 1429, 1367, 1339, 1305, 1250, 1211, 1115, 1055, 1013, 988, 948, 896, 862, 795, 757, 702, 658. **HRMS** (ESI): *m/z*: calculated for $[M+Na]^+$ $C_{13}H_{18}O_2Na$: 229.1199, found: 229.1205.

5.3.2 Synthesis of starting materials

General procedure for the synthesis of bromocyclopropanes

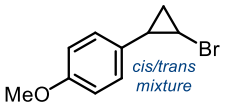


Bromocyclopropanes were synthesized using a modified procedure of An *et al*.[139] In a round-bottom flask, the corresponding alkene (1.0 eq.) and benzyltriethylammonium chloride (0.1 eq.) were dissolved in bromoform (3.0 eq.) and cooled down to 0 °C. An aqueous solution of NaOH (4.0 eq., 20 M) was added dropwise via syringe pump over 30 min to the stirring reaction mixture. After the addition was complete, the mixture was stirred for 30 min at room temperature and then heated overnight at 60 °C. The reaction was allowed to cool and was then quenched by the addition of water and the organic phase was extracted with CH_2Cl_2. The combined organic phase was washed with brine, dried over Na_2SO_4 and concentrated under reduced pressure. The 2,2-dibromocyclopropane was filtered over a plug of silica and used in the next step without further analysis.

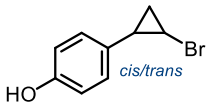
The obtained 2,2-dibromocyclopropane (1.0 eq.) and $Ti(O^iPr)_4$ (0.1 eq.) were dissolved in anhydrous THF (1 M) under Ar at 0 °C. A solution of ethylmagnesium bromide (3 M in THF) was added dropwise via syringe pump over 1h to the stirring reaction mixture. The reaction mixture was further stirred at room temperature until full conversion of the starting material (monitored by TLC or GC-MS). Then, the reaction was quenched by slow addition of water and the aqueous layer was extracted with Et_2O. The combined organic layers were washed with brine, dried over Na_2SO_4 and concentrated under reduced pressure. The crude products were

purified by silica gel column chromatography. *Note: The pure trans- or cis-isomers can be obtained by using pure pentane or hexane as the eluent. The trans-isomers were generally less polar than cis-isomers. The assignment of the cis- and trans-isomers was determined according to the coupling constant between the protons of the cyclopropane. The vicinal coupling constant of cyclopropane, J_{cis} is generally larger than that of J_{trans}.*[140]

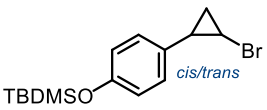
1-(2-bromocyclopropyl)-4-methoxybenzene: The titled compound was synthesized in two different batches following general procedure using 1-(2,2-dibromocyclopropyl)-4-methoxybenzene (Batch 1: 9.18 g, 30 mmol; Batch 2: 57 mmol, 17.4 g). Flash column chromatography (Batch 1: 20:1 hexane:EtOAc; Batch 2: 50:1 hexane:EtOAc) afforded the titled product as diastereomeric mixture as a colorless oil (Batch 1: 4.77 g, 70% yield, 73:27 cis/trans (^{1}H NMR); Batch 2: 9.69 g, 75%, 64:36 cis/trans (^{1}H NMR)). **Rf** = 0.4 (50:1 hexane:EtOAc). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.17 (d, *J* = 8.8 Hz, 2H, *cis*-isomer), 7.01 (d, *J* = 8.8 Hz, 2H, *trans*-isomer), 6.88 (d, *J* = 8.7 Hz, 2H, *cis*-isomer), 6.83 (d, *J* = 8.7 Hz, 1H, *trans*-isomer), 3.81 (s, 3H, *cis*-isomer), 3.79 (s, 3H, *trans*-isomer), 3.29 (td, *J* = 7.5, 4.5 Hz, 1H, *cis*-isomer), 3.01 – 2.93 (m, 1H, *trans*-isomer), 2.37 (ddd, *J* = 10.0, 6.5, 3.5 Hz, 1H, *trans*-isomer), 2.25 (dt, *J* = 9.7, 7.5 Hz, 1H, *cis*-isomer), 1.56 (ddd, *J* = 9.6, 7.5, 6.7 Hz, 1H, *cis*-isomer), 1.45 (dddd, *J* = 9.9, 6.7, 4.4, 0.7 Hz, 1H, *trans*-isomer), 1.40 (dt, *J* = 7.8, 6.6 Hz, 1H, *trans*-isomer), 1.26 (ddd, *J* = 7.7, 6.8, 4.5 Hz, 1H, *cis*-isomer). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 158.6, 158.5, 130.4, 129.4, 127.3, 127.0, 114.1, 113.5, 55.5, 55.4, 26.3, 24.4, 21.7, 21.5, 18.5, 14.4. The data are in agreement with those previously reported in the literature.[139]



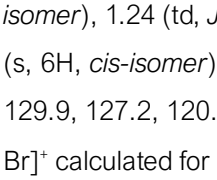
4-(2-bromocyclopropyl)phenol: To an oven dried flask 1-(2-bromocyclopropyl)-4-methoxybenzene (2.27 g, 10 mmol, 1.0 eq.) was added and dissolved in dry DCM (20 mL, 0.5 M). The mixture was cooled to 0 °C and a solution of tribromoborane (15 mL, 3.7 g, 15 mmol, 1.5 eq.) in dry DCM (15 mL, 1 M) was added dropwise. The reaction was stirred for 2 h at 0 °C before it was allowed to warm up to room temperature overnight. The mixture was quenched by slow addition of water (30 mL) and neutralized with sat. $NaHCO_3$ (30 mL). The phases were separated, and the aqueous phase was extracted with DCM (3x 50 mL). The combined organic layers were dried over Na_2SO_4, filtered and concentrated under reduced pressure. Flash column chromatography (4:1 hexane:EtOAc) afforded the title product as a diastereomeric mixture as a brown oil (1.90 g, 8.92 mmol, 89%, 70:30 *cis*/*trans* (^{1}H NMR)). **R_f** = 0.37 (4:1 hexane:EtOAc). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.12 (d, *J* = 8.5 Hz, 2H, *cis-isomer*), 6.94 (d, *J* = 8.5 Hz, 2H, *trans-isomer*), 6.81 (d, *J* = 8.6 Hz, 2H, *cis-isomer*), 6.76 (d, *J* = 8.6 Hz, 2H, *trans-isomer*), 5.15 (bs, 2H, *cis-* + *trans-isomer*), 3.28 (td, *J* = 7.5, 4.5 Hz, 1H, *cis-isomer*), 2.95 (ddd, *J* = 7.7, 4.4, 3.5 Hz, 1H, *trans-isomer*), 2.35 (ddd, *J* = 10.0, 6.5, 3.5 Hz, 1H, *trans-isomer*), 2.24 (dt, *J* = 9.5, 7.5 Hz, 1H, *cis-isomer*), 1.55 (dt, *J* = 9.5, 7.1 Hz, 1H, *cis-isomer*), 1.45 (ddd, *J* = 9.9, 6.7, 4.4 Hz, 1H, *trans-isomer*), 1.38 (dt, *J* = 7.7, 6.7 Hz, 1H, *trans-isomer*), 1.25 (td, *J* = 7.1, 4.5 Hz, 1H, *cis-isomer*). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 154.3, 154.1, 132.1, 130.6, 129.6, 127.5, 115.6, 115.1, 26.2, 24.4, 21.7, 21.4, 18.5, 14.3. **HRMS** (APCI): m/z $[M+H]^+$ calculated for $C_9H_{10}BrO$: 212.9910, found 212.9907.



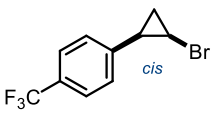
(4-(2-bromocyclopropyl)phenoxy)(*tert*-butyl)dimethylsilane: To an oven-dried flask 4-(2-bromocyclopropyl)phenol (214 mg, 1 mmol, 1.0 equiv) and DMAP (2.5 mg, 2 mol%) were added and dissolved in dry DCM (5 mL, 0.2 M). Next, Et_3N (0.18 mL, 1.3 mmol, 1.3 eq.) was added followed by slow addition of *tert*-butylchlorodimethylsilane (196 mg, 1.3 mmol, 1.3 eq.) in dry DCM (1.3 mL, 1 M). The mixture was stirred for 3 hours at room temperature before it was quenched by addition of water (5 mL). The aqueous phase was extracted with DCM (2x 5 mL) and the combined organic phases were dried over Na_2SO_4, filtered and concentrated under reduced pressure. Flash column chromatography (100:1 hexane:EtOAc) afforded the title product as a diastereomeric mixture as a collorless oil (321 mg, 0.98 mmol, 98%, 63:37 *cis*/*trans* (^{1}H NMR)). **R_f** = 0.35 (100:1 hexane:EtOAc). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.10 (d, *J* = 8.4 Hz, 2H, *cis-isomer*), 6.93 (d, *J* = 8.5 Hz, 2H, *trans-isomer*), 6.80 (d, *J* = 8.5 Hz, 2H, *cis-isomer*), 6.76 (d, *J* = 8.5 Hz, 2H, *trans-isomer*), 3.27 (td, *J* = 7.4, 4.5 Hz, 1H, *cis-isomer*), 2.96 (ddd, *J* = 7.6, 4.4, 3.4 Hz, 1H, *trans-isomer*), 2.34 (ddd, *J* = 10.0, 6.5, 3.5 Hz, 1H, *trans-isomer*), 2.24 (dt, *J* = 9.7, 7.6 Hz, 1H, *cis-isomer*), 1.54 (ddd, *J* = 9.6, 7.6, 6.7 Hz, 1H, *cis-isomer*), 1.44 (ddd, *J* = 9.9, 6.7, 4.4 Hz, 1H, *trans-isomer*), 1.42 – 1.35 (m, 1H, *trans-isomer*), 1.24 (td, *J* = 7.0, 4.6 Hz, 1H, *cis-isomer*), 0.99 (s, 9H, *cis-isomer*), 0.98 (s, 9H, *trans-isomer*), 0.20 (s, 6H, *cis-isomer*), 0.18 (s, 6H, *trans-isomer*). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 154.6, 154.5, 132.5, 130.3, 129.9, 127.2, 120.3, 119.7, 26.4, 25.8, 24.4, 21.8, 21.6, 18.7, 18.4, 14.4, -4.3, -4.3. **HRMS** (ESI): m/z $[M-Br]^+$ calculated for $C_{15}H_{23}OSi$: 247.1513, found 247.1511.



1-(2-bromocyclopropyl)-4-fluorobenzene: General procedure was followed using 1-(2,2-dibromocyclopropyl)-4-fluorobenzene (2.25 g, 7.65 mmol). Flash column chromatography (pentane) afforded the title product as a diastereomeric mixture as a colorless oil (1.12 g, 5.9 mmol, 77%, 62:38 *cis*/*trans* (^{1}H NMR)). **R_f** = 0.4 (pentane). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.21 (dd, *J* = 8.5, 5.4 Hz, 2H, *cis-isomer*), 7.07 – 6.99 (m, 4H, *cis-* + *trans-isomer*), 6.98 (dd, *J* = 8.6 Hz, 2H, *trans-isomer*), 3.30 (ddd, *J* = 7.5, 4.5 Hz, 1H, *cis-isomer*), 2.97 (dd, *J* = 7.7, 3.9 Hz, 1H, *trans-isomer*), 2.39 (ddd, *J* = 9.9, 6.5, 3.5 Hz, 1H, *trans-isomer*), 2.28 (q, *J* = 8.0 Hz, 1H, *cis-isomer*), 1.59 (ddd, *J* = 9.4, 7.1 Hz, 1H, *cis-isomer*), 1.49 (ddd, *J* = 9.9, 6.8, 4.5 Hz, 1H, *trans-isomer*), 1.41 (q, *J* = 6.9 Hz, 1H, *trans-isomer*), 1.27 (ddd, *J* = 7.2, 4.5 Hz, 1H, *cis-isomer*). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 161.9 (d, *J* = 245.2 Hz), 161.7 (d, *J* = 245.0 Hz), 135.5 (d, *J* = 3.5 Hz), 132.9 (d, *J* = 3.1 Hz), 130.8 (d, *J* = 8.1 Hz), 127.7 (d, *J* = 7.9 Hz), 115.5 (d, *J* = 21.4 Hz), 114.9 (d, *J* = 21.3 Hz), 26.3, 23.8, 21.5, 21.4, 18.8, 14.5. The data are in agreement with those previously reported in the literature.[141]

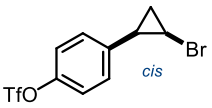


1-(*cis*-2-bromocyclopropyl)-4-(trifluoromethyl)benzene: General procedure was followed using 1-(2,2-dibromocyclopropyl)-4-(trifluoromethyl)benzene (500 mg, 1.45 mmol). Flash column chromatography (50:1 hexane:EtOAc) afforded the title product as a colorless oil (130 mg, 0.55 mmol, 38%). **R_f** = 0.27 (50:1 hexane:EtOAc). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.59 (d, *J* = 8.0 Hz, 2H), 7.35 (d, *J* = 8.0 Hz, 2H), 3.35 (td, *J* = 7.6, 4.7 Hz, 1H), 2.37 (q, *J* = 8.0 Hz, 1H), 1.66 (dt, *J* = 9.3, 7.3 Hz, 1H), 1.37 (td, *J* = 7.2, 4.7 Hz, 1H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 141.3 (q, *J* = 1.3 Hz), 129.6, 128.9 (q, *J* = 32.4 Hz), 124.8 (q, *J* = 3.8 Hz), 124.2 (q, *J* = 271.9 Hz), 23.4, 21.9, 14.7. **^{19}F NMR**



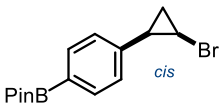
(564 MHz, $CDCl_3$) δ -62.40 (s, 3F). The data are in agreement with those previously reported in the literature.[141]

4-(*cis*-2-bromocyclopropyl)phenyl trifluoromethanesulfonate: To an oven-dried flask 4-(2-



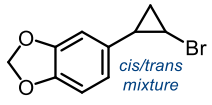
bromocyclopropyl)phenol (426 mg, 2 mmol, 1.0 equiv) was added and dissolved in dry DCM (10 mL, 0.2 M). Next, Et_3N (1.11 mL, 8.0 mmol, 4.0 eq.) was added. The mixture was cooled to 0 °C and triflic anhydride (0.5 mL, 3 mmol, 1.5 eq.) was added dropwise at this temperature. The mixture was allowed to warm up to room temperature and stirred overnight. It was quenched by addition of water (10 mL) and phases were separated. The aqueous phase was extracted with DCM (2x 10 mL) and the combined organic phases were dried over Na_2SO_4, filtered and concentrated under reduced pressure. Flash column chromatography (30:1 hexane:EtOAc) afforded the title product as a colorless oil (156 mg, 0.45 mmol, 23%). R_f = 0.33 (9:1 hexane:EtOAc). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.34 – 7.29 (m, 2H), 7.26 – 7.21 (m, 2H), 3.32 (td, *J* = 7.6, 4.6 Hz, 1H), 2.33 (dt, *J* = 9.5, 7.5 Hz, 1H), 1.65 (dt, *J* = 9.5, 7.3 Hz, 1H), 1.30 (td, *J* = 7.2, 4.6 Hz, 1H). **^{19}F NMR** (564 MHz, $CDCl_3$) δ -72.89 (d, *J* = 3.4 Hz). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 148.5, 138.0, 131.1, 120.9, 118.9 (q, *J* = 321.0 Hz), 23.5, 21.6, 15.0. **HRMS** (ESI): m/z $[M-Br]^+$ calculated for $C_{10}H_8F_3O_3S$: 265.0141, found 265.0142.

2-(4-(*cis*-2-bromocyclopropyl)phenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane: Synthesized according to



a modified procedure of Masuda *et al*.[142] Inside an argon-filled glovebox a 20 mL screw-cap vial was charged with 4-(*cis*-2-bromocyclopropyl)phenyl trifluoromethanesulfonate (345 mg, 1 mmol, 1.0 eq.) and dry dioxane (5 mL, 0,2 M). Next, 4,4,5,5-tetramethyl-1,3,2-dioxaborolane (0.42 mL, 2.9 mmol, 2.9 eq.), $PdCl_2$(dppf) (37 mg, 5 mol%) and Et_3N (0.83 mL, 6 mmol, 6.0 eq.) were added in this order and the vial was closed with the cap. The mixture was stirred at 100 °C for 24 hours. Then, the mixture was let to cool down to room temperature and water (10 mL) was added, phases were seperated and the aqueous phase was extracted with DCM (2x 10 mL). The combined organic phases were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. Flash column chromatography (30:1 pentane:Et_2O) afforded the title product as a white solid (278 mg, 0.86 mmol, 86%). R_f = 0.4 (20:1 pentane:Et_2O). **mp** = 125.2 – 129.6 °C. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.78 (d, *J* = 8.0 Hz, 2H), 7.25 (d, *J* = 7.8 Hz, 2H), 3.32 (td, *J* = 7.6, 4.6 Hz, 1H), 2.33 (dt, *J* = 9.5, 7.6 Hz, 1H), 1.59 (dt, *J* = 9.4, 7.2 Hz, 1H), 1.37 (dt, *J* = 7.2, 3.6 Hz, 1H), 1.34 (s, 12H). **^{11}B NMR** (193 MHz, $CDCl_3$) δ 30.98 (bs). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 140.5, 134.6, 128.7, 83.9, 25.1, 25.0, 24.1, 22.5, 14.4. **HRMS** (ESI): m/z $[M-Br]^+$ calculated for $C_{15}H_{20}O_2B$: 243.1551, found 243.1550.

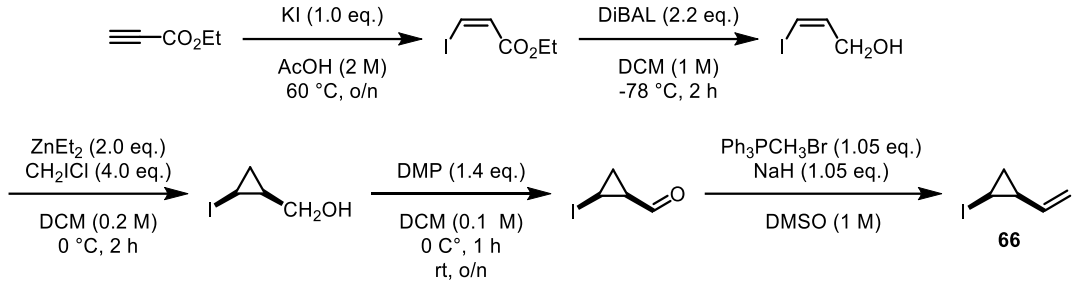
5-(2-bromocyclopropyl)benzo[*d*][1,3]dioxole: General procedure was followed using 5-(2,2-



dibromocyclopropyl)benzo[*d*][1,3]dioxole (6.7 g, 21 mmol). Flash column chromatography (50:1 hexane:EtOAc) afforded the title product as a diastereomeric mixture as a brownish oil (3.85 g, 16.2 mmol, 77%, 57:43 *cis*/*trans* (^{1}H NMR)). R_f = 0.4 (10:1 hexane:EtOAc). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 6.78 (d, *J* = 7.9 Hz, 1H, *cis-isomer*), 6.74 – 6.70 (m, 2H *cis-isomer* + 1H *trans-isomer*), 6.57 (dd, *J* = 7.9, 1.8 Hz, 1H, *trans-isomer*), 6.55 (d, *J* = 1.7 Hz, 1H, *trans-*

isomer), 5.96 (s, 2H, *cis-isomer*), 5.93 (s, 2H, *trans-isomer*), 3.26 (td, *J* = 7.5, 4.5 Hz, 1H, *cis-isomer*), 2.94 (ddd, *J* = 7.7, 4.4, 3.5 Hz, 1H, *trans-isomer*), 2.34 (ddd, *J* = 9.9, 6.5, 3.5 Hz, 1H, *trans-isomer*), 2.23 (dt, *J* = 9.5, 7.5 Hz, 1H, *cis-isomer*), 1.55 (ddd, *J* = 9.6, 7.5, 6.8 Hz, 1H, *cis-isomer*), 1.44 (ddd, *J* = 9.8, 6.7, 4.4 Hz, 1H, *trans-isomer*), 1.38 (dt, *J* = 7.5, 6.6 Hz, 1H, *trans-isomer*), 1.23 (td, *J* = 7.1, 4.5 Hz, 1H, *cis-isomer*). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 148.0, 147.4, 146.6, 146.4, 133.7, 131.2, 122.7, 119.5, 109.8, 108.4, 108.0, 106.7, 101.1, 101.1, 26.8, 24.1, 22.0, 21.6, 18.7, 14.6. **HRMS** (APCI): *m/z* $[M+H]^+$ calculated for $C_{10}H_{10}{}^{79}BrO_2$: 240.9859, found 240.9865.

Synthesis of *cis*-1-iodo-2-vinyl cyclopropane (66)



Ethyl-(*Z*)-3-iodoprop-2-enoate: To a solution of sodium iodide (14.99 g, 100 mmol, 1.0 eq.) in glacial acetic acid (100 mL, 2.0 M), ethyl propiolate (10.13 mL, 100 mmol, 1.0 eq.) was added and heated to 70 °C. The solution was then stirred overnight at 70 °C. After cooling down to room temperature, water was added, and the mixture was extracted with Et_2O (2 x 80 mL). The combined organic extracts were successively washed with KOH (3 M) until pH = 7, and brine, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The title product was obtained without further purification as a colorless oil (20.57 g, 91 mmol, 91%). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.44 (d, *J* = 8.9 Hz, 1H), 6.89 (d, *J* = 8.9 Hz, 1H), 4.25 (q, *J* = 7.1 Hz, 2H), 1.32 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 164.7, 130.1, 94.7, 60.9, 14.3. The data are in agreement with those previously reported in the literature.[143]

(*Z*)-3-Iodoprop-2-en-1-ol: Diisobutylaluminium hydride (88 mL, 1.0 M in hexane, 2.2 eq.) was added dropwise at –78 °C to a stirred solution of ethyl-(*Z*)-3-iodoprop-2-enoate (9.04 g, 40.0 mmol, 1.0 eq.) in DCM (40 mL, 1 M). The mixture was stirred for 2 h at 0 °C and HCl (1 M, 50 mL) was then slowly added. The aqueous layer was extracted with Et_2O (2 x 100 mL) and the combined organic extracts were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. Filtration over a silica pad afforded the title product (6.9 g, 37.5 mmol, 94%) as a yellow oil. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 6.49 (dt, *J* = 7.7, 5.7 Hz, 1H), 6.36 (d, *J* = 7.7 Hz, 1H), 4.24 (t, *J* = 5.1 Hz, 2H), 1.71 (m, *J* = 5.6 Hz, 1H, OH). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 140.0, 82.7, 65.8. The data are in agreement with those previously reported in the literature.[143]

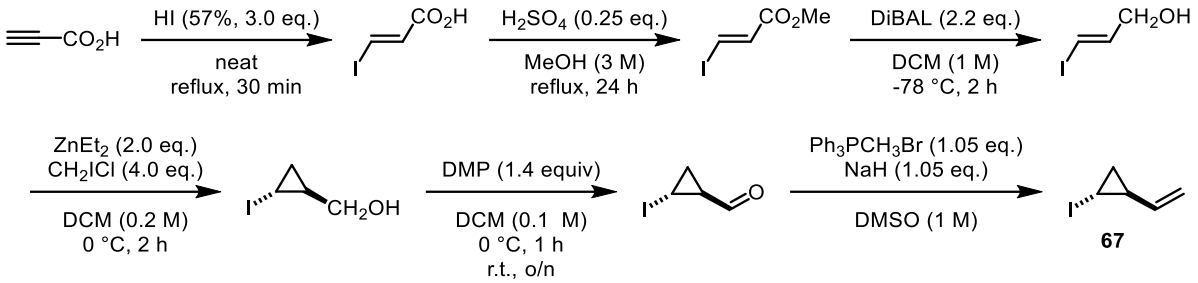
***cis*-(2-Iodocyclopropyl)methanol:** Chloroiodomethane (12.5 mL, 170.9 mmol, 4.0 eq.) was added at 0 °C to a stirred solution of diethylzinc (85.4 mL, 85.4 mmol, 1.0 M in hexane, 2.0 eq.) in DCM (170 mL). After 10 min stirring at 0 °C, a solution of **SI-5** (7.86 g, 42.7 mmol, 1.0 eq.) in DCM (50 mL) was slowly added and the mixture was stirred for 2 h at 0 °C. The reaction was quenched with saturated NH_4Cl solution, and the aqueous layer was extracted with DCM (2 x 100 mL). The combined organic layers were dried over Na_2SO_4

and concentrated. Flash silica gel column chromatography (3:1 hexane:EtOAc) afforded the title product as an orange liquid (4.36 g, 22.1 mmol, 52%). **R_f** (3:1 hexane:EtOAc) = 0.49. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 3.93 (ddd, *J* = 12.5, 7.8, 5.1 Hz, 1H), 3.49 (ddd, *J* = 12.1, 8.7, 3.4 Hz, 1H), 2.61 (td, *J* = 7.5, 4.9 Hz, 1H), 1.82 (s, 1H), 1.32 (ddd, *J* = 9.2, 7.7, 6.3 Hz, 1H), 0.94 (ttd, *J* = 9.0, 6.9, 5.1 Hz, 1H), 0.67 (q, *J* = 6.3 Hz, 1H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 68.1, 17.7, 13.9, -10.3. The data are in agreement with those previously reported in the literature.[144]

***cis*-2-iodocyclopropane-1-carbaldehyde:** *cis*-(2-Iodocyclopropyl)methanol (4.36 g, 22.0 mmol, 1.0 eq.) was weighed into an oven dried flask and dissolved in dry DCM (220 mL, 0.1 M). The solution was cooled to 0 °C before DMP (13.1 g, 30.9 mmol, 1.4 eq.) was added and the reaction mixture was stirred for 1 h at 0 °C before allowing it to warm up to room temperature overnight. The mixture was quenched by adding 50 mL of an aqueous 1:1 mixture of sat. $NaHCO_3$ and sat. $Na_2S_2O_3$. Phases were separated and the aqueous phase was extracted with DCM (3 x 75 mL). The combined organic layers were dried over Na_2SO_4 and concentrated under reduced pressure. Flash silica gel column chromatography (6:1 hexane:EtOAc) afforded the title product as a yellowish oil (3.92 g, 20.3 mmol, 92%). **R_f** (6:1 hexane:EtOAc) = 0.44. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 9.17 – 9.12 (m, 1H), 2.87 – 2.79 (m, 1H), 1.75 – 1.64 (m, 2H), 1.62 – 1.58 (m, 1H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 202.6, 24.4, 16.6, -17.1. **MS** (70eV, EI): *m/z* (%): 195 (36) [M^+], 166 (8), 126 (31), 69 (100). *Note:* The product is volatile and trace solvent impurities could hence not be removed fully. The data are in agreement with those previously reported in the literature.[62]

***cis*-1-Iodo-2-vinylcyclopropane (66):** An oven dried round-bottom flask was charged with sodium hydride (1.02 g, 42.31 mmol, 1.0 eq.) dissolved in DMSO (50 mL) in a glovebox and heated to 70 °C until no solid remained. After cooling to room temperature, Ph_3PCH_3Br (15.11 g, 42.31 mmol, 1.0 eq.) was added and stirred overnight. A solution of *cis*-2-iodocyclopropane-1-carbaldehyde (7.90 g, 40.30 mmol, 1.0 eq.) in DMSO (10 mL) was then added dropwise at room temperature. After stirring overnight, the reaction mixture was treated with water (40 mL) and extracted with pentane (3 x 50 mL). The combined organic phase was dried over Na_2SO_4 and slowly concentrated at 30 °C under slightly reduced pressure. The crude product was filtered over silica gel using a minimal amount of pentane and concentrated again at 30 °C under slightly reduced pressure. Pentane residues were removed by freeze pump thawing to give **66** as a colorless oil (3.85 g, 19.8 mmol, 49%). **R_f** (pentane) = 0.72. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 5.53 (ddd, *J* = 17.0, 10.1, 8.2 Hz, 1H), 5.29 – 5.15 (m, 2H), 2.73 (td, *J* = 7.7, 5.3 Hz, 1H), 1.52 (td, *J* = 8.7, 7.1 Hz, 1H), 1.39 (q, *J* = 7.8 Hz, 1H), 0.84 (t, *J* = 6.1 Hz, 1H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 141.0, 116.4, 19.5, 17.3, -7.7. **MS** (70eV, EI): *m/z* (%): 193 (6) [M^+], 126 (15), 67 (100). **HRMS** (EI, dodecane): *m/z* [M]$^+$ calculated for C_5H_7I: 193.9587, found 193.9589; *m/z* [M-I]$^+$ calculated for C_5H_7: 67.0542, found 67.0542. *Note: The product is volatile and trace solvent impurities could hence not be removed fully.* The data are in agreement with those previously reported in the literature.[62]

Synthesis of *trans*-1-iodo-2-vinyl cyclopropane (67)



Methyl (*E*)-3-iodoacrylate: To aq. HI (57%, 27.8 mL, 210 mmol, 3.0 eq.) was added propiolic acid (3.8 mL, 70 mmol, 1.0 eq.) and the mixture was heated to reflux (ca. 120 °C) for 45 min and then cooled down to room temperature. The solid was filtered off and the grey crystals were washed with water and subsequently dried under vacuum with occasional careful heating using a heat gun to afford crude the title product which was used directly without further purification. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 8.09 (d, *J* = 14.9 Hz, 1H), 6.90 (d, *J* = 14.8 Hz, 1H). *Note*: The acid proton was not observed in ^{1}H NMR due to H-D exchange. **^{13}C NMR** (151 MHz, $CDCl_3$) δ 169.2, 135.8, 103.0. Next, the crude crystals (ca. 9.7 g) were dissolved in MeOH (20 mL) and H_2SO_4 (1 mL) was added at room temperature. The mixture was heated under reflux overnight, cooled to room temperature, and concentrated. The residue was dissolved in water, Et_2O was added and the phases were separated. The aqueous phase was extracted 2 x with Et_2O, and the combined organic phase was washed with aq. $NaHCO_3$, aq. $Na_2S_2O_3$, brine, dried over Na_2SO_4, filtered, and concentrated. The resulting solid was dried under vacuum affording the title product without further purification as an off-white solid (8.2 g, 38.7 mmol, 55% over 2 steps). **R_f** = 0.45 (97:3 pentane:Et_2O) **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.89 (d, *J* = 14.8 Hz, 1H), 6.88 (d, *J* = 14.9 Hz, 1H), 3.75 (s, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 164.8, 136.2, 99.7, 52.1. The data are in agreement with those previously reported in the literature.[145]

(*E*)-3-iodoprop-2-en-1-ol: Diisobutylaluminium hydride (76 mL, 1.0 M in hexane 2.2 eq.) was added dropwise at –78 °C to a stirred solution of (*E*)-3-iodoprop-2-en-1-ol (7.3 g, 34.4 mmol) in DCM (40 mL, 1 M). The mixture was stirred for 1 h at 0 °C and HCl (1 M, 50 mL) was then slowly added. The aqueous layer was extracted with Et_2O (2 x 100 mL) and the combined organic extracts were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude material was purified by a short filtration over a silica pad to give the title product (5.73 g, 31.2 mmol, 90%) as a yellow oil. The product is volatile and was used without further purification. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 6.69 (dt, *J* = 14.6, 5.5 Hz, 1H), 6.39 (d, *J* = 14.5 Hz, 1H), 4.08 (d, *J* = 5.1 Hz, 2H), 1.88 (s, 1H). **MS** (70eV, EI): *m/z* (%): 184 (46) [M^+], 152 (7), 126 (54), 57 (100). The data are in agreement with those previously reported in the literature.[146]

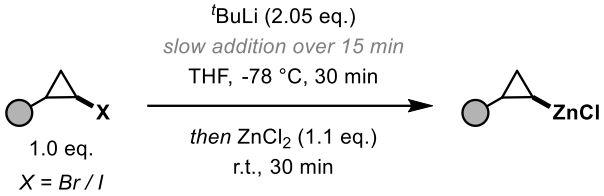
***trans*-(2-iodocyclopropyl)methanol:** Chloroiodomethane (13.8 mL, 124 mmol, 4.0 eq.) was added at 0 °C to a stirred solution of diethylzinc (62 mL, 62 mmol, 1.0 M in hexane, 2.0 eq.) in DCM (170 mL). After 10 min stirring at 0 °C, a solution of (*E*)-3-iodoprop-2-en-1-ol (5.7 g, 31.0 mmol, 1.0 eq.) in DCM (15 mL) was slowly added and the mixture was stirred 2 h at 0 °C. The reaction was quenched with sat. aq. NH_4Cl solution, and the aqueous layer was extracted with DCM (2x100 mL). The combined organic layers were dried over Na_2SO_4 and evaporated at 40 °C under reduced pressure. Flash column chromatography

(hexane/EtOAc 5:1) afforded the title product as a colourless liquid (4.4 g, 22.0 mmol, 71%). R_f = 0.1 (hexane/EtOAc 5:1). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 3.59 (dd, *J* = 11.4, 6.2 Hz, 1H), 3.51 (dd, *J* = 11.5, 6.7 Hz, 1H), 2.26 (dt, *J* = 8.2, 4.3 Hz, 1H), 1.56 (s, 1H), 1.55 – 1.49 (m, 1H), 1.04 – 0.95 (m, 2H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 64.9, 25.5, 14.6, -18.5. **MS** (70eV, EI): *m/z* (%): 198 (100) [M^+], 167 (8), 154 (47), 127 (53), 71 (39). The data are in agreement with those previously reported in the literature.[147]

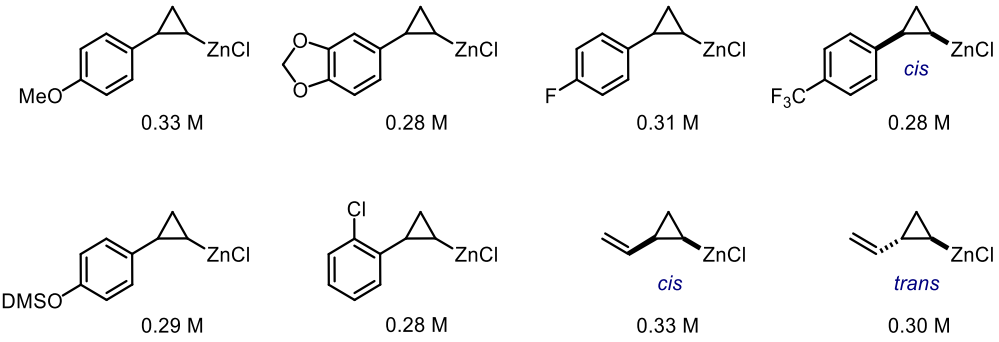
***trans*-2-iodocyclopropane-1-carbaldehyde:** *trans*-(2-iodocyclopropyl)methanol (4.04 g, 20.4 mmol, 1.0 eq.) was weighed into an oven-dried Schlenk flask and dissolved in dry DCM (200 mL, 0.1 M). It was cooled to 0 °C before DMP (12.12 g, 28.6 mmol, 1.4 eq.) was added and the reaction mixture was stirred for 1 h at 0 °C before allowing it to warm up to room temperature overnight. The mixture was quenched by adding 50 mL of an aqueous 1:1 mixture of sat. $NaHCO_3$ and sat. $Na_2S_2O_3$. Phases were separated and the aqueous phase was extracted with DCM (3 x 50 mL). The combined organic layers were dried over Na_2SO_4 and concentrated under reduced pressure (40 °C, 600 mbar). The title product was obtained as a clear oil without further purification (3.5 g, 18 mmol, 88%). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 9.41 (d, *J* = 3.7 Hz, 1H), 2.85 (ddd, *J* = 8.3, 5.8, 3.7 Hz, 1H), 2.29 (ddd, *J* = 9.0, 5.5, 3.7 Hz, 1H), 1.76 (ddd, *J* = 8.3, 5.6 Hz, 1H), 1.52 – 1.44 (m, 1H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 198.6, 33.1, 20.4, -17.7. **MS** (70eV, EI): *m/z* (%): 196 (48) [M^+], 167 (12), 154 (1), 127 (32), 69 (100), 50 (2). *Note: The product is volatile and trace solvent impurities could hence not be removed fully.* The data are in agreement with those previously reported in the literature.[62]

***trans*-1-iodo-2-vinylcyclopropane (67):** To dry DMSO (9 mL) was added NaH (90% in mineral oil, 505 mg, 19 mmol, 1.06 eq.) in small portions. The suspension was stirred at 80 °C for 30 min, then cooled down to room temperature and a solution of PPh_3MeBr (6.9 g, 19 mmol, 1.06 eq.) in dry DMSO (18 mL) was added and the yellow mixture was stirred at room temperature for 1 h. Then, neat *trans*-2-iodocyclopropane-1-carbaldehyde (3.5 g, 18 mmol, 1.0 eq.) was added slowly and the resulting mixture stirred at room temperature for 3 h. Pentane (10 mL) was added, the mixture was vigorously stirred, and subsequently the phases were separated. The DMSO phase was extracted with pentane (2 x 10 mL) and the combined pentane layers were dried over Na_2SO_4, filtered and carefully concentrated until most of the pentane was removed. Alternatively, the organic phase can also be used as received for the next step. **67** was obtained as a colourless solution in pentane (1.9 g, 40% in pentane, 21% yield). R_f = 0.8 (pentane). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 5.41 (ddd, *J* = 17.1, 10.3, 8.3 Hz, 1H), 5.13 (d, *J* = 17.0 Hz, 1H), 5.01 (dd, *J* = 10.3, 1.3 Hz, 1H), 2.33 – 2.28 (m, 1H), 1.86 – 1.79 (m, 1H), 1.16 (dd, *J* = 8.0, 5.9 Hz, 2H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 138.3, 114.8, 26.8, 18.4, -14.6. **MS** (70eV, EI): *m/z* (%): 194 (3) [M^+], 127 (15), 67 (100), 65 (12). **HRMS** (EI, dodecane): *m/z* $[M]^+$ calculated for C_5H_7I 193.9587, found 193.9587; *m/z* $[M\text{-}I]^+$ calculated for C_5H_7 67.0542, found 67.0542. *Note: The product is even more volatile than the corresponding cis-isomer **66**.* The data are in agreement with those previously reported in the literature.[62]

Synthesis of cyclopropyl organozinc



An oven dried Schlenk flask equipped with a magnetic stir bar was evacuated and backfilled with argon three times. The appropriate cyclopropyl halide (1.0 eq.) was added, dissolved in dry THF (1 M) and cooled to -78 °C. Next, *t*BuLi (2.05 eq., 1.7 M in hexane) was added dropwise over a period of 15 min using a syringe pump. After complete addition the mixture was stirred for further 30 min at –78 °C before a solution of $ZnCl_2$ (1.1 eq., 1 M in THF, see below) was added. The mixture was allowed to warm up to room temperature and stirred for additional 30 minutes. Titration was performed with iodine following Knochel's protocol.[134] *Note: The cyclopropyl organozinc were stored at room temperature in an argon filled glove box over several weeks without decomposition.*

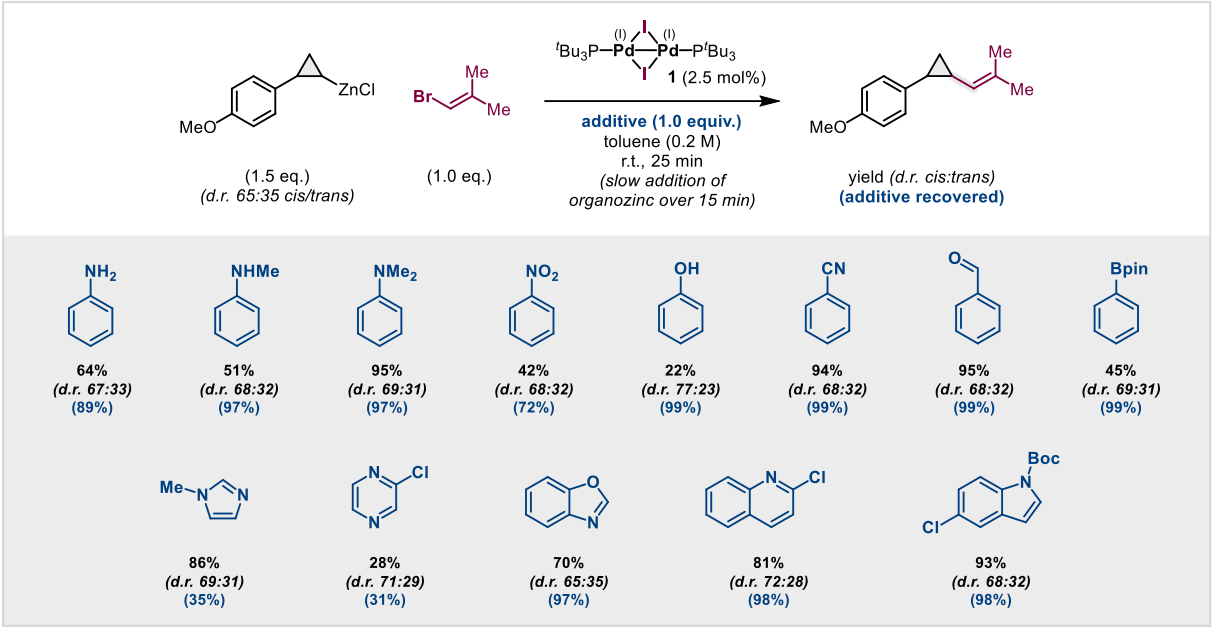


5.3.4 Compatibility screen

The functional group tolerance of the $Pd^{(I)}$ coupling strategy was further assessed by performing a compatibility screen.[89] Therefore, the cross-coupling was demonstrated in the presence of various additives (arenes containing amine, nitro, aldehyde, nitrile, OH, Bpin functionalities, or heterocycles) and analyzed for product yield and recovered additive. The results are shown in **Table 2**, indicating a broad substrate scope could be feasible.

Experimental procedure: Following general procedure A using vinyl bromide (0.1 mmol, 1.0 eq.) and a suspension of freshly prepared (2-(4-methoxyphenyl)cyclopropyl)zinc chloride (1.5 or 2.0 eq., *d.r. 65:35 cis/trans*). Furthermore, an additive (0.1 mmol, 1.0 eq.) was added to the reaction mixture before zinc addition. The tolerance of the reaction towards each additive was assessed by quantification of product yield, the diastereomeric ratio of the product *d.r. cis/trans cyclopropane, E/Z alkene),* and remaining additive using quantitative ^{1}H NMR using mesitylene as internal standard (0.1 mmol, 1.0 eq.).

Table 2 | Compatibility screen to assess various functional groups in the cross-coupling.



5.3.5 Mechanistical investigation

In the $Pd^{(I)}$ catalysis concept, the order of the elementary steps is reversed. The first step involves the transmetallation towards the "mixed" $Pd^{(I)}$ dimer, which is associated with different driving forces at $Pd^{(I)}$ than exchange at $Pd^{(II)}$. The second step involves the oxidative addition of the electrophile to the "mixed" $Pd^{(I)}$ dimer. Furthermore, no reactivity between the electrophile and the $Pd^{(I)}$ dimer is observed unless nucleophilic activation takes place. Mechanistical investigation data is shown below (**Figure 2–4**). The NMR studies are consistent with this dinuclear $Pd^{(I)}$ catalysis concept: No reactivity between $Pd^{(I)}$ dimer **1** and alkenyl bromide is observed while $Pd^{(I)}$ dimer **1** is rapidly consumed once organozinc is added. A structural characterization of the formed species is challenging however, as it is short-lived at r.t. (less than 2 min) generating unreactive *bis*-ligated $Pd^{(0)}(PtBu_3)_2$ and palladium black. The liberation of a low valent $Pd^{(0)}$ species, *e.g.* $Pd^{(0)}(PtBu_3)$, cannot be unambiguously ruled out in the case of vinylcyclopropane formation and is a mechanistic alternative.

Experimental procedure: Inside an argon filled glove box $Pd^{(I)}$ dimer **1** (22 mg, 0.025 mmol, 1.0 eq.) was placed to an oven dried 4 ml screw top vial and THF-d_8 (0.6 mL) was added. The vial was gently shaken until all palladium complex was dissolved and the solution was then transferred into an oven dried NMR tube and closed with a Teflon septum. Next, a solution of 1-bromo-2-methylprop-1-ene (3.4 mg, 0.025 mmol, 1.0 eq.) in THF-d_8 (0.3 mL) was added and NMR spectra were recorded after 2 and 20 minutes (**Figure 2** and **Figure 3**).

Figure 2 | ^{1}H NMR of $Pd^{(I)}$ dimer **1** in presence of vinyl bromide.

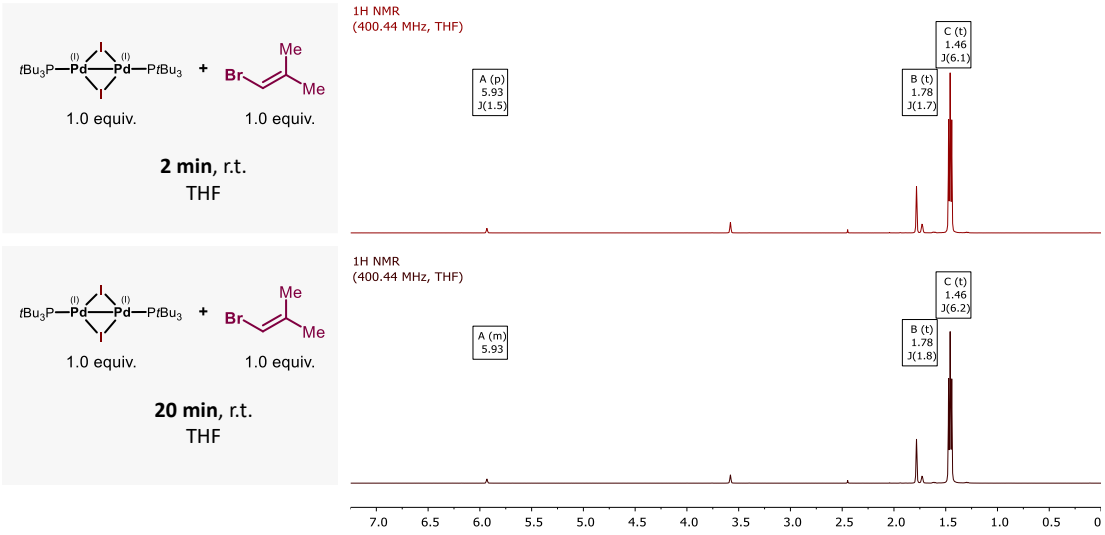
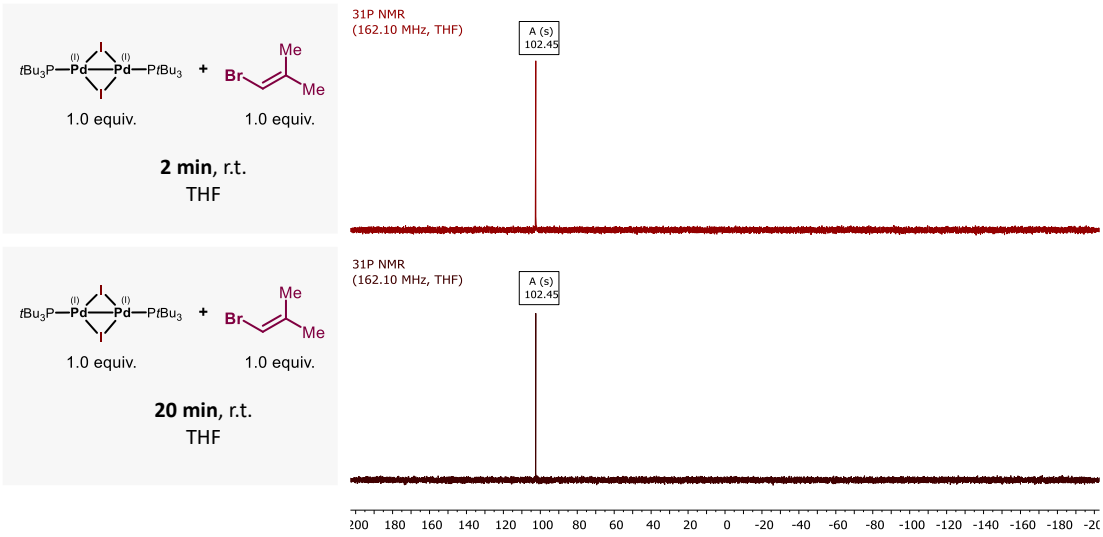
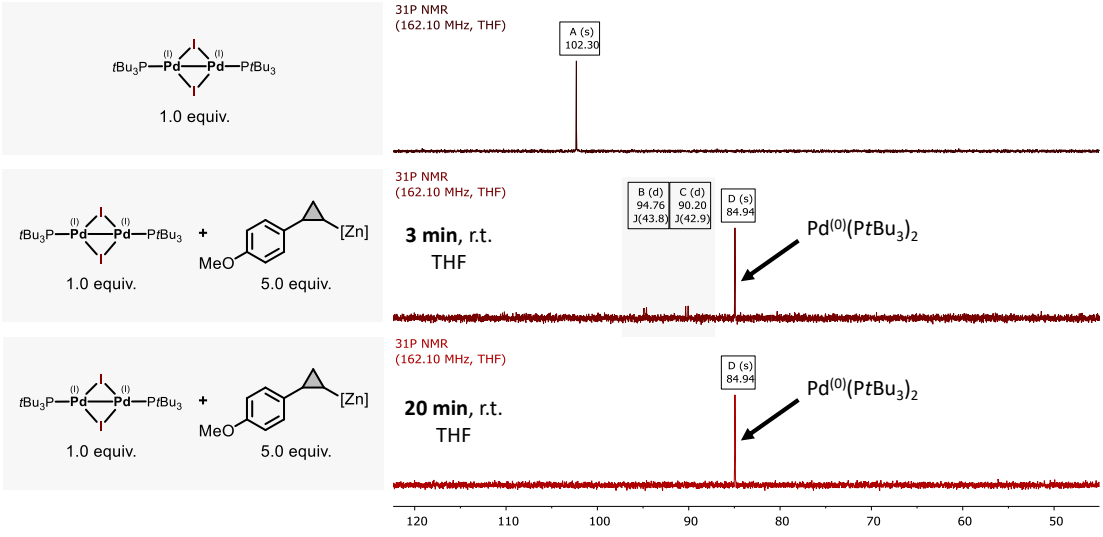


Figure 3 | ^{31}P NMR of Pd$^{(I)}$ dimer **1** in presence of vinyl bromide.



Experimental procedure: Inside an argon filled glove box Pd$^{(I)}$ dimer **1** (22 mg, 0.025 mmol) was placed to an oven dried 4 mL screw top vial equipped with a magnetic stir bar and THF-d_8 (0.6 mL) was added. Next, a suspension of (2-(4-methoxyphenyl)cyclopropyl)zinc chloride (0.42 mL, 0.125 mmol, 5.0 eq.) was added at once. The mixture was gently stirred for one minute before it was transferred to an oven dried NMR tube and closed with a Teflon septum. ^{31}P NMR spectra were recorded after 3 and 20 minutes. An instantaneous consumption of Pd$^{(I)}$ dimer and formation of Pd$^{(0)}$(P*t*Bu$_3$)$_2$ was observed (**Figure 4**).

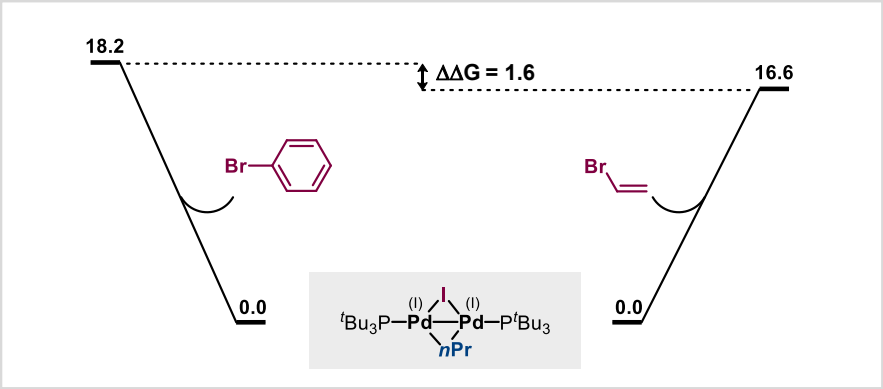
Figure 4 | ^{31}P NMR of Pd$^{(I)}$ dimer **1** before (top) and after (3 min, middle and 20 min, bottom) addition of organozinc.



5.3.6 Computational details

DFT calculations were performed using Gaussian 16, Revision A.03.[148] Geometry optimization was conducted in the gas-phase at the ωB97XD/6-31G(d) level of theory employing LANL2DZ as an ECP for palladium and iodine. Frequencies were calculated at the same level of theory and used to verify the nature of all stationary points as either minima (no imaginary frequencies) or transition states (one imaginary frequency). Additionally, transition states were confirmed by following the intrinsic reaction coordinate (IRC) to their corresponding intermediates. Single point energies were calculated at the M06L/def2-TZVP level of theory employing the CPCM solvation model for toluene. All energies were corrected to 1M standard state (addition of 1.89 kcal/mol to every species). Images were created using the CYLview software.[149] Initial coordinates were extracted from the Ph.D. thesis of Dr. Theresa Sperger.[150]

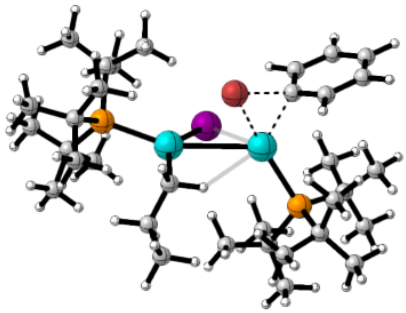
Figure 5 | Calculated Gibbs free energy for oxidative addition of phenyl bromide (left) and vinyl bromide (right) to mixed iodo and *n*-propyl bridged Pd(I) dimer.[a]



[a]Values are given kcal mol^{-1} and refer to Gibbs free energies calculated at the CPCM (toluene) M06L/def2-TZVP//ωB97XD/6-31G(d)(LANL2DZ, Pd, I) level of theory. Initial coordinates were extracted from the Ph.D. thesis of Dr. Theresa Sperger.[150]

XYZ coordinates and energies for optimized structures

Oxidative addition to phenyl bromide

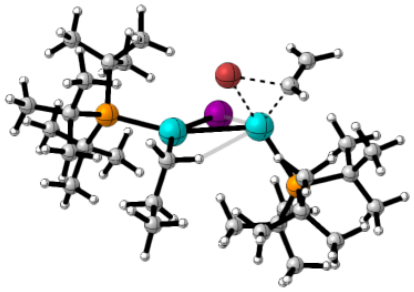


C	4.05843	-4.23454	-0.36019
C	2.97287	-2.68481	-1.86833
C	1.97925	-2.46661	-0.90562
C	1.96345	-3.20425	0.28569
H	1.14582	-3.08859	0.98906
H	2.92982	-2.16814	-2.81941
C	3.03202	-4.05488	0.56291
C	4.01472	-3.55704	-1.57960
H	3.04390	-4.59346	1.50603
H	4.79923	-3.70696	-2.31606
Pd	1.51720	-0.46232	-0.26182
Pd	-1.47872	0.31063	-0.00521
Br	0.08983	-1.94539	-1.72473
H	4.87702	-4.91325	-0.14223
H	3.32904	2.87588	-3.26228
C	2.99818	2.69304	-2.23191
C	3.99811	1.73509	-1.55873
H	2.00122	2.24260	-2.28272
H	2.92309	3.66520	-1.74096
P	3.27221	1.12567	0.11571
C	5.37454	2.41699	-1.50155
C	4.08104	0.53052	-2.51763
C	2.68934	2.68012	1.08545
C	4.69189	0.31853	1.12299
H	6.16611	1.72267	-1.20933
H	5.62917	2.78999	-2.50249
H	5.39975	3.26865	-0.81883
H	4.71745	-0.27717	-2.15760
H	3.08274	0.11832	-2.69101
H	4.48590	0.87345	-3.47931
C	3.60266	3.91415	0.99801
C	1.28523	3.05148	0.56976
C	2.49108	2.34225	2.57469
C	4.05852	-0.51853	2.25470
C	5.43619	-0.69454	0.23597
C	5.72815	1.28071	1.72639
H	4.62099	3.70528	1.33493
H	3.65606	4.33280	-0.00949
H	3.19654	4.69853	1.65003
H	0.57978	2.23637	0.76333
H	0.92833	3.93786	1.11153
H	1.25530	3.28280	-0.49482

H	1.96883	3.18336	3.04857
H	1.86678	1.45573	2.71115
H	3.43166	2.20688	3.11227
H	3.50549	0.07353	2.98261
H	3.37638	-1.27237	1.85153
H	4.86212	-1.03909	2.79252
H	6.05784	-0.22017	-0.52749
H	6.10518	-1.28668	0.87319
H	4.74567	-1.39067	-0.24633
H	6.51508	0.68951	2.21294
H	6.21021	1.90856	0.97336
H	5.30116	1.93320	2.49087
P	-3.82227	0.10949	-0.07567
C	-4.64360	1.36852	1.11654
C	-4.72726	0.20608	-1.77921
C	-4.15136	-1.67419	0.62282
C	-6.04316	0.96894	1.61809
C	-3.71064	1.57617	2.32577
C	-4.77451	2.74473	0.44167
C	-4.37005	1.47305	-2.58262
C	-4.24363	-0.97323	-2.64532
C	-6.26706	0.19797	-1.69518
C	-3.94889	-1.73650	2.14889
C	-5.55580	-2.24040	0.34400
C	-3.10547	-2.63731	0.02300
H	-6.75527	0.81196	0.80569
H	-6.03335	0.07483	2.24167
H	-6.43118	1.78694	2.23802
H	-2.73912	1.97257	2.01476
H	-4.17791	2.30378	3.00162
H	-3.52077	0.66736	2.89526
H	-5.06497	3.47354	1.20812
H	-3.82776	3.08313	0.01466
H	-5.54861	2.76719	-0.32895
H	-4.59005	2.40205	-2.06021
H	-3.32936	1.48546	-2.89513
H	-4.97999	1.46561	-3.49463
H	-4.62863	-1.93900	-2.31524
H	-4.59630	-0.81880	-3.67244
H	-3.14959	-1.02602	-2.67462
H	-6.66366	0.07113	-2.71045
H	-6.68294	-0.59852	-1.08300
H	-6.64960	1.15223	-1.32209
H	-2.97960	-1.34605	2.45795
H	-4.73684	-1.23317	2.71143
H	-3.97286	-2.79360	2.44039
H	-5.74663	-2.42232	-0.71510
H	-5.62805	-3.21089	0.84974
H	-6.35449	-1.61070	0.74374
H	-3.34417	-3.65483	0.35741
H	-3.08376	-2.64619	-1.06682
H	-2.09920	-2.40160	0.37656
I	-0.31479	-0.57697	2.36612
C	-1.18442	1.44685	-1.64413
H	-1.57151	0.99726	-2.56270
H	-0.09233	1.29068	-1.63926
C	-1.50751	2.92440	-1.52054
H	-1.15513	3.30668	-0.55574
H	-2.58595	3.08902	-1.54528
C	-0.86630	3.73324	-2.65543
H	-1.11077	4.79713	-2.56409
H	0.22453	3.63606	-2.64740
H	-1.22317	3.38521	-3.63197

Zero-point correction = 0.945153 (Hartree/Particle)
Thermal correction to Energy = 0.998989
Thermal correction to Enthalpy = 0.999933
Thermal correction to Gibbs Free Energy = 0.859419
Sum of electronic and zero-point Energies = -4817.441958
Sum of electronic and thermal Energies = -4817.388123
Sum of electronic and thermal Enthalpies = -4817.387178
E(M06L) = -5108.34751208

Oxidative addition to vinyl bromide



C	2.20282	-1.59409	-2.32179
C	2.44025	-2.89574	-2.07942
H	1.73808	-3.52262	-1.53887
Pd	1.56492	-0.75124	-0.54018
Pd	-1.20954	0.18410	0.00038
Br	0.13948	-1.04254	-2.66074
H	2.95098	3.86599	-1.38042
C	2.85175	3.12928	-0.57293
C	3.88405	2.01085	-0.79617
H	1.83118	2.73861	-0.60482
H	2.99411	3.66454	0.36793
P	3.43980	0.51114	0.32111
C	5.28882	2.61030	-0.61961
C	3.70081	1.58979	-2.26833
C	3.14037	1.18839	2.09846
C	4.98386	-0.63575	0.39976
H	6.07859	1.92608	-0.93798
H	5.37216	3.50922	-1.24481
H	5.49322	2.90865	0.41091
H	4.35548	0.77203	-2.57146
H	2.66518	1.29021	-2.45804
H	3.93036	2.44870	-2.91242
C	4.13248	2.25175	2.60001
C	1.72121	1.78813	2.16840
C	3.14524	0.01472	3.09600
C	4.53266	-2.01724	0.92166
C	5.51710	-0.88914	-1.02303
C	6.15811	-0.13982	1.25987
H	5.16998	1.91264	2.57595
H	4.06607	3.18568	2.03653
H	3.88993	2.49082	3.64377
H	0.96771	1.08633	1.79827
H	1.48350	2.00840	3.21713
H	1.63067	2.72239	1.61527
H	2.78072	0.38242	4.06325
H	2.47544	-0.78972	2.78015
H	4.14367	-0.39312	3.26615
H	4.15115	-1.99456	1.94157
H	3.75502	-2.44622	0.28394
H	5.39788	-2.69357	0.90788
H	5.99982	-0.01453	-1.46396
H	6.27435	-1.68167	-0.97050
H	4.72788	-1.23791	-1.69258
H	6.99560	-0.84110	1.14853
H	6.51660	0.84753	0.95931
H	5.91191	-0.10619	2.32330
P	-3.57004	0.26058	0.14957
C	-4.11862	0.74729	1.92279
C	-4.57116	1.34048	-1.10297
C	-4.10504	-1.58008	-0.16484
C	-5.52841	0.27333	2.31966
C	-3.09762	0.18239	2.92909
C	-4.07708	2.27591	2.09359
C	-4.10020	2.80960	-1.15891
C	-4.33279	0.78015	-2.51929
C	-6.08639	1.41438	-0.82272
C	-3.82324	-2.47479	1.05702
C	-5.58895	-1.78934	-0.51829
C	-3.23662	-2.14451	-1.30931
H	-6.30606	0.64363	1.64958

H	-5.61128	-0.81272	2.37193
H	-5.75068	0.65980	3.32231
H	-2.09760	0.59112	2.75522
H	-3.41418	0.47058	3.93968
H	-3.01338	-0.90322	2.90488
H	-4.19154	2.50376	3.16031
H	-3.12067	2.69798	1.77275
H	-4.89069	2.78295	1.56993
H	-4.10945	3.31590	-0.19594
H	-3.11076	2.91228	-1.59409
H	-4.79542	3.35030	-1.81324
H	-4.84037	-0.16849	-2.69921
H	-4.72522	1.49969	-3.24832
H	-3.26609	0.64545	-2.72724
H	-6.57125	1.87525	-1.69259
H	-6.56540	0.45248	-0.65706
H	-6.30017	2.05660	0.03634
H	-2.79221	-2.40139	1.40003
H	-4.49621	-2.28611	1.89522
H	-3.98138	-3.51484	0.74674
H	-5.87626	-1.34659	-1.47328
H	-5.75958	-2.86914	-0.60632
H	-6.26354	-1.42106	0.25893
H	-3.58546	-3.15924	-1.53904
H	-3.28656	-1.56320	-2.23054
H	-2.18668	-2.21597	-1.01441
I	-0.08577	-1.90067	1.53172
C	-0.93022	1.88795	-1.03922
H	0.08833	1.65451	-1.38083
H	-1.55999	1.95257	-1.92970
C	-0.93397	3.16246	-0.21236
H	-1.90304	3.32086	0.26596
H	-0.20455	3.07543	0.59934
C	-0.60387	4.38932	-1.07291
H	-1.37263	4.54716	-1.83876
H	-0.54628	5.29552	-0.46014
H	0.35457	4.26645	-1.58840
H	2.80806	-0.98190	-2.98198
H	3.37403	-3.34403	-2.41172

Zero-point correction = 0.896642 (Hartree/Particle)
Thermal correction to Energy = 0.947805
Thermal correction to Enthalpy = 0.948749
Thermal correction to Gibbs Free Energy = 0.815887
Sum of electronic and zero-point Energies = -4663.887296
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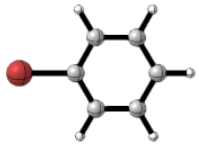
Sum of electronic and thermal Enthalpies = -4663.835189
E(M06L) = -4954.66093582

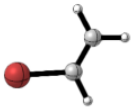
Phenyl bromide



C	-0.00000	-0.00000	-0.09703
C	-0.00000	-1.21185	-0.77826
C	0.00000	1.21185	-0.77826
C	-0.00000	-1.20454	-2.17007
C	0.00000	1.20454	-2.17007
C	-0.00000	-0.00000	-2.86804
H	-0.00000	-2.14617	-0.22758
H	0.00000	2.14617	-0.22758
H	-0.00000	-2.14795	-2.70739
H	0.00000	2.14795	-2.70739
H	-0.00000	-0.00000	-3.95348
Br	0.00000	0.00000	1.79982

Zero-point correction = 0.091965 (Hartree/Particle)
Thermal correction to Energy = 0.097582
Thermal correction to Enthalpy = 0.098526
Thermal correction to Gibbs Free Energy = 0.061817
Sum of electronic and zero-point Energies = -2803.203284
Sum of electronic and thermal Energies = -2803.197667
Sum of electronic and thermal Enthalpies = -2803.196723
E(M06L) = -2805.75812311

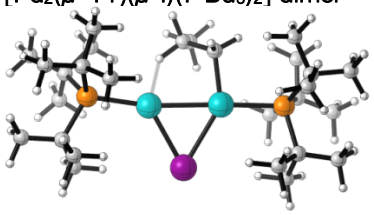
Vinyl bromide



C	-2.10047	-0.31327	0.00001
C	-1.07836	0.52799	0.00002
H	-1.96856	-1.39006	-0.00001
Br	0.72384	-0.04513	-0.00001
H	-1.17809	1.60670	0.00003
H	-3.11474	0.07455	0.00002

Zero-point correction = 0.042798 (Hartree/Particle)
Thermal correction to Energy = 0.046417
Thermal correction to Enthalpy = 0.047361
Thermal correction to Gibbs Free Energy = 0.016183
Sum of electronic and zero-point Energies = -2649.643225
Sum of electronic and thermal Energies = -2649.639606
Sum of electronic and thermal Enthalpies = -2649.638662
E(M06L) = -2652.06691900

[$Pd_2(\mu\text{-}^n Pr)(\mu\text{-}I)(P^tBu_3)_2$] dimer[150]



Pd	1.31075400	0.15395000	0.06392600
Pd	-1.41109700	0.01567200	-0.21562300
I	0.01845500	-2.26219600	-0.40559900
P	-3.77006200	0.18955800	0.12278700
C	-4.62751600	-1.52536100	0.19910400
C	-3.98295700	1.04129300	1.83556200
C	-4.68893000	1.25304600	-1.18375600
C	-6.16452100	-1.51927400	0.21056800
C	-4.14493500	-2.37208200	-0.99801500
C	-4.12625400	-2.26925300	1.45129000
C	-2.90745800	0.47243900	2.78789500
C	-3.64811200	2.53958400	1.70883000
C	-5.36006400	0.90974400	2.50418700
C	-4.87518400	0.43270600	-2.47366200
C	-6.05786300	1.81451500	-0.76779900
C	-3.75894100	2.41612700	-1.58785400
H	-6.58437700	-1.14503100	-0.72681200
H	-6.52240800	-2.55010200	0.33207700
H	-6.58211400	-0.92889600	1.02934400
H	-3.05318900	-2.39952000	-1.05031700
H	-4.50518000	-3.40016500	-0.86318000
H	-4.52510900	-2.02238800	-1.95736800
H	-4.45335100	-3.31450600	1.38904800
H	-3.03235500	-2.26796700	1.50674900
H	-4.53382100	-1.86244400	2.37964800
H	-3.03956800	-0.58505300	3.01325000
H	-1.90329100	0.59648800	2.36486000
H	-2.95242700	1.02120900	3.73815400
H	-4.39926300	3.10575600	1.15447800
H	-3.59883100	2.97129900	2.71649400
H	-2.67140400	2.69342100	1.23864200
H	-5.36650100	1.49921900	3.43070300
H	-6.17158400	1.28102700	1.87340400
H	-5.58851800	-0.12222200	2.78138600
H	-3.94149500	-0.04827400	-2.78340000
H	-5.18162800	1.11356900	-3.27804900
H	-5.65308700	-0.32851200	-2.38531600
H	-5.98279400	2.54768000	0.03893900

H	-6.51166200	2.32709900	-1.62639900
H	-6.75059500	1.03141300	-0.44995600
H	-2.83278500	2.02652100	-2.02219300
H	-4.26274400	3.02559800	-2.34969100
H	-3.49092900	3.07731200	-0.76340700
P	3.70238600	0.21139600	0.16232400
C	4.29991900	-1.61171500	0.38177500
C	4.31716300	0.83497400	-1.54856000
C	4.56794900	1.24834300	1.53242300
C	5.80128400	-1.79128400	0.67110700
C	3.51103100	-2.27278000	1.53327600
C	3.97055200	-2.42450700	-0.88556400
C	3.34326500	0.31367000	-2.62631100
C	4.23033900	2.37094400	-1.61749100
C	5.74946100	0.42845000	-1.93470200
C	4.37956000	0.55102000	2.89301700
C	6.06955700	1.50217000	1.30889900
C	3.88099900	2.61757800	1.69507500
H	6.09184200	-1.40290700	1.64965700
H	6.01993100	-2.86649800	0.67974200
H	6.44303000	-1.33589800	-0.08603800
H	2.43159000	-2.19617200	1.38665300
H	3.76638300	-3.33959200	1.55357000
H	3.75498900	-1.86502800	2.51348300
H	4.14560300	-3.48441100	-0.66565700
H	2.92323000	-2.32551400	-1.18060500
H	4.60820500	-2.16565700	-1.73332600
H	3.32432500	-0.77253600	-2.70813500
H	2.32024400	0.64708800	-2.42622900
H	3.65158300	0.71553500	-3.60006700
H	4.96396000	2.87209300	-0.98242500
H	4.43575000	2.67924300	-2.65002300
H	3.23126100	2.73496100	-1.36573400
H	5.99698600	0.89644800	-2.89608300
H	6.49489800	0.76099000	-1.20899500
H	5.85775100	-0.64936300	-2.06882000
H	3.33454200	0.27037600	3.06188600
H	4.66575700	1.25507000	3.68409200
H	5.00698000	-0.33360100	3.01138200
H	6.25190200	2.17967100	0.47100800
H	6.47710300	1.98638700	2.20572100
H	6.64394300	0.59064500	1.14125200
H	3.86583800	3.21744200	0.78534200
H	2.85714400	2.50398600	2.05357400
H	4.43590000	3.18822600	2.45063400
C	0.96772200	2.16719100	0.33546200
H	-1.09017000	1.87655300	-0.38787800
H	0.78884700	2.23873800	1.41526100
C	-0.22655100	2.60929400	-0.45947900
H	1.84579600	2.75149700	0.06826300
H	-0.67690700	3.49439200	0.01699100
C	0.05904500	2.88694800	-1.93145800
H	-0.83377100	3.24901100	-2.45119900
H	0.84236300	3.64763000	-2.03795700
H	0.39561200	1.97544000	-2.43521900

Zero-point correction = 0.850938 (Hartree/Particle)
Thermal correction to Energy = 0.897931
Thermal correction to Enthalpy = 0.898875
Thermal correction to Gibbs Free Energy = 0.772662
Sum of electronic and zero-point Energies = -2012.144960
Sum of electronic and thermal Energies = -2012.097967
Sum of electronic and thermal Enthalpies = -2012.097023
Sum of electronic and thermal Free Energies = -2012.223236
E(RM06L) = -2302.59647674

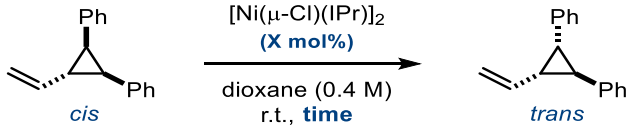
5.4 Supporting information for chapter 4

5.4.1 $Ni^{(I)}$ vinylcyclopropane isomerization

5.4.1.1 Reaction optimization

Experimental procedure: All reactions were carried out inside an argon-filled glovebox. A 4 mL screw-cap vial equipped with a Teflon-coated magnetic stir bar was sequentially charged with the corresponding cyclopropane substrate (1.0 equiv.), anhydrous 1,4-dioxane (0.4 M) and $[Ni(\mu\text{-}Cl)(IPr)]_2$, in that order. The reaction vial was then sealed and allowed to stir inside the glovebox at the indicated temperature. After the indicated time the reaction mixture was removed from the glovebox and was quenched by the addition of wet pentane. A spatula tip of ammonium pyrrolidine-1-dithiocarboxylic acid was added and the mixture stirred for additional 15 min to precipitate nickel.[60] The resulting mixture was filtered through a plug of silica, washing with Et_2O or EtOAc or MeCN and the filtrate was concentrated under reduced pressure. The crude material was analyzed by quantitative ^1H NMR (10 s relaxation delay).

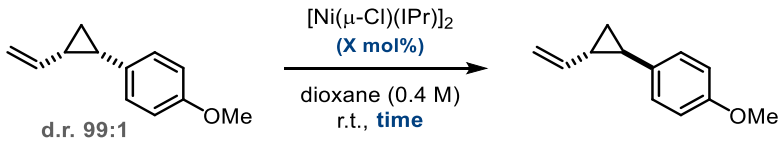
Table 3 | Reaction optimization of diphenyl vinylcyclopropane.



entry	catalyst loading	time	d.r. (*cis*:*trans*)	Yield[a]
1	1 mol%	15 min	74:26	n.d.
2	2 mol%	1 h	33:67	n.d.
3	2 mol%	2 h	24:76	n.d.
4	5 mol%	2 h	17:83	n.d.
5	**5 mol%**	**6 h**	**11:89**	**96%**
6	5 mol%	9 h	11:89	n.d.
7[b]	5 mol%	24 h	12:88	n.d.

a) isolated yield; b) reaction temperature at 60 °C. n.d. = not determined.

Table 4 | Reaction optimization of vinylcyclopropyl arenes.

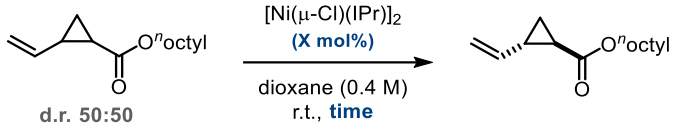


entry	catalyst loading	time	d.r. (*cis*:*trans*)
1	5 mol%	15 min	10:90
2	2.5 mol%	15 min	10:90
3	1 mol%	15 min	10:90
4	5 mol%	5 min	10:90
5	**1 mol%**	**5 min**	**10:90 (98%)[c]**
6[a]	1 mol%	5 min	16:84

7[a]	1 mol%	2 min	22:78
8	1 mol%	2 min	16:84
9	5 mol%	24 h	10:90
10[b]	5 mol%	24 h	12:88

a) THF (0.4 M) was used as solvent; b) 60 °C reaction temperature; c) isolated yield.

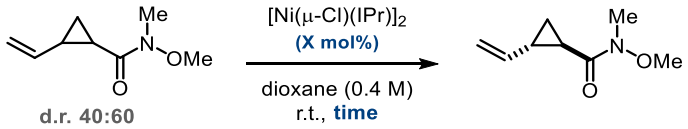
Table 5 | Reaction optimization of vinylcyclopropyl esters.



entry	catalyst loading	time	d.r. (*cis*:*trans*)
1	5 mol%	15 min	80:20
2	5 mol%	30 min	16:84
3	**5 mol%**	**60 min**	**9:91 (94%)[a]**
4	5 mol%	24 h	9:91
5[b]	**5 mol%**	**15 min**	**9:91 (96%)[a]**

a) isolated yield; b) vinylcyclopropyl ketone was applied as starting material.

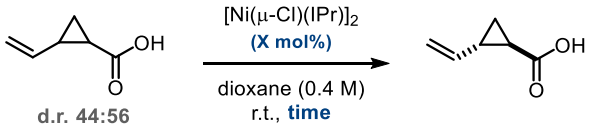
Table 6 | Reaction optimization of vinylcyclopropyl amides.



entry	catalyst loading	time	d.r. (*cis*:*trans*)
1	5 mol%	15 min	17:83
2	5 mol%	30 min	16:84
3	**5 mol%**	**60 min**	**9:91 (97%)[a]**
4	5 mol%	24 h	9:91

a) isolated yield.

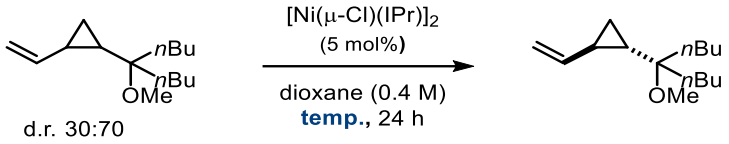
Table 7 | Reaction optimization of vinylcyclopropyl carboxylic acid.



entry	catalyst loading	time	d.r. (*cis*:*trans*)
1	1 mol%	5 min	35:65
2	5 mol%	5 min	31:69
3	1 mol%	15 min	35:65
4	**5 mol%**	**15 min**	**25:75 (94%)[a]**
5	5 mol%	36 h	25:75 (80%)[a]

a) isolated yield.

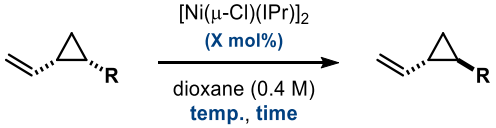
Table 8 | Reaction optimization of vinylcyclopropyl alkyl.



entry	catalyst loading	temperature	d.r. (*cis*:*trans*)
1	5 mol%	45 °C	15:85
2	**5 mol%**	**60 °C**	**1:99 (96%)[a]**

a) isolated yield.

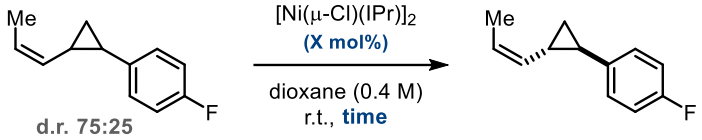
Table 9 | Reaction optimization of vinylcyclopropyl alkylgermane and -boronates.



entry	R (d.r. *cis*:*trans*)	catalyst loading	temperature	time	d.r. (*cis*:*trans*)
1	$GeEt_3$ (100:0)	5 mol%	r.t.	15 min	100:0
2	$GeEt_3$ (100:0)	5 mol%	r.t.	2 h	90:10
3	$GeEt_3$ (100:0)	5 mol%	r.t.	14 h	54:46
4	**$GeEt_3$ (100:0)**	**5 mol%**	**r.t.**	**24 h**	**10:90 (96%)[a]**
5	BMIDA (35:65)	5 mol%	r.t.	24 h	35:65
6	BMIDA (35:65)	5 mol%	60 °C	24 h	22:78
7	**BMIDA (35:65)**	**5 mol%**	**60 °C**	**72 h**	**12:88 (95%)[a]**
8	BPin (41:59)	5 mol%	60 °C	72 h	21:79 (82%)[a]
9[b]	**BPin (41:59)**	**5 mol%**	**60 °C**	**72 h**	**22:78 (88%)[a]**

a) isolated yield; b) addition of 10 mol% pyridine.

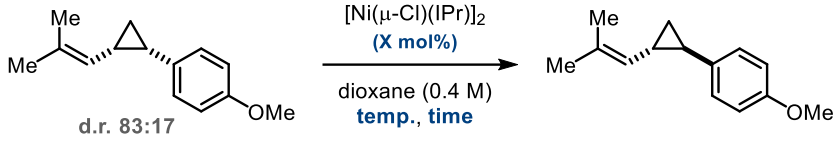
Table 10 | Reaction optimization of *Z*-alkenylcyclopropyl benzene.



entry	catalyst loading	time	d.r. (*cis*:*trans*)
1	1 mol%	5 min	70:30
2	1 mol%	2 h	40:60
3	5 mol%	1 h	22:78
4	**5 mol%**	**2 h**	**11:89 (96%)[a]**
5	5 mol%	24 h	11:89 (88%)[a]

a) isolated yield.

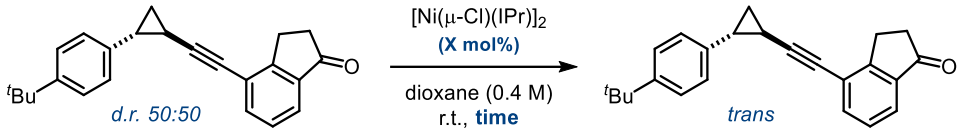
Table 11. Reaction optimization of higher substituted alkenylcyclopropyl benzenes.



entry	catalyst loading	temperature	time	d.r. (*cis*:*trans*)
1	5 mol%	r.t.	2 h	83:17
2	5 mol%	r.t.	24 h	79:21
3	5 mol%	r.t.	48 h	76:24
4	5 mol%	60 °C	72 h	28:72
5	**10 mol%**	**60 °C**	**72 h**	**18:82 (91%)[a]**

a) isolated yield.

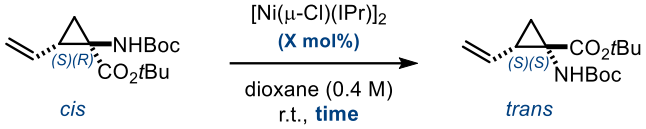
Table 12. Reaction optimization of diphenyl vinylcyclopropane.



entry	catalyst loading	time	Temp.	d.r. (*cis*:*trans*)	Yield[a]
1[a]	5 mol%	2.5 h	r.t.	34:66	n.d.
2	**5 mol%**	**24 h**	**r.t.**	**10:90**	**84%**
3	5 mol%	72 h	60 °C	10:90	n.d.

a) isolated yield.

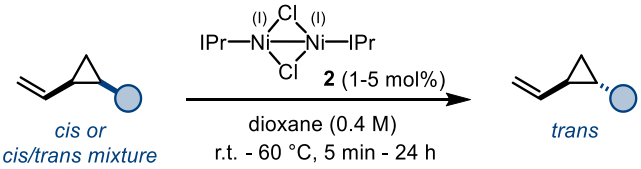
Table 13. Reaction optimization of vinyl-ACCA ester isomerization.



entry	catalyst loading	time	d.r. (*cis*:*trans*)	Yield[b]
1[a]	5 mol%	24 h	25:75	n.d.
2	5 mol%	24 h	20:80	n.d.
3	2 mol%	2 h	16:84	>99%
4	2 mol%	1 h	16:84	>99%
5	2 mol%	30 min	14:86	>99%
6	2 mol%	15 min	15:85	>99%
7	1 mol%	15 min	14:86	n.d.
8	**1 mol%**	**10 min**	**14:86**	**>99% (96%)[c]**
9	1 mol%	5 min	20:80	n.d.

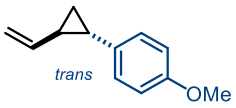
a) 60 °C reaction temperature; b) qNMR yield using ethylenecarbonate as internal standard; c) isolated yield.

5.4.1.2 General Procedure for Ni(I) isomerization

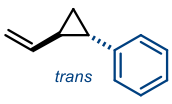


Inside an argon-filled glovebox, an oven dried 4 mL screw-cap vial equipped with a magnetic stir bar was charged with the corresponding cyclopropane substrate (1.0 equiv.), anhydrous 1,4-dioxane (0.4 M) and $[Ni(\mu\text{-}Cl)(IPr)]_2$ **2** (1-5 mol%), in that order. The reaction vial was then sealed and allowed to stir inside the glovebox at the indicated temperature for the indicated time. Upon completion the reaction mixture was removed from the glovebox and quenched by the addition of wet pentane (*i.e.* technical grade pentane that had been distilled and stored on the bench). A spatula tip of ammonium pyrrolidine-1-dithiocarboxylic acid was added and the mixture stirred for additional 15 min to precipitate nickel.[60] The mixture was filtered through a plug of silica, rinsing with Et_2O or EtOAc or MeCN and the filtrate was concentrated under reduced pressure. The *trans*-vinylcyclopropane was then obtained in high purity ranging from 90 to 99%. In case of Nickel impurities, the crude was dissolved in Et_2O and filtered another time over a plug of silica again rinsing the plug with Et_2O. The filtrate was concentrated under reduced pressure. Some compounds were further purified by silica gel column chromatography. *Note: In most cases, the colour of the reaction mixture after completion is dark red. After addition of ammonium pyrrolidine-1-dithiocarboxylic acid and subsequent mixing, the colour changes rapidly to yellow. After further mixing (15 min) the solution becomes clear and precipitation occurs.*

5.4.1.3 Compound characterization data



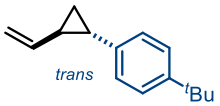
***trans*-1-methoxy-4-(2-vinylcyclopropyl)benzene (96):** General procedure was followed using a *cis*-vinylcyclopropane (17.4 mg, 0.100 mmol, 99:1 *cis*/*trans* (^{1}H NMR)) and Nickel dimer **2** (1.0 mg, 1 mol%). The reaction mixture was stirred for 5 min at room temperature. Purification by filtration over a short silica plug washing with Et_2O afforded the title product as a low-melting solid (17.1 mg, 0.098 mmol, 98%, 10:90 *cis*/*trans* (^{1}H NMR)). **R_f** = 0.41 (50:1 pentane:Et_2O). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.01 (d, *J* = 8.7 Hz, 2H), 6.82 (d, *J* = 8.7 Hz, 2H), 5.53 (ddd, *J* = 16.8, 10.3, 8.5 Hz, 1H), 5.09 (d, *J* = 17.0 Hz, 1H), 4.92 (dd, *J* = 10.3, 1.6 Hz, 1H), 3.78 (s, 3H), 1.89 (dt, *J* = 9.6, 5.0 Hz, 1H), 1.62 (tt, *J* = 8.8, 4.9 Hz, 1H), 1.13 (dt, *J* = 8.4, 5.4 Hz, 1H), 1.05 (dt, *J* = 8.6, 5.3 Hz, 1H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 157.9, 141.0, 134.4, 127.0, 114.0, 112.4, 55.5, 27.0, 24.7, 16.4. **IR** (neat, cm^{-1}): 3074, 3001, 2927, 2837, 2325, 2067, 1997, 1878, 1797, 1680, 1633, 1611, 1513, 1459, 1376, 1295, 1245, 1177, 1112, 1076, 1034, 986, 938, 896, 825, 716. **HRMS** (EI): *m/z*: calculated for $[M]^+$ $C_{12}H_{14}O$: 174.1039, found: 174.1040. The data are in agreement with those previously reported in the literature.[151]



***trans*-(2-vinylcyclopropyl)benzene (99):** General Procedure was followed using a diastereomeric mixture of vinylcyclopropane (14.4 mg, 0.100 mmol, 40:60 *cis*/*trans* (^{1}H NMR)) and Nickel dimer **2** (1.0 mg, 1 mol%). The reaction mixture was stirred for 5 min at room temperature.

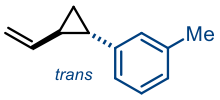
Purification by filtration over a short silica plug rinsing with Et_2O afforded the title product a s a colorless liquid (0.093 mmol, 93% (determined by quantitative ^{1}H NMR), 12:88 *cis*/*trans* (^{1}H NMR)). **R_f** = 0.43 (pentane). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.31 – 7.25 (m, 2H), 7.21 – 7.15 (m, 1H), 7.12 – 7.07 (m, 2H), 5.56 (ddd, *J* = 16.9, 10.3, 8.5 Hz, 1H), 5.13 (dd, *J* = 17.0, 1.5 Hz, 1H), 4.96 (dd, *J* = 10.3, 1.6 Hz, 1H), 1.95 (ddd, *J* = 8.7, 5.7, 4.3 Hz, 1H), 1.77 – 1.68 (m, 1H), 1.22 (dt, *J* = 8.4, 5.4 Hz, 1H), 1.13 (dt, *J* = 8.6, 5.3 Hz, 1H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 142.5, 140.8, 128.5, 125.8, 125.8, 112.7, 27.5, 25.4, 16.9. **IR** (neat, cm^{-1}): 3068, 3026, 2926, 2737, 2340, 2062, 1946, 1727, 1681, 1633, 1604, 1495, 1452, 1372, 1331, 1295, 1217, 1179, 1121, 1074, 1030, 982, 932, 896, 841, 747, 695, 661. **HRMS** (EI): *m/z* $[M]^+$ calculated for $C_{11}H_{12}$: 144.0934, found: 144.0932. The data are in agreement with those previously reported in the literature.[152] *Note: Caution, compound is volatile.*

***trans*-1-(*tert*-butyl)-4-(2-vinylcyclopropyl)benzene (100):** General procedure was followed using a

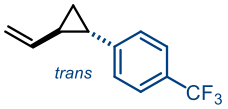


diastereomeric mixture of vinylcyclopropane (19.0 mg, 0.095 mmol, 27:73 *cis*/*trans* (^{1}H NMR)) and Nickel dimer **2** (0.9 mg, 1 mol%). The reaction mixture was stirred for 5 min at room temperature. Purification by filtration over a short silica plug washing with Et_2O afforded the title product as a colorless liquid (0.090 mmol, 95% (determined by quantitative ^{1}H NMR), 10:90 *cis*/*trans* (^{1}H NMR)). **R_f** = 0.4 (pentane). **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.35 – 7.30 (m, 2H), 7.08 – 7.01 (m, 2H), 5.63 – 5.48 (m, 1H), 5.15 – 5.07 (m, 1H), 4.98 – 4.91 (m, 1H), 1.97 – 1.89 (m, 1H), 1.77 – 1.66 (m, 1H), 1.33 (s, 9H), 1.21 (dddd, *J* = 8.4, 5.7, 4.8, 0.7 Hz, 1H), 1.11 (dddd, *J* = 8.7, 5.6, 4.9, 0.6 Hz, 1H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 148.7, 140.9, 139.4, 125.5, 125.4, 112.5, 34.5, 31.5, 27.4, 25.0, 16.8. **IR** (neat, cm^{-1}): 3077, 3003, 2960, 2906, 2869, 2714, 2323, 2199, 2078, 1991, 1900, 1791, 1736, 1688, 1635, 1516, 1462, 1393, 1363, 1268, 1223, 1199, 1118, 1076, 1023, 984, 938, 895, 826, 735, 682. **HRMS** (EI): *m/z* $[M]^+$ calculated for $C_{15}H_{20}$: 200.1560, found: 200.1559. *Note: Caution, compound is volatile.*

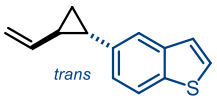
***trans*-1-methyl-3-(2-vinylcyclopropyl)benzene (101):** General procedure was followed using a



diastereomeric mixture of vinylcyclopropane (15.8 mg, 0.100 mmol, 33:67 *cis*/*trans* (^{1}H NMR)) and Nickel dimer **2** (1.0 mg, 1 mol%). The reaction mixture was stirred for 5 min at room temperature. Purification by filtration over a short silica plug washing with Et_2O afforded the title product as a colorless liquid (0.098 mmol, 98% (determined by quantitative ^{1}H NMR), 11:89 *cis*/*trans* (^{1}H NMR)). **R_f** = 0.43 (pentane). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.15 (dd, *J* = 7.5 Hz, 1H), 6.97 (d, *J* = 7.5 Hz, 1H), 6.91 – 6.85 (m, 2H), 5.57 – 5.49 (m, 1H), 5.10 (d, *J* = 17.2 Hz, 1H), 4.93 (dt, *J* = 10.3, 1.3 Hz, 1H), 2.32 (s, 3H), 1.89 (dt, *J* = 9.4, 5.0 Hz, 1H), 1.69 (tt, *J* = 8.8, 5.0 Hz, 1H), 1.19 (dt, *J* = 8.0, 5.2 Hz, 1H), 1.09 (dt, *J* = 8.2, 5.2 Hz, 1H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 142.4, 140.9, 138.0, 128.4, 126.7, 126.5, 122.8, 112.6, 27.4, 25.3, 21.6, 16.8. **IR** (neat, cm^{-1}): 3454, 3010, 2920, 2731, 2324, 2193, 2079, 1725, 1686, 1634, 1607, 1489, 1453, 1375, 1279, 1241, 1197, 1167, 1076, 1037, 985, 961, 895, 837, 776, 696, 660. **HRMS** (EI): *m/z* $[M]^+$ calculated for $C_{12}H_{14}$: 158.1090, found: 158.1088. *Note: Caution, compound is volatile.*

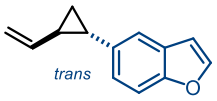


trans-1-(trifluoromethyl)-4-(2-vinylcyclopropyl)benzene (102): General procedure was followed using a diastereomeric mixture of vinylcyclopropane (21.2 mg, 0.100 mmol, 35:65 *cis*/*trans* (^{1}H NMR)) and Nickel dimer **2** (1.0 mg, 1 mol%). The reaction mixture was stirred for 5 min at room temperature. Purification by flash silica gel column chromatography (pentane) afforded the title product as a colorless liquid (0.094 mmol, 94% (determined by quantitative ^{1}H NMR), 9:91 *cis*/*trans* (^{1}H NMR)). **R$_f$** = 0.58 (hexane). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.50 (d, *J* = 8.1 Hz, 2H), 7.15 (d, *J* = 8.1 Hz, 2H), 5.54 (ddd, *J* = 17.0, 10.3, 8.3 Hz, 1H), 5.13 (dt, *J* = 17.1, 1.4 Hz, 1H), 4.97 (dd, *J* = 10.3, 1.4 Hz, 1H), 1.97 (dt, *J* = 9.4, 4.9 Hz, 1H), 1.77 – 1.71 (m, 1H), 1.24 (dt, *J* = 8.6, 5.4 Hz, 1H), 1.19 (dt, *J* = 8.7, 5.5 Hz, 1H). **^{19}F NMR** (282 MHz, $CDCl_3$) δ -62.30 (s, 3F). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 146.8, 140.0, 128.0 (q, *J* = 32.3 Hz), 126.0, 125.4 (q, *J* = 3.9 Hz), 123.6, 113.4, 28.2, 25.2, 17.4. **IR** (neat, cm^{-1}): 3081, 3010, 2684, 2327, 1697, 1618, 1521, 1454, 1418, 1323, 1226, 1162, 1115, 1067, 1015, 986, 902, 832, 735, 665. **HRMS** (EI): *m/z* $[M]^+$ calculated for $C_{12}H_{11}F_3$: 212.0807, found: 212.0808. *Note: Caution, compound is volatile.*

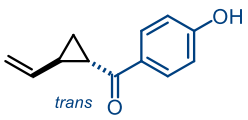


5-(_trans_-2-vinylcyclopropyl)benzo[_b_]thiophene (103): General procedure was followed using 5-(*cis*-2-vinylcyclopropyl)benzo[*b*]thiophene (40.1 mg, 0.200 mmol) and Nickel dimer **2** (9.7 mg, 5 mol%). The reaction mixture was stirred for 60 min at room temperature. Purification by filtration over a short silica plug washing with Et_2O afforded the title product as a colorless oil (36.9 mg, 0.184 mmol, 92%, 11:89 *cis*/*trans* (^{1}H NMR)). **R$_f$** = 0.31 (100:1 pentane:Et_2O). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.76 (d, *J* = 8.4 Hz, 1H), 7.54 (s, 1H), 7.44 – 7.39 (m, 1H), 7.28 – 7.24 (m, 1H), 7.09 (d, *J* = 8.2 Hz, 1H), 5.57 (dt, *J* = 18.3, 9.5 Hz, 1H), 5.13 (d, *J* = 17.0 Hz, 1H), 4.96 (d, *J* = 10.3 Hz, 1H), 2.09 – 2.03 (m, 1H), 1.79 – 1.71 (m, 1H), 1.30 – 1.24 (m, 1H), 1.19 – 1.12 (m, 1H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 140.8, 140.0, 138.6, 137.3, 126.9, 123.7, 123.1, 122.4, 120.6, 112.7, 27.6, 25.4, 16.8. **IR** (neat, cm^{-1}): 3075, 3003, 2326, 2167, 1883, 1728, 1685, 1633, 1604, 1505, 1432, 1374, 1324, 1262, 1227, 1196, 1157, 1084, 1045, 984, 894, 803, 751, 731, 695. **HRMS** (EI): *m/z* $[M]^+$ calculated for $C_{13}H_{12}S$: 200.0654, found 200.0654.

5-(_trans_-2-vinylcyclopropyl)benzofuran (104): General procedure was followed using 5-(*cis*-2-vinylcyclopropyl)benzofuran (18.4 mg, 0.100 mmol) and Nickel dimer **2** (4.8 mg, 5 mol%). The reaction mixture was stirred for 5 min at room temperature. Purification by filtration over a short silica plug washing with Et_2O afforded the title product as a yellowish oil (16.6 mg, 0.090 mmol, 90%, 10:90 *cis*/*trans* (^{1}H NMR)). **R$_f$** = 0.28 (100:1 pentane:Et_2O). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.59 (s, 1H), 7.40 (d, *J* = 8.6 Hz, 1H), 7.31 (s, 1H), 7.04 (dd, *J* = 8.7, 2.3 Hz, 1H), 6.70 (s, 1H), 5.62 – 5.52 (m, 1H), 5.13 (dd, *J* = 17.1, 2.4 Hz, 1H), 4.95 (dd, *J* = 10.3, 2.4 Hz, 1H), 2.08 – 2.01 (m, 1H), 1.75 – 1.68 (m, 1H), 1.27 – 1.19 (m, 1H), 1.16 – 1.09 (m, 1H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 153.7, 145.4, 141.0, 136.8, 127.7, 122.8, 118.0, 112.5, 111.2, 106.5, 27.4, 25.4, 16.7. **IR** (neat, cm^{-1}): 3117, 3075, 3002, 2666, 2325, 2086, 1994, 1871, 1805, 1728, 1687, 1633, 1536, 1469, 1371, 1329, 1261, 1207, 1186, 1128, 1077, 1030, 986, 964, 896, 845, 804, 766, 735, 661. **HRMS** (EI): *m/z* $[M]^+$ calculated for $C_{13}H_{12}O$: 184.0883, found 184.0883.

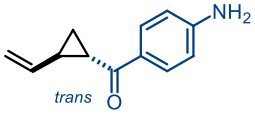


(4-hydroxyphenyl)(*trans*-2-vinylcyclopropyl)methanone (105): General procedure was followed using a



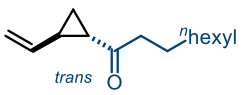
diastereomeric mixture of vinylcyclopropane (18.8 mg, 0.100 mmol, 41:59 *cis*/*trans* (^{1}H NMR)) and Nickel dimer **2** (4.8 mg, 5 mol%). The reaction mixture was stirred for 15 min at room temperature. Purification by filtration over a short silica plug washing with EtOAc afforded the title product as a white solid (17.0 mg, 0.090 mmol, 90%, 10:90 *cis*/*trans* (^{1}H NMR)). **R_f** = 0.25 (4:1 hexane:EtOAc). **M.p.** = 78.2 – 82.3 °C. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.94 (d, *J* = 8.4 Hz, 2H), 6.92 (d, *J* = 8.4 Hz, 2H), 5.54 (ddd, *J* = 17.0, 10.3, 8.5 Hz, 1H), 5.20 (d, *J* = 17.0 Hz, 1H), 5.03 (d, *J* = 10.3 Hz, 1H), 2.66 (dt, *J* = 8.5, 4.4 Hz, 1H), 2.22 – 2.16 (m, 1H), 1.70 (dt, *J* = 9.0, 4.6 Hz, 1H), 1.18 (ddd, *J* = 7.9, 6.4, 4.0 Hz, 1H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 198.4, 160.8, 138.6, 130.9, 130.7, 115.6, 115.2, 29.5, 26.5, 18.2. **IR** (neat, cm^{-1}): 3338, 3014, 2466, 1834, 1638, 1603, 1573, 1515, 1442, 1388, 1316, 1283, 1224, 1165, 1115, 1075, 1051, 1024, 990, 911, 848, 812, 748, 688, 665. **HRMS** (ESI): *m/z* $[M+Na]^+$ calculated for $C_{12}H_{12}O_2Na$: 211.0730, found: 211.0727.

(4-aminophenyl)(*trans*-2-vinylcyclopropyl)methanone (106): General procedure was followed using a



diastereomeric mixture of vinylcyclopropane (18.7 mg, 0.100 mmol, 37:63 *cis*/*trans* (^{1}H NMR)) and Nickel dimer **2** (4.8 mg, 5 mol%). The reaction mixture was stirred for 15 min at room temperature. Purification by filtration over a short silica plug washing with EtOAc afforded the title product as a beige solid (17.0 mg, 0.098 mmol, 91%, 7:93 *cis*/*trans* (^{1}H NMR)). **R_f** = 0.2 (2:1 hexane:EtOAc). **M.p.** = 106.4 – 109.8 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.86 (d, *J* = 8.6 Hz, 2H), 6.66 (d, *J* = 8.5 Hz, 2H), 5.52 (ddd, *J* = 17.2, 10.2, 8.6 Hz, 1H), 5.18 (dd, *J* = 17.1, 1.4 Hz, 1H), 5.00 (dd, *J* = 10.3, 1.4 Hz, 1H), 4.17 – 4.12 (m, 2H), 2.60 (ddd, *J* = 8.5, 5.1, 3.9 Hz, 1H), 2.13 (tdd, *J* = 8.8, 6.0, 3.8 Hz, 1H), 1.63 (ddd, *J* = 8.8, 5.1, 3.9 Hz, 1H), 1.10 (ddd, *J* = 8.1, 6.3, 3.8 Hz, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 196.6, 151.1, 139.1, 130.7, 130.6, 128.4, 114.7, 113.9, 113.9, 28.7, 25.9, 17.7. **IR** (neat, cm^{-1}): 3405, 3330, 3221, 2975, 2686, 2475, 2323, 1743, 1633, 1587, 1515, 1441, 1384, 1305, 1235, 1170, 1081, 1049, 1021, 912, 843, 749, 695, 668. **HRMS** (ESI): *m/z* $[M+Na]^+$ calculated for $C_{12}H_{13}ONNa$: 210.0889, found: 210.0888.

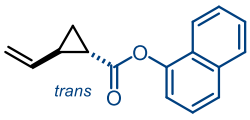
1-(*trans*-2-vinylcyclopropyl)nonan-1-one (107): General procedure was followed using a diastereomeric



mixture of 1-(2-vinylcyclopropyl)nonan-1-one (20.8 mg, 0.100 mmol, 40:60 *cis*/*trans* (^{1}H NMR)) and Nickel dimer **2** (4.8 mg, 5 mol%). The reaction mixture was stirred for 15 min at room temperature. Purification by filtration over a short silica plug washing with Et_2O afforded the title product as a colorless oil (20.0 mg, 0.096 mmol, 96%, 9:91 *cis*/*trans* (^{1}H NMR)). **R_f** = 0.25 (50:1 pentane:Et_2O). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 5.40 (ddd, *J* = 17.0, 10.3, 8.5 Hz, 1H), 5.14 (dd, *J* = 17.1, 1.4 Hz, 1H), 4.97 (dd, *J* = 10.3, 1.4 Hz, 1H), 2.54 (td, *J* = 7.3, 1.9 Hz, 2H), 2.03 – 1.92 (m, 2H), 1.63 – 1.56 (m, 2H), 1.43 (ddd, *J* = 8.9, 5.2, 3.9 Hz, 1H), 1.31 – 1.23 (m, 10H), 0.98 (ddd, *J* = 8.1, 6.3, 4.0 Hz, 1H), 0.87 (t, *J* = 7.0 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 209.5, 138.7, 114.7, 44.1, 32.0, 29.6, 29.5, 29.4, 29.3, 28.4, 24.2, 22.8, 17.6, 14.2. **IR** (neat, cm^{-1}): 3004, 2925, 2856, 2324, 2159, 1697, 1638, 1458,

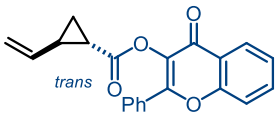
1385, 1305, 1201, 1129, 1083, 987, 902, 838, 722. **HRMS** (ESI): *m/z* $[M+Na]^+$ calculated for $C_{14}H_{24}ONa$: 231.1719, found: 231.1716.

Naphthalen-1-yl *trans*-2-vinylcyclopropane-1-carboxylate (108): General procedure was followed using a



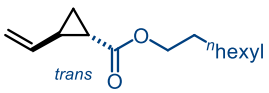
diastereomeric mixture of vinylcyclopropane (12.5 mg, 0.052 mmol, 37:63 *cis*/*trans* (^{1}H NMR)) and Nickel dimer **2** (2.5 mg, 5 mol%). The reaction mixture was stirred for 1 h at room temperature. Purification by filtration over a short silica plug washing with Et_2O afforded the title product as a colorless oil (12.0 mg, 0.052 mmol, 96%, 9:91 *cis*/*trans* (^{1}H NMR)). **R_f** = 0.33 (20:1 pentane:Et_2O). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.94 – 7.84 (m, 2H), 7.75 (d, *J* = 8.2 Hz, 1H), 7.55 – 7.51 (m, 1H), 7.47 (dd, *J* = 7.9 Hz, 1H), 7.27 (d, *J* = 7.6 Hz, 1H), 5.55 (ddd, *J* = 17.0, 10.2, 8.3 Hz, 1H), 5.31 (dd, *J* = 16.9, 1.3 Hz, 1H), 5.12 (dd, *J* = 10.3, 1.3 Hz, 1H), 2.31 (qd, *J* = 8.8, 3.9 Hz, 1H), 2.08 (ddd, *J* = 8.7, 5.1, 4.0 Hz, 1H), 1.65 (dt, *J* = 9.2, 4.8 Hz, 1H), 1.24 (ddd, *J* = 8.3, 6.4, 4.5 Hz, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 172.2, 146.7, 137.8, 134.7, 128.2, 126.9, 126.6, 126.5, 126.1, 125.5, 121.3, 118.2, 115.6, 26.7, 21.9, 16.5. **IR** (neat, cm^{-1}): 3062, 3011, 2325, 2092, 1745, 1637, 1598, 1508, 1445, 1379, 1319, 1222, 1132, 1087, 1046, 987, 909, 872, 845, 792, 770, 729. **HRMS** (ESI): *m/z* $[M+Na]^+$ calculated for $C_{16}H_{14}O_2Na$: 261.0886, found: 261.0884.

4-oxo-2-phenyl-4H-chromen-3-yl *trans*-2-vinylcyclopropane-1-carboxylate (109): General procedure was



followed using a diastereomeric mixture of vinylcyclopropane (33.2 mg, 0.100 mmol, 41:59 *cis*/*trans* (^{1}H NMR)) and Nickel dimer **2** (4.8 mg, 5 mol%). The reaction mixture was stirred for 1 h at room temperature. Purification by filtration (2 times) over a short silica plug washing with EtOAc afforded the title product as a white solid (32.0 mg, 0.096 mmol, 96%, 8:92 *cis*/*trans* (^{1}H NMR)). **R_f** = 0.28 (5:1 hexane:EtOAc). **M.p.** = 103.2 – 107.8 °C. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 8.27 (dd, *J* = 8.0, 1.7 Hz, 1H), 7.87 (dd, *J* = 7.6, 2.0 Hz, 2H), 7.74 – 7.68 (m, 1H), 7.58 – 7.51 (m, 4H), 7.44 (dd, *J* = 7.5 Hz, 1H), 5.47 (ddd, *J* = 17.0, 10.2, 8.3 Hz, 1H), 5.22 (d, *J* = 17.0 Hz, 1H), 5.06 (d, *J* = 10.2 Hz, 1H), 2.22 – 2.16 (m, 1H), 1.96 (dt, *J* = 8.7, 4.5 Hz, 1H), 1.56 (dt, *J* = 9.4, 4.9 Hz, 1H), 1.16 (ddd, *J* = 8.3, 6.4, 4.6 Hz, 1H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 172.4, 170.7, 156.4, 155.8, 137.6, 134.1, 133.7, 131.4, 130.2, 128.8, 128.5, 126.3, 125.3, 123.8, 118.2, 115.6, 26.7, 21.8, 16.4. **IR** (neat, cm^{-1}): 3286, 3074, 2924, 2854, 2186, 1752, 1642, 1612, 1568, 1468, 1386, 1286, 1239, 1188, 1118, 1031, 990, 899, 847, 756, 693. **HRMS** (CI): *m/z* $[M+H]^+$ calculated for $C_{21}H_{17}O_4$: 333.1121, found: 333.1120.

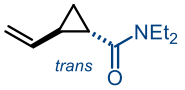
Octyl *trans*-2-vinylcyclopropane-1-carboxylate (110): General procedure was followed using a



diastereomeric mixture of vinylcyclopropane (9.0 mg, 0.041 mmol, 50:50 *cis*/*trans* (^{1}H NMR)) and Nickel dimer **2** (1.9 mg, 5 mol%). The reaction mixture was stirred for 1 h at room temperature. Purification by filtration over a short silica plug washing with Et_2O afforded the title product as a colorless oil (8.5 mg, 0.040 mmol, 94%, 9:91 *cis*/*trans* (^{1}H NMR)). **R_f** = 0.31 (30:1, pentane:Et_2O, $KMnO_4$). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 5.40 (ddd, *J* = 17.0, 10.3, 8.4 Hz, 1H), 5.16 (dd, *J* = 17.0, 1.4 Hz, 1H), 4.99 (dd, *J* = 10.3, 1.4 Hz, 1H), 4.06 (td, *J* = 6.8, 2.3 Hz, 2H), 2.05 – 1.98 (m, 1H), 1.66 – 1.59 (m, 3H), 1.39 – 1.23 (m, 11H), 0.97 (ddd, *J* = 8.4, 6.3, 4.3 Hz, 1H), 0.88

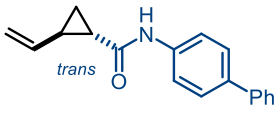
(t, *J* = 6.9 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 173.6, 138.3, 114.9, 65.0, 31.9, 29.4, 29.3, 28.8, 26.1, 25.7, 22.8, 22.0, 15.7, 14.2. **IR** (neat, cm^{-1}): 2926, 2857, 2327, 2111, 1726, 1639, 1459, 1400, 1373, 1266, 1169, 1086, 1048, 987, 905, 853, 818, 731. **HRMS** (ESI): *m/z* $[M+Na]^+$ calculated for $C_{14}H_{24}O_2Na$: 247.1669, found: 247.1664.

***trans*-*N*,*N*-diethyl-2-vinylcyclopropane-1-carboxamide (111):** General procedure was followed using a

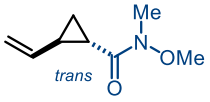


diastereomeric mixture of vinylcyclopropane (33.5 mg, 0.200 mmol, 44:56 *cis*/*trans* (^{1}H NMR)) and Nickel dimer **2** (9.7 mg, 5 mol%). The reaction mixture was stirred for 2 h at room temperature. Purification by filtration over a short silica plug washing with Et_2O afforded the title product as a colorless oil (31.1 mg, 0.186 mmol, 93%, 10:90 *cis*/*trans* (^{1}H NMR)). **R_f** = 0.38 (3:2 hexane:EtOAc, PMA). **^{1}H NMR** (600 MHz, C_6D_6) δ 5.23 (ddt, *J* = 17.0, 10.3, 8.7 Hz, 1H), 5.03 (dd, *J* = 17.1, 1.7 Hz, 1H), 4.87 (dd, *J* = 10.2, 1.6 Hz, 1H), 3.26 (dq, *J* = 14.1, 7.1 Hz, 1H), 3.18 (dq, *J* = 14.0, 7.1 Hz, 1H), 2.85 (q, *J* = 7.1 Hz, 2H), 2.20 (tdd, *J* = 8.8, 5.9, 3.9 Hz, 1H), 1.67 (ddd, *J* = 8.7, 5.2, 3.7 Hz, 1H), 1.45 (ddd, *J* = 8.1, 5.2, 4.0 Hz, 1H), 0.94 (t, *J* = 7.1 Hz, 3H), 0.77 (t, *J* = 7.2 Hz, 3H), 0.65 (ddd, *J* = 8.1, 5.9, 3.7 Hz, 1H). **^{13}C NMR** (151 MHz, C_6D_6) δ 170.2, 139.7, 113.9, 41.9, 41.1, 25.2, 20.9, 15.0, 13.6. **IR** (neat, cm^{-1}): 3479, 3255, 3081, 2975, 2933, 2320, 2158, 1908, 1737, 1629, 1456, 1430, 1374, 1310, 1254, 1221, 1139, 1082, 969, 898, 851, 789, 729, 664. **HRMS** (ESI): *m/z* $[M+Na]^+$ calculated for $C_{10}H_{17}NONa$: 190.1202, found: 190.1209.

***trans*-*N*-([1,1'-biphenyl]-4-yl)-*trans*-2-vinylcyclopropane-1-carboxamide (112):** General procedure was



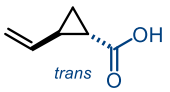
followed using a diastereomeric mixture of vinylcyclopropane (11.0 mg, 0.042 mmol, 39:61 *cis*/*trans* (^{1}H NMR)) and Nickel dimer **2** (2.0 mg, 5 mol%). The reaction mixture was stirred for 1 h at room temperature. Purification by filtration over a short silica plug washing with Et_2O afforded the title product as a white solid (10.6 mg, 0.040 mmol, 96%, 7:93 *cis*/*trans* (^{1}H NMR)). **R_f** = 0.32 (4:1 hexane:EtOAc). **M.p.** = 171.7 – 174.6 °C. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.61 – 7.52 (m, 6H), 7.51 (s, 1H), 7.42 (dd, *J* = 7.7 Hz, 2H), 7.33 (dd, *J* = 7.6 Hz, 1H), 5.46 (dt, *J* = 18.1, 9.6 Hz, 1H), 5.20 (d, *J* = 17.0 Hz, 1H), 5.02 (d, *J* = 10.0 Hz, 1H), 2.13 (dq, *J* = 10.5, 5.3 Hz, 1H), 1.58 – 1.50 (m, 2H), 1.01 (td, *J* = 7.1, 3.8 Hz, 1H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 170.4, 140.6, 138.5, 137.4, 137.1, 128.9, 127.7, 127.2, 127.0, 120.1, 114.9, 25.5, 25.1, 15.4. **IR** (neat, cm^{-1}): 3292, 3035, 2329, 1903, 1812, 1650, 1596, 1532, 1486, 1448, 1401, 1316, 1253, 1203, 1184, 1112, 1077, 1039, 1004, 983, 899, 833, 758, 685. **HRMS** (ESI): *m/z* $[M+Na]^+$ calculated for $C_{18}H_{17}NONa$: 286.1202, found: 286.1204.



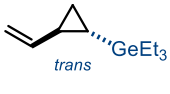
***trans*-*N*-methoxy-*N*-methyl-2-vinylcyclopropane-1-carboxamide (113):** General procedure was followed using a diastereomeric mixture of vinylcyclopropane (15.5 mg, 0.100 mmol, 42:58 *cis*/*trans* (^{1}H NMR)) and Nickel dimer **2** (4.8 mg, 5 mol%). The reaction mixture was stirred for 1 h at room temperature. Purification by filtration over a short silica plug washing with Et_2O afforded the title product as a colorless oil (15.0 mg, 0.096 mmol, 97%, 9:91 *cis*/*trans* (^{1}H NMR)). **R_f** = 0.47 (3:2 pentane:Et_2O, $KMnO_4$). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 5.45 (ddd, *J* = 17.0, 10.2,

8.5 Hz, 1H), 5.16 (ddd, *J* = 17.0, 1.6, 0.7 Hz, 1H), 4.97 (dd, *J* = 10.2, 1.2 Hz, 1H), 3.73 (s, 3H), 3.21 (s, 3H), 2.20 – 2.12 (m, 1H), 1.98 (tdd, *J* = 8.6, 6.1, 4.0 Hz, 1H), 1.41 (ddd, *J* = 8.9, 5.3, 4.1 Hz, 1H), 0.96 (ddd, *J* = 8.3, 6.1, 4.1 Hz, 1H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 138.9, 114.5, 61.8, 32.7, 25.5, 19.3, 15.2. *Note: The carbonyl carbon was not observed in ^{13}C NMR*. **IR** (neat, cm^{-1}): 3083, 3003, 2967, 2937, 2326, 2094, 1651, 1421, 1390, 1335, 1175, 1104, 1048, 1004, 964, 902, 845, 764, 720, 664. **HRMS** (ESI): *m/z* $[M+Na]^+$ calculated for $C_8H_{13}O_2NNa$: 188.0839, found: 188.0843.

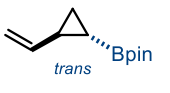
***trans*-2-vinylcyclopropane-1-carboxylic acid (114):** General procedure was followed using a diastereomeric mixture of vinylcyclopropane (22.5 mg, 0.200 mmol, 44:56 *cis*/*trans* (^{1}H NMR)) and Nickel dimer **2** (9.7 mg, 5 mol%). The reaction mixture was stirred for 15 min at room temperature. Purification by filtration over a short silica plug washing with Et_2O afforded the title product as a colorless oil (21.0 mg, 0.187 mmol, 94%, 25:75 *cis*/*trans* (^{1}H NMR)). **R_f** = 0.37 (10:1 pentane:Et_2O, 1% AcOH, $KMnO_4$). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 5.40 (ddd, *J* = 17.0, 10.2, 8.3 Hz, 1H), 5.18 (d, *J* = 17.0 Hz, 1H), 5.02 (dd, *J* = 10.3, 1.3 Hz, 1H), 2.12 – 2.06 (m, 1H), 1.68 – 1.61 (m, 1H), 1.43 (dt, *J* = 9.2, 4.7 Hz, 1H), 1.06 (ddd, *J* = 8.3, 6.4, 4.4 Hz, 1H). *Note*: *The acid proton was not observed in ^{1}H NMR due to H-D exchange.* **^{13}C NMR** (151 MHz, $CDCl_3$) δ 179.7, 137.7, 115.4, 26.6, 21.8, 16.3. **IR** (neat, cm^{-1}): 2923, 2643, 2569, 1690, 1641, 1433, 1360, 1292, 1227, 1084, 1052, 980, 905, 851, 678. **HRMS** (EI): *m/z* $[M]^+$ calculated for $C_6H_8O_2$: 112.0519, found: 112.0504. The data are in agreement with those previously reported in the literature.[153] *Note: Caution, compound is volatile.*



(*trans*-2-vinylcyclopropyl)triethylgermane (115): General procedure was followed using (*cis*-2-vinylcyclopropyl)triethylgermane (22.7 mg, 0.100 mmol) and Nickel dimer **2** (4.8 mg, 5 mol%).The reaction mixture was stirred for 24 h at room temperature. Purification by flash silica gel column chromatography (pentane) afforded the title product as a colorless oil (21.8 mg, 0.096 mmol, 96%, 10:90 *cis*/*trans* (^{1}H NMR)). **R_f** = 0.73 (hexane, $KMnO_4$). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 5.32 (ddd, *J* = 17.0, 10.2, 8.8 Hz, 1H), 5.05 (dd, *J* = 17.0, 1.7 Hz, 1H), 4.81 (dd, *J* = 10.2, 1.8 Hz, 1H), 1.35 – 1.29 (m, 1H), 1.05 – 1.00 (m, 9H+1H), 0.71 – 0.64 (m, 6H+1H), -0.07 (ddd, *J* = 9.7, 7.6, 5.8 Hz, 1H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 143.9, 110.7, 18.6, 10.5, 8.9, 4.9, 3.5. **IR** (neat, cm^{-1}): 2947, 2870, 2826, 2730, 2326, 2094, 1990, 1744, 1457, 1426, 1375, 1215, 1011, 961, 692. **HRMS** (CI): *m/z* $[M-C_2H_5]^+$ calculated for $C_9H_{17}Ge$: 199.0537, found 199.0536. *Note: Attention, compound is volatile*.

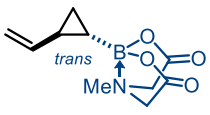


***trans*-4,4,5,5-tetramethyl-2-(*trans*-2-vinylcyclopropyl)-1,3,2-dioxaborolane (116):** General procedure was followed using a diastereomeric mixture of vinylcyclopropane (38.8 mg, 0.200 mmol, 41:59 *cis*/*trans* (^{1}H NMR)) and Nickel dimer **2** (9.7 mg, 5 mol%). The reaction mixture was stirred for 72 h at 60 °C. Purification by flash silica gel column chromatography (50:1 pentane:Et_2O) afforded the title product as a colorless oil (31.8 mg, 0.164 mmol, 82%, 21:79 *cis*/*trans* (^{1}H NMR)). **R_f** = 0.14 (50:1 pentane:Et_2O, PMA). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 5.31 (ddd, *J* = 17.0, 10.2, 8.8 Hz, 1H), 5.10 (dd, *J* = 17.0, 1.7 Hz, 1H), 4.86 (dd, *J* = 10.2, 1.7 Hz, 1H), 1.64 (tt, *J* = 8.3, 5.1 Hz, 1H), 1.24 – 1.20 (m, 12H), 0.92 (ddd, *J* = 7.9, 6.7, 3.6 Hz, 1H), 0.69 (ddd, *J* = 9.7, 5.0, 3.5 Hz, 1H), -0.04 (ddd, *J* = 9.7, 6.7, 5.2 Hz, 1H).



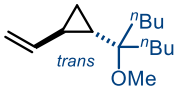
^{11}B NMR (193 MHz, $CDCl_3$) δ 32.9. **^{13}C NMR** (151 MHz, $CDCl_3$) δ 142.4, 112.2, 83.2, 25.2, 24.9, 24.8, 21.6, 12.6. **IR** (neat, cm^{-1}): 3078, 2980, 2931, 1730, 1636, 1513, 1436, 1404, 1372, 1318, 1218, 1144, 1069, 1043, 980, 945, 895, 844, 719, 672. **HRMS** (ESI): *m/z* $[M]^+$ calculated for $C_{11}H_{19}O_2B$: 194.1472, found 194.1469. *Note: Attention, compound is volatile*.

***trans*-6-methyl-2-(*trans*-2-vinylcyclopropyl)-1,3,6,2-dioxazaborocane-4,8-dione (117):** General procedure



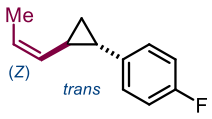
was followed using a diastereomeric mixture of vinylcyclopropane (22.3 mg, 0.100 mmol, 35:65 *cis*/*trans* (^{1}H NMR)) and Nickel dimer **2** (4.8 mg, 5 mol%). The reaction mixture was stirred for 72 h at 60 °C. Purification by flash silica gel column chromatography (20:1 DCM:MeOH) afforded the title product as a white solid (21.2 mg, 0.095 mmol, 95%, 12:88 *cis*/*trans* (^{1}H NMR)). **R_f** = 0.17 (20:1 DCM:MeOH, PMA). **M.p.** = 90.2 – 96.7 °C. **^{1}H NMR** (600 MHz, CD_3CN) δ 5.37 (dt, *J* = 18.2, 9.6 Hz, 1H), 5.10 (d, *J* = 17.0 Hz, 1H), 4.82 (d, *J* = 10.2 Hz, 1H), 3.94 (d, *J* = 17.1 Hz, 2H), 3.81 (d, *J* = 17.1 Hz, 2H), 2.94 (s, 3H), 1.33 – 1.26 (m, 1H), 0.65 – 0.58 (m, 2H), -0.12 – -0.19 (m, 1H). **^{11}B NMR** (193 MHz, CD_3CN) δ 12.4. **^{13}C NMR** (151 MHz, CD_3CN) δ 169.2, 169.1, 144.0, 111.9, 63.0, 62.9, 47.4, 19.5, 10.7. *Note: The carbon attached to boron was not observed in ^{13}C NMR.* **IR** (neat, cm^{-1}): 3502, 3073, 3002, 2960, 2920, 2851, 2164, 1744, 1634, 1540, 1456, 1337, 1290, 1248, 1194, 1123, 1075, 991, 961, 891, 861, 709, 663. **HRMS** (ESI): *m/z* $[M+Na]^+$ calculated for $C_{10}H_{14}O_4NBNa$: 246.0908, found: 246.0906.

***trans*-1-(5-methoxynonan-5-yl)-2-vinylcyclopropane (118):** General procedure was followed using a



diastereomeric mixture of vinylcyclopropane (49.8 mg, 90w%, 0.200 mmol, 30:70 cis/trans (^{1}H NMR)) and Nickel dimer **2** (9.65 mg, 5 mol%). The reaction mixture was stirred for 24 h at 60 °C. Flash silica gel column chromatography (100:1 hexane:EtOAc) afforded the title compound as a colorless oil (48 mg, 90w%, 0.192 mmol, 96%, 1:99 *cis*/*trans* (^{1}H NMR)). **R_f** = 0.18 (100:1 hexane:EtOAc, PMA). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 5.37 (ddd, *J* = 17.1, 10.2, 8.7 Hz, 1H), 5.05 (dd, *J* = 17.0, 1.7 Hz, 1H), 4.86 (dd, *J* = 10.2, 1.8 Hz, 1H), 3.14 (s, 3H), 1.48 – 1.37 (m, 4H), 1.34 – 1.25 (m, 9H), 0.93 – 0.89 (m, 6H), 0.84 – 0.74 (m, 2H), 0.52 (ddd, *J* = 8.8, 5.1, 4.1 Hz, 1H). **^{13}C NMR** (151 MHz, $CDCl_3$): δ 142.0, 112.0, 76.5, 49.1, 35.6, 34.8, 27.7, 25.8, 25.6, 23.6, 23.6, 18.1, 14.3, 9.9. **IR** (neat, cm^{-1}): 3183, 3148, 3074, 2957, 2868, 2292, 2190, 2066, 2033, 1934, 1796, 1702, 1635, 1590, 1535, 1461, 1399, 1380, 1329, 1268, 1201, 1176, 1081, 986, 936, 890, 802, 738, 708, 659. **HRMS** (ESI): *m/z* $[M+Na]^+$ calculated for $C_{15}H_{28}ONa$: 247.2032, found 247.2021.

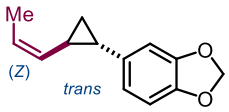
***trans*-(Z)-1-fluoro-4-(2-(prop-1-en-1-yl)cyclopropyl)benzene (119):** General procedure was followed using



a diastereomeric mixture of vinylcyclopropane (17.6 mg, 0.100 mmol, 65:35 *cis*/*trans* (^{1}H NMR)) and Nickel dimer **2** (4.8 mg, 5 mol%). The reaction mixture was stirred for 2 h at room temperature. Purification by filtration over a short silica plug washing with Et_2O afforded the title product as a colorless oil (17.0 mg, 0.096 mmol, 96%, 11:89 *cis*/*trans* (^{1}H NMR)). **R_f** (pentane) = 0.88. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.07 – 7.02 (m, 2H), 6.98 – 6.92 (m, 2H), 5.46 (dq, *J* = 10.5, 6.8 Hz, 1H), 4.96 (ddq, *J* = 10.9, 9.2, 1.8 Hz, 1H), 1.86 (ddd, *J* = 9.3, 5.0 Hz, 1H), 1.81 – 1.75 (m, 1H),

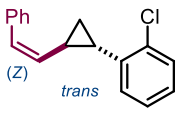
1.72 (dd, *J* = 6.9, 1.7 Hz, 3H), 1.17 (ddd, *J* = 8.6, 5.3 Hz, 1H), 1.00 (ddd, *J* = 8.6, 5.2 Hz, 1H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 161.3 (d, *J* = 243.2 Hz), 138.4 (d, *J* = 3.1 Hz), 133.0, 127.3 (d, *J* = 7.8 Hz), 123.5, 115.2 (d, *J* = 21.2 Hz), 24.5, 22.3, 17.1, 13.4. **^{19}F NMR** (565 MHz, $CDCl_3$) δ -118.0 (m). **HRMS** (EI): *m/z* $[M]^+$ calculated for $C_{12}H_{13}F$: 176.0996, found 176.0987. *Note: The product is volatile.*

***trans*-5-(2-((*Z*)-prop-1-en-1-yl)cyclopropyl)benzo[*d*][1,3]dioxole (120):** General procedure was followed



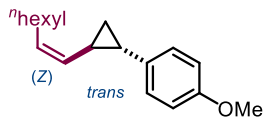
using a diastereomeric mixture of vinylcyclopropane (20.2 mg, 0.100 mmol, 65:35 *cis*/*trans* (^{1}H NMR)) and Nickel dimer **2** (4.8 mg, 5 mol%). The reaction mixture was stirred for 2 h at room temperature. Purification by filtration over a short silica plug washing with Et_2O afforded the title product as a yellowish oil (19.0 mg, 0.093 mmol, 94%, 10:90 *cis*/*trans* (^{1}H NMR)). **R_f** = 0.3 (100:1 pentane:Et_2O). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 6.72 (d, *J* = 8.0 Hz, 1H), 6.60 (dd, *J* = 8.0, 1.8 Hz, 1H), 6.57 (d, *J* = 1.8 Hz, 1H), 5.91 (s, 2H), 5.44 (dqd, *J* = 10.7, 6.8, 1.0 Hz, 1H), 4.94 (ddq, *J* = 11.0, 9.3, 1.8 Hz, 1H), 1.83 (ddd, *J* = 8.7, 5.6, 4.3 Hz, 1H), 1.78 – 1.73 (m, 1H), 1.72 (dd, *J* = 6.9, 1.8 Hz, 3H), 1.14 (ddd, *J* = 8.6, 5.6, 4.8 Hz, 1H), 0.95 (dt, *J* = 8.6, 5.2 Hz, 1H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 147.8, 145.6, 136.7, 133.1, 123.3, 119.2, 108.2, 106.4, 100.9, 25.1, 22.1, 16.9, 13.4. **IR** (neat, cm^{-1}): 3781, 3674, 3566, 3070, 3011, 2886, 2776, 2322, 2079, 1857, 1653, 1608, 1493, 1441, 1236, 1207, 1103, 1074, 1037, 965, 933, 880, 804, 743, 700. **HRMS** (EI): *m/z* $[M]^+$ calculated for $C_{13}H_{14}O_2$: 202.0988, found 202.0988.

***trans*-(*Z*)-1-chloro-2-(2-styrylcyclopropyl)benzene (121):** General procedure was followed using a



diastereomeric mixture of vinylcyclopropane (12.7 mg, 0.050 mmol, 69:31 *cis*/*trans* (^{1}H NMR)) and Nickel dimer (2.4 mg, 5 mol%). The reaction mixture was stirred for 2 h at room temperature. Purification by filtration over a short silica plug washing with Et_2O afforded the title product as a colorless oil (12.0 mg, 0.047 mmol, 94%, 19:81 *cis*/*trans* (^{1}H NMR)). **R_f** = 0.4 (50:1 hexane:EtOAc). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.41 – 7.37 (m, 2H), 7.33 – 7.27 (m, 2H), 7.26 – 7.18 (m, 2H), 7.17 (ddd, *J* = 7.6, 7.6, 1.2 Hz, 1H), 7.12 (ddd, *J* = 7.6, 7.6, 1.6 Hz, 1H), 6.94 (dd, *J* = 7.6, 1.3 Hz, 1H), 6.47 (d, *J* = 11.5 Hz, 1H), 5.34 (dd, *J* = 11.3, 9.8 Hz, 1H), 2.40 – 2.34 (m, 1H), 2.14 – 2.06 (m, 1H), 1.33 (dt, *J* = 8.6, 5.5 Hz, 1H), 1.19 (dt, *J* = 8.7, 5.2 Hz, 1H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 139.2, 137.7, 135.4, 134.8, 129.4, 128.9, 128.6, 128.3, 127.1, 126.9, 126.7, 126.3, 24.1, 22.7, 16.8. **MS** (70eV, EI): *trans isomer* (GC retention time 10.350 min), *m/z* (%): 254 (13) $[M^+]$, 215 (5), 202 (10), 189 (4), 178 (4), 163 (5), 149 (2), 141 (11), 129 (100), 91 (23). **HRMS** (APCI): *m/z* $[M+H]^+$ calculated for $C_{17}H_{16}Cl$: 255.0935, found 255.0933.

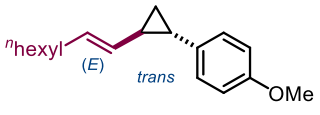
***trans*-(*Z*)-1-methoxy-4-(2-(oct-1-en-1-yl)cyclopropyl)benzene (122):** General procedure was followed using



a diastereomeric mixture of vinylcyclopropane (25.8 mg, 0.100 mmol, 54:46 *cis*/*trans*, 91:9 *Z*/*E* (^{1}H NMR)) and Nickel dimer **2** (4.8 mg, 5 mol%). The reaction mixture was stirred for 2 h at room temperature. Purification by filtration over a short silica plug washing with Et_2O afforded the title product as a colorless oil (25.3 mg, 0.098 mmol, 98%, 12:88 *cis*/*trans*, 91:9 *Z*/*E* (^{1}H NMR)). **R_f** = 0.5 (50:1 hexane:EtOAc). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.05 –

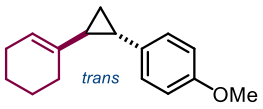
7.00 (m, 2H), 6.84 – 6.80 (m, 2H), 5.37 (dt, *J* = 10.7, 7.4 Hz, 1H), 4.96 – 4.89 (m, 1H), 3.79 (s, 3H), 2.19 – 2.09 (m, 2H), 1.83 (ddd, *J* = 9.1, 5.1 Hz, 1H), 1.78 – 1.70 (m, 1H), 1.40 – 1.33 (m, 2H), 1.34 – 1.22 (m, 6H), 1.14 (ddd, *J* = 8.5, 5.2 Hz, 1H), 0.95 (ddd, *J* = 8.6, 5.2 Hz, 1H), 0.87 (t, *J* = 6.9 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 157.9, 134.8, 132.5, 129.3, 127.0, 113.9, 55.5, 31.9, 29.9, 29.1, 27.9, 24.6, 22.8, 22.2, 16.9, 14.3. **HRMS** (APCI): *m/z* $[M+H]^+$ calculated for $C_{18}H_{27}O$: 259.2056, found 259.2062.

***trans*-(*E*)-1-methoxy-4-(2-(oct-1-en-1-yl)cyclopropyl)benzene (123):** General procedure was followed using



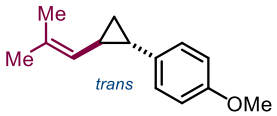
a diastereomeric mixture of vinylcyclopropane (15.0 mg, 0.058 mmol, 59:41 *cis*/*trans*, 14:86 *Z*/*E* (^{1}H NMR)) and Nickel dimer **2** (2.8 mg, 5 mol%). The reaction mixture was stirred for 48 h at 60 °C. Flash silica gel column chromatography (100:1 pentane:Et_2O) afforded the title compound as a colorless oil (13.9 mg, 0.054 mmol, 93%, 9:91 *cis*/*trans*, 15:85 *Z*/*E* (^{1}H NMR)). **R_f** = 0.24 (100:1 pentane:Et_2O). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 6.99 (d, *J* = 8.6 Hz, 2H), 6.81 (d, *J* = 8.5 Hz, 2H), 5.52 (dt, *J* = 14.3, 6.8 Hz, 1H), 5.13 (dd, *J* = 15.2, 8.2 Hz, 1H), 3.78 (s, 3H), 1.99 (q, *J* = 6.9 Hz, 2H), 1.80 (dt, *J* = 9.4, 5.1 Hz, 1H), 1.56 – 1.51 (m, 1H), 1.38 – 1.23 (m, 8H), 1.06 (dt, *J* = 8.5, 5.3 Hz, 1H), 0.98 (dt, *J* = 8.5, 5.3 Hz, 1H), 0.88 (t, *J* = 6.8 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 157.8, 134.9, 132.2, 129.3, 126.9, 113.9, 55.5, 32.7, 31.9, 29.8, 29.0, 26.1, 24.3, 22.8, 16.4, 14.3. **HRMS** (APCI): *m/z* $[M+H]^+$ calculated for $C_{18}H_{27}O$: 259.2056, found 259.2061.

***trans*-1-(2-(cyclohex-1-en-1-yl)cyclopropyl)-4-methoxybenzene (124):** General procedure was followed



using a diastereomeric mixture of vinylcyclopropane (45.7 mg, 0.200 mmol, 25:75 *cis*/*trans* (^{1}H NMR)) and Nickel dimer **2** (9.7 mg, 5 mol%). The reaction mixture was stirred for 24 h at 60 °C. Flash silica gel column chromatography (30:1 hexane:EtOAc) afforded the title compound as a colorless oil (42.9 mg, 0.188 mmol, 94%, 5:95 *cis*/*trans* (^{1}H NMR)). **R_f** = 0.67 (10:1 hexane:EtOAc). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.04 – 7.00 (m, 2H), 6.83 – 6.78 (m, 2H), 5.51 – 5.46 (m, 1H), 3.78 (s, 3H), 2.04 – 1.98 (m, 2H), 1.96 – 1.90 (m, 2H), 1.86 (ddd, *J* = 9.0, 5.2 Hz, 1H), 1.67 – 1.60 (m, 2H), 1.61 – 1.54 (m, 2H), 1.53 – 1.46 (m, 1H), 1.16 – 1.09 (m, 1H), 0.93 (ddd, *J* = 8.8, 5.2 Hz, 1H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 157.8, 137.5, 135.5, 127.0, 120.3, 113.9, 55.5, 29.8, 27.1, 25.4, 23.1, 22.8, 22.5, 13.9. **HRMS** (APCI): *m/z* $[M+H]^+$ calculated for $C_{16}H_{21}O$: 229.1587, found 229.1591.

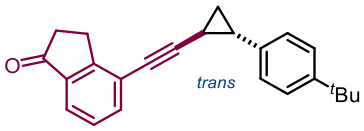
***trans*-1-methoxy-4-(2-(2-methylprop-1-en-1-yl)cyclopropyl)benzene (125):** General procedure was



followed using a diastereomeric mixture of vinylcyclopropane (40.5 mg, 0.200 mmol, 57:43 *cis*/*trans* (^{1}H NMR)) and Nickel dimer **2** (19.3 mg, 10 mol%). The reaction mixture was stirred for 72 h at 60 °C. Flash silica gel column chromatography (50:1 pentane:Et_2O) afforded the title compound as a colorless oil (36.8 mg, 0.182 mmol, 91%, 19:81 *cis*/*trans* (1H NMR)). **R_f** = 0.25 (50:1 pentane:Et_2O). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.01 (d, *J* = 8.7 Hz, 2H), 6.81 (d, *J* = 8.6 Hz, 2H), 4.73 (dt, *J* = 9.1, 1.6 Hz, 1H), 3.78 (s, 3H), 1.78 (dt, *J* = 9.1, 4.9 Hz, 1H), 1.72 – 1.70 (m, 6H), 1.63 (tt, *J* = 9.0, 4.9 Hz, 1H), 1.10 (dt, *J* = 8.6, 5.2 Hz, 1H), 0.90 (dt, *J* = 8.6, 5.1

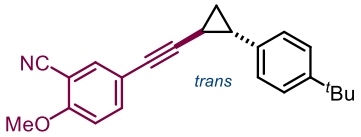
Hz, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 157.8, 135.1, 131.5, 127.5, 126.9, 113.9, 55.5, 25.7, 24.3, 22.8, 18.5, 16.7. **HRMS** (ESI): *m/z* $[M]^+$ calculated for $C_{14}H_{19}O$: 203.1430, found 203.1428.

4-((*trans*-2-(4-(*tert*-butyl)phenyl)cyclopropyl)ethynyl)-2,3-dihydro-*1H*-inden-1-one (126): General



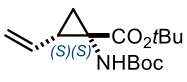
procedure was followed using a diastereomeric mixture of alkynyl cyclopropane (65.7 mg, 0.2 mmol, 50:50 *cis*/*trans* (^{1}H NMR)) and Nickel dimer **2** (9.7 mg, 5 mol%). The reaction mixture was stirred for 24 h at room temperature. Flash silica gel column chromatography (10:1 hexane:EtOAc) afforded the title compound as a white solid (51 mg, 0.168 mmol, 84%, 10:90 *cis*/*trans* (^{1}H NMR)). **M.p.** = 78.3 – 81.5 °C. **R_f** = 0.40 (10:1 hexane:EtOAc). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.58 (d, *J* = 7.6 Hz, 1H), 7.38 (dd, *J* = 7.5, 1.1 Hz, 1H), 7.37 – 7.32 (m, 2H), 7.28 – 7.24 (m, 2H), 7.22 (dd, *J* = 7.6, 7.6 Hz, 1H), 2.61 – 2.56 (m, 2H), 2.52 (dddd, *J* = 7.8, 4.4, 1.0 Hz, 2H), 2.46 (ddd, *J* = 8.0 Hz, 1H), 2.01 (ddd, *J* = 8.5, 5.6 Hz, 1H), 1.47 (dddd, *J* = 8.6, 5.1, 1.0 Hz, 1H), 1.37 – 1.31 (m, 1H), 1.31 (s, 9H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 207.0, 157.3, 149.6, 137.1, 137.1, 134.9, 128.6, 127.3, 125.0, 122.9, 122.6, 96.1, 76.4, 36.2, 34.6, 31.6, 25.2, 24.0, 14.7, 10.1. **IR** (neat, cm^{-1}): 3405, 3054, 2958, 2925, 2865, 2330, 2220, 2097, 2010, 1903, 1772, 1708, 1574, 1516, 1470, 1430, 1397, 1364, 1325, 1265, 1198, 1160, 1110, 1042, 990, 899, 825, 788, 719. **HRMS** (ESI): *m/z* $[M+Na]^+$ calculated for $C_{24}H_{24}ONa$: 351.1719, found 351.1729.

***trans*-1-(2-(cyclohex-1-en-1-yl)cyclopropyl)-4-methoxybenzene (127):** General procedure was followed



using a diastereomeric mixture of vinylcyclopropane (65.9 mg, 0.2 mmol, 45:55 *cis*/*trans* (^{1}H NMR)) and Nickel dimer **2** (9.7 mg, 5 mol%). The reaction mixture was stirred for 24 h at room temperature. Flash silica gel column chromatography (5:1 hexane:EtOAc) afforded the title compound as a colorless oil (56 mg, 0.173 mmol, 87%, 10:90 *cis*/*trans* (^{1}H NMR)). **R_f** = 0.23 (hexane/EtOAc 10:1). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.38 (dd, *J* = 8.2, 1.3 Hz, 2H), 7.30 – 7.22 (m, 4H), 6.79 (d, *J* = 8.6 Hz, 1H), 3.90 (s, 3H), 2.42 (ddd, *J* = 8.0 Hz, 1H), 1.93 (dddd, *J* = 8.5, 6.5, 1.2 Hz, 1H), 1.44 (dddd, *J* = 8.6, 5.1, 1.2 Hz, 1H), 1.36 (s, 9H), 1.29 (ddd, *J* = 5.7, 5.2 Hz, 1H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 160.2, 149.5, 137.3, 136.5, 134.9, 128.2, 124.8, 117.1, 115.8, 111.3, 102.1, 90.9, 77.6, 56.3, 34.6, 31.6, 23.8, 14.9, 9.9. **IR** (neat, cm^{-1}): 3012, 2959, 2869, 2557, 2229, 2029, 1906, 1717, 1665, 1605, 1569, 1499, 1460, 1401, 1364, 1277, 1182, 1127, 1019, 991, 901, 824, 775, 742, 669. **HRMS** (APCI): *m/z* $[M+Na]^+$ calculated for $C_{23}H_{23}ONNa$: 352.1617, found 352.1682.

***tert*-butyl (1*S*,2*S*)-1-((*tert*-butoxycarbonyl)amino)-2-vinylcyclopropane-1-carboxylate (129):** General



isomerization procedure was followed using tert-butyl (1*R*,2*S*)-1-((*tert*-butoxycarbonyl)amino)-2-vinylcyclopropane-1-carboxylate **128** (28.3 mg, 0.100 mmol, >99% ee) and Nickel dimer **2** (0.9 mg, 1 mol%). The reaction mixture was stirred for 10 min at room temperature. Filtration over a short plug of silica eluting with Et_2O afforded the crude compound as a diastereomeric mixture as a viscous oil (27 mg, 0.096 mmol, 96%, 14:86 *cis*/*trans* (^{1}H NMR)). *Note: The diastereomers can either be separated by using silica flash column chromatography (4:1 pentane:Et_2O) or crystallization from hot hexane (100 mg/1 mL).* **R_f** (*trans*-isomer) = 0.32 (4:1 pentane:Et_2O, PMA). **$[\alpha]_D^{25}$** =

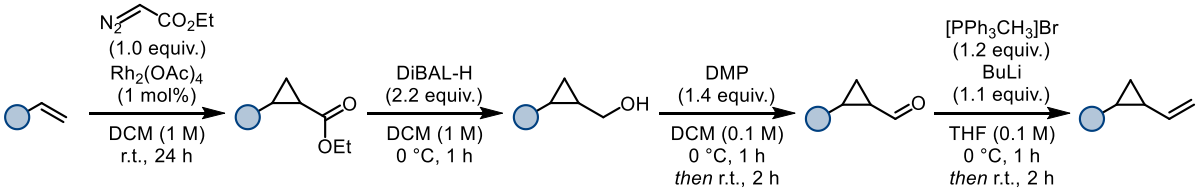
–37.6 (*c* 1.0 $CHCl_3$, 99% ee). **M.p.** = 101.6 – 104.1 °C. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 5.52 (dt, *J* = 18.2, 9.4 Hz, 1H), 5.25 (d, *J* = 17.2 Hz, 1H), 5.14 (d, *J* = 10.3 Hz, 1H), 4.90 (s, 0.6H, NH major rotamer), 4.69 (s, 0.3H, NH minor rotamer), 2.27 (q, *J* = 9.0, 8.6 Hz, 1H), 1.86 – 1.79 (m, 1H), 1.44 (s, 18H), 1.22 – 1.16 (m, 1H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 171.5, 156.1, 134.5, 117.9, 81.5, 79.8, 40.2, 30.8, 28.4, 28.1, 22.7. **IR** (neat, cm^{-1}): 3338, 3092, 2979, 2935, 2324, 2199, 2169, 2112, 1968, 1704, 1640, 1515, 1364, 1346, 1252, 1159, 1085, 1059, 991, 951, 905, 847, 762, 735, 697, 662. **HRMS** (ESI): *m/z* $[M+Na]^+$ calculated for $C_{15}H_{25}O_4NNa$: 306.1676, found 306.1682.

5.4.2 Synthesis of starting materials

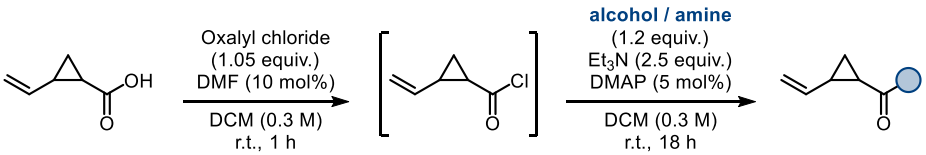
5.4.2.1 General procedures

General overview for starting material synthesis

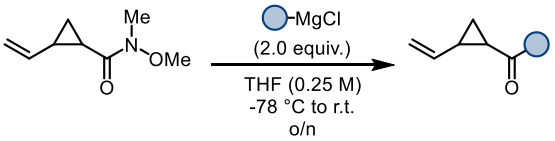
General Procedure A: Cyclopropanation with ethyl diazoacetate



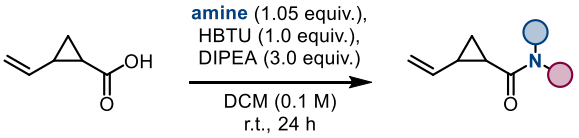
General Procedure B: Synthesis of vinylcyclopropyl ester



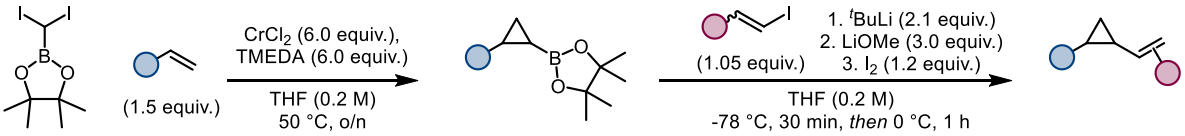
General Procedure C: Synthesis of vinylcyclopropyl ketones



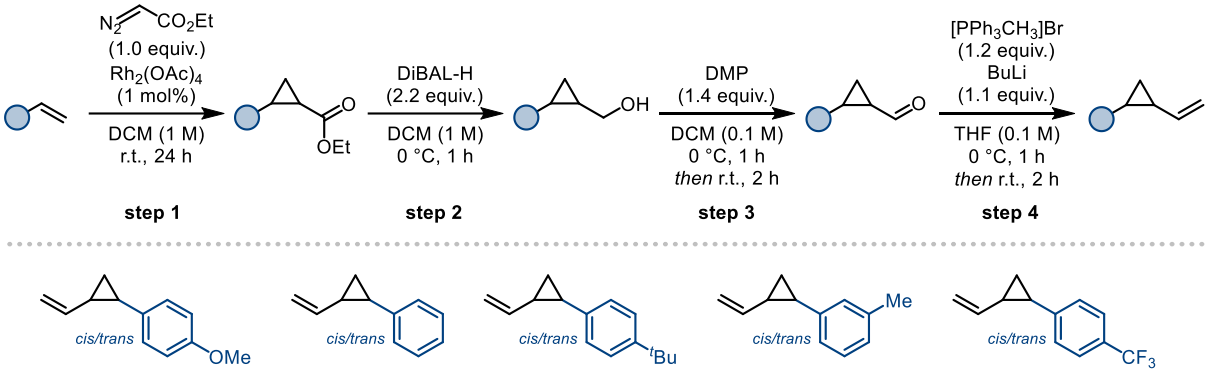
General Procedure D: Synthesis of vinylcyclopropyl amides



General Procedure E: Synthesis of vinylcyclopropyl boronates and Zweifel olefination

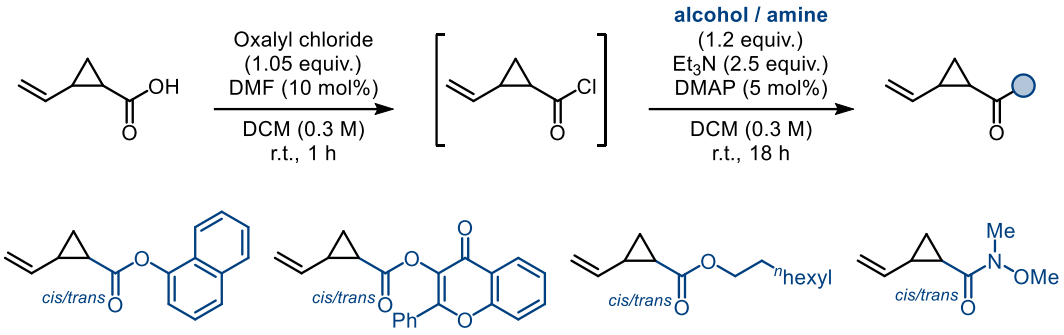


General procedure A: Cyclopropanation with ethyl diazoacetate



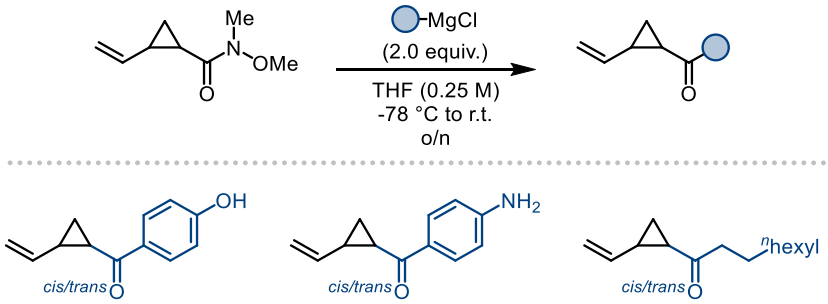
- **Step 1**: An oven dried flask equipped with a magnetic stir bar was charged with the corresponding styrene (1.0 equiv.), $Rh_2(OAc)_4$ (1 mol%) and dry DCM (1 M). Next, a solution of diazo ethyl diazoacetate (1.0 equiv.) in DCM (2 M) was added via syringe pump and over the course of 1 hour. After complete addition the resulting green mixture was stirred for further 24 hours before it was filtered through a short pad of silica gel. The mixture was concentrated under reduced pressure and flash silica gel column chromatography afforded corresponding product as a diastereomeric mixture.
- **Step 2**: Diisobutylaluminium hydride (1.0 M in toluene, 2.2 equiv.) was added dropwise over the course of 15 min to a stirred solution of the respective cyclopropyl ester (1.0 equiv.) in DCM (1 M) at –78 °C. The mixture was stirred for 1 h at 0 °C and HCl (1 M, 30 mL) was then slowly added. The aqueous layer was extracted with DCM (2 x 20 mL) and the combined organic extracts were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. Flash silica gel column chromatography afforded the corresponding cyclopropyl alcohol as a diastereomeric mixture.
- **Step 3**: The corresponding alcohol (1 mmol, 1.0 equiv.) was weighed into an oven dried flask and dissolved in dry DCM (10 mL, 0.1 M). The solution was cooled to 0 °C before DMP (600 mg, 1.4 mmol, 1.4 equiv.) was added and the reaction mixture was stirred for 1 h at 0 °C and then for 2 h at room temperature. The mixture was quenched by adding 10 mL of an aqueous 1:1 mixture of sat. $NaHCO_3$ and sat. $Na_2S_2O_3$ and it was stirred until both phases were clear. Next, the phases were separated, and the aqueous phase was extracted with DCM (3 x 10 mL). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude aldehydes were obtained quantitative in high purity and were used directly for the next step without further purification.
- **Step 4**: An oven dried flask was charged with methyltriphenylphosphonium bromide (1.2 mmol, 1.2 equiv.) before it was evacuated and backfilled with argon for three times. It was suspended in dry THF (10 mL, 0.1 M), cooled to 0 °C and ^{n}BuLi (1.1 mmol, 1.1 equiv., 2.5 M in hexane) was added dropwise and the reaction mixture stirred for 30 min at 0 °C. Then, a solution of the corresponding aldehyde (1.0 mmol, 1.0 equiv., 0.5 M in THF) was added and the resulting mixture was stirred for 1 h at 0 °C followed by 2 h at room temperature. The mixture was quenched by adding 5 mL of sat. aqueous NH_4Cl and phases were separated. The aqueous phase was extracted with DCM (2 x 10 mL). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude vinylcyclopropane was purified by silica silica gel column chromatography.

General Procedure B: Synthesis of vinylcyclopropyl esters



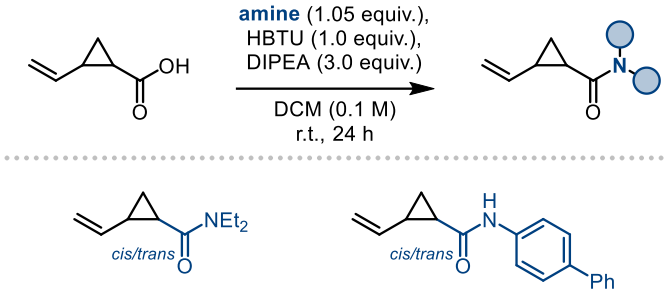
2-Vinylcyclopropane-1-carboxylic acid (1.0 equiv.) was dissolved in anhydrous DCM (0.3 M) and DMF (10 mol%) was added. The mixture was cooled to 0 °C and stirred for 5 minutes before a solution of oxalyl chloride (1.05 equiv.) in anhydrous DCM (2 M) was added dropwise to the reaction mixture. The reaction was then stirred at room temperature for 1 hour (until no gas evolution was observed). The freshly prepared acid chloride was then added to a stirred solution of the corresponding alcohol or amine (1.2 equiv.), Et_3N (2.5 equiv.) and DMAP (5 mol%) in anhydrous DCM (0.3 M) at 0 °C. After stirring for 5 minutes the reaction mixture was allowed to warm up to room temperature and stirred overnight. The mixture was quenched by adding 10 mL of sat. aqueous NH_4Cl and the phases were separated. The aqueous phase was extracted with DCM (2 x 10 mL). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude vinylcyclopropane was purified by silica gel column chromatography.

General Procedure C: Synthesis of vinylcyclopropyl ketones



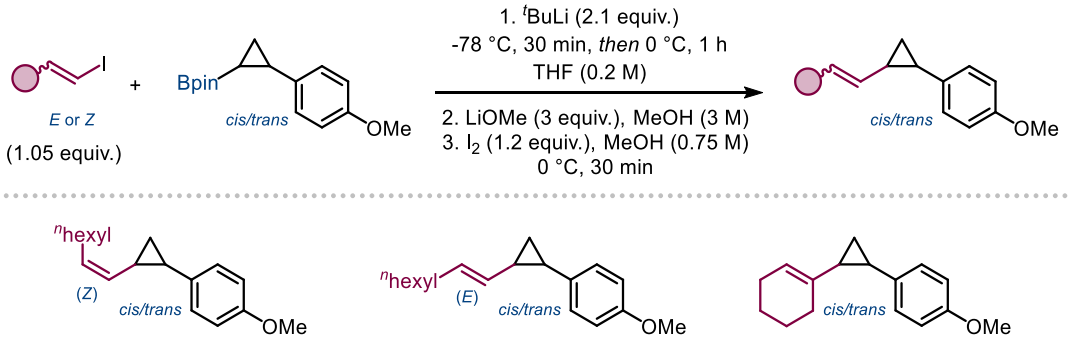
N-methoxy-*N*-methyl-2-vinylcyclopropane-1-carboxamide (1.0 mmol, 1.0 equiv.) was dissolved in anhydrous THF (0.25 M). The mixture was cooled to -78 °C before a solution of the corresponding organomagnesium compound (2.0 equiv.) in anhydrous THF or Et_2O (0.5 - 2 M) was added dropwise to the reaction mixture. After stirring for 5 minutes the reaction mixture was allowed to warm up to room temperature and stirred over night. The mixture was quenched by adding 10 mL of sat. aqueous NH_4Cl and phases were separated. The aqueous phase was extracted with DCM (2 x 10 mL). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude vinylcyclopropane was purified by silica gel column chromatography.

General procedure D: Synthesis of vinylcyclopropyl amides



2-Vinylcyclopropane-1-carboxylic acid (1.0 equiv.), HBTU (1.05 equiv.) and DIPEA (3.0 equiv.) were dissolved in anhydrous DCM (0.1 M) and stirred for 5 minutes before the amine (1.05 equiv.) was added. The reaction was then stirred at room temperature overnight. The reaction mixture was then diluted with DCM (10 mL) and washed with saturated $NaHCO_3$ solution (10 mL), 2 M HCl solution (10 mL) and brine (10 mL). The organic phase was dried over $MgSO_4$ and concentrated *in vacuo* before purification by silica gel silica gel column chromatography.

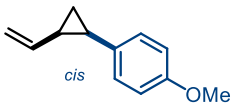
General Procedure E: Zweifel olefination



The corresponding vinyl iodide (0.525 mmol, 1.05 equiv.) was added to an oven dried Schlenk flask and dissolved in dry THF (2.5 mL, 0.2 M). The solution was then cooled to -78 °C and ^{t}BuLi (0.62 mL, 1.05 mmol, 2.1 equiv, 1.7 M in pentane) was added dropwise over a period of 10 min. After complete addition the mixture was stirred for 30 min at this temperature before a solution of 2-(2-(4-methoxyphenyl)cyclopropyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (137 mg, 0.5 mmol, 1.0 equiv.) in THF (2 mL, 0.25 M) was added dropwise. The reaction mixture was stirred for additional 15 min at -78 °C then warmed up to 0 °C and stirred for 1 h. Next, a suspension of LiOMe (57 mg, 1.5 mmol, 3.0 equiv.) in MeOH (0.5 mL, 3 M) was added and the mixture was cooled to 0 °C before a solution of iodine (153 mg, 0.6 mmol, 1.2 equiv.) in MeOH (0.8 mL, 0.75 M) was added dropwise at this temperature. The reaction was stirred for 30 min before it was quenched with sat. aqueous Na_2SO_3 solution (10 mL). Phases were separated and the aqueous phase was extracted with DCM (3x 10 mL), dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude material was then purified by silica gel column chromatography.

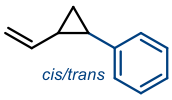
5.4.2.2 Compound characterization data

1-methoxy-4-(*cis*-2-vinylcyclopropyl)benzene: Prepared following General Procedure A from *cis*-2-(4-methoxyphenyl)cyclopropane-1-carbaldehyde (159 mg, 0.9 mmol). The title product was obtained after purification by silica gel column chromatography (50:1 pentane:Et_2O) as a colorless oil (110 mg, 0.63 mmol, 70%, 99:1 *cis*/*trans* (^{1}H NMR)).



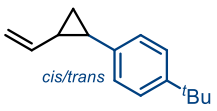
R_f = 0.38 (50:1 hexane:Et_2O). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.17 – 7.10 (m, 2H), 6.86 – 6.79 (m, 2H), 5.14 – 5.06 (m, 2H), 4.89 – 4.81 (m, 1H), 3.79 (s, 3H), 2.29 (td, *J* = 8.5, 6.4 Hz, 1H), 1.88 – 1.75 (m, 1H), 1.23 (td, *J* = 8.4, 5.1 Hz, 1H), 0.96 (q, *J* = 5.5 Hz, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 158.1, 138.6, 130.9, 130.3, 113.9, 113.6, 55.4, 22.8, 22.6, 12.0. **IR** (neat, cm^{-1}): 3074, 3001, 1633, 1611, 1512, 1458, 1295, 1244, 1177, 1034, 985, 894, 830, 798. **HRMS** (ESI): *m/z* $[M+H]^+$ calculated for $C_{12}H_{15}O$: 175.1117, found 175.1114.

(2-vinylcyclopropyl)benzene: Prepared following General Procedure A from 2-phenylcyclopropane-1-carbaldehyde (142 mg, 1 mmol). The title product was obtained after purification by silica gel column chromatography (pentane) as a colorless oil (105 mg, 0.728 mmol, 73%, 40:60 *cis*/*trans* (^{1}H NMR)).



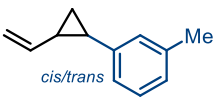
R_f = 0.4 (hexane). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.31 – 7.25 (m, 2H *cis* + 2H *trans*), 7.24 – 7.15 (m, 3H *cis* + 1H *trans*), 7.09 (d, *J* = 7.6 Hz, 2H *trans*), 5.56 (ddd, *J* = 17.3, 10.2, 8.5 Hz, 1H, *trans*), 5.17 – 5.08 (m, 2H *cis* + 1H *trans*), 4.95 (dd, *J* = 10.3, 1.4 Hz, 1H, *trans*), 4.89 – 4.85 (m, 1H, *cis*), 2.37 (td, *J* = 8.6, 6.4 Hz, 1H, *cis*), 1.94 (dt, *J* = 9.4, 5.1 Hz, 1H, *trans*), 1.92 – 1.85 (m, 1H, *cis*), 1.72 (tt, *J* = 8.8, 5.0 Hz, 1H, *trans*), 1.28 (td, *J* = 8.4, 5.2 Hz, 1H, *cis*), 1.22 (dt, *J* = 8.5, 5.4 Hz, 1H, *trans*), 1.12 (dt, *J* = 8.9, 5.3 Hz, 1H, *trans*), 1.06 (q, *J* = 5.7 Hz, 1H, *cis*). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 142.5, 140.8, 138.9, 138.2, 129.3, 128.5, 128.2, 126.1, 125.8, 125.8, 114.2, 112.7, 27.5, 25.4, 23.4, 23.1, 16.9, 11.8. **IR** (neat, cm^{-1}): 3075, 3025, 1635, 1603, 1496, 1453, 1077, 1030, 985, 895, 838, 747, 696. **HRMS** (EI): *m/z* $[M]^+$ calculated for $C_{11}H_{12}$: 144.0934, found 144.0937.

1-(*tert*-butyl)-4-(2-vinylcyclopropyl)benzene: Prepared following General Procedure A from 2-(4-(*tert*-butyl)phenyl)cyclopropane-1-carbaldehyde (101 mg, 0.5 mmol). The title product was obtained after purification by silica gel column chromatography (pentane) as a colorless oil (99 mg, 0.49 mmol, 98%, 27:73 *cis*/*trans* (^{1}H NMR)).

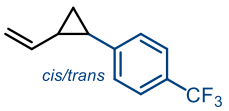


R_f = 0.34 (hexane). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.31 (dd, *J* = 8.4, 2.6 Hz, 2H *cis* + 2H *trans*), 7.15 (d, *J* = 7.8 Hz, 2H, *cis*), 7.05 – 7.01 (m, 2H, *trans*), 5.54 (ddd, *J* = 17.5, 10.2, 8.4 Hz, 1H, *trans*), 5.21 – 5.12 (m, 2H, *cis*), 5.10 (dd, *J* = 17.1, 1.6 Hz, 1H, *trans*), 4.93 (dd, *J* = 10.3, 1.6 Hz, 1H, *trans*), 4.87 (dd, *J* = 8.6, 3.7 Hz, 1H, *cis*), 2.32 (q, *J* = 8.4 Hz, 1H, *cis*), 1.91 (dt, *J* = 9.3, 5.0 Hz, 1H, *trans*), 1.86 (qd, *J* = 8.1, 5.3 Hz, 1H, *cis*), 1.70 (tt, *J* = 8.9, 5.0 Hz, 1H, *trans*), 1.34 – 1.30 (m, 9H *cis* + 9H *trans*), 1.28 – 1.23 (m, 1H, *cis*), 1.19 (dt, *J* = 8.7, 5.5 Hz, 1H, *trans*), 1.10 (dt, *J* = 9.3, 5.4 Hz, 1H, *trans*), 1.01 (q, *J* = 5.7 Hz, 1H, *cis*). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 148.8, 148.7, 140.9, 139.4, 138.6, 135.8, 128.9, 125.5, 125.4, 125.1, 114.0, 112.5, 34.5, 34.5, 31.5, 31.5, 27.4, 25.0, 23.1, 23.0, 16.8, 12.0. **IR** (neat, cm^{-1}): 3077, 2960, 1635, 1516, 1463, 1363, 1268, 1197, 1118, 1024, 984, 894, 830, 688. **HRMS** (EI): *m/z* $[M]^+$ calculated for $C_{15}H_{20}$: 200.1560, found 200.1554.

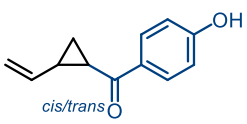
1-methyl-3-(2-vinylcyclopropyl)benzene: Prepared following General Procedure A from 2-(m-tolyl)cyclopropane-1-carbaldehyde (161 mg, 1.0 mmol). The title product was obtained after purification by silica gel column chromatography (pentane) as a colorless oil (126 mg, 0.796 mmol, 80%, 34:66 *cis*/*trans* (^{1}H NMR)). R_f = 0.43 (hexane). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.19 – 7.14 (m, 1H *cis*, 1H *trans*), 7.06 – 6.99 (m, 3H, *cis*), 6.98 (ddt, *J* = 7.6, 1.9, 0.8 Hz, 1H, *trans*), 6.89 (dt, *J* = 9.5, 1.8 Hz, 2H, *trans*), 5.54 (ddd, *J* = 17.0, 10.3, 8.5 Hz, 1H, *trans*), 5.15 – 5.09 (m, 2H *cis*, 1H *trans*), 4.94 (dd, *J* = 10.3, 1.6 Hz, 1H, *trans*), 4.86 (dd, *J* = 7.3, 5.0 Hz, 1H, *cis*), 2.34 (s, 3H, *cis*), 2.34 – 2.32 (m, 3H *trans*, 1H *cis*), 1.90 (ddd, *J* = 8.7, 5.8, 4.3 Hz, 1H, *trans*), 1.88 – 1.84 (m, 1H, *cis*), 1.70 (tdd, *J* = 8.6, 5.6, 4.3 Hz, 1H, *trans*), 1.25 (td, *J* = 8.4, 5.2 Hz, 1H, *cis*), 1.20 (ddd, *J* = 8.5, 5.8, 4.9 Hz, 1H, *trans*), 1.10 (ddd, *J* = 8.7, 5.7, 5.0 Hz, 1H, *trans*), 1.04 (dt, *J* = 6.4, 5.4 Hz, 1H, *cis*). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 142.4, 140.9, 138.7, 138.4, 138.1, 137.7, 130.1, 128.4, 128.0, 126.9, 126.7, 126.6, 126.2, 122.8, 114.1, 112.6, 27.5, 25.3, 23.4, 23.1, 21.6, 21.6, 16.8, 11.8. **HRMS** (EI): *m/z* $[M]^+$ calculated for $C_{12}H_{14}$: 158.1090, found 158.1090.



1-(trifluoromethyl)-4-(2-vinylcyclopropyl)benzene: Prepared following General Procedure A from 2-(4-(trifluoromethyl)phenyl)cyclopropane-1-carbaldehyde (215 mg, 1.0 mmol). The title product was obtained after purification by silica gel column chromatography (pentane) as a colorless oil (150 mg, 0.706 mmol, 71%, 36:64 *cis*/*trans* (^{1}H NMR)). R_f = 0.52 (hexane). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.55 – 7.49 (m, 2H *cis* + 2H *trans*), 7.31 (d, *J* = 8.0 Hz, 2H, *cis*), 7.16 (d, *J* = 8.0 Hz, 2H, *trans*), 5.55 (dddd, *J* = 17.0, 9.8, 8.3, 1.1 Hz, 1H, *trans*), 5.18 – 5.11 (m, 1H *cis* + 1H *trans*), 5.11 – 5.04 (m, 1H, *cis*), 5.00 – 4.96 (m, 1H, *trans*), 4.90 (dt, *J* = 10.1, 1.6 Hz, 1H, *cis*), 2.38 (q, *J* = 8.1 Hz, 1H, *cis*), 2.00 – 1.91 (m, 1H *cis* + 1H *trans*), 1.74 (tt, *J* = 8.9, 5.0 Hz, 1H, *trans*), 1.36 – 1.30 (m, 1H, *cis*), 1.27 – 1.22 (m, 1H, *trans*), 1.22 – 1.17 (m, 1H, *trans*), 1.09 (q, *J* = 5.9 Hz, 1H, *cis*). **^{19}F NMR** (565 MHz, $CDCl_3$) δ -62.29 (s, 3F, *trans*), -62.32 (s, 3F, *cis*). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 146.8, 143.2, 140.0, 137.3, 129.5, 128.3 (q, *J* = 32.3 Hz), 128.0 (q, *J* = 32.3 Hz), 126.0, 125.4 (q, *J* = 3.7 Hz), 125.1 (q, *J* = 3.7 Hz), 123.6, 123.6, 115.2, 113.4, 28.2, 25.2, 23.4, 23.3, 17.4, 12.1. **HRMS** (EI): *m/z* $[M]^+$ calculated for $C_{12}H_{11}F_3$: 212.0807, found 212.0800.

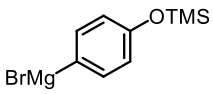


(4-hydroxyphenyl)(2-vinylcyclopropyl)methanone: Prepared from *N*-methoxy-*N*-methyl-2-vinylcyclopropane-1-carboxamide (233 mg, 1.5 mmol) and (4(4-((trimethylsilyl)oxy)phenyl)magnesium bromide (9.1 mL, 2.0 equiv., 0.33 M in THF, see below) following General Procedure C with a reaction time of 20 h. The title product was obtained after purification by silica gel column chromatography (4:1 hexane:EtOAc) as a beige solid (268 mg, 1.43 mmol, 95%, 41:59 *cis*/*trans* (^{1}H NMR)). R_f = 0.22 (4:1 hexane:EtOAc). **M.p.** = 80.2 – 85.1 °C. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.96 – 7.91 (m, 2H *cis* + 2H *trans*), 6.95 – 6.88 (m, 2H *cis* + 2H *trans*), 6.73 (s, 1H, *trans*), 6.65 (s, 1H, *cis*), 5.63 (ddd, *J* = 17.1, 10.3, 9.2 Hz, 1H, *cis*), 5.54 (ddd, *J* = 17.0, 10.3, 8.5 Hz, 1H, *trans*), 5.24 – 5.17 (m, 1H *cis* + 1H *trans*), 5.03 (dd, *J* = 10.3, 1.3 Hz, 1H, *trans*), 4.97 (dd, *J* = 10.3, 1.7 Hz, 1H, *cis*), 2.92 (ddd, *J* = 8.9, 7.5, 6.0 Hz, 1H, *cis*), 2.66 (ddd, *J* = 8.0, 5.2, 3.8 Hz, 1H, *trans*), 2.27 – 2.15 (m, 1H *cis* + 1H *trans*), 1.73 – 1.64 (m, 1H *cis* + 1H *trans*), 1.32 (ddd, *J* = 8.4, 7.5, 4.6



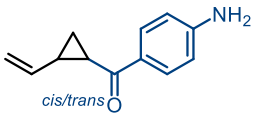
Hz, 1H, *cis*), 1.18 (ddd, *J* = 8.0, 6.4, 4.0 Hz, 1H, *trans*). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 198.4, 197.1, 160.7, 160.5, 138.6, 135.1, 131.5, 130.9, 130.9, 130.7, 116.4, 115.6, 115.5, 115.2, 29.5, 28.2, 26.5, 25.7, 18.2, 14.3. **IR** (neat, cm^{-1}): 3155, 2814, 2469, 1633, 1602, 1566, 1513, 1441, 1386, 1291, 1224, 1163, 1053, 1026, 990, 911, 849, 810, 740, 663. **HRMS** (ESI): *m/z* $[M+Na]^+$ calculated for $C_{12}H_{12}O_2Na$: 211.0730, found 211.0722.

(4-((trimethylsilyl)oxy)phenyl)magnesium bromide: Inside an argon filled glovebox (4-



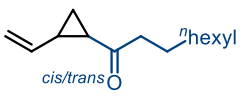
bromophenoxy)trimethylsilane (1.23 g, 5 mmol, 1.0 equiv.) was placed to an oven-dried screw top vial. It was dissolved in dry THF (10 mL, 0.5 M) and fine magnesium shavings (243 mg, 10 mmol, 2.0 equiv.) were added. The mixture was stirred overnight at room temperature. The starting bromide was fully consumed and titration with iodine afforded a concentration of 0.33 M. The compound was used in the next step without further analysis.

(4-aminophenyl)(2-vinylcyclopropyl)methanone: Prepared from *N*-methoxy-*N*-methyl-2-vinylcyclopropane-



1-carboxamide (155 mg, 1.0 mmol) and (4-(bis(trimethylsilyl)amino)phenyl) magnesium chloride (4.0 mL, 2.0 equiv., 0.5 M in THF) following General Procedure C with a reaction time of 16 h. The crude was then dissolved in 10 mL MeOH, aqueous HCl (2.0 mL, 1M) was added and it was stirred over night at room temperature. The mixture was diluted with DCM (10 mL) and H_2O (10 mL) and phases were separated. The aqueous layer was further extracted with DCM (3x10 mL) and the combined organic layers were dried over Na_2SO_4 and concentrated under reduced pressure. The title product was obtained after purification by silica gel column chromatography (2:1 hexane:EtOAc, 1% Et_3N) as a beige solid (72 mg, 0.38 mmol, 38%, 37:63 *cis*/*trans* (^{1}H NMR)). **R_f** = 0.2 (2:1 hexane:EtOAc). **M.p.** = 96.8 – 99.1 °C. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.88 – 7.84 (m, 2H *cis* + 2H *trans*), 6.68 – 6.63 (m, 2H *cis* + 2H *trans*), 5.65 (ddd, *J* = 17.1, 10.3, 9.3 Hz, 1H, *cis*), 5.53 (ddd, *J* = 17.0, 10.3, 8.5 Hz, 1H, *trans*), 5.18 (dt, *J* = 17.1, 1.6 Hz, 1H *cis* + 1H *trans*), 5.00 (dd, *J* = 10.3, 1.4 Hz, 1H, *trans*), 4.94 (dd, *J* = 10.3, 1.9 Hz, 1H, *cis*), 4.16 – 4.08 (m, 2H *cis* + 2H *trans*), 2.87 (ddd, *J* = 8.9, 7.5, 6.0 Hz, 1H, *cis*), 2.60 (ddd, *J* = 8.0, 5.2, 3.8 Hz, 1H, *trans*), 2.18 – 2.10 (m, 1H *cis* + 1H *trans*), 1.66 – 1.59 (m, 1H *cis* + 1H *trans*), 1.28 – 1.22 (m, 1H, *cis*), 1.10 (ddd, *J* = 8.0, 6.2, 3.9 Hz, 1H, *trans*). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 196.6, 195.4, 151.1, 151.0, 139.1, 135.7, 130.7, 130.6, 129.2, 128.5, 115.7, 114.6, 113.9, 113.9, 28.6, 27.5, 26.0, 25.2, 17.6, 13.8. **IR** (neat, cm^{-1}): 3412, 3334, 3223, 3006, 2976, 2681, 2324, 2163, 1829, 1744, 1631, 1586, 1515, 1440, 1386, 1306, 1236, 1170, 1133, 1048, 1002, 910, 842, 790, 750, 696, 667. **HRMS** (ESI): *m/z* $[M+Na]^+$ calculated for $C_{12}H_{13}ONNa$: 210.0889, found 210.0886.

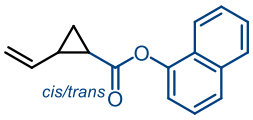
1-(2-vinylcyclopropyl)nonan-1-one: Prepared from *N*-methoxy-*N*-methyl-2-vinylcyclopropane-1-



carboxamide **S23** (155 mg, 1.0 mmol) and octylmagnesium chloride (1.0 mL, 2.0 equiv., 2M in THF) following General Procedure C with a reaction time of 16 h. The title product was obtained after purification by silica gel column chromatography (50:1 pentane:Et_2O) as a colorless oil (199 mg, 0.95 mmol, 95%, 40:60 *cis*/*trans* (^{1}H NMR)). **R_f** = 0.32

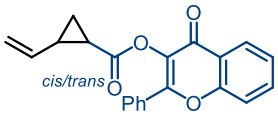
(*trans*) and 0.29 (*cis*) (50:1 pentane:Et_2O, $KMnO_4$). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 5.65 (dt, *J* = 17.1, 9.8 Hz, 1H, *cis*), 5.40 (ddd, *J* = 17.0, 10.3, 8.5 Hz, 1H, *trans*), 5.20 – 5.11 (m, 1H *cis* + 1H *trans*), 5.00 – 4.94 (m, 1H *cis* + 1H *trans*), 2.53 (td, *J* = 7.3, 1.9 Hz, 2H, *trans*), 2.50 (td, *J* = 7.3, 2.0 Hz, 2H, *cis*), 2.26 (ddd, *J* = 8.8, 7.6, 6.0 Hz, 1H, *cis*), 2.04 – 1.92 (m, 1H *cis* + 2H *trans*), 1.63 – 1.54 (m, 2H *cis* + 2H *trans*), 1.44 – 1.37 (m, 1H *cis* + 1H *trans*), 1.31 – 1.22 (m, 10H *cis* + 10H *trans*), 1.15 (td, *J* = 7.9, 4.5 Hz, 1H, *cis*), 0.98 (ddd, *J* = 8.1, 6.3, 3.9 Hz, 1H, *trans*), 0.89 – 0.85 (m, 3H *cis* + 3H *trans*). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 209.4, 208.3, 138.7, 135.4, 115.8, 114.7, 44.9, 44.1, 32.0, 29.6, 29.5, 29.4, 29.4, 29.3, 28.4, 27.6, 24.1, 24.1, 22.8, 17.6, 14.8, 14.2. **IR** (neat, cm^{-1}): 3083, 3005, 2925, 2856, 2324, 2616, 1697, 1637, 1458, 1385, 1288, 1199, 1130, 1080, 990, 902, 839, 786, 723. **HRMS** (ESI): *m/z* $[M+Na]^+$ calculated for $C_{14}H_{24}ONa$: 231.1719, found 231.1716.

Naphthalen-1-yl 2-vinylcyclopropane-1-carboxylate: Prepared from 2-vinylcyclopropane-1-carboxylic acid



(224 mg, 2.0 mmol) and naphthalen-1-ol (346 mg, 2.4 mmol) following General Procedure B with a reaction time of 16 h. The title product was obtained after purification by silica gel column chromatography (20:1 pentane:Et_2O) as a colorless oil (295 mg, 1.24 mmol, 62%, 37:63 *cis*/*trans* (^{1}H NMR)). **R_f** = 0.33 (20:1 pentane:Et_2O). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.92 – 7.85 (m, 2H *cis* + 2H *trans*), 7.78 – 7.71 (m, 1H *cis* + 1H *trans*), 7.56 – 7.43 (m, 3H *cis* + 3H *trans*), 7.28 – 7.22 (m, 1H *cis* + 1H *trans*), 5.87 (ddd, *J* = 17.1, 10.2, 9.2 Hz, 1H, *cis*), 5.55 (ddd, *J* = 17.1, 10.2, 8.3 Hz, 1H, *trans*), 5.39 (dd, *J* = 17.2, 1.7 Hz, 1H, *cis*), 5.30 (d, *J* = 17.1, 1H, *trans*), 5.16 (dd, *J* = 10.3, 1.7 Hz, 1H, *cis*), 5.12 (dd, *J* = 10.3, 1.3 Hz, 1H, *trans*), 2.39 (ddd, *J* = 8.8, 7.8, 5.9 Hz, 1H, *cis*), 2.31 (qd, *J* = 8.8, 3.9 Hz, 1H, *trans*), 2.26 – 2.16 (m, 1H, *cis*), 2.08 (ddd, *J* = 8.7, 5.1, 4.0 Hz, 1H, *trans*), 1.64 (dt, *J* = 9.3, 4.8 Hz, 1H, *trans*), 1.52 – 1.43 (m, 2H, *cis*), 1.24 (ddd, *J* = 8.3, 6.4, 4.4 Hz, 1H, *trans*). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 172.2, 170.8, 146.9, 146.7, 137.8, 135.1, 134.8, 128.2, 128.1, 127.0, 127.0, 126.6, 126.5, 126.5, 126.1, 125.5, 121.5, 121.3, 118.3, 118.2, 117.1, 115.6, 26.7, 25.9, 21.9, 21.1, 16.5, 15.0. **IR** (neat, cm^{-1}): 3061, 3011, 2326, 1745, 1636, 1598, 1508, 1443, 1378, 1318, 1222, 1130, 1047, 1012, 988, 909, 872, 846, 823, 769, 726. **HRMS** (ESI): *m/z* $[M+Na]^+$ calculated for $C_{16}H_{14}O_2Na$: 261.0886, found 261.0884.

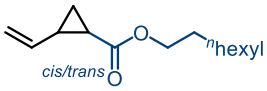
4-oxo-2-phenyl-*4H*-chromen-3-yl 2-vinylcyclopropane-1-carboxylate: Prepared from 2-vinylcyclopropane-



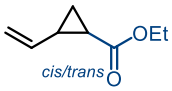
1-carboxylic acid (224 mg, 2.0 mmol) and 3-hydroxy-2-phenyl-4*H*-chromen-4-one (572 mg, 2.4 mmol) following General Procedure B with a reaction time of 18 h. The title product was obtained after purification by silica gel column chromatography (5:1 hexane:EtOAc) as a beige solid (329 mg, 1.0 mmol, 50%, 41:59 *cis*/*trans* (^{1}H NMR)). **R_f** = 0.18 (5:1 hexane:EtOAc). **M.p.** = 89.8 – 101.4 °C. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 8.29 – 8.23 (m, 1H *cis* + 1H *trans*), 7.87 (d, *J* = 6.7 Hz, 2H *trans*), 7.83 (d, *J* = 7.6 Hz, 2H *cis*), 7.71 – 7.68 (m, 1H *cis* + 1H *trans*), 7.57 – 7.46 (m, 4H *cis* + 4H *trans*), 7.44 – 7.38 (m, 1H *cis* + 1H *trans*), 5.73 (dt, *J* = 18.8, 10.0 Hz, 1H, *cis*), 5.46 (dt, *J* = 18.1, 9.4 Hz, 1H, *trans*), 5.29 (d, *J* = 14.8 Hz, 1H, *cis*), 5.22 (d, *J* = 17.0 Hz, 1H, *trans*), 5.09 – 5.03 (m, 1H *cis* + 1H *trans*), 2.29 (q, *J* = 7.9 Hz, 1H, *cis*), 2.22 – 2.16 (m, 1H, *trans*), 2.12 (t, *J* = 8.6 Hz, 1H, *cis*), 1.96 (q, *J* = 4.2 Hz, 1H, *trans*), 1.56 (q, *J* = 4.2 Hz, 1H, *trans*), 1.45 – 1.37 (m, 2H, *cis*), 1.19 –

1.14 (m, 1H, *trans*). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 172.4, 172.3, 170.6, 169.4, 156.4, 156.3, 155.7, 137.6, 134.7, 134.0, 134.0, 133.8, 133.7, 131.3, 131.3, 130.1, 130.1, 128.7, 128.7, 128.4, 128.4, 126.3, 126.2, 125.3, 125.2, 123.8, 118.2, 118.2, 116.8, 115.6, 26.7, 26.1, 21.8, 20.7, 16.3, 15.2. **IR** (neat, cm^{-1}): 3074, 2324, 2168, 1752, 1642, 1570, 1468, 1385, 1287, 1239, 1188, 1117, 987, 956, 899, 848, 757, 692. **HRMS** (ESI): *m/z* $[M+Na]^+$ calculated for $C_{21}H_{16}O_4Na$: 355.0941, found 355.0930.

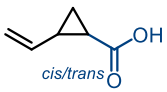
Octyl 2-vinylcyclopropane-1-carboxylate: Prepared from 2-vinylcyclopropane-1-carboxylic acid (224 mg, 2.0 mmol) and octan-1-ol (313 mg, 2.4 mmol) following General Procedure B with a reaction time of 16 h. The title product was obtained after purification by silica gel column chromatography (30:1 pentane:Et_2O) as a colorless oil (214 mg, 0.95 mmol, 48%, 50:50 *cis*/*trans* (^{1}H NMR)). **R_f** = 0.4 (25:1 pentane:Et_2O, $KMnO_4$). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 5.77 (dddd, *J* = 17.4, 9.5, 7.4, 1.7 Hz, 1H, *cis*), 5.39 (ddd, *J* = 17.0, 10.3, 8.4 Hz, 1H, *trans*), 5.22 (dd, *J* = 17.1, 1.8 Hz, 1H, *cis*), 5.15 (dd, *J* = 17.1, 1.3 Hz, 1H, *trans*), 5.03 (dd, *J* = 10.3, 1.8 Hz, 1H, *cis*), 4.98 (dd, *J* = 10.3, 1.4 Hz, 1H *trans*), 4.09 – 4.02 (m, 2H *cis* + 2H *trans*), 2.05 – 1.97 (m, 1H, *trans*), 1.97 – 1.87 (m, 2H, *cis*), 1.66 – 1.57 (m, 2H *cis* + 3H *trans*), 1.39 – 1.23 (m, 11H *cis* + 11H *trans*), 1.21 (td, *J* = 8.2, 4.8 Hz, 1H, *cis*), 0.96 (ddd, *J* = 8.3, 6.2, 4.3 Hz, 1H, *trans*), 0.90 – 0.84 (m, 3H *cis* + 3H *trans*). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 173.6 (*trans*), 172.1 (*cis*), 138.3 (*trans*), 135.6 (*cis*), 116.2 (*cis*), 114.8 (*trans*), 65.0 (*trans*), 64.8 (*cis*), 31.9 (*cis* + *trans*), 29.3 (*cis* + *trans*), 29.3 (*cis* + *trans*), 28.9 (*cis*), 28.8 (*trans*), 26.0 (*cis* + *trans*), 25.6 (*trans*), 24.9 (*cis*), 22.8 (*cis* + *trans*), 22.0 (*trans*), 21.1 (*cis*), 15.7 (*trans*), 14.2 (*cis*), 14.2 (*cis* + *trans*). **IR** (neat, cm^{-1}): 2926, 2857, 2326, 2090, 1726, 1638, 1460, 1401, 1372, 1266, 1167, 1084, 1049, 991, 904, 854, 815, 790, 726. **HRMS** (ESI): *m/z* $[M+Na]^+$ calculated for $C_{14}H_{24}O_2Na$: 247.1669, found 247.1665.



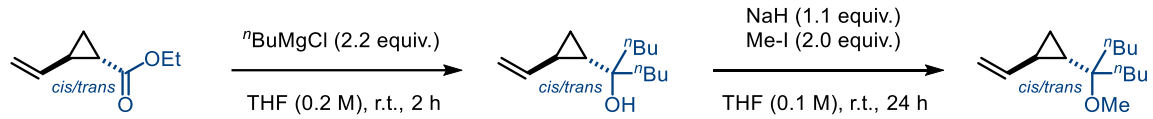
Ethyl 2-vinylcyclopropane-1-carboxylate : Prepared from butadiene (55 mL, 10 equiv., 15% in hexane) and ethyl diazoacetate (1.14 g, 10 mmol, 1.0 equiv.) following General Procedure A - step 1. The title product was obtained after purification by silica gel column chromatography (50:1 → 20:1 → 10:1 pentane:Et_2O) as a colorless oil (627 mg, 4.47 mmol, 45%, 44:56 *cis*/*trans* (^{1}H NMR)). **R_f** = 0.18 (50:1 pentane:Et_2O, PMA). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 5.82 – 5.73 (m, 1H, *cis*), 5.39 (ddd, *J* = 17.1, 10.3, 8.4 Hz, 1H, *trans*), 5.23 (dd, *J* = 17.1, 1.9 Hz, 1H, *cis*), 5.16 (dd, *J* = 17.1, 1.6 Hz, 1H, *trans*), 5.04 (dd, *J* = 10.3, 1.9 Hz, 1H, *cis*), 4.98 (dd, *J* = 10.2, 1.5 Hz, 1H, *trans*), 4.16 – 4.11 (m, 2H *cis*, 2H *trans*), 2.01 (tdd, *J* = 8.8, 6.1, 3.9 Hz, 1H, *trans*), 1.95 – 1.89 (m, 2H, *cis*), 1.63 (ddd, *J* = 8.7, 5.2, 3.9 Hz, 1H, *trans*), 1.38 – 1.34 (m, 1H, *trans*), 1.29 – 1.23 (m, 3H *trans,* 4H *cis*), 1.21 (dt, *J* = 8.3, 4.2 Hz, 1H, *cis*), 0.97 (ddd, *J* = 8.4, 6.2, 4.3 Hz, 1H, *trans*). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 173.5, 172.0, 138.3, 135.6, 116.2, 114.9, 60.7, 60.6, 25.6, 24.8, 22.0, 21.1, 15.6, 14.5, 14.4, 14.2. **IR** (neat, cm^{-1}): 2983, 1723, 1638, 1448, 1384, 1269, 1168, 1093, 1036, 987, 906. **HRMS** (ESI): *m/z* $[M]^+$ calculated for $C_8H_{12}O_2$: 140.0832, found 140.0833.



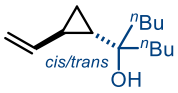
2-vinylcyclopropane-1-carboxylic acid: Synthesized according to a modified literature procedure:[154, 155] Ethyl 2-vinylcyclopropane-1-carboxylate (627 mg, 4.47 mmol, 1.0 equiv.) was placed into a 25 mL round bottom flask and aqueous KOH (2.5 mL, 1.5 equiv. 3 M) was added before



it was heated at reflux for 3 h. The mixture was cooled down to room temperature and it was diluted with DCM (10 mL) and 10 mL of an aqueous HCl solution (1 M) was added. The phases were separated, and the aqueous phase was extracted with DCM (2 x 10 mL). The combined organic extracts were dried over Na_2SO_4, filtered, and concentrated under reduced pressure (600 mbar, 40 °C). The crude acid was obtained as a colourless liquid in high purity and was used directly for the next step without further purification (464 mg, 4.14 mmol. 88%, 44:56 *cis*/*trans* (^{1}H NMR)). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 5.79 (ddd, *J* = 17.1, 10.3, 9.2 Hz, 1H, *cis*), 5.40 (ddd, *J* = 17.0, 10.2, 8.3 Hz, 1H, *trans*), 5.26 (dd, *J* = 17.1, 1.7 Hz, 1H, *cis*), 5.18 (dt, *J* = 17.0, 1.0 Hz, 1H, *trans*), 5.08 (dd, *J* = 10.3, 1.8 Hz, 1H, *cis*), 5.01 (dd, *J* = 10.3, 1.3 Hz, 1H, *trans*), 2.09 (tdd, *J* = 8.6, 6.3, 3.8 Hz, 1H, *trans*), 2.07 – 1.98 (m, 1H, *cis*), 1.92 (ddd, *J* = 8.7, 7.5, 6.2 Hz, 1H, *cis*), 1.64 (ddd, *J* = 8.6, 5.1, 3.8 Hz, 1H, *trans*), 1.43 (dt, *J* = 9.2, 4.8 Hz, 1H, *trans*), 1.32 – 1.28 (m, 2H, *cis*), 1.06 (ddd, *J* = 8.3, 6.4, 4.4 Hz, 1H, *trans*). *Note*: The acid proton was not observed in ^{1}H NMR due to H-D exchange. **^{13}C NMR** (151 MHz, $CDCl_3$) δ 180.2, 178.9, 137.7, 135.0, 116.9, 115.5, 26.6, 26.0, 21.9, 21.0, 16.3, 15.1. **IR** (neat, cm^{-1}): 2916, 2648, 2567, 1690, 1640, 1434, 1357, 1292, 1228, 1084, 1052, 980, 905, 854, 677. **HRMS** (ESI): *m/z* $[M\text{-}CO_2H]^+$ calculated for C_5H_7: 67.0542, found 67.0542.

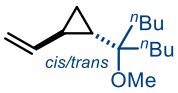


5-(2-vinylcyclopropyl)nonan-5-ol: Ethyl 2-vinylcyclopropane-1-carboxylate (1.40 g, 10.00 mmol, 1.0 equiv.)



was dissolved in dry THF (50 mL, 0.2 M) and cooled down to 0 °C. Butyl magnesium chloride solution (25.00 mmol, 2.5 equiv., 1.0 M in THF) was added dropwise over the course of 15 min to the stirring solution at 0 °C. The reaction mixture was allowed to warm to room temperature and was stirred overnight. The mixture was quenched by slowly adding 50 mL of sat. NH_4Cl. Next, the phases were separated, and the aqueous layer was extracted with Et_2O (2 x 50 mL). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude was used directly for the next step without further purification and analysis.

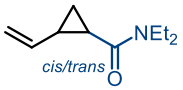
1-(5-methoxynonan-5-yl)-2-vinylcyclopropane: To a suspension of NaH (293.3 mg, 11.00 mmol, 1.1 equiv.)



in THF (100 mL, 0.1 M) was added dropwise a solution of 5-(2-vinylcyclopropyl)nonan-5-ol (2.10 g, 10.00 mmol, 1.0 equiv.) in THF (20 mL) at 0 °C. After stirring for 2 h at room temperature, a solution of MeI (1.87 mL, 30.00 mmol, 3.0 equiv.) in THF (20 mL) was added at 0 °C. The solution was stirred at room temperature for 24 h. The mixture was quenched by adding H_2O (100 mL). Next, the phases were separated, and the aqueous layer was extracted with Et_2O (3 x 100 mL). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. Purification by silica gel column chromatography (100:1 hexane:EtOAc) afforded the title compound as a colorless oil in two separate fractions (*fraction 1*: 110 mg, 0.490 mmol, 5%, 30:70 cis/trans (^{1}H NMR); *fraction 2*: 210 mg, 0.935 mmol, 9%, 12:88 cis/trans (^{1}H NMR)). *Note: Fraction 1 was obtained in 90% purity and was used without further purification for all further reactions.* **R_f** = 0.2 (100:1 hexane:EtOAc, PMA). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 5.85 (dt, *J* = 17.5, 9.9 Hz, 1H *cis*), 5.37 (ddd, *J* = 17.3,

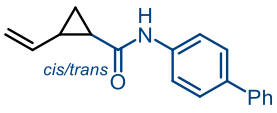
10.2, 8.7 Hz, 1H *trans*), 5.11 – 5.00 (m, 1H *cis*, 1H *trans*), 4.90 – 4.80 (m, 1H *cis*, 1H *trans*), 3.14 (s, 3H *trans*), 3.12 (s, 3H *cis*), 1.98 (q, *J* = 7.5, 6.9 Hz, 2H *cis*), 1.58 – 1.21 (m, 13H *trans,* 14H *cis*), 0.98 – 0.82 (m, 6H *trans*, 6H *cis*), 0.85 – 0.72 (m, 2H *trans*), 0.52 (ddd, *J* = 7.9, 5.1, 3.4 Hz, 1H *trans*). **^{13}C NMR** (101 MHz, $CDCl_3$): δ 142.0, 140.6, 112.4, 112.0, 77.0, 76.5, 49.2, 48.6, 36.8, 36.6, 35.6, 34.8, 27.7, 26.5, 26.3, 25.8, 25.6, 23.6, 23.6, 20.4, 18.1, 14.3, 10.0, 9.9. **IR** (neat, cm^{-1}): 3080, 2936, 2868, 2827, 2325, 2194, 2164, 2069, 2029, 1924, 1791, 1701, 1635, 1461, 1379, 1335, 1259, 1199, 1170, 1081, 1040, 985, 889, 826, 779, 730, 659. **HRMS** (ESI): *m/z* $[M+Na]^+$ calculated for $C_{15}H_{28}ONa$: 247.2032, found 247.2031.

***N*,*N*-diethyl-2-vinylcyclopropane-1-carboxamide:** Prepared from 2-vinylcyclopropane-1-carboxylic acid (56 mg, 0.5 mmol) and diethylamine (55 µL, 0.525 mmol) following General Procedure D. The title product was obtained after purification by silica gel column chromatography (3:2 hexane:EtOAc) as a colorless oil (46 mg, 0.275 mmol, 55%, 44:56 *cis*/*trans* (^{1}H NMR)).



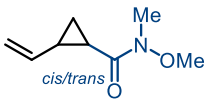
R$_f$ = 0.32 (3:2 hexane:EtOAc, PMA). **^{1}H NMR** (600 MHz, C_6D_6) δ 5.94 (dt, *J* = 17.3, 9.6 Hz, 1H, *cis*), 5.28 – 5.20 (m, 1H, *trans*), 5.15 (dd, *J* = 17.2, 2.0 Hz, 1H, *cis*), 5.03 (dd, *J* = 17.0, 1.4 Hz, 1H, *trans*), 4.96 (dd, *J* = 10.3, 2.0 Hz, 1H, *cis*), 4.87 (dd, *J* = 10.2, 1.4 Hz, 1H, *trans*), 3.36 – 3.23 (m, 1H *cis* + 1H *trans*), 3.23 – 3.09 (m, 1H *cis* + 1H *trans*), 2.99 (dq, *J* = 14.2, 7.1 Hz, 1H, *cis*), 2.86 (q, *J* = 7.1 Hz, 2H, *trans*), 2.78 (dq, *J* = 14.3, 7.1 Hz, 1H, *cis*), 2.20 (tdd, *J* = 8.8, 5.7, 4.3 Hz, 1H, *trans*), 1.72 (q, *J* = 5.9 Hz, 1H, *cis*), 1.67 (dt, *J* = 8.7, 4.4 Hz, 1H, *trans*), 1.55 – 1.48 (m, 2H, *cis*), 1.48 – 1.44 (m, 1H, *trans*), 0.97 – 0.92 (m, 3H *cis* + 3H *trans*), 0.81 – 0.75 (m, 4H *cis* + 3H *trans*), 0.65 (ddd, *J* = 8.2, 5.9, 3.7 Hz, 1H, *trans*). **^{13}C NMR** (151 MHz, C_6D_6) δ 170.2, 168.4, 139.7, 137.5, 114.7, 113.9, 41.9, 41.7, 41.1, 40.7, 25.2, 24.1, 20.9, 20.6, 15.0, 14.7, 13.6, 12.5. **IR** (neat, cm^{-1}): 2975, 2932, 1631, 1456, 1430, 1375, 1255, 1221, 1138, 1082, 899, 786. **HRMS** (ESI): *m/z* $[M+Na]^+$ calculated for $C_{10}H_{17}ONNa$: 190.1202, found 190.1201.

***N*-([1,1'-biphenyl]-4-yl)-2-vinylcyclopropane-1-carboxamide:** Prepared from 2-vinylcyclopropane-1-carboxylic acid (112 mg, 0.5 mmol) and 4-aminobiphenyl (180 mg, 1.05 mmol) following General Procedure D. The title product was obtained after purification by silica gel column chromatography (3:2 pentane:EtOAc) as a beige solid (88 mg, 0.33 mmol, 67%, 39:61 *cis*/*trans* (^{1}H NMR)).

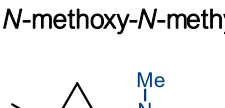


M.p. = 138.6 – 145.6 °C. **R$_f$** = 0.32 (*trans*) and 0.15 (*cis*) (4:1 hexane:EtOAc). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.64 – 7.51 (m, 7H *cis* + 7H *trans*), 7.42 (dd, *J* = 7.7 Hz, 2H *cis* + 2H *trans*), 7.33 (dd, *J* = 7.4 Hz, 1H *cis* + 1H *trans*), 5.87 (ddd, *J* = 17.2, 10.4, 9.2 Hz, 1H *cis*), 5.45 (ddd, *J* = 17.1, 10.3, 8.5 Hz, 1H *trans*), 5.25 (dd, *J* = 17.1, 1.8 Hz, 1H *cis*), 5.20 (dd, *J* = 17.0, 1.3 Hz, 1H *trans*), 5.05 (dd, *J* = 10.3, 1.8 Hz, 1H *cis*), 5.02 (dd, *J* = 10.3, 1.4 Hz, 1H *trans*), 2.13 (tdd, *J* = 8.7, 6.2, 3.9 Hz, 1H *trans*), 1.96 (qd, *J* = 8.7, 6.7 Hz, 1H *cis*), 1.89 (td, *J* = 8.3, 5.8 Hz, 1H *cis*), 1.57 (dt, *J* = 8.5, 4.5 Hz, 1H *trans*), 1.52 (dt, *J* = 9.2, 4.7 Hz, 1H *trans*), 1.45 (q, *J* = 5.8 Hz, 1H *cis*), 1.24 (tt, *J* = 8.2, 4.2 Hz, 1H *cis*), 1.01 (ddd, *J* = 8.0, 6.2, 4.3 Hz, 1H *trans*). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 170.5, 168.9, 140.6, 140.6, 138.5, 137.5, 137.4, 137.1, 137.1, 135.7, 128.9, 127.7, 127.2, 126.9, 120.1, 116.1, 114.9, 25.5, 25.1, 25.1, 24.0, 15.4, 13.3. **IR** (neat, cm^{-1}): 3292, 3033, 1650, 1596, 1532, 1487, 1448, 1401, 1316, 1203, 1077, 1004, 899, 833, 758, 685. **HRMS** (ESI): *m/z* $[M+Na]^+$ calculated for $C_{18}H_{17}ONNa$: 286.1202, found 286.1206.

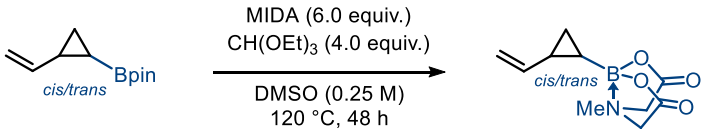
_N_-methoxy-_N_-methyl-2-vinylcyclopropane-1-carboxamide: Prepared from 2-vinylcyclopropane-1-carboxylic acid (560 mg, 5.0 mmol), _N_,_O_-dimethylhydroxylamine hydrochloride (585 mg, 6.0 mmol) and Et_3N (2.1 mL, 3.0 equiv.) following General Procedure B with a reaction time of 18 h. The crude was then dissolved in a minimum amount of Et_2O and filtered over a plug of silica washed with Et_2O and concentrated. The title product was obtained in high purity as a clear oil and was used without further purification (732 mg, 4.7 mmol, 94%, 42:58 *cis*/*trans* (^{1}H NMR)). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 5.67 (dt, *J* = 17.0, 9.9 Hz, 1H *cis*), 5.44 (ddd, *J* = 17.2, 10.2, 8.5 Hz, 1H *trans*), 5.24 – 5.10 (m, 1H *cis* + 1H *trans*), 5.03 – 4.92 (m, 1H *cis* + 1H *trans*), 3.72 (s, 3H *trans*), 3.70 (s, 3H *cis*), 3.20 (s, 3H *cis* + 3H *trans*), 2.44 (br, 1H *cis*), 2.16 (br, 1H *trans*), 2.03 – 1.87 (m, 1H *cis* + 1H *trans*), 1.46 – 1.31 (m, 1H *cis* + 1H *trans*), 1.15 (td, *J* = 8.1, 4.6 Hz, 1H *cis*), 0.94 (ddd, *J* = 8.3, 6.0, 4.0 Hz, 1H *trans*). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 138.9, 136.3, 115.6, 114.5, 61.8, 61.7, 32.7, 25.5, 24.7, 19.3, 18.9, 15.1, 12.6. *Note: The carbonyl carbon was not observed in ^{13}C NMR*. **IR** (neat, cm^{-1}): 3082, 3004, 2967, 2938, 2821, 2325, 2172, 2090, 1651, 1421, 1390, 1333, 1175, 1101, 1048, 1000, 966, 903, 845, 823, 791, 765, 720, 665. **HRMS** (ESI): *m/z* $[M+Na]^+$ calculated for $C_8H_{13}O_2NNa$: 178.0839, found 178.0837.



(*cis*-2-vinylcyclopropyl)triethylgermane: Inside the Glovebox an oven dried flask was charged with *cis*-1-Iodo-2-vinylcyclopropane (194 mg, 1mmol, 1.0 equiv.) and anhydrous THF (2.5 mL, 0.4 M). Outside the Glovebox the mixture was connected to the Schlenk line and cooled to -78 °C. Next, ^{t}BuLi (1.18 mL, 2.05 equiv., 1.7 M in hexane) was added dropwise over a period of 15 min using a syringe pump. After complete addition the mixture was stirred for further 30 min at –78 °C before neat Et_3GeCl (0.2 mL, 1.2 mmol, 1.2 equiv.) was added. The mixture was allowed to warm up to room temperature and stirred overnight. At the next day water (10 mL) and pentane (10 mL) were added, phases were separated and the aqueous phase was extracted with pentane (2x 10 mL). The combined organic phases were dried over Na_2SO_4, filtered and concentrated under reduced pressure. Flash column chromatography (pentane) afforded the title product as a colorless liquid (51 mg, 0.22 mmol, 22%). **R_f** = 0.8 (pentane, PMA). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 5.36 (ddd, *J* = 16.9, 10.1, 9.2 Hz, 1H), 5.12 (dd, *J* = 16.9, 1.9 Hz, 1H), 4.87 (dd, *J* = 10.2, 1.9 Hz, 1H), 1.68 (tdd, *J* = 9.1, 7.8, 4.7 Hz, 1H), 1.04 (t, *J* = 7.9 Hz, 10H), 0.74 (p, *J* = 7.9 Hz, 6H), 0.41 (dt, *J* = 7.8, 4.4 Hz, 1H), 0.18 (td, *J* = 9.6, 7.8 Hz, 1H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 142.4, 112.7, 19.2, 10.3, 9.1, 5.1, 4.9. **HRMS** (ESI): *m/z* $[M-Et]^+$ calculated for $C_9H_{17}Ge$: 199.0536, found 199.0532. *Note: Attention, compound is volatile*.



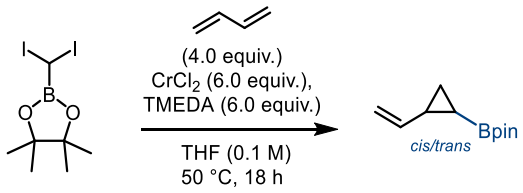
6-methyl-2-(2-vinylcyclopropyl)-1,3,6,2-dioxazaborocane-4,8-dione:



A 20 mL screw cap vial was charged with 4,4,5,5-tetramethyl-2-(2-vinylcyclopropyl)-1,3,2-dioxaborolane (100 mg, 0.52 mmol, 1.0 equiv.), _N_-methyliminodiacetic acid (455 mg, 3.1 mmol, 6.0 equiv.), triethyl orthoformate (0.342 mL, 2.1 mmol, 4.0 equiv.) and anhydrous DMSO (2 mL, 0.25 M). The vial was closed properly using a standard screw cap and the mixture was stirred vigorously at 120 °C for 48 hours. The

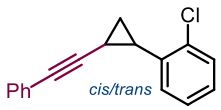
reaction was then allowed to cool to room temperature, diluted with ethyl acetate (20 mL) and washed with sat. $NaHCO_3$ (2x10 mL) and brine (10 mL), dried over Na_2SO_4 and concentrated *in vacuo*. Purification by silica gel column chromatography (20:1 DCM:MeOH) afforded the title compound as a diastereomeric mixture as a white solid (60 mg, 0.27 mmol, 52%, 35:65 *cis/trans* (^{1}H NMR)). **R_f** = 0.17 (20:1 DCM:MeOH, PMA). **M.p.** = 44.8–48.6 °C. **^{1}H NMR** (600 MHz, CD_3CN) δ 5.58 (dt, *J* = 17.3, 10.1 Hz, 1H, *cis*), 5.37 (dt, *J* = 17.5, 9.6 Hz, 1H, *trans*), 5.15 (dd, *J* = 17.1, 2.1 Hz, 1H, *cis*), 5.10 (dd, *J* = 17.2, 1.8 Hz, 1H, *trans*), 4.90 (dd, *J* = 10.3, 2.1 Hz, 1H, *cis*), 4.83 (dd, *J* = 10.2, 1.8 Hz, 1H, *trans*), 3.97 – 3.89 (m, 2H *cis* + 2H *trans*), 3.85 – 3.78 (m, 2H *cis* + 2H *trans*), 2.96 (s, 3H, *cis*), 2.94 (s, 3H, *trans*), 1.66 (dt, *J* = 14.7, 9.1 Hz, 1H, *cis*), 1.31 (tt, *J* = 8.7, 5.2 Hz, 1H, *trans*), 1.01 – 0.95 (m, 1H, *cis*), 0.66 – 0.58 (m, 2H, *trans*), 0.42 (dt, *J* = 8.3, 4.3 Hz, 1H, *cis*), 0.08 (q, *J* = 9.1 Hz, 1H, *cis*), -0.16 (dt, *J* = 9.8, 6.3 Hz, 1H, *trans*). **^{11}B NMR** (193 MHz, CD_3CN) δ 17.9, 17.6. **^{13}C NMR** (151 MHz, CD_3CN) δ 169.2, 169.2, 169.1, 169.0, 144.0, 141.9, 113.9, 111.9, 63.1, 63.1, 63.0, 63.0, 47.4, 47.4, 20.6, 19.6, 10.8, 10.7, 7.5, 6.6. **MS** (70eV, EI): *trans isomer* (GC retention time 11.11 min), *m/z* (%): 223 (1) [M^+], 156 (100) [$MIDA^+$], 128 (15), 100 (42), 70 (10), 66 (3) [vinyl $cyclopropyl^+$]; *cis isomer* (GC retention time 11.24 min), *m/z* (%): *m/z* (%): 223 (1) [M^+], 207 (1), 156 (100) [$MIDA^+$], 128 (14), 100 (41), 70 (10), 66 (3) [vinyl $cyclopropyl^+$]. **IR** (neat, cm^{-1}): 3001, 2960, 2923, 1744, 1634, 1456, 1337, 1289, 1248, 1124, 1075, 993, 961, 890, 861, 709, 664. **HRMS** (ESI): *m/z* $[M+Na]^+$ calculated for $C_{10}H_{14}O_4N^{11}BNa$: 246.0908, found 246.0907.

4,4,5,5-tetramethyl-2-(2-vinylcyclopropyl)-1,3,2-dioxaborolane:



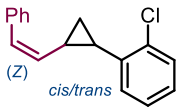
Synthesized according to a modified literature procedure:[156] In an argon-filled glovebox, a 50 mL round-bottom flask equipped with a magnetic stir bar and a rubber septum was charged sequentially with $CrCl_2$ (740 mg, 6.0 mmol, 6.0 equiv.), dry THF (10 mL, 0.1 M) and TMEDA (900 µL, 6.0 mmol, 6.0 equiv.). The reaction was stirred for 20 minutes inside the glovebox before 2-(diiodomethyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane[157] (394 mg, 1.0 mmol, 1.0 equiv.) was added in one portion. The reaction mixture was stirred for 30 minutes and then removed from the glovebox. Next, a solution of 1,3-butadiene (2.0 mL, 4.0 mmol, 4.0 equiv., 2.0 M in THF) was added. After further stirring for 18 hours at 50 °C the resulting reaction mixture was filtered through a plug of silica gel eluting with diethyl ether. The organic phase was then washed with water and brine, dried over Na_2SO_4, filtered and concentrated *in vacuo* to afford the product as a clear and colorless oil (157.2 mg, 0.81 mmol, 81%, 41:59 *cis/trans* (^{1}H NMR)). The compound showed sufficient purity at this stage and subsequent silica gel column chromatography was not required. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 5.64 (dt, *J* = 16.7, 10.0 Hz, 1H, *cis*), 5.30 (dt, *J* = 16.5, 9.4 Hz, 1H, *trans*), 5.16 – 5.07 (m, 1H *cis* + 1H *trans*), 4.90 – 4.83 (m, 1H *cis* + 1H *trans*), 1.78 – 1.71 (m, 1H, *cis*), 1.63 (tt, *J* = 8.9, 5.3 Hz, 1H, *trans*), 1.24 – 1.21 (m, 12H *cis* + 12H *trans*), 1.04 – 0.99 (m, 1H, *cis*), 0.91 (td, *J* = 7.2, 3.4 Hz, 1H, *trans*), 0.76 – 0.71 (m, 1H, *cis*), 0.69 (dt, *J* = 9.2, 4.2 Hz, 1H, *trans*), 0.23 (td, *J* = 9.2, 7.3 Hz, 1H, *cis*), -0.04 (dt, *J* = 9.3, 6.0 Hz, 1H, *trans*). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 142.4, 140.7, 112.9, 112.2, 83.3, 83.2, 25.2, 24.9 (2C),

24.8, 21.9, 21.6, 12.6, 12.3. **^{11}B NMR** (193 MHz, $CDCl_3$) δ 33.0. **IR** (neat, cm^{-1}): 3078, 2979, 2930, 1635, 1437, 1405, 1372, 1319, 1216, 1144, 979, 944, 895, 847, 803, 671. **HRMS** (EI): *m/z* $[M]^+$ calculated for $C_{11}H_{19}O_2{}^{11}B$: 194.1473, found 194.1477. *Note: Caution compound is volatile.*

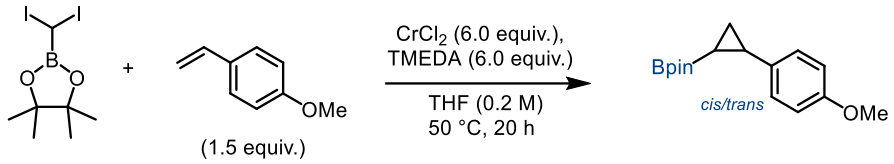


1-chloro-2-(2-(phenylethynyl)cyclopropyl)benzene: Synthesized following the Pd$^{(I)}$ coupling using (bromoethynyl)benzene (218 mg, 1.2 mmol, 1.2 equiv.) and a suspension of freshly prepared (2-(2-chlorophenyl)cyclopropyl)zinc(II) chloride[62] (1.0 mmol). Flash silica gel column chromatography (hexane) afforded the title product as a diastereomeric mixture as a colorless oil (117 mg, 0.46 mmol, 46%, 62:38 *cis*/*trans* (^{1}H NMR)). R_f = 0.28 (hexane). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.44 – 7.37 (m, 4H), 7.30 – 7.27 (m, 2H), 7.25 – 7.13 (m, 8H), 7.05 – 6.99 (m, 4H), 2.66 – 2.58 (m, 2H), 2.11 (ddd, *J* = 8.5, 5.6 Hz, 1H, *cis*), 1.71 (ddd, *J* = 8.8, 5.2 Hz, 1H, *trans*), 1.51 – 1.44 (m, 2H), 1.38 – 1.30 (m, 2H). The product was directly used in the following step without further analysis.

(*Z*)-1-chloro-2-(2-styrylcyclopropyl)benzene: 1-chloro-2-(2-(phenylethynyl)cyclopropyl)benzene (50 mg, 0.2 mmol, 1.0 equiv.) was dissolved in a 1:1 mixture of hexane/EtOAc (1 mL, 0.25 M). Next, Lindlar catalyst (10 mg, 20 mol%) and pyridine (0.016 mL, 0.2 mmol, 1.0 equiv.) were added and the flask was sealed with a septum. The flask was connected to a hydrogen balloon and the atmosphere was exchanged by bubbling hydrogen through the solution for 5 min before the reaction was stirred for 3 hours at room temperature under hydrogen. The reaction mixture was filtered over a plug of silica washing with Et_2O. The solution was then concentrated under reduced pressure. Flash silica gel column chromatography (pentane) afforded the title product as a diastereomeric mixture as a colorless oil (36 mg, 0.14 mmol, 71%, 69:31 *cis*/*trans*, 93:7 *Z*/*E* (^{1}H NMR)). **R_f** = 0.26 (hexane). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.48 (d, *J* = 7.5 Hz, 2H, *cis*), 7.41 – 7.33 (m, 3H *cis* + 2H *trans*), 7.30 (t, *J* = 7.6 Hz, 2H, *trans*), 7.25 – 7.09 (m, 4H *cis* + 4H *trans*), 6.94 (dd, *J* = 7.8, 1.0 Hz, 1H, *trans*), 6.47 (d, *J* = 11.4 Hz, 1H, *trans*), 6.31 (d, *J* = 11.6 Hz, 1H, *cis*), 5.34 (dd, *J* = 11.2, 9.9 Hz, 1H, *trans*), 4.80 (dd, *J* = 11.3, 10.1 Hz, 1H, *cis*), 2.54 (q, *J* = 8.3 Hz, 1H, *cis*), 2.47 (qd, *J* = 9.0, 6.0 Hz, 1H, *cis*), 2.37 (dt, *J* = 8.9, 5.5 Hz, 1H, *trans*), 2.10 (tt, *J* = 9.5, 5.0 Hz, 1H, *trans*), 1.42 (td, *J* = 8.3, 5.3 Hz, 1H, *cis*), 1.33 (dt, *J* = 8.6, 5.6 Hz, 1H, *trans*), 1.19 (dt, *J* = 9.0, 5.2 Hz, 1H, *trans*), 1.14 (q, *J* = 5.5 Hz, 1H, *cis*). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 139.2, 137.9, 137.7, 136.8, 136.7, 135.4, 134.8, 131.3, 129.8, 129.6, 129.4, 129.4, 129.0, 128.9, 128.6, 128.3, 128.3, 127.6, 127.1, 126.9, 126.7, 126.6, 126.5, 126.4, 24.1, 23.3, 22.7, 19.2, 16.8, 13.6. **MS** (70eV, EI): *trans isomer* (GC retention time 10.358 min), *m/z* (%): 254 (13) $[M^+]$, 215 (6), 202 (11), 189 (4), 176 (3), 163 (5), 130 (11), 129 (100), 91 (23); *cis isomer* (GC retention time 10.482 min), *m/z* (%): 254 (15) $[M^+]$, 217 (32), 202 (32), 189 (7), 178 (4), 163 (6), 151 (2), 141 (11), 129 (100), 91 (23). **HRMS** (ESI): *m/z* $[M]^+$ calculated for $C_{17}H_{15}Cl$: 254.0857, found 254.0862.



2-(2-(4-methoxyphenyl)cyclopropyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane:



This compound was synthesized according to a modified literature procedure.[156] In an argon-filled glovebox, a 50 mL round-bottom flask equipped with a magnetic stir bar and a rubber septum was charged sequentially with $CrCl_2$ (2.62 g, 30 mmol, 6.0 equiv.), dry THF (25 mL, 0.2 M) and TMEDA (4.53 mL, 30 mmol, 6.0 equiv.). The mixture was stirred for 20 minutes inside the glovebox before 2-(diiodomethyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane[4] (1.97 g, 5.0 mmol, 1.0 equiv.) was added in one portion. The reaction mixture was stirred for 30 minutes and then removed from the glovebox. Next, 1-methoxy-4-vinylbenzene (1.0 mL, 7.5 mmol, 1.5 equiv.) was added. The green/brown reaction mixture was then stirred for 20 hours at 50 °C. The mixture was allowed to cool to room temperature and water (50 mL) was added. Phases were separated and the aqueous phase was extracted with EtOAc (3x 50 mL). The combined organic layers were dried over Na_2SO_4, filtered and concentrated under reduced pressure. Flash silica gel column chromatography (50:1 hexane:EtOAc) afforded the title product as a diastereomeric mixture as a pale yellow oil (412 mg, 1.5 mmol, 30%, 23:77 *cis*/*trans* (^{1}H NMR)). **R_f** = 0.3 (20:1 hexane:EtOAc). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.19 (dd, *J* = 8.6, 2.1 Hz, 2H, *cis*), 7.01 (dd, *J* = 8.5, 2.2 Hz, 2H, *trans*), 6.82 – 6.74 (m, 2H *cis* + 2H *trans*), 3.79 – 3.75 (m, 3H *cis* + 3H *trans*), 2.33 – 2.24 (m, 1H, *cis*), 2.11 – 2.02 (m, 1H, *trans*), 1.27 – 1.22 (m, 12H, *trans*), 1.22 – 1.18 (m, 1H, *cis*), 1.14 – 1.08 (m, 1H, *trans*), 1.08 – 1.05 (m, 1H, *cis*), 1.03 (s, 3H, *cis*), 0.97 – 0.91 (m, 1H, *trans*), 0.90 (s, 3H, *cis*), 0.44 – 0.34 (m, 1H, *cis*), 0.26 – 0.17 (m, 1H, *trans*). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 158.0 (*cis*), 157.9 (*trans*), 135.5 (*trans*), 133.2 (*cis*), 130.0 (*cis*), 127.0 (*trans*), 113.9 (*trans*), 113.3 (*cis*), 83.3 (*trans*), 83.0 (*cis*), 55.5 (*cis*), 55.5 (*trans*), 25.0 (*cis*), 24.9 (*trans*), 24.9 (*trans*), 24.6 (*cis*), 21.4 (*trans*), 21.2 (*cis*), 14.6 (*trans*), 9.1 (*cis*). **MS** (70eV, EI): *cis isomer* (GC retention time 9.15 min), *m/z* (%): 274 (100) [M^+], 215 (12), 175 (44), 156 (37), 147 (39), 115 (49), 83 (34); *trans isomer* (GC retention time 9.80 min), *m/z* (%): 274 (100) [M^+], 215 (11), 175 (42), 156 (23), 147 (40), 115 (44), 83 (30). The data are in agreement with those previously reported in the literature.[156]

(*Z*)-1-methoxy-4-(2-(oct-1-en-1-yl)cyclopropyl)benzene: Prepared following General Procedure E using (*E*)-1-iodooct-1-ene (125 mg, 0.525 mmol). Flash silica gel column chromatography (50:1 hexane:EtOAc) afforded the title compound as a diastereomeric mixture as a colorless oil (60 mg, 0.23 mmol, 46%, 53:47 *cis*/*trans*, 92:8 *Z*/*E* (^{1}H NMR)). **R_f** = 0.5 (50:1 hexane:EtOAc). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.13 – 7.09 (m, 2H, *cis*), 7.04 – 7.00 (m, 2H, *trans*), 6.84 – 6.79 (m, 2H *cis* + 2H *trans*), 5.37 (dt, *J* = 10.7, 7.4 Hz, 1H, *trans*), 5.29 (dt, *J* = 10.8, 7.4 Hz, 1H, *cis*), 4.92 (t, *J* = 10.1 Hz, 1H, *trans*), 4.62 (t, *J* = 10.3 Hz, 1H, *cis*), 3.78 (s, 3H *cis* + 3H *trans*), 2.30 – 2.23 (m, 1H, *cis*), 2.18 – 2.10 (m, 2H *cis* + 2H *trans*), 1.97 – 1.88 (m, 1H, *cis*), 1.86 – 1.80 (m, 1H, *trans*), 1.77 – 1.70 (m, 1H, *trans*), 1.41 – 1.21 (m, 9H *cis* + 8H *trans*), 1.17 – 1.11 (m, 1H, *trans*), 0.98 – 0.91 (m, 1H, *trans*), 0.92 – 0.84 (m, 4H *cis* + 3H *trans*). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 157.9 (*cis*), 157.9 (*trans*), 134.8 (*trans*), 132.5 (*trans*), 131.2 (*cis*), 130.4 (*cis*), 130.3 (*cis*), 129.3 (*trans*), 129.1 (*cis*), 127.1 (*trans*), 113.9

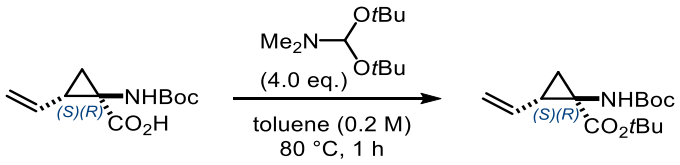
(*trans*), 113.6 (*cis*), 55.5 (*trans*), 55.4 (*cis*), 32.0 (*cis*), 31.9 (*trans*), 29.9 (*trans*), 29.9 (*cis*), 29.1 (*cis*), 29.1 (*trans*), 27.9 (*trans*), 27.8 (*cis*), 24.6, 22.8 (*cis*), 22.8 (*trans*), 22.4 (*cis*), 22.2 (*trans*), 17.3 (*cis*), 16.9 (*trans*), 14.3 (*cis*), 14.3 (*trans*), 12.6 (*cis*). *Note: Only Z-isomers were assigned.* **MS** (70eV, EI): *cis isomer* (GC retention time 10.22 min), *m/z* (%): 258 (20) [M^+], 173 (84), 159 (27), 147 (11), 134 (92), 121 (100); *trans isomer* (GC retention time 10.09 min), *m/z* (%): 258 (23) [M^+], 173 (87), 159 (28), 147 (12), 134 (92), 121(100). The data are in agreement with those previously reported in the literature.[62]

(E)-1-methoxy-4-(2-(oct-1-en-1-yl)cyclopropyl)benzene: Prepared following General Procedure E using (*Z*)-1-iodooct-1-ene (125 mg, 0.525 mmol). Flash silica gel column chromatography (50:1 hexane:EtOAc) afforded the title compound as a diastereomeric mixture as a colorless oil (53 mg, 0.20 mmol, 41%, 59:41 *cis*/*trans*, 14:86 *Z*/*E* (^{1}H NMR)). **R_f** = 0.52 (50:1 hexane:EtOAc). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.13 – 7.09 (m, 2H, *cis*), 7.00 – 6.98 (m, 2H, *trans*), 6.82 – 6.79 (m, 2H *cis* + 2H *trans*), 5.51 (dq, *J* = 15.2, 6.6 Hz, 1H *cis* + 1H *trans*), 5.13 (dd, *J* = 15.3, 8.4 Hz, 1H, *trans*), 4.73 (dd, *J* = 15.2, 8.9 Hz, 1H, *cis*), 3.79 (s, 3H, *cis*), 3.78 (s, 3H, *trans*), 2.20 (td, *J* = 8.6, 6.2 Hz, 1H, *cis*), 2.01 – 1.97 (m, 2H, *trans*), 1.86 (q, *J* = 7.4 Hz, 2H, *cis*), 1.80 (dt, *J* = 9.3, 5.0 Hz, 1H, *trans*), 1.74 (qd, *J* = 8.7, 5.6 Hz, 1H, *cis*), 1.57 – 1.52 (m, 1H, *trans*), 1.37 – 1.13 (m, 10H *cis* + 8H *trans*), 1.06 (dt, *J* = 8.5, 5.2 Hz, 1H, *trans*), 0.98 (dt, *J* = 8.4, 5.1 Hz, 1H, *trans*), 0.89 (t, *J* = 7.0 Hz, 3H, *trans*), 0.86 (t, *J* = 7.2 Hz, 3H, *cis*). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 157.9 (*cis*), 157.8 (*trans*), 134.9 (*trans*), 132.2 (*trans*), 131.3 (*cis*), 130.8 (*cis*), 130.3 (*cis*), 129.4 (*cis*), 129.3 (*trans*), 126.8 (*trans*), 113.9 (*trans*), 113.5 (*cis*), 55.5 (*trans*), 55.4 (*cis*), 32.7 (*cis*), 32.7 (*trans*), 31.9 (*trans*), 31.9 (*cis*), 29.7 (*trans*), 29.7 (*cis*), 29.0 (*trans*), 28.8 (*cis*), 26.0 (*trans*), 24.3 (*trans*), 22.8 (*cis* + *trans*), 22.2 (*cis*), 21.6 (*cis*), 16.4 (*trans*), 14.4 (*cis*), 14.3 (*trans*), 11.8 (*cis*). *Note*: Only *E*-isomers were assigned. **MS** (70eV, EI): *cis isomer* (GC retention time 9.93 min), *m/z* (%): 258 (24) [M^+], 173 (96), 159 (30), 147 (12), 134 (88), 121 (100); *trans isomer* (GC retention time 10.44 min), *m/z* (%): 258 (26) [M^+], 173 (97), 159 (30), 147 (12), 134 (89), 121(100).

1-(2-(cyclohex-1-en-1-yl)cyclopropyl)-4-methoxybenzene: Prepared following General Procedure E using 1-iodocyclohex-1-ene (109 mg, 0.525 mmol). Flash silica gel column chromatography (30:1 hexane:EtOAc) afforded the title compound as a diastereomeric mixture as a colorless oil (60 mg, 0.23 mmol, 46%, 25:75 *cis*/*trans* (^{1}H NMR)). **R_f** = 0.67 (10:1 hexane:EtOAc). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.04 – 6.97 (m, 2H *cis* + 2H *trans*), 6.81 (dd, *J* = 8.7, 2.1 Hz, 2H, *trans*), 6.77 – 6.72 (m, 2H, *cis*), 5.48 (s, 1H, *trans*), 5.46 (s, 1H, *cis*), 3.80 – 3.76 (m, 3H *cis* + 3H *trans*), 2.16 – 2.08 (m, 1H, *cis*), 2.02 – 1.98 (m, 2H, *trans*), 1.95 – 1.90 (m, 2H, *trans*), 1.90 – 1.83 (m, 1H, *trans*), 1.75 – 1.66 (m, 2H, *cis*), 1.67 – 1.60 (m, 1H *cis* + 2H *trans*), 1.61 – 1.52 (m, 1H *cis* + 2H *trans*), 1.53 – 1.46 (m, 1H, *trans*), 1.45 – 1.34 (m, 3H, *cis*), 1.28 – 1.18 (m, 2H, *cis*), 1.16 – 1.07 (m, 1H *cis* + 1H *trans*), 1.08 – 1.02 (m, 1H, *cis*), 0.93 (dt, *J* = 8.7, 5.3 Hz, 1H, *trans*). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 157.8 (*cis*+*trans*), 137.5 (*trans*), 135.6 (*trans*), 134.3 (*cis*), 131.5 (*cis*), 129.0 (*cis*), 127.0 (*trans*), 123.8 (*cis*), 120.2 (*trans*), 113.9 (*trans*), 113.0 (*cis*), 55.5 (*trans*), 55.4 (*cis*), 29.7 (*trans*), 29.5 (*cis*), 27.2 (*trans*), 26.8 (*cis*), 25.4 (*cis*+*trans*), 23.1 (*trans*), 22.9 (*cis*), 22.8 (*trans*), 22.6 (*cis*), 22.6 (*trans*), 21.4 (*cis*),

13.9 (*trans*), 8.9 (*cis*). **MS** (70eV, EI): *cis isomer* (GC retention time 9.34 min), *m/z* (%): 228 (100) [M^+], 213 (24), 199 (24), 185 (40), 171 (51), 159 (30), 121 (94), 91 (58); *trans isomer* (GC retention time 9.95 min), *m/z* (%): 228 (100) [M^+], 213 (22), 199 (22), 185 (36), 171 (46), 159 (27), 121 (77), 91 (48).

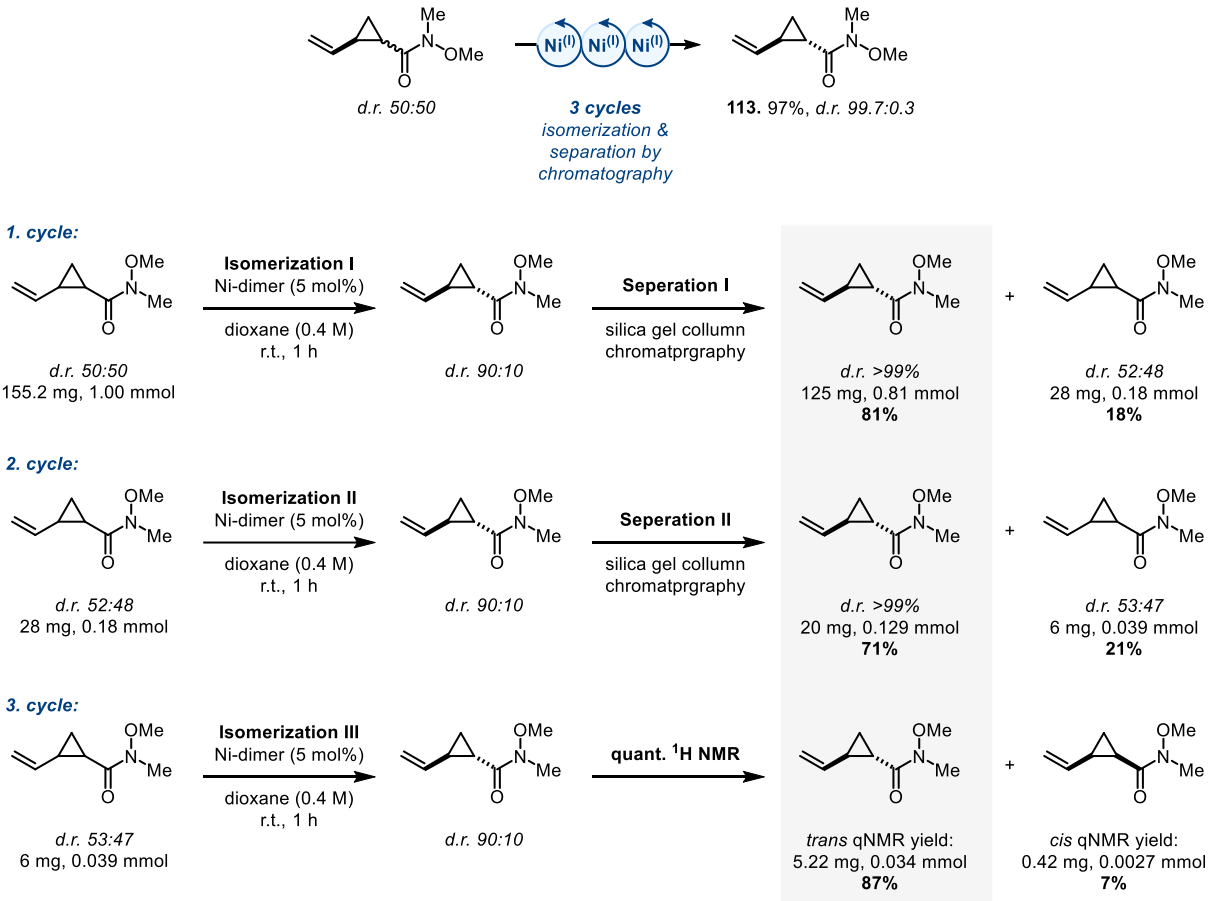
tert-butyl (1*R*,2*S*)-1-((_tert_-butoxycarbonyl)amino)-2-vinylcyclopropane-1-carboxylate (128):



Under argon atmosphere, a solution of (1*R*,2*S*)-1-((*tert*-butoxycarbonyl)amino)-2-vinylcyclopropane-1-carboxylic acid (562 mg, 2.47 mmol, 1.0 equiv.) in dry toluene (12 mL, 0.2 M) was heated to 80 °C. Then, 1,1-di-*tert*-butoxy-*N,N*-dimethylmethanamine (2.01 g, 9.89 mmol, 4.0 equiv.) was added dropwise over the course of 15 minutes and the mixture was stirred for 1 hour at 80 °C. The mixture was cooled down to 0 °C and it was diluted with EtOAc (12 mL) before sat. $NaHCO_3$ (15 mL) was added. The phases were separated and the organic layer was washed with water (3x10 mL), dried over $MgSO_4$, filtered and concentrated under reduced pressure. Flash column chromatography (4:1 pentane:Et_2O) afforded the title product as a white solid (420 mg, 1.48 mmol, 60%, >99% ee). R_f = 0.37 (4:1 pentane:Et_2O, PMA). $[\alpha]_D^{25}$ = +38.5 (*c* 1.0 $CHCl_3$, >99% ee). M.p. = 84.6 – 86.9 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 5.75 (dt, *J* = 18.0, 9.5 Hz, 1H), 5.25 (d, *J* = 17.2 Hz, 1H), 5.14 (brs, 1H), 5.09 (d, *J* = 10.3 Hz, 1H), 2.05 (q, *J* = 8.8 Hz, 1H), 1.72 (brs, 1H), 1.46 – 1.43 (m, 19H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 169.9, 155.9, 134.1, 117.4, 81.7, 80.0, 41.5, 33.6, 28.5, 28.3, 22.7. IR (neat, cm^{-1}): 3325, 3086, 2978, 2933, 2287, 2111, 1703, 1638, 1501, 1390, 1359, 1328, 1250, 1154, 1094, 1045, 1027, 1000, 975, 941, 906, 848, 784, 758, 694, 661. HRMS (ESI): *m/z* [M+Na]$^+$ calculated for $C_{15}H_{25}O_4NNa$: 306.1676, found 306.1680. *Note: The corresponding racemate (rac-128) was synthesized following the literature procedure of Beaulieu and co-workers starting from tert-butyl (E)-2-(benzylideneamino)acetate (2.1 g, 9.58 mmol).*[158]

5.4.3 Dynamic thermodynamic resolution

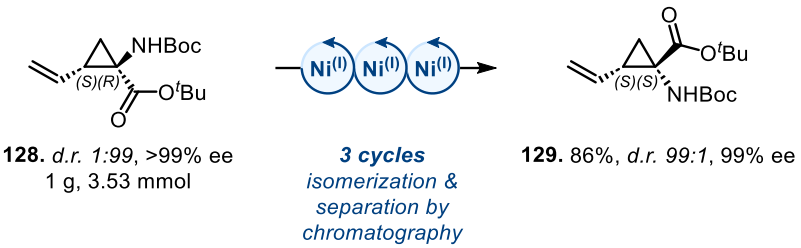
5.4.3.1 Thermodynamic resolution of vinyl cyclopropyl-Weinreb amide



- ***Step 1, isomerization:*** Inside an argon-filled glovebox *N*-methoxy-*N*-methyl-2-vinylcyclopropane-1-carboxamide **S23** (155.2 mg, 1.0 mmol, d.r. 50:50 (^{1}H NMR)) was dissolved in dioxane (2.5 mL, 0.4 M) and Nickel dimer (48 mg, 5 mol%) was added. The reaction mixture was stirred for 60 min at room temperature. The reaction mixture was removed from the glovebox and 6 mL Et_2O were added followed by 4 spatula tips of ammonium pyrrolidine-1-dithiocarboxylic acid and the mixture was stirred for additional 15 min to precipitate nickel.[60] The mixture was filtered through a plug of silica, rinsing with Et_2O and the filtrate was concentrated under reduced pressure affording the crude compound as a diastereomeric mixture (10:90 *cis/trans* (^{1}H NMR)).
- ***Step 2, silica chromatography:*** The diastereomers were then separated by flash silica column chromatography (4:1 pentane:Et_2O) affording two main fractions: the pure *trans* diastereomer (125 mg, 0.81 mmol, 81%, d.r. >1:99 *cis/trans* (^{1}H NMR)) as a colorless oil and a mixture of both diastereomers (28 mg, 0.18 mmol, 18%, 48:52 *cis/trans* (^{1}H NMR)).
- ***Iteration*:** The mixture of diastereomers was subjected to two additional iterations of isomerization and separation (3 cycles in total) and the *trans* enriched product fractions were combined to give **23** as a colorless oil (150.22 mg, 0.967 mmol, 97%, 1:99 *cis*/*trans* (^{1}H NMR)).

5.4.3.2 Thermodynamic resolution of vinyl-ACCA ester (128)

trans-enrichment by flash silica column chromatography



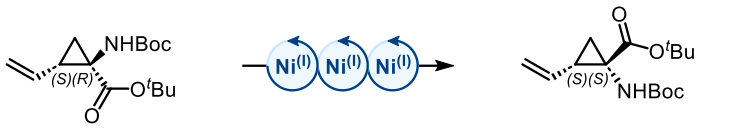
128. *d.r. 1:99*, >99% ee
1 g, 3.53 mmol

3 cycles
isomerization & separation by chromatography

129. 86%, *d.r. 99:1*, 99% ee

- ***Step 1, isomerization:*** Inside an argon-filled glovebox *tert*-butyl (1*R*,2*S*)-1-((*tert*-butoxycarbonyl)amino)-2-vinylcyclopropane-1-carboxylate **128** (1.0 g, 3.53 mmol, >99% ee) was dissolved in dioxane (8.8 mL, 0.4 M) and Nickel dimer **1** (34 mg, 1 mol%) was added. The reaction mixture was stirred for 10 min at room temperature. The reaction mixture was removed from the glovebox and 6 mL Et_2O were added followed by 4 spatula tips of ammonium pyrrolidine-1-dithiocarboxylic acid and the mixture was stirred for additional 15 min to precipitate nickel.[60] The mixture was filtered through a plug of silica, rinsing with Et_2O and the filtrate was concentrated under reduced pressure affording the crude compound as a diastereomeric mixture as dark green solid.
- ***Step 2, silica chromatography:*** The diastereomers were then separated by flash silica column chromatography (4:1 pentane:Et_2O) affording two main fractions: the pure (1*S*,2*S*)-diastereomer **129** as a white solid and a mixture of both diastereomers.
- ***Iteration***: The mixture of diastereomers was subjected to two additional iterations of isomerization and separation (3 cycles in total) and the (1*S*,2*S*)-enriched product fractions were combined to give *tert*-butyl (1*S*,2*S*)-1-((*tert*-butoxycarbonyl)amino)-2-vinylcyclopropane-1-carboxylate (**38**) as a white solid (861 mg, 3.04 mmol, 86%, 99% ee, 1:99 *cis*/*trans* (^{1}H NMR)).

trans-enrichment by crystallization



128. *d.r. 1:99*, >99% ee
1 g, 3.53 mmol

3 cycles
isomerization & separation by chromatography

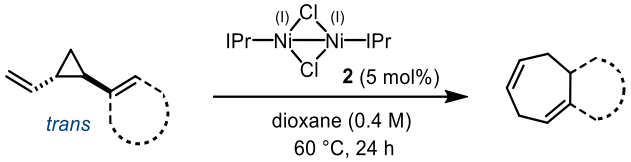
129. 91%, *d.r. 99:1*, >99% ee

- *Step 1, isomerization:* Inside an argon-filled glovebox *tert*-butyl (1*R*,2*S*)-1-((*tert*-butoxycarbonyl)amino)-2-vinylcyclopropane-1-carboxylate **128** (1.0 g, 3.5 mmol, >99% ee) was dissolved in dioxane (8.8 mL, 0.4 M) and Nickel dimer (34 mg, 1 mol%) was added. The reaction mixture was stirred for 10 min at room temperature. The reaction mixture was removed from the glovebox and 6 mL Et_2O were added followed by 4 spatula tips of ammonium pyrrolidine-1-dithiocarboxylic acid and the mixture was stirred for additional 15 min to precipitate nickel.[60] The mixture was filtered through a plug of silica, rinsing with Et_2O and the filtrate was concentrated under reduced pressure affording the crude compound as a diastereomeric mixture as dark green solid.

- *Step 2, crystallization*: The crude was dissolved in refluxing hexane (100 mg/1 mL) for 15 minutes and let cool down to room temperature before it was stored in the fridge overnight. The mother liquid was decantated and the solid washed with a minimum amount of hexane (2x1 mL) to afford the (1*S*,2*S*)-diastereomer **129** as colorless crystals. The combined hexane phases were concentrated to afford the crude compound as a diastereomeric mixture.
- *Iteration*: The mixture of diastereomers was subjected to two additional cycles of isomerization and separation (3 cycles in total) and the crystallized product portions were combined to give *tert*-butyl (1*S*,2*S*)-1-((*tert*-butoxycarbonyl)amino)-2-vinylcyclopropane-1-carboxylate (**129**) as colorless crystals (905 mg, 3.19 mmol, 91%, >99% ee, 1:99 *cis*/*trans* (^{1}H NMR)).

5.4.4 *Trans* to *cis* isomerization/Cope sequence

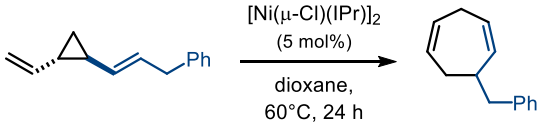
5.4.4.1 General procedure for *trans* to *cis* isomerization/Cope sequence



Inside an argon-filled glovebox, an oven dried 4 mL screw-cap vial equipped with a magnetic stir bar was charged with the corresponding divinylcyclopropane (1.0 equiv.), anhydrous 1,4-dioxane (0.4 M) and [Ni(μ-Cl)(IPr)]$_2$ **2** (5 mol%), in that order. The reaction vial was then sealed and allowed to stir inside the glovebox at 60 °C for 24 hours. Upon completion the reaction mixture was removed from the glovebox and quenched by the addition of wet pentane (*i.e.* technical grade pentane that had been distilled and stored on the bench). A spatula tip of ammonium pyrrolidine-1-dithiocarboxylic acid was added and the mixture stirred for additional 15 min to precipitate nickel.[60] The mixture was filtered through a plug of silica, rinsing with Et_2O and the filtrate was concentrated under reduced pressure. *Note: In most cases, the colour of the reaction mixture after completion is dark red. After addition of ammonium pyrrolidine-1-dithiocarboxylic acid and subsequent mixing, the colour changes rapidly to yellow. After further mixing (15 min) the solution becomes clear and precipitation occurs.*

5.4.4.2 Characterization data of cyclized products

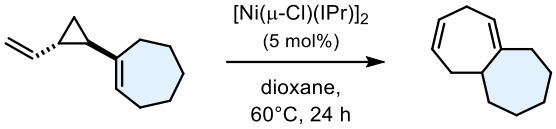
6-benzylcyclohepta-1,4-diene (76):



General procedure was followed using ((*E*)-3-(*trans*-2-vinylcyclopropyl)allyl)benzene **79** (18.4 mg, 0.100 mmol) and Nickel dimer **2** (4.8 mg, 5 mol%). Pyridine (0.8 mg, 10 mol%) was added as additive and the reaction mixture was stirred at 60 °C for 24 h. Purification by filtration over a short silica plug washing with Et_2O afforded the title product **76** as a colourless oil (18.0 mg, 0.098 mmol, 98%). R_f = 0.4 (hexane). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.33 – 7.27 (m, 2H), 7.24 – 7.17 (m, 3H), 5.73 – 5.65 (m, 2H), 5.65 – 5.61 (m, 2H), 2.95 (dd, *J* = 19.4, 2.6 Hz, 1H), 2.81 – 2.70 (m, 3H), 2.63 (dd, *J* = 13.1, 7.8 Hz, 1H), 2.30 – 2.23 (m,

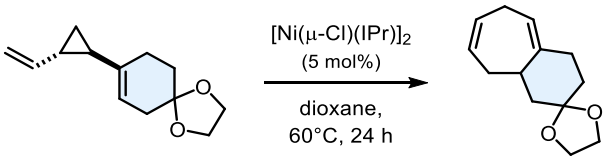
1H), 2.15 – 2.07 (m, 1H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 140.9, 135.7, 129.7, 129.2, 128.9, 128.3, 127.6, 126.0, 42.4, 39.2, 32.2, 28.6. **HRMS** (EI): *m/z* $[M]^+$ calculated for $C_{14}H_{16}$: 184.1247, found 184.1238. The data are in agreement with those previously reported in the literature.[62]

1,2,3,4,5,5a,6,9-octahydroheptalene (130):



General procedure was followed using 1-((*trans*)-2-vinylcyclopropyl)cyclohept-1-ene **80** (16.2 mg, 0.100 mmol) and Nickel dimer **2** (4.8 mg, 5 mol%). The reaction mixture was stirred at 60 °C for 24 h. Purification by filtration over a short silica plug washing with Et_2O afforded the title product **130** as a colourless oil (15 mg, 92%). **R_f** = 0.5 (hexane). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 5.64 (dd, *J* = 8.3, 4.3 Hz, 1H), 5.60 – 5.49 (m, 2H), 3.14 – 3.05 (m, 1H), 3.06 – 2.97 (m, 1H), 2.37 (dt, *J* = 18.1, 7.7 Hz, 1H), 2.18 – 2.13 (m, 2H), 2.01 (ddt, *J* = 8.0, 5.5, 2.6 Hz, 2H), 1.89 – 1.77 (m, 2H), 1.76 – 1.63 (m, 2H), 1.42 – 1.32 (m, 1H), 1.33 – 1.17 (m, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 149.5, 129.8, 126.7, 124.6, 40.7, 35.4, 35.0, 34.8, 31.8, 31.0, 28.3, 26.8. **IR** (neat, cm^{-1}): 3387, 3027, 2922, 2854, 2692, 2326, 2159, 2100, 1990, 1723, 1691, 1448, 1392, 1230, 1169, 983, 847, 741, 660. *Note: Caution, compound is volatile.*

1,3,4,6,9,9a-hexahydrospiro[benzo[7]annulene-2,2'-[1,3]dioxolane] (131):

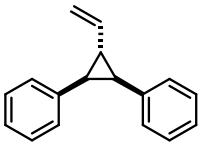


General procedure was followed using 8-((trans)-2-vinylcyclopropyl)-1,4-dioxaspiro[4.5]dec-7-ene **81** (20.6 mg, 0.100 mmol) and Nickel dimer **2** (4.8 mg, 5 mol%). The reaction mixture was stirred at 60 °C for 24 h. Flash column chromatography (10:1 pentane:Et_2O) afforded the title product **131** as a colorless oil (18.0 mg, 0.087 mmol, 87%). **R_f** = 0.19 (10:1 pentane:Et_2O). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 5.96 (dt, *J* = 9.8, 6.0 Hz, 1H), 5.83 (dt, *J* = 9.8, 6.9 Hz, 1H), 5.43 (t, *J* = 5.7 Hz, 1H), 4.00 – 3.91 (m, 4H), 2.84 – 2.75 (m, 1H), 2.69 – 2.60 (m, 1H), 2.35 (d, *J* = 11.7 Hz, 1H), 2.30 (ddd, *J* = 13.8, 7.2, 3.9 Hz, 1H), 2.22 (ddd, *J* = 13.7, 9.3, 6.6 Hz, 2H), 2.07 (ddd, *J* = 13.6, 4.8, 2.9 Hz, 1H), 1.80 – 1.73 (m, 1H), 1.67 (ddd, *J* = 12.8, 4.2, 2.9 Hz, 1H), 1.58 (t, *J* = 12.8 Hz, 1H), 1.53 (td, *J* = 13.4, 4.9 Hz, 1H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 141.8, 133.0, 129.8, 119.8, 109.2, 64.5, 64.4, 42.9, 36.4, 35.9, 35.5, 31.9, 25.8. **IR** (neat, cm^{-1}): 3353, 3025, 2936, 2880, 2327, 2089, 1992, 1721, 1441, 1353, 1279, 1251, 1120, 1061, 945, 923, 830, 761, 731, 687. **HRMS** (EI): *m/z*: calculated for $[M]^+$ $C_{13}H_{18}O_2$: 206.1301, found: 206.1297.

5.4.5 Initial experimental investigation

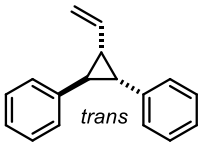
5.4.5.1 Characterization of radical probe

cis-1,2-diphenyl-trans-3-vinylcyclopropane (82): Prepared following the literature procedure.[36] The title



product was obtained after purification by silica gel column chromatography (100:1 pentane:Et_2O) as a colorless oil (2.59 g, 11.76 mmol, 76%). R_f = 0.25 (100:1 pentane:Et_2O). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.21 – 7.08 (m, 6H), 7.03 – 6.95 (m, 4H), 5.85 (ddd, *J* = 17.5, 10.3, 7.9 Hz, 1H), 5.33 (d, *J* = 17.1 Hz, 1H), 5.11 (dd, *J* = 10.4, 1.8 Hz, 1H), 2.59 (d, *J* = 5.7 Hz, 2H), 2.45 – 2.35 (m, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$): δ 140.2, 137.6, 129.0, 127.9, 126.0, 113.4, 32.9, 30.0. **IR** (neat, cm^{-1}): 3850, 3391, 3059, 3026, 2663, 2325, 2113, 1990, 1881, 1805, 1751, 1635, 1602, 1496, 1445, 1361, 1298, 1239, 1196, 1148, 1076, 1027, 984, 946, 899, 848, 755, 726, 695. **HRMS** (EI): *m/z* $[M]^+$ calculated for $C_{17}H_{16}$: 220.1247, found 220.1249. The data are in agreement with those previously reported in the literature.[36]

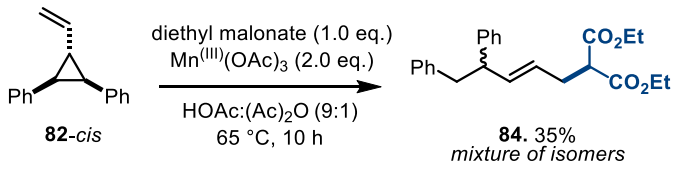
trans-1,2-diphenyl-3-vinylcyclopropane (83): General isomerization procedure was followed using *cis*-



vinylcyclopropane **82** (44.0 mg, 0.200 mmol) and Nickel dimer **2** (9.65 mg, 5 mol%). The reaction mixture was stirred for 6 h at room temperature. Flash silica gel column chromatography (100:1 pentane:Et_2O) afforded the title compound as a colorless oil (42.5 mg, 0.192 mmol, 96%, 11:89 *cis*/*trans* (^{1}H NMR)). R_f = 0.16 (100:1 pentane:Et_2O) **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.30 – 7.23 (m, 6H), 7.21 – 7.15 (m, 4H), 5.25 (ddd, *J* = 17.0, 10.2, 9.1 Hz, 1H), 5.14 (dd, *J* = 17.0, 2.0 Hz, 1H), 4.90 (dd, *J* = 10.2, 2.0 Hz, 1H), 2.70 (dd, *J* = 9.3, 6.0 Hz, 1H), 2.47 (t, *J* = 5.5 Hz, 1H), 2.16 (td, *J* = 9.2, 5.1 Hz, 1H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 141.7, 138.1, 136.8, 129.3, 128.6, 128.3, 126.4, 126.3, 126.1, 115.0, 34.2, 33.4, 30.4. **IR** (neat, cm^{-1}) 3850, 3394, 3060, 3026, 2664, 2325, 2115, 1992, 1882, 1807, 1633, 1601, 1495, 1447, 1299, 1210, 1178, 1154, 1074, 1027, 987, 900, 751, 695. **HRMS** (EI): *m/z* $[M]^+$ calculated for $C_{17}H_{16}$: 220.1247, found 220.1249.

5.4.5.2 Free organic radical reactivity

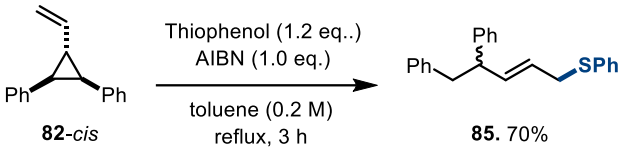
Synthesis of diethyl 2-(3,4-diphenylbut-1-en-1-yl)malonate (84):



Synthesized following a modified literature procedure of *Huang and co-worker*.[105] Inside an argon filled glovebox, vinylcyclopropane **82** (66.1 mg, 0.3 mmol, 1.0 eq.) and manganese acetate (161 mg, 0.6 mmol, 2.0 eq.) was placed to an oven dried flask equipped with a magnetic stir bar. The flask was then closed with Teflon septum and brought outside. Next, a mixture of acetic acid and acid anhydride (9:1, 1.5 mL) was added as solvent followed by the addition of malonic acid diethyl ester (45.8 µL, 0.3 mmol, 1.0 eq.). The mixture was then heated to 65 °C for 10 hours. The reaction mixture was allowed to cool down to room temperature before 15 mL water was added. The aqueous phase was extracted with DCM (3x 10 mL) and EtOAc (1x 10 mL). The combined organic layers were dried over Na_2SO_4 and volatiles were removed under

reduced pressure. Column chromatography (10:1 pentane:EtOAc) afforded **84** as a complex mixture of four diastereomers as a clear oil (40 mg, 0.109 mmol, 35% yield). R_f = 0.3 (10:1 pentane:EtOAc). Analysis with **^{1}H NMR** (complex spectra of 4 diastereomers) and **GCMS** strongly indicated the consumption of **82** and the formation of the ring-opened product **84**, however, the compound structure was not further verified. **GC**: retention time (min): 9.80, 10.03, 10.14, 10.29; four compounds with similar/identical fragmentation: **MS** (EI): m/z (%): 380 (1) [M^+], 378 (9), 333 (5), 332 (16), 289 (21), 243 (53), 218 (28), 197 (80), 169 (36), 149 (19), 141 (38), 130 (100) [malonate-Et]$^+$, 107 (69), 91 (37), 77 (15), 65 (4).

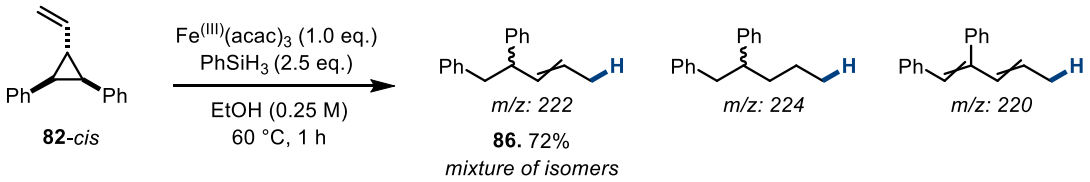
Synthesis of (*R,E*)-(4,5-diphenylpent-2-en-1-yl)(phenyl)sulfane (85):



Synthesized following a modified literature procedure of *Huang and co-worker*.[106] An oven dried two neck round bottom flask equipped with a magnetic stir bar was charged with vinylcyclopropane **82** (66.1 mg, 0.3 mmol, 1.0 eq.), AIBN (49.3 mg, 0.3 mmol, 1.0 eq.) and the flask was capped with a heating condenser and Teflon septa. The system was flushed with argon and toluene was added. Subsequently thiophenol (37 µL, 0.36 mmol, 1.2 eq.) was added and it was heated to reflux for 3 hours (100% consumption of SM). The reaction mixture was allowed to cool down to room temperature before solvent was removed under reduced pressure. Column chromatography (100:1 pentane:EtOAc) afforded the product **85** as a clear oil (69 mg, 0.209 mmol, 70%). R_f = 0.3 (100:1 pentane:EtOAc). **^{1}H NMR** (600 MHz, $CDCl_3$): δ 7.30-7.14 (m, 11H), 7.03 (d, *J*=7.4 Hz, 2H), 6.98 (d, *J*=7.3 Hz, 2H), 5.73 (dd, *J*=15.1, 7.3 Hz, 1H), 5.43 (dt, *J*=14.7, 6.9 Hz, 1H), 3.53 (m, 1H), 3.48 (d, *J*=7.1 Hz, 2H), 2.93 (d, *J*=7.5 Hz, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$): δ 143.7, 140.0, 136.7, 130.5, 129.3, 128.9, 128.5, 128.2, 127.9, 126.4, 126.0, 125.7, 50.3, 42.5, 36.7. **HRMS** (ESI) *m/z* [M]$^+$ calculated for $C_{23}H_{22}S$: 330.1437, found 330.1449.

5.4.5.3 Transition metal hydride reactivity

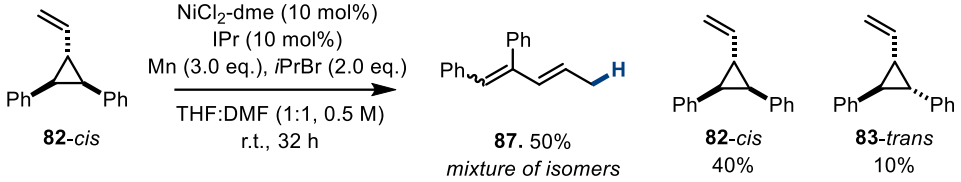
Synthesis of pent-3-ene-1,2-diyldibenzene (86):



Synthesized following a modified literature procedure of *Baran and co-worker*.[107] Inside the Glovebox an oven dried flask equipped with a magnetic stir bar was charged with vinylcyclopropane **82** (66.1 mg, 0.3 mmol, 1.0 eq.), dry EtOH (1.5 mL, 0.25 M) and $Fe^{(III)}(acac)_3$ (106 mg, 0.3 mmol, 1.0 eq.). Then $PhSiH_3$ (93 µL, 0.75 mmol, 2.5 eq.) was added in one shot and the reaction was stirred for 1 hour at 60 °C. The reaction mixture was allowed to cool down to room temperature before pentane (3 mL) and a minimal amount of water (few drops) were added. The mixture was filtered over a short plug of silica washing with Et_2O and the solvent was removed under reduced pressure. Column chromatography (50:1 hexane:EtOAc) afforded

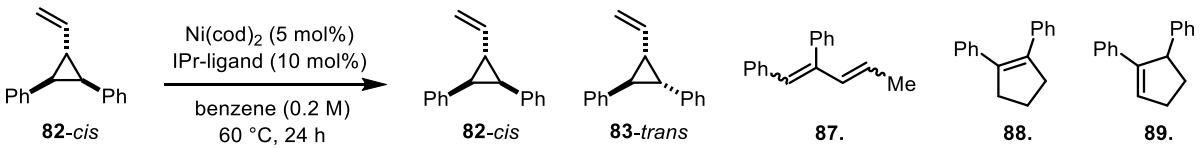
86 as a complex mixture of isomers as a clear oil (48 mg, 0.216 mmol, 72%). R_f = 0.2 (50:1 hexane:EtOAc). Analysis with **^{1}H NMR** (complex spectra of numerous diastereomers) and **GCMS** strongly indicated the consumption of **82** and the formation of the ring-opened product **86**, however, the compound structure was not further verified. **GC**: retention time (min): 7.35 (m/z: 220 [M$^+$]), 8.48 (m/z: 224 [M$^+$]), 8.59 (m/z: 222 [M$^+$]), 8.60 (m/z: 222 [M$^+$]), 8.63 (m/z: 222 [M$^+$]), 9.10 (m/z: 222 [M$^+$]) several compounds with similar/identical fragmentation: **MS** (EI): m/z (%): 222 (1) [M$^+$], 193 (1), 179 (1), 165 (1), 131 (100) [M-Bn]$^+$, 115 (9), 91 (27), 77 (3), 65 (4).

Synthesis of penta-1,3-diene-1,2-diyl)dibenzene (87):



Synthesized following a modified literature procedure of *Schoenebeck and co-worker*.[108] Inside the Glovebox a 4 mL screw-cap vial equipped with a magnetic stir bar was charged with $NiCl_2$(dme) (8.8 mg, 10 mol%), IPr ligand (15.6 mg, 10 mol%), dry THF (0.4 mL, 1 M), manganese (66 mg, 1.2 mmol, 3.0 eq.) and *i*PrBr (75.1 µL, 0.8 mmol, 2.0 eq.). The mixture was stirred for 15 minutes at room temperature before a solution of vinylcyclopropane **82** (88.1 mg, 0.4 mmol, 1.0 eq.) in DFM (0.4 mL, 1 M) was added. The mixture was stirred inside the glovebox at room temperature for 32 hours. The reaction was brought outside the Glovebox, filtered over a short plug of silica washing with Et_2O and the solvent was removed under reduced pressure. Analysis of the crude with **^{1}H NMR** and **GCMS** strongly indicated the partial consumption of **82** and the formation of the ring-opened product **87** (40% qNMR yield) accompanied with **83** (10% qNMR yield). **^{1}H NMR** (600 MHz, $CDCl_3$): δ 7.51 (d, *J* = 7.7 Hz, 2H), 7.47 (d, *J* = 7.6 Hz, 2H), 7.40 – 7.27 (m, 6H), 6.77 (s, 1H), 6.37 (dd, *J* = 11.8, 2.1 Hz, 1H), 5.86 – 5.74 (m, 1H), 1.81 (d, *J* = 6.8 Hz, 1H *minor isomer*), 1.33 (dd, *J* = 7.0, 1.7 Hz, 3H). **MS** (EI): m/z (%): 220 (46) [M$^+$], 205 (100), 190 (15), 178 (14), 163 (2), 141 (9), 129 (22), 115 (15), 101 (8) 91 (13), 77 (7), 63 (4). *<u>Note</u>: **87** decomposed due to silica column chromatography and/or storage on air.*

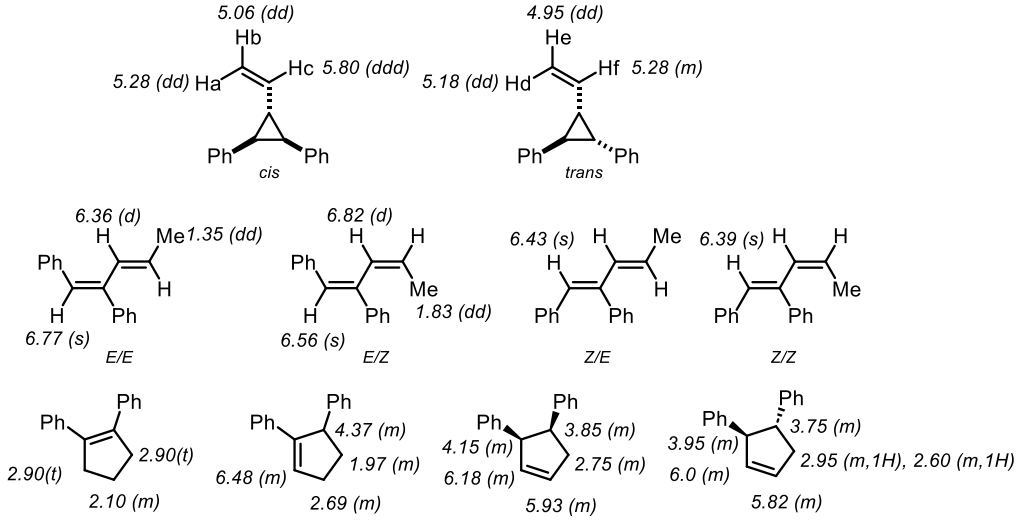
5.4.5.4 Investigation on Ni$^{(0)}$IPr reactivity



Following the literature procedure of *Louie and co-worker*,[109] inside an argon filled Glovebox a 4 mL screw-cap vial equipped with a magnetic stir bar was charged with $Ni(cod)_2$ (1.4 mg, 10 mol%) and IPr ligand (3.9 mg, 10 mol%) were premixed in benzene (0.25 mL, 0.4 M) at room temperature for 3 hours. Then a solution of vinylcyclopropane **82** (22 mg, 0.1 mmol, 1.0 eq.) in benzene (0.25 mL, 0.4 M) was added and the reaction mixture was stirred at 60 °C for 24 hours. The reaction was brought outside the Glovebox, filtered over a short plug of silica washing with Et_2O and the solvent was removed under reduced pressure. Analysis of the

crude with **^{1}H NMR** and **GCMS** indicated the partial cyclopropane isomerization (**82**:**83** *d.r. 81:19*) accompanied with minor signals of opened and rearranged isomers (for potential isomers see **Figure 6**).

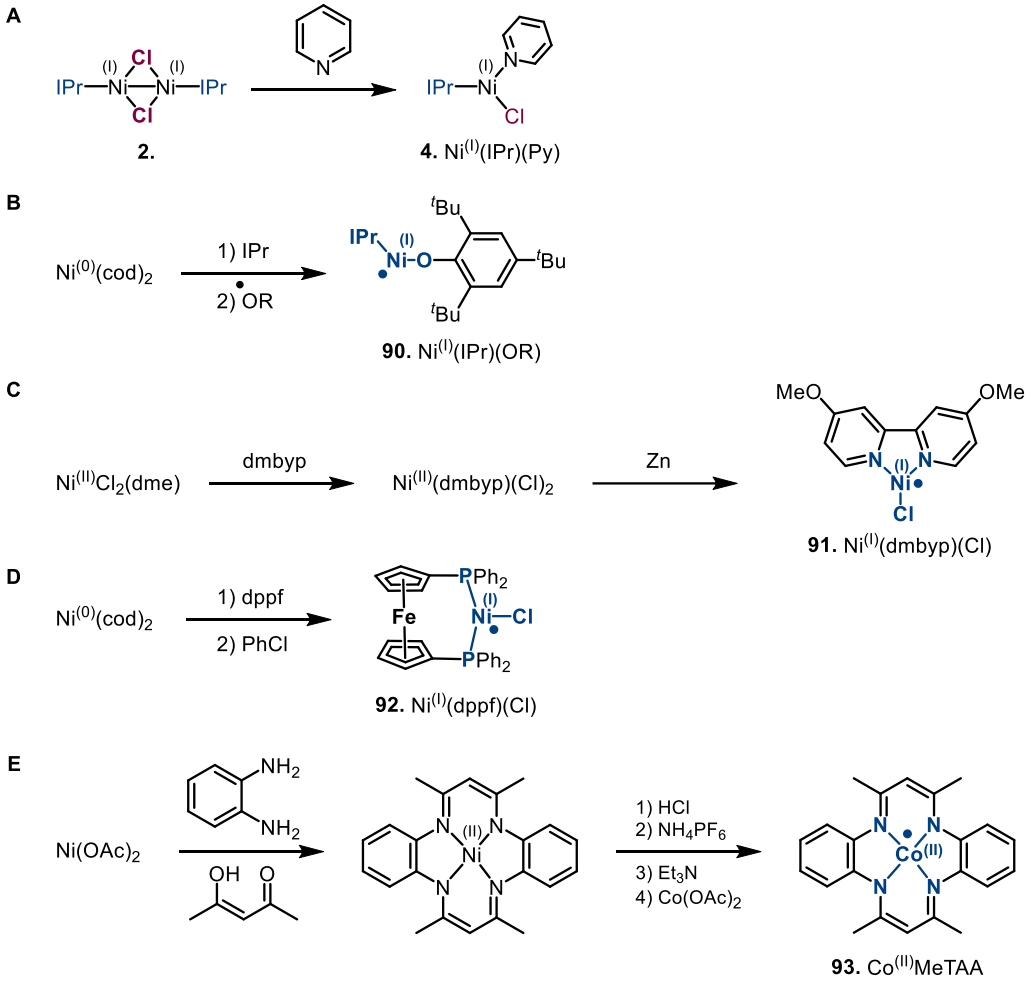
Figure 6 | Potential isomers of vinylcyclopropane **82** and characteristic ^{1}H NMR signals.



5.4.5.5 Pre-defined metalloradical reactivity

Synthesis of pre-defined metalloradicals

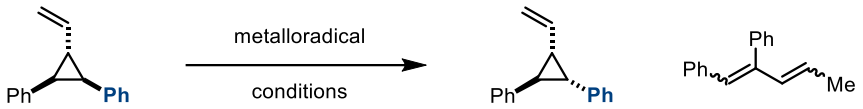
The metal complexes below were synthesized following the corresponding literature procedures: **4**,[34] **90**,[112] **91** (in situ synthesis from $Ni^{(II)}$(dmbyp)-precursor[159]), **92**,[160] **93**.[161]



Experimental comparison of pre-defined metalloradicals and $Ni^{(I)}$ dimer

Experimental procedure: All reactions were carried out inside an argon-filled glovebox. A 4 mL screw-cap vial equipped with a magnetic stir bar was sequentially charged with vinylcyclopropane **82** (22 mg, 0.1 mmol, 1.0 equiv.), anhydrous solvent (0.4 M) and metal catalyst (5-10 mol%), in that order. The reaction vial was then sealed and allowed to stir inside the glovebox at the indicated temperature for the indicated time. The reaction mixture was then removed from the glovebox and was quenched by the addition of wet pentane. The resulting mixture was filtered through a plug of silica, washing with Et_2O and the filtrate was concentrated under reduced pressure. The crude material was analyzed by qualitative ^1H NMR.

Table 14 | Metalloradical reactivity comparison.



82-*cis* **83**-*trans* **88**-*opening*

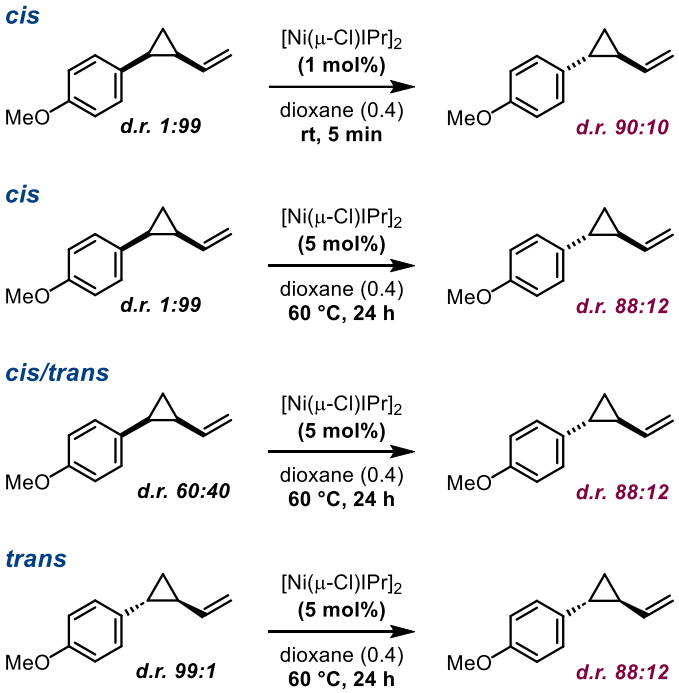
entry	catalyst	conditions	cis:trans:opening[a]
1[b]	**2.** $Ni^{(I)}$ dimer (5 mol%)	PhCl, 3 h, r.t.	72:28:n.d.
2[b]	**2.** $Ni^{(I)}$ dimer (5 mol%)	PhCl, 6 h, r.t.	60:40:n.d.
3	**2.** $Ni^{(I)}$ dimer (5 mol%)	PhCl, 24 h, 60 °C	62:23:15
4[c]	**2.** $Ni^{(I)}$ dimer (25 mol%)	PhCl, 24 h, r.t.	0:57:43
5	**2.** $Ni^{(I)}$ dimer (5 mol%)	PhH, 24 h, 60 °C	13:81:6
6	**4.** $Ni^{(I)}$(IPr)(Py) (10 mol%)	PhCl, 24 h, r.t.	55:35:10
7	**90.** $Ni^{(I)}$(IPr)(OR) (10 mol%)	PhCl, 24 h, r.t.	45:41:14
8	**91.** $Ni^{(I)}$(dmbpy)(Cl)[b] (10 mol%)	PhMe, 24 , r.t.	100:0:0
9	**92.** $Ni^{(I)}$(dppf)(Cl)[c] (10 mol%)	PhMe, 48 h, r.t.	100:0:0
10	**93.** $Co^{(II)}$(MeTAA) (5 mol%)	PhMe, 24 h, r.t.	100:0:0
11	**93.** $Co^{(II)}$(MeTAA) (5 mol%)	PhMe, 24 h, 60 °C	100:0:0
12	**93.** $Co^{(II)}$(MeTAA) (5 mol%)	PhMe, 24 h, 100 °C	100:0:0
13	**93.** $Co^{(II)}$(MeTAA) (5 mol%)	PhMe, 24 h, r.t., near UV	100:0:0

a) product ratios determined by qualitative ^{1}H NMR; b) original observation[36]; c) unpublished result of Dr. Sherif J. Kaldas; d) generated in situ from $Ni^{(II)}$(dmbpy)$(Cl)_2$ and excess of Zn; dmbyp = 4,4′-dimethoxy-2,2′-bipyridyl; dppf = 1,1′-bis(diphenylphosphino)ferrocene; n.d. = not determined.

5.4.6 Mechanistic studies

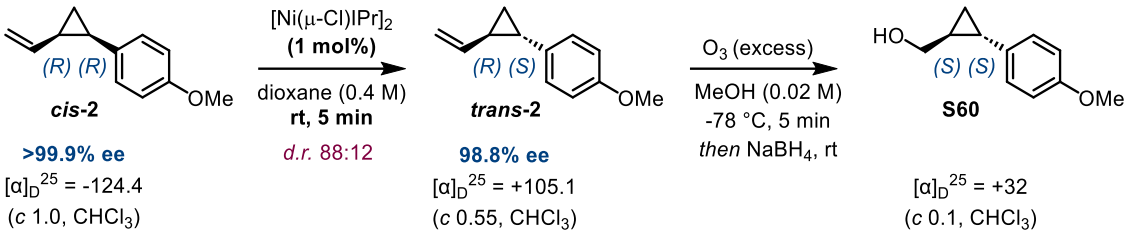
5.4.6.1 Study on the driving force

Inside an argon-filled glovebox, an oven dried 4 mL screw-cap vial equipped with a magnetic stir bar was charged with the corresponding (*cis*, *cis*/*trans*, or *trans*) 1-methoxy-4-(2-vinylcyclopropyl)benzene (17.4 mg, 0.1 mmol, 1.0 eq.), anhydrous 1,4-dioxane (0.4 M) and [Ni(μ-Cl)(IPr)]$_2$ **2** (1-5 mol%), in that order. The reaction vial was then sealed and allowed to stir inside the glovebox at the indicated temperature for the indicated time. Upon completion the reaction mixture was removed from the glovebox and quenched by the addition of wet pentane (*i.e.* technical grade pentane that had been distilled and stored on the bench). A spatula tip of ammonium pyrrolidine-1-dithiocarboxylic acid was added and the mixture stirred for additional 15 min to precipitate nickel.[60] The mixture was filtered through a plug of silica, rinsed with Et_2O and the filtrate was concentrated under reduced pressure. The crude was analyzed by quantitative ^{1}H NMR spectroscopy. The isomerization is driven by a thermodynamic equilibrium. Increased catalyst loadings, higher temperatures or longer reaction times do not influence the diastereomeric ratio as well as whether *cis*, *cis*/*trans*, or *trans* vinylcyclopropanes are exposed to isomerization.



5.4.6.2 Enantioinvertive vinylcyclopropane isomerization

Enantioinvertive isomerization and downstream derivatization



>99.9% ee
$[\alpha]_D^{25}$ = -124.4
(*c* 1.0, $CHCl_3$)

d.r. 88:12

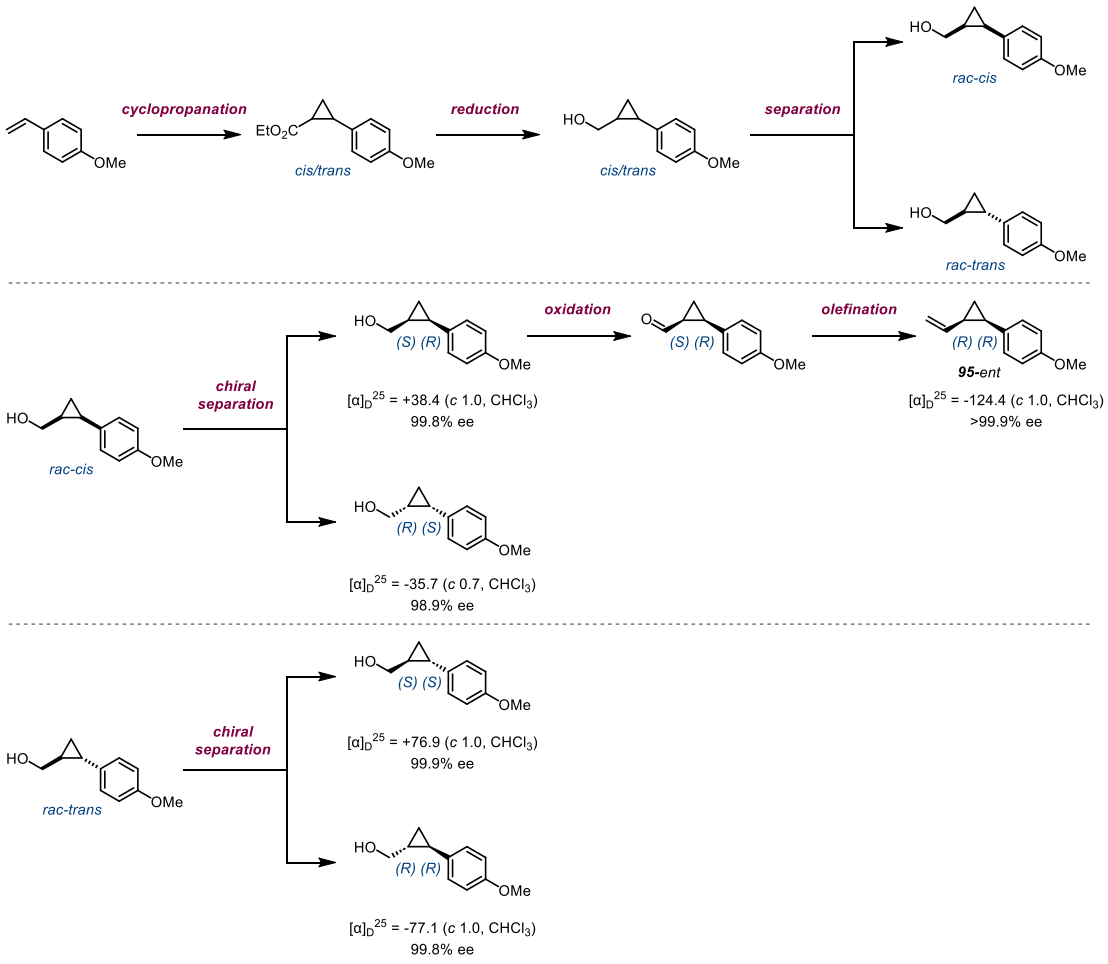
98.8% ee
$[\alpha]_D^{25}$ = +105.1
(*c* 0.55, $CHCl_3$)

$[\alpha]_D^{25}$ = +32
(*c* 0.1, $CHCl_3$)

- ***Isomerization.*** Inside an argon-filled glovebox, an oven dried 4 mL screw-cap vial equipped with a magnetic stirring bar was charged with 1-methoxy-4-((1*R*,2*R*)-2-vinylcyclopropyl)benzene ***cis*-2** (17.4 mg, 0.100 mmol, 1.0 equiv.), anhydrous 1,4-dioxane (0.25 mL, 0.4 M) and [Ni(μ-Cl)(IPr)]$_2$ (1.0 mg, 1 mol%), in that order. The reaction vial was then sealed and allowed to stir inside the glovebox at the indicated temperature for the indicated time. Upon completion the reaction mixture was removed from the glovebox and quenched by the addition of wet pentane (*i.e.* technical grade pentane that had been distilled and stored on the bench). A spatula tip of ammonium pyrrolidine-1-dithiocarboxylic acid was added and the mixture stirred for additional 15 min to precipitate nickel.[60] Purification by filtration over a short silica plug washing with Et_2O and concentration under reduced pressure afforded ***trans*-2** as a low-melting solid (17.1 mg, 0.098 mmol, 98%, 12:88 *cis*/*trans* (^{1}H NMR), 98.8% ee). **$[\alpha]_D^{25}$** = +105.1 (*c* 0.55 $CHCl_3$).
- ***Derivatization*** According to Taylor and coworkers,[162] a dry Schlenk tube was charged with ***trans*-2** (17.1 mg, 0.098 mmol, *from previous step*) was dissolved in dry MeOH (5 mL, 0.02 M) fitted with a stir bar and cooled to -78°C. Ozone was bubbled through the cooled solution until a blue color persisted in the flask (usually 5-10 min). Then, $NaBH_4$ (3.8 mg, 0.100 mmol) was added in one portion to the solution and the reaction was allowed to warm to room temperature. TLC analysis showed complete conversion of the starting material after 120 minutes. The mixture was diluted with Et_2O, filtered over a short silica plug washing with Et_2O and concentrated under reduced pressure. Purification by silica gel column chromatography (6:4:0.5 hexanes:EtOAc:MeOH) afforded ((*1S,2S)*-2-(4-methoxyphenyl)cyclopropyl) methanol) as a colorless oil (12.0 mg, 0.067 mmol, 69%). **$[\alpha]_D^{25}$** = +32 (*c* 0.1, $CHCl_3$). *Note: Characterization data and optical rotation values match with previously prepared compound.*

Synthesis and characterization of enantiopure vinylcyclopropanes

The enantiopure vinylcyclopropanes were synthesized according to reaction sequence shown below.



Ethyl 2-(4-methoxyphenyl)cyclopropane-1-carboxylate: An oven dried flask equipped with a magnetic stirring bar was charged with 4-vinylanisole (30 mmol, 4.03 g, 1.0 equiv.), $Rh_2(OAc)_4$ (0.3 mmol, 133 mg, 1 mol%) and dry DCM (30 mL, 1 M). Next, a solution of diazo ethylacetate (3.42 g, 30 mmol, 1.0 equiv.) in DCM (15 ml, 2 M) was added via syringe pump and over the course of 12 hours. The green mixture was stirred for further 12 hours before it was filtered through a short pad of silica gel. The mixture was concentrated under reduced pressure and flash column chromatography (10:1 pentane:Et_2O) afforded the title product as a diastereomeric mixture as a yellowish solid (4.62 g, 21 mmol, 70%, 63:37 *trans*/*cis* (^{1}H NMR)). **R_f** (*trans*) = 0.30 (10:1 hexane:Et_2O). **R_f** (*cis*) = 0.22 (10:1 hexane:Et_2O). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.21 – 7.16 (m, 2H, *cis*), 7.06 – 7.01 (m, 2H, *trans*), 6.84 – 6.78 (m, 2H *cis* + 2H *trans*), 4.17 (q, *J* = 7.1 Hz, 2H, *trans*), 3.89 (q, *J* = 7.1 Hz, 2H, *cis*), 3.78 (s, 3H, *trans*), 3.77 (s, 3H, *cis*), 2.56 – 2.45 (m, 1H *cis* + 1H *trans*), 2.03 (ddd, *J* = 9.2, 7.8, 5.6 Hz, 1H, *cis*), 1.82 (ddd, *J* = 8.4, 5.2, 4.1 Hz, 1H, *trans*), 1.69 – 1.62 (m, 1H, *cis*), 1.58 – 1.52 (m, 1H, *trans*), 1.35 – 1.28 (m, 1H, *cis*), 1.28 (t, *J* = 7.2 Hz, 3H, *trans*), 1.27 – 1.19 (m, 1H, *trans*), 1.02 (t, *J* = 7.1 Hz, 3H, *cis*). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 173.7, 171.2, 158.5, 158.4, 132.2, 130.4, 128.7, 127.5, 114.0, 113.5, 60.8, 60.3, 55.5, 55.3, 25.8, 25.0, 24.0, 21.8, 16.9, 14.4, 14.3, 11.4. **MS** (70eV, EI): *trans isomer* (GC retention time 8.85 min), *m/z* (%): 220 (40) $[M]^+$, 191 (20), 175 (18), 163 (16), 147 (100), 131 (18), 115 (23), 91 (27). **MS** (70eV, EI): *cis isomer* (GC retention time 8.48 min), *m/z* (%): 220 (41) $[M]^+$,

191 (20), 175 (22), 163 (16), 147 (100), 131 (18), 115 (23), 91 (26). The data are in accordance with the data previous reported in literature.[163]

General procedure for reduction: Diisobutylaluminium hydride (48 mL, 1.0 M in toluene, 2.2 equiv.) was added dropwise over the course of 15 min to a stirred solution of ethyl 2-(4-methoxyphenyl)cyclopropane-1-carboxylate (4.62 g, 20.970 mmol, 1.0 equiv.) in DCM (25 mL, 1 M) at –78 °C. After completion of the addition the mixture was stirred for 1 h at 0 °C and HCl (1 M, 30 mL) was then slowly added. The aqueous layer was extracted with DCM (2 x 100 mL) and the combined organic extracts were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. Filtration over a short plug of silica afforded the title product as a diastereomeric mixture. Purification by silica gel flash column chromatography (6:4:0.5 hexane:DCM:MeOH) afforded *cis*-2-(4-methoxyphenyl)cyclopropyl)methanol (600 mg, 3.370 mmol, 16%) as a colorless oil, *trans*-2-(4-methoxyphenyl)cyclopropyl)methanol (1.11 g, 6.220 mmol, 30%) as a white solid and a mixture of diastereomers (1.76 g, 9.860 mmol, 47%) as a colorless oil. Chiral separation of the pure fractions performed on preparative HPLC afforded the single enantiomers (*see chapter 0 for HPLC information).*

((1*S*,2*R*)-2-(4-methoxyphenyl)cyclopropyl)methanol: The title compound was obtained after enantiomeric separation of the corresponding *cis* racemate (600 mg, 3.370 mmol) as a colorless oil (213 mg, 1.2 mmol, 36%, 99.8% ee). R_f = 0.38 (6:4:0.5, hexane:DCM:MeOH). $[\alpha]_D^{25}$ = +38.4 (*c* 1.0, $CHCl_3$). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.17 (d, *J* = 8.4 Hz, 2H), 6.83 (d, *J* = 8.6 Hz, 2H), 3.79 (s, 3H), 3.47 (dd, *J* = 11.6, 6.3 Hz, 1H), 3.25 (dd, *J* = 11.6, 8.5 Hz, 1H), 2.23 (td, *J* = 8.4, 6.0 Hz, 1H), 1.44 (dtd, *J* = 14.4, 8.5, 5.8 Hz, 1H), 1.22 (s, 1H), 1.01 (td, *J* = 8.4, 5.2 Hz, 1H), 0.80 (q, *J* = 5.6 Hz, 1H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 158.2, 130.3, 130.0, 113.9, 63.1, 55.4, 20.7, 20.0, 7.8. **MS** (70eV, EI): *cis isomer* (GC retention time 7.893 min), *m/z* (%): 178.1 (21) $[M]^+$, 160.1 (13), 159.1 (15), 147.1 (100), 115.1 (25), 91.1 (34), 77.1 (12). **IR** (neat, cm^{-1}): 3364, 2936, 1886, 1611, 1511, 1459, 1410, 1294, 1243, 1177, 1026, 832, 798. **HRMS** (APCI): *m/z*: calculated for $[M+Na]^+$ $C_{11}H_{14}O_2Na$: 201.0886, found 201.0878. *Note: The absolute configuration was assigned by comparison of optical rotation with close analog (1S,2R)-2-phenylcyclopropylmethanol* $[\alpha]_D^{25}$ *= +38.4 (c 3.8,* $CHCl_3$*; e.r. 86:14).*[164]

((1*R*,2*S*)-2-(4-methoxyphenyl)cyclopropyl)methanol: The title compound was obtained after enantiomeric separation of the corresponding *cis* racemate (600 mg, 3.370 mmol) as a colorless oil (236 mg, 1.3 mmol, 39%, 98.9% ee). R_f = 0.38 (6:4:0.5 hexane:DCM:MeOH). $[\alpha]_D^{25}$ = –35.7 (*c* 0.7, $CHCl_3$). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.17 (d, *J* = 8.4 Hz, 2H), 6.83 (d, *J* = 8.6 Hz, 2H), 3.79 (s, 3H), 3.47 (dd, *J* = 11.6, 6.3 Hz, 1H), 3.25 (dd, *J* = 11.6, 8.5 Hz, 1H), 2.23 (td, *J* = 8.4, 6.0 Hz, 1H), 1.44 (dtd, *J* = 14.4, 8.5, 5.8 Hz, 1H), 1.22 (s, 1H), 1.01 (td, *J* = 8.4, 5.2 Hz, 1H), 0.80 (q, *J* = 5.6 Hz, 1H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 158.2, 130.3, 130.0, 113.9, 63.1, 55.4, 20.7, 20.0, 7.8. **MS** (70eV, EI): *cis isomer* (GC retention time 7.893 min), *m/z* (%): 178.1 (21) $[M]^+$, 160.1 (13), 159.1 (15), 147.1 (100), 115.1 (25), 91.1 (34), 77.1 (12). **IR** (neat, cm^{-1}): 3365, 2930, 1883, 1611, 1511,

1459, 1410, 1294, 1243, 1177, 1027, 832, 798. **HRMS** (APCI): *m/z*: calculated for $[M+Na]^+$ $C_{11}H_{14}O_2Na$: 201.0886, found 201.0877. *Note: The absolute configuration was assigned by comparison of optical rotation with close analog (1R,2S)-2-phenylcyclopropylmethanol* $[\alpha]_D^{25}$ *= -30.1 (c 1.0,* $CHCl_3$*; e.r. 77.5:22.5).*[165]

((1*S*,2*S*)-2-(4-methoxyphenyl)cyclopropyl)methanol: The title compound was obtained after enantiomeric separation of the corresponding *trans* racemate (1.11 g, 6.220 mmol) as a white solid (528 mg, 2.96 mmol, 48%, 99.9% ee). R_f = 0.35 (6:4:0..5 hexane:DCM:MeOH). **M.p.** = 57.9 – 59.3 °C. $[\alpha]_D^{25}$ = +76.9 (*c* 1.0, $CHCl_3$). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.01 (d, *J* = 8.6 Hz, 2H), 6.81 (d, *J* = 8.6 Hz, 2H), 3.78 (s, 3H), 3.65 – 3.57 (m, 2H), 1.79 (dt, *J* = 9.3, 4.9 Hz, 1H), 1.46 (s, 1H), 1.43 – 1.34 (m, 1H), 0.89 (ddt, *J* = 13.9, 8.8, 5.1 Hz, 2H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 157.9, 134.5, 127.1, 114.0, 66.8, 55.5, 24.9, 20.7, 13.4. **MS** (70eV, EI): *trans isomer* (GC retention time 8.045 min), *m/z* (%): 178.1 (25) $[M]^+$, 160.1 (16), 159.1 (17), 147.1 (100), 115.1 (26), 91.1 (31), 77.1 (11). **IR** (neat, cm^{-1}): 3304, 2927, 1613, 1511, 1458, 1361, 1291, 1248, 1178, 1113, 1074, 1026, 919, 885, 847, 814. **HRMS** (ESI): *m/z*: calculated for $[M]^+$ $C_{11}H_{14}O_2$: 178.0988, found 178.0990. The data are in agreement with those previously reported in the literature.[151] *Note: The absolute configuration was assigned by comparison of optical rotation with reported values* $[\alpha]_D^{25}$ *= +21.1 (c 0.4,* $CHCl_3$*; e.r. 99:1).*[166]

((1*R*,2*R*)-2-(4-methoxyphenyl)cyclopropyl)methanol: The title compound was obtained after enantiomeric separation of the corresponding *trans* racemate (1.11 g, 6.220 mmol) as a white solid (490 mg, 2.75 mmol, 44%, 99.8% ee). R_f = 0.35 (6:4:0.5 hexane:DCM:MeOH). **M.p.** = 57.9 – 59.3 °C. $[\alpha]_D^{25}$ = –77.1 (*c* 1.0, $CHCl_3$). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.01 (d, *J* = 8.6 Hz, 2H), 6.81 (d, *J* = 8.6 Hz, 2H), 3.78 (s, 3H), 3.61 (qd, *J* = 11.2, 6.8 Hz, 2H), 1.79 (dt, *J* = 9.3, 4.9 Hz, 1H), 1.47 (s, 1H), 1.39 (dtdd, *J* = 8.5, 6.8, 5.7, 4.5 Hz, 1H), 0.89 (ddt, *J* = 13.9, 8.8, 5.1 Hz, 2H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 157.9, 134.5, 127.1, 114.0, 66.8, 55.5, 24.9, 20.7, 13.4. **MS** (70eV, EI): *trans isomer* (GC retention time 8.045 min), *m/z* (%): 178.1 (25) $[M]^+$, 160.1 (16), 159.1 (17), 147.1 (100), 115.1 (26), 91.1 (31), 77.1 (11). **IR** (neat, cm^{-1}): 3305, 2929, 1613, 1512, 1458, 1361, 1291, 1249, 1179, 1112, 1074, 1026, 918, 885, 847, 813. **HRMS** (ESI): *m/z*: calculated for $[M]^+$ $C_{11}H_{14}O_2$: 178.0988, found 178.0990. The data are in agreement with those previously reported in the literature.[151] *Note: The absolute configuration was assigned by comparison of optical rotation with reported values* $[\alpha]_D^{25}$ *= -21.5 (c 0.4,* $CHCl_3$*; e.r. 99:1).*[166]

General procedure for DMP oxidation: The cyclopropyl alcohol (1.0 equiv.) was weighed into an oven dried flask and dissolved in dry DCM (10 mL, 0.1 M). The solution was cooled to 0 °C before DMP (1.4 equiv.) was added and the reaction mixture was stirred for 1 h at 0 °C and then for 2 h at room temperature. The reaction was quenched by adding 10 mL of an aqueous 1:1 mixture of sat. $NaHCO_3$ and sat. $Na_2S_2O_3$ and the resulting mixture was stirred until both phases were clear. Next, the phases were separated, and the aqueous phase was extracted with DCM (3 x 10 mL). The combined organic layers were dried over Na_2SO_4,

filtered, and concentrated under reduced pressure. The crude aldehydes were obtained quantitatively in high purity and were used directly for the next step without further purification.

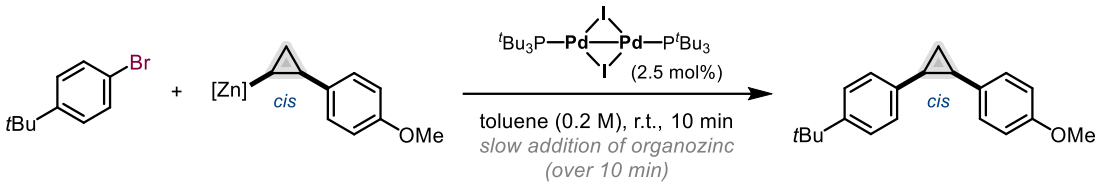
(1*S*,2*R*)-2-(4-methoxyphenyl)cyclopropane-1-carbaldehyde: Following general procedure using ((1*S*,2*R*)-2-(4-methoxyphenyl)cyclopropyl)methanol (160.0 mg, 0.897 mmol). The title compound was obtained as a yellowish solid (156.6 mg, 0.888 mmol, 99%). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 8.68 (d, *J* = 6.7 Hz, 1H), 7.23 (d, *J* = 8.3 Hz, 2H), 6.83 (dd, *J* = 8.5, 1.3 Hz, 2H), 3.79 (s, 3H), 2.77 (q, *J* = 8.1 Hz, 1H), 2.09 (tdd, *J* = 8.2, 6.7, 5.2 Hz, 1H), 1.83 (dt, *J* = 6.8, 5.3 Hz, 1H), 1.56 (td, *J* = 8.2, 5.5 Hz, 1H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 201.7, 158.8, 130.4, 127.9, 114.1, 55.4, 29.8, 26.0, 12.0. **IR** (neat, cm^{-1}): 2938, 2836, 1699, 1612, 1513, 1457, 1297, 1245, 1176, 1030, 946, 829. **HRMS** (EI): *m/z*: calculated for $[M]^+$ $C_{11}H_{12}O_2$: 176.0832, found: 176.0832. *Note: The absolute configuration was assigned based on the employed starting material.*

General procedure for Wittig olefination: An oven dried flask was charged with methyltriphenylphosphonium bromide (1.2 equiv.) before it was evacuated and backfilled with argon (3x). It was suspended in dry THF (10 mL, 0.1 M), cooled to 0 °C and ^{n}BuLi (1.1 equiv., 2.5 M in hexane) was added dropwise and the resulting mixture stirred for 30 min at 0 °C. Then, a solution of the cyclopropyl aldehyde (1.0 equiv., 0.5 M in THF) was added and the reaction mixture stirred for 1 h at 0 °C followed by 1 h at room temperature. The mixture was quenched by adding 5 mL of sat. aqueous NH_4Cl and phases were separated. The aqueous phase was extracted with DCM (2 x 10 mL). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude vinylcyclopropane was purified by silica column chromatography (50:1 pentane:Et_2O).

1-methoxy-4-((1*R*,2*R*)-2-vinylcyclopropyl)benzene (95-*ent*): Following general procedure using (1*S*,2*R*)-2-(4-methoxyphenyl)cyclopropane-1-carbaldehyde (156.6 mg, 0.888 mmol). Column chromatography (50:1 pentane:Et_2O) afforded the title compound as a colorless oil (110.0 mg, 0.631 mmol, 71%, 99.9% ee). **R_f** = 0.38 (50:1 hexane:Et_2O). **$[\alpha]_D^{25}$** = – 124.4 (*c* 1.0, $CHCl_3$). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.17 – 7.10 (m, 2H), 6.86 – 6.79 (m, 2H), 5.14 – 5.06 (m, 2H), 4.89 – 4.81 (m, 1H), 3.79 (s, 3H), 2.29 (td, *J* = 8.5, 6.4 Hz, 1H), 1.88 – 1.75 (m, 1H), 1.23 (td, *J* = 8.4, 5.1 Hz, 1H), 0.96 (q, *J* = 5.5 Hz, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 158.1, 138.6, 130.9, 130.3, 113.9, 113.6, 55.4, 22.8, 22.6, 12.0. **IR** (neat, cm^{-1}): 3074, 3002, 2953, 2834,1633, 1612, 1512, 1459, 1295, 1245, 1177, 1034, 985, 893, 831, 795. **MS** (70eV, EI): *cis isomer* (GC retention time 6.900 min), *m/z* (%): 174.1 (100) $[M]^+$, 173.1 (46), 159.1 (90), 158.1 (43), 145.1 (18), 144.1 (71), 143.1 (42), 131.1 (28), 128.1 (51), 115.1 (49), 108.1 (22), 91.1 (47), 77.1 (25), 65.1 (17). **HRMS** (EI): *m/z*: calculated for $[M]^+$ $C_{12}H_{14}O$: 174.1039, found: 174.1040. *Note: The absolute configuration was assigned based on the employed starting material.*

5.4.6.3 Control reactions without vinyl handle

Synthesis and characterization of 1-(*tert*-butyl)-4-(*cis*-2-(4-methoxyphenyl)cyclopropyl) benzene (97)



Synthesized according to modified literature procedure.[62] In an argon filled glovebox, 1-bromo-4-(*tert*-butyl)benzene (107 mg, 0.5 mmol, 1.0 equiv.) was placed into an oven dried 20 mL screw top vial equipped with a magnetic stir bar. It was dissolved in dry toluene (2.5 mL, 0.2 M) and [Pd(μ-I)(P^tBu_3)]$_2$ (11 mg, 2.5 mol%) was added. The vial was sealed with a rubber septum, brought outside the glovebox, and connected to a Schlenk line. Then, a solution of (*cis*-2-(4-methoxyphenyl)cyclopropyl)zinc(II) chloride[62] (3 mL, 1.5 equiv., 0.24 M) was added slowly to the reaction mixture via syringe pump (during 10 min). The reaction mixture was stirred for additional 10 min, before it was opened to air and quenched by the addition of hexane. A spatula tip of ammonium pyrrolidine-1-dithiocarboxylic acid was added and the mixture stirred for additional 5 min to precipitate palladium.[60] The resulting mixture was filtered through a plug of silica, washing with Et_2O and the filtrate was concentrated under reduced pressure. Purification by silica gel column chromatography (20:1, hexane:EtOAc) afforded the title product **97** as a colorless oil (136 mg, 0.485 mmol, 97%). R_f = 0.42 (20:1, hexane:EtOAc). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.12 (d, *J* = 8.3 Hz, 2H), 6.90 (d, *J* = 8.6 Hz, 2H), 6.85 (d, *J* = 8.3 Hz, 2H), 6.67 (d, *J* = 8.6 Hz, 2H), 3.73 (s, 3H), 2.39 (dt, *J* = 8.7, 6.0 Hz, 2H), 1.43 (td, *J* = 8.8, 5.2 Hz, 1H), 1.24 (s, 10H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 157.7, 148.3, 135.8, 130.8, 130.3, 128.5, 124.7, 113.3, 55.3, 34.4, 31.5, 23.7, 23.6, 12.1. **HRMS** (EI): *m/z* $[M]^+$ calculated for $C_{20}H_{24}O$: 280.1822, found: 280.1821. The data are in agreement with those previously reported in the literature.[167] *Note: The compound contained 5% 1-cyclopropyl-4-methoxybenzene as impurity.*

Isomerization of 1-(*tert*-butyl)-4-(*cis*-2-(4-methoxyphenyl)cyclopropyl) benzene (97)

Inside an argon filled glovebox 1-(*tert*-butyl)-4-(*cis*-2-(4-methoxyphenyl)cyclopropyl)benzene **97** (56 mg, 0.2 mmol) was placed to an oven dried 4 mL screw-cap vial and dissolved in dry dioxane (0.5 mL, 0.4 M). Then, [Ni(μ-Cl)(IPr)]$_2$ **2** (10 mg, 5 mol%) was added. The reaction vial was then sealed and allowed to stir in a pre-heated aluminium block inside the glovebox for 24 h at 60 °C. The mixture was removed from the glovebox, diluted with wet hexane and a spatula tip of ammonium pyrrolidine-1-dithiocarboxylic acid was added and the mixture stirred for additional 15 min to precipitate nickel.[60] It was filtered over plug of silica diluted with Et_2O and solvent was removed under reduced pressure. The crude was analyzed by ^{1}H NMR spectroscopy and GC-MS showing no isomerization took place.

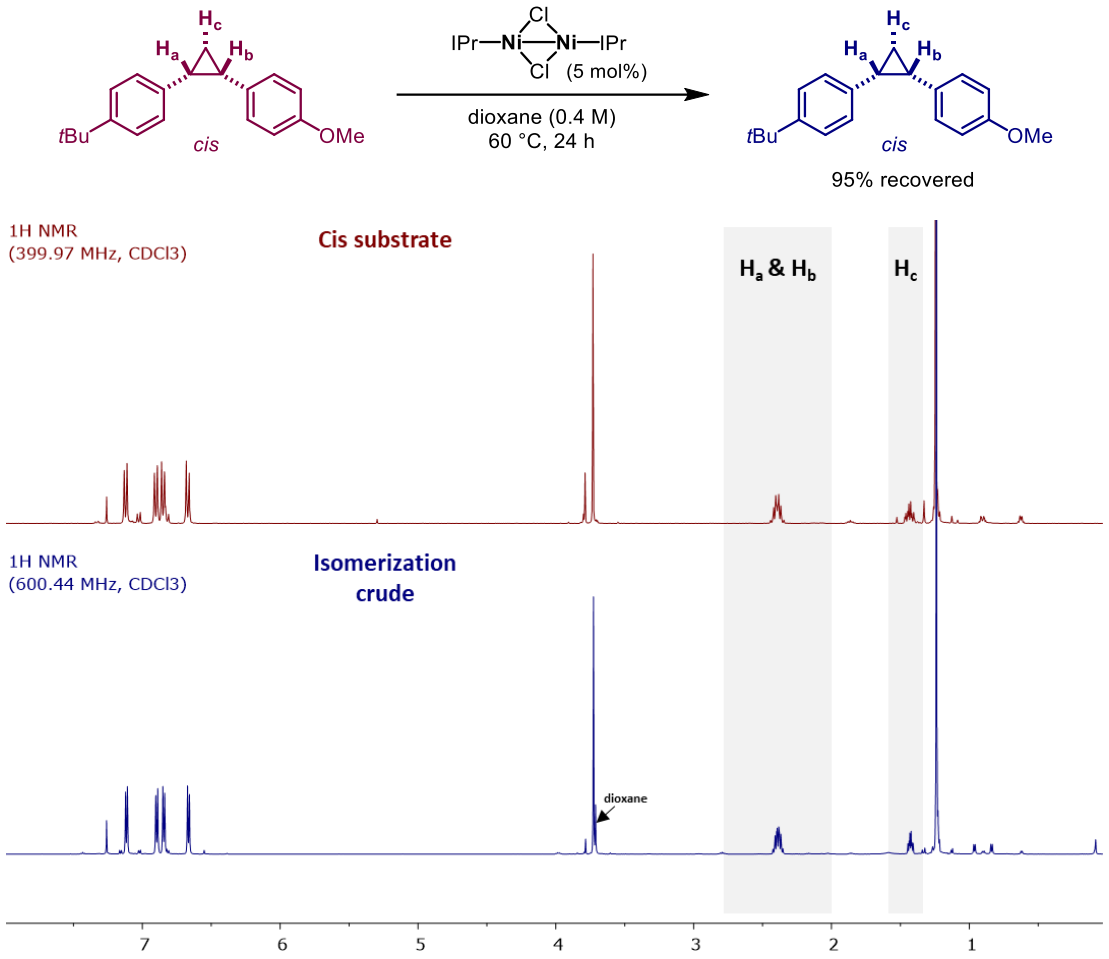
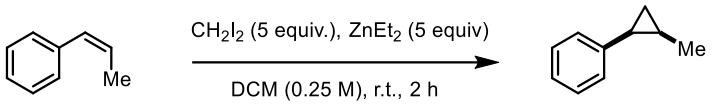


Figure 7 | Isomerization study on 1,2-biarylcyclopropane: no isomerization was observed.

Synthesis and characterization of (*cis*-2-methylcyclopropyl)benzene (98)



Synthesized following literature procedure.[168] Under argon atmosphere, a flame dried round bottom flask was charged with dry DCM (40 mL), *cis*-1-phenyl-1-propene (1.3 mL, 10.0 mmol, 1.0 equiv.) and diiodomethane (4.03 mL, 50.0 mmol, 5.0 equiv.). The solution was cooled to -10 °C and a solution of diethylzinc (50.0 mL, 50.0 mmol, 5 equiv., 1 M in hexane) was added dropwise over 10 min. The reaction was then allowed to warm up to room temperature over 2 h. Next, the reaction was cooled to 0 °C and sat. aqueous NaEDTA (20 mL) solution was added dropwise. The resulting suspension was then diluted with Et_2O (100 mL) and the phases were separated. The organic layer was further washed with H_2O (20 mL), brine (20 mL), dried over $MgSO_4$, filtered and concentrated under reduced pressure. The crude product was further purified by HPLC (*Column: LiChrosorb Si (250x25)mm, 7 µm, Mobile Phase: n-hexane, flow rate: 18 mL/min, pressure: 30 bar*) to afford (*cis*-2-methylcyclopropyl)benzene **98** (207 mg, 1.57 mmol, 16%) as a colorless oil. R_f = 0.9 (hexane). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.28 (dd, *J* = 7.6 Hz, 2H), 7.23 – 7.16 (m, 3H), 2.09 (td, *J* = 8.7, 5.9 Hz, 1H), 1.15 (dddd, *J* = 14.8, 12.2, 8.7, 6.2 Hz, 1H), 0.99 (td, *J* = 8.4, 4.9 Hz, 1H), 0.81 (d, *J* = 6.3 Hz, 3H), 0.59 (q, *J* = 5.5 Hz, 1H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 139.7, 129.4, 128.0, 125.7, 21.2, 13.7, 12.8, 11.0. **IR** (neat, cm^{-1}): 3063, 3005, 2952, 2872, 2333, 2186, 2104, 1998,

1943, 1879, 1802, 1748, 1603, 1496, 1450, 1388, 1353, 1304, 1229, 1170, 1070, 1029, 994, 909, 864, 841, 755, 725, 696. **MS** (70eV, EI): *m/z* (%): 132 (37%) [M$^+$], 117 (100), 103 (6), 91 (29), 77 (9), 65 (7), 58 (1), 51 (7). The data are in agreement with those previously reported in the literature.[169]

Isomerization of (*cis*-2-methylcyclopropyl)benzene (98)

Inside an argon filled glovebox (*cis*-2-methylcyclopropyl)benzene **98** (26.4 mg, 0.200 mmol) was placed to an oven dried 4 mL screw-cap vial and dissolved in dry dioxane (0.5 mL, 0.4 M). Then, [Ni(μ-Cl)(IPr)]$_2$ **2** (38.6 mg, 20 mol%) was added. The reaction vial was then sealed and allowed to stir in a pre-heated aluminium block inside the glovebox for 24 h at 60 °C. The mixture was removed from the glovebox, diluted with wet hexane and a spatula tip of ammonium pyrrolidine-1-dithiocarboxylic acid was added and the mixture stirred for additional 15 min to precipitate nickel.[60] It was filtered over plug of silica diluted with pentane and solvent was removed under reduced pressure. The crude was dissolved in a minimum amount of pentane and filtered again over a short plug of silica diluted with pentane and solvent was removed under reduced pressure. The recovered substrate **98** (24 mg, 0.181 mmol, 91%) was analyzed by ^{1}H NMR spectroscopy showing no isomerization took place.

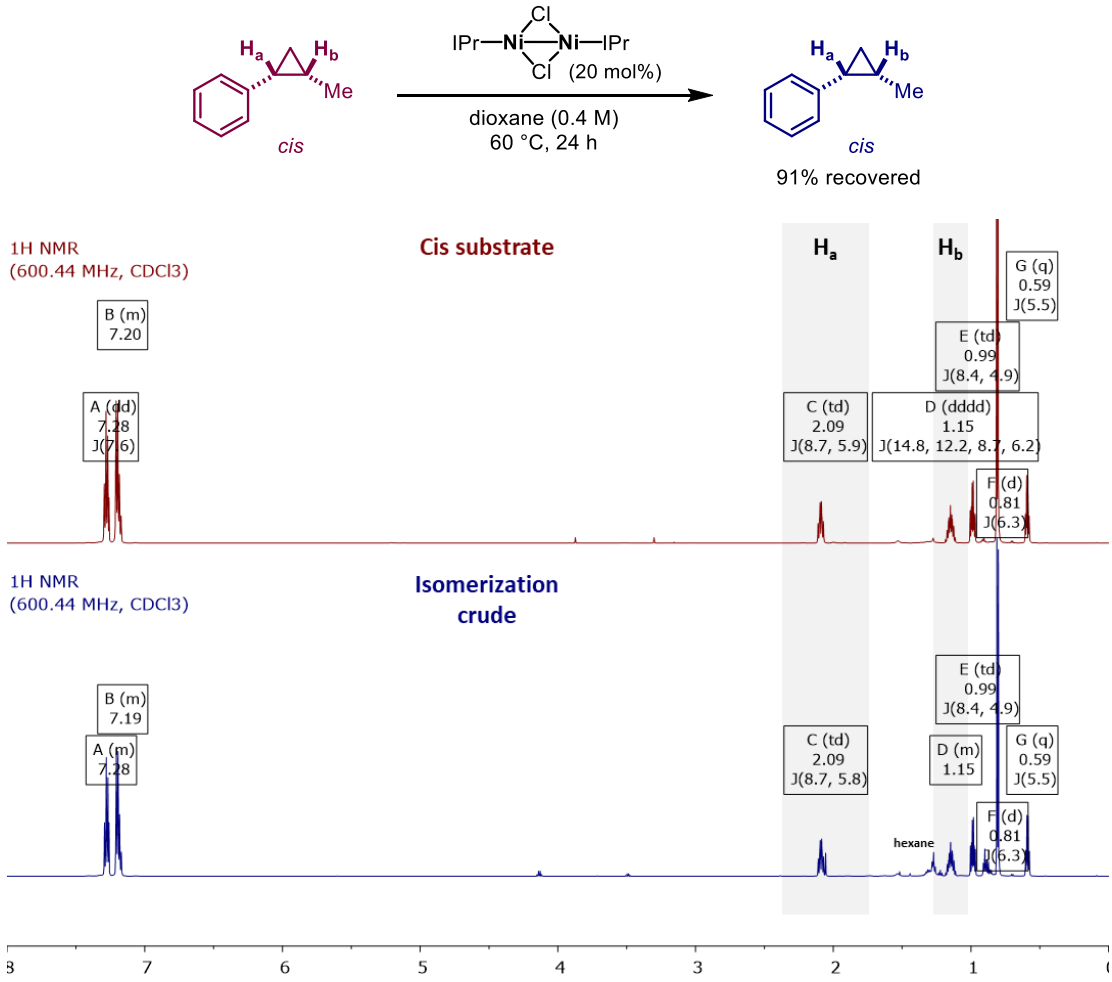
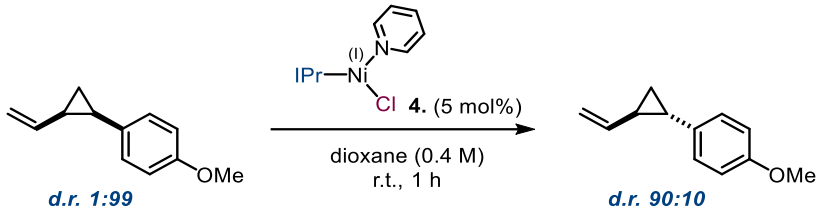


Figure 8 | No isomerization was observed with 1-phenyl-2-methyl cyclopropane.

5.4.6.4 Isomerization reaction using Nickel(I) metalloradical (4)



d.r. 1:99 *d.r. 90:10*

Inside an argon-filled glovebox, an oven dried 4 mL screw-cap vial equipped with a magnetic stirring bar was charged with 1-methoxy-4-(*cis*-2-vinylcyclopropyl)benzene (17.4 mg, 0.100 mmol, 1.0 equiv.), anhydrous 1,4-dioxane (0.25 mL, 0.4 M) and Ni(Cl)(IPr)(pyridine) **4** (2.8 mg, 5 mol%), in that order. The reaction vial was then sealed and allowed to stir inside the glovebox at room temperature for 1 h. Upon completion the reaction mixture was removed from the glovebox and quenched by the addition of wet pentane (*i.e.* technical grade pentane that had been distilled and stored on the bench). A spatula tip of ammonium pyrrolidine-1-dithiocarboxylic acid was added and the mixture stirred for additional 15 min to precipitate nickel.[60] The mixture was filtered through a plug of silica, rinsed with Et_2O and the filtrate was concentrated under reduced pressure. The crude was analyzed by quantitative ^1H NMR spectroscopy using ethylene carbonate (2.0 mg, 0.023 mmol) as internal standard. The *trans* (0.089 mmol, 89%) and *cis* (0.010 mmol, 10%) isomers were obtained in similar ratio as under standard conditions using $[Ni(\mu\text{-}Cl)(IPr)]_2$ **2**.

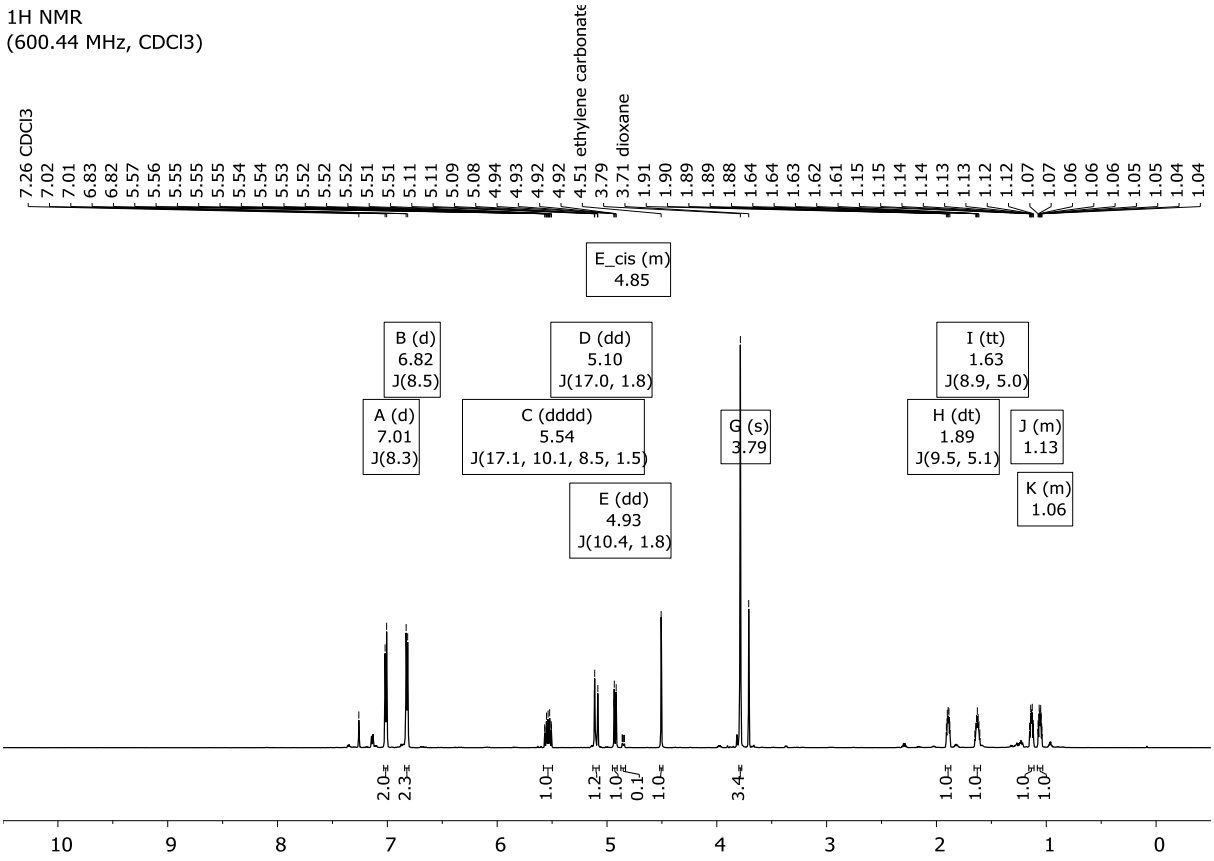


Figure 9 | Quantitative 1H NMR analysis of reaction crude using ethylene carbonate (4.51 ppm) as internal standard.

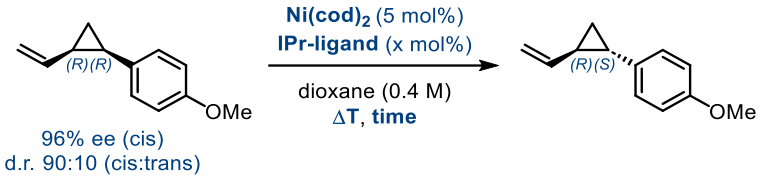
5.4.7 Reactivity comparison $Ni^{(I)}$ vs. $Ni^{(0)}$

5.4.7.1 $Ni^{(0)}$ reactivity with terminal vinylcyclopropanes

General Procedure for $Ni^{(0)}$ isomerization: Inside an argon-filled glovebox, an oven dried 4 mL screw-cap vial equipped with a magnetic stirring bar was charged with 1-methoxy-4-((*R,R*)-2-vinylcyclopropyl)benzene (17.4 mg, 0.100 mmol, 1.0 equiv., 96% ee), anhydrous dioxane (0.25 mL, 0.4 M), $Ni(cod)_2$ (1.38 mg, 5 mol%) and IPr-ligand (1.94 mg, 5 mol% or 3.89 mg, 10 mol%) in that order. The reaction vial was then sealed and allowed to stir inside the glovebox at room temperature for 1 hour. Upon completion the reaction mixture was removed from the glovebox and quenched by the addition of wet pentane (*i.e.* technical grade pentane that had been distilled and stored on the bench). A spatula tip of ammonium pyrrolidine-1-dithiocarboxylic acid was added and the mixture stirred for additional 15 min to precipitate nickel.[60] The mixture was filtered through a plug of silica, rinsed with Et_2O and the filtrate was concentrated under reduced pressure. The crude was analyzed by quantitative ^1H NMR spectroscopy using ethylene carbonate (2.0 mg, 0.023 mmol) as internal standard.

Data interpretation: $Ni(cod)_2$/IPr-system mediates isomerization of vinylcyclopropane less efficient and elongated reaction times or elevated temperatures are necessary. The applied ratio of $Ni(cod)_2$ to IPr-ligand has only minor influence on isomerization but a 1:1 ratio is more convenient.

Table 15 | Vinylcyclopropane isomerization mediated by $Ni^{(0)}$/IPr-ligand system.



entry	IPr-ligand	conditions	d.r. (*cis*:*trans*)[a]	yield[b]
1	5 mol%	r.t., 5 min	70:30	99%
2	10 mol%	r.t., 5 min	82:18	99%
3	10 mol%	r.t., 1 h	18:82	99%
4	5 mol%	60 °C, 1 h	11:89	99%
5	10 mol%	60 °C, 1 h	11:89	99%
6	5 mol%	60 °C, 24 h	11:89	n.d.
7	10 mol%	60 °C, 24 h	12:88	95%

a) Quantitative ^1H NMR ratio; b) quantitative ^1H NMR yield of cis+trans diastereomers using ethylene carbonate as internal standard.

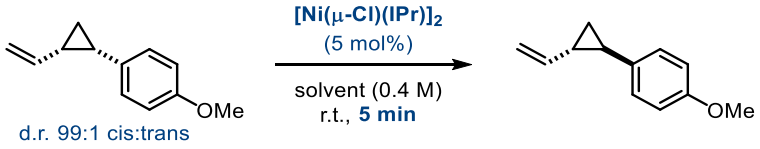
5.4.7.2 Solvent effect on isomerization

General Procedure for $Ni^{(I)}$ solvent screen: Inside an argon-filled glovebox, an oven dried 4 mL screw-cap vial equipped with a magnetic stirring bar was charged with 1-methoxy-4-(*cis*-2-vinylcyclopropyl)benzene (8.7 mg, 0.050 mmol, 1.0 equiv.), anhydrous solvent (0.125 mL, 0.4 M) and $[Ni(\mu\text{-}Cl)(IPr)]_2$ **2** (2.4 mg, 5 mol%) in that order. The reaction vial was then sealed and allowed to stir outside the glovebox at room temperature for 5 minutes. Upon completion the reaction mixture was quenched by the addition of wet pentane (*i.e.* technical grade pentane that had been distilled and stored on the bench). A spatula tip of ammonium pyrrolidine-1-dithiocarboxylic acid was added and the mixture stirred for additional 15 min to

precipitate nickel.[60] The mixture was filtered through a plug of silica, rinsed with Et_2O and the filtrate was concentrated under reduced pressure. The crude was analyzed by quantitative ^1H NMR spectroscopy using ethylene carbonate (2.0 mg, 0.023 mmol) as internal standard.

***Data interpretation**:* No significant solvent effect on the isomerization potential of $Ni^{(I)}$ dimer **2** was observed. The reaction is characterized by its rapid isomerization within minutes at room temperature.

Table 16 | Solvent effect on isomerization mediated by $Ni^{(I)}$ dimer **1**.



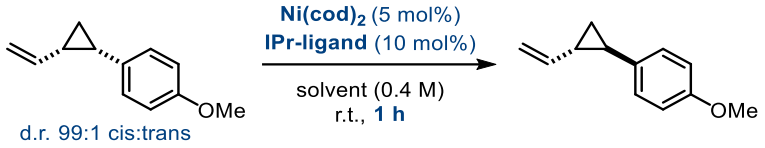
entry	solvent	d.r. (*cis:trans*)	yield[a]
1	dioxane[b]	10:90	98
2	dioxane[c]	10:90	98
3	THF	10:90	97
4	Et_2O	11:89	94
5	benzene	11:89	96
6	toluene	11:89	97
7	pentane	29:71	96

a) Quantitative 1H NMR yield using ethylene carbonate as internal standard; b) contains 35 ppm BHT inhibitor; c) inhibitor free.

***General Procedure for $Ni^{(0)}$ solvent screen**:* Inside an argon-filled glovebox, an oven dried 4 mL screw-cap vial equipped with a magnetic stirring bar was charged with 1-methoxy-4-(*cis*-2-vinylcyclopropyl)benzene (8.7 mg, 0.050 mmol, 1.0 equiv.), anhydrous solvent (0.125 mL, 0.4 M), $Ni(cod)_2$ (0.7 mg, 5 mol%) and IPr-ligand (1.94 mg, 10 mol%) in that order. The reaction vial was then sealed and allowed to stir inside the glovebox at room temperature for 1 hour. Upon completion the reaction mixture was removed from the glovebox and quenched by the addition of wet pentane (*i.e.* technical grade pentane that had been distilled and stored on the bench). A spatula tip of ammonium pyrrolidine-1-dithiocarboxylic acid was added and the mixture stirred for additional 15 min to precipitate nickel.[60] The mixture was filtered through a plug of silica, rinsed with Et_2O and the filtrate was concentrated under reduced pressure. The crude was analyzed by quantitative ^1H NMR spectroscopy using ethylene carbonate (2.0 mg, 0.023 mmol) as internal standard.

***Data interpretation**:* $Ni(cod)_2$/IPr-system mediates the isomerization of vinylcyclopropane less efficient. The isomerization potential of $Ni^{(0)}$/IPr-system is significantly affected by the corresponding solvent and particular for dioxane a positive effect was observed.

Table 17 | Solvent effect on isomerization mediated by Ni(0)/IPr-ligand (1:2).



entry	solvent	d.r. (*cis*:*trans*)	yield[a]
1	dioxane[b]	18:82	99
2	dioxane[c]	15:85	99
3	THF	61:39	99
4	Et_2O	65:35	95
5	benzene	64:36	97
6	toluene	6040	94
7	pentane	96:4	96

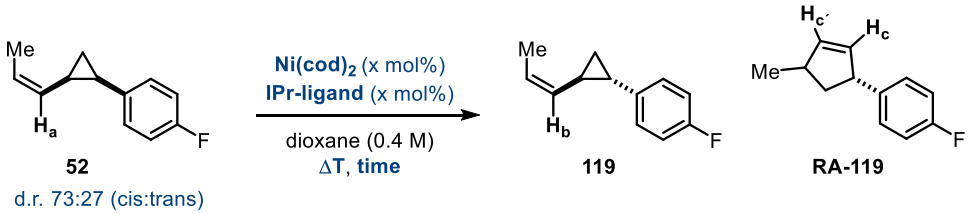
a) Quantitative ^{1}H NMR yield using ethylene carbonate as internal standard; b) contains 35 ppm BHT inhibitor; c) inhibitor free.

5.4.7.4 $Ni^{(0)}$ reactivity with internal vinylcyclopropane

General Procedure for Ni(0) isomerization: Inside an argon-filled glovebox, an oven dried 4 mL screw-cap vial equipped with a magnetic stirring bar was charged with 1-fluoro-4-(2-((Z)-prop-1-en-1-yl)cyclopropyl)benzene (17.6 mg, 0.100 mmol, 1.0 equiv., 73:27 cis/trans (^{1}H NMR)), anhydrous dioxane (0.25 mL, 0.4 M), $Ni(cod)_2$ (1.38 mg, 5 mol%) and IPr-ligand (1.94 mg, 5 mol% or 3.89 mg, 10 mol%) in that order. The reaction vial was then sealed and allowed to stir inside the glovebox at indicated temperature for indicated time. Upon completion the reaction mixture was removed from the glovebox and quenched by the addition of wet pentane (*i.e.* technical grade pentane that had been distilled and stored on the bench). A spatula tip of ammonium pyrrolidine-1-dithiocarboxylic acid was added and the mixture stirred for additional 15 min to precipitate nickel.[60] The mixture was filtered through a plug of silica, rinsed with Et_2O and the filtrate was concentrated under reduced pressure. The crude was analyzed by quantitative ^{1}H NMR spectroscopy using ethylene carbonate (2.0 mg, 0.023 mmol) as internal standard.

Data interpretation: With an additional substituent on the vinyl unit, the reactivity of $Ni^{(0)}$ is significantly lower and side-products resulting from cyclopentene formation are seen. By contrast, under $Ni^{(I)}$ dimer catalysis, no cyclopentene is seen regardless of the reaction time or temperature.

Table 18 | Internal vinylcyclopropane isomerization: comparison of $Ni^{(I)}$ dimer and $Ni^{(0)}$/IPr system.



entry	catalyst	conditions	d.r. (cis:trans)[a]	Yield (52+119)[b]	Yield RA-119[b]
1	-	starting material **52**	73:27	-	-
2	$Ni^{(I)}$ dimer **2** (5 mol%)	r.t., 2 h	11:89	96%c	n.d.
3	$Ni(cod)_2$ (5 mol%) IPr (5 mol%)	r.t., 2 h	72:28	96%	n.d.
4	Ni(cod)2 (5 mol%) IPr (10 mol%)	r.t., 2 h	72:28	95%	4%
5	$Ni(cod)_2$ (5 mol%) IPr (5 mol%)	60 °C, 24 h	21:79	38%	27%
6	$Ni(cod)_2$ (5 mol%) IPr (10 mol%)	60 °C, 24 h	23:77	61%	11%
7	$Ni^{(I)}$ dimer **2** (5 mol%)	60 °C, 24 h	14:86	81%	n.d.

a) Quantitative ^{1}H NMR ratio, E and Z diastereomers are neglected for clarity; b) quantitative ^{1}H NMR yield using ethylene carbonate as internal standard; c) isolated yield; n.d. = not determined.

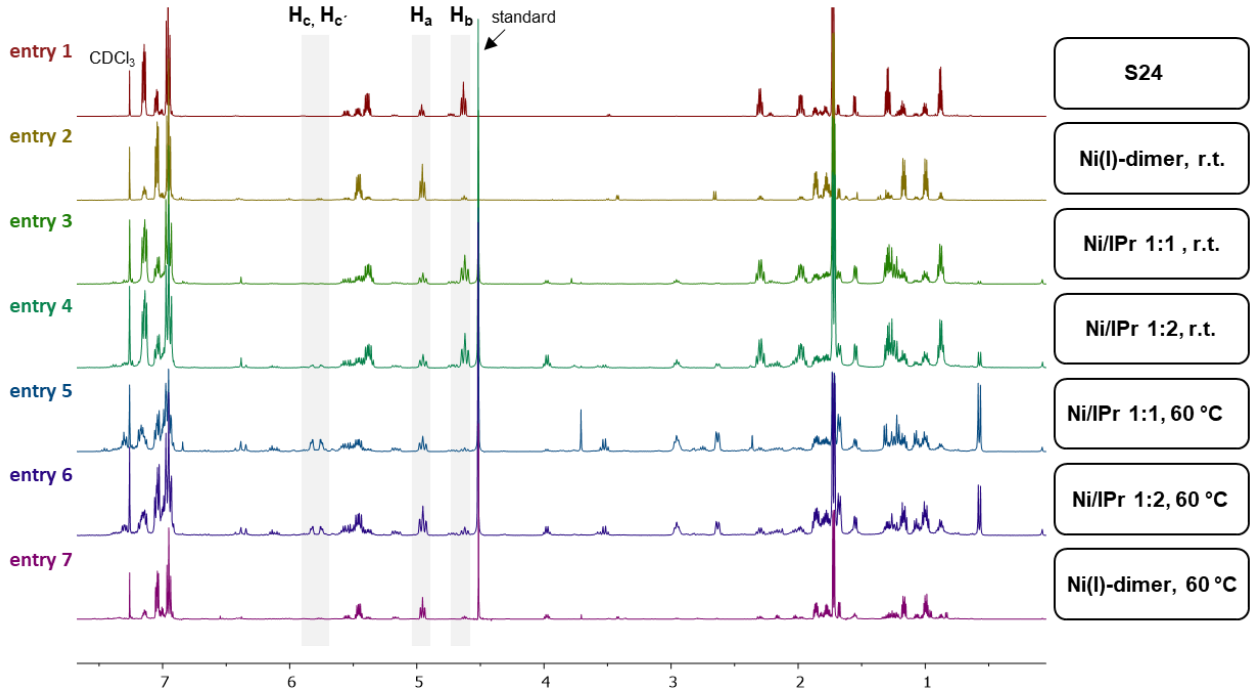


Figure 10 | Internal vinylcyclopropane isomerization: comparison of $Ni^{(I)}$ dimer and $Ni^{(0)}$/IPr system. Stacked 1H NMR spectra (horizontal zoom: 7.6 – 0.5 ppm).

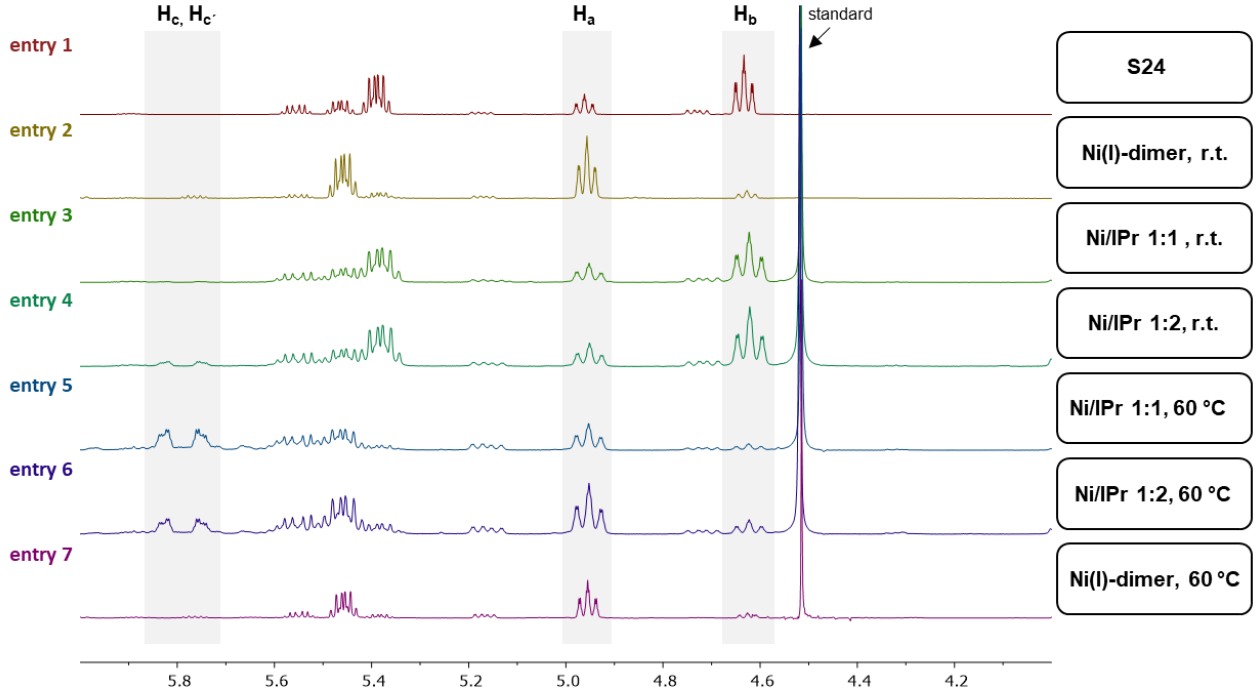
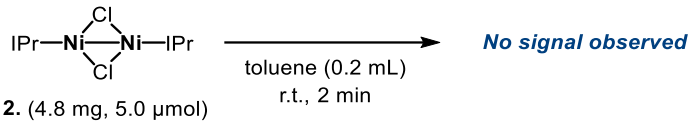


Figure 11 | Internal vinylcyclopropane isomerization: comparison of $Ni^{(I)}$ dimer and $Ni^{(0)}$/IPr system. Stacked 1H NMR spectra (horizontal zoom: 6.0 – 4.0 ppm).

5.4.8 Spectroscopic investigation on Ni(I) intermediate

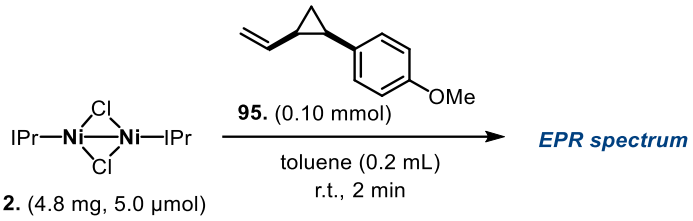
5.4.8.1 EPR spectroscopy[8]

EPR study of [Ni(μ-Cl)IPr]2 (2)

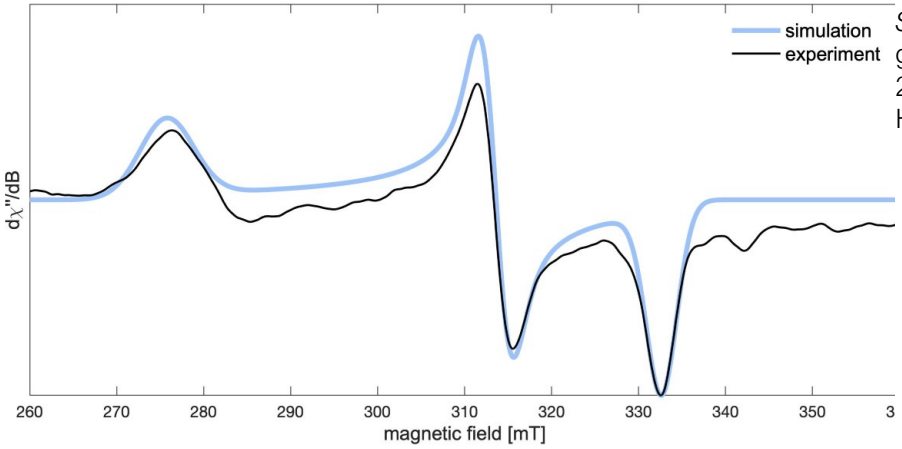


Inside an Argon-filled glovebox, [Ni(μ-Cl)(IPr)]$_2$ **2** (4.8 mg, 5.0 μmol) was dissolved in dry toluene (0.20 mL, 0.05 M). The solution was stirred for 2 min at ambient temperature inside the glovebox before being transferred inside an EPR capillary tube and sealed inside the glove box. After removing from the glovebox, the capillary tube was frozen immediately by immerging it in liquid nitrogen. No paramagnetic species was detected.

EPR study of isomerization reaction with [Ni(μ-Cl)IPr]2 (2)



Inside an Argon-filled glovebox, [Ni(μ-Cl)(IPr)]$_2$ **2** (4.8 mg, 5.0 μmol, 10 mol% Ni) was placed to a 4 mL screw-capped vial and a stock solution of vinylcyclopropane (17.4 mg, 0.100 mmol) in dry toluene (0.20 mL, 0.5 M) was added. The solution was stirred for 2 min at ambient temperature inside the glovebox before being transferred inside an EPR capillary tube and sealed inside the glove box. After removing from the glovebox, the capillary tube was frozen immediately by immerging it in liquid nitrogen. A new paramagnetic species was detected.

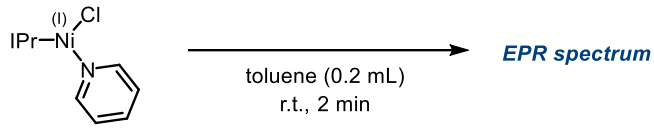


Simulation parameters:
g = [2.4526 2.1560 2.0323]
HStrain = [250 110 117]

Figure 12. CW EPR spectrum of 2 + VCP at 77 K of a frozen solution in toluene at X-band (9.464 GHz).

[8] EPR spectra simulation and plotting was conducted by Dr. T. Sperger.

EPR study of Ni(Cl)(IPr)(pyridine) 4



4. (2.8 mg, 10.0 µmol)

Inside an Argon-filled glovebox, Ni(Cl)(IPr)(pyridine) **4** (2.8 mg, 10.0 µmol) was dissolved in dry toluene (0.20 mL, 0.05 M). The solution was stirred for 2 min at ambient temperature inside the glovebox before being transferred inside an EPR capillary tube and sealed inside the glove box. After removing from the glovebox, the capillary tube was frozen immediately by immerging it in liquid nitrogen. A paramagnetic species was detected.

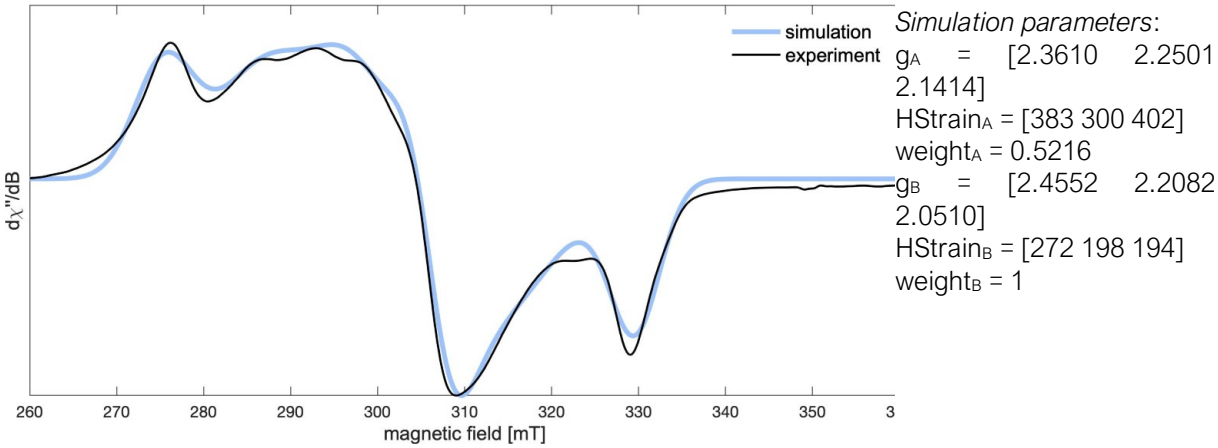
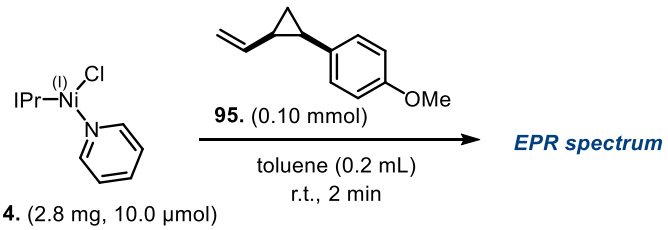


Figure 13. CW EPR spectrum of 4 at 77 K of a frozen solution in toluene at X-band (9.464 GHz).

EPR study of isomerization reaction with Ni(Cl)(IPr)(pyridine) 4



4. (2.8 mg, 10.0 µmol)

Inside an Argon-filled glovebox, Ni(Cl)(IPr)(pyridine) **4** (2.8 mg, 10.0 µmol, 10 mol% Ni) was placed to a 4 mL screw-capped vial and a stock solution of vinylcyclopropane (14.7 mg, 0.100 mmol) in dry toluene (0.20 mL, 0.5 M) was added. The solution was stirred for 2 min at ambient temperature inside the glovebox before being transferred inside an EPR capillary tube and sealed inside the glove box. After removing from the glovebox, the capillary tube was frozen immediately by immerging it in liquid nitrogen. A new paramagnetic species was detected.

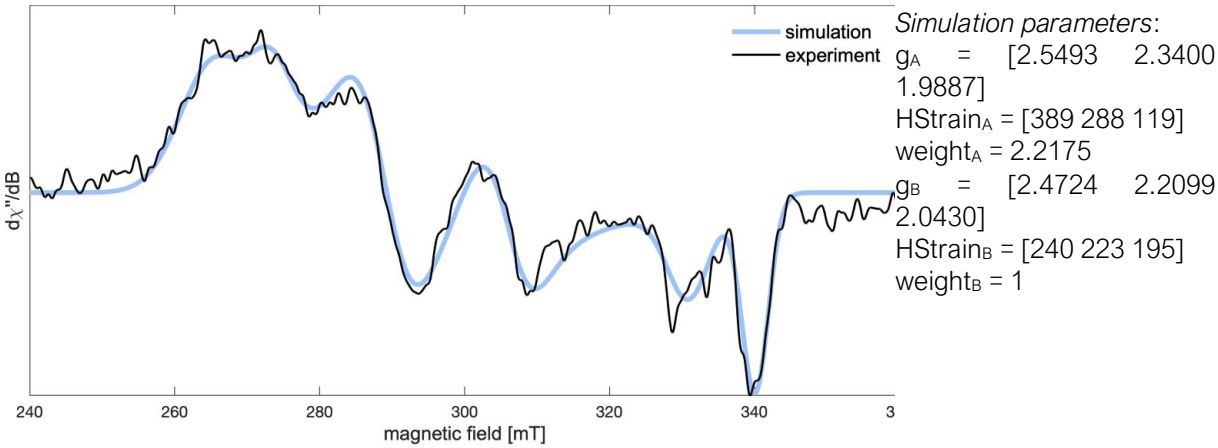
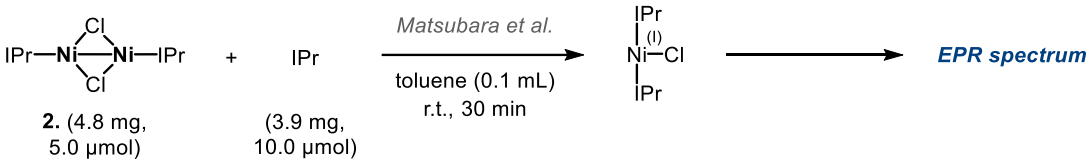


Figure 14. CW EPR spectrum of 4 + VCP at 77 K of a frozen solution in toluene at X-band (9.464 GHz).

EPR study of in situ-formed $Ni^{(I)}(Cl)(IPr)_2$



$Ni(Cl)(IPr)_2$ was formed in situ according to Matsubara and co-worker.[35]: Inside an Argon-filled glovebox, $[Ni(\mu\text{-}Cl)(IPr)]_2$ **2** (4.8 mg, 5.0 µmol, 10 mol% Ni) and IPr ligand (3.9 mg, 10.0 µmol) were weighed into a 4 mL screw-capped vial and dissolved in dry toluene (0.10 mL, 1.0 M). The solution was stirred for 30 min at ambient temperature inside the glovebox before being transferred inside an EPR capillary tube and sealed inside the glove box. After removing from the glovebox, the capillary tube was frozen immediately by immerging it in liquid nitrogen. A new paramagnetic species was detected.

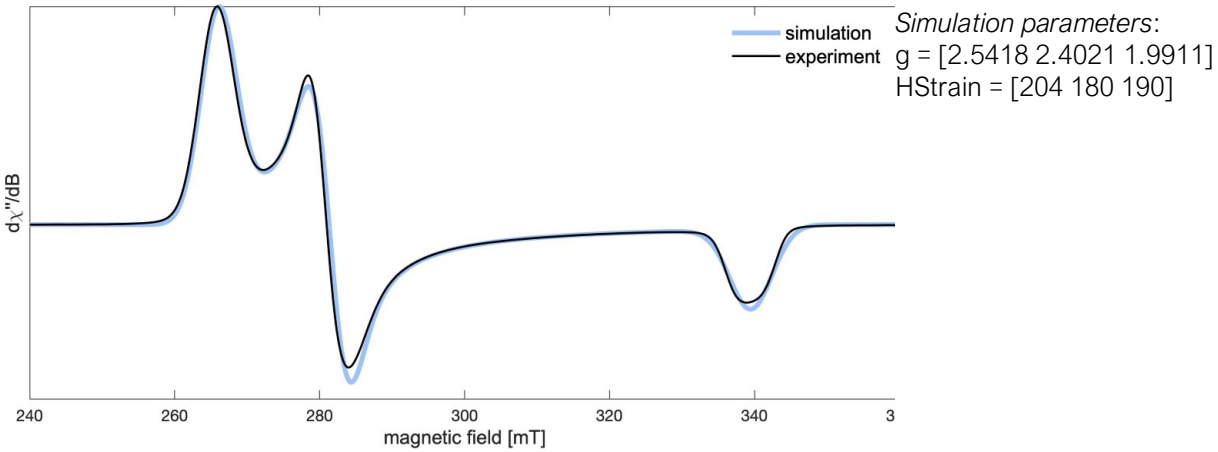
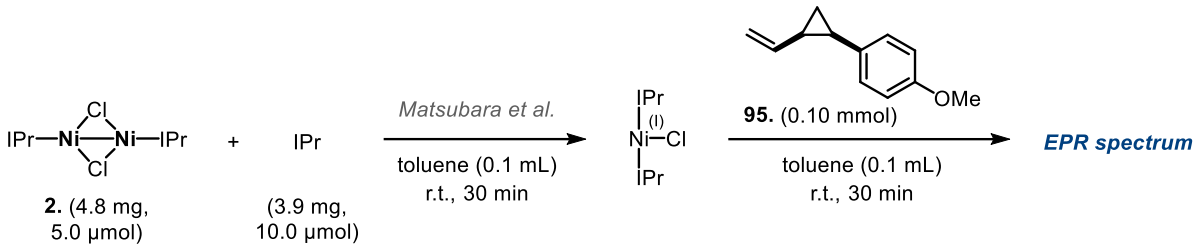


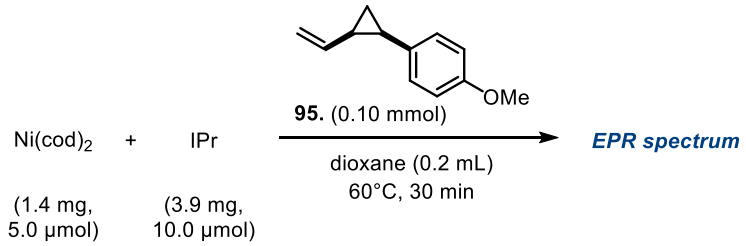
Figure 15. CW EPR spectrum of $Ni^{(I)}(Cl)(IPr)_2$ at 77 K of a frozen solution in toluene at X-band (9.464 GHz).

EPR study of isomerization reaction with in situ-formed $Ni(Cl)(IPr)_2$



$Ni(Cl)(IPr)_2$ was formed in situ according to Matsubara and co-worker.[35]: Inside an Argon-filled glovebox, $[Ni(\mu\text{-}Cl)(IPr)]_2$ **2** (4.8 mg, 5.0 µmol, 10 mol% Ni) and IPr ligand (3.9 mg, 10.0 µmol) were weighed into a 4 mL screw-capped vial and dissolved in dry toluene (0.10 mL, 1.0 M). The solution was stirred for 30 min at ambient temperature inside the glovebox before a stock solution of vinylcyclopropane (14.7 mg, 0.100 mmol) in dry toluene (0.10 mL) was added. The solution was stirred for 30 min at ambient temperature inside the glovebox before being transferred inside an EPR capillary tube and sealed inside the glove box. After removing from the glovebox, the capillary tube was frozen immediately by immerging it in liquid nitrogen. The recorded EPR spectrum showed no change compared to the spectrum recorded without the addition of vinylcyclopropane.

EPR study of isomerization reaction with $Ni^{(0)}(IPr)_2$



Inside an Argon-filled glovebox, $Ni(cod)_2$ (1.4 mg, 5.0 µmol) and IPr ligand (3.9 mg, 10.0 µmol) were weighed into a 4 mL screw-capped vial and dissolved in dry dioxane (0.10 mL, 1.0 M). The solution was stirred for 2 min at ambient temperature inside the glovebox before a stock solution of vinylcyclopropane (14.7 mg, 0.100 mmol) in dry dioxane (0.10 mL) was added. The solution was stirred for 30 min at 60°C inside the glovebox before allowing to cool and being transferred inside an EPR capillary tube and sealed inside the glove box. After removing from the glovebox, the capillary tube was frozen immediately by immerging it in liquid nitrogen. The recorded EPR spectrum showed a very weak signal. Notably, no signal was observed when the reaction was performed in toluene instead of dioxane.

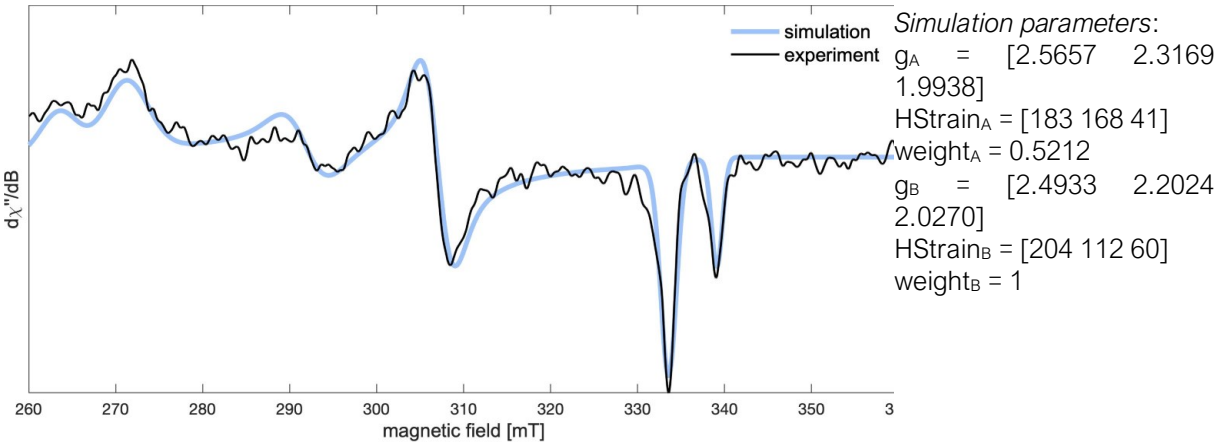


Figure S16. CW EPR spectrum of $Ni(IPr)_2$ + VCP at 77 K of a frozen solution in dioxane at X-band (9.464 GHz).

5.4.8.2 UV-vis absorption spectroscopy

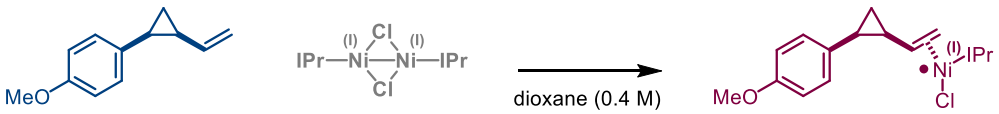
UV-vis study of 1-methoxy-4-(2-vinylcyclopropyl)benzene (95-cis)

Inside an Argon-filled glovebox, 1-methoxy-4-(2-vinylcyclopropyl)benzene (**95-**cis, (8.71 mg, 0.050 mmol) was placed to a 4 mL screw-capped vial and dry dioxane (0.125, 0.4 M) was added. After everything was dissolved an aliquot (2 µL) was taken and diluted with dry dioxane (1 mL). The diluted sample was transferred inside an UV-vis quartz cuvette and sealed inside the glove box. The cuvette was removed from the glovebox and the absorption spectra was measured immediately.

UV-vis study of $Ni^{(I)}$ dimer (2)

Inside an Argon-filled glovebox, $[Ni(\mu\text{-}Cl)(IPr)]_2$ **2** (2.41 mg, 2.5 µmol, 5 mol%) was placed to a 4 mL screw-capped vial and dry dioxane (0.125 mL) was added. After everything was dissolved an aliquot (2 µL) was taken and diluted with dry dioxane (1 mL). The diluted sample was transferred inside an UV-vis quartz cuvette and sealed inside the glove box. The cuvette was removed from the glovebox and the absorption spectra was measured immediately.

UV-vis study of isomerization reaction (95-cis + 2)



Inside an Argon-filled glovebox, $[Ni(\mu\text{-}Cl)(IPr)]_2$ **2** (2.41 mg, 2.5 µmol, 5 mol%) was placed to a 4 mL screw-capped vial and a stock solution of 1-methoxy-4-(2-vinylcyclopropyl)benzene (**95-**cis, (8.71 mg, 0.050 mmol) in dry dioxane (0.125 mL, 0.4 M) was added. The solution was stirred for 2 min at room temperature inside the glovebox before an aliquot (2 µL) was taken and diluted with dry dioxane (1 mL). The diluted sample was transferred inside an UV-vis quartz cuvette and sealed inside the glove box. The cuvette was removed from the glovebox and the absorption spectra was measured immediately.

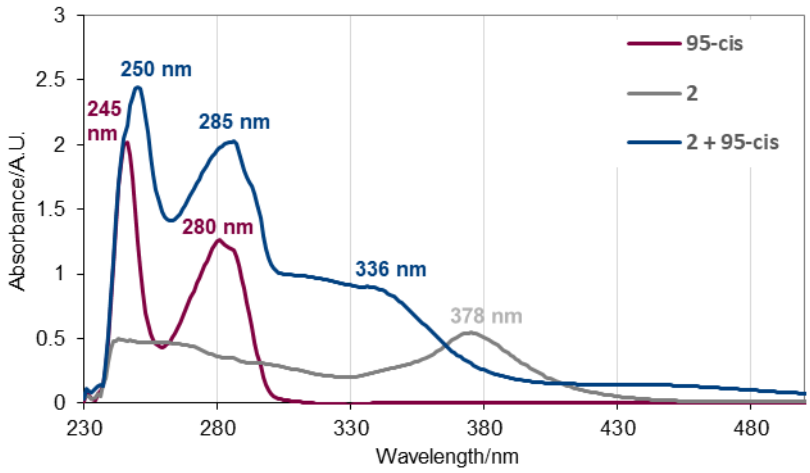
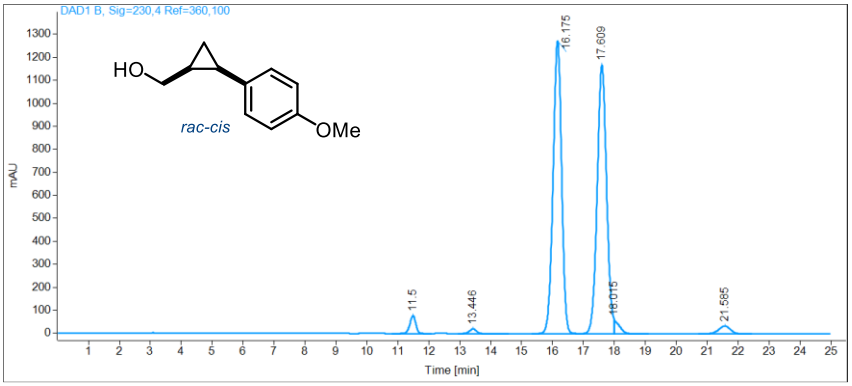


Figure 17 | UV-vis spectra of $Ni^{(I)}$ dimer (**2**, grey), 1-methoxy-4-(2-vinylcyclopropyl)benzene (**95**-cis, red) and the corresponding reaction mixture (**2**+**95**-cis, blue).

5.4.9 Chiral HPLC and GC Analyses

Racemic ((*cis*)-2-(4-methoxyphenyl)cyclopropyl)methanol

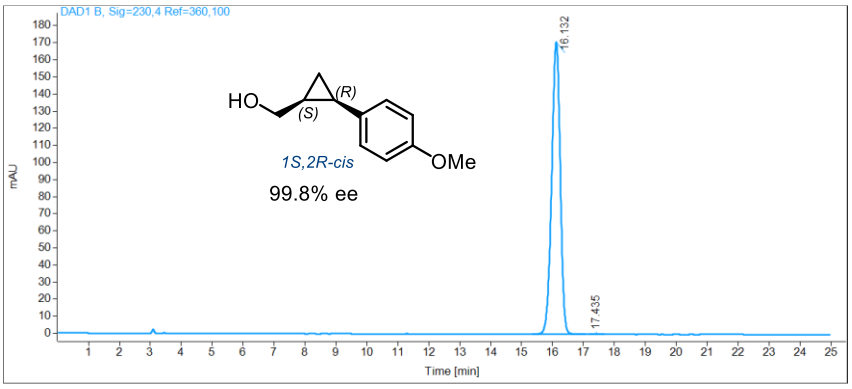
The compound was obtained as racemate ($\tau_{(S,R)}$ = 16.2 min, $\tau_{(R,S)}$ = 17.6 min).



Mobile phase: 95:5 *n*-hexane/EtOH. **Column**: Chiralpak IA, (250 x 4,6) mm. **Pressure at start**: 38 bar. **Start flow**: 1.000 mL/min. **Column oven**: 30 °C.

((1*S*,2*R*)-2-(4-methoxyphenyl)cyclopropyl)methanol

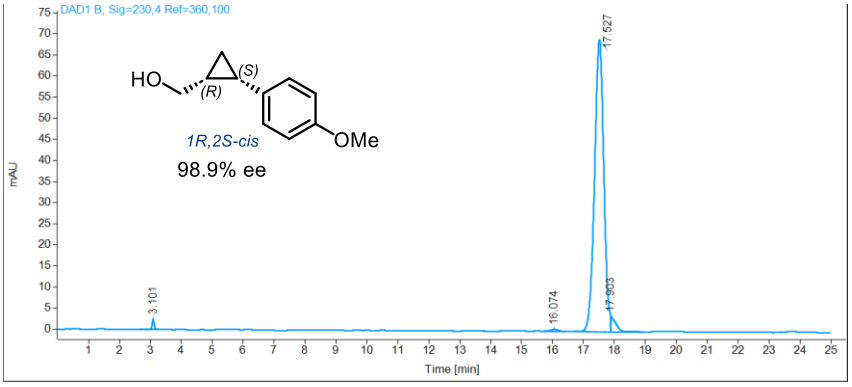
The compound was obtained with 99.8% ee (major: $\tau_{(S,R)}$ = 16.1 min, minor: $\tau_{(R,S)}$ = 17.4 min).



Mobile phase: 95:5 *n*-hexane/EtOH. **Column**: Chiralpak IA, (250 x 4,6) mm. **Pressure at start**: 37 bar. **Start flow**: 1.000 mL/min. **Column oven**: 30 °C.

((1*R*,2*S*)-2-(4-methoxyphenyl)cyclopropyl)methanol

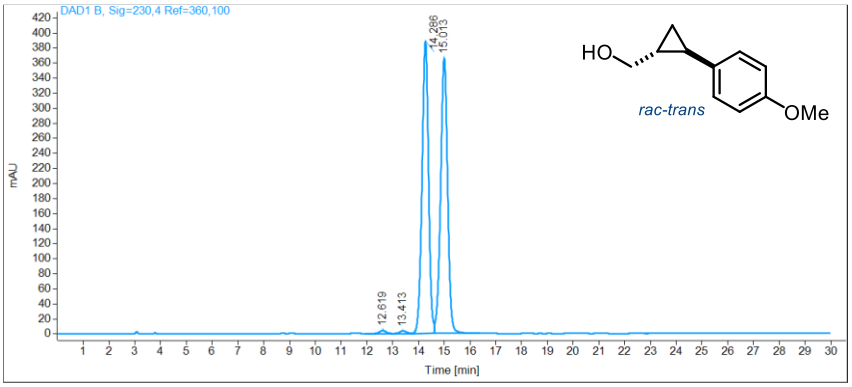
The compound was obtained with 98.8% ee (minor: $\tau_{(S,R)}$ = 16.1 min, major: $\tau_{(R,S)}$ = 17.5 min).



Mobile phase: 95:5 *n*-hexane/EtOH. **Column**: Chiralpak IA, (250 x 4,6) mm. **Pressure at start**: 38 bar. **Start flow**: 1.000 mL/min. **Column oven**: 30 °C.

Racemic ((*trans*)-2-(4-methoxyphenyl)cyclopropyl)methanol

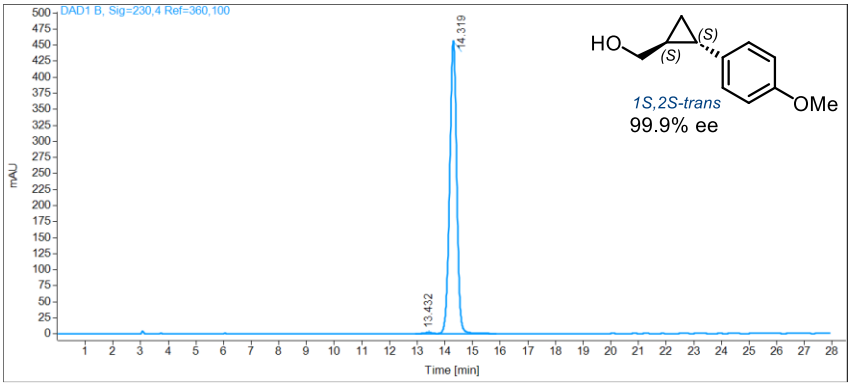
The compound was obtained as racemate ($\tau_{(S,S)}$ = 14.3 min, $\tau_{(R,R)}$ = 15.0 min).



Mobile phase: 95:5 *n*-hexane/*i*-PrOH. **Column**: Chiralpak IA, (250 x 4,6) mm. **Pressure at start**: 38 bar. **Start flow**: 1.000 mL/min. **Column oven**: 29.99 °C.

((1*S*,2*S*)-2-(4-methoxyphenyl)cyclopropyl)methanol

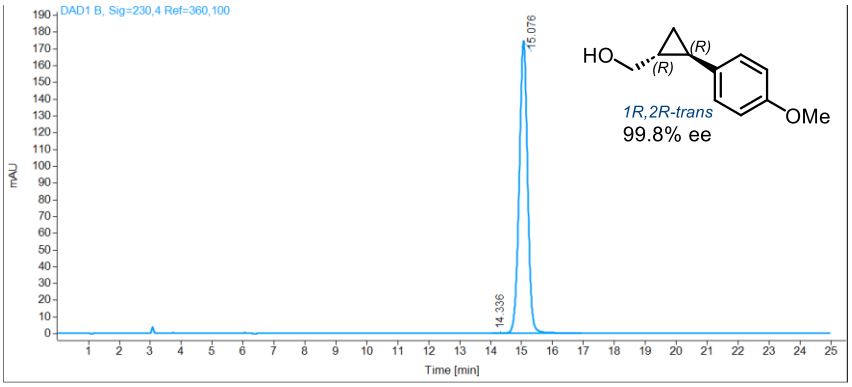
The compound was obtained with >99.9% ee (major: $\tau_{(S,S)}$ = 14.3 min, $\tau_{(R,R)}$ = not detected).



Mobile phase: 95:5 *n*-hexane/*i*-PrOH. **Column**: Chiralpak IA, (250 x 4,6) mm. **Pressure at start**: 38 bar. **Start flow**: 1.000 mL/min. **Column oven**: 30.01 °C.

((1*R*,2*R*)-2-(4-methoxyphenyl)cyclopropyl)methanol

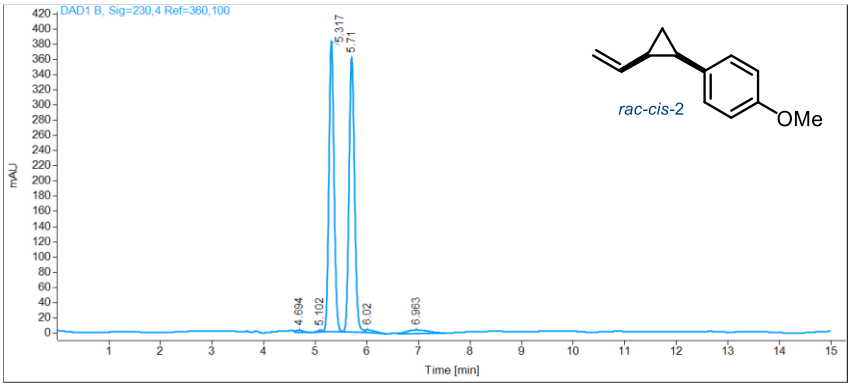
The compound was obtained with 99.8% ee (minor: $\tau_{(S,S)}$ = 14.3 min, major: $\tau_{(R,R)}$ = 15.1 min).



Mobile phase: 95:5 *n*-hexane/*i*-PrOH. **Column**: Chiralpak IA, (250 x 4,6) mm. **Pressure at start**: 38 bar. **Start flow**: 1.000 mL/min. **Column oven**: 29.99 °C.

Racemic 1-methoxy-4-((*cis*)-2-vinylcyclopropyl)benzene (95-*rac*)

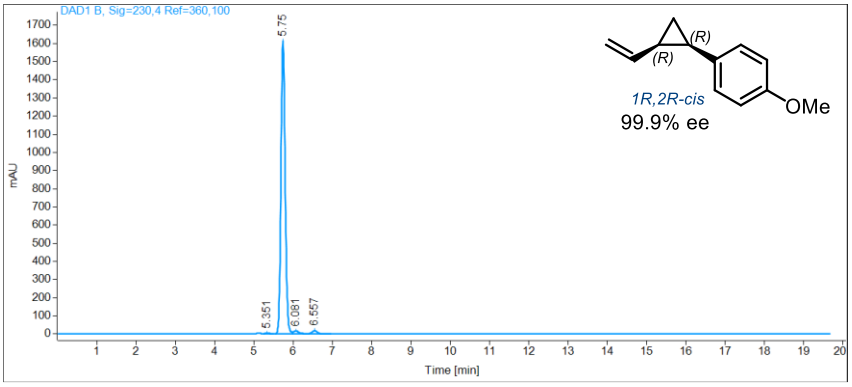
The compound was obtained as racemate ($\tau_{(S,S)}$ = 5.3 min, $\tau_{(R,R)}$ = 5.7 min).



Mobile phase: 99:1 *n*-hexane/EtOH. **Column**: Chiralpak IG, (150 x 4,6) mm, 5 µm. **Pressure at start**: 13 bar. **Start flow**: 0.500 mL/min. **Column oven**: 19.99 °C.

1-methoxy-4-((1*R*,2*R*)-2-vinylcyclopropyl)benzene (95-*ent*)

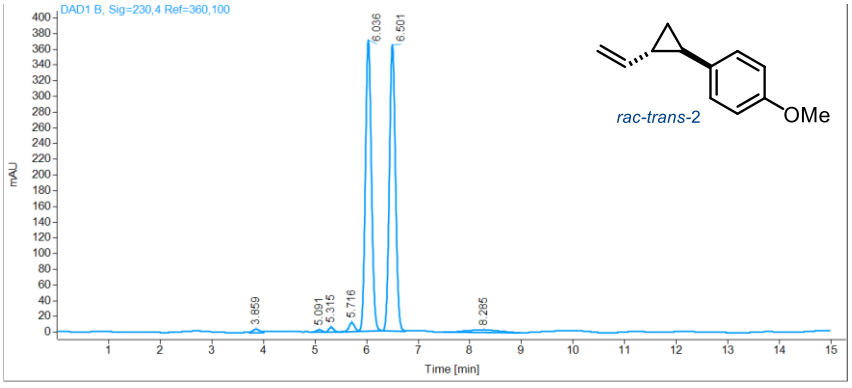
The compound was obtained with 99.9% ee (minor: $\tau_{(S,S)}$ = 5.35 min, major: $\tau_{(R,R)}$ = 5.75 min).



Mobile phase: 99:1 *n*-hexane/EtOH. **Column**: Chiralpak IG, (150 x 4,6) mm, 5 µm. **Pressure at start**: 13 bar. **Start flow**: 0.500 mL/min. **Column oven**: 19.99 °C.

Racemic 1-methoxy-4-((*trans*)-2-vinylcyclopropyl)benzene (96-*rac*)

The compound was obtained as racemate ($\tau_{(S,S)}$ = 6.03 min, $\tau_{(R,R)}$ = 6.50 min).



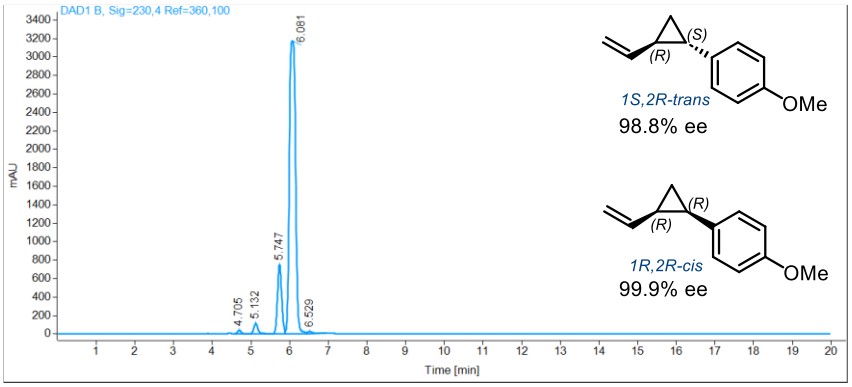
Mobile phase: 99:1 *n*-hexane/EtOH. **Column**: Chiralpak IG, (150 x 4,6) mm, 5 µm. **Pressure at start**: 13 bar. **Start flow**: 0.500 mL/min. **Column oven**: 20 °C.

Isomerization to 1-methoxy-4-((1*S*,2*R*)-2-vinylcyclopropyl)benzene (96-*ent*)

Starting material: 1-methoxy-4-((1*R*,2*R*)-2-vinylcyclopropyl)benzene.

Conditions: [Ni(μ-Cl)(IPr)]$_2$ **2** (1 mol%), room temperature., 5 minutes.

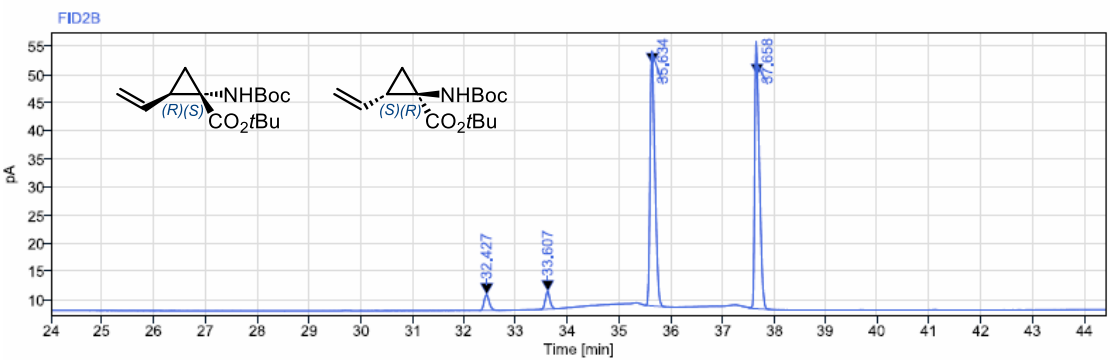
The *trans* isomer was obtained with 98.8% ee (major: $\tau_{(S,R)}$ = 6.061 min, minor: $\tau_{(R,S)}$ = 6.529 min). The *cis* isomer was obtained with 99.9% ee (minor: $\tau_{(S,S)}$ = not detected, major: $\tau_{(R,R)}$ = 5.747 min).



Mobile phase: 99:1 *n*-hexane/EtOH. **Column**: Chiralpak IG, (150 x 4,6) mm, 5 μm. **Pressure at start**: 13 bar. **Start flow**: 0.500 mL/min. **Column oven**: 20 °C.

tert-butyl (1*RS*,2*SR*)-1-((*tert*-butoxycarbonyl)amino)-2-vinylcyclopropane-1-carboxylate (128-*rac*)

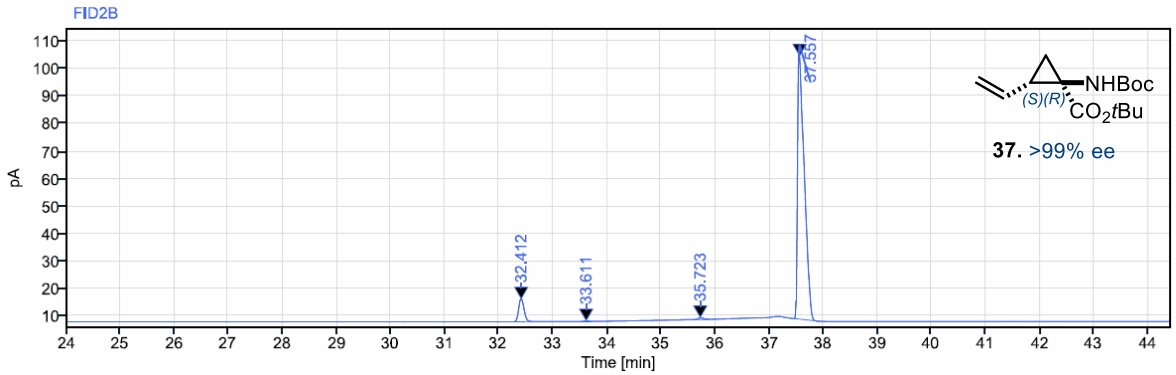
The compound was obtained as racemate ($\tau_{(S,R)}$ = 35.63 min, $\tau_{(R,S)}$ = 37.66 min).



Instrument: 8890 GC. **Mobile phase**: helium. **Column**: Chirasil-dex, 25 m, 0.25 mm. **Pressure**: 0.8 bar. **Method:** 120 °C–10 min, isothermal; 1 °C/min-140 °C; 3 °C/min-190 °C–30 min, isothermal.

tert-butyl (1*R*,2*S*)-1-((*tert*-butoxycarbonyl)amino)-2-vinylcyclopropane-1-carboxylate (128)

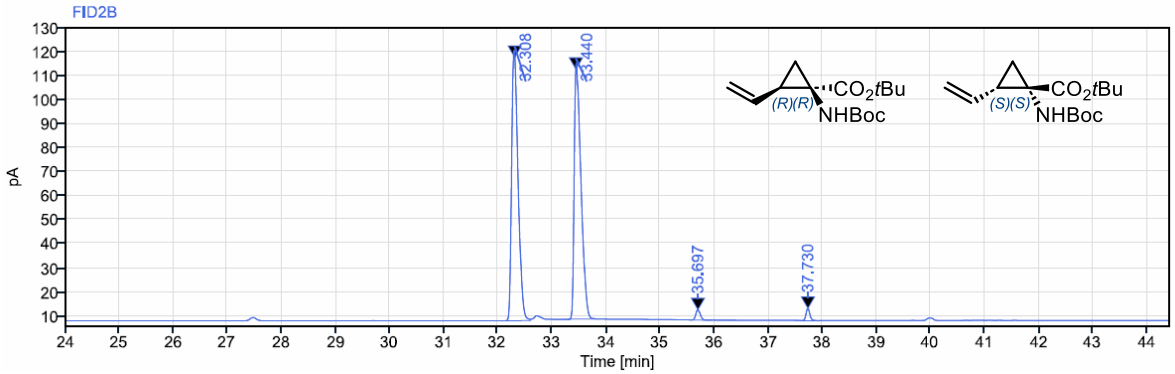
The compound was obtained with >99% ee (minor: $\tau_{(S,R)}$ = 35.72 min, major: $\tau_{(R,S)}$ = 37.56 min).



Instrument: 8890 GC. **Mobile phase**: helium. **Column**: Chirasil-dex, 25 m, 0.25 mm. **Pressure**: 0.8 bar. **Method:** 120 °C–10 min, isothermal; 1 °C/min-140 °C; 3 °C/min-190 °C–30 min, isothermal.

tert-butyl (1*SR*,2*SR*)-1-((*tert*-butoxycarbonyl)amino)-2-vinylcyclopropane-1-carboxylate (129-*rac*)

The compound was obtained as racemate ($\tau_{(R,R)}$ = 32.31 min, $\tau_{(S,S)}$ = 33.44 min) after isomerization of **128**-*rac*.

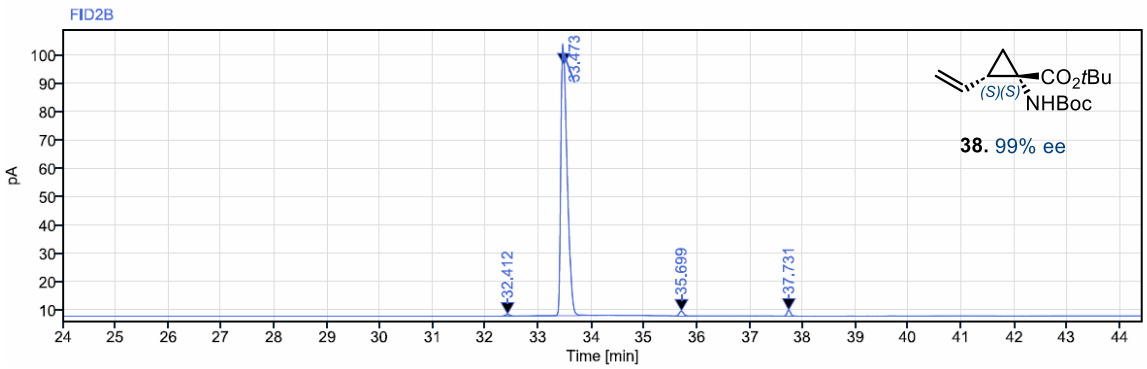


Instrument: 8890 GC. **Mobile phase**: helium. **Column**: Chirasil-dex, 25 m, 0.25 mm. **Pressure**: 0.8 bar. **Method:** 120 °C–10 min, isothermal; 1 °C/min-140 °C; 3 °C/min-190 °C–30 min, isothermal.

Isomerization to *tert*-butyl (1*S*,2*S*)-1-((*tert*-butoxycarbonyl)amino)-2-vinylcyclopropane-1-carboxylate (129)

Starting material: 1*R*,2*S*-enantiomer (**128**). **Conditions:** [Ni(μ-Cl)(IPr)]$_2$ **2** (1 mol%), r.t., 10 min. **Diastereomer separation**: flash silica column chromatography. **Iterations**: 3 cycles.

The compound was obtained with 99% ee (minor: $\tau_{(R,R)}$ = 32.41 min, major: $\tau_{(S,S)}$ = 33.47 min).

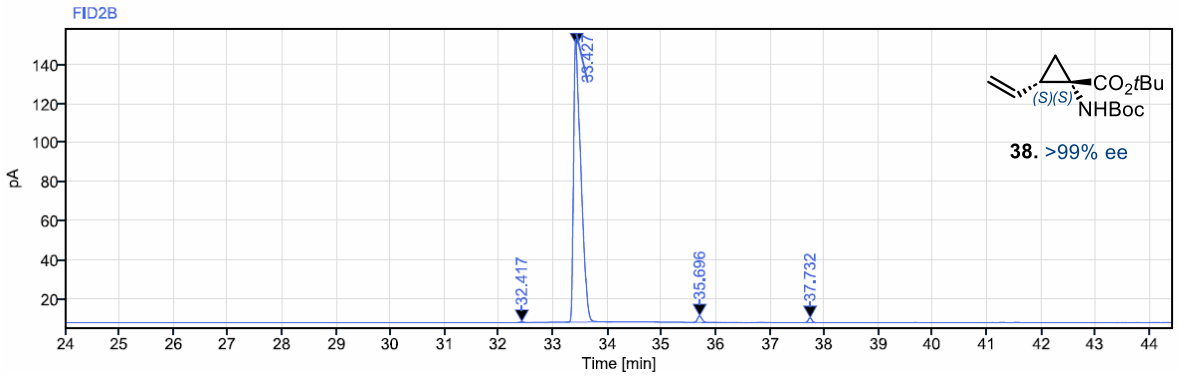


Instrument: 8890 GC. **Mobile phase**: helium. **Column**: Chirasil-dex, 25 m, 0.25 mm. **Pressure**: 0.8 bar. **Method:** 120 °C–10 min, isothermal; 1 °C/min-140 °C; 3 °C/min-190 °C–30 min, isothermal.

Isomerization to *tert*-butyl (1*S*,2*S*)-1-((*tert*-butoxycarbonyl)amino)-2-vinylcyclopropane-1-carboxylate (129)

Starting material: 1*R*,2*S*-enantiomer (**37**). **Conditions:** [Ni(μ-Cl)(IPr)]$_2$ (1 mol%), r.t., 10 min. **Diastereomer separation**: Crystallization. **Iterations**: 3 cycles.

The compound was obtained with >99% ee (minor: $\tau_{(R,R)}$ = 32.42 min, major: $\tau_{(S,S)}$ = 33.43 min).



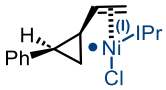
Instrument: 8890 GC. **Mobile phase**: helium. **Column**: Chirasil-dex, 25 m, 0.25 mm. **Pressure**: 0.8 bar. **Method:** 120 °C–10 min, isothermal; 1 °C/min-140 °C; 3 °C/min-190 °C–30 min, isothermal.

5.4.10 Computational details

All calculations were performed with the Gaussian 16 program package (revision A.03).[148] Gas phase geometry optimizations and frequency calculations were performed with ωB97XD along with 6-31G(d) basis set on C, H, N, and Cl atoms, and the effective core potential (ECP) SDD on Ni. Single point energy calculations were performed using the M06L[170] functional and def2-TZVP basis set on all atoms. Solvation energies were described using CPCM model for 1,4-dioxane. Frequency calculations were performed to confirm the structures minima (no imaginary frequencies) or transition states (exactly one imaginary frequency). Transition states were identified by selective bond scan. Intrinsic reaction coordinate (IRC) analysis was used to confirm that the obtained transition states connect the corresponding reactants and products. Conformational searches were conducted manually on all the species.

XYZ coordinates and energies for optimized structures

int1_planar

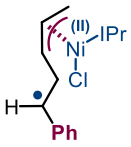


Ni	-1.33826	0.39364	-1.43138
C	1.12620	0.63152	-2.85277
H	0.63147	0.81405	-3.80397
C	0.49452	-0.44810	-2.05270
C	-0.55001	-1.20387	-2.52613
H	-0.88994	-2.09681	-2.00870
H	-0.93424	-1.05419	-3.53323
H	1.00404	-0.74520	-1.13881
C	-1.33815	0.24115	0.53896
Cl	-2.93022	1.57172	-2.41838
N	-2.09552	-0.66633	1.20556
N	-0.95288	1.11230	1.50845
C	-2.20579	-0.35647	2.55224
C	-1.48466	0.77058	2.74322
H	-2.77890	-0.96352	3.23448
H	-1.28432	1.35008	3.63012
C	-2.55530	-1.88244	0.59624
C	-3.87239	-1.95204	0.13083
C	-1.63580	-2.94023	0.47052
C	-4.28867	-3.16266	-0.42888
C	-2.10124	-4.12402	-0.09901
C	-3.41757	-4.23736	-0.53523
H	-5.30504	-3.25947	-0.79686
H	-1.42701	-4.96652	-0.21478
H	-3.76043	-5.16887	-0.97607
C	0.11858	2.05094	1.32457
C	1.40211	1.64395	1.72189
C	-0.14448	3.29748	0.74151
C	2.45153	2.54371	1.52762
C	0.94010	4.15923	0.56841
C	2.22265	3.78883	0.95630
H	3.45919	2.26057	1.81845
H	0.78048	5.13291	0.11747
H	3.05066	4.47562	0.80638
C	-0.19050	-2.80031	0.93312
H	0.08352	-1.74665	0.82590
C	0.81093	-3.59434	0.08675
H	0.72056	-4.67492	0.24668
H	0.68683	-3.39289	-0.98181
H	1.83101	-3.30584	0.36309
C	-0.04863	-3.17144	2.41698
H	0.98716	-3.03188	2.74777
H	-0.69076	-2.55222	3.05094
H	-0.31976	-4.22123	2.57900
C	-4.81928	-0.76828	0.24042
H	-4.21266	0.13474	0.36202
C	-5.71773	-0.91637	1.47758
H	-6.34285	-1.81392	1.39834
H	-5.12971	-0.99868	2.39843
H	-6.37958	-0.04892	1.57447
C	-5.65504	-0.56384	-1.02716
H	-6.22879	0.36440	-0.93971
H	-5.01078	-0.47166	-1.90553
H	-6.37011	-1.38021	-1.18470
C	1.66349	0.29089	2.36873
H	0.74524	-0.29877	2.32067
C	2.74682	-0.50928	1.64121
H	2.83090	-1.51145	2.07718
H	2.52624	-0.61767	0.57480
H	3.72865	-0.03257	1.72099
C	2.01042	0.45934	3.85461
H	2.93899	1.02824	3.98029
H	1.21787	0.99150	4.39161
H	2.14623	-0.51967	4.32770
C	-1.55770	3.70901	0.36454
H	-2.11943	2.80629	0.10930
C	-2.24555	4.36735	1.57048
H	-1.71489	5.27820	1.87334
H	-3.27586	4.63917	1.31716
H	-2.27571	3.69108	2.43235
C	-1.61547	4.61192	-0.86921
H	-1.20079	5.60862	-0.67363
H	-1.08116	4.15883	-1.70939
H	-2.65719	4.73674	-1.17799
C	3.57325	0.05113	-2.03569
C	3.57194	-1.34826	-2.09174
C	4.51824	0.66939	-1.22029
C	4.46576	-2.09777	-1.34298
H	2.84610	-1.85488	-2.72191
C	5.44217	-0.06594	-0.47928
H	4.52774	1.75429	-1.15413
C	5.40899	-1.46019	-0.53008
H	4.45614	-3.18255	-1.37422
H	6.16233	0.45697	0.14021
C	1.70501	1.85319	-2.17410
H	1.52561	2.82234	-2.62823
H	1.70101	1.85295	-1.08790
C	2.62616	0.87631	-2.84826
H	3.02277	1.18996	-3.81302
O	6.23762	-2.27902	0.16874
C	7.17893	-1.68394	1.03014
H	6.68927	-1.08367	1.80895
H	7.72217	-2.50556	1.49881
H	7.88747	-1.05046	0.48048

Zero-point correction = 0.816162 (Hartree/Particle)
Thermal correction to Energy = 0.862549

Thermal correction to Enthalpy = 0.863493
Thermal correction to Gibbs Free Energy = 0.734811
Sum of electronic and zero-point Energies = -2330.832031
Sum of electronic and thermal Energies = -2330.785643
Sum of electronic and thermal Enthalpies = -2330.784699
Sum of electronic and thermal Free Energies = -2330.913382
E(M06L) = -3669.93890047

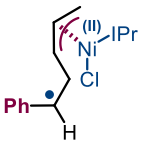
Int 2



Ni	-0.46903	-0.90272	-0.75278
C	2.31318	-3.37936	-2.11945
C	-0.10469	-2.71719	-1.76189
H	-1.11107	-2.71464	-2.18588
C	0.04871	-2.83342	-0.38880
C	-0.96248	-2.34620	0.47939
H	-0.74592	-2.30023	1.54399
H	-2.01048	-2.52582	0.23609
H	1.04962	-2.99898	0.00407
C	-1.12486	0.50519	0.32873
Cl	-0.10030	0.34411	-2.55129
N	-2.42114	0.73808	0.66783
N	-0.44932	1.53878	0.89306
C	-2.55152	1.89734	1.41647
C	-1.30766	2.39333	1.57033
H	-3.51152	2.25149	1.75427
H	-0.94213	3.26336	2.09030
C	-3.53018	-0.10556	0.32189
C	-4.09657	0.02007	-0.95444
C	-4.00801	-1.00700	1.28617
C	-5.18158	-0.80579	-1.25532
C	-5.09950	-1.80245	0.93710
C	-5.67848	-1.70600	-0.32212
H	-5.64669	-0.74000	-2.23347
H	-5.49830	-2.51214	1.65520
H	-6.52456	-2.33743	-0.57729
C	0.96596	1.79567	0.85250
C	1.81176	1.07407	1.70635
C	1.42412	2.84695	0.04407
C	3.14493	1.47486	1.78444
C	2.76582	3.21302	0.16723
C	3.61585	2.54623	1.03913
H	3.83078	0.93135	2.42692
H	3.15117	4.03063	-0.43452
H	4.66038	2.83211	1.10763
C	-3.38545	-1.11111	2.67107
H	-2.37114	-0.70113	2.61371
C	-3.26835	-2.55748	3.16980
H	-4.24846	-2.98175	3.41513
H	-2.79398	-3.20629	2.42833
H	-2.66652	-2.58501	4.08466
C	-4.17814	-0.27382	3.68723
H	-3.71577	-0.33561	4.67864
H	-4.22186	0.78068	3.40024
H	-5.20735	-0.64263	3.76742
C	-3.60107	1.05671	-1.94925
H	-2.55760	1.28298	-1.71886
C	-4.41455	2.35163	-1.80021
H	-5.47454	2.17683	-2.02113
H	-4.34335	2.75433	-0.78355
H	-4.04243	3.11459	-2.49270
C	-3.61481	0.55701	-3.39587
H	-3.11323	1.28853	-4.03655
H	-3.06744	-0.38554	-3.48653
H	-4.63296	0.41909	-3.77992
C	1.33004	-0.10653	2.53081
H	0.30656	-0.33925	2.22770
C	2.17689	-1.35366	2.24418
H	1.72424	-2.23668	2.71049
H	2.26093	-1.52703	1.16720
H	3.19395	-1.25355	2.64025
C	1.30360	0.23202	4.02654
H	2.30658	0.47844	4.39417
H	0.65223	1.09043	4.22461
H	0.93218	-0.62081	4.60639
C	0.51696	3.58806	-0.92609
H	-0.40152	3.00482	-1.04194
C	0.15092	4.98061	-0.39160
H	1.04882	5.59684	-0.26312
H	-0.51324	5.49505	-1.09492
H	-0.35909	4.92877	0.57589
C	1.14752	3.69636	-2.32016
H	2.02435	4.35475	-2.32109
H	1.44031	2.70986	-2.68718
H	0.41910	4.11641	-3.02212
C	3.22833	-2.48373	-1.51767
C	3.08666	-1.07027	-1.60782
C	4.32370	-2.96726	-0.76053
C	3.97380	-0.22085	-0.98596
H	2.25899	-0.64139	-2.16332
C	5.21091	-2.11326	-0.12059
H	4.46662	-4.04138	-0.66900
C	5.04030	-0.72885	-0.22833
H	3.84842	0.85350	-1.05994
H	6.02734	-2.53595	0.45452
H	2.49869	-4.44449	-1.99326
C	1.01757	-2.97888	-2.75593
H	0.68947	-3.77676	-3.43395
H	1.12892	-2.07892	-3.37545
O	5.84630	0.19591	0.36210
C	6.90758	-0.26931	1.16013
H	7.62261	-0.86518	0.57774
H	7.41175	0.61931	1.54338
H	6.54448	-0.87136	2.00443

Zero-point correction = 0.815467 (Hartree/Particle)
Thermal correction to Energy = 0.861384
Thermal correction to Enthalpy = 0.862328
Thermal correction to Gibbs Free Energy = 0.736263
Sum of electronic and zero-point Energies = -2330.812393
Sum of electronic and thermal Energies = -2330.766476
Sum of electronic and thermal Enthalpies = -2330.765532
Sum of electronic and thermal Free Energies = -2330.891597
E(M06L) = -3669.93292195

Int-3

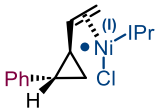


Ni	-0.48537	-0.34180	-1.14309
C	2.51798	0.09948	-2.62415
C	0.44148	-1.32991	-2.70162
H	-0.45874	-1.56501	-3.27279
C	0.64229	-1.96392	-1.47610
C	-0.47265	-2.26106	-0.66032
H	-0.29291	-2.61359	0.35126
H	-1.40847	-2.60464	-1.10511
H	1.62446	-1.91697	-1.01001
C	-1.32641	0.28363	0.43637
Cl	-0.67500	1.55681	-2.26499
N	-2.58211	0.05219	0.89395
N	-0.79097	1.13036	1.35266
C	-2.83458	0.75536	2.06222
C	-1.70136	1.42558	2.35715
H	-3.79082	0.71330	2.55732
H	-1.44934	2.07755	3.17717
C	-3.51897	-0.84014	0.27249
C	-4.27588	-0.37097	-0.80991
C	-3.63377	-2.14328	0.78141

C	-5.18436	-1.26112	-1.38596
C	-4.56057	-2.99010	0.17319
C	-5.32723	-2.55425	-0.90046
H	-5.78964	-0.93680	-2.22614
H	-4.68068	-4.00546	0.53777
H	-6.04088	-3.22957	-1.36341
C	0.54567	1.66278	1.32673
C	1.60670	0.83245	1.72436
C	0.72597	3.00260	0.95649
C	2.87886	1.39811	1.78231
C	2.02075	3.52032	1.03705
C	3.08382	2.73215	1.45263
H	3.72407	0.78448	2.07448
H	2.19732	4.55638	0.76550
H	4.08301	3.15549	1.50797
C	-2.80545	-2.62117	1.96536
H	-1.91599	-1.98455	2.03044
C	-2.32501	-4.07061	1.81425
H	-3.14815	-4.78396	1.93430
H	-1.86474	-4.24771	0.83807
H	-1.58530	-4.29822	2.58948
C	-3.58997	-2.46893	3.27806
H	-2.98167	-2.79801	4.12793
H	-3.88608	-1.43148	3.45708
H	-4.50039	-3.07899	3.25315
C	-4.16201	1.06317	-1.29995
H	-3.17125	1.43893	-1.03360
C	-5.21127	1.93854	-0.59767
H	-6.22704	1.59950	-0.83477
H	-5.09200	1.91051	0.49136
H	-5.11459	2.98049	-0.92179
C	-4.26375	1.18776	-2.82208
H	-4.03267	2.21567	-3.11752
H	-3.53678	0.53521	-3.31385
H	-5.26819	0.95143	-3.19402
C	1.38225	-0.61902	2.11824
H	0.53234	-0.98583	1.53899
C	2.57332	-1.52367	1.78350
H	2.28023	-2.57447	1.88505
H	2.93026	-1.36132	0.76160
H	3.41872	-1.35794	2.46170
C	1.00935	-0.72908	3.60440
H	1.82050	-0.34871	4.23641
H	0.10320	-0.15811	3.83356
H	0.82746	-1.77540	3.87659
C	-0.42545	3.88953	0.50890
H	-1.26132	3.23978	0.23283
C	-0.87483	4.81696	1.64867
H	-0.05960	5.48749	1.94590
H	-1.71973	5.43511	1.32554
H	-1.18616	4.25935	2.53782
C	-0.07584	4.71176	-0.73736
H	0.67237	5.48377	-0.52131
H	0.29543	4.06406	-1.53464
H	-0.97389	5.22075	-1.10359
C	3.63812	-0.42016	-1.93852
C	4.05603	-1.77967	-2.02092
C	4.39207	0.41852	-1.07906
C	5.11786	-2.25435	-1.28033
H	3.51669	-2.46708	-2.66638
C	5.46315	-0.05331	-0.33666
H	4.09982	1.46026	-0.98501
C	5.83172	-1.40078	-0.42463
H	5.42172	-3.29469	-1.33943
H	5.99805	0.63289	0.31124
H	2.23792	1.13053	-2.42545
C	1.57061	-0.67888	-3.48578
H	2.09739	-1.44511	-4.07364
H	1.11199	0.00902	-4.20288
O	6.85071	-1.97349	0.26855
C	7.57111	-1.16437	1.16678
H	6.92001	-0.75393	1.95084
H	8.31989	-1.81204	1.62493
H	8.07665	-0.33707	0.65131

Zero-point correction = 0.815191 (Hartree/Particle)
Thermal correction to Energy = 0.861222
Thermal correction to Enthalpy = 0.862166
Thermal correction to Gibbs Free Energy = 0.734613
Sum of electronic and zero-point Energies = -2330.808857
Sum of electronic and thermal Energies = -2330.762827
Sum of electronic and thermal Enthalpies = -2330.761883
Sum of electronic and thermal Free Energies = -2330.889436
E(M06L) = -3669.93180355

Int4_planar

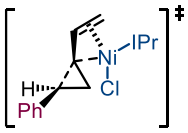


Ni	-0.59150	-0.57495	-1.14179
C	3.25386	-0.30958	0.56028
C	2.17231	-0.75359	-0.40567
H	2.51943	-1.15074	-1.35704
C	0.92459	-1.37263	0.10594
C	0.25936	-2.38874	-0.53367
H	-0.54053	-2.93879	-0.04391
H	0.64312	-2.81219	-1.45958
H	0.64288	-1.11665	1.12599
C	2.44725	0.71776	-0.17710
C	-1.81153	0.39213	0.07942
Cl	-0.90709	-0.42626	-3.32780
N	-2.99576	-0.12987	0.49095
N	-1.90381	1.70226	0.42809
C	-3.81330	0.82999	1.06538
C	-3.12265	1.99081	1.02382
H	-4.79505	0.59433	1.44354
H	-3.36711	2.98314	1.36773
C	-3.27378	-1.53745	0.46117
C	-3.98504	-2.06592	-0.62196
C	-2.78272	-2.32237	1.51834
C	-4.25347	-3.43647	-0.59944
C	-3.07749	-3.68472	1.49216
C	-3.81298	-4.23434	0.44743
H	-4.80478	-3.88656	-1.41850
H	-2.72064	-4.32893	2.28932
H	-4.03122	-5.29825	0.44392
C	-0.79101	2.60833	0.40649
C	-0.08876	2.79785	1.60577
C	-0.44407	3.24488	-0.79376
C	0.99617	3.67623	1.58587
C	0.65918	4.09897	-0.76294
C	1.36963	4.31618	0.41216
H	1.56542	3.84585	2.49561
H	0.96819	4.60336	-1.67209
H	2.22368	4.98698	0.41005
C	-1.95892	-1.71281	2.64505
H	-1.44780	-0.83436	2.23787
C	-0.86774	-2.65012	3.17368
H	-1.28649	-3.49217	3.73627
H	-0.25339	-3.05243	2.36196
H	-0.21065	-2.09967	3.85603
C	-2.85815	-1.23418	3.79456
H	-2.25534	-0.76379	4.58031
H	-3.59430	-0.50130	3.45061
H	-3.39924	-2.07791	4.23851
C	-4.46219	-1.18524	-1.76535
H	-3.82597	-0.29470	-1.78852
C	-5.91168	-0.73711	-1.52330
H	-6.58414	-1.60262	-1.48697
H	-6.01596	-0.19155	-0.57903
H	-6.24716	-0.07960	-2.33263
C	-4.31672	-1.85891	-3.13313
H	-4.54940	-1.13560	-3.92108
H	-3.28983	-2.19851	-3.29150
H	-5.00324	-2.70609	-3.25024

C	-0.45128	2.06920	2.89225
H	-1.31805	1.43086	2.70053
C	0.68551	1.14865	3.35348
H	0.38572	0.59399	4.25019
H	0.94048	0.42456	2.57393
H	1.59317	1.71361	3.59372
C	-0.85495	3.05340	3.99766
H	-0.02196	3.70973	4.27368
H	-1.68787	3.68762	3.67604
H	-1.16575	2.51006	4.89687
C	-1.27116	3.05621	-2.05494
H	-1.67898	2.04176	-2.04734
C	-2.45035	4.04198	-2.05440
H	-2.09173	5.07845	-2.05403
H	-3.06705	3.89352	-2.94733
H	-3.09024	3.90463	-1.17557
C	-0.45326	3.17797	-3.34192
H	-0.11795	4.20670	-3.52382
H	0.41591	2.51453	-3.31802
H	-1.07027	2.87227	-4.19161
H	1.70921	1.29146	0.37341
H	2.92505	1.25795	-0.98888
H	2.99935	-0.43386	1.61354
C	4.69561	-0.53819	0.23563
C	5.18666	-1.82295	0.01856
C	5.59741	0.52951	0.16583
C	6.53316	-2.05479	-0.25918
H	4.50143	-2.66607	0.05921
C	6.93933	0.32028	-0.10828
H	5.23398	1.54144	0.32551
C	7.41718	-0.97667	-0.32277
H	6.87205	-3.07069	-0.42758
H	7.63989	1.14698	-0.16695
O	8.74564	-1.08106	-0.58777
C	9.27225	-2.36535	-0.82484
H	10.33671	-2.22459	-1.01746
H	9.14690	-3.02096	0.04713
H	8.80636	-2.83782	-1.69967

Zero-point correction = 0.815653 (Hartree/Particle)
Thermal correction to Energy = 0.862386
Thermal correction to Enthalpy = 0.863331
Thermal correction to Gibbs Free Energy = 0.731395
Sum of electronic and zero-point Energies = -2330.826131
Sum of electronic and thermal Energies = -2330.779398
Sum of electronic and thermal Enthalpies = -2330.778453
Sum of electronic and thermal Free Energies = -2330.910389
E(M06L) = -3669.93485022

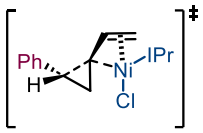
TS1_opening



Ni	-0.56562	0.10605	-1.16543
C	3.30739	0.46818	-3.09210
C	1.34350	-0.01975	-2.57141
H	0.89329	-0.49086	-3.44176
C	1.29088	-0.68661	-1.32222
C	0.37147	-1.70299	-1.05589
H	0.39456	-2.22329	-0.10440
H	-0.10724	-2.24038	-1.87536
H	1.91379	-0.30874	-0.51232
C	-1.56844	0.08928	0.48860
Cl	-1.35149	1.90070	-2.23078
N	-2.81107	-0.34133	0.81017
N	-1.10585	0.64140	1.64120
C	-3.12253	-0.06265	2.13320
C	-2.04511	0.56103	2.65822
H	-4.07337	-0.33141	2.56423
H	-1.85846	0.95639	3.64357
C	-3.66061	-1.07133	-0.08767
C	-4.57112	-0.36247	-0.88268
C	-3.53571	-2.46799	-0.12168
C	-5.40477	-1.11114	-1.71516
C	-4.39289	-3.16895	-0.96987
C	-5.32134	-2.49695	-1.75520
H	-6.12458	-0.60206	-2.34754
H	-4.33307	-4.25176	-1.02099
H	-5.98034	-3.05848	-2.41110
C	0.21869	1.18229	1.77706
C	1.24382	0.32932	2.21574
C	0.43588	2.52737	1.44318
C	2.52355	0.87035	2.34240
C	1.73710	3.01643	1.57769
C	2.76773	2.20130	2.02809
H	3.34207	0.24131	2.67700
H	1.94726	4.05034	1.32550
H	3.77218	2.60407	2.12562
C	-2.53136	-3.19884	0.75604
H	-1.74842	-2.48465	1.02884
C	-1.84285	-4.36238	0.03434
H	-2.52947	-5.19775	-0.14328
H	-1.43493	-4.04641	-0.93023
H	-1.01846	-4.74460	0.64656
C	-3.19470	-3.68258	2.05407
H	-2.46274	-4.18541	2.69642
H	-3.62362	-2.84830	2.61816
H	-4.00102	-4.39219	1.83463
C	-4.67284	1.15283	-0.81666
H	-3.69813	1.53745	-0.50232
C	-5.72388	1.57237	0.22277
H	-6.71553	1.19397	-0.05353
H	-5.48420	1.19092	1.22103
H	-5.78183	2.66469	0.28487
C	-4.96893	1.79100	-2.17656
H	-4.87937	2.87881	-2.09369
H	-4.24784	1.45657	-2.92662
H	-5.98539	1.56934	-2.52447
C	0.97993	-1.12651	2.56685
H	0.08345	-1.44109	2.02234
C	2.12355	-2.06122	2.15183
H	1.80285	-3.10409	2.25082
H	2.43455	-1.89603	1.11586
H	3.00479	-1.93254	2.79011
C	0.68799	-1.27883	4.06757
H	1.55103	-0.95611	4.66143
H	-0.17512	-0.67957	4.37265
H	0.47695	-2.32580	4.31278
C	-0.70246	3.43017	0.99676
H	-1.44531	2.80616	0.49206
C	-1.36445	4.08814	2.21783
H	-0.64608	4.71687	2.75772
H	-2.19986	4.72148	1.89993
H	-1.75517	3.34354	2.91934
C	-0.26753	4.48883	-0.01958
H	0.37668	5.25454	0.43010
H	0.25061	4.02761	-0.86442
H	-1.15320	4.99460	-0.41617
C	4.32356	0.09879	-2.14622
C	4.37050	0.60429	-0.82550
C	5.33073	-0.81571	-2.50956
C	5.34968	0.20783	0.06440
H	3.62826	1.32090	-0.48823
C	6.32482	-1.21348	-1.62478
H	5.32866	-1.22747	-3.51576
C	6.33703	-0.70628	-0.32208
H	5.37529	0.60117	1.07585
H	7.07613	-1.92042	-1.95851
H	3.40924	0.09449	-4.10737
C	2.08858	1.25568	-2.78315
H	1.69217	1.84146	-3.61271
H	2.13551	1.88293	-1.89057
O	7.25058	-1.03171	0.62957
C	8.26520	-1.94514	0.28392
H	8.88759	-1.56561	-0.53717

H	8.88189	-2.06414	1.17586
H	7.85015	-2.92098	-0.00111

Zero-point correction = 0.813234 (Hartree/Particle)
Thermal correction to Energy = 0.859602
Thermal correction to Enthalpy = 0.860546
Thermal correction to Gibbs Free Energy = 0.731160
Sum of electronic and zero-point Energies = -2330.788470
Sum of electronic and thermal Energies = -2330.742102
Sum of electronic and thermal Enthalpies = -2330.741158
Sum of electronic and thermal Free Energies = -2330.870544
E(M06L) = -3669.91181324



TS4_closing

Ni	-0.61387	0.68365	0.93438
C	3.29796	1.67551	2.53737
C	1.53159	1.07139	1.72094
H	1.93017	0.57559	0.83736
C	0.61196	0.36338	2.52634
C	0.07187	-0.85800	2.08371
H	-0.65054	-1.38155	2.70389
H	0.65351	-1.47548	1.40510
H	0.23176	0.84245	3.42862
C	-1.60184	-0.25636	-0.42265
Cl	-0.95191	2.80128	0.30777
N	-1.00527	-0.85389	-1.49002
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H	4.18444	-1.75865	-1.26085
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H	1.14322	3.30824	-2.51527
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H	-3.62901	3.78857	0.07720
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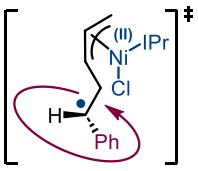
C	4.42081	1.28297	1.73057
C	4.56751	1.67166	0.37866
C	5.42193	0.45169	2.26680
C	5.64049	1.24690	-0.37958
H	3.82235	2.30919	-0.08625
C	6.50677	0.02168	1.51346
H	5.34120	0.13093	3.30236
C	6.62052	0.41395	0.17641
H	5.74793	1.55062	-1.41637
H	7.25016	-0.61826	1.97530
H	3.28939	1.35780	3.57608
C	2.10143	2.40546	2.04638
H	2.24072	3.05947	1.18494
H	1.54338	2.93253	2.82129
O	7.62785	0.04694	-0.65621
C	8.64586	-0.77788	-0.13856
H	8.24947	-1.74451	0.19954
H	9.34600	-0.94403	-0.95824
H	9.17253	-0.29375	0.69417

Zero-point correction = 0.813181 (Hartree/Particle)
Thermal correction to Energy = 0.859551
Thermal correction to Enthalpy = 0.860495
Thermal correction to Gibbs Free Energy = 0.730879
Sum of electronic and zero-point Energies = -2330.787495
Sum of electronic and thermal Energies = -2330.741125
Sum of electronic and thermal Enthalpies = -2330.740181
Sum of electronic and thermal Free Energies = -2330.869797
E(M06L) = -3669.91174375

TS_rotation



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C	-2.77802	-0.13353	-1.99242
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H	0.17702	-1.50698	-3.24874
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H	1.81216	1.74452	-2.30954
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N	0.96954	1.03651	1.34875
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C	1.82070	1.17893	2.43430

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C	3.65652	-0.97623	0.24170
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C	4.54798	-0.34231	-0.63991
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C	5.48976	-1.14217	-1.28581
C	5.53710	-2.51255	-1.05786
H	4.69095	-4.18049	-0.01492
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C	-0.19347	2.98520	0.46400
C	-1.44192	1.26480	1.71257
C	-1.37828	3.70476	0.31488
C	-2.59721	2.03201	1.54703
C	-2.56893	3.23538	0.85685
H	-1.37172	4.64719	-0.22349
H	-3.53622	1.66965	1.95219
H	-3.48172	3.81235	0.73655
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H	3.50837	1.50975	-0.65163
C	4.88362	1.59117	-2.27395
H	5.94630	1.43711	-2.49295
H	4.29957	1.04197	-3.01817
H	4.67967	2.66002	-2.40173
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H	5.16670	1.64195	1.19371
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H	2.71415	-3.58691	3.57527
C	2.19596	-4.35729	0.99489
H	1.41411	-4.70722	1.67646
H	1.75082	-4.26391	0.00114
H	2.97997	-5.12398	0.96953
C	1.11936	3.53188	-0.07383
H	1.79161	2.68462	-0.23109
C	0.96962	4.24431	-1.42247
H	1.95901	4.45054	-1.84561
H	0.41163	3.63476	-2.14045
H	0.45421	5.20612	-1.32273
C	1.78072	4.46132	0.95505
H	1.13811	5.32407	1.16583
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H	2.73940	4.83302	0.57559
C	-1.48633	-0.03919	2.48906
H	-0.61719	-0.63343	2.19467
C	-1.40030	0.23998	3.99734
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H	-1.40745	-0.70113	4.55802
H	-0.48478	0.78228	4.25919
C	-2.72350	-0.87923	2.15413
H	-3.64840	-0.42290	2.52739
H	-2.81357	-1.02781	1.07536
H	-2.62974	-1.86514	2.62072
C	-4.06695	-0.45699	-1.51059
C	-4.70171	-1.70699	-1.75123
C	-4.79099	0.47821	-0.73072
C	-5.94678	-1.99287	-1.23321
H	-4.19467	-2.46164	-2.34378
C	-6.04246	0.19549	-0.20623
H	-4.33966	1.44617	-0.53362
C	-6.63147	-1.05007	-0.45163
H	-6.42091	-2.95252	-1.41304
H	-6.55001	0.94809	0.38748
H	-2.37315	0.82929	-1.68949
C	-1.94099	-1.03795	-2.84466
H	-2.32946	-1.05629	-3.87877
H	-2.02523	-2.06700	-2.47405
O	-7.84863	-1.43758	0.01299
C	-8.56556	-0.53214	0.81683
H	-8.80311	0.39202	0.27298
H	-9.49409	-1.03683	1.08771
H	-8.01274	-0.27831	1.73127

Zero-point correction = 0.814386 (Hartree/Particle)
Thermal correction to Energy = 0.859744
Thermal correction to Enthalpy = 0.860688
Thermal correction to Gibbs Free Energy = 0.735711
Sum of electronic and zero-point Energies = -2330.802987
Sum of electronic and thermal Energies = -2330.757629
Sum of electronic and thermal Enthalpies = -2330.756685
Sum of electronic and thermal Free Energies = -2330.881662
E(M06L) = -3669.92794001

6

Literature

6 Literature

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