Aluminum or Calcium-Catalyzed Electrophilic Cyclizations of Alkynes via Vinyl Cations

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

vorgelegt von

Master of Science

Liang Fu

aus Wuhan, China

Berichter: Prof. Dr. rer. nat. Meike Niggemann

Univ.-Prof. Dr. rer. nat. Dieter Enders

Tag der mündlichen Prüfung: 21. Januar 2016

Diese Dissertation ist auf den Internetseiten der Universitätsbibliothek online verfügbar.

This work was done from October 2012 to June 2015 under the guidance of Prof. Dr. Meike Niggemann at the Institute of Organic Chemistry, RWTH Aachen University.

I would like to thank my PhD supervisor, Prof. Dr. Meike Niggemann for offering me a great opportunity to pursue my PhD in her group and my scienticfic research under her helpful guidance is presented herein.

I am very grateful to Prof. Dr. Dieter Enders for agreeing to be my "Zweitgutachter" as well.

Scientific research papers have already been published:

" Calcium-Catalyzed Cycloisomerization of Enynes"
V. J. Meyer, **L. Fu**, F. Marquardt, M. Niggemann, *Adv. Synth. Cat.* **2013**, *355*, 1943-1947.

"Calcium-Catalyzed Carboarylation of Alkynes"
L. Fu, M. Niggemann, *Chem. Eur. J.* **2015**, *21*, 6367-6370 (selected as hot paper and the cover picture of the corresponding issue).

Unpublished scientific research papers:

" Insertion of an Unactivated Alkyne into an Unstrained C-C σ Bond"
L. Fu, H. Damsen, M. Niggemann, *J. Am. Chem. Soc.* to be submitted

"A Novel Approach to 2*H*-Chromenes through $Al(OTf)_3$-Catalyzed Unstrained C-C σ Bond Activation"
L. Fu, A. Wang, M. Niggemann, *Angew. Chem. Int. Ed.* to be submitted

" Calcium-Catalyzed Synthesis of 4*H*-Chromenes through the [4+2] Cycloaddition Reaction of Alkynes with In Situ Generated *ortho*-Quinone Methides"
L. Fu, S. Gao, M. Niggemann, *Chem. Eur. J.* manuscript in preparation

Acknowledgements

First, I would like to appreciate my PhD supervisor, Prof. Dr. Meike Niggemann, who gave me a precious opportunity to study and complete my PhD in her group. In addition, I am very grateful to her for teaching me how to do scientific research and write scientific paper. It is very lucky and glorious for me to study and enjoy my life in her group.

Second, it is my glory to invite Prof. Dr. Dieter Enders to be my “Zweitgutachter”.

Third, I do appreciate China Scholarship Council (CSC) for offering me all the living expense in Germany. Meanwhile, I am very grateful to my good friends in the Niggemann group: Dr. Vera J. Meyer, Helena Damsen, Dr. Stefan Haubenreisser, Dr. Jeanne-Marie Begouin, Dr. Francesca Capitta, Dr. Xian Wu, Dr. Fa-Rong Gou, Dr. David Skinner, Tobias Stopka, Christoph Ascheberg, Marian Rauser, Sebastian Schroeder and Shuang Gao for their kind help. I also thank all the faculties in our institute for their help. Particularly, I thank Dr. Christoph Räuber for analysis of NMR data, Prof. Dr. Ulli Englert and Prof. Dr. Gerhard Raabe for their contribution to structural determination of products by X-ray diffraction analysis.

Finally, I am very grateful to my parents, my sister and my brother for their love, support, encouragement and understanding over the past few years. It is impossible for me to write down all my friends’ names here, but I do really appreciate them for their support during this journey in Germany.

ABSTRACT

Aluminum or Calcium-Catalyzed Electrophilic Cyclizations of Alkynes via Vinyl Cations

In the research projects presented in my PhD thesis, the environmentally friendly aluminum or calcium-catalyzed electrophilic cyclizations of alkynes via vinyl cations were investigated. In these reactions, trisubstituted highly reactive vinyl cations were generated by the nucleophilic addition of alkynes to the carbocations that were produced from alcohols by aluminum or calcium catalysis. Subsequently, it was intercepted by hydroxyl groups or aromatic nucleophiles, leading to the formation of 4*H*-chromenes and all-carbon tetrasubstituted olefins respectively. Furthermore, the first transition-metal free alkyne insertion reaction through unstrained C-C σ bond activation was efficiently promoted by the trisubstituted highly reactive vinyl cations in the presence of 10 mol% $Al(OTf)_3$ as a catalyst, which provided a novel protocol for the straightforward and efficient synthesis of structurally diverse 1,2-dihydroquinolines and 2*H*-chromenes.

In a first project, an unprecedented inverse electron demand hetero-Diels-Alder reaction (IED/HDA) of alkynes with in situ generated *ortho*-quinone methides was described. The reaction itself features low catalyst loading, wide substrate scope and high functional group tolerance. In addition, it offers a new protocol for the straightforward and efficient synthesis of structurally diverse multi-substituted 4*H*-chromenes from readily available starting materials under very mild reaction conditions. Furthermore, either a concerted mechanism or a stepwise mechanism via vinyl cations was proposed for the reaction. In the stepwise mechanism, the trisubstituted highly reactive vinyl cations would be trapped by the tethered phenolic hydroxyl group.

In a second project, the first transition-metal free carboarylation of alkynes with readily available alcohols was realized in the presence of non-toxic and abundant calcium catalysts, which allowed for the one-step synthesis of all-carbon tetrasubstituted olefins from alkynes. A trisubstituted highly reactive vinyl cation was generated in the carboarylation process, which was intercepted even by deactivated arenes as the tethered nucleophiles.

In a third project, a new concept for a redox-neutral C-C bond functionalization based on intramolecular 1,3-aryl migration was demonstrated. The redox-neutral C-C σ bond activation

reaction was selectively and efficiently promoted by trisubstituted highly reactive vinyl cations in the presence of 10 mol% $Al(OTf)_3$ as a catalyst. Importantly, a plausible retro Friedel-Crafts/Povarov reaction mechanism was clearly excluded from this transformation by reacting acetals with alkynes. Furthermore, an unsaturated constrained four-membered spiro ring intermediate leading to the rearrangement products was proposed in the reaction.

In the last project, a novel approach to 2*H*-chromenes through $Al(OTf)_3$-catalyzed unstrained C-C σ bond activation was developed. The first transition-metal free process of insertion of an unactivated alkyne into an unstrained C-C σ bond was selectively and efficiently promoted by trisubstituted highly reactive vinyl cations in the presence of 10 mol% $Al(OTf)_3$ as a catalyst. In addition, this alkyne insertion reaction proceeding through the C-C σ bond cleavage of benzylic alcohols features operational simplicity and allows for the direct and efficient synthesis of structurally diverse multi-substituted 2*H*-chromenes under very mild reaction conditions.

Abbreviations

Å	Angstrom
Ar	Aryl
Ac	Acetyl
Bn	Benzyl
Bu	Butyl
n-BuLi	*n*-Butyllithium
CI	Chemical ionization
DTBP	Di-tert-butyl peroxide
dr	Diastereoselectivity
DCE	1,2-Dichloroethane
DCM	Dichloromethane
DMF	*N*,*N*-dimethylformamide
DMSO	Dimethyl sulfoxide
DMSO-d^6	Dimethyl sulfoxide-d^6
DIAD	Diisopropyl azodicarboxylate
dppp	1,3-Bis(diphenylphosphino)propane
Eq.	Equivalent
ESI	Electrospray ionization
EI	Electronic impact (in mass spectroscopy)
Et	Ethyl
EE	Ethyl acetate
HMPA	Hexamethylphosphoramide
Hz	Hertz
HPLC	High-performance liquid chromatography
HRMS	High-resolution mass spectrometer
IR	Infrared spectroscopy
KHMDS	Potassium bis(trimethylsilyl)amide
LAH	Lithium aluminum hydride
Me	Methyl
NBS	*N*-Bromosuccinimide
NIS	*N*-Iodosuccinimide
Nu	Nucleophile
PCC	Pyridinium chlorochromate
Py	Pyridine
Ph	Phenyl
PMP	4-Methoxyphenyl

ppm	Parts per million
Pr	Propyl
δ	Chemical shift
s	Singlet (NMR signal)
d	Doublet (NMR signal)
t	Triplet (NMR signal)
q	Quartet (NMR signal)
m	Multiplet (NMR signal)
TLC	Thin layer chromatography
THF	Tetrahydrofuran
TMS	Trimethylsilyl
TIPS	Tri-isopropylsilyl
Ts	Tosyl
Tf	Trifluoromethyl
p-Tolyl	4-Methylpheny
hv	Irradiation with light

Table of Contents

Table of Contents

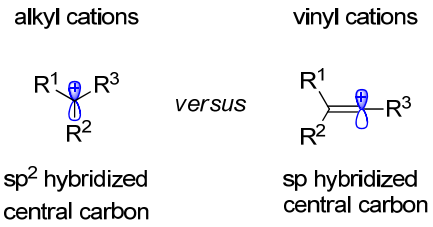
Table of Contents

1. Introduction

1.1. Reactions via Vinyl Cations

1.1.1 Vinyl Cations

Although vinyl cations as well as the well-known alkyl cations possess a positively charged carbon atom, their chemical properties are very different from each other, because of different orbital hybridizations of the carbon atoms bearing the positive charge (Scheme 1). For the vinyl cation, it is located on sp carbon atoms, there is 50% of s orbital, while the alkyl



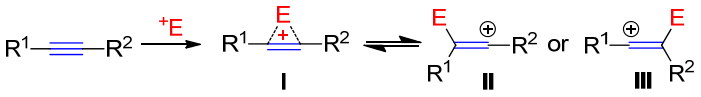
Scheme 1. Differences between alkyl cations and vinyl cations.

cation is located on sp^2 carbon atoms, there is only 33% of s orbital. Because the sp carbon has more s-character than the sp^2 carbon, the vinyl cation is much less stable than the alkyl cation. Over the past a few decades, as the alkyl cation is very reactive and easily accessed, it has broad applications in natural product total synthesis, materials science and medicinal chemistry.[1] In contrast, the vinyl cations have been less developed. In fact, several challenging reactions can be promoted by vinyl cations, which are impossible for alkyl cations,[2] such as activation of unreactive sp^3 C-H bonds.[16,17,18]

In the following part, representative examples of synthetic applications of vinyl cations will be shown. In order to make reading easier, the introduction will be organized with respect to different types of reactions via vinyl cations including electrophilic cyclization reactions of alkynes, vinyl cation-promoted 1,5-hydride shift reactions and vinyl cation-promoted 1,4-aryl shift reactions.

1.1.2 Electrophilic Cyclizations of Alkynes via Vinyl Cations

Alkynes have nucleophilic characteristics, because the C-C triple bond has regions of high electron density. Therefore, the addition of electrophilic sources to alkynes proceeding through the coordination of an electrophilic source with π bonds offers the simplest protocol for the generation of vinyl cations (Scheme 2). The R group that is adjacent to the positively charged carbon atom significantly affects vinyl-cation formation. For example, aryl groups and heteroatoms (such as oxygen and nitrogen atoms) can stabilize the highly reactive vinyl cations through a p-π conjugated system and thus induce the formation of vinyl cations.

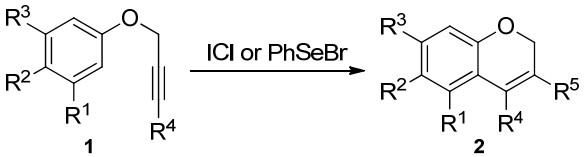


Scheme 2. Concept of electrophilic activation of alkynes.

In recent years, because of the high reactivity of vinyl cations, different electrophiles and alkynes have been used to efficiently construct carbocycles, heterocycles and multi-substituted alkenes.[2]

1.1.2.1 Halogen and Organoselenium as Electrophiles

In 2007, Larock et al. reported electrophilic cyclizations of substituted propargylic aryl ethers **1** by using I_2, ICl or PhSeBr as the electrophiles (Figure 1).[3] This transition-metal free reaction provided an efficient access to 3,4-disubstituted 2*H*-benzopyrans **2** under mild reaction conditions. Notably, the reaction is quite tolerant with respect to functional groups, such as methoxy, hydroxyl, aldehyde and nitro groups. Furthermore, the propargylic aryl ethers **1** containing an unactivated alkyne moiety (R^4 = alkyl groups) can be employed as the reaction substrates when using PhSeBr as the electrophile.

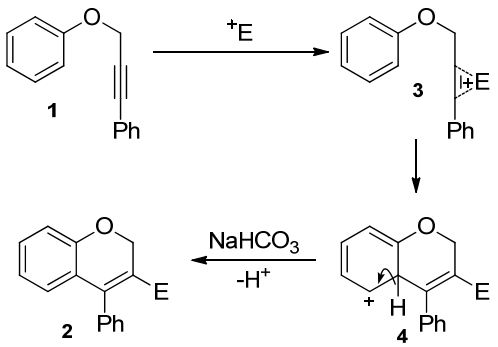


38 examples
39-96% yields

R^1 = ^{t}Bu, Cl, OMe
R^2 = Me, ^{t}Bu, OMe, Cl, CHO
R^3 = ^{t}Bu, Cl, OMe
R^4 = Ph, *p*-Tolyl, PMP, $C_6H_4NO_2$-*p*, C_6H_4Me-*o*
cyclohexenyl, CH_2OH, Me
R^5 = I, SePh

Figure 1

A plausible reaction mechanism for the electrophilic cyclizations of substituted propargylic aryl ethers **1** was proposed by the authors (Scheme 3). The reaction was initiated by the activation of the C-C triple bond with ICl or PhSeBr as the electrophiles, producing an



Scheme 3. Possible mechanism for the electrophilic cyclizations of propargylic aryl ethers.

iodonium or selenonium intermediate **3**. Subsequently, Friedel-Crafts type reactions occurred in the presence of $NaHCO_3$ as a base, leading to the eventual cyclization product **2**. Furthermore, the 3-iodo-2*H*-chromene adducts **2** obtained by this methodology have other advantages. The introduced iodo atom can be easily functionalized by Sonogashira reaction to produce alkynyl chromenes **7** and a Pd-catalyzed CO insertion reaction to provide lactones **9** (Figure 2).

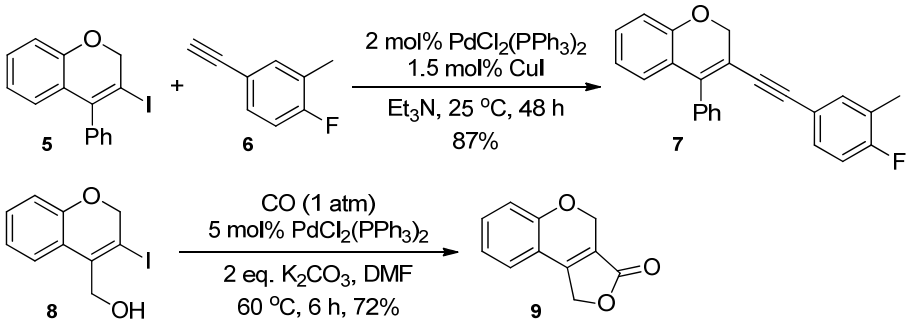
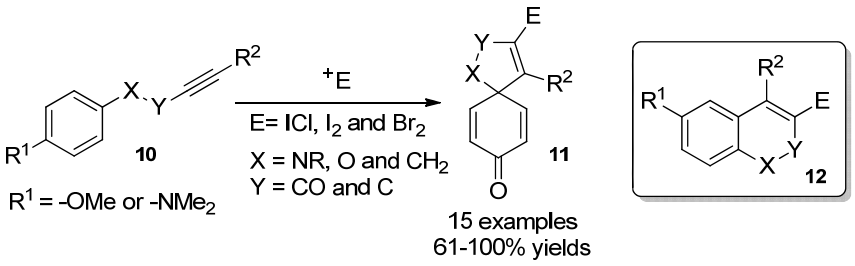


Figure 2

Electrophilic cyclizations of alkynes with a 5-*endo* cyclization by using I_2, ICl or Br_2 as the electrophiles have also been developed by the same group. Larock et al. found that spiro [4.5] trienones **11** were exclusively produced by intramolecular 5-*endo* halocyclization of 4-(*p*-methoxyaryl)-1-alkynes **10**, but none of the expected product **12** via a 6-*endo* cyclization was observed (Scheme 4).[4] Importantly, an electron-rich substituent such as methoxyl group



Scheme 4. 5-*endo* Electrophilic cyclization of alkynes.

and *N*,*N*-dimethylamino group on the aromatic ring at the *para*-position is crucial to the reaction. The author proposed a mechanism to explain the formation of the product **11** (Figure 3). Initially, a highly reactive vinyl iodonium intermediate **13** was produced by the activation of the C-C triple bond by halogen electrophiles. Subsequently, a 5-*ipso* cyclization occurred on the benzene ring, leading to intermediates **14**, which then underwent the removal of methyl group by nucleophilic displacements to afford the product **11**.

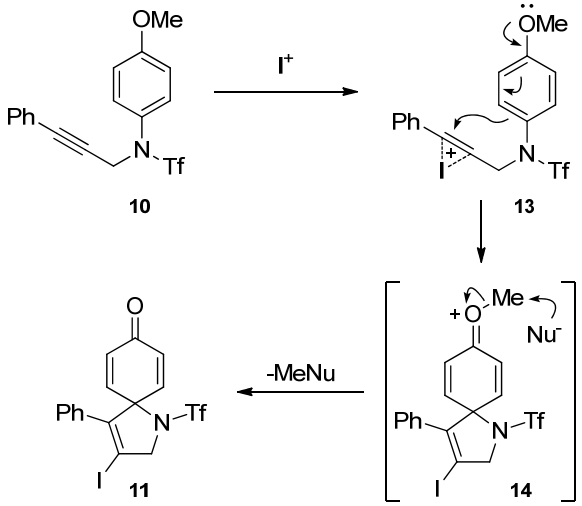
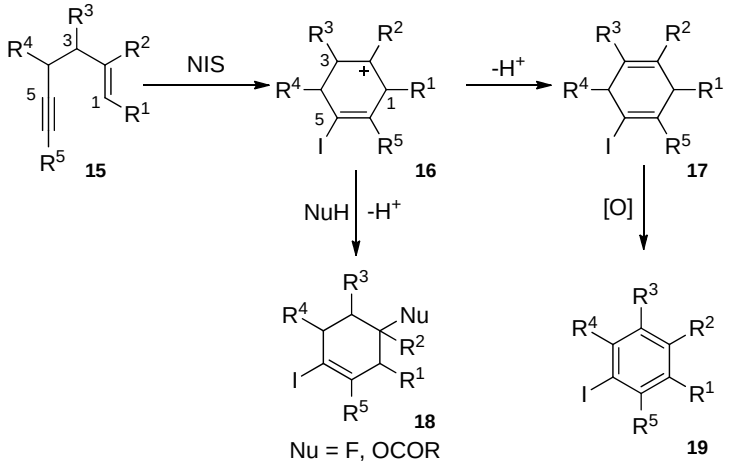


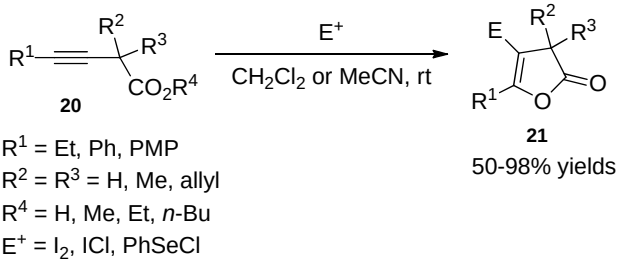
Figure 3

Not only arenes but also alkenes can be regarded as good nucleophiles for halogen electrophile-induced electrophilic cyclizations of alkynes. In 2010 Kirsch et al. demonstrated the iodonium-mediated electrophilic cyclizations of 1,5-enynes **15**. This transition-metal free reaction allowed for the direct and efficient synthesis of highly valuable six-membered ring products, such as 1,4-cyclohexadienes **17**, 4-fluorocyclohexenes **18** and highly substituted benzenes **19** (Scheme 5).[5]



Scheme 5. Electrophilic cyclizations of 1,5-enynes.

The nucleophilic oxygen atom of esters and carboxylic acids can be used as excellent nucleophiles as well for halogen electrophile-induced electrophilic cyclizations of alkynes.



Scheme 6. Iodolactonization of 3-alkynoate esters and acids.

Therefore, Larock et al. developed the electrophilic cyclizations of 3-alkynoate esters and acids by using I_2, ICl or PhSeBr as the electrophiles, which provided a novel protocol for the straightforward and efficient synthesis of highly substituted 2(*3H*)-furanones **21** (Scheme 6).[6]

1.1.2.2 Brønsted Acids as Electrophiles

Brønsted acid is the simplest and smallest electrophile in nature, which played an important role in the development of chemistry. In 1997, Swager et al. reported the trifluoroacetic acid (TFA)-mediated electrophilic cyclizations of alkynes, which provided an efficient access to fused polycyclic aromatics **23** that can't be obtained by other existing methods (Figure 4).[7] The synthesis of such a complex framework proceeded through two synthetic steps. First, the preparation of nonfused ring systems was realized by transition-metal catalyzed coupling reactions. Second, Brønsted acid-induced electrophilic cyclizations of alkynes were crucial to the ring-forming step in quantitative yields.

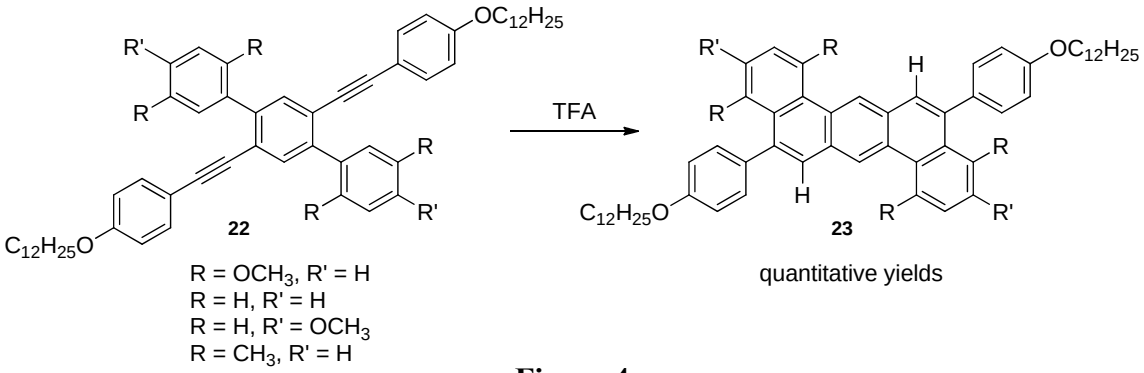
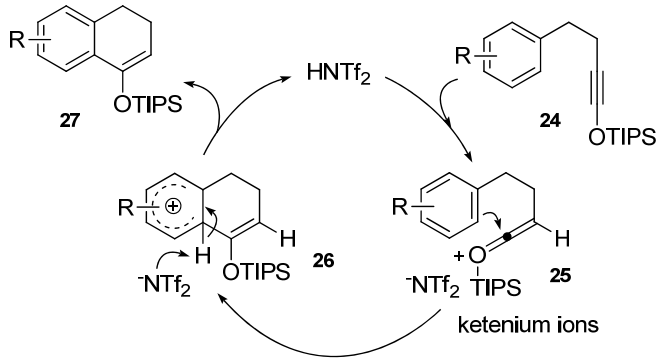


Figure 4

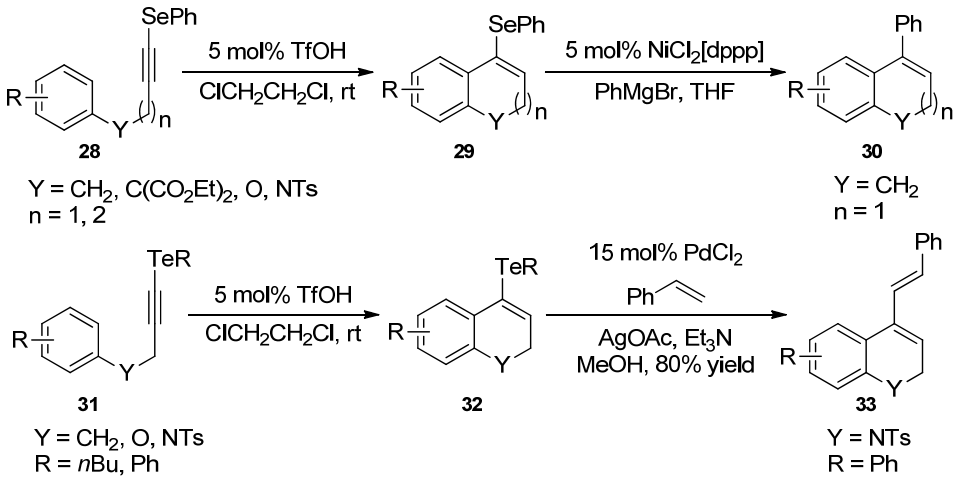
In 2004, Kozmin et al. developed the Tf_2NH-promoted electrophilic carbocyclizations of siloxyalkynes **24**, which provided a novel platform for the direct and efficient synthesis of a variety of structurally diverse enol silyl ethers **27**, tetralones and cyclohexenones.[8] Importantly, the oxygen atom is the key to stabilize vinyl cations. A proposed mechanism for this transformation is outlined in Scheme 7. Highly reactive ketenium ions **25** were



Scheme 7. $HNTf_2$-promoted carbocyclizations of siloxyalkynes.

produced upon the protonation of the siloxyalkynes **24**, which can be subsequently intercepted by both arenes and alkenes as the tethered carbon nucleophiles to afford the eventual adducts **27**.

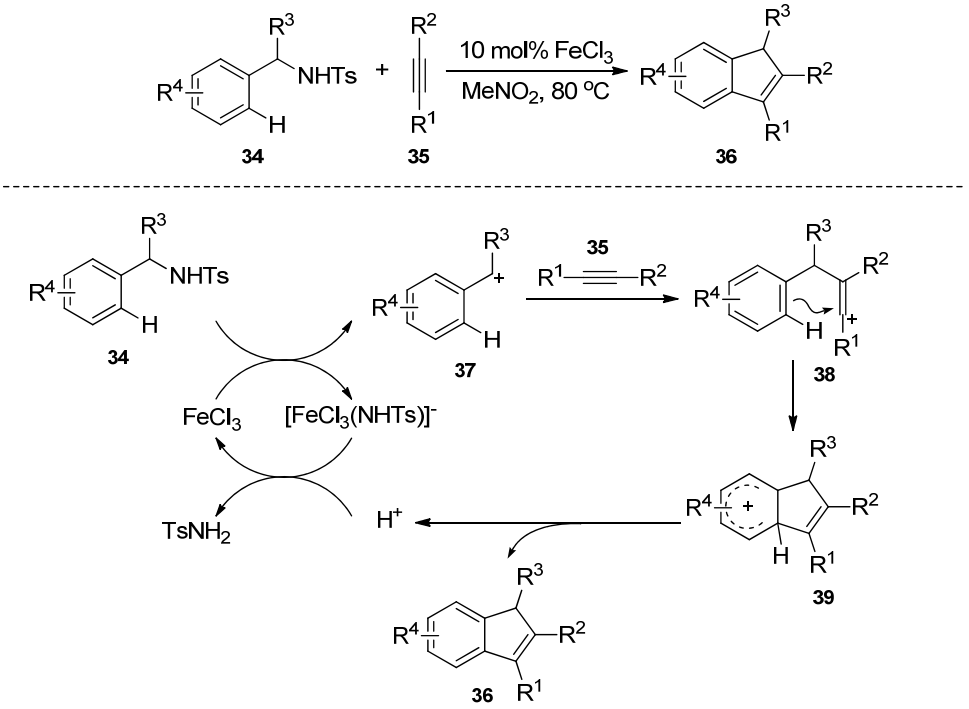
Not only the oxygen atom but also the heteroatoms selenium and tellurium are able to enhance the stability of intermediary vinyl cations by positive charge delocalization. Therefore, recently triflic acid-catalyzed intramolecular hydroarylation of alkynyl selenides **28** and tellurides **31** was described by the Lee group, which provided an efficient access to a variety of structurally diverse cycloalkenyl selenides **29** and tellurides **32**.[9] Furthermore, the cycloalkenyl selenides and tellurides can be easily functionalized by transition-metal catalyzed coupling reactions (Scheme 8).



Scheme 8. Electrophilic carbocyclizations of alkynyl selenides and tellurides.

1.1.2.3 Carbocations and Iodonium Salts as Electrophiles

Carbocations are excellent electrophiles and common reactive intermediates that can be easily accessed in laboratories. Therefore, considerable effort of chemists has been directed toward applications of the carbocations over the past decades. For example, in 2010 Tian et al. described an iron-catalyzed electrophilic [3+2] cycloaddition reaction of *N*-benzylic sulphonamides **34** with internal alkynes **35**, which allowed for the direct and efficient synthesis of structurally diverse indene derivatives **36** (Scheme 9).[10] A proposed mechanism for the iron-catalyzed electrophilic [3+2] cycloaddition reaction is depicted in Scheme 9. The reaction began with the iron-catalyzed C-N bond cleavage of the *N*-benzylic sulphonamides **34**, producing stable benzylic carbocations **37**. Subsequently, trisubstituted highly reactive vinyl cations **38** were generated by the nucleophilic addition of the alkyne **35** to the benzylic carbocation **37**, which were then trapped by the tethered aryl nucleophiles to give the eventual adducts **36**.



Scheme 9. Electrophilic [3+2] cycloaddition of alkynes with benzylic carbocations.

Several similar electrophilic [3+2] cycloaddition reactions of alkynes with benzylic carbocations have been developed by other groups as well.[11] The only difference is the ways of generating the benzylic carbocations. In 2011, Li et al. demonstrated that benzylic carbocations **41** can be formed through iron-catalyzed C-C σ bond cleavage with 1,3-dicarbonyl groups as a leaving group (Figure 5, a).[11a] In the same year, Zhou et al. disclosed that benzylic alcohols **42** were efficiently converted into the corresponding benzylic carbocations **43** through the iron-catalyzed dehydroxylation process of the benzylic alcohol **42** (Figure 5, b).[11b] In 2013, Chen et al. utilized an oxidative strategy to produce the benzylic carbocations **43** by iron catalysis (Figure 5, c).[11c]

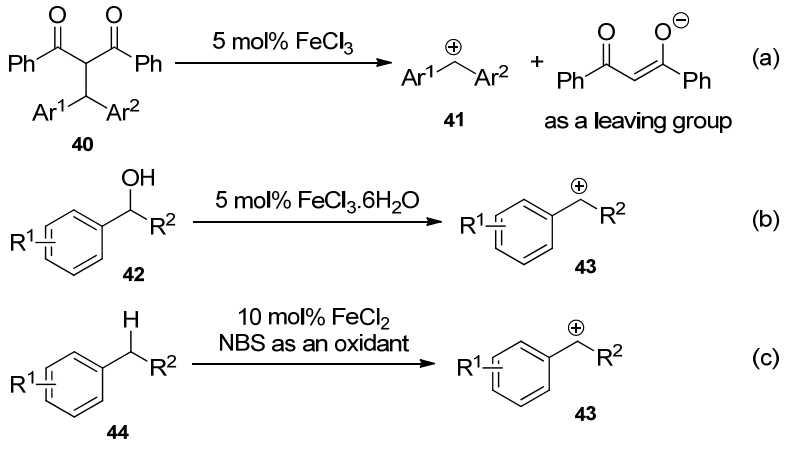
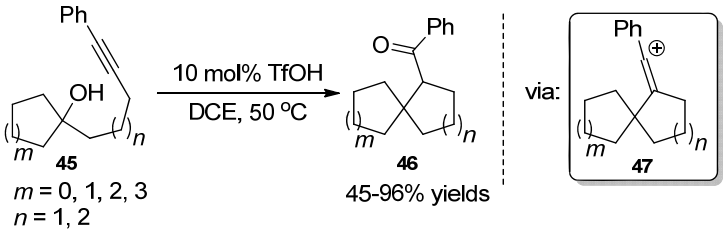


Figure 5

Spirocyclic hydrocarbon frameworks are important structural motifs with a broad range of biological activities, which are frequently found in natural isolates and pharmaceuticals.[12] Therefore, in 2009 Yamamoto and co-workers developed intramolecular electrophilic cyclizations of alkynyl cyclic tertiary alcohols **45**, which offered a novel protocol for the straightforward and efficient synthesis of spirocycles **46** with rings of different sizes and bridged bicyclic compounds (Scheme 10).[13] Tertiary carbocations were produced from the corresponding tertiary alcohol **45** in the presence of 10 mol% TfOH. Subsequently, trisubstituted highly reactive vinyl cations **47** were generated by the intramolecular nucleophilic addition of the alkyne moiety to the tertiary carbocation, which were then intercepted by water produced in the reaction system to provide the eventual spirocycles **46**.



Scheme 10. Tertiary carbocation-induced electrophilic cyclizations of alkynes.

Phenyl electrophiles **50** which are generated through oxidative addition of copper (I) to the C-I bond of diaryliodonium salts **48** (Figure 6) can be used as carbon electrophiles as well for electrophilic cyclizations of alkynes. Recently, Gaunt et al. developed copper (I)-catalyzed carboarylation of alkynes **51** by using diaryliodonium salts **52** as carbon electrophile

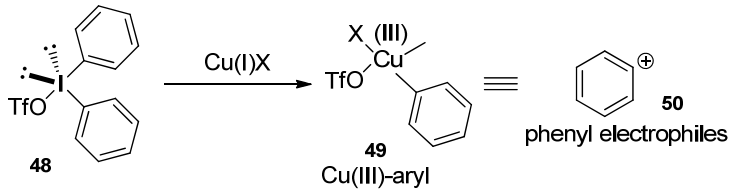


Figure 6

equivalent, which provided an easy access to all-carbon tetrasubstituted alkenes **53** containing dihydronaphthalene motifs (Figure 7).[14] Notably, the reaction features high functional group tolerance and wide substrate scope in both the aryl alkyne and diaryliodonium salt components. Furthermore, the intermolecular carboarylation of alkynes **54** was also feasible,

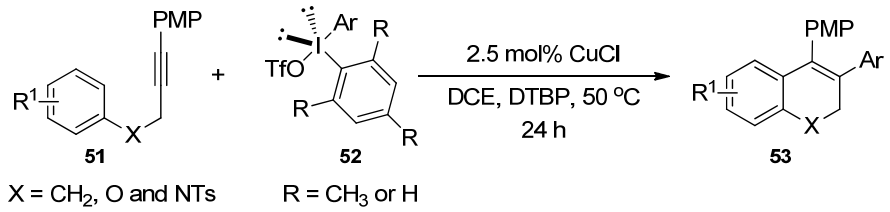
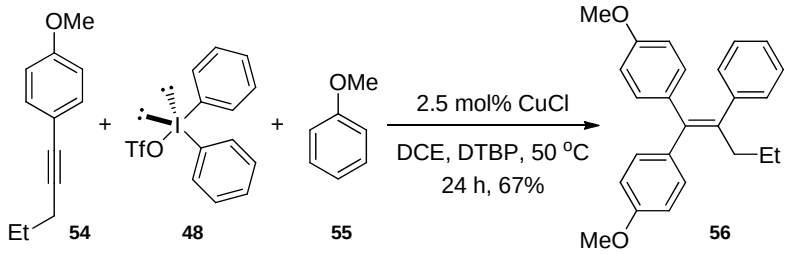


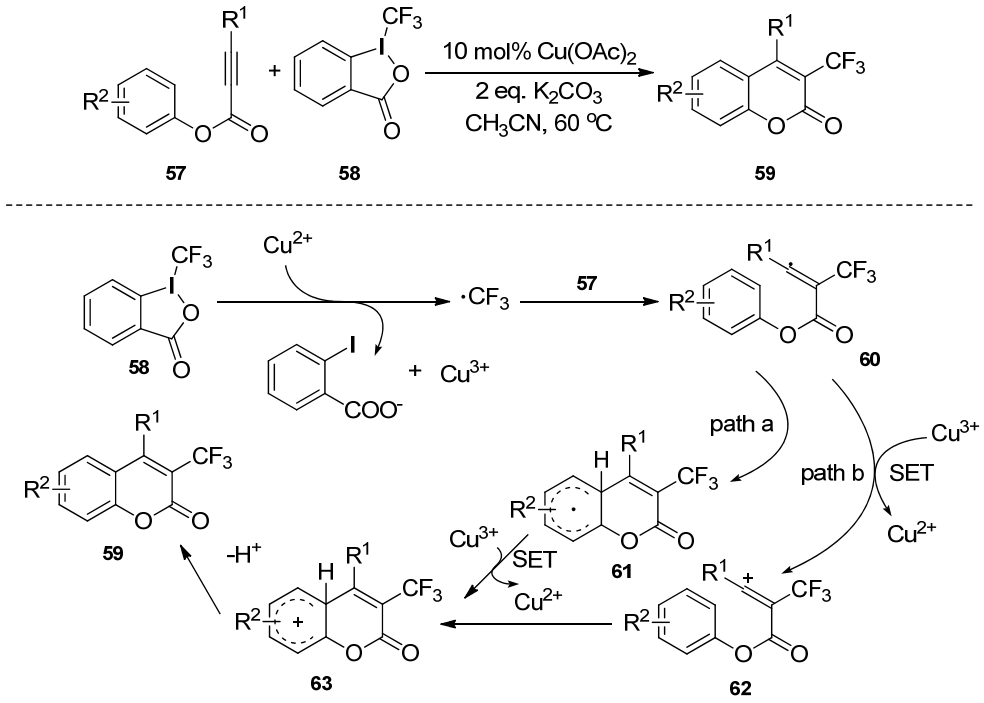
Figure 7

leading to the formation of acyclic all-carbon tetrasubstituted alkenes **56** (Scheme 11).



Scheme 11. Intermolecular carboarylation of alkynes via vinyl cations.

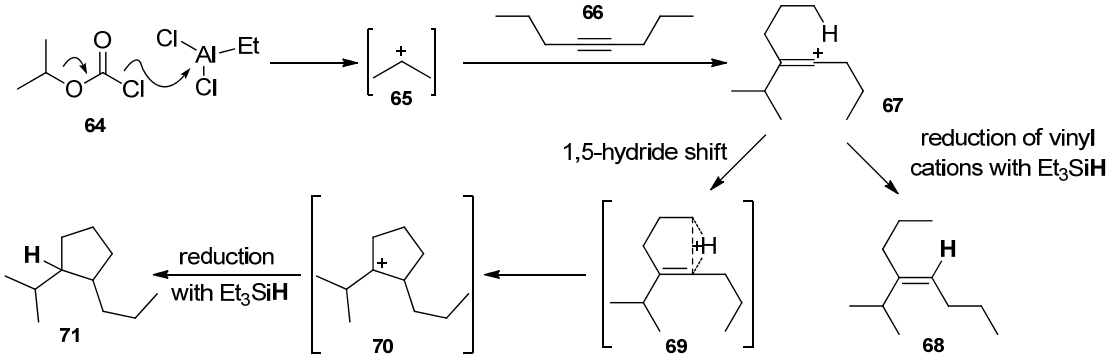
The reagent of Togni **58** is a kind of iodonium salts with a trifluoromethyl group. In 2014, Ding and co-workers described copper (II) acetate-catalyzed trifluoromethylation of propiolates **57** by using the Togni's reagent **58** as carbon electrophile equivalent, which allowed for the straightforward and efficient synthesis of trifluoromethylated coumarins **59**.[15] A proposed mechanism for the Togni's reagent-induced electrophilic cyclizations of alkynes is outlined in Scheme 12. Radical addition of trifluoromethyl radicals generated from the Togni's reagent and copper (II) acetate to the alkyne **57** provided vinyl radicals **60**, which were then further oxidized by copper (III) via single electron transfer (SET) to produce trisubstituted highly reactive vinyl cations **62**. Subsequently, the trisubstituted highly reactive vinyl cations **62** were intercepted by the tethered aryl nucleophiles, leading to the formation of the eventual adducts **59** (Scheme 12, path b).



Scheme 12. Togni's reagent-induced carboarylation of alkynes via vinyl cations.

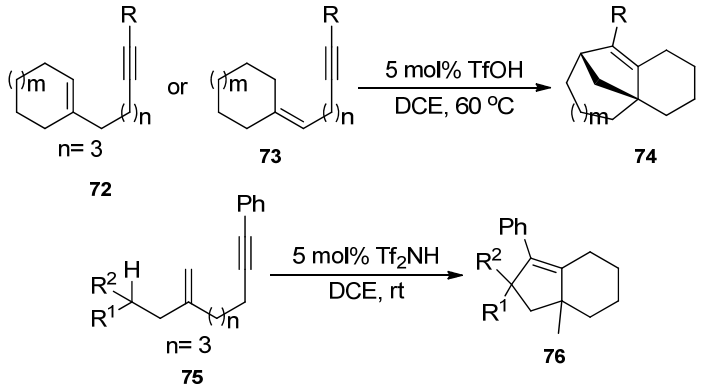
1.1.3 Vinyl Cation-Promoted Hydride Shift Reactions

There are a few examples of vinyl cation-promoted hydride shift reactions, which involve concerted 1,5-hydride shift processes. In 2006, Metzger et al. reported the first example of intramolecular insertion of vinyl cations into C-H bonds. At the beginning, the author designed processes of hydroalkylation of alkynes **66** by reducing highly reactive vinyl cations **67** with Et_3SiH as an additional hydride donor. To their surprise, they just obtained the expected hydroalkylation adduct **68** as a by-product (< 5%), but cyclopentanes **71** as the major product in good yield (Scheme 13).[16] The formation of the cyclopentane **71** can be explained as follows: the highly reactive vinyl cations **67** were formed by the nucleophilic addition of the alkyne **66** to alkyl carbocations **65** produced from alkyl chloroformates **64** and ethylaluminum sesquichlorides ($Et_3Al_2Cl_3$). If a C-H bond was available at the C5 position, intramolecular 1,5-hydride shift processes would occur, leading to cyclopentyl cations **70**. Subsequently, the cyclopentyl carbocation **70** was reduced by Et_3SiH to afford the eventual cyclopentane **71** (Scheme 13). Furthermore, calculations demonstrated that insertion of the highly reactive vinyl cations **67** into sp^3 C-H bonds proceeded in a concerted manner.



Scheme 13. The first example of 1,5-hydrogen shift reactions via vinyl cations.

In 2010, Yamamoto and co-workers developed Brønsted acid TfOH or $NHTf_2$-catalyzed activation of unreactive sp^3 C-H bonds based on vinyl cation-promoted 1,5-hydride shift reactions, which allowed for the direct and efficient synthesis of complex bridged multi-cyclic



Scheme 14. Tertiary carbocation-induced 1,5-hydride shift reactions via vinyl cations.

molecules **74** from versatile enynes (Scheme 14).[17] Vinyl cations **78** produced by the intramolecular nucleophilic addition of the alkyne moiety to tertiary carbocations **77** can efficiently promote 1,5-hydride shift processes and the formation of new C-C bonds.

A plausible mechanism for the 1,5-hydride shift reaction is outlined in Figure 8. Initially, tertiary carbocations **77** were produced from the corresponding alkenes in the presence of Brønsted acids. Subsequently, the trisubstituted highly reactive vinyl cations **78** were generated by the intramolecular nucleophilic addition of the alkyne moiety to the tertiary carbocation **77**. There are two possible pathways for the 1,5-hydride shift processes. A concerted pathway was promoted by the anion of deprotonated Brønsted acids and the highly reactive vinyl cations **78**, thus directly leading to the eventual adduct **76** (Figure 8, path A). Meanwhile, a stepwise mechanism can not be ruled out. Because the 1,5-hydride shift processes occurred, leading to the formation of alkyl carbocations **80**, which then underwent the addition/elimination sequences to provide the same adduct **76** (Figure 8, path B).

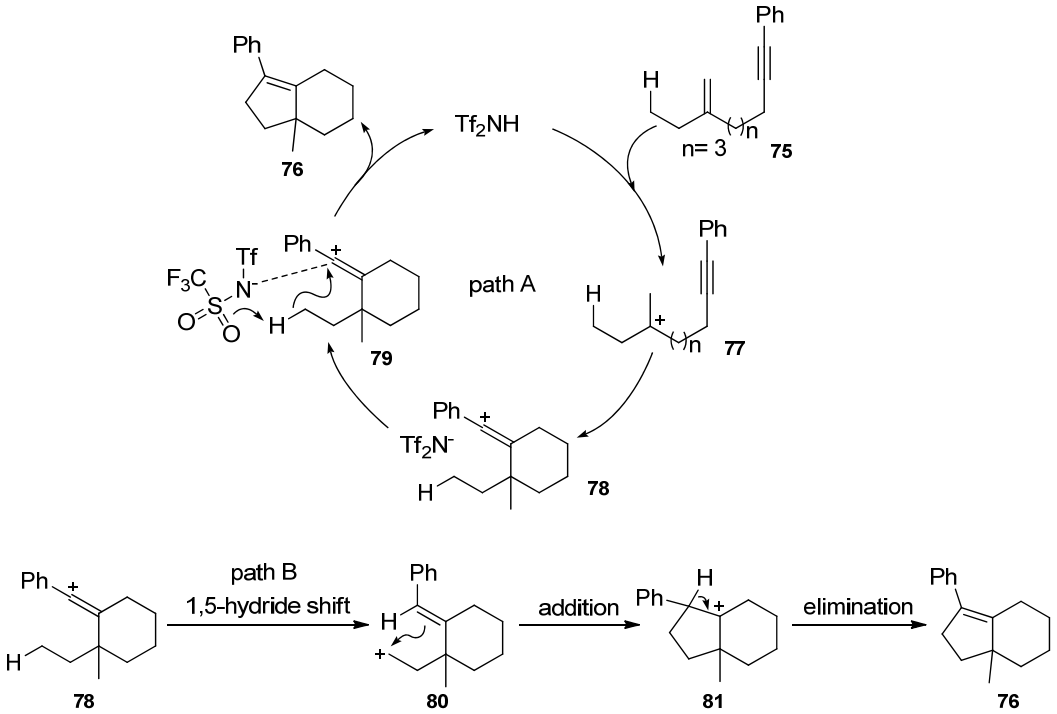
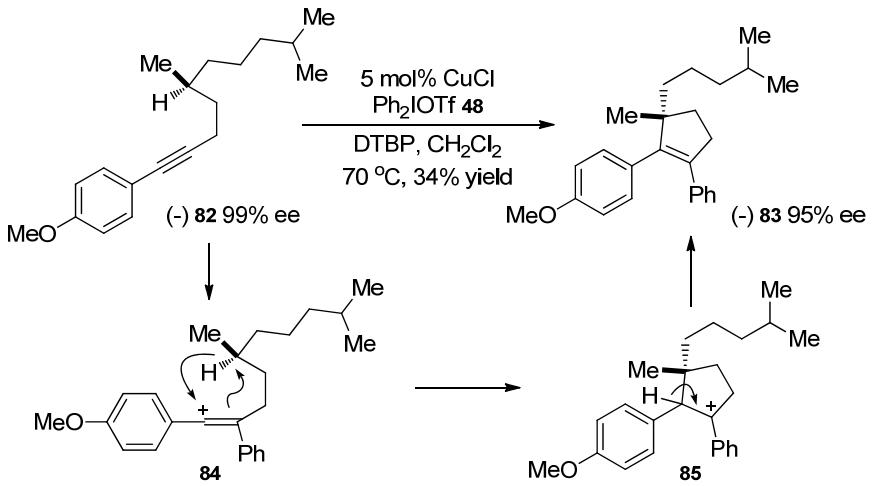


Figure 8

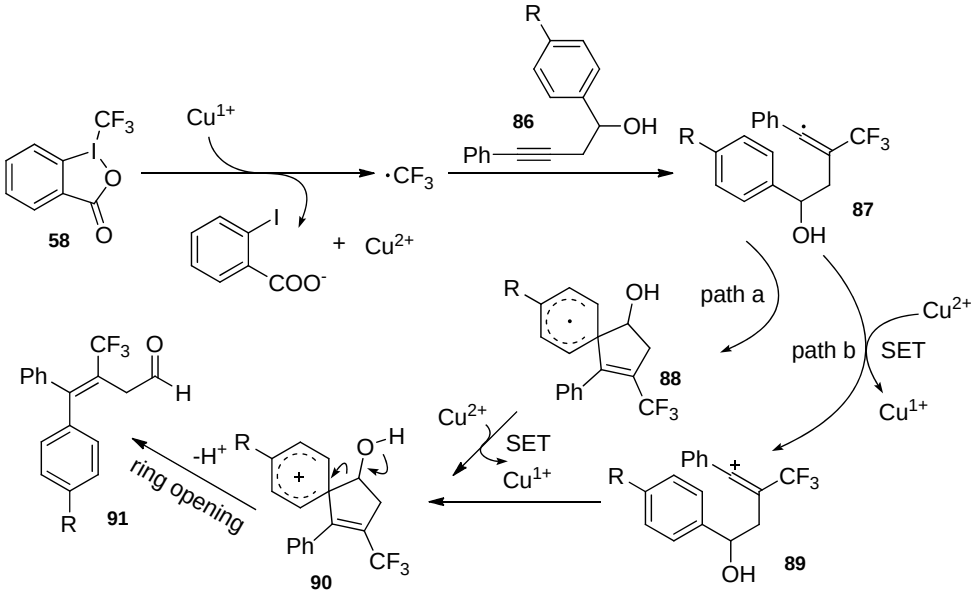
In 2014, Gaunt and co-workers have demonstrated that vinyl cations **84** produced by the intermolecular nucleophilic addition of alkynes **82** to aromatic electrophile equivalent **48** can promote 1,5-hydride shift reactions as well, which allowed for the straightforward and efficient synthesis of cyclopentenes **83** from readily available starting materials. Furthermore, it was the first time for them to demonstrate the concerted mechanism for insertion of vinyl cations into sp^3 C-H bonds by experiments (Scheme 15).[18]



Scheme 15. Experimental proofs for the concerted 1,5-hydride shift mechanism.

1.1.4 Vinyl Cation-Promoted Aryl Shift Reactions

The electrons in a C-H σ bond can transfer to the vacant *p*-orbital of a vinyl cation, thus leading to hydride shift processes, such as vinyl cation-promoted 1,5-hydride shift reactions as already discussed in chapter 1.1.3. Similar to the hydride shift processes, the cleavage of a C-C σ bond via electron transfer to the empty *p*-orbital of a vinyl cation would lead to carbon transfer processes. Recently, Liang and co-workers have demonstrated the feasibility of the carbon transfer processes by vinyl cation-promoted 1,4-aryl shift reactions.[19] A proposed mechanism for the cascade reaction is outlined in Scheme 16. Initially, radical addition of trifluoromethyl radicals generated from the Togni's reagent **58** and Cu^{I} to alkynes **86** provided vinyl radicals **87**. There are two possible pathways for the generation of intermediates **90**. In the first pathway, a 5-*ipso* cyclization would occur on the phenyl ring,



Scheme 16. One example of aryl shift reactions via vinyl cations.

leading to radicals **88**, which were then oxidized by Cu^{2+} via single electron transfer (SET) to produce the intermediate **90** (Scheme 16, path a). In the other pathway, the vinyl radicals **87** would be oxidized directly by Cu^{2+} via single electron transfer (SET), producing trisubstituted highly reactive vinyl cations **89**, which can also lead to the intermediate **90** via a 5-*endo* cyclization (Scheme 16, path b). Finally, the intermediate **90** underwent intramolecular 1,4-aryl migration, leading to the rearrangement product **91**.

1.1.5 Conclusions and Perspectives

Recent advances in reactions via vinyl cations were illustrated and summarized. Different electrophiles and alkynes have been used to efficiently construct carbocycles, heterocycles and multi-substituted alkenes.[2] Particularly, halogen atom-induced electrophilic cyclizations of alkynes provided an efficient access to a variety of heterocycles that can be further functionalized by transition-metal catalysis to give the highly substituted heterocycles. Despite advances, electrophilic sources for the activation of the alkyne moiety are often limited to halogen, organoselenium, carbon electrophiles (carbocations and iodonium salts) and Brønsted acids. Among these electrophilic sources, the carbon electrophile seems to be privileged, for the reactions by using the carbon electrophiles serve as a rapid and atom-economic approach for constructing at least one new C-C bond. Therefore, developing the new reactions by using the carbon electrophiles is highly desirable in the future, especially for vinyl cation-promoted hydride shift reactions and vinyl cation-promoted aryl shift reactions.

1.2. Calcium-Catalyzed Reactions

1.2.1 Why Developing Calcium-Catalyzed Reactions?

Over the past few decades, transition-metal catalysis has become the most powerful tool for the creation of C-C bonds and carbon-heteroatom bonds in organic synthesis, which played an important role in natural product total synthesis, pharmaceuticals and materials.[20] Nevertheless, there are some inherent disadvantages for transition-metal catalysts. First, the transition-metal catalysts are oftentimes highly toxic, thus to remove metallic impurities from the final pharmaceutical products is a major purification problem from transition-metal catalyzed reactions. Second, they are expensive, most transition metals such as palladium, gold, rhodium and ruthenium are precious metals. Third, in most transition-metal catalyzed reactions, the combination of transition metals and the complex ligands is required to improve the reaction efficiency. Finally, the availability of the transition metals is more and more restricted, as our limited natural resources are used up. Therefore, wherever possible, the creation of more sustainable alternatives is in strong demand. In this regard, the reactions catalyzed by inexpensive, non-toxic and abundant metals open a new avenue for sustainability.

Calcium is the fifth most abundant elements in the earth's crust and essentially non-toxic even in substantial amounts, which perfectly meets the requirements for sustainability. Therefore, it is highly desirable to develop the calcium-catalyzed reactions in synthetic organic chemistry, from the viewpoint of ecological and economic benefits.

In the following part, representative examples of calcium-catalyzed reactions will be shown. In order to make reading easier, the introduction will be organized with respect to different types of the calcium-catalyzed reactions based on alcohols, olefins and carbonyl compounds as the reaction substrates.

1.2.2 Reactions of Alcohols

An easily accessible calcium-based inorganic salt that was synthesized from calcium carbonate and $HNTf_2$ acid in water can efficiently convert many different alcohols into the corresponding carbocations. Therefore, highly interesting organic reactions were designed and realized based on these reactive intermediates. A plausible activation model of hydroxyl groups for the generation of carbocations is depicted in Figure 9. Wherein, a real reactive species, $CaNTfPF_6$ was proposed for the dehydroxylation process, which was in situ generated by anion exchange between calcium salts and ammonium additives (Figure 9).

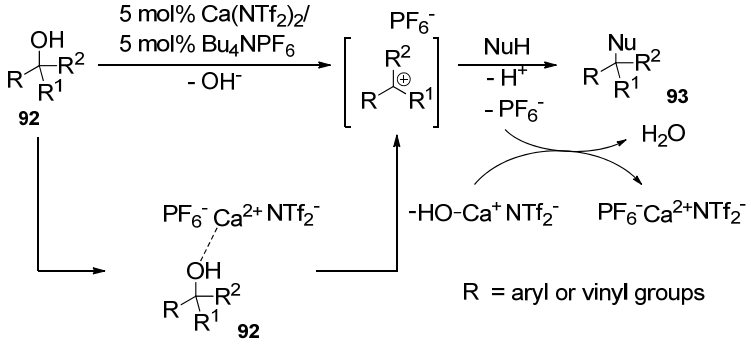
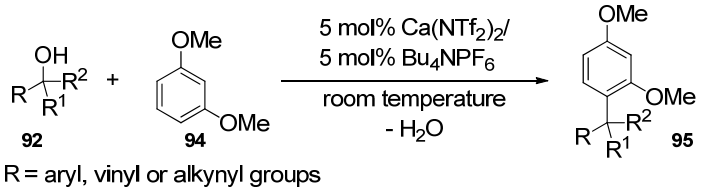
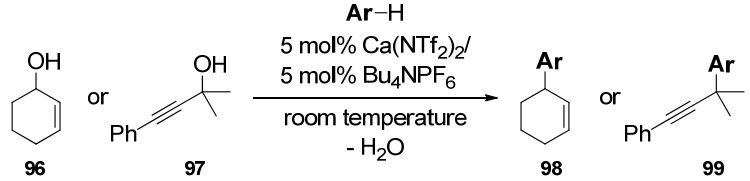


Figure 9

When this highly efficient protocol for the generation of carbocations was first discovered, electron-rich arenes were used to trap these highly reactive carbocations, and thus

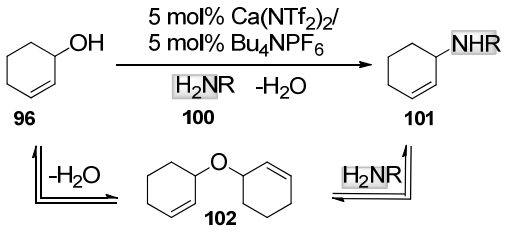




Scheme 17. The first example of calicum-catalyzed Friedel-Crafts alkylation reactions.

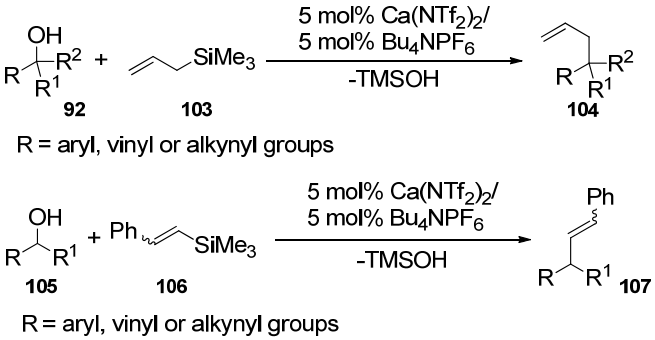
providing an environmentally benign protocol for the alkylation of electron-rich arenes under mild reaction conditions (Scheme 17).[21] Notably, not only π-activated secondary alcohols but also tertiary alcohols can be transformed into the corresponding carbocations by calcium catalysis, which were subsequently intercepted by aromatic nucleophiles. Furthermore, a variety of electron-rich heteroarenes reacted smoothly with allylic and tertiary alcohols in the presence of calcium catalysts.

Amines have good nucleophilic characteristics, a series of nitrogen nucleophiles **100** such as carbamates, tosylamides and anilines can be used to trap the highly reactive carbocations. Therefore, in 2011 the calcium-catalyzed direct amination of π-activated alcohols was developed. For tertiary, allylic and propargyl alcohols, they were successfully aminated by this methodology (Scheme 18).[22]



Scheme 18. Calcium-catalyzed direct amination of π-activated alcohols.

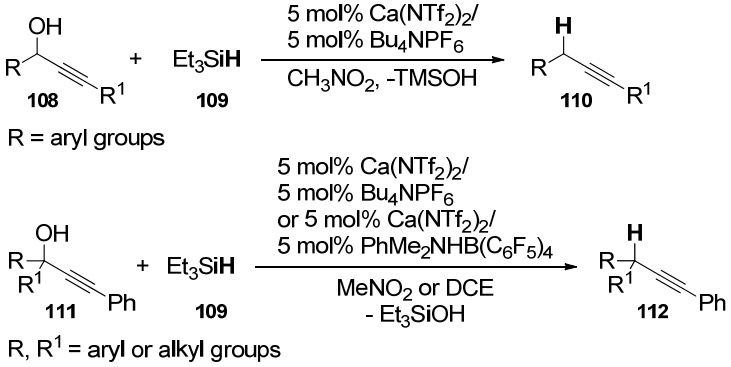
Allyltrimethylsilanes **103** are good nucleophiles that are widely used as coupling partners in transition-metal catalyzed reactions. Thus, in 2011 the calcium-catalyzed direct coupling reaction of π-activated alcohols **92**/**105** with organosilanes **103**/**106** was described. The highly reactive carbocations produced from π-activated alcohols by calcium catalysis were smoothly intercepted by the organosilanes **103** or **106** (Scheme 19).[23] In addition, tertiary, allylic and propargyl alcohols were quite suitable for the coupling reaction as well.



Scheme 19. Calcium-catalyzed coupling reactions of π-activated alcohols with organosilanes.

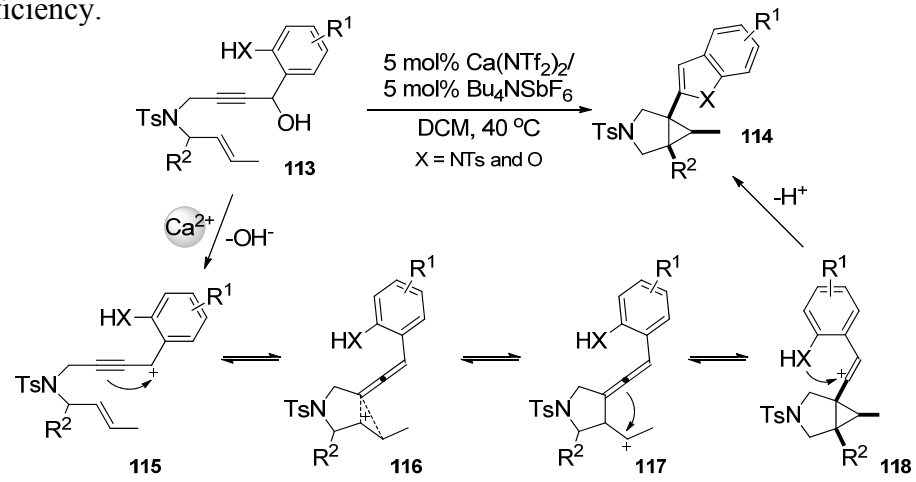
Silanes are excellent nucleophiles that have broad applications in reduction reactions, such as the reduction of carbonyl groups and imines. In 2012, the calcium-catalyzed deoxygenation of π-activated alcohols by using triethylsilanes **109** as an inexpensive and environmentally benign reductant was therefore developed (Scheme 20).[24] The tiethylsilane

109 successfully reduced not only secondary alcohols **108**, but also tertiary alcohols **111**. Normally, the elimination of tertiary carbocations leading to alkenes is always preferred over the reduction of tertiary carbocations. However, in this case, the elimination products were significantly prevented by using CH_3NO_2 as the solvent or *N*,*N*-dimethylanilinium tetra(pentafluorophenyl)borate as the additive.



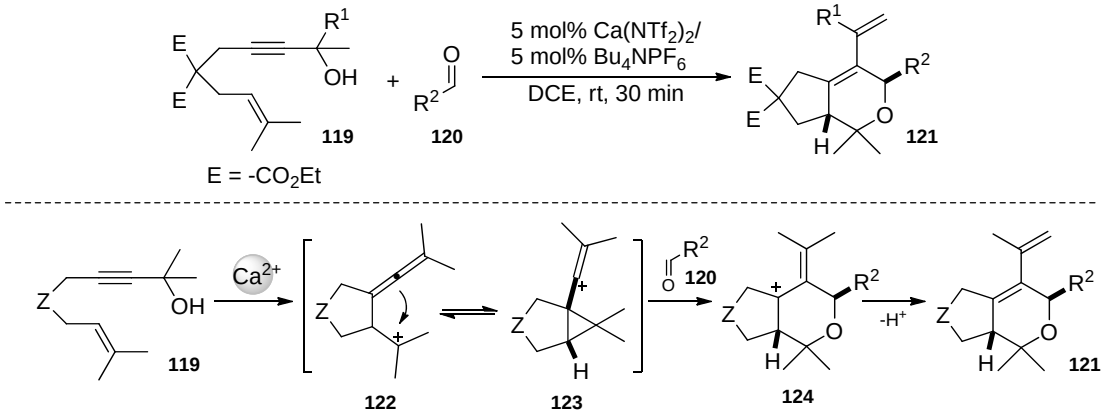
Scheme 20. Calcium-catalyzed deoxygenation of alcohols.

In 2013, the first calcium-catalyzed carbocation cascade reaction was demonstrated, which provided a highly elegant protocol for the diastereoselective synthesis of cyclopropanes **114** containing heterocycles that were essential structural motifs found in a myriad of natural isolates and pharmaceuticals.[25] A proposed mechanism for the cascade reaction is outlined in Scheme 21. The reaction began with the calcium-catalyzed dehydroxylation process of compounds **113**, producing propargylic cations **115** and carbocations **116** bearing the positive charge on the allenic position. Subsequently, cyclopropanation started when the carbocations **116**, which were stabilized by the through-space cation-π interaction of the positive charge with alkenes, formed in the pool of random conformers. Importantly, DFT calculations demonstrated that the successive two C-C and one C-X bond-forming events, eventually leading to the cyclopropanes **114**, were merged in a concerted manner. Furthermore, two different geometries of olefins were found to have great effect on the reaction efficiency.



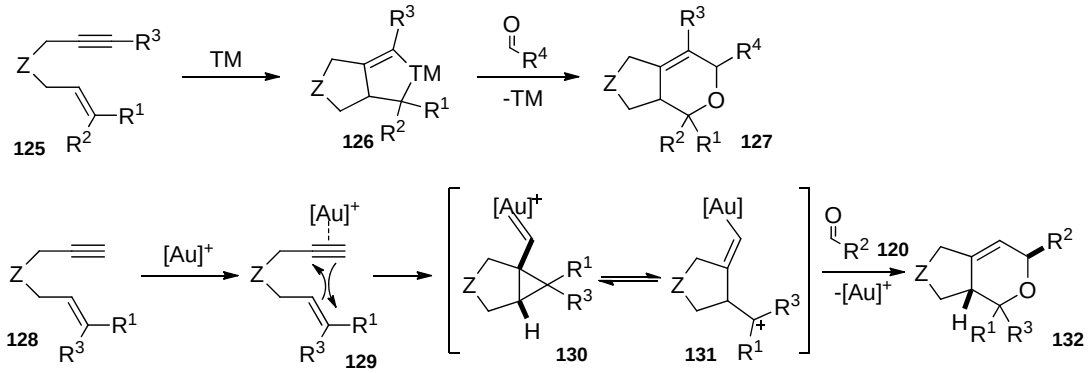
Scheme 21. The first example of calcium-catalyzed carbocation cascade reactions.

In 2015, the first calcium-catalyzed formal [2+2+2] cycloaddition reaction of enynes **119** with aldehydes **120** was disclosed, which allowed for a one-step synthesis of highly valuable bicyclic building blocks **121** with excellent chemo, region- and diastereoselectivity from readily available starting materials (Scheme 22).[26] A highly reactive homoallenyl cation **122** and its cyclopropyl form **123**, which were trapped by the tethered nucleophiles in the calcium-catalyzed cyclopropanation, can also be intercepted by the aldehyde **120**.



Scheme 22. Formal [2+2+2] cycloaddition reactions of enynes with aldehydes.

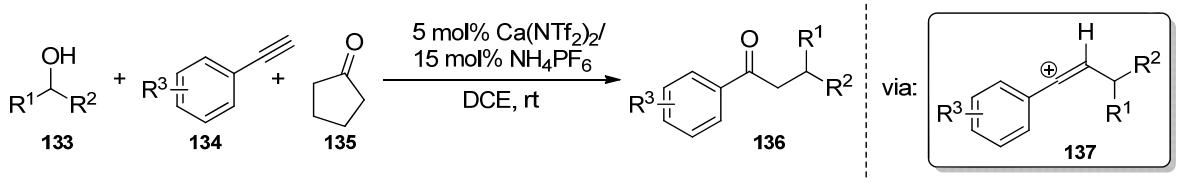
Typically, [2+2+2] cycloaddition reactions of enynes with aldehydes rely on transition-metal catalyzed reactions via Co-, Rh-, Ru- and Ni metallacycles **126** or C-gold bond species **130** and **131** (Scheme 23).[27] Therefore, the similar type of reactions demonstrates that calcium catalysts can replace transition-metal catalysts in synthetic organic chemistry.



Scheme 23. Transition-metal catalyzed [2+2+2] cycloaddition reactions of enynes with aldehydes.

The alkyne moiety has nucleophilic characteristics, which can trap highly reactive carbocations to produce highly reactive vinyl cations. Therefore, in 2015 the calcium-catalyzed intermolecular carbohydroxylation of alkynes was developed (Scheme 24).[28] Notably, cyclopentanones **135** can significantly improve the yields for the intermolecular carbohydroxylation of alkynes. The role of the cyclopentanone **135** is to

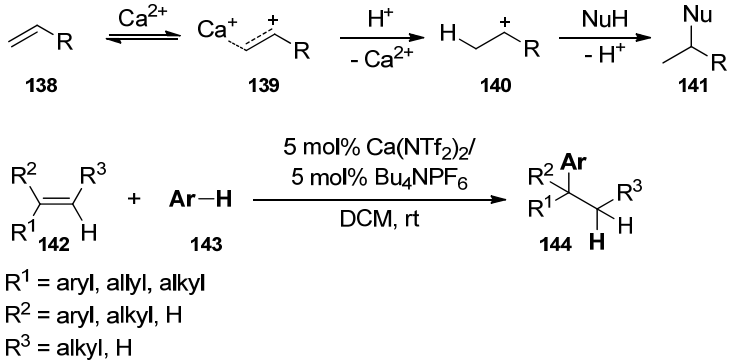
stabilize transient reactive carbocations produced from π-activated alcohols **133** by calcium catalysis and vinyl cations **137**.



Scheme 24. Cyclopentanone-promoted carbohydroxylation of alkynes.

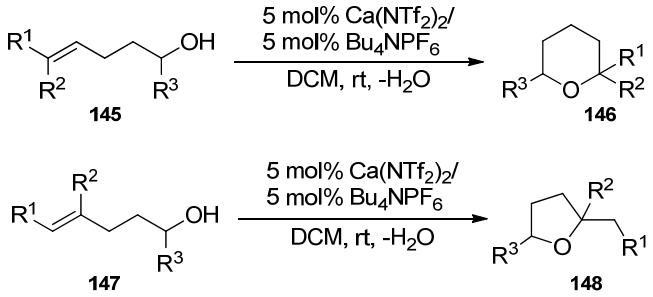
1.2.3 Reactions of Olefins

Not only alcohols but also alkenes can be efficiently transformed into the corresponding carbocations by calcium catalysis, which are subsequently trapped by aromatic nucleophiles. Therefore, in 2010 the first calcium-catalyzed hydroarylation of alkenes was described (Scheme 25).[29] In addition, a wide array of trisubstituted olefins and dienes were successfully hydroarylated in the presence of the calcium catalyst.



Scheme 25. Calcium-catalyzed hydroarylation of alkenes.

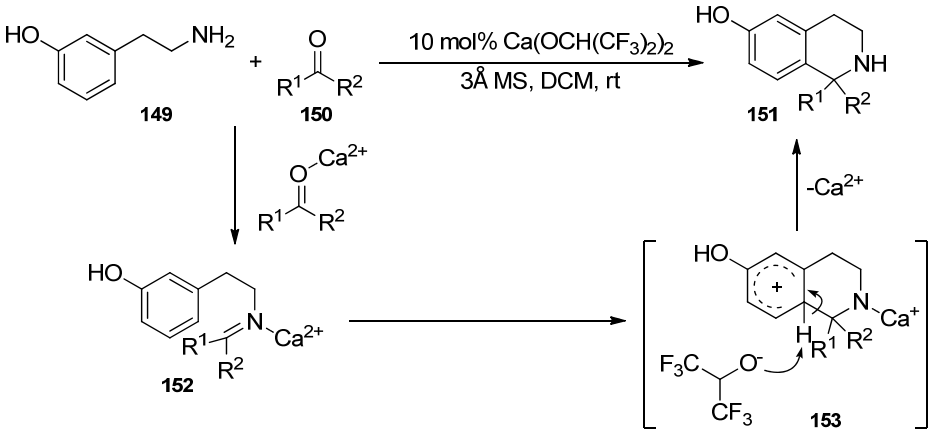
Hydroxyl groups are regarded as excellent nucleophiles, which can trap these highly reactive carbocations as well. In 2012 the calcium-catalyzed intramolecular hydroalkoxylation of alkenes was developed here, which offered an elegant protocol for the direct and efficient synthesis of structurally diverse cyclic tetrahydropyrans **146** and tetrahydrofurans **148** under mild reaction conditions (Scheme 26).[30]



Scheme 26. Calcium-catalyzed hydroalkoxylation of alkenes.

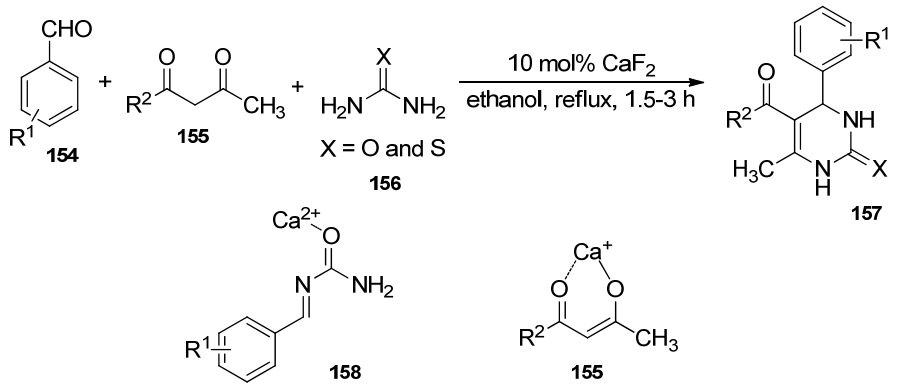
1.2.4 Reactions of Carbonyl Compounds

In 2008, Stambuli and co-workers developed the first example of the calcium-catalyzed regioselective Pictet-Spengler reactions of *m*-tyramines **149** with aldehydes **150** (Scheme 27).[31] The Pictet-Spengler reaction is a classic synthetic route to prepare tetrahydroisoquinolines and *β*-carbonyl alkaloids. However, it was generally promoted by stoichiometric amounts of strong Brønsted acids, and thus resulting in many disadvantages caused by the harsh reaction conditions, such as limited functional group tolerance. Therefore, Stambuli and co-workers developed the Pictet-Spengler reaction catalyzed by environmentally benign calcium salts to overcome these disadvantages.[31a] The role of calcium catalysts is to activate the aldehyde **150** and imines **152**. Two years later, Stambuli et al. found that unreactive ketones were quite suitable for the calcium-catalyzed Pictet-Spengler reaction as well.[31b]



Scheme 27. Calcium-catalyzed Pictet-Spengler reactions.

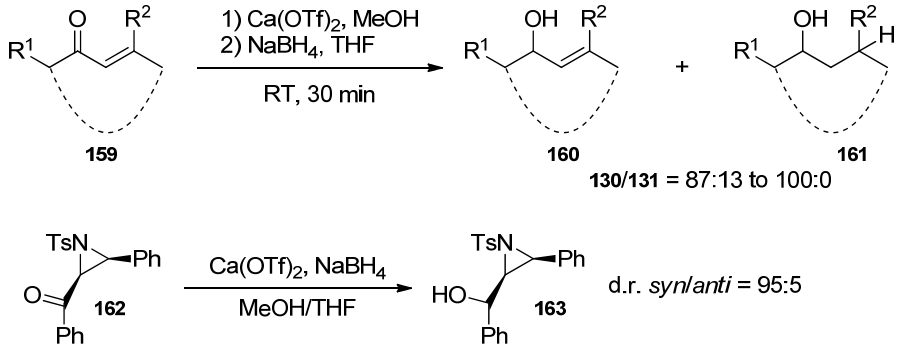
In 2009, Pandiarajan described the calcium-catalyzed Biginelli reaction among aldehydes **154**, 1,3-dicarbonyl compounds **155** and urea/thiourea **156** (Scheme 28),[32] which provided an elegant protocol for the straightforward and efficient synthesis of dihydropyrimidones **157**. In addition, a variety of metal-halides and metal-triflates have been



Scheme 28. Calcium-catalyzed Biginelli reactions.

explored for the optimization of the Biginelli reaction. Among these inorganic salts, calcium fluoride was identified to exhibit superior levels of catalytic activities. The role of the Lewis acidic calcium catalyst is to facilitate the formation of acyl iminium intermediates **158**, which is the rate-determining step in the Biginelli reaction (Scheme 28). In addition, the calcium catalyst can increase the nucleophilicity of 1,3-dicarbonyl compounds **155** by enolization (Scheme 28).

In 2012, Fuchter and co-workers demonstrated the $Ca(OTf)_2$-promoted regioselective Luche-type reduction of α,β-unsaturated ketones **159** with $NaBH_4$ (Scheme 29).[33] Before this approach, the 1,2-reduction of α,β-unsaturated ketones **159** was generally promoted by $CeCl_3$, thus it was not eco-friendly. The challenging 2-cyclopentenone was quite suitable for the calcium-promoted Luche-type reduction reaction. In addition, aziridinyl ketones **162** were also smoothly reduced by this methodology to give the stereoselective reduction adducts **163**.



Scheme 29. Calcium-mediated Luche-type reduction reactions.

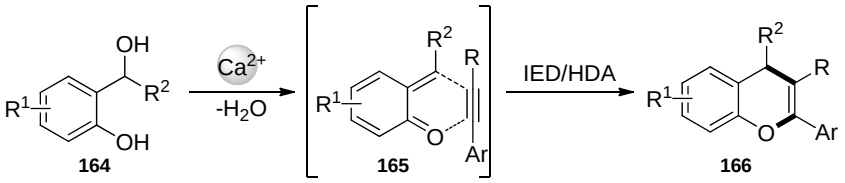
1.2.5 Conclusions and Perspectives

Recent advances in calcium-catalyzed reactions were illustrated and summarized. Lewis acidic calcium salts have exhibited excellent activities toward alcohols, olefins and carbonyl compounds. Particularly, the $Ca(NTf_2)_2$ catalyst can transform not only alcohols but also alkenes into the corresponding carbocations. Importantly, calcium-catalyzed carbocation cascade reactions provide a powerful platform for the construction of molecular complexity, from readily available starting materials. Furthermore, [2+2+2] cycloaddition reactions of enynes with aldehydes demonstrate that non-toxic and abundant calcium catalysts can replace transition-metal catalysts in synthetic organic chemistry.

Future developments in this area will involve the screening of suitable chiral ligands to realize calcium-catalyzed asymmetric reactions. In addition, calcium-catalyzed and vinyl cation-promoted hydride shift reactions and aryl shift reactions may be discovered by designing reasonable substrates.

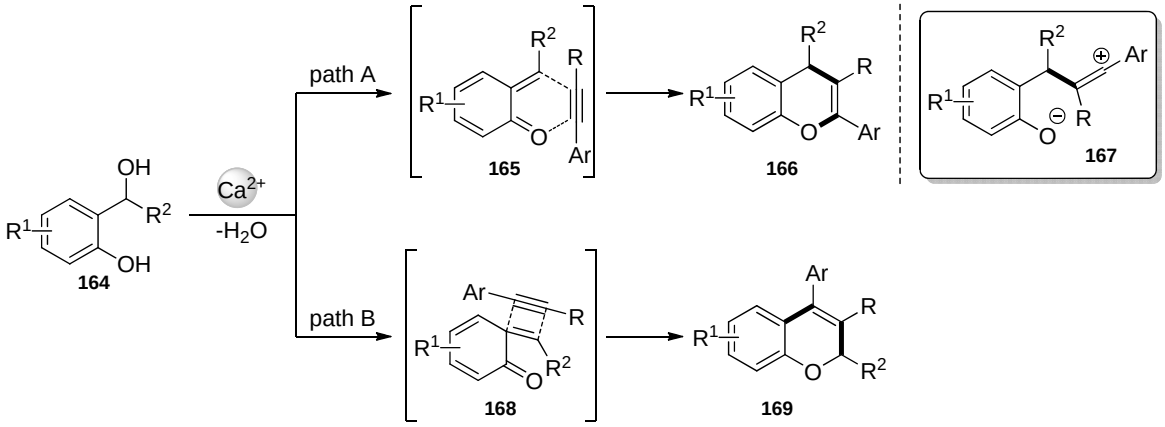
2. Aims of My Research Projects

The first goal of the presented work was to develop an efficient and sustainable approach for the synthesis of 4*H*-chromenes. The established methods for the preparation of 4*H*-chromenes are dependent on organocatalytic reactions that are often limited to salicylaldehyde derivatives and *α,β*-unsaturated carbonyl compounds as the reaction substrates, and transition-metal catalyzed reactions. Thus, the approaches are not general and eco-friendly. Therefore, the development of more efficient and sustainable alternatives is highly desirable. In this regard, inverse electron demand hetero-Diels-Alder reactions (IED/HDA) of alkynes with in situ generated *ortho*-quinone methides **165** are investigated in this project, which provides an elegant protocol for the straightforward synthesis of multi-substituted 4*H*-chromenes **166** (Scheme 30).



Scheme 30. Calcium-catalyzed synthesis of 4*H*-chromenes.

In principle, there are two different types of cyclization of alkynes with the in situ generated *ortho*-quinone methides **165**, leading to 4*H*-chromenes **166** and 2*H*-chromenes **169** respectively (Scheme 31). Electron-donating groups are therefore introduced on the aromatic ring in the aryl alkyne component, which are able to stablize highly reactive vinyl cations **167** and are thus beneficial to the inverse electron demand hetero-Diels-Alder reaction (IED/HDA) (Scheme 31, path A).

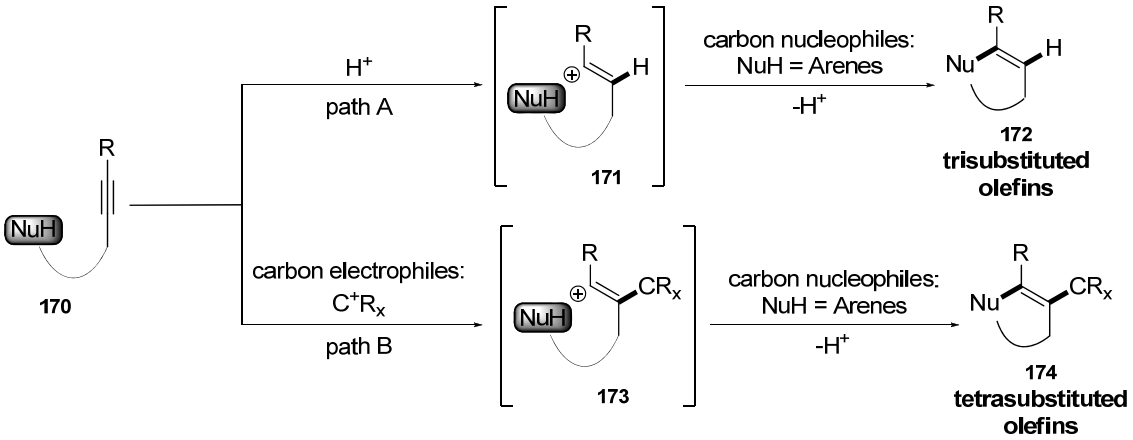


Scheme 31. Two different types of cyclization of alkynes with *ortho*-quinone methides.

As a second part of my work, investigations of the calcium-catalyzed carboarylation of alkynes were undertaken. Although there are several catalytic protocols for the one-step synthesis of all-carbon tetrasubstituted olefins from alkynes, transition-metal catalysts, such

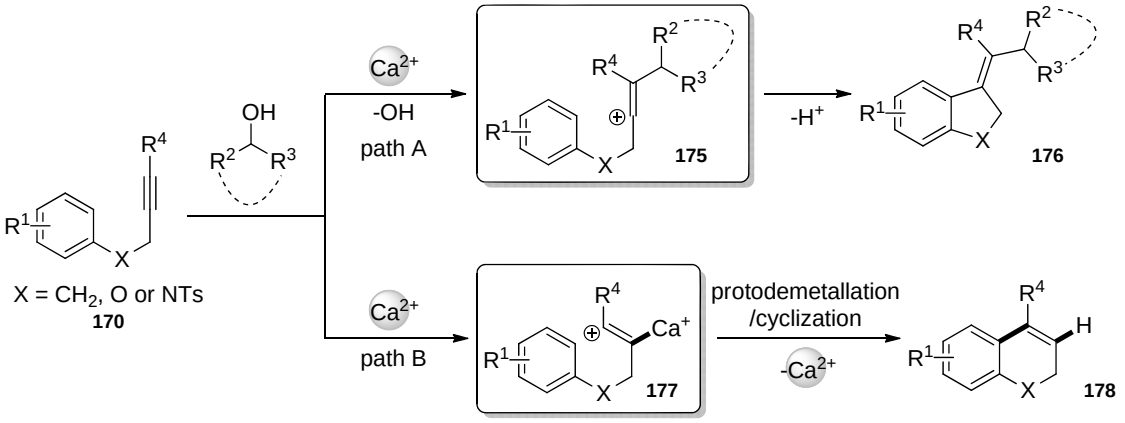
as nickel,[49] palladium,[50] copper[14] and iron salts,[51] and air and moisture sensitive stoichiometric organometallic reagents are required for these processes. Therefore, the development of more sustainable alternatives is certainly highly desirable.

Inspired by Brønsted acid-mediated hydroarylation of alkynes (Scheme 32, path A),[52] the first transition-metal free approach for the one-step synthesis of all-carbon tetrasubstituted olefins **174** from alkynes is investigated in this project. It involves the activation of the alkyne moiety by carbocations followed by the introduction of carbon nucleophiles (Scheme 32, path B). In other words, a transient, highly reactive vinyl cation **173** is generated by the nucleophilic addition of alkynes to the carbon electrophiles. Subsequently, the highly reactive vinyl cation **173** is intercepted by the carbon nucleophiles, leading to the all-carbon tetrasubstituted olefins **174** (Scheme 32, path B).



Scheme 32. Hydroarylation *versus* carboarylation of alkynes.

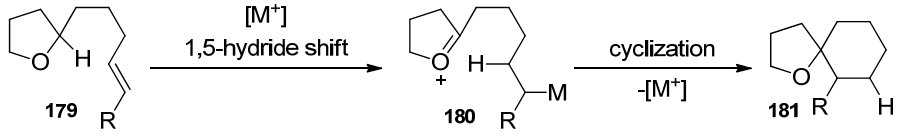
There are several possibilities for the calcium-catalyzed carboarylation of alkynes. First, in theory, two different trisubstituted highly reactive vinyl cations **173** and **175** might be generated by the nucleophilic addition of alkynes to carbocations, potentially leading to the formation of regio-isomeric mixtures of products **174** (Scheme 32, path B) and products **176** (Scheme 33, path A). Therefore, aryl alkynes and ynamides are selected as the reaction



Scheme 33. Different calcium-catalyzed electrophilic cyclizations of alkynes.

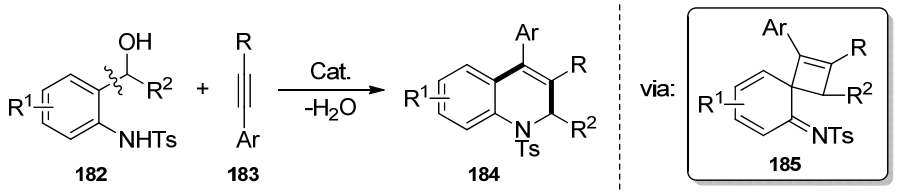
substrates to selectively induce the formation of the trisubstituted highly reactive vinyl cations **173**. Alternatively, Lewis acid-bound vinyl cations **177** might be produced by the direct activation of alkynes by the calcium catalyst. Subsequently, protodemetallation of the Lewis acid-bound vinyl cations **177** would lead to the formation of hydroarylation products **178** (Scheme 33, path B). Hence, many factors such as solvents, additives and reaction temperature must be considered to prevent the generation of the Lewis acid-bound vinyl cations **177**.

As a third part of my work, the development of a new concept for a redox-neutral C-C bond functionalization was projected. In 2005, Sames described redox-neutral C-H bond functionalizations based on intramolecular 1,5-hydrogen transfer processes (Scheme 34).[54]



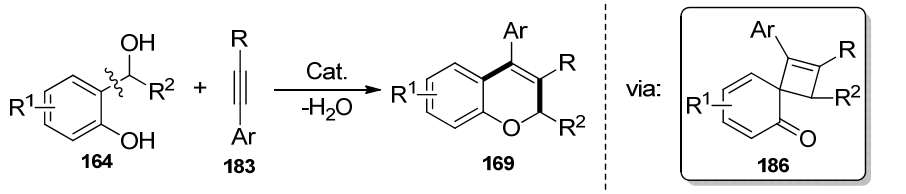
Scheme 34. Redox-neutral C-H bond functionalizations presented by Sames.

Inspired by his pioneering work, the new concept for the redox-neutral C-C bond functionalization based on intramolecular 1,3-aryl migration is investigated in this project (Scheme 35).



Scheme 35. New concept for a redox-neutral C-C bond functionalization.

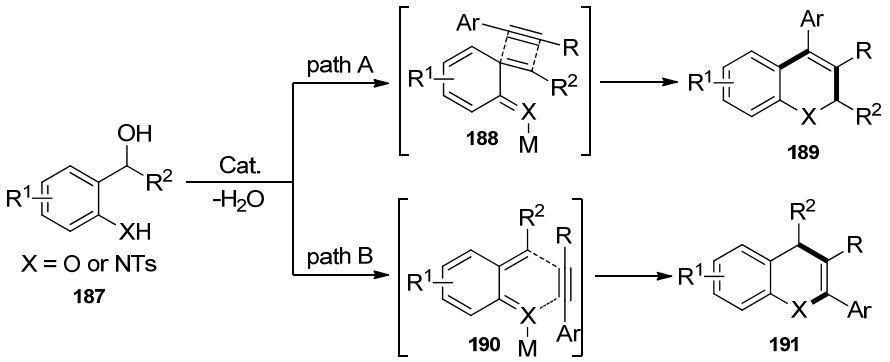
As an extension of the redox-neutral C-C bond activation reaction, the development of more efficient and sustainable approaches for the synthesis of 2*H*-chromenes was also projected. Although a variety of methods for the synthesis of 2*H*-chromenes are documented in the literature,[61c] the approaches suffer from multi-step reaction sequences, limited functional group tolerance and formation of regio-isomeric mixtures. Particularly, transition-metal catalysts and complex prefunctionlized fragments are required in most cases. Therefore, the first transition-metal free alkyne insertion reaction proceeding through the C-C



Scheme 36. Synthesis of 2*H*-chromenes through unstrained C-C σ bond activation.

σ bond cleavage of benzylic alcohols **164** is investigated in this project, which provides an elegant protocol for the direct synthesis of multi-substituted 2*H*-chromenes **169** (Scheme 36).

Theoretically, there are two different types of cyclization of alkynes with in situ generated *ortho*-azaquinone methides or *ortho*-quinone methides, leading to the rearrangement products **189** and the direct [4+2] cyclization products **191** (Scheme 37). Many factors such as metal catalysts, additives, solvents and reaction temperature must be taken into account to avoid the formation of the [4+2] cyclization products **191**. Among these factors, metal catalysts seem to be particularly interesting, for the coordination between the metal catalysts and the *ortho*-azaquinone methides or *ortho*-quinone methides might play an important role in the selectivity of these two different reactions.



Scheme 37. [2+2] Cyclization *versus* [4+2] cyclization of alkynes.

3. Results and Discussion

3.1. Calcium-Catalyzed Synthesis of 4*H*-Chromenes

3.1.1 Background

4*H*-Chromenes belong to the privileged structural motifs frequently found in both natural isolates and pharmaceutically active compounds (such as these molecules shown in Figure 10).[34] Therefore, considerable effort of chemists has been directed toward the synthesis of such a framework over the past decade. The established methods for the preparation of 4*H*-chromenes include: (1) ruthenium-catalyzed cycloaddition reactions of propargylic alcohols with phenol derivatives via allenylidene intermediates;[35] (2) ruthenium-catalyzed

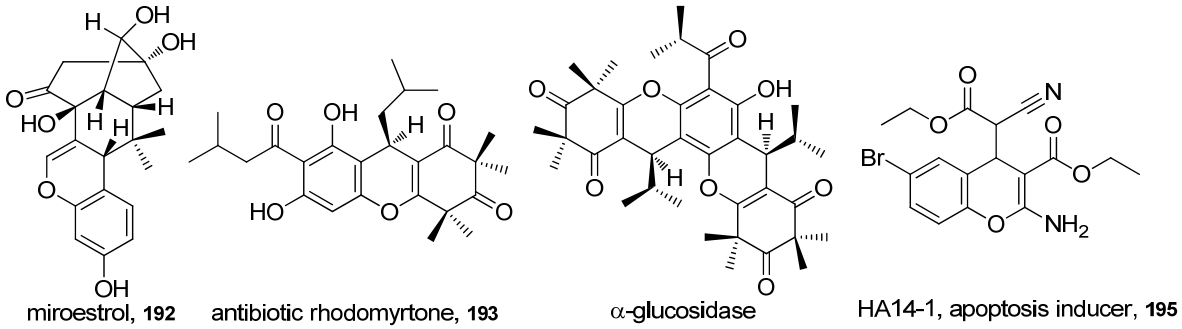


Figure 10

RCM reactions of aryl vinyl ethers;[36] (3) CuI-catalyzed intramolecular O-arylation of aryl bromides with 1,3-dicarbonyl groups;[37] (4) the tetrahydrothiophene-catalyzed tandem annulation reactions by Michael addition/elimination/substitution sequences;[38] (5) tandem reactions of 1,3-dicarbonyls with salicylaldehyde derivatives;[39] (6) organocatalytic tandem annulation reactions of *α,β*-unsaturated alkynes with salicylaldehyde derivatives;[40] (7) organocatalytic tandem annulation reactions of allenic esters or ketones with salicylaldehyde derivatives;[41,42] (8) metal-free reactions of chalcones with kojic acids, indoles or phenols through intermolecular Michael addition/intramolecular condensation sequences;[43] (9) further synthetic transformations of benzopyrans.[44] However, the approaches suffer from the limited diversity of readily available starting materials, multi-step reaction sequences or the use of transition-metal catalysts. Therefore, the development of more general and sustainable alternatives is highly desirable.

Based on previous studies here, *ortho*-quinone methides **165** can be in situ generated from benzylic alcohols **164** by calcium catalysis. Subsequently, inverse electron demand hetero-Diels-Alder reactions (IED/HDA) of the *ortho*-quinone methides **165** with alkynes allow for the straightforward synthesis of 4*H*-chromenes **166** (Scheme 30).

3.1.2 Aims

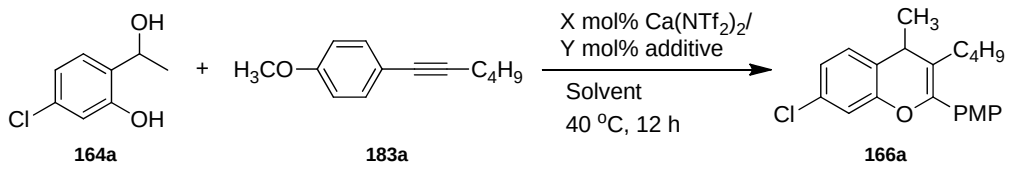
The goal of this work was to develop an efficient and sustainable approach for the synthesis of 4*H*-chromenes. The established methods for the preparation of 4*H*-chromenes are dependent on organocatalytic reactions that are often limited to salicylaldehyde derivatives and *α,β*-unsaturated carbonyl compounds as the reaction substrates, and transition-metal catalyzed reactions. Thus, the approaches are not general and eco-friendly. Therefore, the development of more efficient and sustainable alternatives is highly desirable. In this regard, inverse electron demand hetero-Diels-Alder reactions (IED/HDA) of alkynes with in situ generated *ortho*-quinone methides **165** are investigated in this project, which provides an elegant protocol for the straightforward synthesis of multi-substituted 4*H*-chromenes **166** (Scheme 30).

In principle, there are two different types of cyclization of alkynes with the in situ generated *ortho*-quinone methides **165**, leading to 4*H*-chromenes **166** and 2*H*-chromenes **169** respectively (Scheme 31). Therefore, electron-donating groups are introduced on the aromatic ring in the aryl alkyne component, which are able to stablize highly reactive vinyl cations **167** and are thus beneficial to the inverse electron demand hetero-Diels-Alder reaction (IED/HDA) (Scheme 31, path A).

3.1.3 Optimization of the [4+2] Cycloaddition Reaction of Alkynes

Initially, the reaction of 5-chloro-2-(1-hydroxyethyl)phenol **164a** with 1-*p*-methoxyphenyl-1-hexyne **183a** in DCE, in the presence of 5 mol% $Ca(NTf_2)_2$ and 5 mol% Bu_4NPF_6 at 40 ^oC for 12 h was examined. Gratifyingly, the desired product **166a** was obtained in 92% isolated yield (table 1, entry 1). The reaction also worked well in CH_3NO_2 as media (table 1, entry 2) or when using other additives such as Bu_4NBF_4 and Bu_4NSbF_6 (table 1, entry 3-4). Notably, the desired adduct **166a** was obtained in excellent yield even when 2.5 mol% $Ca(NTf_2)_2$ and 2.5 mol% Bu_4NPF_6 were used (table 1, entry 5, 91%). However, the reaction didn't work in the absence of additives (table 1, entry 6) and 5 mol% $HNTf_2$ exhibited lower catalytic activities compared to 2.5 mol% $Ca(NTf_2)_2$/2.5 mol% Bu_4NPF_6 (table 1, entry 5 *versus* entry 7-8). From these optimization results, 2.5 mol% $Ca(NTf_2)_2$ and 2.5 mol% Bu_4NPF_6 in DCE at 40 ^oC for 12 h were selected as the standard reaction conditions (table 1, entry 5).

Table 1. Optimization of the calcium-catalyzed [4+2] cycloaddition reaction.



164a **183a** **166a**

Entry [a]	$Ca(NTf_2)_2$ (X mol%)	Additive (Y mol%)	Solvent	Yield (%)[b]
1	5	Bu_4NPF_6 (5)	DCE	92
2	5	Bu_4NPF_6 (5)	CH_3NO_2	73
3	5	Bu_4NBF_4 (5)	DCE	84
4	5	Bu_4NSbF_6 (5)	DCE	79
5	**2.5**	**Bu_4NPF_6 (2.5)**	**DCE**	**91**
6	2.5	------	DCE	------
7[c]	------	Bu_4NPF_6 (2.5)	DCE	84
8[c]	------	------	DCE	83

[a] Additives and $Ca(NTf_2)_2$ were added to **164a** (0.4 mmol) and **183a** (0.6 mmol) in 4 mL solvent and the reaction was then stirred at 40 ^oC for 12 h. [b] The isolated yield. [c] 5 mol% $HNTf_2$ was used.

3.1.4 Synthesis of Substrates

Benzylic alcohols **164** were synthesized from the corresponding commercial ketones **196** and aldehydes **197** according to the known methods.[39a] For example, reduction of the ketones **196** by $NaBH_4$ provided the benzylic alcohols **164a-164d** directly (Figure 11). The nucleophilic addition of organometallic reagents **198** to the aldehydes **197** allowed for the continuation of synthesis of the benzylic alcohols **164e-164i** (Figure 12).

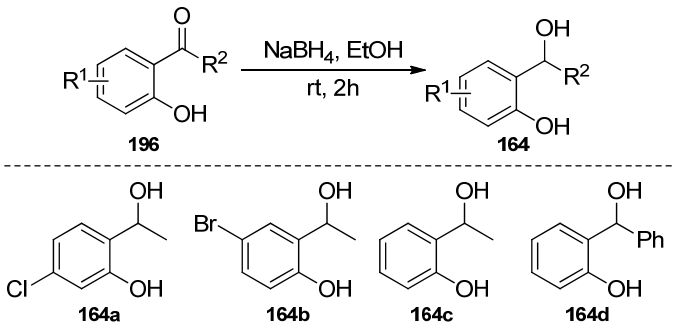
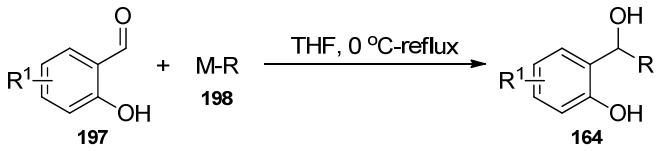


Figure 11



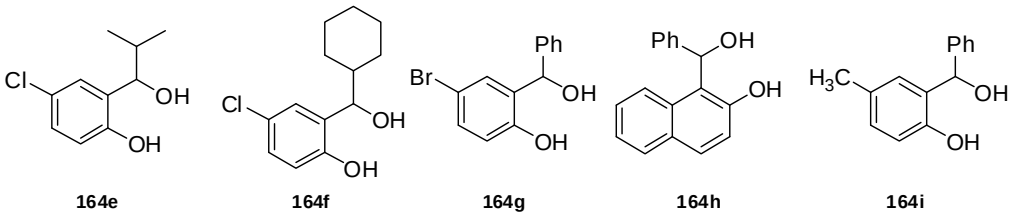


Figure 12

For the synthesis of alkynes **183**, they can be obtained by the Sonogashira coupling reaction of terminal alkynes **199** with aryl iodides **200** (Figure 13).[45] In addition, it can also be prepared from terminal alkynes **201** and methyl iodides **202** in the presence of *n*-butyllithium as a strong base (Figure 13).[46]

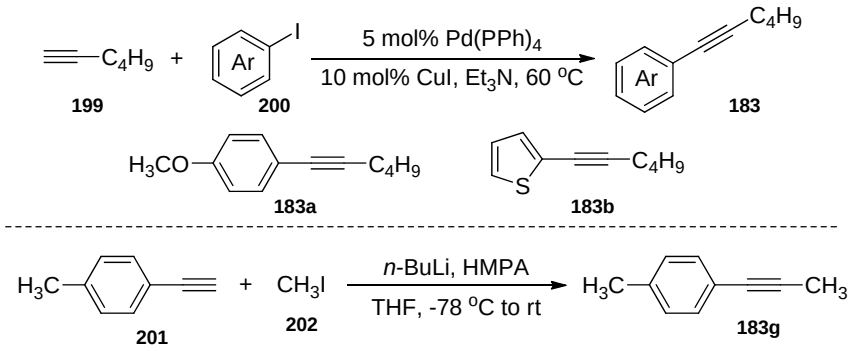
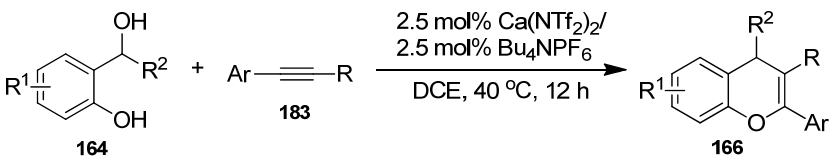


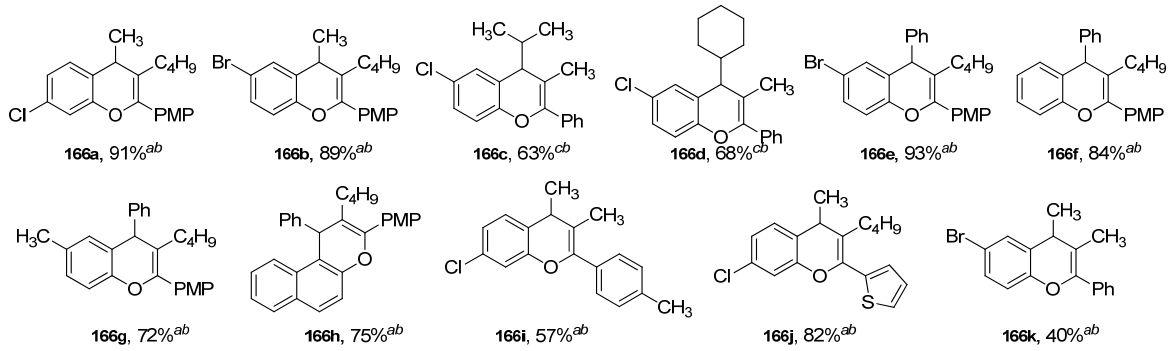
Figure 13

3.1.5 Scope of the Calcium-Catalyzed [4+2] Cycloaddition Reaction

With the optimal reaction conditions in hand, the scope of the inverse electron demand hetero-Diels-Alder reaction of alkynes **183** with in situ generated *ortho*-quinone methides was next examined. Bromo atom and chloro atom, which not only can prevent polymerization of benzylic alcohols **164** by decreasing the electron density on the benzene ring, but also are regarded as excellent coupling functional groups in transition-metal catalyzed reactions, can be introduced on the 2-(1-hydroxyethyl)phenol at the C4 and C5 positions without loss in reaction efficiency (table 2, **166a-166b**). Importantly, a wide variety of structurally diverse secondary benzylic alcohols **164**, which bear sterically hindered groups, can be employed as the reaction substrates and the reactions afforded the desired [4+2] cycloaddition adducts in moderate to excellent yields (table 2, **166c-166e**). Furthermore, the aryl framework of the

Table 2. Scope of the calcium-catalyzed [4+2] cycloaddition reaction.



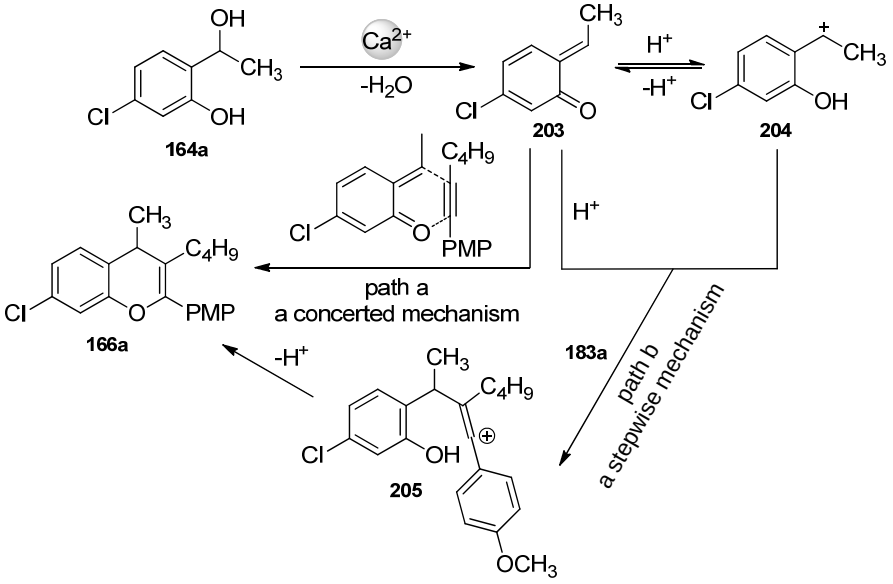


[a] 2.5 mol% Bu_4NPF_6 and 2.5 mol% $Ca(NTf_2)_2$ were added to benzylic alcohols **164** (0.4 mmol) and alkynes **183** (0.6 mmol) in 4 mL DCE and the reaction was then stirred at 40 °C for 12 h. [b] Isolated yields. [c] 5 mol% $Al(OTf)_3/NH_4PF_6/Bu_4NSbF_6$ were used and the reaction was stirred at 80 °C.

benzylic alcohols **164** can be successfully extended to electron-rich aromatic and naphthalene-derived systems (table 2, **166f-166h**). More importantly, structural variation in the aryl alkyne component can also be realized. Both the aryl and heteroaromatic alkynes reacted smoothly with **164a** and **164b** under the standard reaction conditions (table 2, **166i-166k**).

3.1.6 Mechanistic Discussion

Based on previous studies here, plausible reaction mechanisms for the inverse electron demand hetero-Diels-Alder reaction of alkynes with the in situ generated *ortho*-quinone methides are outlined in Scheme 38. The reaction started with the calcium-catalyzed dehydroxylation process of **164a**, generating *ortho*-quinone methides **203** and carbocations **204**. There are two possible pathways for the [4+2] cycloaddition processes. In the first pathway, the inverse electron demand hetero-Diels-Alder reaction (IED/HDA) proceeded in a concerted manner (Scheme 38, path a), thus directly leading to the eventual product **166a**. In



Scheme 38. Proposed pathways for the [4+2] cycloaddition reaction of alkynes.

the other pathway, a stepwise mechanism can't be ruled out. A trisubstituted highly reactive vinyl cation **205** was produced by the nucleophilic addition of alkynes **183a** to the electrophilic intermediates **203**/**204**, which was subsequently intercepted by the tethered phenolic hydroxyl group to afford the same product **166a** (Scheme 38, path b).

3.1.7 Conclusion

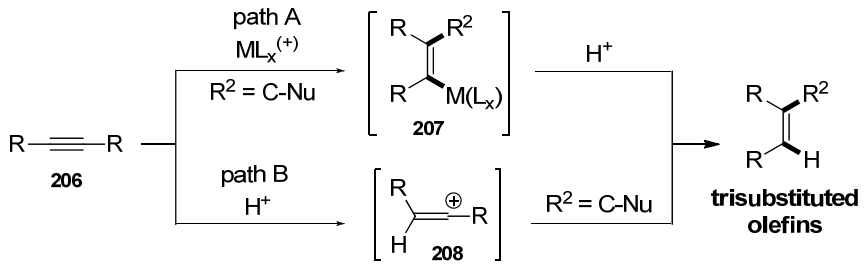
In summary, the first [4+2] cycloaddition reaction of alkynes with in situ generated *ortho*-quinone methides has been developed, which provides an elegant protocol for the straightforward and efficient synthesis of structurally diverse multi-substituted 4*H*-chromenes **166**. In addition, eleven representative adducts were readily obtained by this methodology in moderate to excellent yields (40-93%) under very mild reaction conditions.

The reaction proceeded through either a concerted inverse electron demand hetero-Diels-Alder reaction (IED/HDA) or a stepwise mechanism via trisubstituted highly reactive vinyl cations. In the stepwise mechanism, the trisubstituted highly reactive vinyl cation would be trapped by the tethered phenolic hydroxyl group.

3.2. Calcium-Catalyzed Carboarylation of Alkynes

3.2.1 Background

All-carbon tetrasubstituted olefins are ubiquitous structural motifs that widely occur in not only natural isolates, but also pharmaceuticals and materials.[47] In addition, they are versatile starting materials for the synthesis of complex fine chemicals through hydrogenation, dihydroxylation and epoxidation. However, their synthesis is very difficult by conventional olefination methods such as olefin metathesis and carbonyl olefination,[47a] because of the congested nature of densely substituted olefins. Over the past decade, transition-metal catalysis has became a powerful tool for the introduction of substituents to the alkyne moiety. Nevertheless, most transition-metal catalyzed reactions proceeded through vinyl-metal species **207**, which subsequently underwent protodemetallation, leading to the formation of trisubstituted olefins (Scheme 39, path A). Although a few methods have been demonstrated to obtain all-carbon tetrasubstituted olefins from alkynes in a stepwise reaction



Scheme 39. Synthesis of olefins through hydroarylation of alkynes.

sequence,[47a, 48] the development of catalytic protocols for the one-step synthesis of all-carbon tetrasubstituted olefins from alkynes still remains one of the major challenges in synthetic organic chemistry. Particularly, transition-metal catalysts, such as nickel,[49] palladium,[50] copper[14] and iron salts,[51] and air and moisture sensitive stoichiometric organometallic reagents are required for these processes. Therefore, the development of more efficient and sustainable alternatives is highly desirable.

Inspired by Brønsted acid-mediated hydroarylation of alkynes (Scheme 39, path B),[52] an ideal strategy for the synthesis of all-carbon tetrasubstituted olefins is envisaged, which involves the activation of the alkyne moiety by carbon electrophiles such as carbocations followed by the subsequent introduction of carbon nucleophiles (Scheme 32, path B). In other words, a transient, highly reactive vinyl cation **173** is generated by the nucleophilic addition of alkynes **170** to the carbon electrophiles. Subsequently, the highly reactive vinyl cation **173** is trapped by the carbon nucleophiles, and thus leading to the formation of all-carbon tetrasubstituted olefins **174** (Scheme 32, path B). Therefore, this strategy is able to avoid the formation of the vinyl-metal species **207**, and two carbon substituents are concomitantly introduced to the C-C triple bond.

3.2.2 Aims

As a second part of my work, investigations of the calcium-catalyzed carboarylation of alkynes were undertaken. Although there are several catalytic protocols for the one-step synthesis of all-carbon tetrasubstituted olefins from alkynes, transition-metal catalysts, such as nickel,[49] palladium,[50] copper[14] and iron salts,[51] and air and moisture sensitive stoichiometric organometallic reagents are required for these processes. Therefore, the development of more sustainable alternatives is highly desirable.

Inspired by Brønsted acid-mediated hydroarylation of alkynes (Scheme 32, path A),[52] the first transition-metal free approach for the one-step synthesis of all-carbon tetrasubstituted olefins from alkynes is investigated in this project. It involves the activation of the alkyne moiety by carbocations followed by the introduction of carbon nucleophiles (Scheme 32, path B). In other words, a transient, highly reactive vinyl cation **173** is generated by the nucleophilic addition of alkynes to the carbon electrophiles. Subsequently, the highly reactive vinyl cation **173** is trapped by the carbon nucleophiles, leading to the formation of all-carbon tetrasubstituted olefins **174** (Scheme 32, path B).

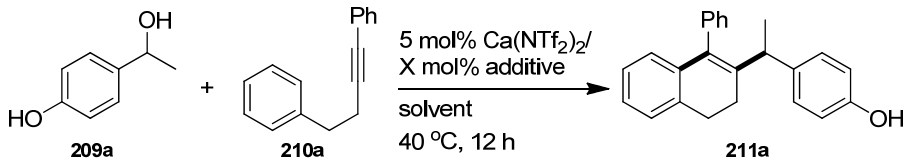
There are several possibilities for the calcium-catalyzed carboarylation of alkynes. First, in theory, two different trisubstituted highly reactive vinyl cations **173** and **175** might be generated by the nucleophilic addition of alkynes to carbocations, potentially leading to the regio-isomeric mixtures of products **174** (Scheme 32, path B) and products **176** (Scheme 33, path A). Aryl alkynes and ynamides are therefore chosen as the reaction substrates to

selectively induce the formation of the trisubstituted highly reactive vinyl cations **173**. Alternatively, Lewis acid-bound vinyl cations **177** might be produced by the direct activation of alkynes by the calcium catalyst. Subsequently, protodemetallation of the Lewis acid-bound vinyl cations **177** would lead to the formation of hydroarylation products **178** (Scheme 33, path B). Hence, many factors such as solvents, additives and reaction temperature must be considered to prevent the generation of the Lewis acid-bound vinyl cations **177**.

3.2.3 Optimization of the Calcium-Catalyzed Carboarylation of Alkynes

In the initial investigation, the reaction of 4-hydroxyphenylethanol **209a** with acetylene **210a** in DCE, in the presence of 5 mol% $Ca(NTf_2)_2$ and 5 mol% Bu_4NPF_6 at 40 °C for 12 h was examined. Gratifyingly, the reaction did occur and the desired carboarylation adduct **211a** was obtained in 56% isolated yield (table 3, entry 1). Inspired by this result, further optimization of reaction conditions was then explored. It was pleased to find that solvents had great effect on the reaction efficiency, and the reaction yield was significantly improved when using CH_3NO_3 as media (table 3, entry 2). In addition, decreasing the additive Bu_4NPF_6 loading to 2.5 mol% slightly improved the reaction yield (Table 3, entry 3). The reaction also worked well when using other additives such as NH_4PF_6 and Bu_4NSbF_6 (table 3, entry 4-5). Furthermore, mixed solvents and two equivalents of **209a** were investigated as well in order to improve the reaction efficiency further, but no better results were obtained (table 3, entry 6-7). Notably, the reaction didn't work in the absence of additives (table 3, entry 8) and 10 mol% $HNTf_2$ exhibited lower catalytic activities than 5 mol% $Ca(NTf_2)_2$/2.5 mol% Bu_4NPF_6 (Table 3, entry 3 *versus* entry 9-10). From these optimization results, 5 mol% $Ca(NTf_2)_2$ and 2.5 mol% Bu_4NPF_6 in CH_3NO_2 at 40 °C for 12 h were selected as the standard reaction conditions (Table 3, entry 3).

Table 3. Optimization of the calcium-catalyzed carboarylation of alkynes.



209a **210a** **211a**

Entry [a]	Additive (X mol%)	Solvent	Yield (%)[b]
1	Bu_4NPF_6 (5)	DCE	56
2	Bu_4NPF_6 (5)	CH_3NO_2	83
3	**Bu_4NPF_6 (2.5)**	**CH_3NO_2**	**85**
4	NH_4PF_6 (2.5)	CH_3NO_2	80

5	Bu_4NSbF_6 (2.5)	CH_3NO_2	81
6	Bu_4NPF_6 (2.5)	CH_3NO_2/DCE (1:1)	77
7[c]	Bu_4NPF_6 (2.5)	CH_3NO_2	82
8	------	CH_3NO_2	------
9[d]	Bu_4NPF_6 (2.5)	CH_3NO_2	70
10[d]	------	CH_3NO_2	71

[a] Additives and $Ca(NTf_2)_2$ were added to **210a** (0.48 mmol) and **209a** (0.4 mmol) in 2 mL solvent and the reaction was then stirred at 40 °C for 12 h. [b] The isolated yield. [c] Two equivalents of **209a** were used. [d] 10 mol% $HNTf_2$ was used.

3.2.4 Synthesis of Substrates

π-Activated alcohols were sythesized from the corresponding ketones **212** and aldehydes **213** according to the known methods (Figure 14 and 15).[39a] Notably, cyclic allylic alcohols **209f** and **209g** were obtained by the $Ca(OTf)_2$-promoted selective 1,2-reduction of *α,β*-unsaturated ketones with $NaBH_4$.[33]

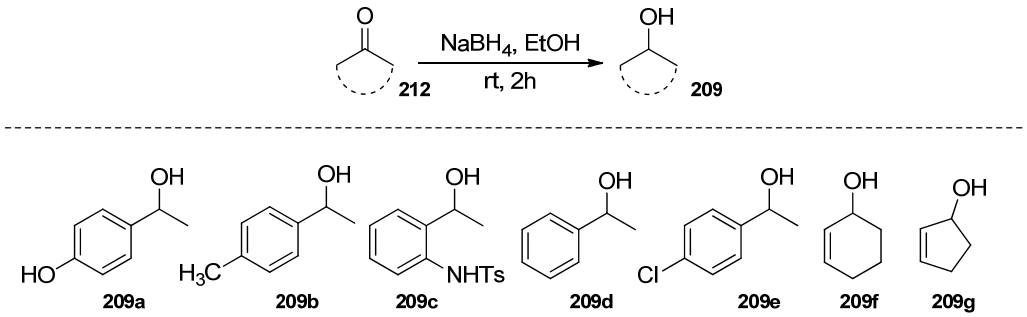


Figure 14

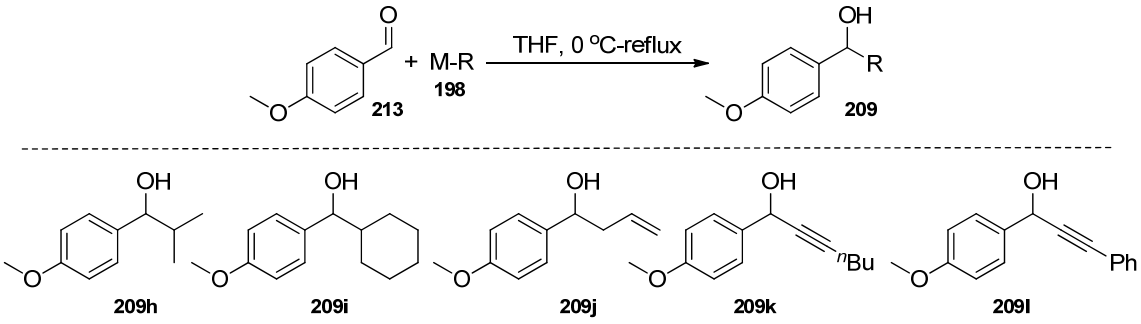


Figure 15

For the synthesis of alkynes **210**, they can be obtained by the Sonogashira coupling reaction of terminal alkynes **214** with aryl iodides **200** (Figure 16).[45] In addition, the nucleophilic displacement reactions of bromides **215** with 4-ethynylanisoles **216** allowed for

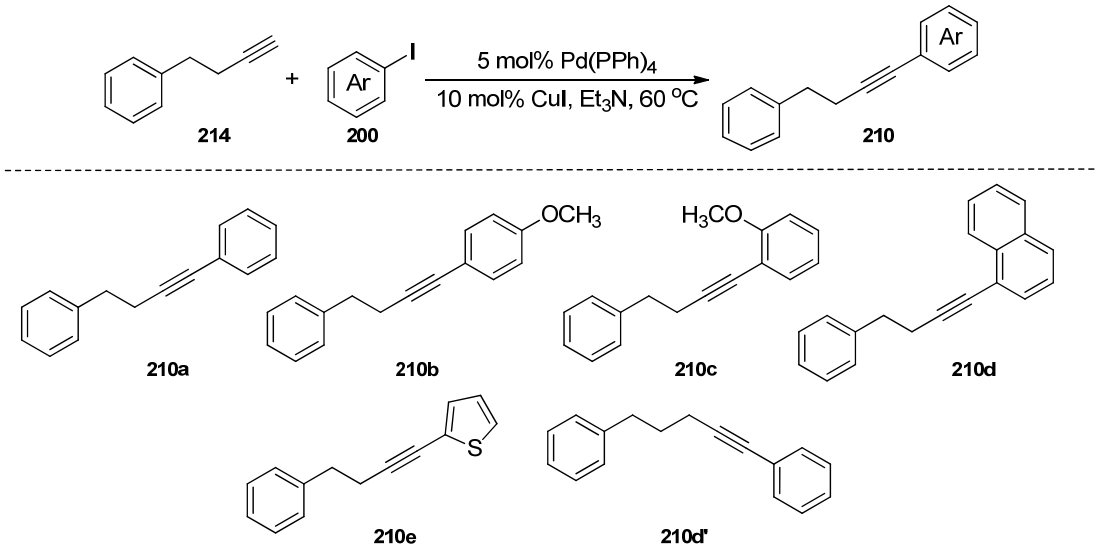


Figure 16

the concise synthesis of other different alkynes **210** (Figure 17).[14] Furthermore, copper-catalyzed aerobic oxidative C-N bond coupling of terminal alkynes **214** with oxazolidin-2-ones **217** provided an efficient access to ynamides **210l** (Figure 18).[14]

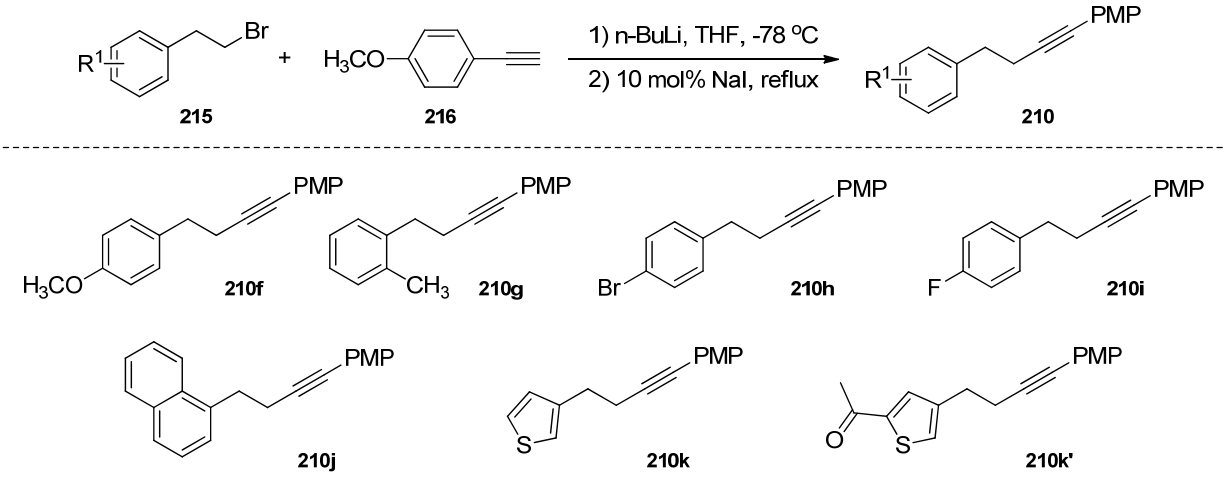


Figure 17

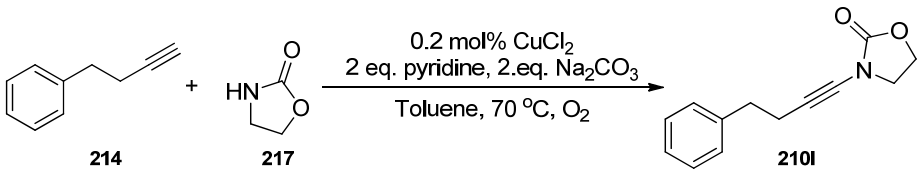


Figure 18

The rest of alkynes **210** containing the oxygen atom and nitrogen atom were prepared by classic reactions from readily available starting materials (Figure 19 and 20).[14]

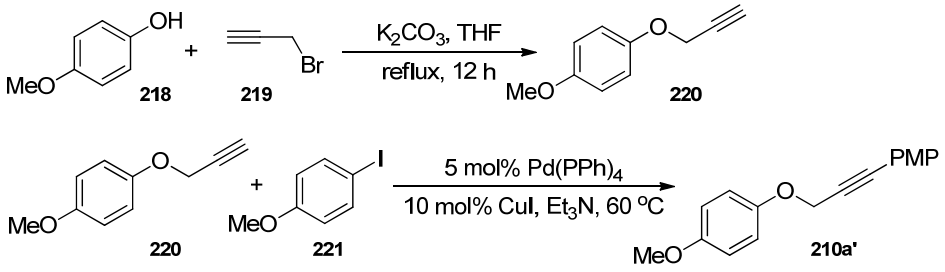


Figure 19

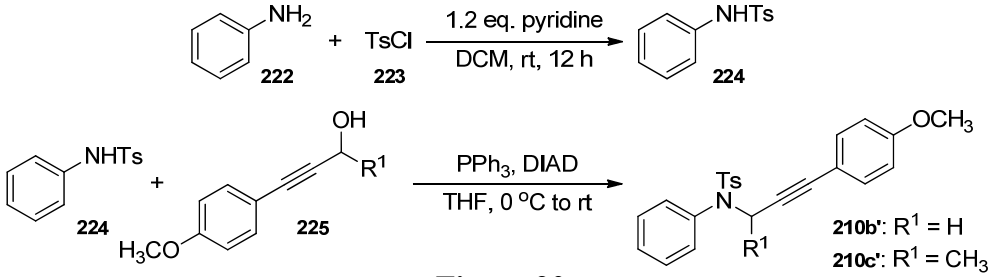
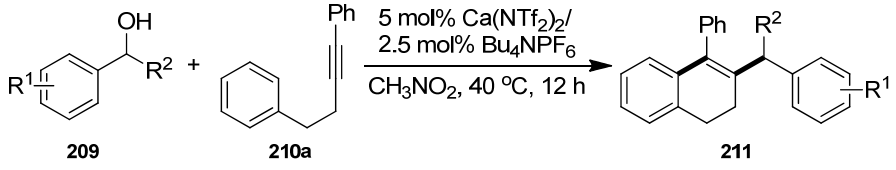


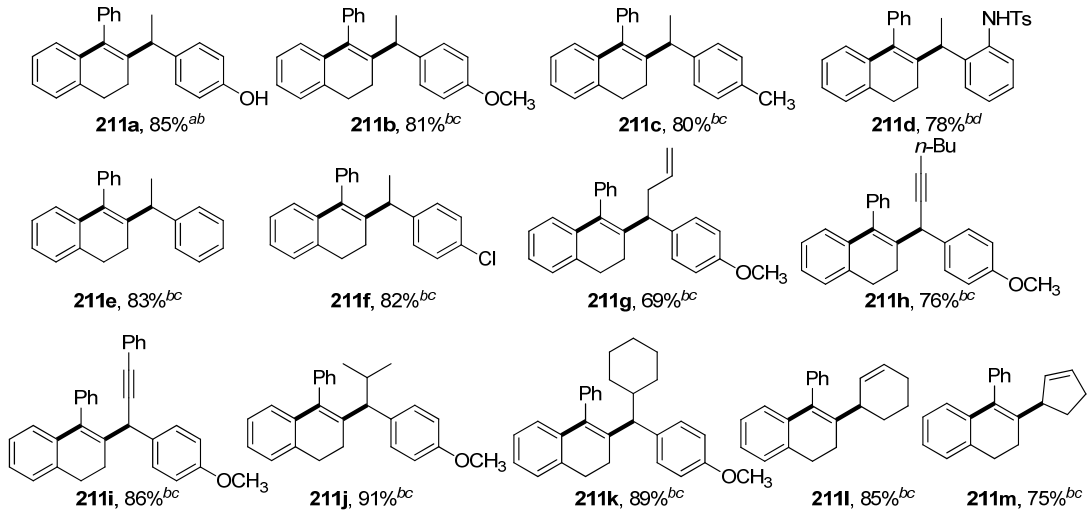
Figure 20

3.2.5 Scope of the Calcium-Catalyzed Carboarylation of Alkynes

With the optimized reaction conditions in hand, the scope of the calcium-catalyzed carboarylation of alkynes was next investigated. As revealed in table 4, π-activated alcohols as carbon electrophiles were first examined. The reaction is quite general with respect to the electronic nature of substituents on the aromatic ring of benzylic alcohols (table 4, **211a-211f**). For example, OH, MeO, Me, Cl and NHTs can be introduced on the 1-phenylethanol at the C2 and C4 positions without loss in reaction efficiency. Furthermore, the reaction seems quite tolerant with respect to functional groups in the π-activated alcohol component, such as C-C double bonds and C-C triple bonds (table 4, **211g-211i**). More importantly, sterically hindered secondary benzylic alcohols and cyclic allylic alcohols can be employed as the reaction substrates and the reactions provided the desired carboarylation adducts in good to excellent yields (table 4, **211j-211m**).

Table 4. Scope of the π-activated alcohols as carbon electrophiles.



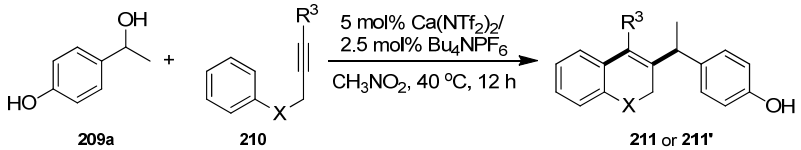


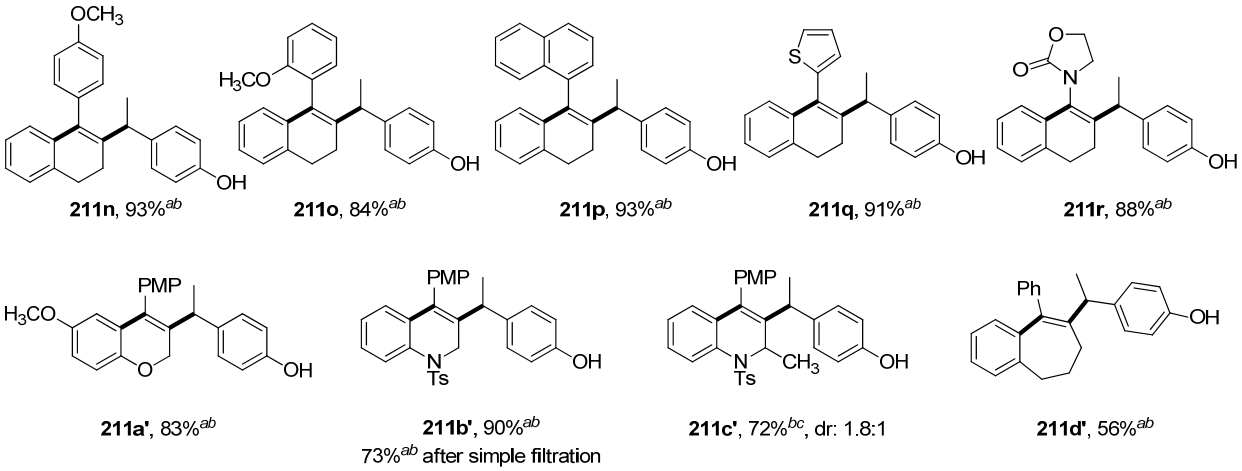
[a] 2.5 mol% Bu_4NPF_6 and 5 mol% $Ca(NTf_2)_2$ were added into **210a** (0.48 mmol) and **209** (0.4 mmol) in 2 mL CH_3NO_2 and the reaction was then stirred at 40 °C for 12 h. [b] Isolated yields after column chromatography. [c] 2 mL DCE/CH_3NO_2 (1:1) was used. [d] 2 mL DCE was used.

Next the substituents on the C-C triple bond were examined, both aryl and heteroaromatic groups gave the corresponding carboarylation adducts in excellent yields (table 5, **211n-211q**). Notably, an axial scaffold that has broad applications in asymmetric catalysis was successfully installed by this methodology (table 5, **211o-211p**), although obtaining the racemic compounds. Furthermore, ynamides **210l** reacted smoothly with **209a**, providing more complex dihydronaphthalene derivatives (table 5, **211r**).

The linkage between aryl nucleophiles and the C-C triple bond was investigated as well. Not only an ethylene linking unit but also oxygen and nitrogen substituents can be incorporated into the substrates (table 5, **211a'-211c'**), which allowed for the direct and efficient synthesis of multi-substituted 2*H*-chromenes and 1,2-dihydroquinolines. In addition, the 1,2-dihydroquinoline **211b'** was obtained in 73% isolated yield through simple filtration after reaction completion (table 5, **211b'**). Furthermore, the diastereoselectivity of the reaction was examined by introducing an additional substituent in the linkage (table 5, **211c'**), although the result was moderate. More importantly, a seven-membered carbocyclic ring can be formed by this methodology, which further expands the substrate scope (table 5, **211d'**).

Table 5. Scope of alkyne substituents and linking units.





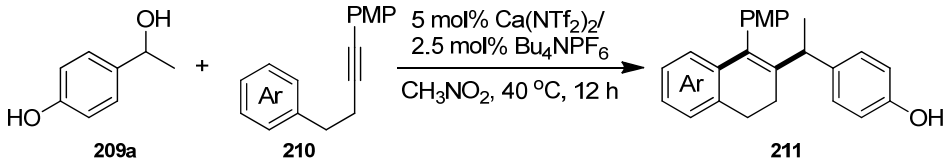
211n, 93%[ab] **211o**, 84%[ab] **211p**, 93%[ab] **211q**, 91%[ab] **211r**, 88%[ab]

211a', 83%[ab] **211b'**, 90%[ab] 73%[ab] after simple filtration **211c'**, 72%[bc], dr: 1.8:1 **211d'**, 56%[ab]

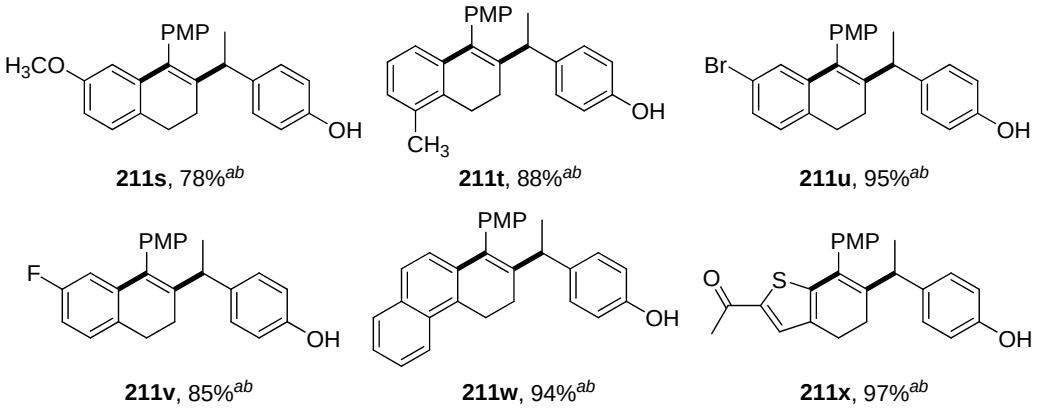
[a] 2.5 mol% Bu_4NPF_6 and 5 mol% $Ca(NTf_2)_2$ were added into **210** (0.48 mmol) and **209a** (0.4 mmol) in 2 mL CH_3NO_2 and the reaction was then stirred at 40 °C for 12 h. [b] Isolated yields after column chromatography. [c] Reactions stirred at 80 °C for 12 h and the dr was determined by ^1H NMR analysis of the crude mixture.

Finally, the scope of aryl nucleophiles was examined. The reaction seems quite general with respect to the electronic nature of substituents on the nucleophilic aromatic ring, both electron-donating and electron-withdrawing groups can be introduced without loss in reaction efficiency (table 6, **211s-211v**). Furthermore, the aryl framework can be successfully extended to heteroaromatic and naphthalene-derived systems (table 6, **211w-211x**).

Table 6. Scope of aromatic nucleophiles.



209a **210** **211**



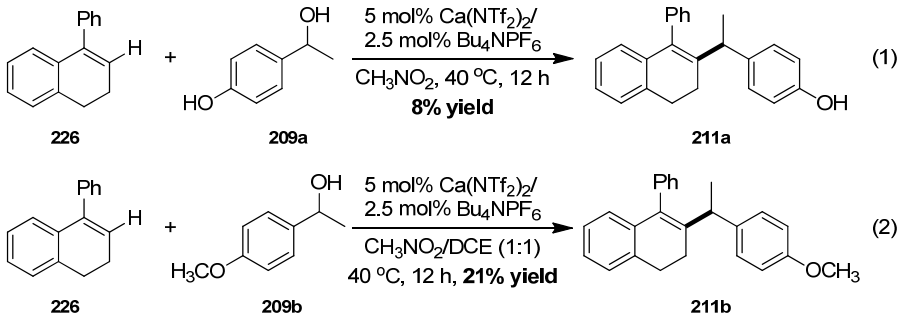
211s, 78%[ab] **211t**, 88%[ab] **211u**, 95%[ab]

211v, 85%[ab] **211w**, 94%[ab] **211x**, 97%[ab]

[a] 2.5 mol% Bu_4NPF_6 and 5 mol% $Ca(NTf_2)_2$ were added into **210** (0.48 mmol) and **209a** (0.4 mmol) in 2 mL CH_3NO_2 and the reaction was then stirred at 40 °C for 12 h. [b] Isolated yields after column chromatography.

3.2.6 Mechanistic Study

To gain insight into a plausible reaction mechanism, dihydronaphtalenes **226** that were seperated as a by-product in the reaction mixture reacted with **209a** and **209b** under the standard reaction conditions (eqn(1) and eqn(2)). The desired products **211a** and **211b** were obtained in 8% and 21% yields respectively together with the unreacted dihydronaphtalene **226**. Therefore, trisubstituted highly reactive vinyl cations generated by the nucleophilic addition of alkynes to the carbocations that were produced from π-activated alcohols by calcium catalysis were clearly demonstrated in the calcium-catalyzed carboarylation of alkynes.



3.2.7 Conclusion

In conclusion, the first transition-metal free carboarylation of alkynes with readily available alcohols was realized in the presence of non-toxic and abundant calcium catalysts, which provides a novel protocol for the one-step synthesis of all-carbon tetrasubstituted olefins from alkynes. A trisubstituted highly reactive vinyl cation **173** was generated by the nucleophilic addition of alkynes to carbocations, which was subsequently intercepted even by deactivated arenes as the tethered nucleophiles. In addition, twenty eight representative adducts were readily obtained by this methodology in moderate to excellent yields (56-97%) under very mild reaction conditions.

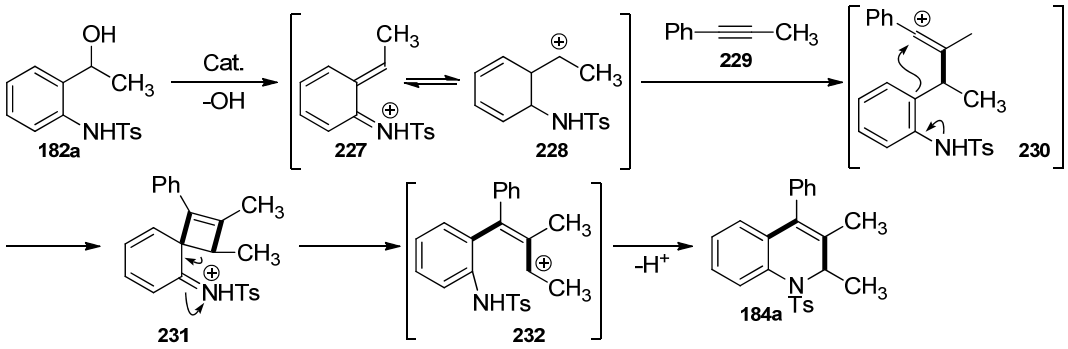
3.3. $Al(OTf)_3$-Catalyzed Insertion of an Unactivated Alkyne into an Unstrained C-C σ Bond

3.3.1 Background

Over the past decade, considerable effort of chemists has been devoted to addressing the long-standing problem of the direct functionalization of unactivated C-H bonds, and therefore remarkable progress has been made in this area.[53] Complementing the more classical, directing group/transition metal-triggered strategies, in 2005 Sames revived an alternative approach to C-H bond activation based on intramolecular 1,5-hydrogen transfer processes.[54] As opposed to the aforementioned transition-metal catalyzed C-H bond transformations, no

terminal oxidants were required for the C-H bond activation reaction, thus this strategy was called as the "redox-neutral C-H bond functionalizations" (Scheme 34).

Despite advances in the field of the direct C-H functionalizations, the cleavage and activation of C-C σ bonds still remains one of the major challenges in modern synthetic chemistry, from the viewpoint of practicability and mechanistic understanding.[55] Reactions generally rely on the C-C σ bond cleavage of constrained small-ring molecules by the release of strain energy.[55k] In recent years, notable achievements have been made by transition-metal catalyzed reactions, which are limited to nitriles, acylquinolines and carbonyl compounds as the unconstrained reaction substrates.[55l] In addition, several transition-metal free C-C σ bond cleavage reactions have been recently demonstrated, which were enabled by oxidative processes.[56] Therefore, in analogy to the redox-neutral C-H bond functionalization presented by Sames, a new concept for a redox-neutral C-C bond functionalization based on the first transition-metal free alkyne insertion reaction through unstrained C-C σ bond activation has been developed here, such as the one described in Scheme 40.



Scheme 40. New concept for a redox-neutral C-C bond functionalization.

3.3.2 Aims

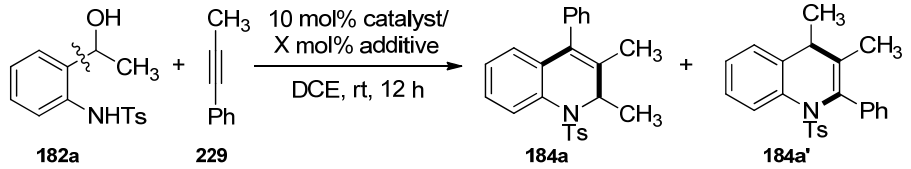
As a third part of my work, the development of a new concept for a redox-neutral C-C bond functionalization was projected. In 2005, Sames described redox-neutral C-H bond functionalizations based on intramolecular 1,5-hydrogen transfer processes (Scheme 34).[54] Inspired by his pioneering work, the new concept for the redox-neutral C-C bond functionalization based on intramolecular 1,3-aryl migration is investigated in this project (Scheme 40).

3.3.3 Optimization of the 1,3-Aryl Shift Reaction

Initially, the reaction of *N*-(2-(1-hydroxyethyl)phenyl)-4-methylbenzenesulfonamide **182a** with 1-phenyl-1-propyne **229** in DCE, in the presence of 10 mol% $Ca(NTf_2)_2$ and 10 mol% Bu_4NPF_6 at room temperature for 12 h was investigated. Gratifyingly, the reaction did occur and gave both the desired rearrangement product **184a** and the direct [4+2] cylcoaddition product **184a'** in 65% isolated yield, albeit with poor selectivity (table 7, entry

1, **184a**/**184a'** = 68:32). In addition, the structure of the rearrangement product **184a** was confirmed by X-ray diffraction analysis unambiguously. Thus, further optimization of reaction conditions was then explored. Notably, the reaction efficiency was slightly improved

Table 7. Optimization of the unstrained C-C σ bond activation reaction.



Entry [a]	Catalyst (10 mol%)	Additive (X mol%)	Solvent	Yield (%)[b]	Ratio[c] **184a**/**184a'**
1	$Ca(NTf_2)_2$	Bu_4NPF_6 (10)	DCE	65	68:32
2	$Ca(NTf_2)_2$	Bu_4NPF_6 (5)	DCE	69	77:23
3	$LiNTf_2$	Bu_4NPF_6 (5)	DCE	60	64:36
4	$Mg(NTf_2)_2$	Bu_4NPF_6 (5)	DCE	84	73:27
5	$Al(OTf)_3$	Bu_4NPF_6 (5)	DCE	91	88:12
6	$Al(NTf_2)_3$	Bu_4NPF_6 (5)	DCE	81	74:26
7	$Al(OTf)_3$	------	DCE	------	------
8	TfOH (10)	Bu_4NPF_6 (5)	DCE	39	83:17
9	TfOH (10)	------	DCE	43	86:14
10	$Al(OTf)_3$	Bu_4NPF_6 (5)	CH_3NO_2	89	82:18
11	$Al(OTf)_3$	Bu_4NPF_6 (5)	DCM	84	95:5
12	$Al(OTf)_3$	Bu_4NSbF_6 (5)	DCE	50	95:5
13	$Al(OTf)_3$	Bu_4NBF_4 (5)	DCE	71	95:5
14[d]	**$Al(OTf)_3$**	**Bu_4NPF_6 (5)**	**DCE**	**87**	**95:5**
15[e]	$Al(OTf)_3$	Bu_4NPF_6 (5)	DCE	86	95:5
16[f]	$Al(OTf)_3$	Bu_4NPF_6 (5)	DCE	83	91:9

[a] Alcohols **182a** (0.3 mmol) and alkynes **229** (0.36 mmol) were added at room temperature to additives and catalysts in 1.5 mL solvent and the reaction was then stirred for 12h at rt. [b] The isolated and combined yield of **184a** and **184a'**. [c] Ratio for **184a**/**184a'** determined by ^{1}H NMR spectroscopy of the crude mixture. [d] Reaction at 40 ^{o}C. [e] Reaction at 80 ^{o}C. [f] Reaction in 3 mL DCE.

by deceasing the additive Bu_4NPF_6 loading to 5 mol% (table 7, entry 2), and $Al(OTf)_3$ (10 mol%) was identified to exhibit excellent selectivity toward the formation of the rearrangement product **184a** (table 7, entry 5, 91%, **184a**/**184a'** = 88:12) after the investigations of a series of environmentally benign catalysts (table 7, entry 3-6). However, the reaction didn't work in the absence of additives (table 7, entry 7), and 10 mol% TfOH gave low yield for the rearrangement product **184a** with good selectivity (table 7, entry 8-9). The rearrangement reaction also worked well in DCM or CH_3NO_2 as media (table 7, entry 10-11). Furthermore, the influence of several other additives such as Bu_4NSbF_6 and Bu_4NBF_4 were examined as well, but no better results were obtained (table 7, entry 12-13). After the further investigations of the reaction temperature and reaction concerntrations (table 7, entry 14-16), 10 mol% $Al(OTf)_3$/5 mol% Bu_4NPF_6 in 0.2 M DCE at 40 ^oC for 12 h were selected as the standard reaction conditions (table 7, entry 14).

3.3.4 Synthesis of Substrates

Benzylic alcohols **182** were obtained from the corresponding commercial ketones **233** and alcohols **236** according to the known methods.[57] For example, protection of amines **233** by tosyl group and subsequent reduction of ketones **235** with $NaBH_4$ gave the substrates **182a** and **182b** (Figure 21).[57a]

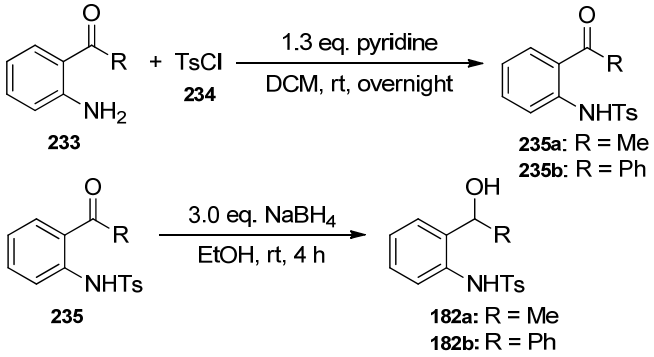
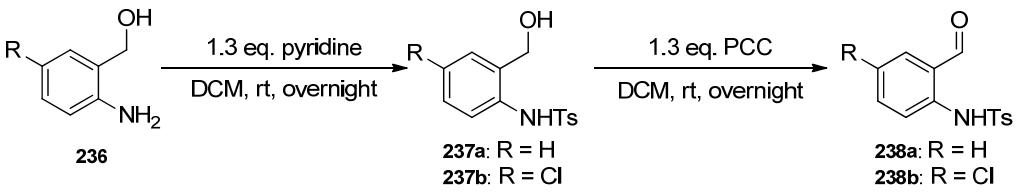


Figure 21

Aldehydes **238** were prepared from the commercial benzylic alcohols **236** through amino protection by tosyl group and subsequent oxidation of hydroxyl groups by PCC (Figure 22). Then, the nucleophilic addition of organometallic reagents **198** to the aldehyde **238** provided an easy access to the benzylic alcohols **182c**-**182e** (Figure 22).[57b]



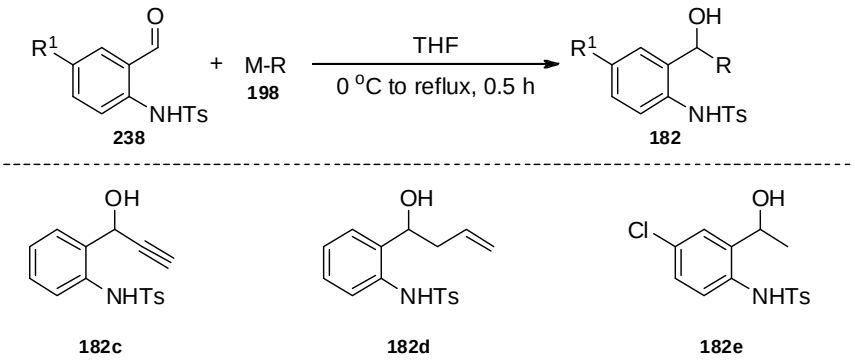


Figure 22

For the synthesis of alkynes **183**, they can be obtained by the Sonogashira coupling reaction of terminal alkynes **239** with aryl iodides **200** (Figure 23).[45] In addition, it can also be prepared from terminal alkynes **240** and methyl iodides **202** in the presence of *n*-butyllithium as a strong base (Figure 24).[46]

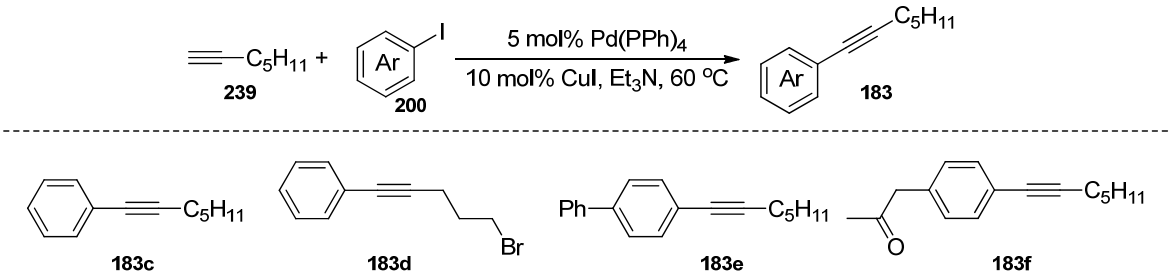


Figure 23

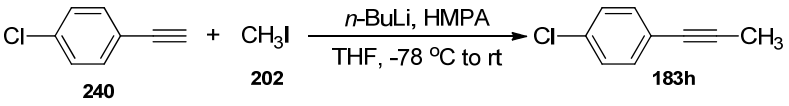


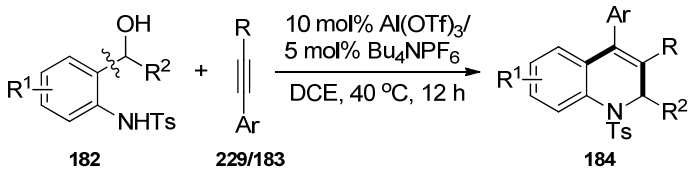
Figure 24

3.3.5 Scope of the Al(OTf)$_3$-Catalyzed 1,3-Aryl Shift Reaction

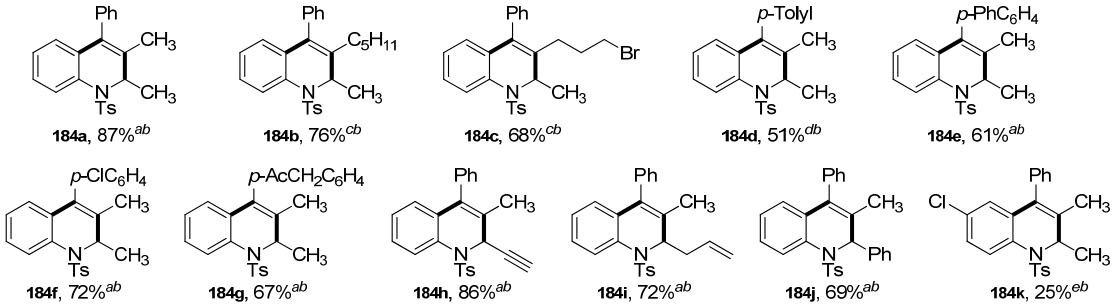
With the optimal reaction conditions in hand, the scope of this Al(OTf)$_3$-catalyzed unstrained C-C σ bond activation reaction was next investigated. As revealed in table 8, not only the aryl alkynes with long carbon chains (table 8, **184b**), the carbon chain containing bromo atom (table 8, **184c**), but also the aryl alkynes with both electron-donating (table 8, **184d-184e**) and electron-withdrawing groups (table 8, **184f-184g**) on the aromatic ring, reacted smoothly with **182a** under the standard reaction conditions. Furthermore, the reaction seems quite tolerant with respect to functional groups in both the aryl alkyne and benzylic alcohol components, such as acetyl group (table 8, **184g**) and unsaturated C-C bonds (table 8, **184h-184i**). More importantly, a wide variety of structurally diverse secondary benzylic alcohols, which bear alkynyl group, allyl group and phenyl group, can be employed as the reaction substrates and the reactions provided the desired rearrangement products in good to

excellent yields (table 8, **184h**-**184j**). However, an electron-withdrawing chloro atom on the *N*-(2-(1-hydroxyethyl)phenyl)-4-methylbenzenesulfonamide at the C4 position was not beneficial to this transformation (table 8, **184k**).

Table 8. Scope of the $Al(OTf)_3$-catalyzed 1,3-aryl shift reaction.



182 **229/183** **184**



[a] Alcohols **182** (0.3 mmol) and alkynes **229**/**183** (0.36 mmol) were added at room temperature to Bu_4NPF_6 and $Al(OTf)_3$ in 1.5 mL DCE and the reaction was then stirred at 40 °C for 12h. [b] Isolated yields of **184**. [c] Alkynes **183** (0.9 mmol) were used and the reaction was stirred at 80 °C. [d] 20 mol% $Al(OTf)_3$/10 mol% Bu_4NPF_6 were used. [e] Alkynes **229** (0.9 mmol) were used.

3.3.6 Mechanistic Study

To gain insight into a plausible reaction mechanism, more experiments have been done to understand the $Al(OTf)_3$-catalyzed unstrained C-C σ bond activation reaction. Further analysis of the reaction mixture at various reaction time revealed that the ratio for **184a**/**184a'** was rising from beginning to end with the increasing conversion of the starting materials (Figure 25).

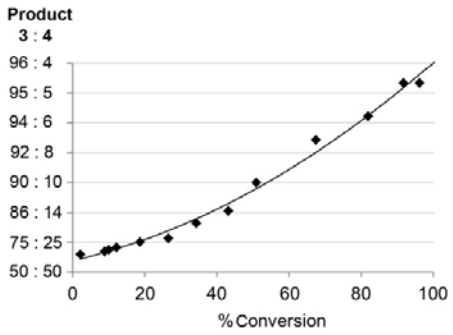
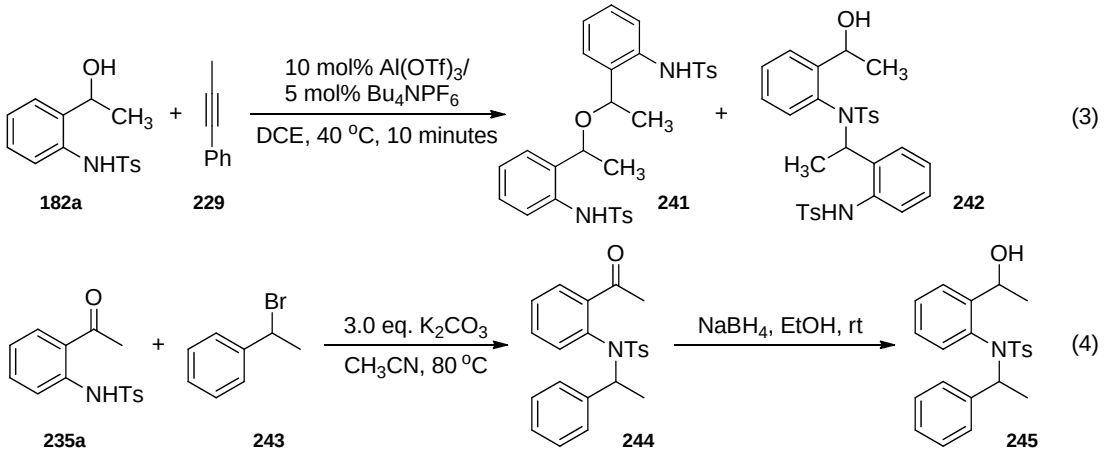
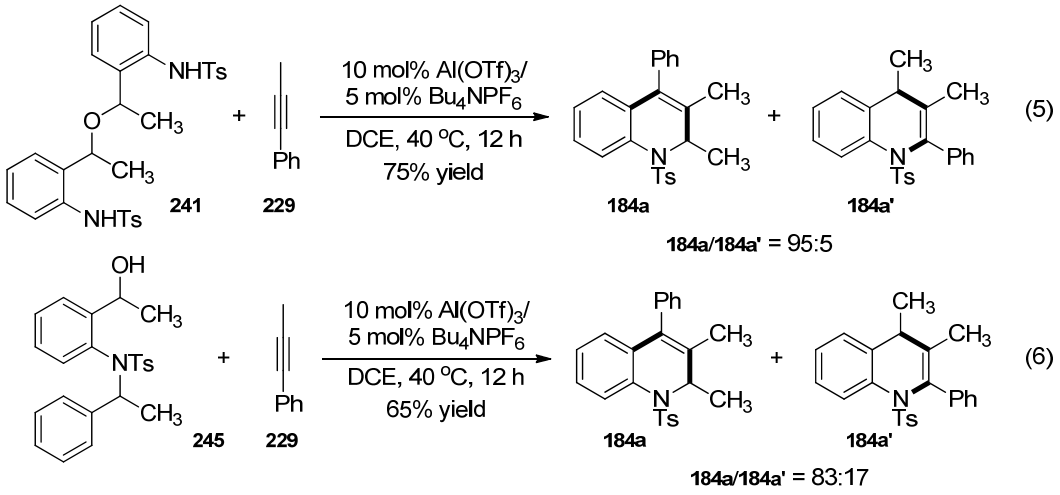


Figure 25

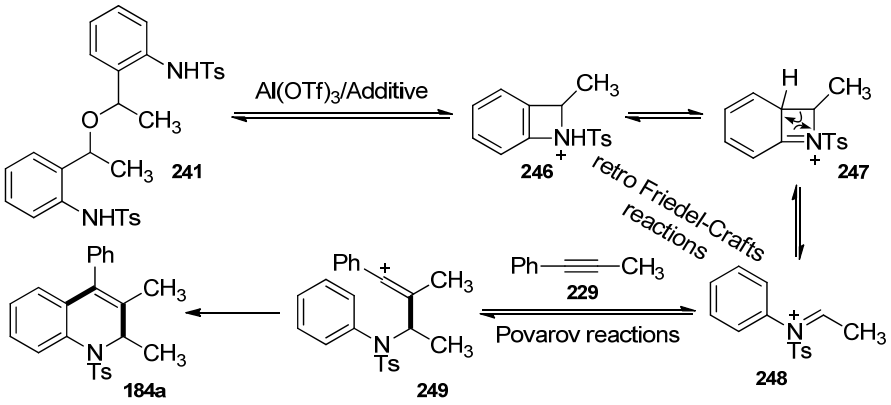
Dimers **241** as well as small amounts of asymmetric dimers **242** were obtained by preparative HPLC when the model reaction was quenched after 10 minutes (eqn(3)). Because the isolation of the asymmetric dimer **242** was very difficult, its analogue **245** was prepared



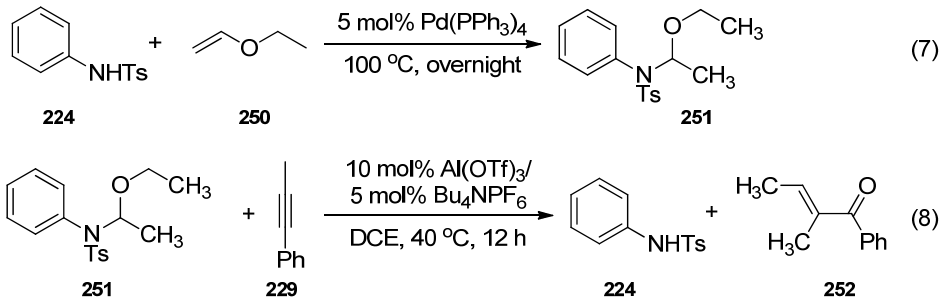
according to the literature (eqn(4)).[58] Then, **241** and **245** reacted with **229** under the standard reaction conditions. The rearrangement product **184a** was exclusively obtained when using the dimer **241** (eqn(5)). However, the selectivity decreased for the compound **245**, presumably because of the more difficult ionization of C-N bonds (eqn(6)).



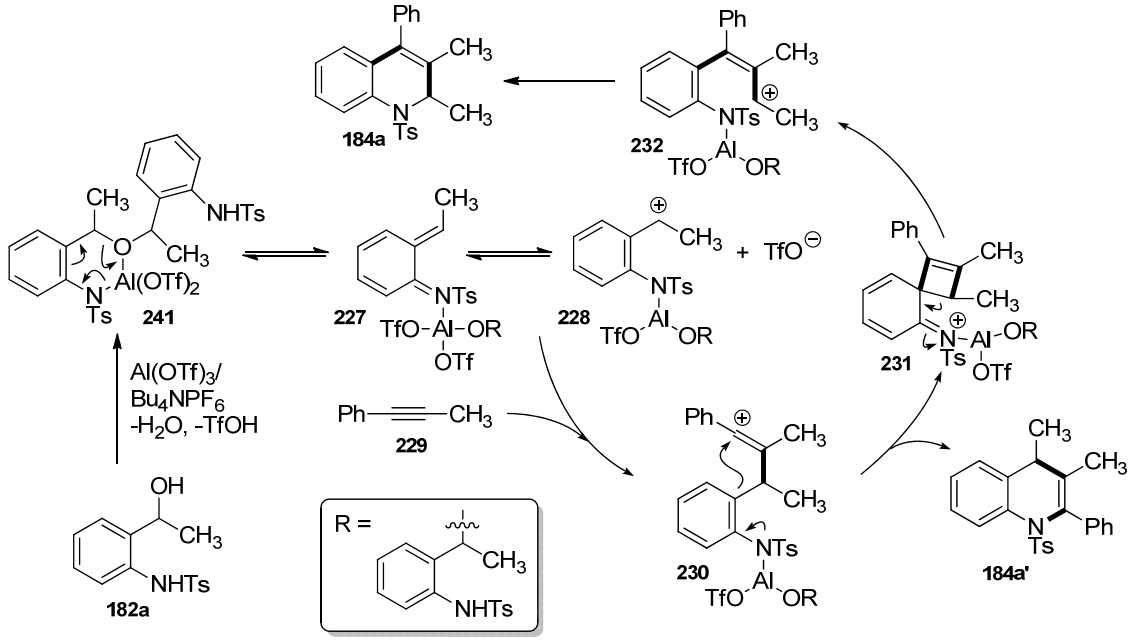
There is an alternative reaction pathway to explain the formation of the rearrangement product **184a**. The reaction might proceed through retro Friedel-Crafts/Povarov reaction sequences, such as these illustrated in Scheme 41. To prove the hypothesis, acetals **251** that can be easily converted into iminiums **248** under the acidic reaction conditions were prepared according to the literature (eqn(7)).[59] Then, the acetal **251** reacted with **229** under the standard reaction conditions, whereas none of the desired product **184a** was observed, unsaturated ketones **252** were obtained by alkyne-carbonyl metathesis reactions in high yield (eqn(8)).[60] Therefore, the retro Friedel-Crafts/Povarov reaction mechanism was clearly excluded from this transformation.



Scheme 41. Retro Friedel-Crafts reaction/Povarov reaction pathways.



While a precise reaction mechanism for the $Al(OTf)_3$-catalyzed unstrained C-C σ bond activation reaction awaits further study, a plausible reaction mechanism is outlined in Scheme 42. The reaction began with the $Al(OTf)_3$-catalyzed dehydroxylation process of **182a** to generate dimers **241**, which were then further transformed into *ortho*-azaquinone methides **227** and carbocations **228**. Subsequently, trisubstituted highly reactive vinyl cations **230** were



Scheme 42. Possible mechanism for the $Al(OTf)_3$-catalyzed 1,3-aryl shift reaction.

produced by the nucleophilic addition of alkynes **229** to the electrophilic intermediates **227**/**228**, which were then trapped by the tethered nitrogen nucleophiles to give the direct [4+2] cycloaddition product **184a'**. Meanwhile, a 4-*ipso* cyclization would occur on the phenyl ring, providing highly unstable four-membered spiro ring intermediates **231**. Thereupon, the highly unstable four-membered spiro ring intermediate **231** underwent intramolecular 1,3-aryl migration, leading to a stable allylic carbocation intermediate **232**, which was subsequently intercepted by the tethered nitrogen nucleophiles to afford the eventual rearrangement product **184a**. The excellent selectivity toward the formation of the rearrangement product **184** seems to be derived from the Al-coordination at the nitrogen atom.

3.3.7 Conclusion

In summary, a new concept for a redox-neutral C-C bond functionalization based on intramolecular 1,3-aryl migration has been developed. The redox-neutral C-C σ bond activation reaction was selectively and efficiently promoted by trisubstituted highly reactive vinyl cations in the presence of 10 mol% $Al(OTf)_3$ as a catalyst. Furthermore, a plausible retro Friedel-Crafts/Povarov reaction mechanism was clearly excluded from this novel transformation by reacting acetals **251** with alkynes, and a highly unstable four-membered spiro ring intermediate **231** leading to the rearrangement product **184a** was proposed in the reaction.

3.4. A Novel Approach to 2*H*-Chromenes through $Al(OTf)_3$-Catalyzed Unstrained C-C σ Bond Activation

3.4.1 Background

2*H*-Chromenes are ubiquitous structural motifs frequently found in not only natural isolates (such as tannins and polyphenols found in teas, fruits, and vegetables), but also pharmaceuticals and materials (such as sex-pheromones, breast cancer treatment and photochromic materials, and selected examples shown in Figure 26).[61] Therefore, the synthesis of such a framework has intrigued and inspired synthetic organic chemists over the past decade, and a variety of methods are documented in the literature.[61c] Most of them are dependent on transition-metal catalyzed reactions, such as Co^{II}-catalyzed radical reactions of salicyl *N*-tosylhydrazones with phenylacetylenes,[62] Au-catalyzed cyclization of aryl propargyl ethers,[63] Ru-catalyzed ring-closing methathesis (RCM) reactions of styrenyl ethers[64] and Ni-catalyzed functional group transformations between chromene acetals and boronic acids.[65] In recent years, organocatalysis has become an ideal tool for the synthesis of 2*H*-chromenes.[61c] Despite advances, the approaches suffer from multi-step reaction sequences, limited functional group tolerance and formation of regio-isomeric mixtures.[61c,14]

Particularly, transition-metal catalysts or complex prefunctionlized fragments are required in most cases.[61c] Therefore, the development of more efficient and sustainable alternatives is certainly highly desirable.

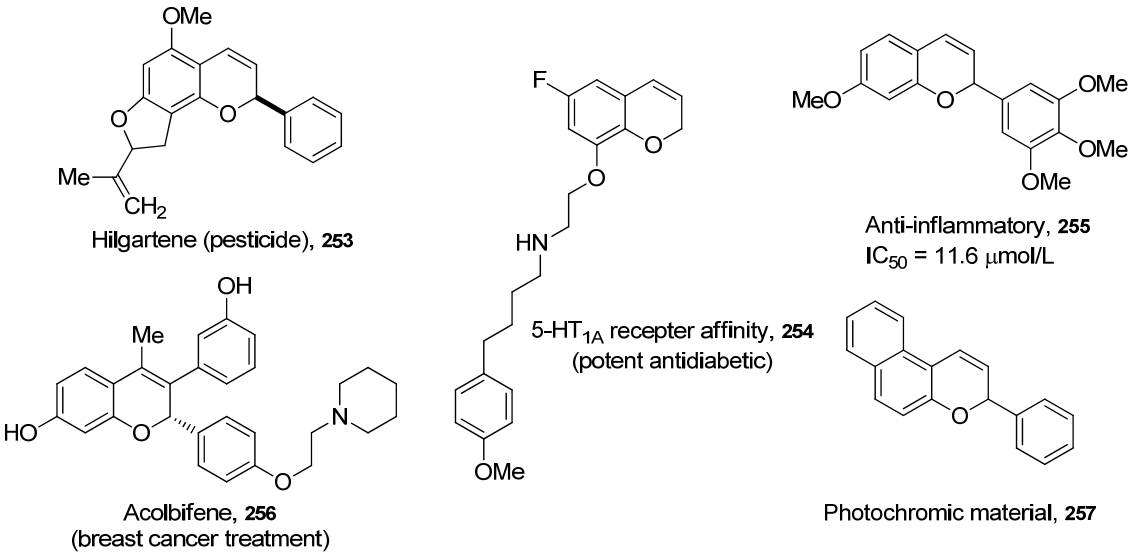
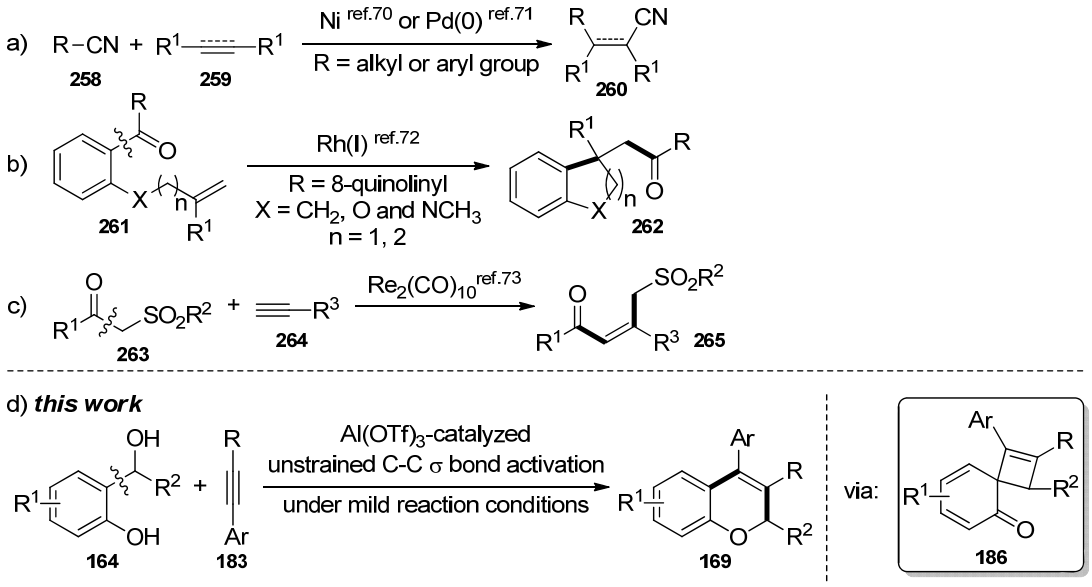


Figure 26

Ever-increasing demand for "green chemistry" urges to develop highly economical and eco-friendly C-C bond-forming reactions.[66] In this regard, cleavage of a C-C σ bond followed by insertion of an unsaturated C-C bond unit, namely, simultaneous formation of two new C-C bonds should have extremely great synthetic potentials.[67] Nevertheless, reported examples with regard to success of these processes rely on the C-C σ bond cleavage of constrained small-ring molecules by the release of strain energy.[68,69] In addition, remarkable progress has recently been made in transition-metal catalyzed reactions, which are limited to nitriles **258**[70,71] (Scheme 43, a), acylquinolines **261**[72] (Scheme 43, b) and



Scheme 43. Insertion of an unsaturated C-C bond into an unstrained C-C σ bond.

β-keto sulfones **263**[73] (Scheme 43, c) as the unconstrained reaction substrates. Consequently, they lack generality and are not environmentally friendly. On the contrary, no such transition-metal free reactions through unstrained C-C σ bond activation are documented to date. Therefore, the first $Al(OTf)_3$-catalyzed process of insertion of an unactivated alkyne into an unstrained C-C σ bond has been developed here (Scheme 43, d). This alkyne insertion reaction proceeds through the C-C σ bond cleavage of benzylic alcohols **164** and allows for the direct and efficient synthesis of structurally diverse multi-substituted 2*H*-chromenes **169** under very mild reaction conditions.

3.4.2 Aims

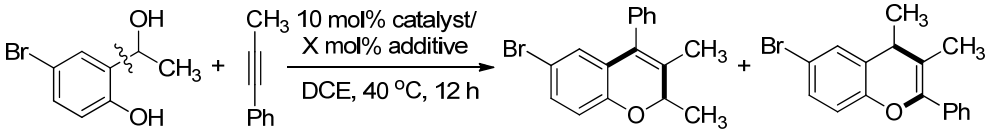
As an extension of the redox-neutral C-C bond activation reaction, the development of more efficient and sustainable approaches for the synthesis of 2*H*-chromenes was also projected. Although a variety of methods for the synthesis of 2*H*-chromenes are documented in the literature,[61c] the approaches suffer from multi-step reaction sequences, limited functional group tolerance and formation of regio-isomeric mixtures. Particularly, transition-metal catalysts and complex prefunctionlized fragments are required in most cases. Therefore, the first transition-metal free alkyne insertion reaction proceeding through the C-C σ bond cleavage of benzylic alcohols **164** is investigated in this project, which provides an elegant protocol for the direct synthesis of multi-substituted 2*H*-chromenes **169** (Scheme 43, d).

3.4.3 Optimization of the Unstrained C-C σ Bond Activation Reaction

Initially, the reaction of 4-bromo-2-(1-hydroxyethyl)phenol **164b** with 1-phenyl-1-propyne **229** in DCE, in the presence of 10 mol% $Al(OTf)_3$ and 5 mol% Bu_4NPF_6 at 40 ^oC for 12 h was investigated. Gratifyingly, the alkyne insertion reaction did occur and gave both the rearrangement adduct **169a** and the direct [4+2] cylcoaddition product **166k** in 78% isolated yield, albeit with poor selectivity (table 9, entry 1, **169a**/**166k** = 60:40). In addition, the structure of the adduct **169a** was confirmed by X-ray diffraction analysis unambiguously. Thus, the influence of several additives was then investigated (table 9, entry 2-4), and it was pleased to find that the additives had great effect on the reaction efficiency. For example, the additive NH_4PF_6 afforded an excellent yield for the products with poor selectivity (table 9, entry 3, **169a**/**166k** = 61:39), while the additive Bu_4NSbF_6 provided improved selectivity but low yields (table 10, entry 4, **169a**/**166k** = 80:20). Based on these observations, the mixed additives by the combination of 15 mol% NH_4PF_6 and 5 mol% Bu_4NSbF_6 were therefore examined for the reaction. Gratifyingly, the product **169a** was obtained in 70% yield with excellent selectivity (table 9, entry 5, **169a**/**166k** = 92:8). Furthermore, other environmentally benign catalysts were explored as well in order to improve the reaction efficiency further (table 9, entry 6-9), but no better results were obtained. Notably, the reaction didn't work in the absence of additives (table 9, entry 10) and 30 mol%

TfOH provided poor selectivity for the reaction without additives (table 9, entry 11, **169a**/**166k** = 65:35). From these optimization results, 10 mol% $Al(OTf)_3$/15 mol% NH_4PF_6/5 mol% Bu_4NSbF_6 in DCE at 40 °C for 12 h were selected as the standard reaction conditions (table 9, entry 5).

Table 9. Optimization of reaction conditions.



164b **229** **169a** **166k**

Entry [a]	Catalyst (10 mol%)	Additive (X mol%)	Yield (%)	Ratio (**169a**/**166k**)
1	$Al(OTf)_3$	Bu_4NPF_6 (5)	78	60:40
2	$Al(OTf)_3$	Bu_4NBF_4 (5)	82	62:38
3	$Al(OTf)_3$	NH_4PF_6 (5)	89	61:39
4	$Al(OTf)_3$	Bu_4NSbF_6 (5)	46	80:20
5	**$Al(OTf)_3$**	**NH_4PF_6 (15)/Bu_4NSbF_6 (5)**	**70**	**92:8**
6	$Al(NTf_2)_3$	NH_4PF_6 (15)/Bu_4NSbF_6 (5)	74	84:16
7	$Ca(NTf_2)_2$	NH_4PF_6 (15)/Bu_4NSbF_6 (5)	72	81:19
8	$Mg(NTf_2)_2$	NH_4PF_6 (15)/Bu_4NSbF_6 (5)	69	86:14
9	$Zn(OTf)_2$	NH_4PF_6 (15)/Bu_4NSbF_6 (5)	75	88:12
10	$Al(OTf)_3$	none	NR	------
11	TfOH (30)	none	87	65:35
12	TfOH (30)	NH_4PF_6 (15)/Bu_4NSbF_6 (5)	68	92:8

[a] Reaction conditions: to a suspension of 10 mol% catalysts in 4 mL dried DCE, **164b** (86.8 mg, 0.4 mmol), **229** (69.7 mg, 0.6 mmol) and additives were added, the reaction was then stirred at 40 °C for 12 h. [b] Yields of the isolated and combined products. [c] Ratio for **169a**/**166k** was determined by ^{1}H NMR spectroscopy of the crude mixture.

3.4.4 Synthesis of Substrates

Benzylic alcohols **164** were obtained according to the aforementioned methods.[39a] The nucleophilic addition of organometallic reagents **198** to aldehydes **197** allowed for the straightforward synthesis of the benzylic alcohols **164j**-**164o** (Figure 27).

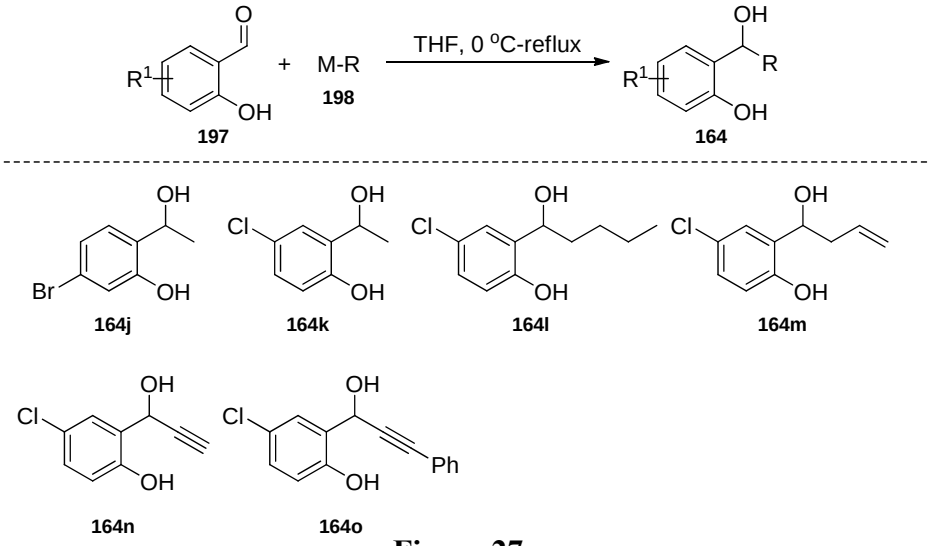
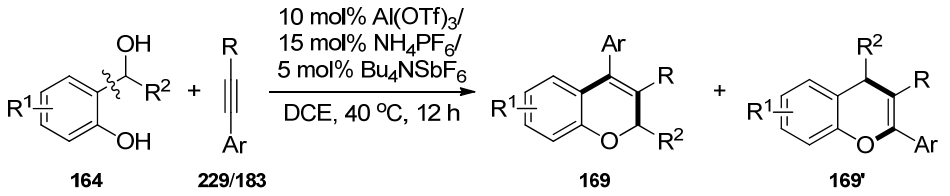


Figure 27

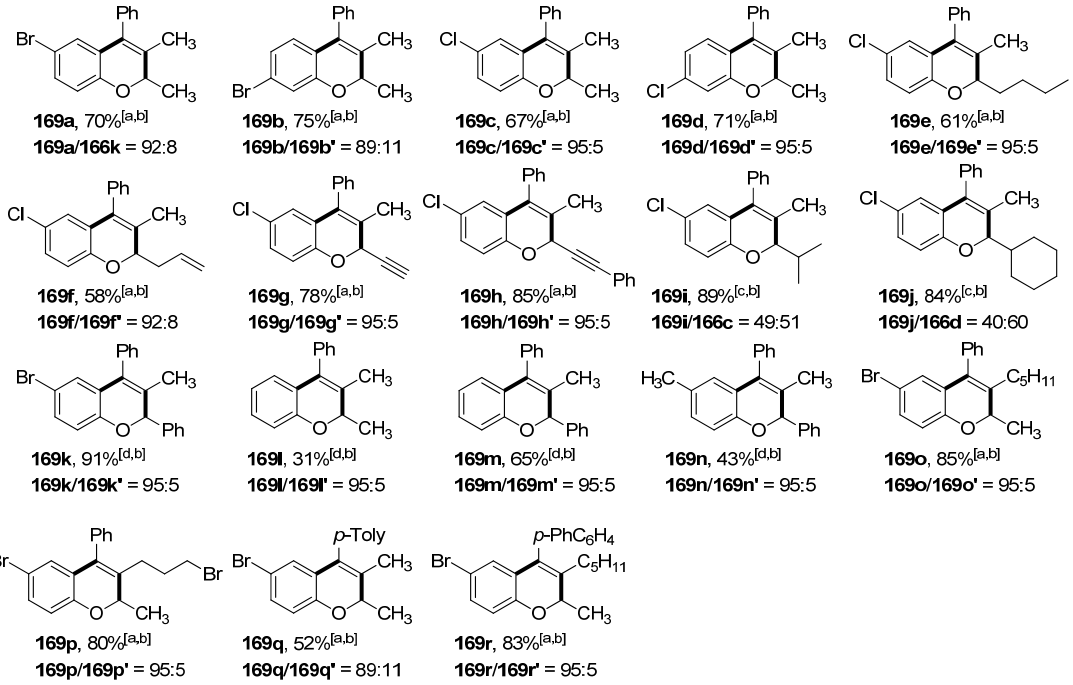
3.4.5 Scope of the $Al(OTf)_3$-Catalyzed Unstrained C-C σ bond activation reaction

With the optimized reaction conditions in hand, the substrate scope of this $Al(OTf)_3$-catalyzed unstrained C-C σ bond activation reaction was next investigated. Bromo atom and chloro atom, which not only can prevent polymerization of benzylic alcohols by decreasing the electron density on the benzene ring, but also are regarded as excellent coupling functional groups in transition-metal catalyzed reactions, can be introduced on the 2-(1-hydroxyethyl)phenol at both the C4 and C5 positions without loss in reaction efficiency (table 10, **169a**-**d**). Importantly, a wide variety of structurally diverse secondary benzylic alcohols, which bear *n*-butyl group, allyl group, alkynyl group and even sterically hindered groups, can be employed as the reaction substrates and the reactions afforded the desired 2*H*-chromene adducts in good to excellent yields with excellent selectivity (table 10, **169e**-**169k**), except for the products **169i** and **169j** with poor selectivity. Although the reaction of 2-(1-hydroxyethyl)phenol **164c** gave the corresponding product **169l** in 31% yield, due to its polymerization (table 10, **169l**), the reactivity was restored by changing the R^2 group from methyl group to phenyl group (table 10, **169m**). Furthermore, an electron-donating methyl group can be introduced on the 2-(hydroxy(phenyl)methyl)phenol at the C4 position by the same strategy (table 10, **169n**). More importantly, structural variation in the aryl alkyne component can also be realized. Not only the aryl alkynes with long carbon chains (table 10, **169o**), the carbon chain containing bromo atom (table 10, **169p**), but also the aryl alkynes with electron-donating groups on the aromatic ring (table 10, **169q**-**169r**) reacted successfully with **164b** under the standard reaction conditions.

Table 10. Scope of the unstrained C-C σ bond activation reaction.



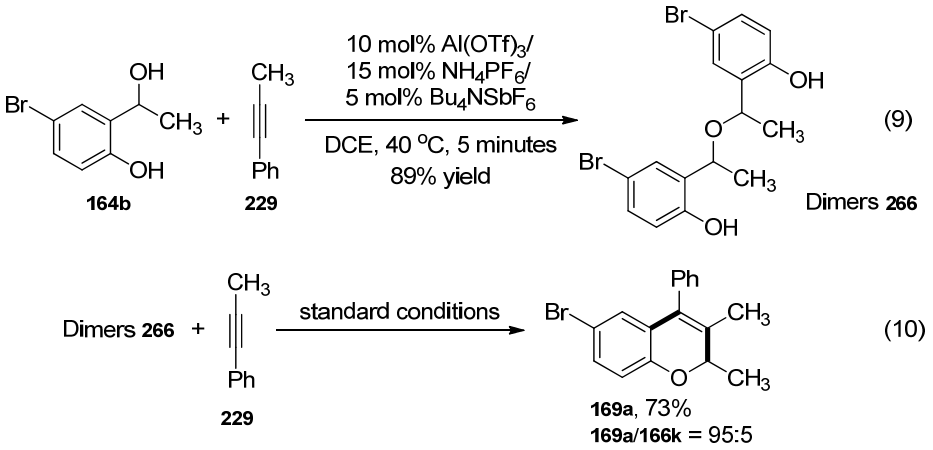
164 **229/183** **169** **169'**



[a] Reaction conditions: to a suspension of 10 mol% $Al(OTf)_3$ (19.0 mg, 0.04 mmol) in 4 mL dried DCE, **164** (0.4 mmol), **183**/**229** (0.6 mmol), NH_4PF_6 (9.8 mg, 0.06 mmol) and Bu_4NSbF_6 (9.6 mg, 0.02 mmol) were added, the reaction was then stirred at 40 °C for 12 h. [b] Yields of isolated products. [c] 10 mol% $Al(OTf)_3$ and 5 mol% NH_4PF_6 were used. [d] 10 mol% $Mg(OTf)_2$/5 mol% NH_4PF_6 and 4 mL DCE/CH_3NO_2 (1:1) were used. [e] Ratio for **169**/**169'** determined by ^1H NMR spectroscopy of the crude mixture.

3.4.6 Mechanistic Study

To gain insight into a plausible reaction mechanism for the $Al(OTf)_3$-catalyzed unstrained C-C σ bond activation reaction, the model reaction was stopped after 5 minutes and dimers **266** were obtained in 89% isolated yield (eqn (9)). The dimer **266** then reacted with **229** under the standard reaction conditions, both the yield and selectivity were slightly improved compared to the model reaction (eqn (10)). Moreover, further analysis of the model reaction mixture at various reaction time revealed that the ratio for **169a**/**166k** was rising from beginning to end. At the beginning of the reaction, the ratio was very low, but it was remarkably improved within two hours (up to 87:13). Therefore, based on these experiments, a proposed reaction mechanism is described as these shown in Scheme 42.



3.4.7 Conclusion

In conclusion, the first transition-metal free process of insertion of an unactivated alkyne into an unstrained C-C σ bond has been developed. This alkyne insertion reaction proceeds through the C-C σ bond cleavage of benzylic alcohols **164** and provides an efficient access to potentially biologically active multi-substituted 2*H*-chromenes **169** from readily available starting materials. Eighteen representative adducts were obtained by this methodology in moderate to excellent yields (31-91%) under very mild reaction conditions. In addition, 10 mol% $Al(OTf)_3$/15 mol% NH_4PF_6/5 mol% Bu_4NSbF_6 were identified to exhibit excellent selectivity toward the formation of the rearrangement products **169**. Furthermore, a highly unstable four-membered spiro ring intermediate **186** leading to the rearrangement products **169** was proposed in the reaction.

4. Summary and Outlook

In conclusion, the environmentally friendly aluminum or calcium-catalyzed electrophilic cyclizations of alkynes via vinyl cations have been developed. In these reactions, trisubstituted highly reactive vinyl cations were generated by the nucleophilic addition of alkynes to the carbocations that were produced from alcohols by aluminum or calcium catalysis. Subsequently, it was intercepted by hydroxyl groups or aromatic nucleophiles, leading to the formation of 4*H*-chromenes and all-carbon tetrasubstituted olefins respectively. Furthermore, the first transition-metal free alkyne insertion reaction through unstrained C-C σ bond activation was efficiently promoted by the trisubstituted highly reactive vinyl cations in the presence of 10 mol% $Al(OTf)_3$ as a catalyst, which provided a novel protocol for the straightforward and efficient synthesis of structurally diverse 1,2-dihydroquinolines and 2*H*-chromenes.

In a first project, an unprecedented inverse electron demand hetero-Diels-Alder reaction (IED/HDA) of alkynes with in situ generated *ortho*-quinone methides has been described, which offers a new protocol for the straightforward and efficient synthesis of structurally diverse multi-substituted 4*H*-chromenes from readily available starting materials under very mild reaction conditions. Either a concerted mechanism or a stepwise mechanism via vinyl cations was proposed for the reaction. In the stepwise mechanism, the trisubstituted highly reactive vinyl cations would be trapped by the tethered phenolic hydroxyl group.

In a second project, the first transition-metal free carboarylation of alkynes with readily available alcohols has been realized in the presence of non-toxic and abundant calcium catalysts, which allows for the one-step synthesis of all-carbon tetrasubstituted olefins from alkynes. A trisubstituted highly reactive vinyl cation was generated in the carboarylation process, which was intercepted even by deactivated arenes as the tethered nucleophiles.

In a third project, a new concept for a redox-neutral C-C bond functionalization based on intramolecular 1,3-aryl migration has been demonstrated. The redox-neutral C-C σ bond activation reaction was selectively and efficiently promoted by trisubstituted highly reactive vinyl cations in the presence of 10 mol% $Al(OTf)_3$ as a catalyst.

In the last project, a novel approach to 2*H*-chromenes through $Al(OTf)_3$-catalyzed unstrained C-C σ bond activation has been developed. The first transition-metal free process of insertion of an unactivated alkyne into an unstrained C-C σ bond was selectively and efficiently promoted by trisubstituted highly reactive vinyl cations in the presence of 10 mol% $Al(OTf)_3$ as a catalyst. This alkyne insertion reaction proceeds through the C-C σ bond cleavage of benzylic alcohols and allows for the direct and efficient synthesis of structurally diverse multi-substituted 2*H*-chromenes from readily available starting materials under very mild reaction conditions.

Future developments in the redox-neutral C-C bond activation reaction will involve the screening of suitable chiral ligands to realize a catalytic asymmetric version of alkyne insertion reactions. In addition, other different nucleophiles such as alkenes and cyclopropanes might react with in situ generated *ortho*-azaquinone methides or *ortho*-quinone methides, giving the different [4+2] cycloaddition products and the [4+3] cycloaddition products respectively. Furthermore, aluminum or calcium-catalyzed 1,5-hydride shift reactions might be realized and promoted by a vinyl cation generated by the nucleophilic addition of alkynes to the carbocations produced from π-activated alcohols.

5. Experimental Part

5.1. General Techniques

All the experimetal operations were carried out in a well ventilated hood according to the standard requirements for experimental safety in our institute. All reactions were performed in standard glassware with no special precautions taken for the exclusion of moisture or air. For air and moisture sensitive reactions, they were performed in Schlenk flasks under an inert atmosphere of argon.

5.2. Solvents

Solvents for anhydrous reactions were dried and distilled before used, DCM was dried over calcium hydride and THF was distilled from sodium/benzophenone. Ethyl acetate (EtOAc) and *n*-pentane/hexane were distilled before used for flash column chromatography. DMF, DMSO, acetonitrile, methanol and ethanol were HPLC grade solvents and they were used directly as received. DCE and CH_3NO_2 were filtered through neutral alumina before used.

5.3. Methods for Determination of Synthesized Compounds

5.3.1 NMR Spectroscopy

NMR spectra was collected on a Varian Mercury 300 spectrometer (300 MHz), a Varian Inova 400 spectrometer (400 MHz), or a Varian VNMRS 600 spectrometer (600 MHz). For ^{1}H NMR, $CHCl_3$ (7.26 ppm) or DMSO-d^6 (2.50 ppm) are used as internal standard in the same solvent; for ^{13}C NMR, $CDCl_3$ (77.00 ppm) or DMSO-d^6 (39.50 ppm) are used as internal standard in the same solvent; integrals in accordance with assignments, coupling constants are measured in Hz and always constitute $J_{H,H}$ coupling constants.

5.3.2 Mass Spectroscopy

Low-resolution and high-resolution mass spectra were obtained by using electron impact ionisation (EI) and chemical ionisation (CI) techniques, or positive and/or negative electrospray ionisation (ESI) on Finnigan SSQ or 7000 Thermo Deca XP mass spectrometers.

5.3.3 Infrared Spectroscopy

IR Spectra was recorded on a Perkin-Elmer 1760 series FT-IR as neat films on KBr plates.

5.4. Chromatography

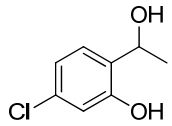
Column chromatography was performed in glass columns (10-50 mm diameter) on Merck silica gel 60, particle size 0.035-0.070 mm. Analytical thin layer chromatography (TLC) was conducted with precoated aluminium-backed plates (silica gel 60 F254) and visualized with UV radiation at 254 nm.

5.5. Experiments for Calcium-Catalyzed Synthesis of 4*H*-Chromenes

5.5.1 Experiments for Preparation of Substrates

To a solution of ketones **196** (5 mmol) in 20 mL EtOH at 0 °C was added $NaBH_4$ (15 mmol) in portions, the reaction was then warmed to room temperature and stirred for 2 h. After reaction completion, EtOH solvent was removed under reduced pressure and the residue was washed by 20 mL saturated brine. The aqueous phase was extracted with Et_2O (3×20 mL), the combined organic phases were dried over Na_2SO_4 and concentrated under reduced pressure. The crude product was purified by column chromatography.

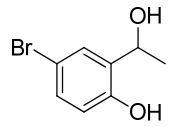
5-Chloro-2-(1-hydroxyethyl)phenol (164a)



164a

Colorless oil, R_f (pentane: EtOAc 5:1) = 0.32. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.21–8.13 (m, 1H), 6.88 (d, J = 8.1, 1H), 6.86 (s, 1H), 6.80 (dd, J = 8.1, 2.1, 1H), 5.04 (d, J = 3.6, 1H), 2.72 (s, 1H), 1.60–1.54 (m, 3H); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 156.17, 134.06, 127.28, 126.81, 119.99, 117.38, 71.21, 23.49; *m/z* (EI)(%): 172.1 (M, 78.8), 157.0 (39.3), 155.1 (100), 154.0 (74.1), 91.2 (63.8); [M+Na] HRMS calcd. for $C_8H_9O_2ClNa$: 195.01833, found: 195.01804; IR (KBr): ν = 3297, 2978, 1593 1485, 1414, 1233, 1072, 897 cm^{-1}.

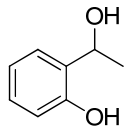
4-Bromo-2-(1-hydroxyethyl)phenol (164b)



164b

White solid, R_f (pentane: EtOAc 10:1) = 0.14. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.06 (s, 1H), 7.22 (dd, J = 8.6, 2.5, 1H), 7.07 (d, J = 2.4, 1H), 6.70 (d, J = 8.6, 1H), 4.97 (q, J = 6.6, 1H), 3.04 (s, 1H), 1.53 (d, J = 6.6, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 154.28, 131.52, 130.42, 129.12, 118.78, 111.83, 70.78, 23.30; *m/z* (EI)(%): 217.9 (M+2, 61.1), 229.9 (M, 60.6), 200.9 (94.6), 199.9 (75.5), 199.0 (100), 197.9 (75.7), 120.0 (42.2), 91.1 (63.3); IR (KBr): ν = 3348, 2977, 1586, 1477, 1361, 1234, 1071, 814, 551 cm^{-1}.

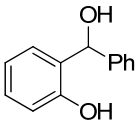
2-(1-Hydroxyethyl)phenol (164c)



164c

White solid, R_f (hexane: EtOAc 5:1) = 0.27. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.04–7.84 (m, 1H), 7.15 (td, J = 8.2, 1.6, 1H), 6.97 (dd, J = 7.5, 1.4, 1H), 6.83 (ddd, J = 14.9, 7.3, 1.0, 2H), 5.04 (d, J = 6.2, 1H), 2.76 (s, 1H), 1.56 (dd, J = 6.6, 1.9, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 155.31, 128.90, 128.36, 126.43, 119.87, 117.04, 71.56, 23.39; *m/z* (EI)(%): 138.1 (M, 56.7), 121.1 (26.2), 120.1 (100), 119.1 (29.6), 92.1 (24.6), 91.1 (81.5), 77.2 (25.1); IR (KBr): ν = 3327, 2976, 2929, 1593 1491, 1455, 1372, 1238, 1072, 893, 755 cm^{-1}.

2-(Hydroxy(phenyl)methyl)phenol (164d)

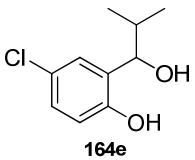


164d

White solid, R_f (hexane: EtOAc 5:1) = 0.29. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.98 (s, 1H), 7.41–7.27 (m, 5H), 7.22–7.14 (m, 1H), 6.84 (dt, J = 14.6, 7.8, 3H), 5.96 (s, 1H), 3.27 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 155.25, 141.77, 129.23, 128.66, 128.21, 128.14, 126.76, 119.93, 119.92, 117.15, 76.85; *m/z* (EI)(%): 200.1 (M, 4.1), 183.1 (8.1), 182.1 (50.4), 181.1 (100), 152.1 (10.3), 77.1 (10.1); IR (KBr): ν = 3500, 3185, 1598, 1456, 1227, 1009, 883, 748, 694 cm^{-1}.

To a solution of organometallic reagents R-M **198** (10.5 mmol) in 20 mL THF at 0 ^{o}C was added aldehydes **197** (5 mmol) slowly under an argon protective atmosphere, the reaction was then heated under reflux for 30 minutes. After the reaction cooled down to room temperature, it was quenched by 20 mL saturated NH_4Cl solution and the aqueous phase was extracted with Et_2O (2×30 mL). The combined organic phases were dried over Na_2SO_4 and concentrated under reduced pressure. The crude product was purified by column chromatography.

4-Chloro-2-(1-hydroxy-2-methylpropyl)phenol (164e)

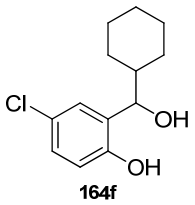


164e

Yellow oil, R_f (pentane: EtOAc 3:1) = 0.60. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.04 (s, 1H), 7.09 (dd, J = 8.7, 2.6, 1H), 6.86 (d, J = 2.6, 1H), 6.77 (d, J = 8.6, 1H), 4.47 (dd, J = 6.8, 2.2, 1H), 2.63 (s, 1H), 2.06 (dq, J = 13.1, 6.6, 1H), 1.02 (d, J = 6.7, 3H), 0.86 (d, J = 6.8, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 154.40, 128.54, 127.78, 127.36, 124.06, 118.52, 81.52, 34.37, 19.18, 17.89; *m/z* (EI)(%): 202.1 (M+2, 19.8), 200.0 (M, 58.5), 183.0 (100), 182.0 (52.7),

167.0 (37.1), 157.0 (69.4), 141.0 (39.8), 129.0 (23.6); IR (KBr): ν = 3352, 2954, 1596 1470, 1234, 1009, 814, 708 cm^{-1}.

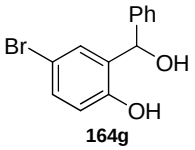
4-Chloro-2-(cyclohexyl(hydroxy)methyl)phenol (164f)



164f

Light yellow solid, R_f (pentane: EtOAc 5:1) = 0.58. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.06 (s, 1H), 7.08 (dd, J = 8.6, 2.6, 1H), 6.83 (d, J = 2.6, 1H), 6.75 (d, J = 8.6, 1H), 4.45 (dd, J = 7.1, 2.9, 1H), 2.77 (d, J = 3.2, 1H), 1.98–1.87 (m, 1H), 1.81–1.57 (m, 4H), 1.50–1.36 (m, 1H), 1.28–0.87 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 154.30, 128.46, 127.81, 127.36, 124.05, 118.41, 80.75, 43.70, 29.39, 28.40, 26.15, 25.88, 25.79; *m/z* (EI)(%): 242.0 (M+2, 21.5), 240.0 (M, 63.3), 224.9 (34.6), 224.0 (27.9), 223.0 (100), 222.0 (40.7), 156.9 (18.0), 81.1 (34.3); IR (KBr): ν = 3427, 3073, 2921, 2726, 1594, 1430, 1236, 1097, 1010, 891, 816, 727 cm^{-1}.

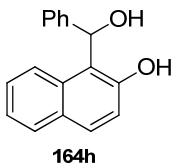
4-Bromo-2-(hydroxy(phenyl)methyl)phenol (164g)



164g

White solid, R_f (hexane: EtOAc 10:1) = 0.15. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.02 (s, 1H), 7.42–7.30 (m, 5H), 7.26 (dd, J = 8.7, 2.3, 1H), 6.97 (d, J = 2.3, 1H), 6.75 (d, J = 8.7, 1H), 5.91 (d, J = 2.7, 1H), 3.10 (d, J = 3.1, 1H); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 154.45, 141.04, 131.95, 130.69, 128.90, 128.58, 128.48, 126.77, 119.06, 111.90, 76.49; *m/z* (EI)(%): 279.9 (M+2, 12.1), 277.9 (M, 10.8), 261.9 (61.8), 260.9 (100), 259.9 (60.4), 258.9 (85.2), 151.9 (20.4); [M+Na] HRMS calcd. for $C_{13}H_{11}O_2BrNa$: 300.98346, found: 300.98309; IR (KBr): ν = 3439, 3216, 1580, 1478, 1368, 1228, 1101, 1025, 820, 692 cm^{-1}.

1-(Hydroxy(phenyl)methyl)naphthalen-2-ol (164h)

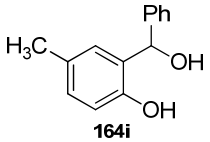


164h

Light yellow solid, R_f (hexane: EtOAc 10:1) = 0.18. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.32 (s, 1H), 7.80–7.68 (m, 2H), 7.61 (d, J = 8.4, 1H), 7.43–7.37 (m, 2H), 7.37–7.24 (m, 5H), 7.16 (d, J = 8.9, 1H), 6.71 (d, J = 2.7, 1H), 3.23 (d, J = 2.9, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 154.39, 141.19, 131.41, 130.11, 128.85, 128.73, 128.67, 128.42, 127.14, 126.76, 123.00, 121.42, 119.90, 115.74, 74.61; *m/z* (EI)(%): 250.0 (M, 25.8), 232.0 (67.7), 231.0 (100), 202.0

(15.4); IR (KBr): ν = 3368, 3027, 1604, 1464, 1405, 1326, 1216, 1157, 1062, 935, 812, 739 cm^{-1}.

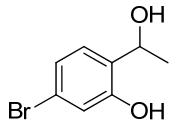
2-(Hydroxy(phenyl)methyl)-4-methylphenol (164i)



164i

White solid, R_f (hexane: EtOAc 10:1) = 0.19. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.88 (s, 1H), 7.42–7.26 (m, 5H), 6.97 (dd, J = 8.2, 2.0, 1H), 6.76 (d, J = 8.2, 1H), 6.68 (s, 1H), 5.88 (s, 1H), 3.58 (s, 1H), 2.21 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 152.72, 142.00, 129.56, 129.09, 128.61, 128.56, 127.95, 126.71, 126.54, 116.85, 76.67, 20.42; *m/z* (EI)(%): 213.9 (M, 8.2), 196.9 (9.9), 195.9 (59.4), 194.9 (100), 180.9 (6.9), 151.9 (7.0), 76.9 (13.2); IR (KBr): ν = 3331, 3035, 2925, 1607, 1493, 1377, 1232, 1011, 921, 817, 709 cm^{-1}.

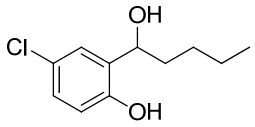
5-Bromo-2-(1-hydroxyethyl)phenol (164j)



164j

Colorless oil, R_f (pentane: EtOAc 5:1) = 0.27. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.21 (s, 1H), 6.99 (d, J = 1.9, 1H), 6.95 (dd, J = 8.1, 1.9, 1H), 6.82 (d, J = 8.2, 1H), 5.07–4.95 (m, 1H), 2.97 (s, 1H), 1.54 (d, J = 6.6, 3H); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 156.06, 127.60, 127.39, 122.98, 121.81, 120.17, 71.02, 23.36; *m/z* (EI)(%): 218.0 (M+2, 83.5), 216.0 (M, 79.3), 201.0 (64.1), 200.0 (99.0), 199.0 (55.5), 198.0 (100), 94.1 (28.0), 91.2 (83.9); [M+Na] HRMS calcd. for $C_8H_9O_2BrNa$: 238.96781, found: 238.96741; IR (KBr): ν = 3345, 2976, 1589, 1482, 1413, 1224, 1068, 878 cm^{-1}.

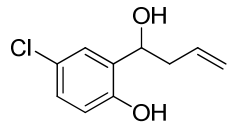
4-Chloro-2-(1-hydroxypentyl)phenol (164l)



164l

Light yellow oil, R_f (pentane: EtOAc 5:1) = 0.51. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.97 (s, 1H), 7.09 (dd, J = 8.6, 2.6, 1H), 6.89 (d, J = 2.6, 1H), 6.77 (d, J = 8.6, 1H), 4.75 (t, J = 5.8, 1H), 2.66 (s, 1H), 1.92–1.81 (m, 1H), 1.80–1.69 (m, 1H), 1.48–1.22 (m, 4H), 0.89 (t, J = 7.1, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 154.12, 128.86, 128.55, 126.83, 124.35, 118.50, 75.78, 36.78, 27.71, 22.41, 13.94; *m/z* (EI)(%): 216.1 (M+2, 38.8), 214.1 (M, 100), 199.1 (33.4), 198.1 (31.6), 197.1 (90.2), 196.1 (64.0), 169.0 (21.9), 167.0 (66.3), 157.0 (26.0), 141.0 (61.6), 132.1 (26.6); HRMS calcd. for $C_{11}H_{15}O_2{}^{35}Cl$: 214.07551, found: 214.07583; IR (KBr): ν = 3344, 2936, 1598, 1469, 1235, 1009, 844, 811 cm^{-1}.

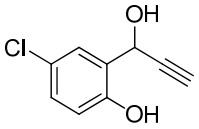
4-Chloro-2-(1-hydroxybut-3-en-1-yl)phenol (164m)



164m

Colorless oil, R_f (pentane: EtOAc 3:1) = 0.50. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.27 (s, 1H), 7.06 (dd, *J* = 8.6, 2.6, 1H), 6.93 (d, *J* = 2.6, 1H), 6.73 (d, *J* = 8.7, 1H), 5.84–5.69 (m, 1H), 5.15–5.11 (m, 1H), 5.05–4.94 (m, 1H), 4.77 (t, *J* = 6.6, 1H), 3.68 (s, 1H), 2.53 (ddd, *J* = 7.9, 4.5, 1.0, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 153.78, 133.51, 128.43, 126.75, 124.36, 119.12, 118.16, 116.17, 73.56, 41.81; *m/z* (EI)(%): 200.1 (M+2, 8.9), 198.1 (M, 23.3), 159.1 (17.4),157.0 (54.5), 85.0 (63.5), 83.0 (100); IR (KBr): ν = 3333, 2922, 1608, 1481, 1426, 1239, 1105, 1015, 905, 814 cm^{-1}.

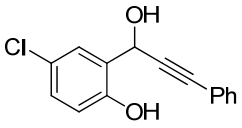
4-Chloro-2-(1-hydroxyprop-2-yn-1-yl)phenol (164n)



164n

Yellow solid, R_f (pentane: EtOAc 3:1) = 0.30. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.37 (d, *J* = 2.5, 1H), 7.24–7.17 (m, 2H), 6.82 (dd, *J* = 8.6, 2.1, 1H), 5.64 (d, *J* = 3.1, 1H), 3.22 (s, 1H), 2.79 (t, *J* = 2.0, 1H); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 153.54, 129.96, 127.43, 125.50, 125.13, 118.37, 80.80, 76.87, 62.94; *m/z* (EI)(%): 183.9 (M+2, 27.5), 181.9 (M, 87.5), 165.9 (33.3), 165.0 (33.6), 163.9 (100), 137.9 (29.7), 135.9 (84.8), 128.9 (22.3), 101.0 (33.6); IR (KBr): ν = 3287, 1600, 1484, 1421, 1231, 1109, 1011, 815 cm^{-1}.

4-Chloro-2-(1-hydroxy-3-phenylprop-2-yn-1-yl)phenol (164o)



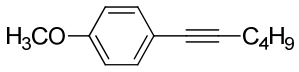
164o

Yellow solid, R_f (pentane: EtOAc 3:1) = 0.51. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.54–7.44 (m, 2H), 7.40 (d, *J* = 2.6, 1H), 7.38–7.29 (m, 4H), 7.19 (dd, *J* = 8.6, 2.6, 1H), 6.84 (t, *J* = 9.5, 1H), 5.86 (d, *J* = 5.7, 1H), 3.01 (d, *J* = 5.8, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 153.96, 131.86, 129.88, 129.10, 128.41, 127.48, 125.85, 124.94, 121.62, 118.51, 88.69, 85.72, 63.96; *m/z* (EI)(%): 258.0 (M, 12.9), 241.0 (56.6), 240.0 (69.3), 239.0 (100), 239.0 (35.3), 205.0 (98.3), 177.0 (19.2), 176.0 (33.2); IR (KBr): ν = 3296, 1596, 1484, 1412, 1235, 1111, 907, 743 cm^{-1}.

To a solution of aryl iodides **200** (5 mmol) and terminal alkynes **199**/**239** (10 mmol) in 5 mL degassed Et_3N were added $Pd(PPh_3)_4$ (0.25 mmol) and CuI (0.5 mmol) under an argon protective atmosphere, the reaction was then stirred at 60 ^{o}C for 3 hours. After the reaction cooled down to room temperature, the mixture was diluted with 30 mL EE and washed by 20

mL 1N HCl and 10 mL saturated $NaHCO_3$ solution. The aqueous phase was extracted with EE (2×30 mL), the combined organic phases were dried over Na_2SO_4 and concentrated under reduced pressure. The crude product was purified by column chromatography.

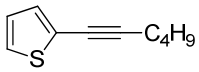
1-(*p*-Methoxyphenyl)-1-hexyne (183a)



183a

Colorless oil, R_f (hexane) = 0.41. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.36–7.27 (m, 2H), 6.83–6.73 (m, 2H), 3.78 (s, 3H), 2.37 (t, J = 7.0, 2H), 1.62–1.52 (m, 2H), 1.51–1.41 (m, 2H), 0.93 (t, J = 7.3, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 158.93, 132.81, 116.24, 113.76, 88.72, 80.18, 55.22, 30.95, 22.01, 19.08, 13.65; *m/z* (EI)(%): 188.0 (M, 100), 172.9 (38.3), 158.9 (38.2), 144.9 (84.2), 114.9 (23.4), 101.8 (28.8); IR (KBr): ν = 2933, 2867, 1605, 1506, 1458, 1287, 1243, 1173, 1032, 829 cm^{-1}.

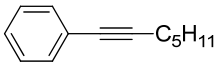
1-(2-Thienyl)-1-hexyne (183b)



183b

Colorless oil, R_f (pentane) = 0.43. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.16 (dd, J = 5.2, 1.1, 1H), 7.12–7.09 (m, 1H), 6.93 (dd, J = 5.2, 3.6, 1H), 2.43 (t, J = 7.1, 2H), 1.63–1.56 (m, 2H), 1.51–1.42 (m, 2H), 0.94 (t, J = 7.3, 3H); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 130.83, 126.71, 125.78, 124.22, 94.48, 73.59, 30.63, 22.02, 19.35, 13.62; *m/z* (EI)(%): 165.0 (M+1, 20.4), 164.0 (M, 100), 149.0 (63.7), 135.0 (59.1), 121.0 (85.4), 115.1 (23.3); IR (KBr): ν = 2936, 1519, 1441, 1189, 832, 694 cm^{-1}.

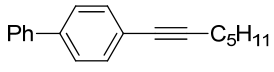
1-Phenyl-1-heptyne (183c)



183c

Brown oil, R_f (hexane) = 0.53. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.41–7.35 (m, 2H), 7.30–7.20 (m, 3H), 2.39 (t, J = 7.1, 2H), 1.60 (dt, J = 11.4, 7.1, 2H), 1.48–1.19 (m, 4H), 0.90 (dd, J = 12.9, 5.8, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 131.52, 128.15, 127.42, 124.10, 90.47, 80.53, 31.13, 28.48, 22.24, 19.39, 14.00; *m/z* (EI)(%): 165.1 (14.9), 117.1 (15.4), 105.1 (21.6), 91.1 (52.8), 57.1 (63.9), 55.1 (100); IR (KBr): ν = 3058, 2931, 2862, 1598, 1489, 1458, 755, 691 cm^{-1}.

4-(hept-1-yn-1-yl)-1,1'-biphenyl (183e)

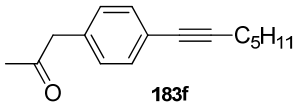


183e

Brown oil, R_f (hexane) = 0.32. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.58 (dt, J = 3.0, 1.8, 2H), 7.55–7.49 (m, 2H), 7.49–7.39 (m, 4H), 7.37–7.30 (m, 1H), 2.43 (t, J = 7.1, 2H), 1.68–1.58 (m, 2H), 1.50–1.30 (m, 4H), 0.94 (t, J = 7.2, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 140.50,

140.15, 131.92, 128.78, 127.41, 126.94, 126.84, 123.05, 91.20, 80.38, 31.14, 28.48, 22.25, 19.47, 14.01; *m/z* (EI)(%): 249.3 (M+1, 27.9), 248.3 (M, 100), 219.3 (29.1), 206.3 (14.0), 193.2 (23.0), 191.2 (25.8), 189.2 (17.5), 165.2 (12.6); IR (KBr): ν = 3038, 2932, 2320, 2100, 1597, 1476, 836, 754, 701 cm^{-1}.

1-(4-(Hept-1-yn-1-yl)phenyl)propan-2-one (183f)

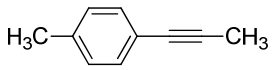


183f

Brown oil, R_f (Hex: EtOAc 5:1) = 0.45. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.34 (d, J = 8 Hz, 2 H), 7.10 (d, J = 8 Hz, 2 H), 3.65 (s, 2 H), 2.37 (t, J = 7 Hz, 2 H), 2.12 (s, 3 H), 1.58 (q, J = 7 Hz, 2 H), 1.41 (m, 2 H), 1.34 (m, 2 H), 0.90 (t, J = 7 Hz, 3 H); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 206.0, 133.5, 131.9, 129.2, 123.0, 90.7, 80.1, 50.8, 31.1, 29.3, 28.4, 22.2, 19.4, 14.0; *m/z* (EI)(%): 228.3 (M-1); IR (KBr): ν = 3853, 3746, 3615, 3530, 3336, 3100, 3013, 2933, 2670, 2324, 2091, 1995, 1901, 1739, 1541, 1453, 1364, 1217, 1098, 990, 897, 839, 782, 696 cm^{-1}.

To a solution of terminal alkynes **201**/**240** (5 mmol) in 10 mL THF at -78 ^{o}C was slowly added *n*-BuLi (7 mmol) under an argon protective atmosphere, the reaction was stirred at -78 ^{o}C for one hour, then a iodomethane solution (10 mmol CH_3I in 10 mL THF) was added dropwise into the flask. The reaction was warmed to room temperature and stirred overnight. After reaction completion, the mixture was quenched by 20 mL saturated brine and the aqueous phase was extracted with Et_2O (3×20 mL). The combined organic phases were dried over Na_2SO_4 and concentrated under reduced pressure. The crude product was purified by column chromatography.

1- (*p*-Tolyl)-1-propyne (183g)



183g

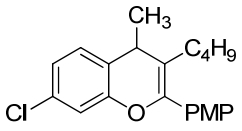
Colorless oil, R_f (hexane) = 0.50. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.28 (d, J = 8.1, 2H), 7.10–7.04 (m, 2H), 2.32 (s, 3H), 2.03 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 137.43, 131.32, 128.93, 120.91, 84.91, 79.72, 21.36, 4.29; *m/z* (EI)(%): 130.7 (M, 14.7), 129.8 (33.3), 128.8 (63.9), 128.1 (32.4), 127.1 (100), 102.5 (23.7), 54.7 (27.2); IR (KBr): ν = 3028, 2919, 2859, 1509, 1445, 1382, 1107, 1031, 816, 526 cm^{-1}.

5.5.2 General Experiment for the Calcium-Catalyzed Synthesis of 4*H*-Chromenes

To a solution of 5-chloro-2-(1-hydroxyethyl)phenols **164a** (0.4 mmol) and 1-(*p*-Methoxyphenyl)-1-hexynes **183a** (0.6 mmol) in 4 mL DCE were added Bu_4NPF_6 (0.01 mmol) and $Ca(NTf_2)_2$ (0.01 mmol), the reaction was then stirred at 40 ^{o}C for 12 h. For the isolation of the product **166a**, 5 mL saturated $NaHCO_3$ solution was added, and the aqueous

phase was extracted with dichloromethane (2×10 mL). The combined organic phases were dried over Na_2SO_4 and concentrated in *vacuo*. The crude product was purified by column chromatography.

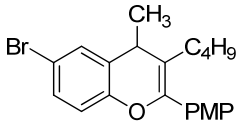
3-Butyl-7-chloro-2-(4-methoxyphenyl)-4-methyl-4*H*-chromene (166a)



166a

Colorless oil, R_f (pentane: EtOAc 40:1) = 0.35. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.38–7.29 (m, 2H), 7.05 (d, J = 8.1, 1H), 7.02–6.94 (m, 2H), 6.94–6.88 (m, 2H), 3.83 (s, 3H), 3.44 (q, J = 6.9, 1H), 2.23 (ddd, J = 14.0, 9.9, 6.7, 1H), 2.11 (ddd, J = 14.2, 9.7, 4.8, 1H), 1.53–1.40 (m, 1H), 1.39–1.10 (m, 6H, 1/2-CH_2, -CH_2 and -CH_3), 0.80 (t, J = 7.3, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 159.44, 152.48, 144.90, 131.94, 130.31, 128.81, 127.58, 125.67, 123.04, 116.18, 114.50, 113.48, 55.27, 32.01, 30.18, 29.27, 23.92, 22.44, 13.88; *m/z* (CI)(%): 345.2(28.6), 344.3(27.1), 343.3 (M+1, 100), 342.3 (16.0), 327.2 (11.7), 307.2 (1.4), 135.3 (0.9); [M+1] HRMS calcd. for $C_{21}H_{24}O_2{}^{35}Cl$: 343.14593, found: 343.14496; IR (KBr): ν = 2944, 1671, 1593, 1485, 1242, 1175, 1083, 898, 830, 729 cm^{-1}.

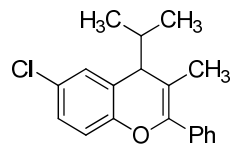
6-Bromo-3-butyl-2-(4-methoxyphenyl)-4-methyl-4*H*-chromene (166b)



166b

Colorless oil, R_f (pentane: EtOAc 40:1) = 0.41. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.37–7.32 (m, 2H), 7.26 (d, J = 2.5, 1H), 7.23 (dd, J = 8.6, 2.4, 1H), 6.94–6.90 (m, 2H), 6.83 (d, J = 8.6, 1H), 3.84 (s, 3H), 3.44 (q, J = 6.9, 1H), 2.23 (ddd, J = 14.1, 9.9, 6.7, 1H), 2.11 (ddd, J = 14.3, 9.8, 4.8, 1H), 1.51–1.42 (m, 1H), 1.38–1.30 (m, 4H, 1/2-CH_2 and -CH_3), 1.30–1.15 (m, 2H), 0.82 (t, J = 7.3, 3H); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 159.46, 151.08, 145.06, 130.54, 130.30, 129.76, 129.27, 127.66, 117.75, 114.78, 114.12, 113.50, 55.28, 32.36, 30.20, 29.25, 23.90, 22.43, 13.88; *m/z* (EI)(%): 388.1 (M+2, 2.1), 386.1 (M, 2.4), 373.1 (12.4), 371.1 (12.2), 268.0 (8.3), 266.0 (8.8), 136.1 (8.5), 135.0 (100), 77.1 (7.3); [M+1] HRMS calcd. for $C_{21}H_{24}O_2{}^{79}Br$: 387.09542, found: 387.09528; IR (KBr): ν = 2942, 1710, 1603, 1475, 1238, 1179, 1099, 1038, 823, 665, 551 cm^{-1}.

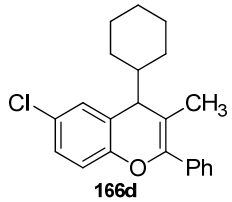
6-Chloro-4-isopropyl-3-methyl-2-phenyl-4*H*-chromene (166c)



166c

Colorless oil, R_f (pentane: EtOAc 40:1) = 0.75. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.51–7.43 (m, 2H), 7.43–7.36 (m, 2H), 7.36–7.30 (m, 1H), 7.14 (dd, *J* = 8.6, 2.5, 1H), 7.05 (d, *J* = 2.5, 1H), 6.95 (d, *J* = 8.6, 1H), 3.10 (d, *J* = 3.6, 1H), 2.04 (dtd, *J* = 13.8, 6.9, 3.7, 1H), 1.88 (s, 3H), 1.00 (d, *J* = 6.9, 3H), 0.80 (d, *J* = 6.9, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 151.99, 146.19, 135.01, 128.93, 128.46, 128.25, 128.04, 127.10, 126.95, 124.84, 116.99, 108.85, 48.18, 33.66, 20.23, 18.50, 18.01; *m/z* (CI)(%): 301.1 (37.1), 300.1 (27.7), 299.1 (M+1, 100), 298.0 (9.6), 257.1 (29.1), 256.1 (14.7), 255.1 (84.5), 105.1 (10.3); HRMS calcd. for $C_{19}H_{19}O^{35}Cl$: 298.11189, found: 298.11138; IR (KBr): ν = 3056, 2954, 1581, 1473, 1241, 1088, 1006, 897, 814, 704 cm^{-1}.

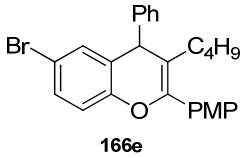
6-Chloro-4-cyclohexyl-3-methyl-2-phenyl-4*H*-chromene (166d)



166d

Colorless oil, R_f (pentane) = 0.40. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.47 (dt, *J* = 8.2, 1.8, 2H), 7.42–7.35 (m, 2H), 7.35–7.30 (m, 1H), 7.13 (dd, *J* = 8.6, 2.5, 1H), 7.03 (d, *J* = 2.5, 1H), 6.94 (d, *J* = 8.6, 1H), 3.06 (d, *J* = 3.7, 1H), 1.89 (s, 3H), 1.82–1.55 (m, 6H), 1.26–1.09 (m, 3H), 1.02 (ddt, *J* = 16.2, 12.6, 6.2, 1H), 0.73 (qd, *J* = 12.4, 3.4, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 152.02, 146.34, 134.98, 128.92, 128.42, 128.23, 128.02, 127.09, 126.86, 125.65, 116.95, 108.89, 48.13, 44.05, 30.80, 28.58, 26.74, 26.62, 26.30, 18.64; *m/z* (CI)(%): 341.2 (28.2), 340.2 (26.2), 339.2 (M+1, 100), 338.1 (M, 17.4), 337.1 (11.4), 257.1 (18.8), 255.1 (47.1); HRMS calcd. for $C_{22}H_{23}O^{35}Cl$: 338.14319, found: 338.14311; IR (KBr): ν = 2923, 2859, 1726, 1595, 1473, 1240, 1084, 1009, 902, 815, 709 cm^{-1}.

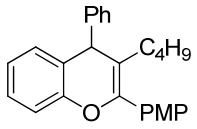
6-Bromo-3-butyl-2-(4-methoxyphenyl)-4-phenyl-4*H*-chromene (166e)



166e

Light yellow oil, R_f (pentane: EtOAc 40:1) = 0.38. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.44–7.38 (m, 2H), 7.34–7.28 (m, 4H), 7.25–7.18 (m, 2H), 7.15 (d, *J* = 2.3, 1H), 6.97–6.91 (m, 2H), 6.88 (d, *J* = 8.7, 1H), 4.59 (s, 1H), 3.84 (s, 3H), 2.14 (ddd, *J* = 14.0, 9.9, 6.6, 1H), 1.80 (ddd, *J* = 14.2, 9.6, 4.7, 1H), 1.51–1.36 (m, 1H), 1.32–1.05 (m, 3H), 0.76 (t, *J* = 7.3, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 159.60, 150.07, 145.42, 145.18, 131.78, 130.36, 130.24, 128.76, 127.93, 127.41, 126.85, 126.55, 118.10, 114.97, 113.55, 112.12, 55.28, 43.98, 29.63, 29.43, 22.30, 13.81; *m/z* (EI)(%): 450.0 (M+2, 100), 449.1 (25.7), 448.0 (M, 97.5), 406.8 (22.4), 392.8 (66.9), 390.9 (56.5), 372.9 (73.7), 371.0 (68.8), 134.9 (20.4); HRMS calcd. for $C_{26}H_{25}O_2{}^{79}Br$: 448.10324, found: 448.10328; IR (KBr): ν = 2955, 2864, 1731, 1604, 1510, 1475, 1242, 1170, 1032, 831, 731, 701 cm^{-1}.

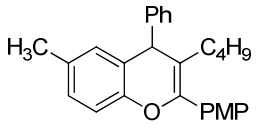
3-Butyl-2-(4-methoxyphenyl)-4-phenyl-4*H*-chromene (166f)



166f

Colorless oil, R_f (pentane: EtOAc 50:1) = 0.25. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.48–7.42 (m, 2H), 7.38–7.33 (m, 2H), 7.31 (dd, *J* = 10.4, 4.9, 2H), 7.23–7.18 (m, 1H), 7.15–7.11 (m, 1H), 7.08–7.03 (m, 1H), 7.03–6.99 (m, 1H), 6.98–6.91 (m, 3H), 4.67 (s, 1H), 3.86 (s, 3H), 2.17 (ddd, *J* = 14.0, 10.0, 6.7, 1H), 1.84 (ddd, *J* = 14.3, 9.8, 4.7, 1H), 1.52–1.43 (m, 1H), 1.35–1.27 (m, 1H), 1.27–1.19 (m, 1H), 1.18–1.09 (m, 1H), 0.78 (t, *J* = 7.3, 3H); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 159.47, 150.92, 146.19, 145.22, 130.40, 129.23, 128.59, 127.99, 127.86, 127.24, 126.52, 124.47, 123.03, 116.22, 113.51, 112.23, 55.28, 44.10, 29.71, 29.53, 22.34, 13.84; *m/z* (EI)(%): 371.1 (M+1, 13.2), 370.1 (M, 51.7), 313.0 (44.5), 293.1 (58.1), 250.0 (20.8), 134.9 (100); HRMS calcd. for $C_{26}H_{26}O_2$: 370.19273, found: 370.19259; IR (KBr): ν = 2946, 2864, 1725, 1600, 1494, 1461, 1241, 1170, 1031, 836, 749, 703 cm^{-1}.

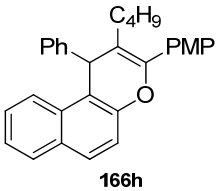
3-Butyl-2-(4-methoxyphenyl)-6-methyl-4-phenyl-4*H*-chromene (166g)



166g

Colorless oil, R_f (pentane: EtOAc 40:1) = 0.32. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.43–7.37 (m, 2H), 7.35–7.25 (m, 4H), 7.21–7.15 (m, 1H), 6.95–6.86 (m, 4H), 6.82 (d, *J* = 0.8, 1H), 4.58 (s, 1H), 3.83 (s, 3H), 2.20 (s, 3H), 2.16–2.07 (m, 1H), 1.79 (ddd, *J* = 14.1, 9.6, 4.7, 1H), 1.49–1.37 (m, 1H), 1.34–1.03 (m, 3H), 0.74 (t, *J* = 7.3, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 159.44, 148.91, 146.34, 145.30, 132.33, 130.40, 129.35, 128.57, 127.98, 126.47, 124.11, 115.97, 113.49, 112.10, 55.28, 44.19, 29.75, 29.51, 22.33, 20.70, 13.84; *m/z* (EI)(%): 384.1 (M, 1.9), 347.0 (4.4), 346.0 (9.3), 265.0 (7.0), 264.0 (20.9), 135.9 (10.7), 134.9 (100), 76.9 (12.0); HRMS calcd. for $C_{27}H_{28}O_2$: 384.20838, found: 384.20839; IR (KBr): ν = 2939, 1723, 1603, 1500, 1241, 1169, 1033, 824, 727 cm^{-1}.

2-Butyl-3-(4-methoxyphenyl)-1-phenyl-1*H*-benzo[*f*]chromene (166h)

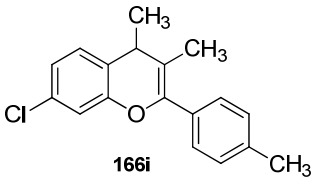


166h

Colorless oil, R_f (pentane: EtOAc 40:1) = 0.32. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.92 (d, *J* = 8.4, 1H), 7.76 (d, *J* = 7.4, 1H), 7.71 (d, *J* = 8.9, 1H), 7.41 (ddd, *J* = 8.2, 5.4, 2.9, 5H), 7.35–7.27 (m, 2H), 7.24 (dd, *J* = 10.3, 4.9, 2H), 7.16–7.09 (m, 1H), 6.97–6.88 (m, 2H), 5.17 (s, 1H), 3.83 (s, 3H), 2.22 (ddd, *J* = 14.0, 9.9, 6.8, 1H), 2.05–1.96 (m, 1H), 1.61 (tdd, *J* = 9.9,

6.4, 4.7, 1H), 1.46–1.35 (m, 1H), 1.32–1.13 (m, 2H), 0.80 (t, J = 7.3, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 159.49, 149.28, 145.59, 144.29, 131.52, 130.80, 130.47, 128.42, 128.37, 128.27, 127.67, 126.43, 126.39, 123.77, 122.98, 117.89, 115.70, 113.60, 113.51, 55.28, 41.23, 29.73, 29.08, 22.42, 13.88; *m/z* (EI)(%): 421.2 (M+1, 10.5), 420.1 (M, 39.0), 363.0 (33.1), 344.1 (21.8), 343.1 (100), 299.0 (6.3); [M+1] HRMS calcd. for $C_{30}H_{29}O_2$: 421.21621, found: 421.21634; IR (KBr): ν = 2955, 2927, 1603, 1511, 1460, 1234, 1175, 1087, 906, 833, 737, 701 cm^{-1}.

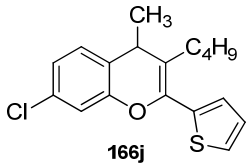
7-Chloro-3,4-dimethyl-2-(*p*-Tolyl)-4*H*-chromene (166i)



166i

Colorless oil, R_f (pentane) = 0.30. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.37–7.30 (m, 2H), 7.23–7.15 (m, 2H), 7.04 (d, J = 8.1, 1H), 7.00–6.94 (m, 2H), 3.33 (q, J = 6.9, 1H), 2.37 (s, 3H), 1.82 (s, 3H), 1.36 (d, J = 6.9, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 152.15, 144.00, 138.05, 132.11, 132.03, 128.86, 128.84, 128.70, 124.86, 123.05, 116.20, 109.85, 35.30, 23.50, 21.31, 17.18; *m/z* (CI)(%): 287.2 (38.6), 286.2 (22.7), 285.2 (M+1, 100), 284.2 (13.5), 249.2 (15.6), 199.1 (41.1), 181.1 (10.5), 121.2 (11.3), 119.2 (19.9); [M-CH_3] HRMS calcd. for $C_{17}H_{14}O^{35}Cl$: 269.07277, found: 269.07229; IR (KBr): ν = 2937, 1715, 1589, 1479, 1420, 1265, 1088, 1010, 817, 728, 587 cm^{-1}.

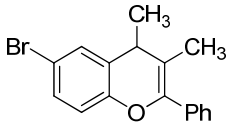
3-Butyl-7-chloro-4-methyl-2-(thiophen-2-yl)-4*H*-chromene (166j)



166j

Colorless oil, R_f (pentane) = 0.42. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.35 (dd, J = 5.1, 0.9, 1H), 7.23 (dd, J = 3.6, 0.9, 1H), 7.08–7.04 (m, 2H), 7.03 (d, J = 1.9, 1H), 7.01 (dd, J = 8.0, 2.0, 1H), 3.44 (q, J = 6.9, 1H), 2.52 (ddd, J = 14.2, 10.5, 6.2, 1H), 2.28–2.22 (m, 1H), 1.58–1.50 (m, 1H), 1.50–1.40 (m, 1H), 1.40–1.28 (m, 5H, -CH_2 and -CH_3), 0.89 (t, J = 7.3, 3H); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 152.14, 139.65, 136.76, 132.09, 128.54, 126.64, 126.62, 125.68, 125.53, 123.34, 117.18, 116.26, 33.44, 30.27, 30.13, 23.81, 22.67, 13.93; *m/z* (CI)(%): 321.1 (32.0), 320.1 (22.0), 319.1 (M+1, 100), 318.1 (13.0), 303.1 (5.9), 283.2 (5.8); [M-CH_3] HRMS calcd. for $C_{17}H_{16}O^{35}Cl^{32}S$: 303.06049, found: 303.06021; IR (KBr): ν = 2945, 2320, 2097, 1725, 1587, 1476, 1416, 1233, 1081, 836, 702, 593 cm^{-1}.

6-Bromo-3,4-dimethyl-2-phenyl-4*H*-chromene (166k)



166k

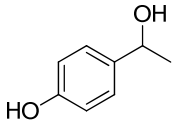
Colorless oil, R_f (pentane: EtOAc 40:1) = 0.8. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.46 (dd, J = 5.1, 3.3, 2H), 7.40 (dd, J = 10.1, 4.7, 2H), 7.37–7.32 (m, 1H), 7.26 (d, J = 2.4, 1H), 7.24 (dd, J = 8.5, 2.4, 1H), 6.84 (d, J = 8.5, 1H), 3.35 (q, J = 6.9, 1H), 1.83 (s, 3H), 1.40 (d, J = 7.0, 3H); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 150.69, 144.13, 135.05, 130.59, 129.93, 128.96, 128.38, 128.21, 128.03, 117.80, 114.86, 109.90, 35.59, 23.48, 17.13; *m/z* (CI)(%): 317.0 (66.4), 315.9 (36.6), 315.0 (68.0), 314.0 (18.6), 301.0 (18.3), 298.9 (17.1), 236.1 (28.6), 123.1 (43.4), 105.2 (100), 85.2 (21.8), 83.2 (30.2); [M-CH_3] HRMS calcd. for $C_{16}H_{12}O^{79}Br$: 299.00660, found: 299.00671; IR (KBr): ν = 3053, 2964, 1581, 1473, 1241, 1092, 807, 763, 695 cm^{-1}.

5.6 Experiments for Calcium-Catalyzed Carboarylation of Alkynes

5.6.1 Experiments for Preparation of Substrates

To a solution of ketones **212** (5 mmol) in 20 mL EtOH at 0 ^{o}C was added $NaBH_4$ (15 mmol) in portions, the reaction was then warmed to room temperature and stirred for 2 h. After reaction completion, EtOH solvent was removed under reduced pressure and the residue was washed by 20 mL saturated brine. The aqueous phase was extracted with Et_2O (3×20 mL), the combined organic phases were dried over Na_2SO_4 and concentrated under reduced pressure. The crude product was purified by column chromatography.

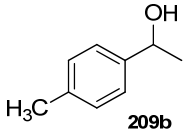
4-(1-Hydroxyethyl)phenol (209a)



209a

White solid, R_f (hexane: EtOAc 1:1) = 0.39. ^{1}H NMR (400 MHz, DMSO-d^6): δ = 9.17 (s, 1H), 7.10 (d, J=5.8, 2H), 6.67 (d, J=5.8, 2H), 4.91 (s, 1H), 4.58 (s, 1H), 1.25 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d^6): δ = 155.96, 137.68, 126.44, 114.66, 67.80, 25.95; *m/z* (EI)(%): 138.1 (M, 42.5), 123.1 (100), 121.1 (26.4), 95.1 (52.7), 77.2 (33.8); IR (KBr): ν = 3388, 3097, 3022, 2971, 1600, 1511, 1458, 1371, 1232, 1072, 1007, 895, 825, 731 cm^{-1}.

1-(*p*-Tolyl)ethanol (209b)

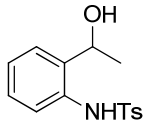


209b

Colorless oil, R_f (hexane: EtOAc 5:1) = 0.32. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.25 (d, J = 8.2, 2H), 7.15 (d, J = 7.9, 2H), 4.85 (q, J = 6.4, 1H), 2.34 (s, 3H), 1.83 (s, 1H), 1.47 (d, J = 6.4, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 142.84, 137.10, 129.12, 125.31, 70.21, 25.05, 21.06;

m/z (EI)(%): 136.0 (M, 73.2), 121.0 (100), 119.0 (69.4), 93.0 (68.3), 91.1 (47.9), 77.1 (22.1); IR (KBr): ν = 3358, 2973, 1513, 1449, 1200, 1078, 1009, 897, 815, 725 cm^{-1}.

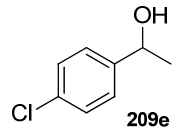
_N_-(2-(1-Hydroxyethyl)phenyl)-4-methylbenzenesulfonamide (209c)



209c

White solid, R_f (hexane: EtOAc 3:1) = 0.20. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.43 (s, 1H), 7.72–7.66 (m, 2H), 7.43 (dd, *J* = 8.1, 1.0 Hz, 1H), 7.24–7.20 (m, 2H), 7.20–7.16 (m, 1H), 7.08 (dd, *J* = 7.7, 1.7 Hz, 1H), 7.04 (td, *J* = 7.5, 1.2 Hz, 1H), 4.84 (q, *J* = 6.6 Hz, 1H), 2.42 (s, 1H), 2.37 (s, 3H), 1.36 (d, *J* = 6.7 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 143.71, 136.88, 135.66, 133.99, 129.59, 128.48, 127.12, 126.97, 124.60, 121.79, 69.75, 22.81, 21.50; *m/z* (EI)(%): 293.3 (3.5), 292.2 (9.8), 291.2 (53.5), 136.2 (63.8), 118.1 (100), 91.1 (40.2); HRMS calcd. for $C_{15}H_{17}NO_3SNa$: 314.08214, found: 314.08121; IR (KBr): ν = 3488, 3243, 2977, 2972, 1549, 1496, 1330, 1159, 1091, 932, 759, 665, 564 cm^{-1}.

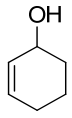
1-(4-Chlorophenyl)ethanol (209e)



209e

Colorless oil, R_f (hexane: EtOAc 3:1) = 0.45. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.31–7.21 (m, 4H), 4.81 (q, *J* = 6.5, 1H), 2.48 (s, 1H), 1.42 (d, *J* = 6.5, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 144.15, 132.93, 128.49, 126.73, 69.60, 25.15; *m/z* (EI)(%): 156.2 (M, 17.2), 155.0 (42.8), 140.8 (83.4), 138.7 (100), 112.3 (14.8), 77.3 (40.3); IR (KBr): ν = 3342, 2973, 1592, 1486, 1406, 1080, 1009, 896, 825 cm^{-1}.

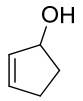
Cyclohex-2-enol (209f)



209f

Colorless oil, R_f (hexane: EtOAc 3:1) = 0.29. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.77–5.84 (m, 1H,), 5.69–5.75 (m, 1H), 4.13–4.21 (m, 1H), 1.78–2.08 (m, 4H), 1.65–1.78 (m, 1H), 1.50–1.65 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 130.5, 129.9, 65.6, 32.1, 25.2, 19.1; *m/z* (EI)(%): 81 (15), 70 (32), 69 (37), 63 (12), 57 (66), 55 (78), 54 (11), 53 (51), 52 (46), 51 (93), 50 (100); IR (KBr): ν = 3353, 3025, 2929, 2864, 2657, 1650, 1578, 1541, 1438, 1385, 1284, 1160, 1131, 1057, 1002, 957, 896, 853, 810, 726, 671, 561 cm^{-1}.

Cyclopent-2-enol (209g)

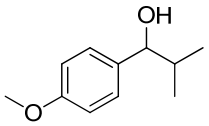


209g

Colorless oil, R_f (hexane: EtOAc 5:1) = 0.19. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.94 (dtd, J = 5.6, 2.2, 1.0, 1H), 5.82–5.77 (m, 1H), 4.87–4.79 (m, 1H), 2.54–2.38 (m, 1H), 2.30–2.15 (m, 1H), 1.83 (s, 1H), 1.75–1.45 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 135.01, 133.24, 77.48, 33.21, 30.91; *m/z* (EI)(%): 84.9 (M, 64.7), 82.9 (100), 48.1 (17.6), 47.1 (31.9); IR (KBr): ν = 2961, 1408, 1258, 1017, 866, 797, 694 cm^{-1}.

To a solution of organometallic reagents R-M **198** (7.5 mmol) in 20 mL THF at 0 ^{o}C was added aldehydes **213** (5 mmol) slowly under an argon protective atmosphere, the reaction was then heated under reflux for 30 minutes. After the reaction cooled down to room temperature, it was quenched by 20 mL saturated NH_4Cl solutuion and the aqueous phase was extracted with Et_2O (2×30 mL). The collected organic phases were dried over Na_2SO_4 and concentrated under reduced pressure. The crude product was purified by column chromatography.

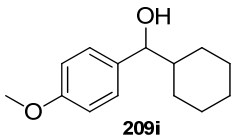
1-(4-Methoxyphenyl)-2-methylpropan-1-ol (209h)



209h

Colorless oil, R_f (hexane: EtOAc 5:1) = 0.26. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.24–7.16 (m, 2H), 6.88–6.81 (m, 2H), 4.27 (d, J = 7.2, 1H), 3.78 (s, 3H), 1.91 (dq, J = 13.6, 6.8, 1H), 1.84 (s, 1H), 0.99 (d, J = 6.7, 3H), 0.75 (d, J = 6.8, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 158.86, 135.82, 127.66, 113.51, 79.70, 55.21, 35.24, 18.92, 18.48; *m/z* (EI)(%): 180.1 (M, 13.1), 163.0 (11.7), 137.0 (100), 109.0 (15.5), 94.0 (8.1), 77.0 (6.8); IR (KBr): ν = 3428, 2957, 1609, 1510, 1461, 1241, 1173, 1025, 938, 828 cm^{-1}.

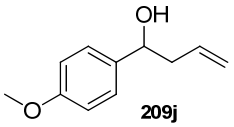
Cyclohexyl(4-methoxyphenyl)methanol (209i)



209i

White solid, R_f (hexane: EtOAc 5:1) = 0.31. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.23–7.15 (m, 2H), 6.91–6.80 (m, 2H), 4.29 (d, J = 7.5, 1H), 3.79 (s, 3H), 2.00 (d, J = 12.7, 1H), 1.76 (dd, J = 10.0, 6.6, 2H), 1.69–1.50 (m, 3H), 1.34 (d, J = 12.8, 1H), 1.28–0.94 (m, 4H), 0.87 (qd, J = 12.4, 3.5, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 158.91, 135.80, 127.74, 113.55, 79.02, 55.25, 44.96, 29.26, 29.09, 26.43, 26.07, 25.99; *m/z* (EI)(%): 220.1 (M, 8.8), 138.1 (7.1), 137.0 (100), 109.0 (8.9); IR (KBr): ν = 3447, 2939, 2856, 1609, 1510, 1448, 1244, 1172, 1001, 820 cm^{-1}.

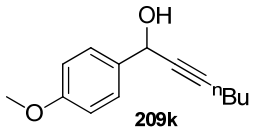
1-(4-Methoxyphenyl)but-3-en-1-ol (209j)



209j

Colorless oil, R_f (hexane: EtOAc 5:1) = 0.24. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.30–7.22 (m, 2H), 6.91–6.83 (m, 2H), 5.78 (ddt, *J* = 17.2, 10.2, 7.1, 1H), 5.19–5.07 (m, 2H), 4.67 (t, *J* = 6.5, 1H), 3.79 (s, 3H), 2.48 (dt, *J* = 7.9, 1.1, 2H), 2.02 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 158.97, 136.02, 134.58, 127.03, 118.17, 113.74, 72.94, 55.24, 43.72; *m/z* (EI)(%): 177.9 (M+1, 1.1), 137.0 (100), 136.1 (99.6), 135.3 (40.0), 108.8 (69.3), 94.4 (25.1), 93.4 (24.6), 77.4 (35.3); IR (KBr): ν = 3400, 2933, 2906, 1610, 1511, 1299, 1242, 1175, 1033, 915, 830 cm^{-1}.

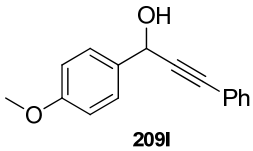
1-(4-Methoxyphenyl)hept-2-yn-1-ol (209k)



209k

Colorless oil, R_f (hexane: EtOAc 5:1) = 0.24. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.50–7.37 (m, 2H), 6.95–6.79 (m, 2H), 5.38 (dd, *J* = 4.0, 1.9, 1H), 3.79 (s, 3H), 2.26 (td, *J* = 7.0, 2.0, 2H), 2.14 (d, *J* = 2.5, 1H), 1.58–1.47 (m, 2H), 1.46–1.35 (m, 2H), 0.90 (t, *J* = 7.3, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 159.48, 133.62, 128.00, 113.81, 87.40, 80.04, 64.39, 55.27, 30.64, 21.95, 18.48, 13.57; *m/z* (EI)(%): 218.1 (M, 100), 217.0 (28.5), 201.1 (27.7), 187.0 (38.9), 175.0 (28.8), 161.0 (26.5), 109.0 (82.2), 107.9 (23.3); IR (KBr): ν = 3399, 2934, 2867, 2285, 2106, 1608, 1509, 1457, 1243, 1026, 833, 768 cm^{-1}.

1-(4-Methoxyphenyl)-3-phenylprop-2-yn-1-ol (209l)



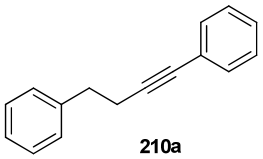
209l

Yellow oil, R_f (hexane: EtOAc 5:1) = 0.24. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.56–7.50 (m, 2H), 7.49–7.42 (m, 2H), 7.34–7.27 (m, 3H), 6.95–6.87 (m, 2H), 5.63 (d, *J* = 5.9, 1H), 3.81 (s, 3H), 2.40 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 159.65, 132.95, 131.69, 128.51, 128.25, 128.14, 122.44, 113.96, 88.90, 86.43, 64.66, 55.30; *m/z* (EI)(%): 238.1 (M, 20.2), 237.1 (23.7), 236.1 (100), 208.1 (70.6), 193.0 (44.0), 165.0 (23.3), 129.0 (28.2); IR (KBr): ν = 3384, 2324, 2108, 1608, 1509, 1245, 1173, 1028, 958, 832, 756, 691 cm^{-1}.

To a solution of aryl iodides **200** (5 mmol) and but-3-yn-1-ylbenzenes **214** (10 mmol) in 5 mL degassed Et_3N were added $Pd(PPh_3)_4$ (0.25 mmol) and CuI (0.5 mmol) under an argon protective atmosphere, the reaction was then stirred at 60 ^{o}C for 3 hours. After the reaction cooled down to room temperature, the mixture was diluted with 30 mL EE and washed by 20 mL 1N HCl and 20 mL saturated $NaHCO_3$ solution. The aqueous phase was extracted with

EE (2×30 mL), the collected organic phases were dried over Na_2SO_4 and concentrated under reduced pressure. The crude product was purified by column chromatography.

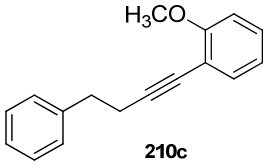
But-1-yne-1,4-diyldibenzene (210a)



210a

Yellow oil, R_f (hexane) = 0.42. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.42–7.36 (m, 2H), 7.36–7.20 (m, 8H), 2.94 (t, J = 7.5, 2H), 2.71 (t, J = 7.5, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 140.67, 131.49, 128.51, 128.35, 128.17, 127.59, 126.28, 123.81, 89.47, 81.29, 35.17, 21.67; *m/z* (EI)(%): 207.2 (M+1, 17.4), 206.2 (M, 92.8), 205.2 (47.7), 191.1 (19.3), 115.1 (73.3), 91.1 (100); IR (KBr): ν = 3028, 2925, 2330, 2096, 1597, 1490, 1444, 749, 693, 531 cm^{-1}.

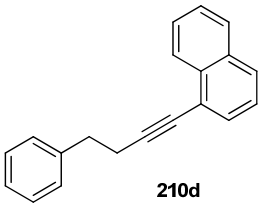
1-Methoxy-2-(4-phenylbut-1-yn-1-yl)benzene (210c)



210c

Yellow oil, R_f (hexane: EtOAc 30:1) = 0.21. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.38–7.19 (m, 7H), 6.91–6.83 (m, 2H), 3.87 (s, 3H), 2.96 (t, J = 7.5, 2H), 2.77 (t, J = 7.5, 2H): ^{13}C NMR (100 MHz, $CDCl_3$): δ = 159.79, 140.79, 133.64, 128.98, 128.55, 128.31, 126.21, 120.37, 112.89, 110.50, 93.68, 55.74, 35.26, 22.06; *m/z* (EI)(%): 236.8 (M, 13.5), 235.7 (99.9), 234.7 (100), 233.7 (72.4), 232.9 (73.0), 145.1 (42.0), 144.2 (44.5), 143.3 (39.2), 116.8 (32.2), 115.8 (44.0), 114.9 (53.3), 114.0 (35.0), 91.5 (38.5), 90.7 (41.2); [M+Na] HRMS calcd. for $C_{17}H_{16}ONa$: 259.10934, found: 259.10934; IR (KBr): ν = 3026, 2933, 2325, 2099, 1595, 1491, 1455, 1258, 1115, 1024, 748, 697 cm^{-1}.

1-(4-Phenylbut-1-yn-1-yl)naphthalene (210d)

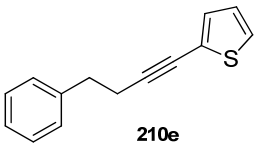


210d

White solid, R_f (hexane) = 0.36. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.23–8.13 (m, 1H), 7.86–7.81 (m, 1H), 7.79 (dd, J = 8.1, 3.2, 1H), 7.62 (dd, J = 8.7, 5.1, 1H), 7.55–7.48 (m, 2H), 7.44–7.39 (m, 1H), 7.39–7.34 (m, 4H), 7.32–7.26 (m, 1H), 3.05 (ddd, J = 7.3, 6.1, 3.3, 2H), 2.93–2.87 (m, 2H); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 140.64, 133.44, 133.11, 129.95, 128.62, 128.44, 128.09, 127.99, 126.43, 126.34, 126.19, 125.17, 121.49, 94.43, 79.37, 35.19, 21.89; *m/z* (EI)(%): 256.1 (M, 29.2), 255.4 (56.5), 254.5 (38.6), 253.7 (57.8), 165.1 (53.7), 164.1

(100), 162.6 (88.6); HRMS calcd. for $C_{20}H_{16}$: 256.12455, found: 256.12425; IR (KBr): ν = 3038, 2922, 2325, 1582, 1494, 1447, 760, 700 cm^{-1}.

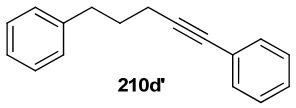
2-(4-Phenylbut-1-yn-1-yl)thiophene (210e)



210e

Yellow oil, R_f (hexane) = 0.41. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.36–7.20 (m, 5H), 7.19–7.15 (m, 1H), 7.12 (d, J = 3.6, 1H), 6.94 (dd, J = 5.2, 3.6, 1H), 2.93 (t, J = 7.6, 2H), 2.72 (t, J = 7.6, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 140.49, 131.01, 128.47, 128.39, 126.74, 126.33, 126.01, 123.92, 93.54, 74.45, 34.97, 21.94; *m/z* (EI)(%): 212.8 (M, 12.6), 211.8 (15.5), 210.5 (100), 208.3 (36.6), 120.8 (48.4), 119.9 (36.3), 91.5 (19.1), 90.7 (26.4); [M+1] HRMS calcd. for $C_{14}H_{13}S$: 213.07325, found: 213.07309; IR (KBr): ν = 3027, 2925, 2324, 2099, 1600, 1495, 1440, 1191, 833, 745, 696 cm^{-1}.

Pent-1-yne-1,5-diyldibenzene (210d')

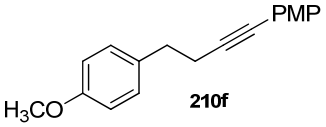


210d'

Colorless oil, R_f (hexane: EtOAc 30:1) = 0.44. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.46–7.38 (m, 2H), 7.34–7.26 (m, 5H), 7.26–7.17 (m, 3H), 2.80 (t, J = 7.6, 2H), 2.43 (t, J = 7.0, 2H), 1.99–1.89 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 141.61, 131.53, 128.54, 128.34, 128.18, 127.53, 125.88, 123.95, 89.81, 81.12, 34.82, 30.30, 18.81; *m/z* (EI)(%): 219.4 (M-1, 50.5), 218.8 (26.0), 218.0 (44.5), 216.9 (67.2), 189.4 (28.2), 141.3 (83.5), 128.3 (72.6), 127.5 (72.4), 126.4 (85.9), 115.0 (100), 102.1 (41.6), 91.5 (64.5), 90.6 (58.3); IR (KBr): ν = 3060, 3027, 2935, 2858, 2111, 1598, 1490, 1448, 749, 693 cm^{-1}.

To a solution of 4-ethynylanisoles **216** (3 mmol) in 15 mL THF at -78 ^{o}C was slowly added *n*-BuLi (3 mmol) under an argon protective atmosphere, the mixture was stirred at -78 ^{o}C for 30 minutes, then NaI (0.3 mmol) and 2-arylethylbromides **215** (3.6 mmol) were added into the flask, the reaction was heated up to reflux overnight. After the reaction cooled down to room temperature, the reaction was quenched by 20 mL saturated NH_4Cl solution and the aqueous phase was extracted with Et_2O (2×20 mL). The collected organic phases were dried over Na_2SO_4 and concentrated under reduced pressure. The crude product was purified by column chromatography.

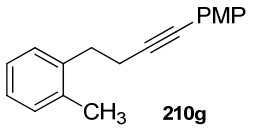
4,4'-(But-1-yne-1,4-diyl)bis(methoxybenzene) (210f)



210f

White solid, R_f (hexane: Et_2O 9:1) = 0.37. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.33 (d, J = 8.8, 2H), 7.20 (d, J = 8.6, 2H), 6.87 (d, J = 8.6, 2H), 6.82 (d, J = 8.8, 2H), 3.80 (d, J = 1.2, 6H), 2.87 (t, J = 7.5, 2H), 2.65 (t, J = 7.5, 2H); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 159.02, 158.04, 132.93, 132.80, 129.44, 115.98, 113.77, 113.71, 87.97, 80.94, 55.21, 55.20, 34.40, 21.97; *m/z* (EI)(%): 266.1 (M, 39.0), 235.1 (11.2), 145.0 (16.9), 121.0 (100); IR (KBr): ν = 3015, 2951, 2309, 2060, 1739, 1603, 1502, 1234, 1173, 1028, 824, 752 cm^{-1}.

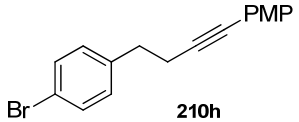
1-(4-(4-Methoxyphenyl)but-3-yn-1-yl)-2-methylbenzene (210g)



210g

Colorless oil, R_f (hexane: DCM 7:3) = 0.41. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.38–7.31 (m, 2H), 7.25 (dd, J = 7.0, 1.8, 1H), 7.22–7.10 (m, 3H), 6.89–6.78 (m, 2H), 3.85–3.75 (m, 3H), 3.00–2.90 (m, 2H), 2.71–2.61 (m, 2H), 2.43–2.36 (m, 3H); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 159.05, 138.90, 135.95, 132.82, 130.17, 128.97, 126.37, 125.95, 115.95, 113.79, 87.94, 80.81, 55.20, 32.56, 20.39, 19.30; *m/z* (EI)(%): 251.3 (M+1, 12.6), 250.2 (M, 55.7), 146.1 (17.5), 145.1 (100), 121.2 (11.6), 105.2 (32.9), 102.1 (17.4); IR (KBr): ν = 3011, 2938, 2079, 1605, 1504, 1456, 1287, 1243, 1172, 1032, 829, 746 cm^{-1}.

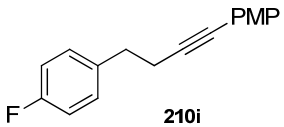
1-Bromo-4-(4-(4-methoxyphenyl)but-3-yn-1-yl)benzene (210h)



210h

White solid, R_f (hexane: DCM 7:1) = 0.51. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.46–7.39 (m, 2H), 7.33–7.27 (m, 2H), 7.14 (t, J = 5.4, 2H), 6.85–6.77 (m, 2H), 3.80 (s, 3H), 2.86 (t, J = 7.4, 2H), 2.65 (t, J = 7.4, 2H); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 159.11, 139.65, 132.80, 131.35, 130.32, 120.07, 115.75, 113.81, 87.30, 81.34, 55.22, 34.58, 21.48; *m/z* (EI)(%): 316.0 (M+2, 18.1), 314.0 (M, 17.8), 146.1 (13.8), 145.0 (100), 102.0 (15.8); IR (KBr): ν = 2930, 2305, 1600, 1494, 1288, 1242, 1168, 1020, 822 cm^{-1}.

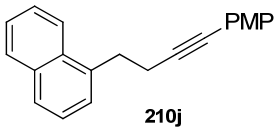
1-Fluoro-4-(4-(4-methoxyphenyl)but-3-yn-1-yl)benzene (210i)



210i

White solid, R_f (hexane: DCM 7:3) = 0.52. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.33–7.27 (m, 2H), 7.25–7.19 (m, 2H), 7.03–6.96 (m, 2H), 6.83–6.78 (m, 2H), 3.80 (s, 3H), 2.88 (t, J = 7.4, 2H), 2.65 (t, J = 7.4, 2H); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 162.33, 160.72, 159.12, 136.38, 133.00, 132.60, 129.69, 113.96, 87.51, 81.26, 55.16, 34.40, 21.79; *m/z* (EI)(%): 255.2 (M+1, 12.6), 254.2 (M, 61.9), 146.1 (13.9), 145.1 (100), 109.1 (17.4), 102.1 (12.5); IR (KBr): ν = 2936, 1605, 1506, 1455, 1288, 1241, 1028, 822 cm^{-1}.

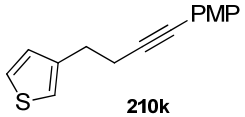
1-(4-(4-Methoxyphenyl)but-3-yn-1-yl)naphthalene (210j)



210j

Colorless oil, R_f (hexane: DCM 7:3) = 0.41. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.10 (d, J = 8.3, 1H), 7.90–7.84 (m, 1H), 7.75 (dd, J = 8.5, 3.8, 1H), 7.56–7.46 (m, 2H), 7.43 (d, J = 5.0, 2H), 7.34–7.27 (m, 2H), 6.88–6.74 (m, 2H), 3.79 (s, 3H), 3.40 (t, J = 7.7, 2H), 2.83 (t, J = 7.7, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 159.07, 136.72, 133.84, 132.83, 131.71, 128.81, 127.08, 126.31, 125.92, 125.49, 123.55, 115.94, 113.79, 87.92, 81.30, 55.22, 32.46, 21.00; *m/z* (EI)(%): 287.2 (M+1, 20.1), 286.2 (M, 90.0), 285.2 (15.3), 255.2 (24.3), 145.1 (100), 141.1 (75.6), 115.1 (28.7), 102.1 (14.1); IR (KBr): ν = 3047, 2953, 2322, 2113, 1603, 1507, 1459, 1288, 1244, 1172, 1029, 829, 788 cm^{-1}.

3-(4-(4-Methoxyphenyl)but-3-yn-1-yl)thiophene (210k)

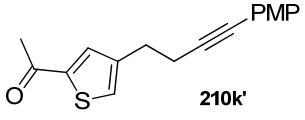


210k

Light yellow oil, R_f (hexane: DCM 7:3) = 0.42. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.35–7.28 (m, 2H), 7.28–7.23 (m, 1H), 7.09–7.05 (m, 1H), 7.03 (dd, J = 4.9, 1.2, 1H), 6.85–6.76 (m, 2H), 3.79 (s, 3H), 2.94 (t, J = 7.4, 2H), 2.68 (t, J = 7.4, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 159.08, 141.13, 132.82, 128.14, 125.29, 120.79, 115.92, 113.80, 87.86, 81.00, 55.21, 29.70, 20.91; *m/z* (EI)(%): 242.1 (M+1, 22.6), 241.1 (M, 81.9), 146.1 (19.9), 145.0 (100), 102.0 (17.0), 97.0 (26.4); [M+1] HRMS calcd. for $C_{15}H_{15}OS$: 242.08381, found: 242.08345; IR (KBr): ν = 2922, 2313, 2090, 1604, 1505, 1452, 1286, 1243, 1172, 1030, 830, 773 cm^{-1}.

To a solution of 2,2,6,6-tetramethylpiperidines (1.8 mmol) in 10 mL THF at -78 ^{o}C was slowly added *n*-BuLi (2.2 mmol) under an argon protective atmosphere, the reaction mixture was stirred at -78 ^{o}C for 30 minutes, then 3-(4-(4-methoxyphenyl)but-3-yn-1-yl)thiophenes **210k** (2.2 mmol) in 10 mL THF were added dropwise into the flask and the mixture was stirred at -78 ^{o}C for one hour. Lastly, *N*-methoxy-*N*-methylacetamides (2.2 mmol) was added into the mixture and the reaction was warmed to 0 ^{o}C and stirred for another one hour. After reaction completion, the mixture was quenched by 20 mL saturated NH_4Cl solution and the aqueous phase was extracted with Et_2O (3×20 mL). The collected organic phases were dried over Na_2SO_4 and concentrated under reduced pressure. The crude product was purified by column chromatography.

1-(4-(4-(4-Methoxyphenyl)but-3-yn-1-yl)thiophen-2-yl)ethanone (210k')

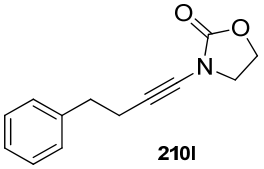


210k'

Yellow oil, R_f (hexane: DCM 7:3) = 0.09. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.62 (d, J = 1.4, 1H), 7.40 – 7.34 (m, 1H), 7.31–7.25 (m, 2H), 6.83–6.75 (m, 2H), 3.77 (s, 3H), 2.89 (t, J = 7.1, 2H), 2.67 (t, J = 7.1, 2H), 2.50 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 190.64, 159.18, 144.12, 142.23, 133.47, 132.76, 129.82, 115.57, 113.83, 87.15, 81.63, 55.20, 29.52, 26.75, 20.74; *m/z* (EI)(%): 285.1 (M+1, 10.2), 284.1 (M, 27.7), 283.1 (M-1, 97.2), 146.1 (11.1), 145.1 (100), 102.1 (11.1); IR (KBr): ν = 2927, 1658, 1606, 1506, 1423, 1248, 1172, 1027, 830 cm^{-1}.

To a solution of oxazolidin-2-ones **217** (57.6 mmol), $CuCl_2$ (2.3 mmol) and Na_2CO_3 (23 mmol) in 57.6 mL toluene were added pyridines (23 mmol) under an oxygen atmosphere, the mixture was heated up to 70 ^{o}C, then a but-3-yn-1-ylbenzene **214** solution (11.5 mmol **214** in 57.6 mL toluene) was added dropwise into the flask for 4 hours by syringe and the reaction was stirred at 70 ^{o}C overnight. After the reaction cooled down to room temperature, the mixture was filtered through a plug of celite and the filter cake was washed with Et_2O. The organic solvent was removed under reduced pressure, and the crude product was purified by column chromatography.

3-(4-Phenylbut-1-yn-1-yl)oxazolidin-2-one (210l)

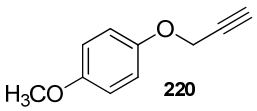


210l

Colorless oil, R_f (hexane: EtOAc 3:1) = 0.14. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.31–7.25 (m, 2H), 7.23–7.15 (m, 3H), 4.38 (dd, J = 8.7, 7.3, 2H), 3.81 (dd, J = 8.7, 7.3, 2H), 2.84 (t, J = 7.6, 2H), 2.59 (dd, J = 9.4, 5.7, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 156.51, 140.48, 128.44, 128.34, 126.28, 70.74, 70.47, 62.78, 46.90, 35.15, 20.64; *m/z* (EI)(%): 216.2 (M+1, 51.8), 229.2 (M, 58.0), 172.2 (61.1), 128.2 (100), 91.2 (68.3), 80.2 (43.1), 53.3 (60.8); IR (KBr): ν = 2918, 2268, 1763, 1482, 1414, 1202, 1112, 1032, 745, 700 cm^{-1}.

To a solution of phenols **218** (10 mmol) and K_2CO_3 (15 mmol) in 30 mL THF were added propargyl bromides **219** (12 mmol), the reaction was then heated up to reflux overnight. After the reaction cooled down to room temperature, the solvent was removed under reduced pressure, and the crude product was purified by column chromatography.

1-Methoxy-4-(prop-2-yn-1-yloxy)benzene (220)



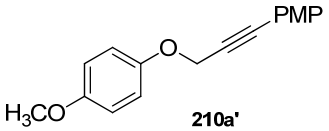
220

Light yellow oil, R_f (hexane: EtOAc 15:1) = 0.36. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.95–6.89 (m, 2H), 6.87–6.80 (m, 2H), 4.63 (d, J = 2.4, 2H), 3.76 (s, 3H), 2.50 (dd, J = 3.4, 1.4, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 154.41, 151.61, 116.07, 114.54, 78.86, 75.25, 56.53, 55.60; *m/z*

(EI)(%): 162.4 (M, 80.2), 161.6 (88.7), 160.7 (100), 159.9 (79.1), 158.3 (67.3); IR (KBr): ν = 3286, 2946, 2325, 2118, 1502, 1455, 1213, 1028, 824, 707 cm^{-1}.

To a solution of 4-iodoanisoles **221** (5 mmol) and terminal alkynes **220** (10 mmol) in 5 mL degassed Et_3N were added $Pd(PPh_3)_4$ (0.25 mmol) and CuI (0.5 mmol) under an argon protective atmosphere, the reaction was then stirred at 60 ^oC for 3 hours. After the reaction cooled down to room temperature, the mixture was diluted with 30 mL EE and washed by 20 mL 1N HCl and 20 mL saturated $NaHCO_3$ solution. The aqueous phase was extracted with EE (2×30 mL), the collected organic phases were dried over Na_2SO_4 and concentrated under reduced pressure. The crude product was purified by column chromatography.

1-Methoxy-4-(3-(4-methoxyphenoxy)prop-1-yn-1-yl)benzene (210a')

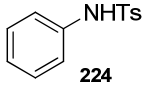


210a'

Yellow solid, R_f (hexane: EtOAc 10:1) = 0.33. ^1H NMR (600 MHz, $CDCl_3$): δ = 7.41–7.36 (m, 2H), 7.01–6.95 (m, 2H), 6.88–6.84 (m, 2H), 6.84–6.81 (m, 2H), 4.85 (s, 2H), 3.80 (s, 3H), 3.78 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 159.78, 154.26, 151.94, 133.27, 116.14, 114.53, 114.35, 113.84, 86.93, 82.79, 57.54, 55.64, 55.22; *m/z* (EI)(%): 268.0 (M, 5.9), 145.1 (100), 123.0 (9.6), 102.0 (20.1); IR (KBr): ν = 3393, 2226, 2067, 1602, 1501, 1451, 1217, 1020, 822, 746 cm^{-1}.

To a solution of anilines **222** (50 mmol) and pyridines (60 mmol) in 50 mL DCM was added TsCl **223** (75 mmol) in portions, the reaction was then stirred at room temperature overnight. The reaction was quenched by 50 mL water and the aqueous phase was extracted with DCM (2×50 mL). The combined organic phases were dried over Na_2SO_4 and concentrated under reduced pressure. The crude product was recrystallized from DCM/hexane.

4-Methyl-*N*-phenylbenzenesulfonamide (224)



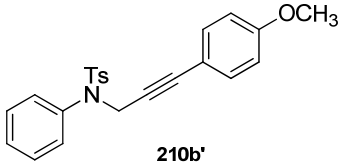
224

White solid, R_f (hexane: EtOAc 5:1) = 0.21. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.68 (d, J = 8.3, 2H), 7.30–7.16 (m, 5H), 7.11–7.01 (m, 3H), 2.35 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 143.83, 136.55, 135.94, 129.61, 129.23, 127.24, 125.14, 121.36, 21.49; *m/z* (EI)(%): 245.8 (M, 41.8), 244.1 (100), 181.8 (32.0), 180.2 (33.4), 166.6 (22.8), 154.9 (26.8), 153.6 (37.8), 92.6 (17.3), 91.4 (84.2), 90.6 (17.2), 65.5 (28.6); IR (KBr): ν = 3247, 1596, 1484, 1414, 1336, 1290, 1153, 1089, 913, 813, 754, 693, 661 cm^{-1}.

To a solution of 4-methyl-*N*-phenylbenzenesulfonamides **224** (3 mmol), PPh_3 (3.3 mmol) and 3-(4-methoxyphenyl)prop-2-yn-1-ols **225** (3.3 mmol) in 30 mL THF at 0 ^oC was added

DIAD (3.3 mmol) under an argon protective atmosphere, the reaction was then stirred at room temperature overnight. After reaction completion, the mixture was diluted with 30 mL Et_2O and washed by 20 mL saturated brine, the aqueous phase was extracted with Et_2O (2×20 mL). The combined organic phases were dried over Na_2SO_4 and concentrated under reduced pressure. The crude product was purified by column chromatography.

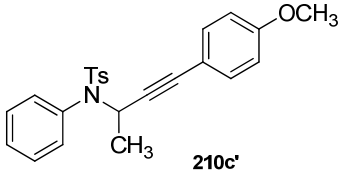
***N*-(3-(4-Methoxyphenyl)prop-2-yn-1-yl)-4-methyl-*N*-phenylbenzenesulfonamide (210b')**



210b'

White solid, R_f (hexane: EtOAc 5:1) = 0.26. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.64–7.52 (m, 2H), 7.36–7.27 (m, 5H), 7.17 (d, J = 8.0, 2H), 7.13–7.05 (m, 2H), 6.81–6.72 (m, 2H), 4.63 (s, 2H), 3.78 (s, 3H), 2.35 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 159.66, 143.41, 139.82, 135.98, 132.91, 129.19, 128.93, 128.46, 128.07, 128.02, 114.43, 113.78, 85.52, 82.16, 55.26, 42.11, 21.50; *m/z* (EI)(%): 233.8 (4.0), 144.4 (100), 91.6 (6.7), 90.7 (7.5); IR (KBr): ν = 3056, 2972, 2309, 2072, 1598, 1499, 1342, 1284, 1243, 1161, 1069, 824, 706 cm^{-1}.

***N*-(4-(4-Methoxyphenyl)but-3-yn-2-yl)-4-methyl-*N*-phenylbenzenesulfonamide (210c')**



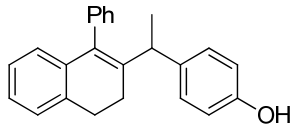
210c'

Light yellow oil, R_f (hexane: EtOAc 5:1) = 0.30. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.64 (d, J = 8.3, 2H), 7.38–7.26 (m, 5H), 7.19 (d, J = 8.0, 2H), 7.11–7.04 (m, 2H), 6.82–6.77 (m, 2H), 5.50 (q, J = 7.1, 1H), 3.80 (s, 3H), 2.37 (s, 3H), 1.34 (d, J = 7.1, 3H); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 159.56, 143.16, 136.59, 135.97, 132.74, 131.46, 129.05, 128.68, 128.65, 128.19, 114.49, 113.76, 86.79, 84.86, 55.26, 47.24, 21.82, 21.49; *m/z* (EI)(%): 405.1 (M, 5.8), 266.1 (10.0), 160.1 (11.7), 159.0 (100), 91.1 (9.6); HRMS calcd. for $C_{24}H_{23}O_3N^{32}S$: 405.13932, found: 405.13950; IR (KBr): ν = 2937, 2086, 1601, 1502, 1454, 1345, 1244, 1163, 1096, 1028, 909, 825, 728 cm^{-1}.

5.6.2 General Experiment for the Calcium-Catalyzed Carboarylation of Alkynes

To a solution of but-1-yne-1,4-diyldibenzenes **210a** (0.48 mmol) and 4-(1-hydroxyethyl)phenols **209a** (0.4 mmol) in 2 mL CH_3NO_2 were added Bu_4NPF_6 (0.01 mmol) and $Ca(NTf_2)_2$ (0.02 mmol), the reaction was then stirred at 40 ^{o}C for 12 h. For the isolation of the product, 5 mL saturated $NaHCO_3$ solution was added, and the aqueous phase was extracted with dichloromethane (2×10 mL). The combined organic phases were dried over Na_2SO_4 and concentrated in *vacuo*. The crude product was purified by column chromatography.

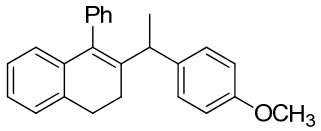
4-(1-(1-Phenyl-3,4-dihydronaphthalen-2-yl)ethyl)phenol (211a)



211a

White solid, R_f (Hex: EtOAc 5:1) = 0.32. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.46 (t, J = 7.7, 2H), 7.35 (dd, J = 19.1, 11.8, 3H), 7.15–7.01 (m, 5H), 6.74 (d, J = 8.6, 2H), 6.62 (d, J = 7.4, 1H), 4.75 (s, 1H), 3.82 (q, J = 7.1, 1H), 2.79–2.68 (m, 2H), 2.28 (ddd, J = 17.1, 10.1, 7.1, 1H), 2.09–1.98 (m, 1H), 1.36 (d, J = 7.1, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 153.53, 142.01, 139.85, 136.97, 136.43, 135.16, 133.66, 130.18, 128.53, 128.39, 126.92, 126.76, 126.16, 125.91, 114.85, 39.96, 28.75, 23.11, 17.10; *m/z* (EI)(%): 327.2 (26.2), 326.2 (100), 312.2 (12.5), 311.2 (49.7), 298.1 (4.5), 233.1 (4.4), 217.1 (30.4), 229.1 (12.0), 202.1 (12.0), 121.1 (7.6), 107.1 (4.9), 91.1 (5.8), 71.1 (3.1); [M+H] HRMS calcd. for $C_{24}H_{23}O$: 327.17434, found: 327.17432; IR (KBr): ν = 3375, 3025, 2934, 2882, 1602, 1506, 1443, 1366, 1226, 1176, 906, 831, 730 cm^{-1}.

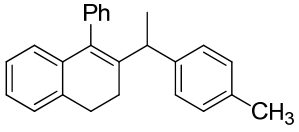
3-(1-(4-Methoxyphenyl)ethyl)-4-phenyl-1,2-dihydronaphthalene (211b)



211b

Colorless oil, R_f (Hex: EtOAc 30:1) = 0.58. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.45 (t, J = 7.8, 2H), 7.40–7.25 (m, 3H), 7.16 (d, J = 8.6, 2H), 7.13–6.99 (m, 3H), 6.85–6.78 (m, 2H), 6.65–6.57 (m, 1H), 3.82 (q, J = 7.1, 1H), 3.78 (s, 3H), 2.79–2.67 (m, 2H), 2.28 (ddd, J = 17.1, 10.0, 7.3, 1H), 2.09–1.97 (m, 1H), 1.37 (d, J = 7.1, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 157.73, 142.07, 139.88, 137.00, 136.21, 135.17, 133.64, 130.18, 128.53, 128.18, 126.92, 126.75, 126.15, 126.14, 125.90, 113.40, 55.18, 39.96, 28.77, 23.14, 17.12; *m/z* (EI)(%): 341.4 (34.5), 340.4 (100), 326.3 (15.1), 325.3 (54.8), 312.3 (3.9), 263.3 (4.3), 249.2 (6.7), 247.2 (6.3), 233.3 (10.5), 217.2 (41.9), 229.2 (15.7), 203.2 (13.5), 202.2 (13.6), 189.2 (4.6), 165.1 (4.1), 135.2 (22.3), 121.2 (8.7), 105.2 (4.4), 91.2 (9.8); [M+Na] HRMS calcd. for $C_{25}H_{24}ONa$: 363.17194, found: 363.17099; IR (KBr): ν = 3019, 2938, 2831, 2326, 2077, 1605, 1505, 1451, 1243, 1177, 1034, 907, 829, 734 cm^{-1}.

4-Phenyl-3-(1-(*p*-Tolyl)ethyl)-1,2-dihydronaphthalene (211c)

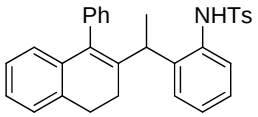


211c

Colorless oil, R_f (Hex: EtOAc 30:1) = 0.62. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.45 (t, J = 7.7, 2H), 7.34 (dd, J = 19.4, 11.9, 3H), 7.15 (d, J = 8.1, 2H), 7.13–7.00 (m, 5H), 6.62 (d, J = 7.3, 1H), 3.84 (q, J = 7.1, 1H), 2.79–2.67 (m, 2H), 2.34–2.24 (m, 4H, Ar-CH_3 and 1/2-CH_2),

2.10–1.99 (m, 1H), 1.38 (d, J = 7.1, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 141.97, 141.06, 139.88, 137.00, 135.29, 135.20, 133.80, 130.19, 128.73, 128.52, 127.16, 126.92, 126.74, 126.15, 126.14, 125.91, 40.37, 28.78, 23.21, 20.95, 17.02; *m/z* (EI)(%): 325.3 (61.5), 324.2 (100), 310.3 (21.9), 309.3 (74.3), 296.3 (9.9), 233.2 (21.0), 232.2 (28.5), 231.2 (32.1), 218.2 (23.3), 217.2 (83.5), 216.2 (23.8), 229.2 (46.1), 205.2 (45.0), 204.2 (16.9), 203.2 (35.8), 202.1 (42.4), 189.1 (12.8), 178.1 (12.5), 165.1 (12.0), 119.1 (30.9), 117.1 (15.3), 115.1 (13.1), 105.1 (17.9), 92.2 (9.8), 91.1 (36.2), 77.2 (6.9); HRMS calcd. for $C_{25}H_{24}$: 324.18725, found: 324.18735; IR (KBr): ν = 3024, 2938, 1596, 1490, 1448, 1035, 904, 817, 738 cm^{-1}.

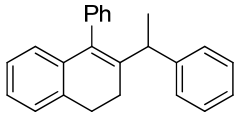
4-Methyl-N-(2-(1-(1-phenyl-3,4-dihydronaphthalen-2-yl)ethyl)phenyl)benzenesulfonamide (211d)



211d

White solid, R_f (Hex: EtOAc 10:1) = 0.43. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.73 (s, 1H), 7.65 (dd, J = 8.0, 1.2, 2H), 7.54 (s, 2H), 7.27 (s, 1H), 7.22–7.15 (m, 2H), 7.13–6.97 (m, 6H), 6.84 (d, J = 8.0, 2H), 6.61 (d, J = 7.8, 1H), 6.47 (s, 1H), 3.24 (q, J = 6.9, 1H), 2.62 (ddd, J = 15.3, 8.9, 6.3, 1H), 2.53–2.42 (m, 1H), 2.25 (s, 3H), 2.01 (ddd, J = 16.3, 8.2, 5.2, 1H), 1.51–1.42 (m, 1H), 1.18 (d, J = 6.9, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 143.18, 139.09, 138.43, 136.21, 135.70, 135.14, 135.08, 134.89, 133.93, 130.14, 129.98, 129.01, 127.74, 127.49, 127.28, 126.99, 126.92, 126.80, 126.37, 126.07, 124.89, 122.32, 36.97, 28.41, 22.94, 21.38, 18.87; *m/z* (EI)(%): 480.3 (4.0), 479.3 (10.5), 464.3 (2.8), 326.3 (3.8), 325.3 (29.0), 324.2 (100), 309.3 (4.9), 245.2 (3.6), 232.2 (2.8), 231.2 (12.5), 229.1 (8.9), 193.1 (40.4), 178.1 (4.3), 144.1 (3.6), 121.1 (5.5), 120.1 (60.9), 91.1 (10.7); [M+Na] HRMS calcd. for $C_{31}H_{29}O_2NSNa$: 502.18112, found: 502.18127; IR (KBr): ν = 3330, 3062, 2971, 2934, 2879, 2830, 1579, 1489, 1451, 1384, 1337, 1162, 1091, 907, 814, 762, 730, 708, 662, 632, 562 cm^{-1}.

4-Phenyl-3-(1-phenylethyl)-1,2-dihydronaphthalene (211e)

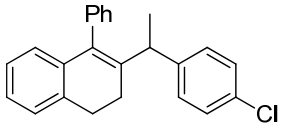


211e

Colorless oil, R_f (Hex: EtOAc 40:1) = 0.41. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.46 (t, J = 7.8, 2H), 7.40–7.23 (m, 7H), 7.18 (ddd, J = 8.5, 5.9, 2.2, 1H), 7.09 (ddd, J = 10.8, 8.5, 4.0, 2H), 7.04 (dd, J = 10.6, 4.3, 1H), 6.63 (d, J = 7.6, 1H), 3.89 (q, J = 7.1, 1H), 2.79–2.69 (m, 2H), 2.30 (ddd, J = 17.1, 10.4, 6.9, 1H), 2.04 (ddd, J = 15.9, 7.7, 6.5, 1H), 1.41 (d, J = 7.1, 3H); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 144.15, 141.78, 139.84, 136.95, 135.17, 133.96, 130.18, 128.55, 128.03, 127.30, 126.93, 126.79, 126.20, 126.17, 125.94, 125.86, 40.77, 28.75, 23.22, 16.92; *m/z* (EI)(%): 311.3 (24.4), 310.3 (100), 296.2 (7.0), 295.2 (29.2), 282.2 (5.8), 232.2

(6.9), 218.2 (8.7), 217.2 (41.0), 216.1 (7.0), 229.1 (16.3), 205.2 (26.2), 203.1 (19.0), 202.1 (24.1), 189.1 (5.9), 178.1 (6.5), 165.1 (5.0), 115.1 (5.6), 105.1 (6.5), 91.1 (8.5), 78.2 (8.4); HRMS calcd. for $C_{24}H_{22}$: 310.17160, found: 310.17204; IR (KBr): ν = 3058, 3024, 2964, 2933, 2880, 2830, 1598, 1487, 1446, 1031, 906, 763, 732, 669 cm^{-1}.

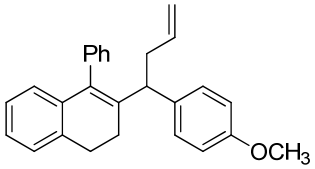
3-(1-(4-Chlorophenyl)ethyl)-4-phenyl-1,2-dihydronaphthalene (211f)



211f

Colorless oil, R_f (Hex: EtOAc 30:1) = 0.61. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.46 (t, J = 7.8, 2H), 7.37 (dd, J = 10.7, 4.1, 1H), 7.29 (s, 2H), 7.24 (dd, J = 7.5, 5.8, 2H), 7.18 (d, J = 8.5, 2H), 7.10 (dt, J = 15.4, 4.0, 2H), 7.04 (t, J = 7.4, 1H), 6.62 (d, J = 7.6, 1H), 3.85 (q, J = 7.0, 1H), 2.80–2.67 (m, 2H), 2.28 (ddd, J = 17.3, 10.9, 6.6, 1H), 2.05–1.95 (m, 1H), 1.38 (d, J = 7.1, 3H); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 142.72, 141.05, 139.66, 136.74, 135.08, 134.31, 131.63, 130.13, 130.01, 128.65, 128.13, 126.97, 126.91, 126.37, 126.23, 126.02, 40.33, 28.69, 23.15, 16.92; *m/z* (EI)(%): 344.7 (2.4), 343.7 (8.5), 328.6 (3.3), 232.0 (5.5), 216.9 (24.0), 229.9 (35.3), 214.6 (70.3), 213.3 (21.6), 212.7 (45.5), 204.9 (17.7), 204.0 (32.2), 203.0 (51.3), 201.9 (62.0), 200.4 (100), 191.1 (10.6), 190.0 (15.7), 187.9 (39.1), 178.1 (15.3), 176.8 (20.6), 175.5 (19.5), 165.1 (12.4), 164.1 (14.3), 162.8 (17.0), 140.4 (11.1), 139.2 (15.3), 138.5 (40.0), 138.0 (17.5), 127.4 (16.2), 126.4 (12.5), 124.7 (23.4), 116.5 (11.7), 115.5 (18.8), 114.1 (29.8), 111.4 (25.0), 103.5 (23.7), 102.2 (34.8), 91.1 (42.8), 77.4 (35.9); HRMS calcd. for $C_{24}H_{21}{}^{35}Cl$: 344.13263, found: 344.13257; IR (KBr): ν = 3059, 3023, 2965, 2933, 2881, 2830, 1597, 1487, 1449, 1092, 1011, 906, 828, 769, 730, 702 cm^{-1}.

3-(1-(4-Methoxyphenyl)but-3-en-1-yl)-4-phenyl-1,2-dihydronaphthalene (211g)

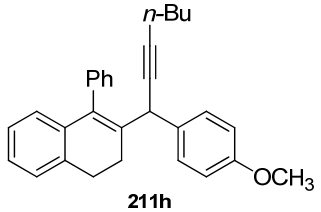


211g

Colorless oil, R_f (Hex: EtOAc 30:1) = 0.39. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.42 (t, J = 7.4, 2H), 7.36–7.31 (m, 1H), 7.25 (d, J = 6.5, 2H), 7.15–6.96 (m, 5H), 6.83–6.75 (m, 2H), 6.60–6.52 (m, 1H), 5.71 (dd, J = 17.1, 10.0, 1H), 5.05–4.94 (m, 2H), 3.79–3.72 (m, 4H, -OCH_3 and -CH), 2.73 (ddd, J = 16.2, 9.2, 6.3, 2H), 2.65–2.47 (m, 2H), 2.30 (ddd, J = 16.4, 10.1, 6.4, 1H), 2.19–2.05 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 157.84, 139.70, 139.49, 137.03, 136.99, 135.23, 134.98, 134.80, 130.87, 130.38, 128.51, 128.39, 126.87, 126.76, 126.20, 126.13, 126.05, 116.00, 113.48, 55.18, 45.83, 36.00, 28.54, 23.21; *m/z* (EI)(%): 365.9 (4.8), 326.5 (7.8), 325.8 (17.3), 324.4 (100), 217.8 (3.7), 216.9 (11.2), 216.1 (42.4), 214.8 (24.8), 214.2 (20.7), 213.3 (35.8), 202.1 (17.2), 200.8 (13.0), 200.1 (9.7), 199.5 (15.3), 187.1 (5.3), 175.6 (4.0), 119.7 (3.4), 91.3 (3.9); [M+Na] HRMS calcd. for $C_{27}H_{26}ONa$: 389.18759,

found: 389.18790; IR (KBr): ν = 3064, 3022, 2933, 2831, 1607, 1507, 1448, 1298, 1245, 1177, 1035, 911, 827, 767, 700 cm^{-1}.

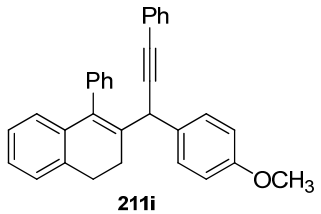
3-(1-(4-Methoxyphenyl)hept-2-yn-1-yl)-4-phenyl-1,2-dihydronaphthalene (211h)



211h

Colorless oil, R_f (Hex: EtOAc 30:1) = 0.38. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.55–7.23 (m, 7H), 7.14–7.05 (m, 2H), 7.05–6.98 (m, 1H), 6.86–6.74 (m, 2H), 6.68–6.58 (m, 1H), 4.65 (s, 1H), 3.77 (s, 3H), 2.75 (tdd, *J* = 15.2, 13.1, 6.6, 2H), 2.52 (ddd, *J* = 16.2, 11.2, 6.6, 1H), 2.27 (td, *J* = 6.9, 2.3, 2H), 2.12 (ddd, *J* = 16.1, 7.4, 6.4, 1H), 1.62–1.39 (m, 4H), 0.93 (t, *J* = 7.2, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 158.24, 139.07, 137.84, 136.70, 135.39, 134.42, 132.26, 130.52, 129.97, 128.69, 128.46, 127.05, 126.52, 126.19, 126.15, 113.45, 84.02, 79.07, 55.22, 39.60, 31.16, 28.76, 23.89, 21.95, 18.60, 13.64; *m/z* (EI)(%): 408.1 (10.2), 406.5 (88.0), 374.7 (15.6), 363.1 (22.0), 348.6 (100), 318.5 (11.5), 317.2 (18.7), 288.3 (11.9), 271.1 (9.3), 255.0 (12.4), 253.0 (18.5), 251.7 (26.0), 239.9 (32.2), 238.5 (45.5), 237.2 (35.5), 225.0 (49.0), 214.7 (43.4), 212.6 (41.3), 203.1 (32.1), 201.9 (48.1), 200.9 (51.7), 199.4 (65.2), 187.8 (15.1), 170.9 (17.3), 158.8 (16.4), 143.1 (13.5), 127.3 (15.9), 121.0 (23.6), 119.8 (18.9), 114.2 (19.1), 91.1 (17.1); [M+Na] HRMS calcd. for $C_{30}H_{30}ONa$: 429.21889, found: 429.21890; IR (KBr): ν = 3059, 3021, 2932, 2836, 1606, 1504, 1451, 1244, 1173, 1034, 834, 768, 701 cm^{-1}.

3-(1-(4-Methoxyphenyl)-3-phenylprop-2-yn-1-yl)-4-phenyl-1,2-dihydronaphthalene (211i)

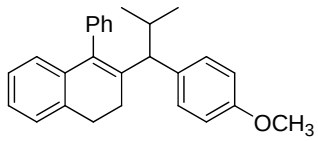


211i

Colorless oil, R_f (Hex: EtOAc 30:1) = 0.41. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.59–7.27 (m, 12H), 7.16–7.09 (m, 2H), 7.06 (td, *J* = 7.6, 1.7, 1H), 6.89–6.83 (m, 2H), 6.69 (d, *J* = 7.6, 1H), 4.93 (s, 1H), 3.80 (s, 3H), 2.90–2.83 (m, 1H), 2.82–2.74 (m, 1H), 2.65 (ddd, *J* = 16.2, 11.5, 6.4, 1H), 2.28–2.20 (m, 1H); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 158.43, 138.93, 136.97, 136.55, 135.37, 135.10, 131.69, 131.57, 130.57, 129.94, 128.84, 128.50, 128.23, 127.86, 127.20, 127.11, 126.71, 126.30, 126.22, 123.68, 113.64, 89.07, 83.99, 55.24, 40.22, 28.76, 24.03; *m/z* (EI)(%): 428.0 (15.1), 426.5 (100), 349.6 (12.3), 348.7 (15.0), 347.5 (14.6), 334.6 (19.1), 333.2 (24.7), 319.5 (13.9), 318.5 (21.5), 317.5 (36.9), 316.5 (29.3), 315.4 (33.1), 303.4 (29.8), 302.3 (39.0), 301.3 (27.6), 300.0 (19.8), 289.2 (20.5), 238.8 (23.8), 237.6 (19.2), 219.8 (32.5), 218.6 (29.3), 217.6 (28.0), 229.8 (17.8), 214.4 (39.8), 213.4 (25.0), 212.7 (20.2), 203.9 (21.7), 202.9 (30.1), 201.8 (51.6), 200.9 (25.7), 200.1 (42.6), 188.1 (24.6), 178.0 (21.7), 177.1

(24.4), 176.2 (27.2), 175.3 (27.3), 150.8 (16.4), 120.1 (10.4), 91.4 (12.7), 90.5 (8.7), 77.7 (8.5); [M+H] HRMS calcd. for $C_{32}H_{27}O$: 427.20564, found: 427.20578; IR (KBr): ν = 3059, 3024, 2935, 2891, 2832, 1603, 1504, 1445, 1245, 1174, 1034, 907, 836, 731, 697 cm^{-1}.

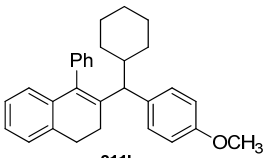
3-(1-(4-Methoxyphenyl)-2-methylpropyl)-4-phenyl-1,2-dihydronaphthalene (211j)



211j

White solid, R_f (Hex: EtOAc 30:1) = 0.54. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.54–7.43 (m, 2H), 7.40 (tt, *J* = 7.4, 1.3, 1H), 7.28–7.19 (m, 2H), 7.12–7.00 (m, 4H), 6.97 (td, *J* = 7.5, 1.5, 1H), 6.83–6.74 (m, 2H), 6.51 (dd, *J* = 7.6, 1.0, 1H), 3.77 (s, 3H), 3.18 (d, *J* = 11.1, 1H), 2.93–2.81 (m, 1H), 2.77–2.64 (m, 1H), 2.49 (ddd, *J* = 15.8, 7.9, 6.3, 1H), 2.40–2.20 (m, 2H), 1.05 (d, *J* = 6.6, 3H), 0.67 (d, *J* = 6.4, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 157.70, 140.12, 140.06, 137.27, 135.24, 134.93, 134.21, 131.10, 130.86, 128.98, 128.41, 128.17, 126.72, 126.66, 126.07, 125.98, 125.94, 113.46, 55.27, 55.13, 29.10, 28.65, 23.30, 21.84, 21.25; *m/z* (EI)(%): 368.4 (1.8), 326.4 (3.3), 325.3 (16.8), 324.4 (18.3), 230.4 (5.5), 217.7 (9.5), 216.8 (47.8), 229.9 (71.7), 214.8 (91.4), 213.2 (100), 201.9 (38.9), 200.8 (53.8), 199.5 (48.1), 188.9 (12.6), 162.5 (11.6), 121.3 (14.9), 120.7 (20.1), 119.9 (26.7), 114.2 (12.7), 107.1 (8.8), 91.5 (17.3), 90.6 (18.3), 77.7 (9.4); [M+Na] HRMS calcd. for $C_{27}H_{28}ONa$: 391.20324, found: 391.20377; IR (KBr): ν = 3058, 3022, 2955, 2833, 1607, 1508, 1456, 1242, 1176, 1036, 907, 829, 766, 730, 704 cm^{-1}.

3-(Cyclohexyl(4-methoxyphenyl)methyl)-4-phenyl-1,2-dihydronaphthalene (211k)

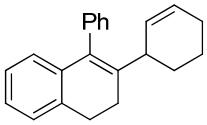


211k

White solid, R_f (Hex: EtOAc 30:1) = 0.52. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.49 (dt, *J* = 6.4, 5.4, 2H), 7.44–7.36 (m, 1H), 7.24 (td, *J* = 8.2, 2.3, 2H), 7.12–7.07 (m, 1H), 7.07–7.00 (m, 3H), 6.97 (td, *J* = 7.5, 1.6, 1H), 6.86–6.74 (m, 2H), 6.51 (dd, *J* = 7.6, 1.1, 1H), 3.78 (s, 3H), 3.24 (d, *J* = 11.0, 1H), 2.94–2.83 (m, 1H), 2.79-2.67 (m, 1H), 2.49 (ddd, *J* = 15.7, 7.9, 6.3, 1H), 2.43–2.29 (m, 1H), 2.04–1.85 (m, 2H), 1.78 (d, *J* = 13.0, 1H), 1.69–1.53 (m, 2H), 1.50–1.41 (m, 1H), 1.35–1.02 (m, 3H), 1.00–0.84 (m, 1H), 0.66–0.44 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 157.69, 140.05, 139.60, 137.26, 134.91, 134.77, 134.45, 131.09, 130.85, 129.06, 128.39, 128.12, 126.70, 126.65, 126.05, 125.94, 125.87, 113.47, 55.12, 54.08, 38.87, 32.27, 31.55, 28.64, 26.77, 26.50, 26.45, 23.40; *m/z* (EI)(%): 408.8 (1.5), 326.4 (3.4), 325.2 (21.0), 324.3 (11.1), 323.4 (5.5), 216.7 (8.7), 229.9 (12.1), 214.7 (18.6), 213.7 (8.6), 202.9 (5.8), 202.0 (12.7), 201.1 (12.6), 200.2 (11.5), 199.3 (6.0), 177.3 (5.2), 151.2 (3.0), 127.6 (5.8), 121.4 (16.5), 120.6 (20.3), 119.8 (13.9), 107.9 (9.1), 91.5 (50.9), 90.7 (46.9), 82.8 (37.1), 77.6

(24.8), 55.7 (100); [M+Na] HRMS calcd. for $C_{30}H_{32}ONa$: 431.23454, found: 431.23450; IR (KBr): ν = 3021, 2924, 2847, 1606, 1505, 1448, 1244, 1177, 1035, 906, 832, 728 cm^{-1}.

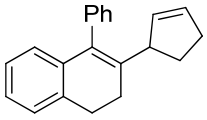
3-(Cyclohex-2-en-1-yl)-4-phenyl-1,2-dihydronaphthalene (211l)



211l

Colorless oil, R_f (Hex: EtOAc 30:1) = 0.46. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.40 (dd, *J* = 11.3, 4.4, 2H), 7.36–7.29 (m, 1H), 7.16 (dd, *J* = 13.0, 6.1, 3H), 7.07 (td, *J* = 7.3, 1.3, 1H), 7.01 (td, *J* = 7.5, 1.3, 1H), 6.56 (dd, *J* = 7.6, 0.8, 1H), 5.78 (ddt, *J* = 9.7, 4.9, 2.5, 1H), 5.46 (d, *J* = 10.0, 1H), 3.08 (ddd, *J* = 9.9, 5.9, 3.4, 1H), 2.90–2.75 (m, 2H), 2.36–2.26 (m, 2H), 2.07–1.88 (m, 2H), 1.77–1.69 (m, 1H), 1.68–1.60 (m, 1H), 1.58–1.45 (m, 1H), 1.45–1.33 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 141.59, 139.78, 137.10, 135.40, 134.02, 130.24, 130.11, 128.57, 128.33, 126.90, 126.58, 126.12, 125.96, 125.70, 40.24, 28.89, 27.76, 24.74, 23.97, 22.03; *m/z* (EI)(%): 288.3 (23.1), 287.3 (62.4), 286.2 (100), 285.1 (28.6), 271.3 (15.4), 259.2 (19.5), 258.2 (40.8), 257.2 (25.1), 242.2 (33.4), 229.1 (29.8), 217.2 (31.1), 229.1 (35.0), 209.1 (35.5), 205.1 (34.7), 203.1 (33.0), 195.1 (30.7), 191.1 (22.9), 181.1 (24.5), 179.1 (24.3), 169.1 (26.3), 167.1 (38.7), 165.1 (37.6), 157.1 (17.9), 143.1 (19.9), 141.1 (12.4), 117.1 (9.7), 81.2 (10.0); HRMS calcd. for $C_{22}H_{22}$: 286.17160, found: 286.17127; IR (KBr): ν = 3020, 2926, 1597, 1481, 1442, 1041, 966, 905, 714 cm^{-1}.

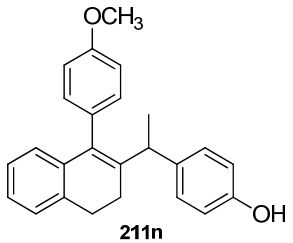
3-(Cyclopent-2-en-1-yl)-4-phenyl-1,2-dihydronaphthalene (211m)



211m

Colorless oil, R_f (Hex: EtOAc 30:1) = 0.56. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.40 (dd, *J* = 10.2, 4.5, 2H), 7.32 (ddd, *J* = 6.3, 2.4, 1.2, 1H), 7.21–7.11 (m, 3H), 7.03 (dtd, *J* = 23.8, 7.4, 1.2, 2H), 6.61–6.55 (m, 1H), 5.80 (dq, *J* = 4.7, 2.3, 1H), 5.49 (dq, *J* = 4.2, 2.1, 1H), 3.57 (tdd, *J* = 6.9, 4.7, 2.4, 1H), 2.82 (t, *J* = 7.8, 2H), 2.46–2.36 (m, 1H), 2.32–2.21 (m, 3H), 2.00–1.89 (m, 1H), 1.72–1.62 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 140.70, 139.93, 137.05, 135.29, 133.66, 133.57, 132.09, 130.36, 128.27, 126.92, 126.54, 126.11, 125.96, 125.68, 49.13, 32.81, 29.09, 28.77, 23.39; *m/z* (EI)(%): 273.3 (24.0), 272.3 (100), 271.3 (11.3), 257.2 (1.9), 243.2 (5.5), 229.2 (7.4), 229.2 (10.4), 202.2 (9.9), 189.1 (4.8), 165.1 (5.5), 128.1 (2.3), 115.1 (2.8), 91.2 (7.3), 77.2 (4.7), 67.2 (16.5), 66.2 (7.3), 65.2 (4.9), 53.2 (2.6); HRMS calcd. for $C_{21}H_{20}$: 272.15595, found: 272.15588; IR (KBr): ν = 3051, 2934, 2886, 2841, 1596, 1483, 1442, 1029, 739, 700 cm^{-1}.

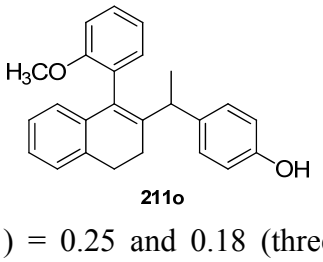
4-(1-(1-(4-Methoxyphenyl)-3,4-dihydronaphthalen-2-yl)ethyl)phenol (211n)



211n

White solid, R_f (Hex: EtOAc 5:1) = 0.26. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.20 (s, 2H), 7.13–6.95 (m, 7H), 6.76–6.69 (m, 2H), 6.67–6.62 (m, 1H), 4.75 (s, 1H), 3.90–3.78 (m, 4H, -OCH_3 and -CH), 2.78–2.63 (m, 2H), 2.31–2.19 (m, 1H), 2.07–1.95 (m, 1H), 1.35 (d, J = 7.1, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 158.35, 153.55, 142.25, 137.26, 136.52, 135.22, 133.18, 132.01, 131.18, 128.38, 126.89, 126.14, 126.09, 125.90, 114.84, 113.97, 55.24, 39.93, 28.76, 23.15, 17.09; *m/z* (EI)(%): 356.7 (6.1), 247.0 (9.2), 234.8 (10.0), 233.8 (14.3), 232.7 (18.0), 231.8 (18.9), 217.7 (12.6), 214.4 (17.0), 201.8 (40.6), 200.8 (29.1), 199.9 (34.8), 190.0 (24.0), 188.9 (34.9), 188.0 (33.5), 187.0 (24.5), 165.0 (25.4), 162.6 (22.7), 131.3 (22.4), 130.4 (20.6), 127.4 (20.7), 121.3 (51.9), 120.7 (85.2), 119.7 (100), 117.5 (20.4), 115.5 (24.5), 114.0 (23.2), 106.0 (46.8), 101.9 (28.5), 94.5 (65.6), 93.3 (79.6), 91.6 (24.7), 90.9 (88.7), 84.7 (28.7), 83.5 (35.4), 82.6 (36.5), 77.3 (81.9), 65.9 (20.2); [M+Na] HRMS calcd. for $C_{25}H_{24}O_2Na$: 379.16685, found: 379.16727; IR (KBr): ν = 3391, 2931, 1602, 1505, 1448, 1365, 1228, 1171, 1025, 905, 824, 775, 729 cm^{-1}.

4-(1-(1-(2-Methoxyphenyl)-3,4-dihydronaphthalen-2-yl)ethyl)phenol (211o)



211o

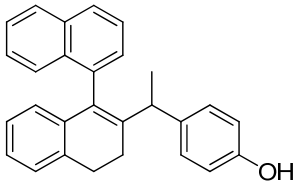
White solid, R_f (Hex: EtOAc 5:1) = 0.25 and 0.18 (three isomers). ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.39–7.32 (m, 1H), 7.22–7.14 (m, 2H), 7.10 (t, J = 8.0, 2H), 7.08–6.98 (m, 4H), 6.75–6.68 (m, 2H), 6.58 (dd, J = 7.1, 3.5, 1H), 4.62 (d, J = 13.0, 1H), 3.77 (d, J = 6.2, 3H), 3.70–3.64 (m, 1H), 2.78–2.67 (m, 2H), 2.37–2.13 (m, 1H), 2.08–1.93 (m, 1H), 1.34 (dd, J = 7.1, 4.5, 3H); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 157.89, 157.38, 153.48, 153.44, 142.62, 142.50, 136.81, 136.73, 136.45, 136.23, 135.15, 135.00, 131.81, 131.78, 130.25, 129.36, 128.70, 128.51, 128.44, 128.37, 128.34, 128.32, 126.92, 126.90, 126.21, 126.17, 125.96, 125.94, 125.25, 125.01, 120.73, 120.63, 114.78, 114.64, 110.81, 110.78, 55.34, 55.17, 40.54, 40.48, 28.79, 28.70, 23.17, 22.99, 16.97, 16.06; *m/z* (EI)(%): 357.7 (16.3), 356.6 (28.2), 356.1 (100), 355.3 (47.8), 354.6 (21.5), 341.6 (24.6), 340.3 (41.8), 339.6 (10.1), 249.0 (11.5), 247.1 (73.5), 244.8 (41.3), 243.6 (48.2), 234.0 (91.4), 232.8 (74.4), 231.8 (81.7), 230.5 (54.4), 229.9 (22.4), 229.1 (39.8), 228.1 (19.0), 219.8 (21.3), 218.7 (33.5), 217.5 (40.8), 229.7 (22.0), 214.7 (32.6), 213.7 (25.8), 212.3 (47.2), 202.1 (35.1), 200.9 (35.4), 199.4 (42.3), 189.0 (15.6), 187.6 (15.0), 120.8 (54.3), 119.7 (18.5), 107.3 (20.6), 106.2 (15.7), 91.5 (11.3), 90.6 (10.2); [M+Na]

HRMS calcd. for $C_{25}H_{24}O_2Na$: 379.16685, found: 379.16656; IR (KBr): ν = 3402, 3019, 2936, 2833, 1598, 1495, 1447, 1235, 1176, 1113, 1028, 906, 831, 734 cm^{-1}.

^1H NMR (600 MHz, $CDCl_3$): δ = 7.34 (tt, J = 7.6, 3.8, 1H), 7.21–7.13 (m, 2H), 7.10 (dd, J = 16.4, 7.7, 2H), 7.07–6.96 (m, 4H), 6.76–6.66 (m, 2H), 6.57 (dd, J = 7.2, 3.6, 1H), 4.54 (d, J = 11.7, 1H), 3.77 (d, J = 3.8, 3H), 3.69–3.62 (m, 1H), 2.78–2.65 (m, 2H), 2.35–2.13 (m, 1H), 2.06–1.91 (m, 1H), 1.33 (dd, J = 7.1, 4.3, 3H); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 157.90, 157.39, 153.48, 153.44, 142.61, 142.49, 136.84, 136.74, 136.45, 136.26, 135.16, 135.00, 131.81, 131.79, 130.27, 129.37, 128.72, 128.51, 128.44, 128.37, 128.35, 126.92, 126.90, 126.21, 126.17, 125.96, 125.93, 125.26, 125.02, 120.73, 120.63, 114.78, 114.63, 110.80, 110.77, 55.34, 55.18, 40.55, 40.48, 28.80, 28.70, 23.18, 22.99, 16.98, 16.06; *m/z* (EI)(%): 357.8 (18.5), 356.5 (100), 355.6 (39.1), 354.9 (67.4), 341.5 (19.3), 340.7 (42.2), 339.8 (23.1), 248.0 (17.0), 247.0 (24.2), 245.1 (34.6), 243.7 (26.6), 234.8 (19.3), 234.0 (30.4), 232.8 (48.8), 231.8 (43.4), 230.7 (23.9), 230.1 (19.1), 229.3 (14.5), 228.4 (10.8), 218.7 (16.1), 217.6 (14.1), 216.7 (10.9), 214.6 (17.6), 213.5 (11.7), 212.2 (18.6), 201.9 (14.4), 200.8 (13.6), 199.6 (15.2), 119.8 (10.7); [M+Na] HRMS calcd. for $C_{25}H_{24}O_2Na$: 379.16685, found: 379.16653; IR (KBr): ν = 3403, 3018, 2934, 2834, 1598, 1495, 1447, 1234, 1176, 1114, 1029, 906, 831, 735 cm^{-1}.

^1H NMR (600 MHz, $CDCl_3$): δ = 7.38–7.32 (m, 1H), 7.21–7.07 (m, 4H), 7.07–6.97 (m, 4H), 6.74–6.68 (m, 2H), 6.60–6.53 (m, 1H), 4.55 (d, J = 11.8, 1H), 3.77 (d, J = 4.0, 3H), 3.69–3.62 (m, 1H), 2.78–2.65 (m, 2H), 2.35–2.13 (m, 1H), 2.06–1.92 (m, 1H), 1.33 (dd, J = 7.1, 4.3, 3H); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 157.90, 157.39, 153.48, 153.44, 142.61, 142.50, 136.84, 136.73, 136.45, 136.25, 135.15, 135.00, 131.81, 131.79, 130.27, 129.36, 128.72, 128.51, 128.44, 128.37, 128.35, 128.32, 126.92, 126.90, 126.21, 126.17, 125.96, 125.93, 125.26, 125.02, 120.73, 120.63, 114.78, 114.63, 110.80, 110.77, 55.34, 55.18, 40.55, 40.48, 28.80, 28.70, 23.18, 22.99, 16.98, 16.06; *m/z* (EI)(%): 357.7 (12.9), 357.0 (12.4), 356.1 (100), 355.2 (28.2), 341.2 (17.3), 340.7 (36.4), 248.0 (24.3), 245.9 (49.4), 244.9 (40.0), 243.5 (58.7), 234.2 (51.4), 232.8 (57.7), 231.8 (64.3), 230.8 (57.8), 229.6 (82.4), 227.7 (24.0), 225.8 (17.9), 219.8 (19.3), 219.0 (55.1), 217.8 (63.4), 216.7 (53.2), 229.7 (41.8), 214.7 (65.3), 213.7 (49.6), 212.3 (79.4), 203.9 (19.1), 203.0 (27.7), 201.9 (78.6), 200.9 (61.6), 199.5 (89.3), 190.2 (25.7), 189.1 (45.2), 188.3 (33.7), 187.0 (63.2), 178.1 (19.1), 177.2 (23.6), 176.4 (17.1), 175.5 (25.2), 165.0 (20.2), 164.0 (30.9), 162.8 (27.5), 150.0 (19.6), 120.7 (74.7), 119.9 (34.1), 114.3 (18.1), 106.9 (58.9), 94.5 (31.0), 93.5 (42.3), 91.3 (40.3), 90.6 (14.2), 77.7 (13.7), 77.2 (30.8); [M+Na] HRMS calcd. for $C_{25}H_{24}O_2Na$: 379.16685, found: 379.16644; IR (KBr): ν = 3403, 3018, 2934, 2834, 1598, 1495, 1447, 1234, 1176, 1113, 1028, 906, 831, 734 cm^{-1}.

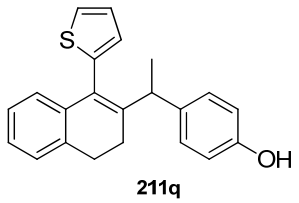
4-(1-(3,4-Dihydro-[1,1'-binaphthalen]-2-yl)ethyl)phenol (211p)



211p

White solid, R_f (Hex: EtOAc 5:1) = 0.22. ^{1}H NMR (400 MHz, DMSO-d^6): δ = 9.14 (d, J = 17.5, 2H), 7.94 (dd, J = 13.2, 7.7, 4H), 7.78–7.55 (m, 4H), 7.55–7.32 (m, 6H), 7.13 (dd, J = 6.7, 3.6, 2H), 7.07–6.93 (m, 4H), 6.90–6.73 (m, 4H), 6.71–6.61 (m, 2H), 6.59–6.48 (m, 2H), 6.17 (ddd, J = 10.9, 7.7, 0.9, 2H), 3.47–3.34 (m, 2H), 2.91–2.65 (m, 4H), 2.40–2.20 (m, 2H), 2.08–1.88 (m, 2H), 1.29 (d, J = 7.1, 3H), 1.11 (d, J = 7.1, 3H); ^{13}C NMR (100 MHz, DMSO-d^6): δ = 155.50, 155.41, 143.79, 143.28, 136.85, 136.55, 136.26, 134.59, 134.43, 133.53, 133.44, 133.33, 133.18, 132.20, 131.81, 130.66, 130.41, 128.34, 127.97, 127.87, 127.60, 127.51, 127.33, 127.00, 126.17, 126.03, 126.00, 125.84, 125.43, 124.92, 114.96, 114.78, 40.38, 39.97, 28.14, 28.06, 22.86, 22.71, 17.16, 16.91; *m/z* (EI)(%): 376.9 (3.7), 361.6 (2.4), 281.1 (8.5), 267.1 (20.6), 266.1 (24.1), 265.2 (21.0), 264.3 (20.0), 254.0 (23.8), 253.1 (32.4), 252.2 (41.3), 251.0 (40.0), 250.0 (31.7), 248.9 (17.4), 238.9 (20.7), 238.0 (22.1), 237.1 (15.3), 200.5 (16.1), 163.6 (18.3), 162.7 (15.0), 152.2 (14.3), 151.2 (16.4), 150.3 (14.3), 149.4 (13.3), 141.4 (19.5), 140.4 (34.8), 139.4 (25.7), 132.8 (15.2), 131.5 (20.3), 130.6 (18.5), 129.6 (21.4), 128.4 (32.1), 127.4 (46.8), 126.5 (52.5), 125.5 (29.4), 121.4 (67.5), 120.7 (97.7), 119.8 (99.9), 118.6 (28.2), 117.5 (38.8), 116.6 (42.2), 115.7 (40.7), 114.8 (29.5), 113.9 (25.7), 107.6 (40.8), 106.8 (78.5), 106.1 (38.4), 103.8 (17.6), 103.0 (22.5), 94.5 (67.8), 93.5 (55.8), 91.4 (100), 90.5 (50.3), 77.8 (38.2), 77.0 (46.7), 66.0 (17.4); [M+Na] HRMS calcd. for $C_{28}H_{24}ONa$: 399.17194, found: 399.17209; IR (KBr): ν = 3375, 3054, 2962, 2933, 2828, 1602, 1509, 1439, 1367, 1227, 1174, 1042, 832, 777, 733 cm^{-1}.

4-(1-(1-(Thiophen-2-yl)-3,4-dihydronaphthalen-2-yl)ethyl)phenol (211q)

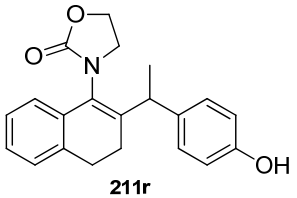


211q

Colorless oil, R_f (Hex: EtOAc 5:1) = 0.31. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.43–7.36 (m, 1H), 7.19–7.12 (m, 3H), 7.12–7.05 (m, 3H), 6.99 (dd, J = 3.4, 1.0, 1H), 6.86–6.82 (m, 1H), 6.78–6.72 (m, 2H), 4.68 (s, 1H), 4.03 (q, J = 7.1, 1H), 2.75–2.64 (m, 2H), 2.31–2.23 (m, 1H), 2.02 (ddd, J = 16.1, 7.9, 6.3, 1H), 1.39 (d, J = 7.1, 3H); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 153.64, 146.75, 140.23, 136.74, 135.99, 134.79, 128.46, 127.54, 127.07, 126.88, 126.45, 126.35, 125.93, 125.66, 125.51, 114.90, 40.35, 28.38, 23.47, 17.05; *m/z* (EI)(%): 334.5 (6.3), 333.5 (27.5), 332.6 (46.5), 332.0 (100), 331.1 (73.3), 330.3 (41.8), 317.3 (32.4), 316.2 (28.3), 315.3 (17.0), 302.5 (12.8), 237.9 (11.2), 236.7 (10.8), 232.8 (10.4), 231.7 (13.7), 230.5 (12.2), 222.8 (14.2), 221.7 (15.5), 220.5 (17.0), 219.5 (12.5), 210.8 (11.0), 209.8 (14.7), 208.8 (17.3), 207.8 (16.1), 206.7 (10.2), 164.8 (9.0), 163.6 (11.6), 119.7 (8.0); [M+Na] HRMS calcd. for

$C_{22}H_{20}OSNa$: 355.11271, found: 355.11249; IR (KBr): ν = 3369, 3024, 2939, 2882, 1606, 1508, 1441, 1364, 1222, 1177, 1112, 1037, 907, 831, 726 cm^{-1}.

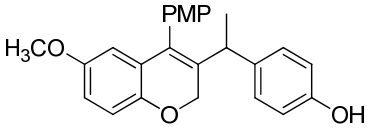
3-(2-(1-(4-Hydroxyphenyl)ethyl)-3,4-dihydronaphthalen-1-yl)oxazolidin-2-one (211r)



211r

White solid, R_f (Hex: EtOAc 1:1) = 0.43. ^{1}H NMR (600 MHz, DMSO-d^6): δ = 9.23 (d, J = 35.2, 1H), 7.20 (td, J = 7.0, 1.3, 1H), 7.17–7.10 (m, 3H), 7.08 (d, J = 8.5, 1H), 7.02 (d, J = 7.6, 1H), 6.72 (d, J = 8.5, 1H), 6.67 (d, J = 8.6, 1H), 4.62–4.45 (m, 2H), 4.04 (dq, J = 55.4, 7.0, 1H), 3.90–3.79 (m, 1H), 3.73 (td, J = 8.8, 6.5, 1H), 2.67–2.43 (m, 2H), 2.27–2.08 (m, 1H), 2.02–1.68 (m, 1H), 1.35 (dd, J = 27.6, 7.1, 3H); ^{13}C NMR (150 MHz, DMSO-d^6): δ = 156.93, 156.88, 155.74, 155.71, 145.51, 144.76, 135.41, 135.32, 133.25, 132.09, 131.31, 131.08, 128.41, 128.10, 127.55, 127.52, 127.15, 127.10, 126.67, 126.62, 126.42, 126.14, 121.79, 121.70, 115.15, 114.83, 62.30, 62.21, 46.63, 46.09, 38.24, 37.73, 27.21, 27.05, 22.88, 22.84, 16.92, 16.25; *m/z* (EI)(%): 335.3 (1.8), 261.8 (3.5), 247.9 (13.6), 247.2 (11.7), 245.6 (15.0), 244.6 (14.1), 231.9 (10.9), 230.9 (13.0), 167.1 (10.6), 153.1 (10.3), 143.2 (10.8), 142.3 (10.9), 130.5 (21.5), 129.5 (14.7), 128.4 (29.0), 127.4 (38.7), 126.6 (23.0), 125.8 (12.0), 121.3 (63.2), 120.6 (41.1), 119.9 (100), 118.7 (25.6), 117.7 (20.9), 116.6 (22.6), 115.6 (48.1), 114.5 (49.8), 107.6 (15.7), 107.0 (19.0), 106.1 (26.1), 104.5 (11.2), 103.5 (26.0), 102.8 (22.9), 102.2 (28.7), 94.5 (37.9), 93.5 (67.7), 92.5 (13.2), 91.5 (71.8), 90.6 (56.9), 89.5 (24.5), 88.6 (26.4), 87.6 (10.3), 78.7 (20.4), 77.7 (65.5), 76.9 (60.5), 66.9 (13.6), 65.9 (45.0), 65.1 (30.3), 64.0 (12.1), 63.2 (11.0), 53.4 (11.5), 45.4 (15.1); [M+Na] HRMS calcd. for $C_{21}H_{21}O_3NNa$: 358.14136, found: 358.14136; IR (KBr): ν = 3237, 2934, 1721, 1596, 1506, 1431, 1252, 1124, 1087, 1033, 831, 760, 721, 674 cm^{-1}.

4-(1-(6-Methoxy-4-(4-methoxyphenyl)-2*H*-chromen-3-yl)ethyl)phenol (211a')

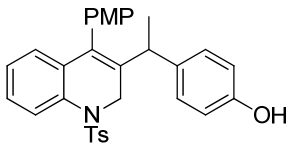


211a'

White solid, R_f (Hex: EtOAc 5:1) = 0.17. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.21 (s, 2H), 7.07 (t, J = 5.7, 2H), 6.99 (dd, J = 7.4, 1.5, 2H), 6.77 (d, J = 8.7, 1H), 6.74–6.69 (m, 2H), 6.64 (dd, J = 8.7, 3.0, 1H), 6.25 (d, J = 3.0, 1H), 5.09 (s, 1H), 4.62 (d, J = 13.9, 1H), 4.38 (d, J = 13.9, 1H), 3.88–3.81 (m, 4H, -OCH_3 and -CH), 3.63 (s, 3H), 1.37 (d, J = 7.2, 3H); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 158.81, 154.03, 153.97, 147.23, 135.49, 134.46, 130.92, 130.65, 128.95, 128.26, 126.82, 115.80, 115.16, 114.12, 112.79, 112.27, 65.10, 55.67, 55.26, 38.26, 17.06; *m/z* (EI)(%): 390.2 (3.9), 389.1 (25.1), 388.2 (94.9), 387.2 (4.9), 373.1 (8.0), 294.1 (3.4), 293.1 (9.1), 281.1 (5.6), 268.1 (34.8), 267.1 (100), 263.1 (10.9), 224.1 (6.8), 209.1 (3.9),

181.1 (4.3), 165.1 (6.3), 152.1 (5.6), 147.1 (5.3), 121.0 (50.5), 107.1 (6.5), 91.1 (7.6), 77.1 (11.3); [M+Na] HRMS calcd. for $C_{25}H_{24}O_4Na$: 411.15668, found: 411.15613; IR (KBr): ν = 3415, 2960, 2839, 1605, 1509, 1485, 1271, 1242, 1216, 1179, 1031, 870, 837, 808, 733, 709 cm^{-1}.

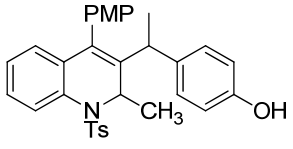
4-(1-(4-(4-Methoxyphenyl)-1-tosyl-1,2-dihydroquinolin-3-yl)ethyl)phenol (211b')



211b'

White solid, R_f (Hex: EtOAc 3:1) = 0.22. ^{1}H NMR (600 MHz, DMSO-d^6): δ = 9.31 (s, 1H), 7.57 (d, *J* = 7.9, 1H), 7.25 (t, *J* = 7.6, 1H), 7.14 (d, *J* = 7.8, 2H), 7.09 (t, *J* = 7.5, 1H), 6.94 (d, *J* = 8.1, 2H), 6.87 (d, *J* = 8.2, 2H), 6.75 (t, *J* = 7.6, 4H), 6.52 (s, 1H), 6.42 (d, *J* = 7.7, 2H), 4.30 (d, *J* = 18.0, 1H), 4.20 (d, *J* = 18.0, 1H), 3.76 (s, 3H), 3.44 (q, *J* = 6.9, 1H), 2.37 (s, 3H), 1.17 (d, *J* = 7.1, 3H); ^{13}C NMR (150 MHz, DMSO-d^6): δ = 158.35, 156.01, 143.54, 137.65, 135.13, 133.01, 132.57, 131.58, 130.34, 130.18, 129.09, 128.38, 128.31, 127.02, 126.82, 126.62, 125.90, 125.66, 115.22, 114.07, 55.05, 44.57, 38.99, 20.92, 17.18; *m/z* (EI)(%): 391.0 (1.0), 390.4 (1.2), 355.7 (3.0), 340.6 (1.7), 289.3 (4.3), 274.0 (5.8), 273.1 (8.1), 272.0 (12.4), 271.0 (8.0), 270.0 (12.3), 244.9 (9.0), 243.9 (9.1), 243.0 (7.6), 242.0 (5.2), 235.8 (6.6), 234.9 (8.4), 233.8 (9.1), 232.8 (6.5), 195.0 (5.7), 193.9 (16.0), 193.1 (48.2), 191.8 (100), 190.7 (29.5), 190.0 (17.1), 189.1 (6.1), 184.0 (8.5), 183.2 (11.3), 181.4 (5.2), 170.9 (5.3), 170.1 (6.0), 169.2 (7.8), 168.5 (15.0), 167.2 (17.4), 165.9 (25.7), 164.8 (18.7), 163.6 (9.5), 139.3 (5.7), 138.3 (6.0), 121.2 (6.2), 119.8 (20.0), 114.1 (12.9), 105.5 (25.0), 104.1 (20.2), 103.1 (5.6), 91.6 (9.4), 90.7 (21.5), 89.6 (17.2), 88.6 (11.6), 78.8 (9.1), 77.8 (13.8), 76.9 (6.7), 63.1 (6.8), 51.6 (12.8); [M+Na] HRMS calcd. for $C_{31}H_{29}O_4NSNa$: 534.17095, found: 534.17200; IR (KBr): ν = 3467, 3067, 3006, 2975, 1605, 1510, 1482, 1451, 1335, 1277, 1245, 1208, 1153, 1087, 1028, 869, 826, 795, 765, 712, 661 cm^{-1}.

4-(1-(4-(4-Methoxyphenyl)-2-methyl-1-tosyl-1,2-dihydroquinolin-3-yl)ethyl)phenol (211c')

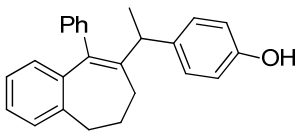


211c'

Light yellow solid, R_f (Hex: EtOAc 3:1) = 0.30. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.81–7.76 (m, 1H), 7.33–7.09 (m, 5H including one proton from $CHCl_3$), 7.06 (dd, *J* = 14.9, 8.0, 2H), 7.03–6.81 (m, 4H), 6.81–6.45 (m, 4H), 6.01–5.81 (m, 1H), 5.31 (s, 0.38H), 5.23 (q, *J* = 6.8, 0.41H), 5.16 (s, 0.59H), 4.85 (q, *J* = 6.8, 0.64H), 3.84 (d, *J* = 10.6, 3H), 3.66 (dq, *J* = 109.1, 7.4, 1H), 2.36 (d, *J* = 58.2, 3H), 1.36 (t, *J* = 6.8, 2.49H), 1.09 (d, *J* = 7.3, 1.89H), 0.44 (d, *J* =

6.8, 1.88H); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 158.62, 158.58, 154.55, 154.37, 143.26, 142.73, 142.56, 141.49, 136.57, 135.60, 135.17, 134.23, 132.02, 131.90, 131.86, 131.66, 131.18, 131.04, 130.67, 130.44, 130.18, 129.96, 129.93, 129.61, 129.19, 128.90, 128.83, 128.74, 127.42, 127.30, 127.23, 127.16, 126.71, 126.54, 126.38, 125.99, 125.64, 115.30, 115.27, 114.25, 113.64, 113.40, 55.25, 50.42, 50.15, 40.37, 38.91, 21.47, 21.44, 21.38, 20.18, 19.86, 18.27; *m/z* (EI)(%): 525.6 (1.5), 512.5 (3.2), 511.6 (12.3), 510.5 (37.1), 340.4 (9.0), 250.3 (17.9), 247.3 (10.5), 245.2 (42.5), 218.3 (6.4), 217.3 (5.6), 204.2 (6.1), 203.3 (7.2), 155.1 (24.4), 121.2 (56.3), 103.2 (9.1), 92.2 (10.3), 91.2 (100), 77.2 (14.8), 65.3 (19.1); [M+Na] HRMS calcd. for $C_{32}H_{31}O_4NSNa$: 548.18660, found: 548.18658; IR (KBr): ν = 3441, 2969, 1605, 1508, 1450, 1336, 1239, 1160, 1088, 1031, 905, 824, 729, 662 cm^{-1}.

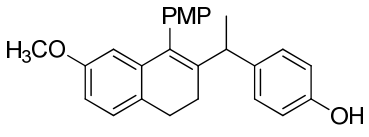
4-(1-(9-Phenyl-6,7-dihydro-5*H*-benzo[7]annulen-8-yl)ethyl)phenol (211d')



211d'

Yellow oil, R_f (Hex: EtOAc 5:1) = 0.34. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.42 (t, *J* = 7.5, 2H), 7.37–7.30 (m, 3H), 7.24 (t, *J* = 7.5, 2H), 7.16 (t, *J* = 7.3, 1H), 7.10 (d, *J* = 7.3, 2H), 7.01 (d, *J* = 8.1, 1H), 6.95 (d, *J* = 2.1, 1H), 6.69 (dd, *J* = 8.1, 2.3, 1H), 4.65 (s, 1H), 3.48 (q, *J* = 7.5, 1H), 2.65–2.50 (m, 3H), 2.35 (ddd, *J* = 14.2, 9.4, 5.0, 1H), 1.92–1.84 (m, 1H), 1.81–1.73 (m, 1H), 1.32 (d, *J* = 7.5, 3H); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 153.31, 150.37, 147.21, 142.15, 138.15, 137.18, 135.62, 129.10, 128.37, 128.34, 128.25, 126.94, 125.70, 119.92, 113.01, 110.65, 44.59, 35.73, 31.62, 26.25, 16.01; *m/z* (EI)(%): 341.0 (4.3), 339.7 (43.6), 236.0 (24.9), 234.9 (68.5), 233.8 (75.2), 232.5 (100), 222.8 (22.9), 221.9 (45.0), 220.8 (62.7), 219.6 (73.1), 218.6 (47.5), 217.1 (62.1), 214.4 (11.0), 206.8 (9.8), 201.9 (20.0), 200.6 (26.1), 199.6 (14.5), 191.0 (11.4), 190.0 (12.8), 188.9 (17.3), 187.7 (13.3), 176.4 (12.9), 154.9 (13.1), 91.5 (14.2), 90.8 (24.9); [M+H] HRMS calcd. for $C_{25}H_{25}O$: 341.18999, found: 341.18948; IR (KBr): ν = 3365, 3026, 2932, 2860, 1739, 1597, 1451, 1362, 1297, 1223, 1169, 1085, 1028, 904, 817, 733, 699 cm^{-1}.

4-(1-(7-Methoxy-1-(4-methoxyphenyl)-3,4-dihydronaphthalen-2-yl)ethyl)phenol (211s)

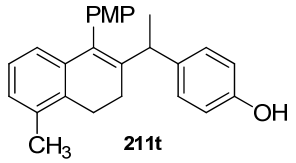


211s

Colorless oil, R_f (Hex: EtOAc 5:1) = 0.21. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.18 (s, 2H), 7.07 (t, *J* = 5.5, 2H), 7.03–6.91 (m, 3H), 6.76–6.66 (m, 2H), 6.61 (dd, *J* = 8.1, 2.7, 1H), 6.24 (d, *J* = 2.6, 1H), 4.81 (s, 1H), 3.89–3.77 (m, 4H, $-OCH_3$ and -CH), 3.63 (s, 3H), 2.70–2.55 (m, 2H), 2.22 (ddd, *J* = 17.0, 10.4, 6.8, 1H), 1.98 (ddd, *J* = 15.9, 7.7, 6.4, 1H), 1.33 (d, *J* = 7.1, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 158.38, 158.03, 153.59, 142.93, 138.44, 136.42, 133.17,

131.80, 131.15, 128.37, 127.58, 127.45, 114.83, 114.00, 112.77, 110.43, 55.23, 55.19, 40.05, 27.85, 23.57, 17.09; *m/z* (EI)(%): 389.4 (3.5), 388.3 (14.6), 387.3 (25.9), 386.3 (100), 385.3 (13.4), 384.3 (44.1), 371.3 (22.2), 277.2 (10.3), 275.2 (22.4), 265.2 (12.7), 121.1 (17.4), 107.1 (7.4); [M+H] HRMS calcd. for $C_{26}H_{27}O_3$: 387.19547, found: 387.19528; IR (KBr): ν = 3406, 2938, 2834, 1604, 1501, 1234, 1176, 1106, 1034, 907, 828, 729 cm^{-1}.

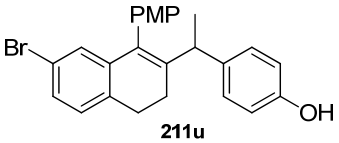
4-(1-(1-(4-Methoxyphenyl)-5-methyl-3,4-dihydronaphthalen-2-yl)ethyl)phenol (211t)



211t

Colorless oil, R_f (Hex: EtOAc 5:1) = 0.22. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.17 (s, 2H), 7.09 (d, *J* = 8.4, 2H), 7.03–6.85 (m, 4H), 6.72 (d, *J* = 8.5, 2H), 6.51 (d, *J* = 6.9, 1H), 4.75 (s, 1H), 3.91–3.74 (m, 4H, -OCH_3 and -CH), 2.78–2.67 (m, 1H), 2.63–2.52 (m, 1H), 2.32–2.13 (m, 4H, Ar-CH_3 and 1/2 -CH_2), 2.01 (dt, *J* = 15.9, 6.2, 1H), 1.34 (d, *J* = 7.1, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 158.30, 153.55, 141.58, 137.13, 136.59, 134.20, 133.47, 133.36, 132.42, 131.21, 128.38, 128.25, 125.46, 124.17, 114.81, 113.92, 55.23, 39.95, 24.51, 22.81, 19.56, 17.07; *m/z* (EI)(%): 371.4 (23.6), 370.3 (79.1), 356.3 (12.2), 355.3 (49.7), 276.2 (18.6), 262.2 (14.3), 261.2 (38.6), 259.2 (13.5), 250.2 (11.4), 249.2 (38.1), 248.2 (13.1), 247.2 (26.7), 245.2 (18.5), 244.2 (17.5), 239.2 (13.4), 237.2 (9.8), 236.2 (12.2), 235.2 (24.4), 234.2 (18.1), 233.2 (14.9), 232.2 (12.2), 231.2 (19.0), 229.2 (14.6), 219.2 (12.4), 218.2 (12.6), 217.2 (13.1), 216.1 (14.9), 229.1 (26.0), 203.1 (25.9), 202.1 (37.3), 191.1 (17.6), 190.1 (16.9), 189.1 (30.9), 185.2 (10.9), 178.1 (15.5), 165.1 (19.1), 152.1 (11.6), 145.0 (15.1), 138.1 (10.9), 135.1 (10.5), 131.2 (24.5), 129.1 (11.9), 128.1 (10.3), 122.1 (10.6), 121.1 (100), 119.1 (13.9), 115.1 (14.8), 108.1 (10.6), 107.1 (48.2), 105.1 (29.4), 103.1 (17.4), 94.1 (28.9), 91.1 (29.4), 77.1 (35.5), 73.1 (10.2), 65.2 (13.8); [M+H] HRMS calcd. for $C_{26}H_{27}O_2$: 371.20056, found: 371.20056; IR (KBr): ν = 3406, 2955, 2833, 1605, 1507, 1454, 1236, 1175, 1107, 1029, 907, 828, 729 cm^{-1}.

4-(1-(7-Bromo-1-(4-methoxyphenyl)-3,4-dihydronaphthalen-2-yl)ethyl)phenol (211u)

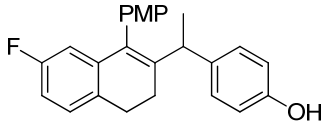


211u

Yellow oil, R_f (Hex: EtOAc 5:1) = 0.24. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.16 (dd, *J* = 7.9, 2.0, 3H), 7.06 (d, *J* = 8.5, 2H), 6.96 (dd, *J* = 19.5, 8.3, 3H), 6.77–6.65 (m, 3H), 4.70 (s, 1H), 3.86 (s, 3H), 3.82 (q, *J* = 7.1, 1H), 2.70–2.54 (m, 2H), 2.21 (ddd, *J* = 17.1, 10.6, 6.7, 1H), 2.04–1.92 (m, 1H), 1.32 (d, *J* = 7.1, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 158.58, 153.65, 143.86, 139.39, 136.19, 134.02, 132.41, 131.13, 131.07, 128.78, 128.62, 128.36, 119.92, 114.91, 114.24, 55.26, 40.01, 28.22, 23.06, 17.04; *m/z* (EI)(%): 437.1 (23.9), 436.1 (86.0), 435.1 (26.9), 434.1 (100), 422.1 (10.7), 421.1 (43.1), 420.1 (11.4), 419.1 (44.0), 342.1 (14.7), 341.1 (9.7), 340.1 (29.8), 327.0 (20.3), 325.0 (20.5), 313.0 (13.7), 265.1 (12.2), 247.1 (17.1),

245.1 (47.6), 244.1 (15.1), 239.1 (13.5), 235.1 (9.2), 234.1 (37.9), 233.1 (14.3), 232.1 (29.1), 231.1 (26.6), 230.1 (9.3), 219.1 (13.9), 218.1 (9.4), 229.1 (22.3), 203.1 (21.4), 202.1 (27.5), 191.1 (11.4), 190.1 (13.8), 189.0 (27.6), 165.0 (10.2), 121.0 (55.4), 107.0 (26.5), 94.0 (19.4), 91.1 (13.1), 77.1 (16.4); [M+H] HRMS calcd. for $C_{25}H_{24}O_2Br$: 435.09542, found: 435.09506; IR (KBr): ν = 3397, 2950, 2833, 1602, 1506, 1469, 1367, 1235, 1174, 1107, 1030, 905, 825, 778, 729 cm^{-1}.

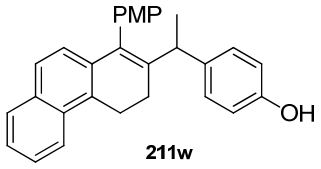
4-(1-(7-Fluoro-1-(4-methoxyphenyl)-3,4-dihydronaphthalen-2-yl)ethyl)phenol (211v)



211v

Yellow solid, R_f (Hex: EtOAc 5:1) = 0.22. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.17 (s, 2H), 7.08 (d, J = 8.4, 2H), 7.04–6.95 (m, 3H), 6.73 (dq, J = 5.3, 3.0, 3H), 6.34 (dd, J = 10.7, 2.7, 1H), 4.80 (s, 1H), 3.89–3.79 (m, 4H, -OCH_3 and -CH), 2.73–2.56 (m, 2H), 2.23 (ddd, J = 17.2, 10.6, 6.7, 1H), 1.99 (ddd, J = 16.0, 7.7, 6.4, 1H), 1.34 (d, J = 7.1, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 162.81, 160.40, 158.55, 153.65, 143.61, 139.20, 139.13, 136.23, 132.74, 131.33, 131.10, 130.57, 130.54, 128.37, 127.80, 127.72, 114.90, 114.17, 112.94, 112.71, 112.33, 112.12, 55.27, 40.05, 27.93, 23.36, 17.06; ^{19}F NMR (376 MHz, $CDCl_3$): δ = -116.80 (dd, J = 15.7, 9.3); *m/z* (EI)(%): 375.2 (25.7), 374.2 (100), 360.1 (8.2), 359.1 (33.7), 280.1 (11.8), 265.0 (21.4), 253.0 (10.5), 251.1 (12.3), 249.0 (7.3), 233.0 (11.8), 220.0 (9.9), 135.0 (7.1), 121.0 (26.1), 107.0 (13.4), 94.0 (6.9), 91.0 (6.2), 77.1 (8.8); [M+H] HRMS calcd. for $C_{25}H_{24}O_2F$: 375.17548, found: 375.17569; IR (KBr): ν = 3401, 2948, 2834, 1604, 1449, 1359, 1238, 1177, 1105, 1030, 979, 907, 818, 729 cm^{-1}.

4-(1-(1-(4-Methoxyphenyl)-3,4-dihydrophenanthren-2-yl)ethyl)phenol (211w)

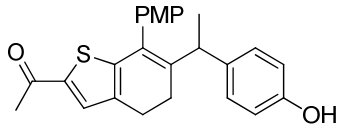


211w

White solid, R_f (Hex: EtOAc 5:1) = 0.21. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.99 (d, J = 8.5, 1H), 7.71 (d, J = 8.0, 1H), 7.49 (d, J = 8.6, 1H), 7.43 (t, J = 7.6, 1H), 7.35 (t, J = 7.4, 1H), 7.23–7.17 (m, 2H), 7.11 (d, J = 8.4, 2H), 6.98 (d, J = 8.6, 2H), 6.86 (d, J = 8.6, 1H), 6.71 (d, J = 8.5, 2H), 4.64 (s, 1H), 3.99–3.74 (m, 4H, -OCH_3 and -CH), 3.25–3.13 (m, 1H), 3.05–2.93 (m, 1H), 2.34 (ddd, J = 18.1, 11.6, 6.6, 1H), 2.18–2.07 (m, 1H), 1.37 (d, J = 7.1, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 158.43, 153.59, 141.85, 136.66, 134.14, 133.62, 132.45, 132.31, 131.29, 130.98, 130.12, 128.42, 128.40, 125.84, 125.71, 124.99, 124.82, 123.51, 114.88, 114.06, 55.26, 39.90, 23.85, 23.00, 17.21; *m/z* (EI)(%): 407.2 (28.6), 406.1 (100), 392.2 (11.5), 391.2 (39.7), 378.1 (13.2), 297.1 (20.0), 285.1 (15.5), 283.1 (11.4), 265.0 (16.1), 253.1 (16.5), 252.1 (17.4), 239.0 (21.1), 164.9 (10.9), 156.2 (20.6), 148.2 (9.4), 141.0 (25.5), 121.0

(27.3), 107.0 (19.3), 94.0 (10.5); [M+H] HRMS calcd. for $C_{29}H_{27}O_2$: 407.20056, found: 407.20020; IR (KBr): ν = 3401, 2952, 1603, 1504, 1449, 1367, 1230, 1026, 907, 821, 730 cm^{-1}.

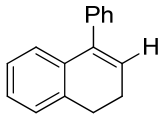
1-(6-(1-(4-Hydroxyphenyl)ethyl)-7-(4-methoxyphenyl)-4,5-dihydrobenzo[b]thiophen-2-yl)ethanone (211x)



211x

Yellow solid, R_f (Hex: EtOAc 1:1) = 0.63. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.41 (s, 1H), 7.25 (s, 2H), 7.04 (d, J = 8.5, 2H), 6.95 (d, J = 8.8, 2H), 6.75 (t, J = 5.7, 2H), 5.35 (s, 1H), 3.93–3.77 (m, 4H, -OCH_3 and -CH), 2.64 (tdd, J = 15.7, 13.3, 7.7, 2H), 2.48–2.30 (m, 4H, -$COCH_3$ and 1/2-CH_2), 2.16–2.05 (m, 1H), 1.36 (d, J = 7.1, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 190.63, 159.13, 154.08, 149.71, 143.21, 139.97, 135.48, 134.46, 132.27, 130.64, 130.42, 129.10, 128.31, 115.07, 114.20, 55.27, 39.65, 26.46, 24.14, 23.39, 17.34; *m/z* (EI)(%): 406.1 (8.8), 405.2 (24.2), 404.2 (100), 390.1 (15.5), 389.1 (59.1), 373.1 (9.9), 361.1 (13.8), 310.1 (17.9), 295.0 (28.9), 283.1 (9.4), 281.0 (9.7), 253.0 (10.7), 252.1 (13.7), 237.0 (10.5), 221.0 (10.1), 208.0 (9.5), 165.0 (8.4), 121.0 (29.9), 107.0 (14.3), 94.0 (32.6), 91.0 (11.5), 77.1 (13.6); [M+Na] HRMS calcd. for $C_{25}H_{24}O_3SNa$: 427.13384, found: 427.13257; IR (KBr): ν = 3226, 2945, 2832, 1607, 1510, 1413, 1243, 1181, 1025, 935, 828, 727 cm^{-1}.

4-Phenyl-1,2-dihydronaphthalene (226)



226

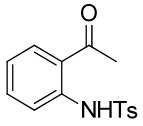
Colorless oil, R_f (Hex: EtOAc 30:1) = 0.58.
^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.43–7.28 (m, 5H), 7.21 (d, J = 7.3, 1H), 7.17 (t, J = 7.3, 1H), 7.12 (t, J = 7.5, 1H), 7.02 (d, J = 7.6, 1H), 6.10 (t, J = 4.7, 1H), 2.87 (t, J = 8.0, 2H), 2.42 (td, J = 7.9, 4.8, 2H); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 140.75, 139.86, 136.75, 135.07, 128.72, 128.19, 127.63, 127.52, 127.04, 126.94, 126.17, 125.41, 28.28, 23.51; *m/z* (EI)(%): 207.3 (19.6), 206.2 (100), 205.2 (20.5), 203.2 (8.8), 202.2 (8.4), 191.2 (18.7), 178.2 (6.9), 165.2 (5.7), 128.2 (5.8), 91.2 (3.9), 77.2 (2.2); IR (KBr): ν = 3030, 2933, 2830, 2326, 2095, 1900, 1593, 1481, 1443, 1354, 1031, 948, 830, 751 cm^{-1}.

5.7 Experiments for $Al(OTf)_3$-Catalyzed Insertion of an Unactivated Alkyne into an Unstrained C-C σ Bond

5.7.1 Experiments for Preparation of Substrates

To a solution of amines **233** (20 mmol) and pyridines (26 mmol) in 15 mL DCM was added TsCl **234** (22 mmol) in portions, the reaction was then stirred at room temperature overnight. The reaction mixture was washed by 15 mL 2N HCl and the aqueous phase was extracted with DCM (2×20 mL). The combined organic phases were dried over Na_2SO_4 and concentrated under reduced pressure. The crude product was recrystallized from DCM/hexane.

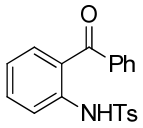
***N*-(2-Acetylphenyl)-4-methylbenzenesulfonamide (235a)**



235a

White solid, R_f (hexane: EtOAc 3:1) = 0.37. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 11.45 (s, 1H), 7.82–7.64 (m, 4H), 7.49–7.37 (m, 1H), 7.25–7.19 (m, 2H), 7.10–6.99 (m, 1H), 2.55 (s, 3H), 2.36 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 202.4, 143.9, 140.1, 136.6, 134.9, 131.9, 129.6, 127.3, 122.5, 122.3, 119.0, 28.1, 21.5; *m/z* (EI)(%): 290.3 (M+1, 39), 289.2 (M, 95), 272.2 (23), 155.1 (20), 134.2 (100), 120.2 (31), 106.2 (51), 92.2 (29), 91.2 (96), 65.3 (43); IR (KBr): ν = 3057, 2182, 2111, 1936, 1816, 1640, 1587, 1493, 1455 cm^{-1}.

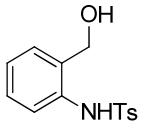
***N*-(2-Benzoylphenyl)-4-methylbenzenesulfonamide (235b)**



235b

White solid, R_f (hexane: EtOAc 3:1) = 0.38. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.97 (s, 1H), 7.78 (dd, J = 8.3, 1.0 Hz, 1H), 7.57–7.47 (m, 4H), 7.41–7.34 (m, 5H), 7.11–7.05 (m, 1H), 7.04–6.99 (m, 2H), 2.22 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 198.4, 143.6, 139.0, 137.6, 135.9, 133.7, 133.0, 132.6, 129.8, 129.5, 128.0, 127.2, 126.2, 123.4, 123.1, 21.4; *m/z* (EI)(%): 352.3 (M+1, 25), 351.3 (M, 100), 196.3 (89), 1953 (31), 167.3 (20), 91.3 (21); IR (KBr): ν = 3242, 3056, 2922, 2657, 2326, 2100, 1998, 1920, 1640, 1593, 1482, 1447, 1390, 1287, 1213, 1160, 1090, 938, 890, 810, 763, 699 cm^{-1}.

***N*-(2-(hydroxymethyl)phenyl)-4-methylbenzenesulfonamide (237a)**



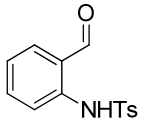
237a

White solid, R_f (hexane: EtOAc 3:1) = 0.13. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.87 (s, 1H), 7.62–7.66 (m, 2H), 7.41–7.45 (m, 2H), 7.18–7.30 (m, 3H), 7.05–7.12 (m, 2H), 4.39 (s, 2H), 2.38 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 143.8, 136.9, 136.4, 131.6, 129.6, 129.3, 129.0, 127.0, 125.3, 123.4, 63.9, 21.5; *m/z* (EI)(%): 277 (M, 30), 194 (20), 122 (100), 121 (32), 104 (19), 94 (43), 93 (96), 92 (18), 91 (72), 77 (53), 65 (51); IR (KBr): ν = 3860, 3435, 3071,

2921, 2874, 2805, 2730, 2644, 2330, 2194, 2120, 2035, 1993, 1918, 1733, 1647, 1594, 1490, 1456, 1410, 1314, 1220, 1183, 1149, 1090, 1029, 951, 926, 885, 843, 806, 760, 729, 714, 659 cm^{-1}.

To a solution of *N*-(2-(hydroxymethyl)phenyl)-4-methylbenzenesulfonamides **237a** (8 mmol) in 40 mL DCM was added PCC (10.4 mmol), the reaction was then stirred at room temperature overnight. After reaction completion, the mixture was filtered through a plug of celite and the filter cake was washed with 50 mL DCM. The collected DCM was removed under reduced pressure and the crude product was purified by column chromatography.

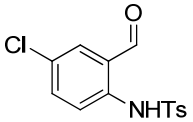
***N*-(2-Formylphenyl)-4-methylbenzenesulfonamide (238a)**



238a

White solid, R_f (hexane: EtOAc 3:1) = 0.37. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 10.79 (s, 1H), 9.83 (d, *J* = 0.7 Hz, 1H), 7.77 (d, *J* = 8.5 Hz, 2H), 7.69 (d, *J* = 8.8 Hz, 1H), 7.59 (dd, *J* = 7.7/1.6 Hz, 1H), 7.55–7.47 (m, 1H), 7.28–7.21 (m, 2H), 7.16 (td, *J* = 7.6, 1.0 Hz, 1H), 2.36 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 194.9, 144.1, 140.0, 136.4, 136.1, 135.8, 129.7, 127.3, 122.9, 121.9, 117.8, 21.5; *m/z* (EI)(%): 277.1 (M+2, 43), 275.2 (M, 4), 194.2 (32), 180.2 (21), 122.2 (100), 121.2 (31), 120.2 (22), 94.3 (30), 93.2 (68), 91.2 (55), 77.2 (34), 65.3 (30); IR (KBr): ν = 3433, 3070, 2921, 2874, 2805, 2731, 2643, 2329, 2111, 1993, 1918, 1743, 1673, 1594, 1492, 1457, 1410, 1314, 1290, 1220, 1149, 1090, 1030, 926, 886, 844, 806, 761, 713, 684, 662 cm^{-1}.

***N*- (4-Chloro-2-formylphenyl)-4-methylbenzenesulfonamide (238b)**



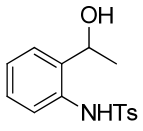
238b

White solid, R_f (hexane: EtOAc 3:1) = 0.55. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 10.62 (s, 1H), 9.77 (d, *J* = 0.7 Hz, 1H), 7.75 (d, *J* = 8.4 Hz, 2H), 7.68 (d, *J* = 8.9 Hz, 1H), 7.55 (d, *J* = 2.5 Hz, 1H), 7.46 (dd, *J* = 8.9, 2.5 Hz, 1H), 7.27–7.23 (m, 2H), 2.38 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 193.7, 144.5, 138.4, 136.1, 135.7, 135.1, 129.8, 128.4, 127.2, 122.8, 119.6, 21.5; *m/z* (EI)(%): 311.2 (M+2, 35), 310.2 (M+1, 23), 309.2 (M, 85), 156.2 (40), 155.2 (36), 154.2 (100), 91.3 (84), 65.4 (23); IR (KBr): ν = 3177, 3051, 2927, 2857, 2749, 2322, 2169, 2107, 2005, 1930, 1809, 1736, 1669, 1595, 1572, 1483, 1385, 1337, 1292, 1222, 1187, 1156, 1089, 928, 866, 820, 720, 660 cm^{-1}.

To a solution of ketones **235** (5 mmol) in 20 mL EtOH at 0 ^{o}C was added $NaBH_4$ (15 mmol) in portions, the reaction was then warmed to room temperature and stirred for 2 h. After reaction completion, EtOH solvent was removed under reduced pressure, the residue

was washed by 20 mL saturated brine and the aqueous phase was extracted with Et_2O (3×20 mL). The collected organic phases were dried over Na_2SO_4 and concentrated under reduced pressure. The crude product was purified by column chromatography.

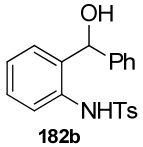
***N*-(2-(1-Hydroxyethyl)phenyl)-4-methylbenzenesulfonamide (182a)**



182a

White solid, R_f (Hex: EtOAc 3:1) = 0.20. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.43 (s, 1H), 7.72–7.66 (m, 2H), 7.43 (dd, J = 8.1, 1.0 Hz, 1H), 7.24–7.20 (m, 2H), 7.20–7.16 (m, 1H), 7.08 (dd, J = 7.7, 1.7 Hz, 1H), 7.04 (td, J = 7.5, 1.2 Hz, 1H), 4.84 (q, J = 6.6 Hz, 1H), 2.42 (s, 1H), 2.37 (s, 3H), 1.36 (d, J = 6.7 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 143.71, 136.88, 135.66, 133.99, 129.59, 128.48, 127.12, 126.97, 124.60, 121.79, 69.75, 22.81, 21.50; *m/z* (EI)(%): 293.3 (3.5), 292.2 (9.8), 291.2 (53.5), 136.2 (63.8), 118.1 (100), 91.1 (40.2); [M+Na] HRMS calcd. for $C_{15}H_{17}NO_3SNa$: 314.08214, found: 314.08121; IR (KBr): ν = 3488, 3243, 2977, 2972, 1549, 1496, 1330, 1159, 1091, 932, 759, 665, 564 cm^{-1}.

***N*-(2-(Hydroxy(phenyl)methyl)phenyl)-4-methylbenzenesulfonamide (182b)**

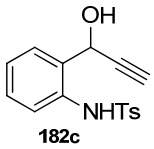


182b

White solid, R_f (Hex: EtOAc 3:1) = 0.25. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.01 (s, 1H), 7.54–7.40 (m, 3H), 7.36–7.27 (m, 3H), 7.22 (td, J = 7.9, 1.5 Hz, 1H), 7.19–7.08 (m, 4H), 7.02 (td, J = 7.5, 1.2 Hz, 1H), 6.92 (dd, J = 7.7, 1.5 Hz, 1H), 5.67 (s, 1H), 2.73 (s, 1H), 2.38 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 143.58, 141.00, 136.43, 135.75, 133.11, 129.52, 129.04, 128.92, 128.57, 127.77, 127.15, 126.28, 124.54, 121.98, 74.57, 21.49; *m/z* (EI)(%): 354.2 (2.3), 353.2 (10.5), 199.2 (15.5), 198.2 (100), 196.1 (25.8), 180.2 (86.5), 179.2 (45.0), 120.2 (27.2); [M+Na] HRMS calcd. for $C_{20}H_{19}NO_3SNa$: 376.09779, found: 376.09778; IR (KBr): ν = 3441, 3104, 1596, 1454, 1320, 1152, 1090, 998, 925, 820, 693 cm^{-1}.

To a solution of organometallic reagents R-M **198** (10.5 mmol) in 20 mLTHF at 0 ^{o}C were added aldehydes **238** (5 mmol) slowly under an argon protective atmosphere, the reaction was then heated under reflux for 30 minutes. After the reaction cooled down to room temperature, it was quenched by 20 mL saturated NH_4Cl solution and the aqueous phase was extracted with Et_2O (2×30 mL). The collected organic phases were dried over Na_2SO_4 and concentrated under reduced pressure. The crude product was purified by column chromatography.

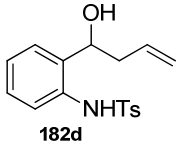
***N*-(2-(1-Hydroxyprop-2-yn-1-yl)phenyl)-4-methylbenzenesulfonamide (182c)**



182c

Yellow oil, R_f (Hex: EtOAc 3:1) = 0.17. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.74 (s, 1H), 7.66 (d, J = 8.3 Hz, 2H), 7.52 (dd, J = 7.7, 1.3 Hz, 1H), 7.37 (d, J = 7.9 Hz, 1H), 7.30–7.24 (m, 1H), 7.22 (d, J = 8.1 Hz, 2H), 7.14 (td, J = 7.5, 1.0 Hz, 1H), 5.30 (dd, J = 5.7, 1.7 Hz, 1H), 2.85 (s, 1H), 2.67 (d, J = 2.3 Hz, 1H), 2.38 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 143.97, 136.61, 135.28, 130.91, 129.77, 129.67, 128.26, 127.18, 125.49, 123.37, 81.28, 76.61, 62.53, 21.54; *m/z* (EI)(%): 303.7 (4.1), 302.7 (16.5), 301.6 (98.0),300.4 (100), 284.0 (53.8), 218.9 (37.8), 204.7 (30.9), 146.7 (19.8); [M+Na] HRMS calcd. for $C_{16}H_{15}NO_3SNa$: 324.06649, found: 324.06543; IR (KBr): ν = 3453, 3284, 2925, 1596, 1490, 1401, 1326, 1161, 1022, 923, 818, 671, 558 cm^{-1}.

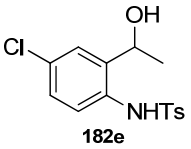
_N_-(2-(1-Hydroxybut-3-en-1-yl)phenyl)-4-methylbenzenesulfonamide (182d)



182d

White solid, R_f (Hex: EtOAc 3:1) = 0.26. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.43 (s, 1H), 7.74–7.62 (m, 2H), 7.46 (d, J = 8.0 Hz, 1H), 7.23 (dd, J = 8.5, 0.6 Hz, 2H), 7.21–7.17 (m, 1H), 7.06–7.02 (m, 2H), 5.73–5.53 (m, 1H), 5.17–5.00 (m, 2H), 4.70–4.60 (m, 1H), 2.52 (s, 1H), 2.37 (s, 3H), 2.35–2.25 (m, 2H); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 143.73, 136.97, 135.81, 133.69, 131.99, 129.61, 128.57, 127.78, 127.11, 124.45, 121.81, 119.22, 73.35, 41.27, 21.49; *m/z* (EI)(%): 319.7 (1.3), 318.7 (5.0), 317.0 (41.4), 300.7 (21.0), 275.9 (100), 247 (20.5), 155.1 (38.2); [M+Na] HRMS calcd. for $C_{17}H_{19}NO_3SNa$: 340.09779, found: 340.09805; IR (KBr): ν = 3474, 3146, 2934, 1740, 1593, 1438, 1318, 1152, 1048, 920, 762, 696 cm^{-1}.

_N_-(4-Chloro-2-(1-hydroxyethyl)phenyl)-4-methylbenzenesulfonamide (182e)



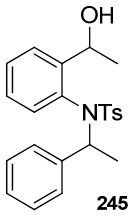
182e

Yellow oil, R_f (Hex: EtOAc 3:1) = 0.18. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.34 (s, 1H), 7.68–7.60 (m, 2H), 7.36 (d, J = 8.7 Hz, 1H), 7.24–7.19 (m, 2H), 7.13 (dd, J = 8.7, 2.5 Hz, 1H), 7.05 (d, J = 2.4 Hz, 1H), 4.76 (q, J = 6.6 Hz, 1H), 2.47 (s, 1H), 2.37 (s, 3H), 1.32 (d, J = 6.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 144.01, 136.56, 135.99, 134.20, 130.10, 129.71, 128.37, 127.12, 127.07, 123.37, 69.23, 22.75, 21.52; *m/z* (EI)(%): 329.1 (2.2), 328.1 (6.6), 327.1 (36.0), 326.1 (17.4), 325.1 (100), 310.1 (25.9), 309.1 (17.4), 308.1 (69.8), 307.1 (19.5), 243.1 (8.1), 172.1 (14.8), 171.1 (10.1), 170.1 (46.1), 169.1 (19.4), 155.1 (18.0), 154.1 (41.3), 153.1 (28.1), 152.1 (86.6), 151.1 (9.2), 128.1 (11.0), 117.1 (50.3), 107.2 (8.3), 93.2 (8.9), 91.2 (45.0), 89.2 (12.0), 65.2 (19.1); [M+Na] HRMS calcd. for $C_{15}H_{16}NO_3ClSNa$: 348.04316,

found: 348.04272; IR (KBr): ν = 3487, 3247, 2927, 1597, 1448, 1389, 1330, 1160, 1091, 1013, 906, 816, 733, 670, 571, 548 cm^{-1}.

To a solution of *N*-(2-acetylphenyl)-4-methylbenzenesulfonamides **235a** (5 mmol) and K_2CO_3 (15 mmol) in 15 mL CH_3CN was added (1-bromoethyl)benzenes **243** (10 mmol), the reaction was then heated up to reflux overnight. After reaction completion, the slovent was removed under reduced pressure, then the residue was dissolved in 20 mL EtOH and $NaBH_4$ (15 mmol) was added in portions at 0 ^oC. The reaction was warmed to room temperature and stirred for 2 h. After reaction completion, EtOH was removed under reduced pressure, the residue was washed by 20 mL saturated brine and the aqueous phase was extracted with Et_2O (3×20 mL). The combined organic phases were dried over Na_2SO_4 and concentrated under reduced pressure. The crude product was purified by column chromatography.

***N*-(2-(1-Hydroxyethyl)phenyl)-4-methyl-*N*-(1-phenylethyl)benzenesulfonamide (245)**

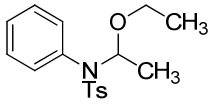


245

White solid, R_f (Hex: EtOAc 3:1) = 0.39. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.75–7.59 (m, 2H), 7.46 (ddd, *J* = 14.5, 8.9, 4.9 Hz, 1H), 7.41–7.08 (m, 9H), 7.08–6.98 (m, 2H), 6.94–6.81 (m, 1H), 6.72 (dd, *J* = 56.6, 7.8 Hz, 1H), 5.98–5.25 (m, 2H), 4.41 (dq, *J* = 19.2, 6.5 Hz, 1H), 3.07 (s, 1H), 2.45 (s, 3H), 1.50 (dt, *J* = 15.8, 7.6 Hz, 2H), 1.32 (dd, *J* = 13.7, 7.2 Hz, 3H), 1.21 (d, *J* = 6.4 Hz, 2H), 0.57 (d, *J* = 6.5 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 149.23, 148.07, 143.58, 143.46, 143.30, 139.88, 139.57, 138.90, 138.08, 137.44, 137.16, 132.65, 132.03, 131.97, 131.36, 130.81, 130.57, 129.76, 129.64, 129.56, 129.23, 129.13, 128.50, 128.43, 128.38, 128.22, 128.17, 128.09, 128.06, 128.00, 127.87, 127.77, 127.70, 127.60, 127.54, 127.08, 126.89, 65.05, 63.53, 63.00, 59.38, 58.53, 58.34, 23.34, 21.56, 21.49, 21.45, 20.05, 19.88, 18.19, 17.73; *m/z* (EI)(%): 379.4 (1.7), 378.3 (7.1), 274.2 (4.3), 239.3 (10.7) 222.2 (11.2), 206.2 (11.0), 194.2 (8.5), 180.1 (13.8), 155.0 (75.4), 106.2 (10.1), 105.1 (100), 104.1 (20.5), 91.2 (41.8), 89.1 (12.9), 77.2 (15.1), 45.5 (17.0); [M+Na] HRMS calcd. for $C_{23}H_{25}NO_3SNa$: 418.14474, found: 418.14484; IR (KBr): ν = 3566, 2975, 2934, 1739, 1594, 1485, 1451, 1331, 1154, 1078, 996, 906, 770, 701cm^{-1}.

To a solution of 4-methyl-*N*-phenylbenzenesulfonamides **224** (5 mmol) in 10 mL ethoxyethene **250** was added $Pd(PPh_3)_4$ (0.025 mmol) under an argon protective atmosphere, the reaction was then heated up to 100 ^oC and stirred overnight. The crude product was purified by column chromatography.

***N*-(1-Ethoxyethyl)-4-methyl-*N*-phenylbenzenesulfonamide (251)**



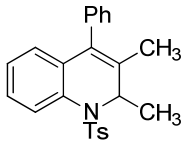
251

Colorless oil, R_f (Hex: EtOAc 5:1) = 0.42. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.53 (d, J = 8.3 Hz, 2H), 7.34–7.26 (m, 3H), 7.22 (d, J = 8.1 Hz, 2H), 7.01–6.96 (m, 2H), 5.68 (q, J = 6.0 Hz, 1H), 3.84 (dq, J = 9.4, 7.1 Hz, 1H), 3.63 (dq, J = 9.4, 7.0 Hz, 1H), 2.41 (s, 3H), 1.21 (t, J = 7.0 Hz, 3H), 1.12 (d, J = 6.1 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 143.19, 137.69, 134.42, 131.96, 129.22, 128.64, 128.57, 127.52, 84.86, 63.49, 21.49, 20.72, 14.89; *m/z* (EI)(%): 319.2 (1.0), 276.1 (1.3), 275.1 (4.1) 274.1 (15.7), 249.1 (6.1), 248.1 (15.9), 247.1 (100), 183.1 (3.6), 182.1 (8.8), 168.1 (6.8), 155.0 (13.5), 119.1 (3.9), 104.1 (6.8), 91.1 (20.6), 77.1 (8.8), 73.1 (45.2), 65.1 (7.1), 45.3 (27.4); [M+Na] HRMS calcd. for $C_{17}H_{21}NO_3SNa$: 342.11344, found: 342.11343; IR (KBr): ν = 2980, 2932, 2880, 2088, 1595, 1490, 1450, 1378, 1339, 1233, 1163, 1087, 1049, 996, 905, 814, 698, 661cm^{-1}.

5.7.2 General Experiment for the Al(OTf)$_3$-Catalyzed Insertion of an Unactivated Alkyne into an Unstrained C-C σ Bond

$Al(OTf)_3$ (14.3 mg, 0.03 mmol, 10 mol%) was suspended in 1.5 mL DCE, alcohols (0.3 mmol), alkynes (0.36 mmol) and Bu_4NPF_6 (5.8 mg, 0.015 mmol, 5 mol%) were then added at room temperature and the reaction was stirred at 40 ^{o}C for 12 h. After reaction completion, 5 mL saturated $NaHCO_3$ solution was added and the aqueous phase was extracted with dichloromethane (3×10 mL). The combined organic phase was dried over anhydrous Na_2SO_4 and concentrated in *vacuo*. The crude product was purified by column chromatography.

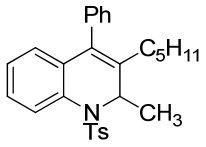
2,3-Dimethyl-4-phenyl-1-tosyl-1,2-dihydroquinoline (184a)



184a

White solid, R_f (Hex: EtOAc 10:1) = 0.35. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.77 (dd, J = 8.0, 1.1 Hz, 1H), 7.32–7.27 (m, 2H), 7.28–7.19 (m, 4H), 7.12 (d, J = 8.0 Hz, 2H), 7.04 (td, J = 7.6, 1.3 Hz, 1H), 6.49 (dd, J = 7.8, 1.4 Hz, 1H), 4.80 (q, J = 6.9 Hz, 1H), 2.38 (s, 3H), 1.51 (s, 3H), 1.22 (d, J = 6.9 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 143.32, 137.16, 136.02, 134.10, 131.34, 130.72, 129.69, 129.05, 128.21, 128.07, 126.96, 126.37, 125.48, 55.56, 21.36, 18.68, 17.98; *m/z* (EI)(%): 391.4 (1.2), 390.4 (3.9), 389.4 (13.6), 375.3 (26.2), 374.3 (100), 234.3 (26), 218.2 (11.5), 155.1 (21.7), 120.1 (13.9), 91.1 (35.7); [M+Na] HRMS calcd. for $C_{24}H_{23}NO_2SNa$: 412.13417, found: 412.13315; IR (KBr): ν = 3056, 2971, 2925, 2864, 1739, 1595, 1483, 1444, 1343, 1160, 1089, 763, 665 cm^{-1}.

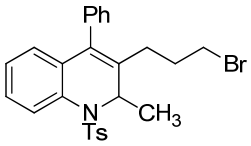
2-Methyl-3-pentyl-4-phenyl-1-tosyl-1,2-dihydroquinoline (184b)



184b

Colorless oil, R_f (Hex: EtOAc 10:1) = 0.40. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.74 (dd, J = 8.0, 1.2 Hz, 1H), 7.23–7.21 (m, 2H), 7.20–7.15 (m, 3H), 7.05–7.02 (m, 2H), 6.98–6.95 (m, 1H), 6.42 (dd, J = 7.8, 1.4 Hz, 1H), 5.84 (s, 1H), 4.83 (q, J = 6.9 Hz, 1H), 2.31 (s, 3H), 1.74 (ddd, J = 13.6, 11.2, 5.2 Hz, 1H), 1.66 (ddd, J = 13.6, 11.0, 5.3 Hz, 1H), 1.24–1.18 (m, 1H), 1.16 (d, J = 6.9 Hz, 3H), 1.11–0.94 (m, 5H), 0.73 (t, J = 7.3 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 143.22, 138.75, 137.34, 136.32, 131.63, 131.58, 131.00, 128.98, 128.10, 127.54, 127.25, 127.05, 126.96, 126.19, 125.83, 53.66, 32.48, 31.97, 28.04, 22.21, 21.39, 19.14, 13.87; *m/z* (EI)(%): 447.3 (1.2), 446.3 (3.9), 445.3 (11.4), 432.3 (8.7), 431.3 (28.5), 430.3 (100), 290.2 (5.0), 220.2 (10.8), 155.0 (16.1), 91.1 (15.3); [M+Na] HRMS calcd. for $C_{28}H_{31}NO_2SNa$: 468.19677, found: 468.19650; IR (KBr): ν = 3063, 2928, 2858, 1596, 1481, 1344, 1161, 1089, 897, 759, 689 cm^{-1}.

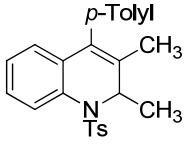
3-(3-Bromopropyl)-2-methyl-4-phenyl-1-tosyl-1,2-dihydroquinoline (184c)



184c

Colorless oil, R_f (Hex: EtOAc 10:1) = 0.22. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.74 (dd, J = 8.0, 1.1 Hz, 1H), 7.31–7.11 (m, 7H), 7.07 (d, J = 8.0 Hz, 2H), 7.01–6.96 (m, 1H), 6.48–6.38 (m, 1H), 5.88 (s, 1H), 4.80 (q, J = 6.8 Hz, 1H), 3.02 (t, J = 6.8 Hz, 2H), 2.33 (s, 3H), 1.96–1.88 (m, 1H), 1.82 (ddd, J = 13.5, 10.8, 4.9 Hz, 1H), 1.76–1.67 (m, 1H), 1.61–1.50 (m, 1H), 1.17 (d, J = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, CDCl3): δ = 143.45, 136.85, 136.66, 136.33, 132.29, 131.64, 131.24, 129.15, 128.36, 127.56, 127.45, 127.27, 127.17, 126.29, 125.97, 53.49, 32.86, 31.45, 30.99, 21.43, 18.99; *m/z* (EI)(%): 498.4 (1.0), 497.4 (3.2), 496.5 (2.6), 495.3 (3.2), 483.3 (19.0), 482.3 (71.0), 481.4 (55.9), 480.1 (100), 479.4 (14.5), 341.7 (10.5), 340.7 (14.3), 260.8, (9.9), 231.3 (17.5), 218.9 (23.1), 217.9 (52.5), 216.6 (32.2), 229.8 (25.6), 155.5 (24.6), 154.4 (18.8); [M+Na] HRMS calcd. for $C_{26}H_{26}BrNO_2SNa$: 518.07598, found: 518.07727; IR (KBr): ν = 2934, 1590, 1468, 1334, 1161, 1084, 888, 757, 684 cm^{-1}.

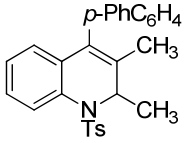
2,3-Dimethyl-4-(*p*-Tolyl)-1-tosyl-1,2-dihydroquinoline (184d)



184d

White solid, R_f (Hex: EtOAc 10:1) = 0.31. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.68 (dd, J = 8.0, 1.1 Hz, 1H), 7.25–7.18 (m, 2H), 7.18–7.13 (m, 1H), 7.03 (d, J = 8.0 Hz, 2H), 6.97 (ddd, J = 12.7, 6.2, 2.4 Hz, 3H), 6.43 (dd, J = 7.8, 1.4 Hz, 1H), 4.72 (q, J = 6.9 Hz, 1H), 2.30 (s, 3H), 2.26 (s, 3H), 1.43 (s, 3H), 1.13 (d, J = 6.9 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 143.28, 136.56, 136.01, 134.08, 133.96, 131.51, 131.35, 130.60, 129.55, 129.01, 128.78, 128.18, 126.96, 126.86, 126.34, 125.50, 55.59, 21.37, 21.13, 18.69, 17.97; *m/z* (EI)(%): 405.6 (0.8), 404.6 (2.8), 403.6 (12.1), 402.7 (13.1), 389.7 (17.5), 388.4 (100), 387.4 (92.1), 262.9 (11.4), 262.0 (18.2), 261.0 (12.7), 248.8 (26.0), 247.9 (22.5), 245.9 (19.4), 232.9 (18.2), 231.8 (16.7), 216.5 (15.7), 189.7 (5.8), 155.5 (9.5), 154.4 (6.8); [M+Na] HRMS calcd. for $C_{25}H_{25}NO_2SNa$: 426.14982, found: 426.14981; IR (KBr): ν = 3063, 2973, 2924, 2866, 1596, 1448, 1445, 1343, 1163, 1090, 895, 813, 763, 732, 665 cm^{-1}.

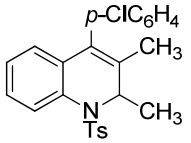
4-([1,1'-Biphenyl]-4-yl)-2-methyl-3-pentyl-1-tosyl-1,2-dihydroquinoline (184e)



184e

White solid, R_f (Hex: EtOAc 10:1) = 0.35. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.83 (dd, J = 8.0, 1.0 Hz, 1H), 7.65–7.59 (m, 2H), 7.46 (t, J = 7.7 Hz, 4H), 7.36 (dd, J = 10.6, 4.2 Hz, 1H), 7.32 (d, J = 8.2 Hz, 2H), 7.26 (td, J = 8.0, 1.4 Hz, 1H), 7.13 (d, J = 8.0 Hz, 2H), 7.07 (td, J = 7.7, 1.2 Hz, 1H), 6.59 (dd, J = 7.8, 1.3 Hz, 1H), 6.00 (s, 1H), 4.93 (q, J = 6.8 Hz, 1H), 2.40 (s, 3H), 1.88 (ddd, J = 13.6, 11.2, 5.4 Hz, 1H), 1.80 (ddd, J = 13.6, 11.1, 5.3 Hz, 1H), 1.37–1.28 (m, 1H), 1.26 (d, J = 6.9 Hz, 3H), 1.22–1.14 (m, 3H), 1.14–1.05 (m, 2H), 0.82 (t, J = 7.3 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 143.24, 140.61, 139.77, 138.93, 136.35, 136.32, 131.65, 131.61, 130.68, 130.00, 128.99, 128.78, 127.60, 127.36, 127.27, 127.12, 126.95, 126.78, 126.24, 125.88, 53.73, 32.59, 31.98, 28.07, 22.23, 21.44, 19.16, 13.88; *m/z* (EI)(%): 523.6 (0.7), 522.7 (2.5), 521.7 (6.3), 508.6 (11.6), 507.5 (38.5), 506.6 (100), 366.5 (7.2), 351.4 (6.4), 308.3 (9.8), 296.4 (21.0), 295.3 (8.2), 294.3 (29.8), 293.3 (11.5), 217.3 (3.8), 155.1 (11.9), 91.2 (11.6); [M+Na] HRMS calcd. for $C_{34}H_{35}NO_2SNa$: 544.22807, found: 544.22791; IR (KBr): ν = 3061, 3029, 2930, 2859, 1597, 1483, 1449, 1348, 1238, 1165, 1089, 987, 905, 761, 731, 694, 663 cm^{-1}.

4-(4-Chlorophenyl)-2,3-dimethyl-1-tosyl-1,2-dihydroquinoline (184f)

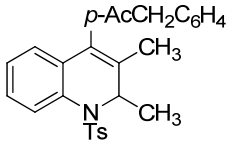


184f

White solid, R_f (Hex: EtOAc 10:1) = 0.28. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.70 (dd, J = 8.0, 1.0 Hz, 1H), 7.24–7.18 (m, 3H), 7.18–7.11 (m, 2H), 7.04 (d, J = 8.0 Hz, 2H), 6.99 (td, J = 7.6,

1.3 Hz, 1H), 6.39 (dd, J = 7.8, 1.4 Hz, 1H), 4.73 (q, J = 6.9 Hz, 1H), 2.31 (s, 3H), 1.44 (s, 3H), 1.13 (d, J = 6.9 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 143.35, 136.03, 135.59, 134.68, 132.97, 131.38, 131.08, 130.96, 129.70, 129.03, 128.37, 127.22, 127.00, 126.49, 125.28, 55.55, 21.39, 18.67, 17.91; *m/z* (EI)(%): 427.2 (0.8), 426.2 (2.8), 425.2 (9.8), 424.2 (7.4), 423.2 (24.7), 411.2 (9.8), 410.1 (40.1), 409.2 (25.0), 408.1 (100), 270.1 (12.6), 268.1 (39.5), 217.1 (10.6), 155.0 (20.9), 91.1 (22.1); [M+Na] HRMS calcd. for $C_{24}H_{22}ClNO_2SNa$: 446.09520, found: 446.09558; IR (KBr): ν = 3060, 2971, 1594, 1484, 1446, 1343, 1162, 1090, 1022, 893, 818, 763, 667 cm^{-1}.

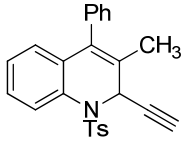
1-(4-(2-Methyl-3-pentyl-1-tosyl-1,2-dihydroquinolin-4-yl)phenyl)propan-2-one (184g)



184g

Colorless oil, R_f (Hex: EtOAc 5:1) = 0.20. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.79 (dd, J = 8.0, 1.0 Hz, 1H), 7.29–7.19 (m, 3H), 7.04 (ddd, J = 12.7, 8.8, 4.6 Hz, 5H), 6.47 (dd, J = 7.8, 1.4 Hz, 1H), 5.87 (s, 1H), 4.88 (q, J = 6.8 Hz, 1H), 3.67 (s, 2H), 2.36 (s, 3H), 2.16 (s, 3H), 1.83–1.66 (m, 2H), 1.30–1.23 (m, 1H), 1.21 (d, J = 6.9 Hz, 3H), 1.18–0.96 (m, 5H), 0.78 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 206.20, 143.22, 138.98, 136.30, 136.11, 132.94, 131.56, 131.50, 130.58, 129.92, 129.20, 128.97, 127.57, 127.25, 127.11, 126.21, 125.77, 53.63, 50.57, 32.42, 31.94, 29.40, 28.00, 22.17, 21.41, 19.10, 13.86; *m/z* (EI)(%): 503.4 (0.8), 502.3 (2.5), 501.3 (5.6), 489. 4 (2.1), 488.3 (10.0), 487.3 (31.4), 486.3 (100), 346.3 (5.9), 276.2 (9.6), 232.2 (7.6), 155.1 (10.5), 91.2 (8.5); [M+Na] HRMS calcd. for $C_{31}H_{35}NO_3SNa$: 524.22299, found: 524.22321; IR (KBr): ν = 2931, 2863, 1715, 1597, 1451, 1346, 1161, 1092, 887, 815, 763, 665 cm^{-1}.

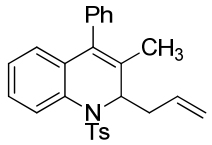
2-Ethynyl-3-methyl-4-phenyl-1-tosyl-1,2-dihydroquinoline (184h)



184h

White solid, R_f (Hex: EtOAc 10:1) = 0.22. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.74 (d, J = 8.0 Hz, 1H), 7.25–7.16 (m, 6H), 7.06 (d, J = 8.5 Hz, 2H), 7.01 (t, J = 7.6 Hz, 1H), 6.47 (d, J = 7.7 Hz, 1H), 5.52 (d, J = 2.4 Hz, 1H), 2.32 (s, 3H), 2.16 (dd, J = 2.4, 0.7 Hz, 1H), 1.58 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 143.82, 136.46, 135.70, 132.30, 131.70, 131.03, 129.56, 129.22, 129.17, 128.14, 127.64, 127.47, 127.30, 127.05, 126.77, 126.03, 79.45, 71.94, 51.59, 21.41, 18.36; *m/z* (EI)(%): 401.5 (1.9), 400.5 (6.6), 399.4 (30.3), 398.5 (21.3), 397.7 (7.7), 243.8 (56.8), 242.8 (100), 241.6 (94.0), 240.8(26.4), 240.0 (19.5), 239.9 (11.3); [M+Na] HRMS calcd. for $C_{25}H_{21}NO_2SNa$: 422.11852, found: 422.11746; IR (KBr): ν = 3283, 2922, 2856, 1595, 1480, 1446, 1338, 1166, 1068, 957, 865, 764, 704, 664 cm^{-1}.

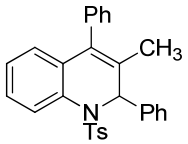
2-Allyl-3-methyl-4-phenyl-1-tosyl-1,2-dihydroquinoline (184i)



184i

White solid, R_f (Hex: EtOAc 10:1) = 0.26. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.68 (d, J = 8.0 Hz, 1H), 7.22 (d, J = 8.1 Hz, 2H), 7.17 (t, J = 5.8 Hz, 4H), 7.04 (d, J = 8.1 Hz, 2H), 6.98 (t, J = 7.6 Hz, 1H), 6.42 (d, J = 7.7 Hz, 1H), 5.84 (ddt, J = 17.1, 10.1, 7.1 Hz, 1H), 5.01 (dd, J = 29.4, 13.6 Hz, 2H), 4.65 (dd, J = 9.4, 4.9 Hz, 1H), 2.31 (s, 3H), 2.21 (dt, J = 12.1, 5.9 Hz, 1H), 2.16–2.04 (m, 1H), 1.46 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 143.33, 137.19, 136.23, 133.81, 132.66, 131.71, 131.56, 131.46, 129.67, 129.05, 128.11, 127.11, 127.04, 126.95, 126.40, 125.57, 117.74, 59.53, 35.91, 21.37, 19.37; *m/z* (EI)(%): 376.6 (4.4),375.7 (11.6), 374.7 (31.4), 374.0 (100), 373.4 (18.1), 219.0 (12.9), 217.8 (19.0), 216.7 (9.9), 154.8 (5.6), 90.9 (5.4); [M+Na] HRMS calcd. for $C_{26}H_{25}NO_2SNa$: 438.14982, found: 438.14951; IR (KBr): ν = 3065, 2983, 2918, 1595, 1482, 1442, 1345, 1164, 1083, 979, 913, 883, 813, 760, 703, 667 cm^{-1}.

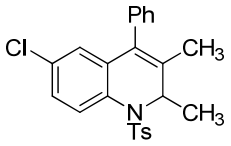
3-Methyl-2,4-diphenyl-1-tosyl-1,2-dihydroquinoline (184j)



184j

White solid, R_f (Hex: EtOAc 10:1) = 0.30. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.53 (dd, J = 8.0, 1.1 Hz, 1H), 7.30 (dd, J = 8.1, 2.2 Hz, 4H), 7.22 (dt, J = 4.1, 2.4 Hz, 3H), 7.20–7.13 (m, 3H), 7.09 (d, J = 8.0 Hz, 2H), 7.08–7.03 (m, 1H), 6.92 (td, J = 7.6, 1.3 Hz, 1H), 6.45 (dd, J = 7.8, 1.4 Hz, 1H), 5.77 (s, 1H), 2.34 (s, 3H), 1.50 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 143.51, 137.11, 137.06, 136.04, 133.62, 131.76, 131.58, 130.75, 129.65, 129.18, 128.52, 128.24, 128.06, 127.87, 127.22, 127.05, 126.41, 125.46, 61.77, 21.42, 19.67; *m/z* (EI)(%): 454.3 (0.6), 453.2 (2.9), 452.2 (9.9), 451.2 (29.8), 375.2 (14.8), 374.2 (54.3), 297.2 (25.3), 296.2 (100), 294.2 (23.5), 280.2 (55), 218.2 (12.4), 217.2 (17.9), 155.1 (13.2), 91.2 (25.3); [M+K] HRMS calcd. for $C_{29}H_{25}NO_2SK$: 490.12376, found: 490.12372; IR (KBr): ν = 3026, 2921, 1740, 1594, 1484, 1336, 1164, 1062, 911, 813, 764, 668 cm^{-1}.

6-Chloro-2,3-dimethyl-4-phenyl-1-tosyl-1,2-dihydroquinoline (184k)

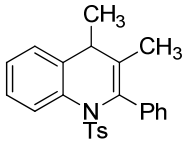


184k

White solid, R_f (Hex: EtOAc 10:1) = 0.31. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.69 (d, J = 8.6 Hz, 1H), 7.32–7.28 (m, 2H), 7.28–7.22 (m, 3H), 7.19 (dd, J = 8.6, 2.4 Hz, 1H), 7.14 (d, J =

8.0 Hz, 2H), 6.44 (d, J = 2.4 Hz, 1H), 4.78 (q, J = 6.9 Hz, 1H), 2.38 (s, 3H), 1.48 (s, 3H), 1.19 (d, J = 6.9 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 143.63, 136.34, 135.82, 132.82, 132.11, 130.03, 129.92, 129.51, 129.24, 128.34, 127.34, 126.94, 125.29, 55.58, 21.41, 18.80, 18.02; *m/z* (EI)(%): 427.1 (1.1), 426.1 (3.8), 425.1 (13.8), 424.1 (10.6), 423.1 (37.0), 410.1 (37.0), 409.1 (24.1), 408.1 (100), 270.1 (24.8), 269.1 (15.4), 268.1 (77.8), 218.1 (12.9), 217.1 (15.9), 155.0 (39.3), 91.1 (41.8); [M+Na] HRMS calcd. for $C_{24}H_{22}NO_2ClSNa$: 446.09520, found: 446.09521; IR (KBr): ν = 3073, 2966, 2924, 1594, 1475, 1343, 1163, 1090, 890, 816, 748, 670 cm^{-1}.

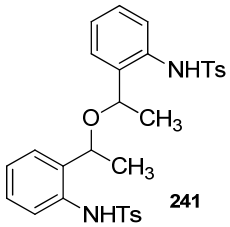
3,4-Dimethyl-2-phenyl-1-tosyl-1,4-dihydroquinoline (184a')



184a'

Colorless oil, R_f (Hex: EtOAc 10:1) = 0.35. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.73 (dd, J = 7.9, 1.3 Hz, 1H), 7.38–7.24 (m, 8H), 7.24–7.18 (m, 1H), 7.10 (dd, J = 8.6, 0.6 Hz, 2H), 7.05 (dd, J = 7.5, 1.3 Hz, 1H), 3.06 (s, 1H), 2.34 (s, 3H), 1.79 (s, 3H), 0.93–0.76 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 143.39, 137.98, 136.43, 129.70, 129.04, 127.90, 127.61, 127.18, 126.37, 126.15, 125.05, 21.44; *m/z* (EI)(%): 390.5 (0.8), 389.4 (3.9), 374.3 (2.1), 250.2 (1.0), 235.3 (9.7), 234.0 (100), 232.1 (9.8), 219.3 (1.9), 218.3 (7.9), 217.2 (8.3), 216.2 (2.3); [M+Na] HRMS calcd. for $C_{24}H_{23}NO_2SNa$: 412.13417, found: 412.13367; IR (KBr): ν = 2929, 1595, 1485, 1447, 1358, 1216, 1163, 1088, 1013, 913, 815, 756, 666 cm^{-1}.

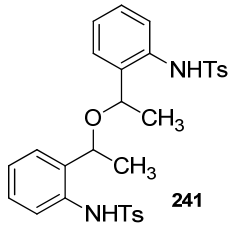
***N*,*N*'-((Oxybis(ethane-1,1-diyl))bis(2,1-phenylene))bis(4-methylbenzenesulfonamide) (241)**



241

Colorless oil (diastereoisomers), R_f (Hex: EtOAc 3:1) = 0.30. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.13 (s, 1H), 7.70 (d, J = 8.3 Hz, 2H), 7.53 (d, J = 8.2 Hz, 1H), 7.22–7.18 (m, 2H), 7.18–7.15 (m, 1H), 6.91 (td, J = 7.5, 0.9 Hz, 1H), 6.71 (dd, J = 7.6, 1.2 Hz, 1H), 4.25 (q, J = 6.7 Hz, 1H), 2.32 (s, 3H), 1.16 (d, J = 6.8 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 143.98, 136.83, 135.64, 129.72, 129.32, 129.05, 128.91, 127.16, 124.18, 120.15, 76.37, 21.79, 21.53; *m/z* (EI)(%): 564.3 (1.3), 291.1 (6.8), 274.1 (32.0), 273.1 (32.3), 210.1 (6.4), 120.1 (14.2), 119.1(40.5), 118.1 (100), 117.0 (19.9), 91.1 (47.5), 65.1 (19.6); [M+Na] HRMS calcd. for $C_{30}H_{32}N_2O_5S_2Na$: 587.16448, found: 587.16284; IR (KBr): ν = 3265, 3065, 2977, 2928, 1730, 1595, 1495, 1450, 1405, 1334, 1281, 1161, 1090, 916, 816, 760, 733, 664, 564 cm^{-1}.

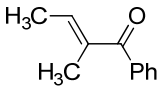
***N*,*N*'-((Oxybis(ethane-1,1-diyl))bis(2,1-phenylene))bis(4-methylbenzenesulfonamide) (241)**



241

Colorless oil (diastereoisomers), R_f (Hex: EtOAc 3:1) = 0.30. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.72 (s, 1H), 7.60 (d, J = 8.3 Hz, 2H), 7.26 (d, J = 7.7 Hz, 1H), 7.22 (d, J = 8.0 Hz, 2H), 7.19–7.14 (m, 1H), 7.02 (dtd, J = 9.3, 7.6, 1.3 Hz, 2H), 4.63 (q, J = 6.6 Hz, 1H), 2.37 (s, 3H), 1.32 (d, J = 6.6 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 143.75, 136.93, 134.95, 132.57, 129.67, 128.71, 128.01, 127.15, 124.89, 121.70, 74.99, 21.52, 20.86; *m/z* (EI)(%): 564.6 (2.5), 292.3 (6.4), 291.2 (33.1), 275.2 (20.7), 274.2 (99.2), 273.2 (85.4), 210.2 (10.6), 136.1 (20.5), 120.2(11.1), 119.2 (28.4), 118.1 (100), 117.1 (21.7), 91.2 (28.2); [M+Na] HRMS calcd. for $C_{30}H_{32}N_2O_5S_2Na$: 587.16448, found: 587.16461; IR (KBr): ν = 3262, 2977, 2927, 1595, 1495, 1451, 1400, 1329, 1281, 1156, 1090, 1067, 912, 814, 758, 733, 661 cm^{-1}.

(*E*)-2-Methyl-1-phenyl-2-buten-1-one (252)



252

Colorless oil, R_f (Hex: EtOAc 10:1) = 0.61. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.63–7.54 (m, 2H), 7.49–7.42 (m, 1H), 7.41–7.33 (m, 2H), 6.38 (qq, J = 6.9, 1.3 Hz, 1H), 1.96–1.92 (m, 3H), 1.85 (ddd, J = 6.9, 2.1, 1.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 198.82, 141.45, 138.76, 137.57, 131.15, 129.11, 127.92, 14.70, 12.07; *m/z* (EI)(%): 160.9 (37.2), 159.9 (55.7), 158.9 (22.8), 144.8 (36.2), 131.9 (67.6), 116.9 (16.5), 104.8 (100), 82.8 (13.1), 76.9 (54.4), 55.0 (17.8),51.0 (24.7); [M+Na] HRMS calcd. for $C_{11}H_{12}ONa$: 183.07804, found: 183.07806; IR (KBr): ν = 3048, 2927, 2328, 2093, 1640, 1442, 1380, 1275, 1167, 1022, 870, 782, 701 cm^{-1}.

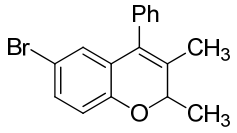
5.8 Experiments for a Novel Approach to 2*H*-Chromenes through Al(OTf)$_3$-Catalyzed Unstrained C-C σ Bond Activation

5.8.1 General Experiment for the synthesis of 2*H*-Chromenes through Al(OTf)$_3$-Catalyzed Unstrained C-C σ Bond Activation

To a suspension of 10 mol% $Al(OTf)_3$ (19.0 mg, 0.04 mmol) in 4 mL dried DCE, 4-bromo-2-(1-hydroxyethyl)phenols **164b** (86.8 mg, 0.4 mmol), 1-phenyl-1-propynes **229** (69.7 mg, 0.6 mmol), Bu_4NSbF_6 (9.6 mg, 0.02 mmol) and NH_4PF_6 (9.8 mg, 0.06 mmol) were added, the reaction was then stirred at 40 ^{o}C for 12 h. After reaction completion, the reaction was quenched by addition of 5 mL saturated $NaHCO_3$ solution and the aqueous phase was

extracted with dichloromethane (3×10 mL). The combined organic phases were dried over Na_2SO_4 and the crude product was purified by column chromatography.

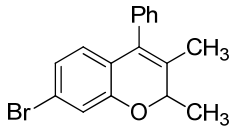
6-Bromo-2,3-dimethyl-4-phenyl-2*H*-chromene (169a)



169a

White solid, R_f (pentane: EtOAc 40:1) = 0.52. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.47–7.33 (m, 3H), 7.15 (dd, J = 8.5, 2.4, 3H), 6.72 (d, J = 8.5, 1H), 6.67 (d, J = 2.4, 1H), 4.86 (q, J = 6.5, 1H), 1.66–1.63 (m, 3H), 1.43 (d, J = 6.6, 3H); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 150.50, 136.51, 132.53, 130.61, 129.73, 129.17, 128.63, 127.84, 127.45, 126.40, 117.94, 113.05, 75.41, 18.65, 17.09; *m/z* (EI)(%): 316.2 (5.4), 314.1 (4.7), 301.1 (17.1), 299.1 (17.6), 145.0 (42.0), 105.0 (51.6), 77.1 (100), 57.2 (65.6); HRMS calcd. for $C_{17}H_{15}O^{79}Br$: 314.03008, found: 314.02876; IR (KBr): ν = 2920, 1744, 1471, 1382, 1234, 1087, 929, 817, 757, 700 cm^{-1}.

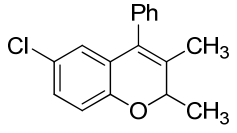
7-Bromo-2,3-dimethyl-4-phenyl-2*H*-chromene (169b)



169b

Colorless oil, R_f (pentane: EtOAc 40:1) = 0.61. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.45–7.32 (m, 3H), 7.15 (d, J = 6.4, 2H), 7.00 (d, J = 2.0, 1H), 6.85 (dd, J = 8.2, 2.0, 1H), 6.42 (d, J = 8.2, 1H), 4.86 (q, J = 6.6, 1H), 1.63 (d, J = 0.5, 3H), 1.43 (d, J = 6.6, 3H); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 152.27, 136.79, 131.44, 129.85, 129.36, 128.51, 127.32, 126.51, 123.76, 123.52, 120.71, 119.33, 75.69, 18.75, 17.04; *m/z* (EI)(%): 316.0 (9.9), 314.0 (9.5), 288.0 (49.7), 277.0 (100), 275.0 (53.0), 261.0 (59.2), 152.1 (30.0), 105.1 (31.6), 77.2 (27.9); [M-CH_3] HRMS calcd. for $C_{16}H_{12}O^{79}Br$: 299.00660, found: 299.00535; IR (KBr): ν = 2976, 1750, 1590, 1479, 1408, 1228, 1074, 932, 857, 809, 755, 700 cm^{-1}.

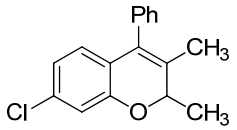
6-Chloro-2,3-dimethyl-4-phenyl-2*H*-chromene (169c)



169c

White solid, R_f (pentane: EtOAc 40:1) = 0.46. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.43 (t, J = 7.7, 2H), 7.39–7.34 (m, 1H), 7.15 (d, J = 2.0, 2H), 7.01 (dd, J = 8.5, 2.5, 1H), 6.77 (d, J = 8.5, 1H), 6.53 (d, J = 2.5, 1H), 4.88–4.82 (m, 1H), 1.64 (s, 3H), 1.42 (d, J = 6.5, 3H); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 149.96, 136.55, 132.52, 129.84, 129.26, 128.61, 127.63, 127.44, 125.88, 125.65, 125.00, 117.41, 75.43, 18.61, 17.09; *m/z* (CI)(%): 272.0 (10.3), 271.1 (18.6), 270.0 (36.0), 85.1 (61.9), 83.1 (100); IR (KBr): ν = 2974, 2922, 1476, 1235, 1080, 934, 814, 762, 699 cm^{-1}.

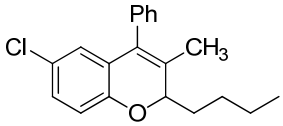
7-Chloro-2,3-dimethyl-4-phenyl-2*H*-chromene (169d)



169d

Colorless oil, R_f (pentane: EtOAc 40:1) = 0.48. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.42 (t, J = 7.6, 2H), 7.35 (dd, J = 10.6, 4.3, 1H), 7.15 (s, 2H), 6.85 (d, J = 2.1, 1H), 6.70 (dd, J = 8.3, 2.1, 1H), 6.48 (d, J = 8.3, 1H), 4.86 (q, J = 6.5, 1H), 1.64 (s, 3H), 1.43 (d, J = 6.5, 3H); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 152.19, 136.87, 132.91, 131.19, 129.87, 129.31, 128.51, 127.31, 126.19, 123.10, 120.82, 116.47, 75.66, 18.75, 16.99; *m/z* (EI)(%): 271.1 (5.5), 270.1 (4.8), 233.2 (62.5), 231.2 (37.1), 155.2 (26.3), 105.2 (37.0), 77.3 (100), 51.3 (51.0); [M-CH_3] HRMS calcd. for $C_{16}H_{12}O^{35}Cl$: 255.05712, found: 255.05669; IR (KBr): ν = 2975, 1596, 1566, 1482, 1412, 1231, 1077, 1002, 938, 859, 810, 758, 701 cm^{-1}.

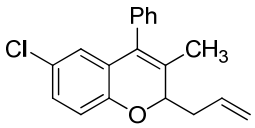
2-Butyl-6-chloro-3-methyl-4-phenyl-2*H*-chromene (169e)



169e

Colorless oil, R_f (pentane: EtOAc 40:1) = 0.52. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.45–7.31 (m, 3H), 7.14 (d, J = 5.9, 2H), 6.99 (dd, J = 8.5, 2.5, 1H), 6.76 (d, J = 8.5, 1H), 6.51 (d, J = 2.5, 1H), 4.64 (dd, J = 9.6, 2.4, 1H), 1.86–1.74 (m, 1H), 1.63 (s, 3H), 1.61–1.51 (m, 2H), 1.48–1.25 (m, 3H), 0.90 (t, J = 7.2, 3H); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 149.99, 136.63, 131.94, 129.85, 129.53, 128.60, 127.62, 127.42, 126.21, 125.55, 124.96, 117.38, 79.41, 32.03, 27.67, 22.47, 17.52, 14.03; *m/z* (CI)(%): 313.0 (1.1), 271.0 (33.6), 259.0 (33.7), 242.0 (31.3), 235.0 (35.6), 233.0 (100), 105.1 (16.7), 103.1 (31.5); HRMS calcd. for $C_{20}H_{21}O^{35}Cl$: 312.12754, found: 312.12711; IR (KBr): ν = 3052, 2937, 1724, 1598, 1472, 1239, 1167, 1094, 818, 757, 703 cm^{-1}.

2-Allyl-6-chloro-3-methyl-4-phenyl-2*H*-chromene (169f)

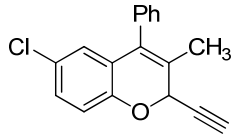


169f

Colorless oil, R_f (pentane: EtOAc 40:1) = 0.43. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.42 (t, J = 7.4, 2H), 7.38–7.32 (m, 1H), 7.13 (d, J = 6.0, 2H), 7.00 (dd, J = 8.5, 2.5, 1H), 6.75 (d, J = 8.5, 1H), 6.52 (d, J = 2.5, 1H), 5.97–5.84 (m, 1H), 5.12 (d, J = 1.1, 1H), 5.10–5.06 (m, 1H), 4.73 (dd, J = 8.4, 3.9, 1H), 2.61–2.50 (m, 1H), 2.45–2.36 (m, 1H), 1.65 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 149.86, 136.46, 133.68, 130.96, 130.19, 129.70, 128.63, 127.79, 127.50, 126.04, 125.72, 125.03, 117.85, 117.46, 78.78, 37.18, 17.65; *m/z* (CI)(%): 298.0 (10.2), 297.0 (40.0), 296.0 (9.4), 271.0 (51.4), 259.0 (44.0), 255.0 (51.2), 235.0 (37.0), 233.0 (100), 121.1

(23.5), 105.1 (43.2); HRMS calcd. for $C_{19}H_{17}O^{35}Cl$: 296.09624, found: 296.09553; IR (KBr): ν = 3063, 2922, 1866, 1638, 1475, 1241, 1047, 919, 817, 761, 701 cm^{-1}.

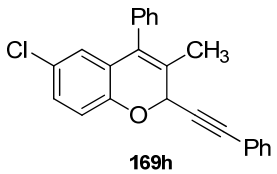
6-Chloro-2-ethynyl-3-methyl-4-phenyl-2*H*-chromene (169g)



169g

Colorless oil, R_f (pentane: EtOAc 40:1) = 0.42. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.44 (dd, J = 11.1, 4.7, 2H), 7.40–7.35 (m, 1H), 7.17 (s, 2H), 7.06 (dd, J = 8.5, 2.5, 1H), 6.87 (d, J = 8.5, 1H), 6.59 (d, J = 2.5, 1H), 5.39 (dd, J = 2.2, 0.6, 1H), 2.49 (d, J = 2.3, 1H), 1.76 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 149.43, 135.70, 130.48, 129.67, 128.67, 128.02, 127.94, 127.76, 126.79, 125.65, 125.44, 117.67, 80.04, 74.28, 68.68, 16.86; *m/z* (EI)(%): 282.0 (20.5), 281.0 (17.1), 280.0 (60.9), 279.0 (15.6), 266.9 (33.8), 266.0 (20.6), 265.0 (100), 244.0 (18.7), 229.0 (24.5), 202.9 (31.6), 202.0 (33.2), 189.0 (14.3); IR (KBr): ν = 3289, 3056, 2915, 2328, 2106, 1593, 1474, 1233, 1031, 896, 817, 705 cm^{-1}.

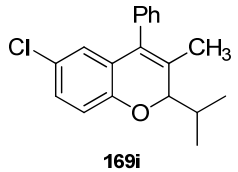
6-Chloro-3-methyl-4-phenyl-2-(phenylethynyl)-2*H*-chromene (169h)



169h

Colorless oil, R_f (pentane: EtOAc 40:1) = 0.40. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.47–7.35 (m, 5H), 7.33–7.25 (m, 3H), 7.19 (d, J = 2.6, 2H), 7.05 (dd, J = 8.5, 2.5, 1H), 6.88 (d, J = 8.5, 1H), 6.60 (d, J = 2.5, 1H), 5.64 (s, 1H), 1.81 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 149.73, 135.92, 131.97, 130.34, 129.75, 128.73, 128.66, 128.28, 128.23, 127.91, 127.70, 126.55, 125.76, 125.38, 122.10, 117.68, 86.17, 85.25, 69.46, 17.07; *m/z* (EI)(%): 358.0 (20.2), 356.0 (55.3), 341.0 (100), 279.0 (28.0), 152.5 (15.8); HRMS calcd. for $C_{24}H_{17}O^{35}Cl$: 356.09624, found: 356.09626; IR (KBr): ν = 3063, 2922, 2287, 2225, 1591, 1476, 1228, 1108, 1027, 900, 820, 754, 695 cm^{-1}.

6-Chloro-2-isopropyl-3-methyl-4-phenyl-2*H*-chromene (169i)

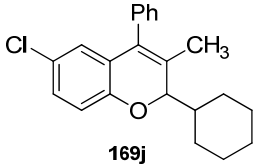


169i

Colorless oil, R_f (pentane: EtOAc 40:1) = 0.61. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.42 (t, J = 7.4, 2H), 7.38–7.32 (m, 1H), 7.15 (s, 2H), 6.97 (dd, J = 8.5, 2.6, 1H), 6.73 (d, J = 8.5, 1H), 6.48 (d, J = 2.5, 1H), 4.50 (d, J = 5.3, 1H), 2.14–2.01 (m, 1H), 1.64 (s, 3H), 1.07 (d, J = 6.9, 3H), 0.98 (d, J = 6.8, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 151.51, 136.85, 130.71, 130.17,

129.34, 128.64, 127.69, 127.45, 125.89, 125.13, 125.02, 116.48, 84.21, 32.23, 19.22, 18.75, 17.27; *m/z* (CI)(%): 300.2 (31.7), 299.2 (99.5), 273.2 (34.6), 271.2 (100); HRMS calcd. for $C_{19}H_{19}O^{35}Cl$: 298.11189, found: 298.11133; IR (KBr): ν = 3419, 2964, 1729, 1600, 1471, 1393, 1241, 1100, 939, 819, 756, 702 cm^{-1}.

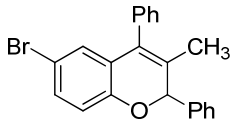
6-Chloro-2-cyclohexyl-3-methyl-4-phenyl-2*H*-chromene (169j)



169j

Colorless oil, R_f (pentane) = 0.23. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.41 (t, *J* = 7.5, 2H), 7.37–7.31 (m, 1H), 7.15 (s, 2H), 6.97 (dd, *J* = 8.5, 2.6, 1H), 6.72 (d, *J* = 8.5, 1H), 6.48 (d, *J* = 2.5, 1H), 4.50 (d, *J* = 5.3, 1H), 1.92 (d, *J* = 10.8, 1H), 1.73 (dddd, *J* = 11.2, 7.4, 5.4, 2.8, 4H), 1.64 (s, 4H, -CH_3 and 1/2-CH_2), 1.38 (qd, *J* = 12.2, 3.4, 1H), 1.29–1.00 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 151.47, 136.90, 130.72, 129.86, 128.61, 127.67, 127.44, 126.06, 125.14, 125.05, 116.59, 83.75, 41.93, 29.56, 27.69, 26.38, 26.32, 26.13, 18.91; *m/z* (CI)(%): 339.2 (100), 338.2 (24.5), 337.2 (9.6), 273.2 (7.0), 271.1 (20.7); HRMS calcd. for $C_{22}H_{23}O^{35}Cl$: 338.14319, found: 338.14307; IR (KBr): ν = 3059, 2929, 1725, 1603, 1469, 1242, 1086, 1014, 901, 820, 717 cm^{-1}.

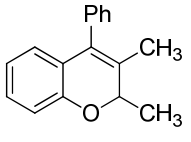
6-Bromo-3-methyl-2,4-diphenyl-2*H*-chromene (169k)



169k

Colorless oil, R_f (pentane: EtOAc 40:1) = 0.31. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.50–7.41 (m, 4H), 7.41–7.30 (m, 4H), 7.24 (s, 2H), 7.10 (dd, *J* = 8.5, 2.4, 1H), 6.72 (d, *J* = 2.4, 1H), 6.62 (d, *J* = 8.5, 1H), 5.72 (s, 1H), 1.55 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 150.57, 138.67, 136.23, 130.90, 130.63, 129.78, 128.84, 128.76, 127.88, 127.68, 127.64, 126.07, 117.82, 113.08, 81.04, 17.81; *m/z* (EI)(%): 378.0 (57.7), 375.9 (61.0), 362.9 (100), 361.0 (93.3), 300.9 (28.6), 298.9 (29.3), 104.8 (31.2), 76.9 (15.0); HRMS calcd. for $C_{22}H_{17}O^{79}Br$: 376.04573, found: 376.04566; IR (KBr): ν = 3062, 3030, 1595, 1475, 1396, 1234, 1025, 907, 815, 730, 700 cm^{-1}.

2,3-Dimethyl-4-phenyl-2*H*-chromene (169l)

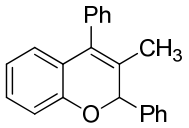


169l

Colorless oil, R_f (pentane: EtOAc 40:1) = 0.36. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.43–7.37 (m, 2H), 7.36–7.31 (m, 1H), 7.16 (d, *J* = 6.7, 2H), 7.08–7.02 (m, 1H), 6.85–6.80 (m, 1H),

6.76–6.69 (m, 1H), 6.56 (dt, *J* = 5.8, 2.9, 1H), 4.85 (q, *J* = 6.5, 1H), 1.64 (d, *J* = 0.5, 3H), 1.43 (d, *J* = 6.5, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 151.39, 137.37, 131.05, 129.95, 128.38, 128.00, 127.09, 125.37, 124.46, 120.72, 116.13, 75.22, 18.68, 17.01; *m/z* (EI)(%): 236.8 (28.5), 235.7 (32.7), 221.9 (71.0), 221.0 (75.8), 220.1 (100), 205.8 (52.0), 189.8 (85.4), 176.6 (60.7), 163.6 (69.3); [M+1] HRMS calcd. for $C_{17}H_{17}O$: 237.12739, found: 237.12738; IR (KBr): ν = 3056, 2973, 2923, 1594, 1483, 1375, 1232, 1089, 1013, 756, 702 cm^{-1}.

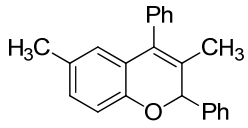
3-Methyl-2,4-diphenyl-2*H*-chromene (169m)



169m

Colorless oil, R_f (pentane: EtOAc 40:1) = 0.35. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.47 (dd, *J* = 16.1, 7.8, 4H), 7.40–7.31 (m, 4H), 7.27 (d, *J* = 16.5, 2H), 7.07–7.00 (m, 1H), 6.74 (dd, *J* = 16.4, 7.9, 2H), 6.63 (dd, *J* = 7.6, 1.2, 1H), 5.74 (s, 1H), 1.57 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 151.51, 139.29, 137.10, 131.40, 129.93, 128.66, 128.60, 128.49, 128.31, 127.71, 127.27, 125.42, 124.07, 120.76, 115.98, 80.96, 17.73; *m/z* (EI)(%): 299.1 (13.6), 298.2 (47.8), 284.1 (23.2), 283.1 (100), 221.1 (34.9); HRMS calcd. for $C_{22}H_{18}O$: 298.13522, found: 298.13514; IR (KBr): ν = 3057, 2920, 1597, 1578, 1483, 1446, 1234, 1050, 749, 698 cm^{-1}.

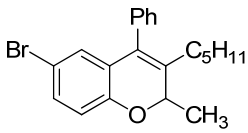
3,6-Dimethyl-2,4-diphenyl-2*H*-chromene (169n)



169n

Colorless oil, R_f (pentane: EtOAc 40:1) = 0.46. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.49–7.41 (m, 4H), 7.39 (dd, *J* = 5.0, 3.6, 1H), 7.36–7.29 (m, 3H), 7.27 (dd, *J* = 8.9, 3.8, 2H), 6.82 (dd, *J* = 8.1, 2.0, 1H), 6.64 (d, *J* = 8.1, 1H), 6.41 (d, *J* = 1.9, 1H), 5.68 (s, 1H), 2.10 (s, 3H), 1.54 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 149.28, 139.34, 137.24, 131.52, 129.95, 129.90, 128.77, 128.63, 128.52, 128.48, 128.43, 127.72, 127.21, 125.83, 123.84, 115.74, 80.84, 20.70, 17.79; *m/z* (EI)(%): 313.0 (16.5), 312.0 (58.3), 297.0 (100), 235.0 (39.6), 104.8 (31.6); HRMS calcd. for $C_{23}H_{20}O$: 312.15087, found: 312.15067; IR (KBr): ν = 3033, 2918, 1600, 1488, 1236, 1005, 913, 823, 705 cm^{-1}.

6-Bromo-2-methyl-3-pentyl-4-phenyl-2*H*-chromene (169o)

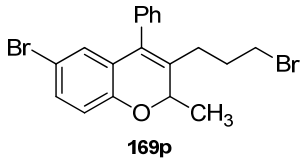


169o

Light yellow oil, R_f (pentane: EtOAc 40:1) = 0.59. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.42 (s, 2H), 7.36 (td, *J* = 7.4, 1.2, 1H), 7.23–7.01 (m, 3H), 6.72 (d, *J* = 8.5, 1H), 6.63 (d, *J* = 2.4, 1H), 4.91 (q, *J* = 6.5, 1H), 2.09 (ddd, *J* = 13.6, 9.9, 6.6, 1H), 1.85–1.79 (m, 1H), 1.43–1.36 (m, 4H,

-CH_3 and 1/2-CH_2), 1.35–1.28 (m, 1H), 1.20–1.08 (m, 4H), 0.79 (dd, J = 9.0, 5.0, 3H); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 150.34, 137.10, 136.52, 130.64, 130.07, 129.67, 129.37, 128.65, 128.49, 128.06, 127.41, 126.86, 118.02, 113.07, 73.31, 31.56, 30.48, 28.08, 22.23, 18.88, 13.84; *m/z* (EI)(%): 372.1 (16.9), 370.1 (16.5), 357.1 (35.0), 355.1 (34.5), 301.0 (34.9), 299.0 (38.6), 277.0 (29.3), 219.1 (29.3), 105.1 (39.5), 99.1 (100), 77.2 (38.0), 71.3 (41.0); [M-CH_3] HRMS calcd. for $C_{20}H_{20}O^{79}Br$: 355.06920, found: 355.06760; IR (KBr): ν = 2935, 1600, 1468, 1383, 1234, 1104, 910, 817, 707 cm^{-1}.

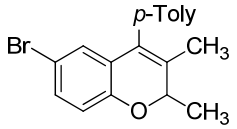
6-Bromo-3-(3-bromopropyl)-2-methyl-4-phenyl-2*H*-chromene (169p)



169p

Colorless oil, R_f (pentane: EtOAc 40:1) = 0.39. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.49–7.34 (m, 3H), 7.16 (dd, J = 8.5, 2.4, 2H), 7.08 (s, 1H), 6.72 (d, J = 8.5, 1H), 6.62 (d, J = 2.4, 1H), 4.89 (q, J = 6.5, 1H), 3.27 (dt, J = 9.9, 6.4, 1H), 3.16 (dt, J = 9.9, 6.7, 1H), 2.24 (ddd, J = 13.3, 9.3, 6.7, 1H), 1.98 (ddd, J = 9.6, 7.2, 3.6, 1H), 1.93–1.80 (m, 2H), 1.40 (d, J = 6.5, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 150.33, 136.02, 134.88, 131.06, 130.70, 129.89, 129.45, 128.89, 128.71, 128.20, 127.71, 126.46, 118.13, 113.18, 73.21, 32.83, 31.54, 29.13, 18.82; *m/z* (EI)(%): 422.0 (5.1), 406.9 (34.2), 301.0 (56.5), 299.0 (58.9), 276.9 (100), 261.0 (63.7), 151.0 (98.3), 105.1 (87.3), 77.2 (97.2); HRMS calcd. for $C_{19}H_{18}O^{79}Br_2$: 419.97189, found: 419.97116; IR (KBr): ν = 2968, 1593, 1475, 1233, 1118, 1073, 911, 817, 734, 702 cm^{-1}.

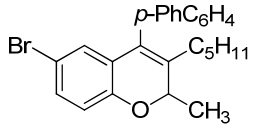
6-Bromo-2,3-dimethyl-4-(*p*-Tolyl)-2*H*-chromene (169q)



169q

White solid, R_f (pentane: EtOAc 40:1) = 0.42. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.26–7.20 (m, 2H), 7.14 (dd, J = 8.5, 2.4, 1H), 7.03 (d, J = 7.5, 2H), 6.70 (t, J = 5.7, 2H), 4.84 (q, J = 6.5, 1H), 2.41 (s, 3H), 1.64 (s, 3H), 1.41 (d, J = 6.6, 3H); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 150.54, 137.06, 133.40, 132.40, 130.51, 129.68, 129.32, 129.06, 127.87, 126.57, 117.89, 113.03, 75.45, 21.27, 18.65, 17.12; *m/z* (EI)(%): 330.0 (25.3), 328.9 (12.5), 328.0 (26.3), 315.0 (94.5), 313.0 (100), 277.0 (38.2), 275.0 (37.1), 165.0 (33.2), 119.0 (41.3), 116.1 (26.4), 91.1 (40.9); [M+1] HRMS calcd. for $C_{18}H_{18}O^{79}Br$: 329.05355, found: 329.05273; IR (KBr): ν = 3023, 2975, 2921, 1511, 1474, 1236, 1170, 1082, 932, 810, 730 cm^{-1}.

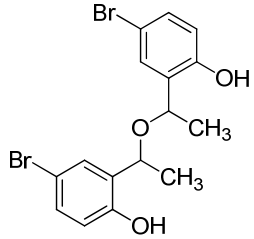
4-((1,1'-Biphenyl)-4-yl)-6-bromo-2-methyl-3-pentyl-2*H*-chromene (169r)



169r

Light yellow oil, R_f (pentane: EtOAc 40:1) = 0.44. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.67 (ddd, J = 6.1, 4.2, 2.1, 4H), 7.52–7.42 (m, 2H), 7.41–7.32 (m, 1H), 7.24 (s, 1H), 7.17 (dd, J = 8.5, 2.4, 2H), 6.73 (dd, J = 8.6, 5.5, 2H), 4.93 (q, J = 6.5, 1H), 2.15 (ddd, J = 13.6, 9.7, 6.8, 1H), 1.91–1.81 (m, 1H), 1.47–1.27 (m, 5H, -CH_3 and –CH_2), 1.23–1.07 (m, 4H), 0.79 (dd, J = 8.5, 5.6, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 150.37, 140.65, 140.13, 137.29, 135.48, 130.69, 130.49, 130.15, 129.02, 128.80, 128.06, 127.38, 127.04, 126.81, 118.07, 113.11, 73.32, 31.55, 30.53, 28.12, 22.25, 18.87, 13.85; *m/z* (EI)(%): 448.1 (5.1), 446.1 (5.1), 431.1 (14.9), 377.0 (22.0), 181.1 (37.4), 154.1 (68.4), 152.1 (75.3), 99.1 (100), 77.2 (46.5), 71.3 (76.6), 55.2 (54.1); HRMS calcd. for $C_{27}H_{27}O^{79}Br$: 446.12398, found: 446.12319; IR (KBr): ν = 3036, 2934, 1599, 1471, 1392, 1236, 1100, 1034, 910, 819, 734 cm^{-1}.

2,2'-(Oxybis(ethane-1,1-diyl))bis(4-bromophenol) (266)



266

Colorless oil, R_f (pentane: EtOAc 5:1) = 0.32. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.30 (dd, J = 8.6, 2.4, 1H), 7.23 (s, 1H), 7.02 (d, J = 2.4, 1H), 6.79 (d, J = 8.6, 1H), 4.54 (q, J = 6.7, 1H), 1.52 (d, J = 6.7, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 154.00, 132.31, 130.50, 127.36, 119.05, 112.28, 76.78, 22.19; *m/z* (EI)(%): 417.8 (14.6), 415.8 (28.8), 413.8 (16.6), 399.8 (15.4), 398.7 (11.6), 397.8 (28.8), 395.8 (16.0), 217.9 (44.7), 229.9 (47.2), 200.9 (97.5), 199.9 (68.9), 198.9 (100), 197.8 (63.0), 120.0 (55.4), 102.0 (22.1), 91.1 (50.6); HRMS calcd. for $C_{16}H_{16}O_3{}^{79}Br_2$: 413.94607, found: 413.94560; IR (KBr): ν = 3385, 2975, 1589, 1469, 1351, 1231, 1070, 903, 814, 732 cm^{-1}.

Literature:

[1] a) R. M. O' Ferrall, *Advances in Physical Organic Chemistry* **2010**, *44*, 19-122; b) D. H. Aue, *Wiley Interdisciplinary Reviews: Computational Molecular Science* **2011**, *1*, 487-508.

[2] a) B. Godoi, R. F. Schumacher, G. Zeni, *Chem. Rev.* **2011**, *111*, 2937-2980; b) K. Gilmore, I. V. Alabugin, *Chem. Rev.* **2011**, *111*, 6513-6556; c) A. Palisse, S. F. Kirsch, *Org. Biomol. Chem.* **2012**, *10*, 8041-8047.

[3] S. A. Worlikar, T. Kesharwani, T.-L. Yao, R. C. Larock, *J. Org. Chem.* **2007**, *72*, 1347-1353.

[4] X.-X. Zhang, R. C. Larock, *J. Am. Chem. Soc.* **2005**, *127*, 12230-12231.

[5] B. Crone, S. F. Kirsch, K.-D. Umland, *Angew. Chem. Int. Ed.* **2010**, *49*, 4661-4664.

[6] Z.-W. W. Just, R. C. Larock, *J. Org. Chem.* **2008**, *73*, 2662-2667.

[7] M. B. Goldfinger, K. B. Crawford, T. M. Swager, *J. Am. Chem. Soc.* **1997**, *119*, 4578-4593.

[8] L.-M. Zhang, S. A. Kozmin, *J. Am. Chem. Soc.* **2004**, *126*, 10204-10205.

[9] D. Eom, S. Park, Y. Park, K. Lee, G. Hong, P.-H. Lee, *Eur. J. Org. Chem.* **2013**, 2672-2682.

[10] C.-R. Liu, F.-L. Yang, Y.-Z. Jin, X.-T. Ma, D.-J. Cheng, N. Li, S.-K. Tian, *Org. Lett.* **2010**, *12*, 3832-3835.

[11] a) H.-R. Li, W.-J. Li, W.-P. Liu, Z.-H. He, Z.-P. Li, *Angew. Chem. Int. Ed.* **2011**, *50*, 2975 -2978; b) X.-L. Bu, J.-Q. Hong, X.-G. Zhou, *Adv. Synth. Catal.* **2011**, *353*, 2111-2118; c) Y.-X. Chen, K.-N. Li, X. Liu, J.-Y. Zhu, B.-H. Chen, *Synlett* **2013**, *24*, 130-134.

[12] a) A. P. Krapcho, *Synthesis* **1974**, 383-419; b) M. Sannigrahi, *Tetrahedron* **1999**, *55*, 9007-9071; c) R. Pradhan, M. Patra, A. K. Behera, B. K. Mishra, R. K. Behera, *Tetrahedron* **2006**, *62*, 779-828; d) S. Kotha, A. C. Deb, K. Lahiri, E. Manivannan, *Synthesis* **2009**, *2*, 165-193.

[13] T.-N. Jin, M. Himuro, Y. Yamamoto, *Angew. Chem. Int. Ed.* **2009**, *48*, 5893-5896.

[14] A. J. Walkinshaw, W.-S. Xu, M. G. Suero, M. J. Gaunt, *J. Am. Chem. Soc.* **2013**, *135*, 12532-12535.

[15] Y.-W. Li, Y. Lu, G.-Y.-S. Qiu, Q.-P. Ding, *Org. Lett.* **2014**, *16*, 4240-4243.

[16] U. Biermann, R. Koch, J.-O. Metzger, *Angew. Chem. Int. Ed.* **2006**, *45*, 3076-3079.

[17] T.-N. Jin, M. Himuro, Y. Yamamoto, *J. Am. Chem. Soc.* **2010**, *132*, 5590-5591.

[18] F-Z. Zhang, S. Das, A. J. Walkinshaw, A. Casitas, M. Taylor, M. G. Suero, M. J. Gaunt, *J. Am. Chem. Soc.* **2014**, *136*, 8851-8854.

Literature:

[19] P. Gao, Y.-W. Shen, R. Fang, X.-H. Hao, Z.-H. Qiu, F. Yang, X.-B. Yan, Q. Wang, X.-J. Gong, X.-Y. Liu, Y.-M. Liang, *Angew. Chem. Int. Ed.* **2014**, *53*, 7629-7633.

[20] For selected reviews on transition-metal catalysis, see: a) K. Nomura, B. Kitiyanan, *Current Organic Synthesis* **2008**, *5*, 217-226; b) J. D. Scholten, B. C. Leal, J. Dupont, *ACS Catal.* **2012**, *2*, 184-200; c) Z.-t. Du, Z.-h. Shao, *Chem. Soc. Rev.* **2013**, *42*, 1337-1378; d) S. H. A. M. Leenders, R. Gramage-Doria, B. de Bruin, J. N. H. Reek, *Chem. Soc. Rev.* **2015**, *44*, 433-448.

[21] M. Niggemann, M. J. Meel, *Angew. Chem. Int. Ed.* **2010**, *49*, 3684-3687.

[22] S. Haubenreissera, M. Niggemanna, *Adv. Synth. Catal.* **2011**, *353*, 469-474.

[23] V. J. Meyer, M. Niggemann, *Eur. J. Org. Chem.* **2011**, 3671-3674.

[24] V. J. Meyer, M. Niggemann, *Chem. Eur. J.* **2012**, *18*, 4687-4691.

[25] T. Haven, G. Kubik, S. Haubenreisser, M. Niggemann, *Angew. Chem. Int. Ed.* **2013**, *52*, 4016-4019.

[26] V. J. Meyer, C. Ascheberg, M. Niggemann, *Chem. Eur. J.* **2015**, *21*, 6371-6374.

[27] For selected examples on metallacycles, see: a) T. Tsuda, T. Kiyoi, T. Miyane, T. Saegusa, *J. Am. Chem. Soc.* **1988**, *110*, 8570-8572; b) B. M. Trost, R. E. Brown, F. D. Toste, *J. Am. Chem. Soc.* **2000**, *122*, 5877-5878; c) B. Bennacer, M. Fujiwara, S.-Y. Lee, I. Ojima, *J. Am. Chem. Soc.* **2005**, *127*, 17756-17767; d) Y. Oonishi, T. Yokoe, A. Hosotani, Y. Sato, *Angew. Chem. Int. Ed.* **2014**, *53*, 1135-1139; for selected examples on C-gold bond species, see: e) E. Jimenez-Nunez, C. K. Claverie, C. Nieto-Oberhuber, A. M. Echavarren, *Angew. Chem. Int. Ed.* **2006**, *45*, 5452-5455; f) M. Schelwies, R. Moser, A. L. Dempwolff, F. Rominger, G. Helmchen, *Chem. Eur. J.* **2009**, *15*, 10888-10900; g) T. Matsuda, Y. Sakurai, *J. Org. Chem.* **2014**, *79*, 2739-2745.

[28] T. Stopka, M. Niggemann, *Org. Lett.* **2015**, *17*, 1437-1440.

[29] M. Niggemann, N. Bisek, *Chem. Eur. J.* **2010**, *16*, 11246-11249.

[30] A. Kena Diba, J.-M. Begouin, M. Niggemann, *Tetrahedron Lett.* **2012**, *53*, 6629-6632.

[31] a) M. J. V. Eynden, J. P. Stambuli, *Org. Lett.* **2008**, *10*, 5289-5291; b) M. J. V. Eynden, K. Kunchithapatham, J. P. Stambuli, *J. Org. Chem.* **2010**, *75*, 8542-8549.

[32] S. Chitra, K. Pandiarajan, *Tetrahedron Lett.* **2009**, *50*, 2222-2224.

[33] N. V. Forkel, D. A. Henderson, M. J. Fuchter, *Green Chem.* **2012**, *14*, 2129-2132.

[34] a) E. E. Schweizer, O. Meeder-Nycz, *in Chromenes, Chromanes, Chromones,* ed. G. P. Ellis, Wiley-Interscience, New York, 1977; b) A. F. Benslimane, Y. F. Pouchus, J.-F. Verbist, J.-Y. Petit, J. D. Brion, L. Welin, *J. Clin. Pharmacol.* **1995**, *35*, 298-301; c) V. Rukachaisirikul, M. Kamkaew, D. Sukavisit, S. Phongpaichit, P. Sawangchote, W. C. Taylor, *J. Nat. Prod.* **2003**, *66*, 1531-1535; d) I. R. Hardcastle, X. l. Cockcroft, N. J.

Literature:

Curtin, M. D. El-Murr, J. J. Leahy, M. Stockley, B. T. Golding, L. Rigoreau, C. Richardson, G. C. M. Smith, R. J. Griffin, *J. Med. Chem.* **2005**, *48*, 7829-7846; e) M. Kidwai, S. Saxena, M. K. R. Khan, S. S. Thukral, *Bioorg. Med. Chem. Lett.* **2005**, *15*, 4295-4298.

[35] Y. Nishibayashi, Y. Inada, M. Hidai, S. Uemura, *J. Am. Chem. Soc.* **2002**, *124*, 7900-7901.

[36] W. A. L. V. Otterlo, E. L. Ngidi, S. Kuzvidza, G. L. Morgans, S. S. Moleele, C. B. Koning, *Tetrahedron* **2005**, *61*, 9996-10006.

[37] a) Y. W. Fang, C. Z. Li, *J. Org. Chem.* **2006**, *71*, 6427-6431; b) C. C. Malakar, D. Schmidt, J. Conrad, U. Beifuss, *Org. Lett.* **2011**, *13*, 1972-1975.

[38] L.-W. Ye, X.-L. Sun, C.-Y. Zhu, Y. Tang, *Org. Lett.* **2006**, *8*, 3853-3856.

[39] a) J.-M. Fan, Z.-Y. Wang, *Chem. Commun.* **2008**, 5381-5383; b) D. Enders, G. Urbanietz, G. Raabe, *Synthesis* **2011**, 1905-1911; c) F.-j. Wang, M.-l. Qu, F. Chen, L. Lia, M. Shi, *Chem. Commun.* **2012**, *48*, 437-439; d) M.-h. Li, B. Zhang, Y.-l. Gu, *Green Chem.* **2012**, *14*, 2421-2428; e) P. P. Ghosh, A. R. Das, *J. Org. Chem.* **2013**, *78*, 6170-6181; f) T. Aoyama, T. Yamamoto, S. Miyota, M. Hayakawa, T. Takido, M. Kodomari, *Synlett* **2014**, *25*, 1571-1576; g) R. Sangsuwan, S. Sangher, T. Aree, C. Mahidol, S. Ruchirawat, P. Kittakoop, *RSC Adv.* **2014**, *4*, 13708-13718; h) O. El-Sepelgy, S. Haseloff, S. K. Alamsetti, C. Schneider, *Angew. Chem. Int. Ed.* **2014**, *53*, 7923-7927.

[40] a) L. Lu, J.-m. Wei, J. Chen, J.-p. Zhang, H.-m. Deng, M. Shao, H. Zhang, W.-g. Cao, *Tetrahedron* **2009**, *65*, 9152-9156; b) C.-l. Liu, X.-s. Zhang, R. Wang, W. Wang, *Org. Lett.* **2010**, *12*, 4948-4951; c) X.-s. Zhang, S.-l. Zhang, W. Wang, *Angew. Chem. Int. Ed.* **2010**, *49*, 1481-1484; d) J. Aleman, A. Nunez, L. Marzo, V. Marcos, C. Alvarado, J. L. G. Ruano, *Chem. Eur. J.* **2010**, *16*, 9453-9456; e) B. Duda, S. N. Tverdomed, G.-V. Roeschenthaler, *J. Org. Chem.* **2011**, *76*, 71-79; f) J. Alemán, C. Alvarado, V. Marcos, A. Núñez, J. L. G. Ruano, *Synthesis* **2011**, 1840-1846; g) S. N. Singh, R. Bopanni, S. Jayaprakash, K. V. Reddy, M. A. Ashfaq, K. S. Kumare, M. Pal, *RSC Adv.* **2014**, *4*, 24870-24873; h) J. Zhang, M. J. Ajitha, L. He, K. Liu, B. Dai, K.-W. Huang, *Adv. Synth. Catal.* **2015**, *357*, 967-973.

[41] Y.-W. Guo, Y.-L. Shi, H.-B. Lia, M. Shi, *Tetrahedron* **2006**, *62*, 5875-5882.

[42] a) Y.-L. Shi, M. Shi, *Org. Lett.* **2005**, *7*, 3057-3060; b) G.-L. Zhao, Y.-L. Shi, M. Shi, *Org. Lett.* **2005**, *7*, 4527-4530; c) Y.-L. Shi, M. Shi, *Chem. Eur. J.* **2006**, *12*, 3374-3378; d) Y.-L. Shi, M. Shi, *Org. Biomol. Chem.* **2007**, *5*, 1499-1504.

[43] a) Y.-k. Liu, J.-q. Qian, S.-j. Lou, J. Zhu, Z.-y. Xu, *J. Org. Chem.* **2010**, *75*, 1309-1312; b) G.-d. Yin, L. Fan, T.-b. Ren, C.-y. Zheng, Q. Tao, A.-x. Wu, N.-f. She, *Org. Biomol. Chem.* **2012**, *10*, 8877-8883; c) H.-J. Li, K. Deng, D.-H. Luo, D.-H. Liu, J.-L. Wang, C.-H. Lin, Y.-C. Wu, *RSC Adv.* **2014**, *4*, 26316-26324; d) C. Bingi, N. R. Emmadi, M.

Literature:

Chennapuram, Y. Poornachandra, C. G. Kumar, J. B. Nanubolu, K. Atmakur, *Bioorg. Med. Chem. Lett.* **2015**, *25*, 1915-1919.

[44] a) S. B. Simelane, H. H. Kinfe, A. Muller, D. B. G. Williams, *Org. Lett.* **2014**, *16*, 4543-4545; b) G. Saidachary, K. V. Prasad, M. Sairam, B. C. Raju, *Tetrahedron Lett.* **2014**, *55*, 4753-4757; c) L. C. Rao, N. S. Kumar, N. J. babu, H. M. Meshram, *Tetrahedron Lett.* **2014**, *55*, 5342-5346.

[45] N. T. Patil, Z. B Huo, G. B. Bajracharya, Y. Yamamoto, *J. Org. Chem*. **2006**, *71*, 3612-3614.

[46] H. M. Weiss, K. M. Touchette, S. Angell, J. Khan, *Org. Biomol. Chem.* **2003**, *1*, 2152-2156.

[47] a) A. B. Flynn, W. W. Ogilvie, *Chem. Rev.* **2007**, *107*, 4698-4745; b) T. Arai, Y. Ikematsu, Y. Suemitsu, *Pure Appl. Chem.* **2010**, *82*, 1485-1490.

[48] a) K. Itami, T. Kamei, J. I. Yoshida, *J. Am. Chem. Soc.* **2003**, *125*, 14670-14671; b) M. Corpet, C. Gosmini, *Chem. Commun.* **2012**, *48*, 11561-11563; c) F. Xue, J. Zhao, T. S. A. Hor, *Chem. Commun*. **2013**, *49*, 10121-10123; d) N. T. Barczak, D. A. Rooke, Z. A. Menard, E. M. Ferreira, *Angew. Chem. Int. Ed*. **2013**, *52*, 7579-7582; e) T. Wakamatsu, K. Nagao, H. Ohmiya, M. Sawamura, *Angew. Chem. Int. Ed.* **2013**, *52*, 11620-11623; f) Y. Q. Zhou, W. You, K. B. Smith, M. K. Brown, *Angew. Chem. Int. Ed*. **2014**, *53*, 3475-3479.

[49] a) S. J. Patel, T. F. Jamison, *Angew. Chem. Int. Ed*. **2003**, *42*, 1364-1367; b) Y. Nakao, S. Oda, T. Hiyama, *J. Am. Chem. Soc*. **2004**, *126*, 13904-13905; c) Y. Nakao, S. Oda, A. Yada, T. Hiyama,*Tetrahedron* **2006**, *62*, 7567-7576; d) Y. Nakao, A.Yada, S. Ebata, T. Hiyama, *J. Am. Chem. Soc.* **2007**, *129*, 2428-2429; e) Y. Nakao, A.Yada, T. Hiyama, *J. Am. Chem. Soc*. **2010**, *132*, 10024-10026; f) Y. Minami, H.Yoshiyasu, Y. Nakao, T. Hiyama, *Angew. Chem. Int. Ed*. **2013**, *52*, 883-887.

[50] a) C. X. Zhou, D. E. Emrich, R. C. Larock, *Org. Lett.* **2003**, *5*, 1579-1582; b) C. X. Zhou, R. C. Larock, *Org. Lett.* **2005**, *7*, 259-262; c) C. X. Zhou, R. C. Larock, *J. Org. Chem*. **2006**, *71*, 3184-3191; d) L. L. Suarez, M. F. Greaney, *Chem. Commun*. **2011**, *47*, 7992-7994.

[51] K. Komeyama, T. Yamada, R. Igawa, K. Takaki, *Chem. Commun*. **2012**, *48*, 6372-6374.

[52] a) M. B. Goldfinger, K. B. Crawford, T. M. Swager, *J. Am. Chem. Soc.* **1997**, *119*, 4578-4593; b) L. M. Zhang, S. A. Kozmin, *J. Am. Chem. Soc.* **2004**, *126*, 10204-10205; c) Y. S. Zhang, R. P. Hsung, X. J. Zhang, J. Huang, B. W. Slafer, A. Davis, *Org. Lett.* **2005**, *7*, 1047-1050; d) Y. S. Zhang, *Tetrahedron Lett.* **2005**, *46*, 6483-6486; e) Y. S. Zhang, *Tetrahedron* **2006**, *62*, 3917-3927; f) L. M. Zhang, J. W. Sun, S. A. Kozmin, *Tetrahedron* **2006**, *62*, 11371-11380; g) Md. A. Rahman, O. Ogawa, J. Oyamada, T. Kitamura, *Synthesis* **2008**, 3755-3760; h) D. Eom, S. Park, Y. Park, K. Lee, G. Hong, P. H. Lee, *Eur. J. Org. Chem.* **2013**, 2672-2682.

Literature:

[53] For selected reviews on C-H bond activation, see: a) V. Ritleng, C. Sirlin, M. Pfeffer, *Chem. Rev.* **2002**, *102*, 1731-1769; b) J. A. Labinger, J. E. Bercaw, *Nature* **2002**, *417*, 507-514; c) I. A. I. Mkhalid, J. H. Barnard, T. B. Marder, J. M. Murphy, J. F. Hartwig, *Chem. Rev.* **2010**, *110*, 890-931; d) D. A. Colby, R. G. Bergman, J. A. Ellman, *Chem. Rev.* **2010**, *110*, 624-655; e) J. Wencel-Delord, T. Droege, F. Liu, F. Glorius, *Chem. Soc. Rev.* **2011**, *40*, 4740-4761; f) S. H. Cho, J. Y. Kim, J. Kwak, S. Chang, *Chem. Soc. Rev.* **2011**, *40*, 5068-5083; g) G.-Y. Song, F. Wang, X.-W. Li, *Chem. Soc. Rev.* **2012**, *41*, 3651-3678; h) S. Gaillard, C. S. J. Cazin, S. P. Nolan, *Acc. Chem. Res.* **2012**, *45*, 778-787; i) P. B. Arockiam, C. Bruneau, P. H. Dixneuf, *Chem. Rev.* **2012**, *112*, 5879-5918.

[54] S. J. Pastine, K. M. McQuaid, D. Sames, *J. Am. Chem. Soc*. **2005**, *127*, 12180-12181.

[55] For reviews on C-C bond activation see: a) R. H. Crabtree, *Chem. Rev.* **1985**, *85*, 245-269; b) W. D. Jones, *Nature.* **1993**, *364*, 676-677; c) B. Rybtchinski, D, Milstein, *Angew. Chem. Int. Ed.* **1999**, *38*, 870-883; d) M. E. van der Boom, D. Milstein, *Chem. Rev.* **2003**, *103*, 1759-1792; e) C. H. Jun, *Chem. Soc. Rev.* **2004**, *33*, 610-618; f) T. Seiser, N. Cramer, *Org. Biomol. Chem.* **2009**, *7*, 2835-2840; g) N. Cramer, T. Seiser, *Synlett* **2011**, 449-460; h) M. Murakami, T. Matsuda, *Chem. Commun.* **2011**, *47*, 1100-1105; i) C. Aissa, *Synthesis* **2011**, 3389-3407; j) T. Seiser, T. Saget, D. N. Tran, N. Cramer, *Angew. Chem. Int. Ed.* **2011**, *50*, 7740-7752; k) K. Ruhland, *Eur. J. Org. Chem.* **2012**, 2683-2706; l) F. Chen, T. Wang, N. Jiao, *Chem. Rev.* **2014**, *114*, 8613-8661; m) H. Liu, M. H. Feng, X. F. Jiang, *Chem. Asian J*. **2014**, *9*, 3360-3389.

[56] a) H. Liu, C. Dong, Z. Zhang, P. Wu, X. Jiang, *Angew. Chem. Int. Ed.* **2012**, *51*, 12570-12574; b) X. Zhang, M. Wang, Y. Zhang, L. Wang, *RSC Adv.* **2013**, *3*, 1311-1316; c) X. Sun, M. Wang, P. Li, X. Zhang, L. Wang, *Green Chem.* **2013**, *15*, 3289-3294; d) N. Y. More, M. Jeganmohan, *Org. Lett*. **2014**, *16*, 804-807; e) B. Tiwari, J. Zhang, Y. R. Chi, *Angew. Chem. Int. Ed*. **2012**, *51*, 1911-1914; f) B. Hu, Y. Li, Z. Li, X. Meng, *Org. Biomol. Chem*. **2013**, *11*, 4138-4141.

[57] a) W. C. Gao, S. Jiang, R. L. Wang, C. Zhang, *Chem. Commun*. **2013**, *49*, 4890-4892; b) M. H. Fonseca, E. Eibler, M. Zabel, B. König, *Tetrahedron: Asymmetry* **2003**, *14*, 1989-1994.

[58] M. K. Schwarz, *J. Med. Chem.* **2005**, *48*, 7882- 7905.

[59] N. K. Pahadi, J. A. Tunge, *Synlett* **2009**, *19*, 3135-3138.

[60] A. Saito, M. Umakoshi, N. Yagyu, Y. Hanzawa, *Org. Lett*. **2008**, *10*, 1783-1785.

[61] a) A. D. Covington, *Chem. Soc. Rev*. **1997**, 111-126; b) G. P. Ellis, I. M. Lockhart, *The Chemistry of Heterocyclic Compounds: Chromenes, Chromanones, and Chromones*, (Eds.: G. P. Ellis), Wiley-VCH, New York, 2009, pp. 1-1196; c) N. Majumdar, N. D. Paul, S. Mandal, B. de Bruin, W. D. Wulff, *ACS Catal*. **2015**, *5*, 2329-2366.

Literature:

[62] N. D. Paul, S. Mandal, M. Otte, X. Cui, X. P. Zhang, B. de Bruin, *J. Am. Chem. Soc.* **2014**, *136*, 1090-1096.

[63] a) C. Nevado, A. M. Echavarren, *Chem. Eur. J.* **2005**, *11*, 3155-3164; b) I. N. Lykakis, C. Efe, C. Gryparis, M. Stratakis, *Eur. J. Org. Chem.* **2011**, 2334-2338.

[64] a) J. P. A. Harrity, D. S. La, D. R. Cefalo, M. S. Visser, A. H. Hoveyda, *J. Am. Chem. Soc.* **1998**, *120*, 2343-2351; b) S. Chang, R. H. Grubbs, *J. Org. Chem.* **1998**, *63*, 864-866; c) R. Doodeman, F. P. J. T. Rutjes, H. Hiemstra, *Tetrahedron Lett.* **2000**, *41*, 5979-5983.

[65] T. J. A. Graham, A. G. Doyle, *Org. Lett.* **2012**, *14*, 1616-1619.

[66] a) B. M. Trost, *Science* **1991**, *254*, 1471-1477; b) B. M. Trost, *Angew. Chem. Int. Ed.* **1995**, *34*, 259-281; c) T. Newhouse, P. S. Baran, R. W. Hoffmann, *Chem. Soc. Rev.* **2009**, *38*, 3010-3021; d) N. Z. Burns, P. S. Baran, R. W. Hoffmann, *Angew. Chem. Int. Ed*. **2009**, *48*, 2854-2867; e) P. Anastas, N. Eghbali, *Chem. Soc. Rev.* **2010**, *39*, 301-312; f) R. A. Sheldon, *Chem. Soc. Rev*. **2012**, *41*, 1437-1451; g) P. J. Dunn, *Chem. Soc. Rev*. **2012**, *41*, 1452-1461; h) P. Gupta, A. Mahajan, *RSC Adv*. **2015**, *5*, 26686-26705.

[67] I. Marek, A. Masarwa, P.-O. Delaye, M. Leibeling, *Angew. Chem. Int. Ed.* **2015**, *54*, 414-429.

[68] For representative examples of the C-C σ bond cleavage of constrained small-ring molecules followed by olefins or alkynes insertion: for biphenylenes, see: a) B. L. Edelbach, R. J. Lachicotte, W. D. Jones, *Organometallics* **1998**, *18*, 4040-4049; b) T. Schau U. Radius, *Chem. Eur. J.* **2005**, *11*, 5024-5030; c) T. Shibata, G. Nishizawa, K. Endo, *Synlett* **2008**, 765-768; d) A. Korotvicka, I. Cisarova, J. Roithova, M. Kotora, *Chem. Eur. J.* **2012**, *18*, 4200-4207; for cyclobutenediones and cyclobutanones, see: e) M. S. South, L. S. Liebeskind, *J. Am. Chem. Soc.* **1984**, *106*, 4181-4185; f) L. S. Liebeskind, S. L. Baysdon, M. S. South, S. Iyer, J. P. Leeds, *Tetrahedron* **1985**, *41*, 5839-5853; g) M. Murakami, T. Itahashi, Y. Ito, *J. Am. Chem. Soc.* **2002**, *124*, 13976-13977; h) M. Murakami, S. Ashida, T. Matsuda, *J. Am. Chem. Soc.* **2005**, *127*, 6932-6933; i) M. Murakami, S. Ashida, *Chem. Commun.* **2006**, 4599-4601; j) M. Murakami, S. Ashida, T. Matsuda, *Tetrahedron* **2006**, *62*, 7540-7546; k) L. Liu, N. Ishida, M. Murakami, *Angew. Chem. Int. Ed*. **2012**, *51*, 2485-2488; for cyclobutenols, see: l) N. Ishida, S. Sawano, Y. Masuda, M. Murakami, *J. Am. Chem. Soc*. **2012**, *134*, 17502-17504; m) T. Matsuda, N. Miura, *Org. Biomol. Chem.* **2013**, *11*, 3424-3427; n) N. Ishida, N. Ishikawa, S. Sawano, Y. Masuda, M. Murakami, *Chem. Commun.* **2015**, *51*, 1882-1885; for azetidinones, see: o) P. Kumar, J. Louie, Org. Lett. 2012, 14, 2026-2029; p) N. Ishida, T. Yuhki, M. Murakami, *Org. Lett.* **2012**, *14*, 3898-3901; q) K. Y. T. Ho, C. Aissa, *Chem. Eur. J.* **2012**, *18*, 3486-3489; r) Y. Li, Z. Y. Lin, *Organometallics* **2013**, *32*, 3003-3011.

[69] For examples with cyclobutenones, see: a) R. L. Danheiser, S. K. Gee, *J. Org. Chem.* **1984**, *49*, 1672-1674; b) R. L. Danheiser, A. Nishida, S. Savariar, M. P. Trova, *Tetrahedron Lett.* **1988**, *29*, 4917-4920; c) M. A. Huffman, L. S. Liebeskind, *J. Am.*

Literature:

Chem. Soc. **1990**, *112*, 8618-8620; d) M. A. Huffman, L, S. Liebeskind, *J. Am. Chem. Soc.* **1991**, *113*, 2771-2772; e) T. Kondo, M. Niimi, M. Nomura, K. Wada, T. Mitsudo, *Tetrahedron Lett.* **2007**, *48*, 2837-2839; f) A.-L. Auvinet, J. P. A. Harrity, *Angew. Chem. Int. Ed.* **2011**, *50,* 2769-2772; g) T. Xu, H. M. Ko, N. A. Savage, G. B. Dong, *J. Am. Chem. Soc.* **2012**, *134*, 20005-20008; h) T. Xu, G. B. Dong, *Angew. Chem. Int. Ed.* **2012**, *51,* 7567-7571; i) P. H Chen, T. Xu, G. B. Dong, *Angew. Chem. Int. Ed.* **2014**, *53,* 1674-1678; j) T. Xu, G. B. Dong, *Angew. Chem. Int. Ed.* **2014**, *53,* 10733-10736.

[70] a) Y. Nakao, S. Oda, T. Hiyama, *J. Am. Chem. Soc.* **2004**, *126*, 13904-13905; b) Y. Nakao, T. Yukawa, Y. Hirata, S. Oda, J. Satoh, T. Hiyama, *J. Am. Chem. Soc*. **2006**, *128*, 7116-7117; c) Y. Nakao, Y. Hirata, T. Hiyama, *J. Am. Chem. Soc.* **2006**, *128*, 7420-7421; d) Y. Nakao, A. Yada, J. Satoh, S. Ebata, S. Oda, T. Hiyama, *Chem. Lett.* **2006**, *35*, 790-791; e) Y. Nakao, A. Yada, S. Ebata, T. Hiyama, *J. Am. Chem. Soc.* **2007**, *129*, 2428-2429; f) M. P. Watson, E. N. Jacobsen, *J. Am. Chem. Soc*. **2008**, *130*, 12594-12595; g) Y. Nakao, S. Ebata, A. Yada, T. Hiyama, M. Ikawa, S. Ogoshi, *J. Am. Chem. Soc.* **2008**, *130*, 12874-12875; h) Y. Hirata, T. Yukawa, N. Kashihara, Y. Nakao, T. Hiyama, *J. Am. Chem. Soc*. **2009**, *131*, 10964-10973; i) A. Yada, T. Yukawa, Y. Nakao, T. Hiyama *Chem. Commun*. **2009**, 3931-3933; j) Y. Nakao, A. Yada, T. Hiyama, *J. Am. Chem. Soc.* **2010**, *132*, 10024-10026; k) Y. Hirata, A. Yada, E. Morita, Y. Nakao, T. Hiyama, M. Ohashi, S. Ogoshi, *J. Am. Chem. Soc.* **2010**, *132*, 10070-10077; l) Y. Minami, H. Yoshiyasu, Y. Nakao, T. Hiyama, *Angew. Chem. Int. Ed.* **2013**, *52*, 883-887.

[71] a) Y. Nishihara, Y. Inoue, M. Itazaki, K. Takagi, *Org. Lett.* **2005**, *7*, 2639-2641; b) Y. Kobayashi, H. Kamisaki, R. Yanada, Y.Takemoto, *Org. Lett*. **2006**, *8*, 2711-2713; c) Y. Nishihara, Y. Inoue, S. Izawa, M. Miyasaka, K. Tanemura, K. Nakajima, K. Takagi, *Tetrahedron* **2006**, *62*, 9872-9882; d) Y. Kobayashi, H. Kamisaki, H. Takeda, Y. Yasui, R. Yanada, Y. Takemoto *Tetrahedron* **2007**, *63*, 2978-2989; e) Y. Yasui, H. Kamisaki, Y. Takemoto, *Org. Lett*. **2008**, *10*, 3303-3306; f) V. J. Reddy, C. J. Douglas, *Org. Lett.* **2010**, *12*, 952-955; g) N. R. Rondla, S. M. Levi, J. M. Ryss, R. A. V. Berg, C. J. Douglas, *Org. Lett.* **2011**, *13*, 1940-1943.

[72] a) M. T. Wentzel, V. J. Reddy, T. K. Hyster, C. J. Douglas, *Angew. Chem. Int. Ed*. **2009**, *48*, 6121-6123; b) A. M. Dreis C. J. Douglas, *J. Am. Chem. Soc.* **2009**, *131*, 412-413; c) C. M. Rathbun, J, B. Johnson, *J. Am. Chem. Soc.* **2011**, *133*, 2031-2033; d) J. P. Lutz, C. M. Rathbun, S. M. Stevenson, B. M. Powell, T. S. Boman, C. E. Baxter, J. M. Zona, J. B. Johnson, *J. Am. Chem. Soc.* **2012**, *134*, 715-722.

[73] Y. Kuninobu, H. Matsuzaki, M. Nishi, K. Takai, *Org. Lett.* **2011**, *13*, 2959-2961.