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Ring Expansion

Arene Ring Expansion by Ruthenium η^6-Arene Complexes

*William G. Whitehurst, Tim Schulte, Zikuan Wang, Felix Waldbach, and Tobias Ritter**

Abstract: Transition metal π-arene complexes enable the dearomatization of benzene rings to access diversified unsaturated carbocycles through multistep synthetic procedures involving sequential addition of nucleophiles and electrophiles. This work details a single-step dearomatization process by reaction of Ru(η^6-arene) complexes with enolates derived from α-halo or α-(tosyloxy)-esters to directly transform π-coordinated arenes to ring-expanded cycloheptatrienes.

Dearomatization of arenes via transition metal π-arene complexes provides a direct approach to access functionalized unsaturated carbocycles.[1,2] Dearomatization is typically achieved with basic carbanion nucleophiles, in combination with a proton source or oxidant, necessitating multistep synthetic sequences. This work reports an alternative strategy employing enolates derived from α-halo or α-(tosyloxy)esters in reactions with Ru(η^6-arene) complexes, resulting in arene ring expansion to form cycloheptatriene products. The reaction proceeds by nucleophilic attack of the enolate to the π-coordinated arene, forming a Ru(η^5-cyclohexadienyl) intermediate, followed by intramolecular displacement of the α-carbonyl leaving group. The mechanism was experimentally supported by the synthesis and thermolysis reaction of an isolable Ru(η^5-cyclohexadienyl) complex derived from an α-chloroester and Ru(η^6-benzene) complex. Computational analysis elucidated additional intermediates in the reaction pathway occurring after leaving group displacement. The discovery and mechanistic investigation of an unprecedented transformation of π-arene complexes provides a basis on which to expand the scope of π-arene activation by transition metals towards the development of catalytic applications.

[*] Dr. W. G. Whitehurst, T. Schulte, Z. Wang, F. Waldbach, Prof. Dr. T. Ritter
Max-Planck-Institut für Kohlenforschung
Kaiser-Wilhelm-Platz 1, Mülheim an der Ruhr, 45470, Germany
E-mail: ritter@kofo.mpg.de

T. Schulte
Institute of Organic Chemistry
RWTH Aachen University
Landoltweg 1, 52074 Aachen, Germany

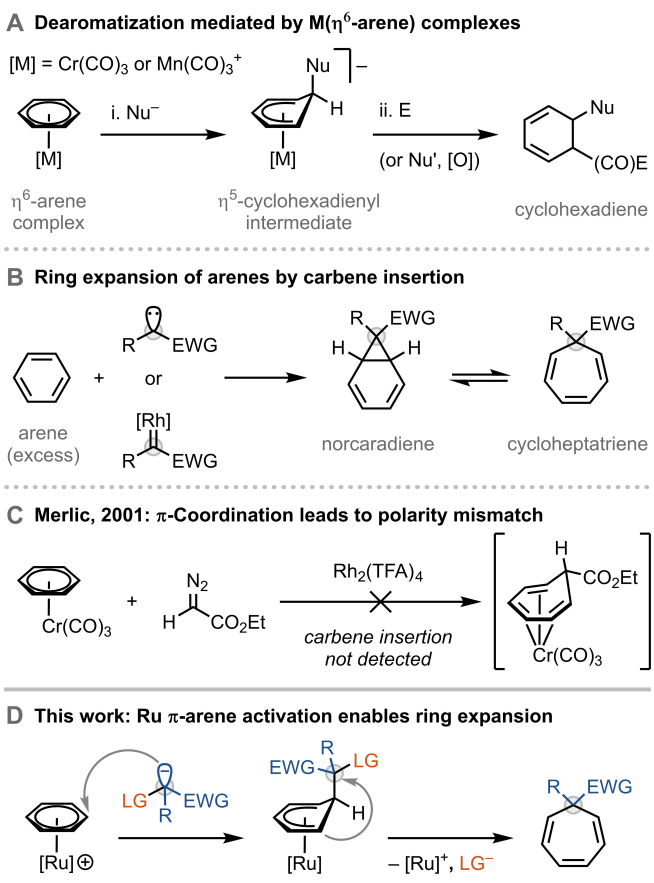
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The abundance and diversity of arenes make them appealing synthetic precursors for chemical transformations. Peripheral modifications that retain the aromatic core are well explored, such as nucleophilic aromatic substitution and cross-coupling, which represent two of the top five reactions used by medicinal chemists.[3,4] Conversely, dearomatization reactions are comparatively limited in their scope and application,[5] despite the utility of the dearomatized products as synthetic intermediates towards complex C(sp^3)-rich frameworks relevant to natural products synthesis and small molecule pharmaceuticals.[6,7] In particular, the larger resonance stabilization of benzenoid rings compared to heteroarenes poses a significant challenge to the development of reactions which disrupt their aromaticity.[5c]

π-Coordination of arenes to transition metals by η^6- or η^2-binding modes has been explored as an approach to stabilize intermediates and products of dearomatization reactions.[1,2] For η^6-arene complexes, ligation to electron-withdrawing metal centers, typically as [$Cr(CO)_3$] or [$Mn(CO)_3$]$^+$ fragments,[1,8] increases the electrophilicity of the arene to facilitate nucleophilic attack (Scheme 1A). The resulting η^5-cyclohexadienyl intermediates undergo reaction with electrophiles, or are oxidized prior to reaction with a second nucleophile,[8b,9] to afford cyclohexadiene products with varying substitution patterns. While these transition metal-mediated reactions provide unrivaled access to valuable, highly functionalized carbocycles from aromatic feedstocks, dearomatization protocols routinely employ organolithium or Grignard reagents, harsh acidic conditions, and strong oxidants such as elemental iodine or nitrosonium cation.[1b,c] Consequently, given that the nucleophiles and electrophiles (or oxidants) would quench one another if present in the same reaction mixture, multistep synthetic sequences are required to access the liberated organic products. Development of single-step procedures is therefore an important target to improve the practicality and thus overall utility of metal-mediated dearomatization reactions by π-arene activation.

A distinct approach to the use of nucleophile-electrophile combinations is to invoke reactive species with ambiphilic character, such as carbenes. A classical example is the Buchner ring expansion involving the reaction of arenes with free carbenes or catalytically generated rhodium carbenes, forming cyclopropanated products (norcaradienes) that undergo valence tautomerism to cycloheptatrienes (Scheme 1B).[10,11] While the Buchner reaction is uniquely capable of directly accessing arene-derived unsaturated carbocycles, a significant drawback is that intermolecular processes currently require large excesses of arene to trap the short-lived carbene intermediate, which limits its application to simple and inexpensive arenes. To date,

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Scheme 1. (A) Prior art for the dearomatization of arenes by π-arene activation. (B) Carbene insertion into arenes, and (C) diminished reactivity with π-complexation. (D) Arene ring expansion by Ru(η6-arene) complexes.

approaches to activate the arene towards carbon group insertion to potentially lower substrate loading have been unsuccessful. For example, it was reported by Merlic that η6-arene coordination by $[Cr(CO)_3]$ deactivates bound arenes towards reaction with rhodium-carbenes due to a philicity mismatch between the electrophilic π-arene ligand and the electrophilic metal-carbene (Scheme 1C).[12] With consideration of Merlic's observation, we envisioned an alternative strategy to exploit π-arene activation by employing a nucleophilic *carbenoid*[13] – a carbon nucleophile bearing an α-leaving group – that would allow for the direct conversion of electrophilic π-arene complexes to ring-expanded cycloheptatrienes (Scheme 1D). Provided that nucleophilic addition to the η6-arene ligand is facile, avoidance of a discrete carbene intermediate circumvents the requirement for large excesses of the arene component as ring expansion results from an intramolecular process within an η5-cyclohexadienyl ligand. Additionally, this distinct mechanistic basis could result in different regioselectivity outcomes compared to established carbene insertions in the case of substituted arenes, opening the possibility to synthesize previously inaccessible isomers of carbon group insertion.

Herein, the realization of this strategy is reported, employing Ru(η6-arene) complexes[14] coordinated by the tripodal hydridotris(pyrazolyl)borate (Tp) ligand with enolates derived from α-halo- or α-(tosyloxy)esters. The current reaction is stoichiometric in ruthenium but demonstrates a fundamentally new reactivity that opens the possibility to promote dearomatization in a single-step procedure with recovery of the ruthenium complex as an adduct with coordinated solvent, at the same oxidation state. Given that the compatibility of all reaction components and maintenance of catalyst fidelity and oxidation state are prerequisites for catalytic turnover,[15] the current study provides a potential blueprint for the development of metal-catalyzed dearomatization reactions.

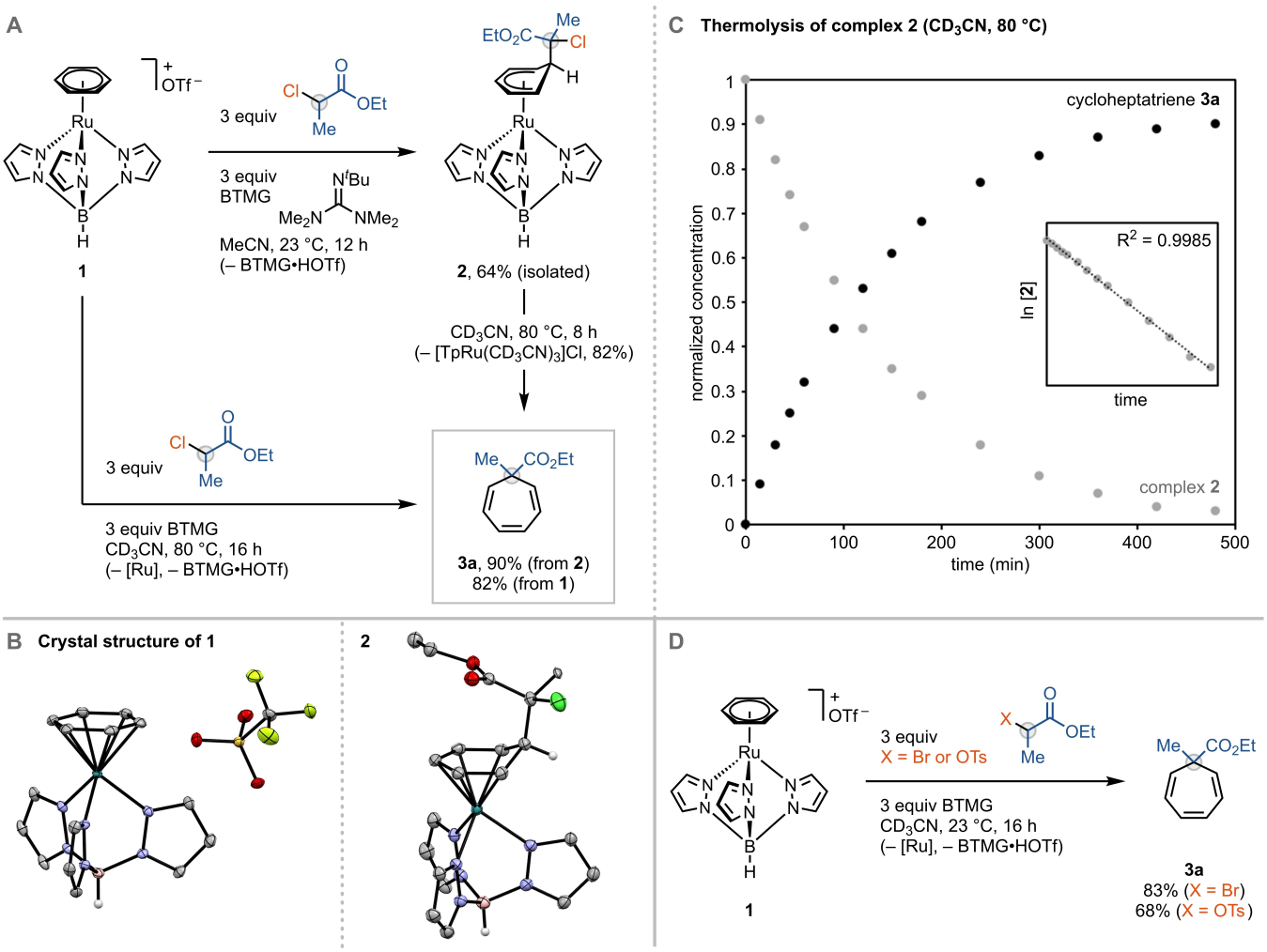
$[(Tp)Ru(\eta^6\text{-}C_6H_6)]OTf$ (**1**)[16,17] was synthesized from commercially available $[(\eta^6\text{-}C_6H_6)RuCl_2]_2$ by reaction with KTp in acetonitrile at 23 °C followed by addition of silver triflate, providing **1** as a yellow solid in 83 % yield. Reaction of complex **1** with ethyl 2-chloropropanoate (3 equivalents) and 2-*tert*-butyl-1,1,3,3-tetramethylguanidine (BTMG, 3 equivalents) in acetonitrile at 23 °C resulted in complete conversion of the cationic starting complex to a neutral η5-cyclohexadienyl-coordinated ruthenium complex **2**, with concomitant elimination of the triflic acid salt of BTMG (Scheme 2A). Nucleophilic addition of the prochiral α-chloroester enolate to the π-coordinated benzene occurs from the *exo* face to generate the cyclohexadienyl ligand, which bears a quaternary carbon stereocenter with chloro, methyl, and ethyl ester substituents and affords the addition product **2** as a racemate. Complex **2** formed quantitatively (> 95 % yield by ^{1}H NMR spectroscopy) and was isolated as a pale-yellow solid in 64 % yield by precipitation at −30 °C from a pentane solution after the reaction. The ^{1}H NMR spectrum of **2** in dichloromethane-d_2 exhibited diagnostic signals for the cyclohexadienyl fragment, including two pairs of diastereotopic C(sp^2)–H signals due to the presence of the α-carbonyl stereocentre. Restricted rotation of the Tp ligand in **2** gave broad pyrazolyl signals at 25 °C[18] that were sharpened by cooling to −40 °C. X-ray diffraction of single crystals of complexes **1** and **2** elucidated their molecular structures (Scheme 2B).[19]

Although complex **2** is stable in the solid state and persistent in solution at ambient temperature, heating **2** in acetonitrile-d_3 at 80 °C generated cycloheptatriene **3a** in high yield (90 % after 8 hours as assessed by ^{1}H NMR spectroscopy) along with formation of the solvent-coordinated ruthenium by-product $[TpRu(CD_3CN)_3]Cl$ (82 % yield).[20,21] Evidently, the cyclohexadienyl anion is sufficiently nucleophilic to promote intramolecular displacement of the tertiary alkyl chloride, leading to a ring expansion process that equates to a formal carbene insertion into benzene. Monitoring the thermolysis by ^{1}H NMR spectroscopy, complex **2** was found to undergo first-order decay, with liberated cycloheptatriene **3a** evolving over the course of the reaction without the accumulation of an intermediate species (Scheme 2C). Further interpretation of the kinetic behavior is made in conjunction with computational analysis (see below).

Conversion of **2** to **3a** did not proceed in benzene-d_6 solvent but did occur in other polar aprotic solvents such as dimethyl sulfoxide-d_6 or nitromethane-d_3 with yields of **3a**

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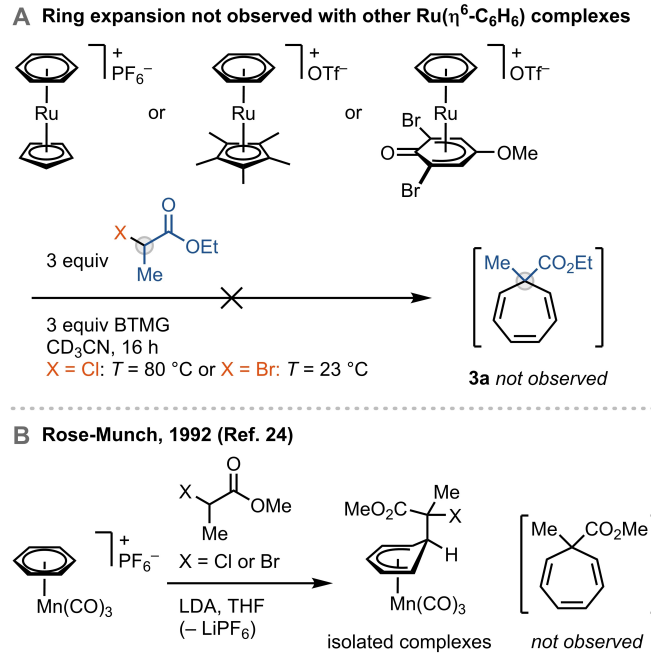
Scheme 2. (A) Ruthenium-mediated ring expansion of benzene. (B) Molecular structures of complexes **1** and **2** with 50% probability ellipsoids.[19] Hydrogen atoms omitted for clarity, except for those bonded to boron or the cyclohexadienyl-C(sp^3) atom. (C) Reaction profile for the thermolysis of complex **2**. (D) Reaction of **1** with α-bromo or α-(tosyloxy) esters. Yields determined by ^{1}H NMR spectroscopy using an internal standard, unless otherwise stated.

of 80% and 55%, respectively. Product **3a** was directly accessed from complex **1** when heating the reaction mixture containing ethyl 2-chloropropanoate and BTMG in acetonitrile-d_3 at 80 °C, resulting in 82% yield of **3a** after 16 hours (Scheme 2A). Replacing BTMG with a weaker organic base, triethylamine, did not result in observed product, whereas other bases with sufficient strength to promote the reaction gave lower yields than BTMG (12–69% **3a** for potassium *tert*-butoxide, 1,1,3,3-tetramethylguanidine, cesium carbonate, phosphazene base P1-t-Bu-tris(tetramethylene), and 1,8-diazabicyclo[5.4.0]undec-7-ene, in order of increasing yield; see the Supporting Information, p. S15). Changing the α-carbonyl leaving group from chloride to more reactive bromide or tosylate groups resulted in the conversion of **1** to **3a** at 23 °C in 83% and 68% yields, respectively (Scheme 2D). Following the reactions by ^{1}H NMR spectroscopy, in the case of a bromide group, the putative Ru(η^5-cyclohexadienyl) intermediate was observed during the conversion of **1** to **3a**, indicating that the rate of bromide displacement by the cyclohexadienyl is comparable to the rate of nucleophilic addition by the enolate. Conversely, for a tosylate group, the Ru(η^5-cyclohexadienyl) intermediate was not observed during the reaction, suggesting that displacement of the leaving group is fast compared to nucleophilic addition.

Control reactions using benzene in place of complex **1** did not result in the formation of cycloheptatriene **3a**. Additionally, commonly employed Ru(η^5-cyclopentadienyl) complexes, [CpRu(η^6-C_6H_6)]PF_6 and [Cp*Ru(η^6-C_6H_6)]OTf, were tested under the reaction conditions and found to give no conversion with either alkyl chloride or bromide coupling partners (Scheme 3A). An η^5-phenoxo supporting ligand, isolobal to Cp, in [(η^5-(2,6-dibromo-4-methoxy-1-phenoxo)-Ru(η^6-C_6H_6)]OTf[22] also did not provide detectable cycloheptatriene. The ability of the Tp supporting ligand to promote dearomatization is, in part, attributed to the greater electrophilicity of the π-coordinated benzene in complex **1** compared to complexes with more electron-donating Cp

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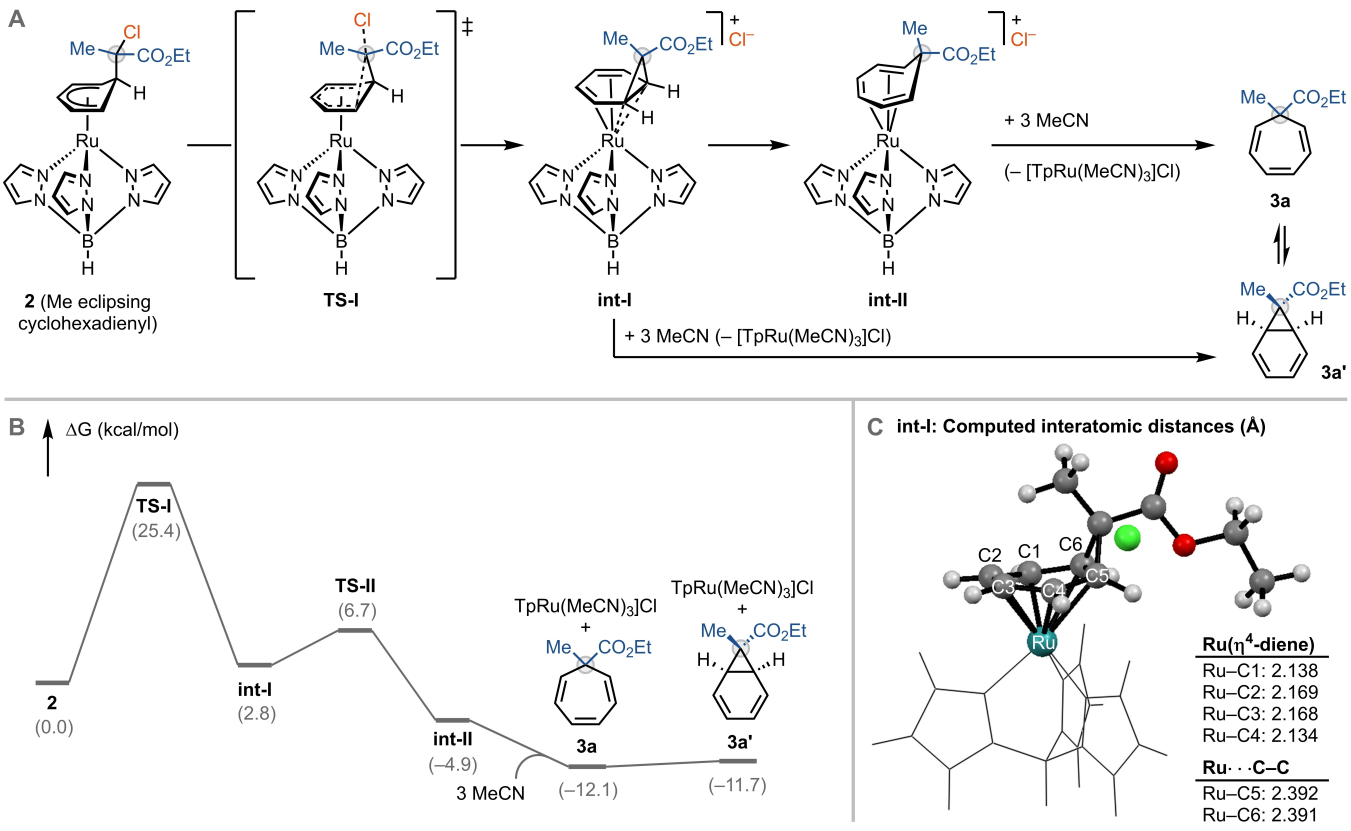
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Scheme 3. (A) No reaction with Cp or η^5-phenoxo Ru complexes. (B) Previously reported addition of α-halo ester enolates to $[(\eta^6\text{-}C_6H_6)Mn(CO)_3]PF_6$.[24]

ligands,[23] which enables nucleophilic addition of the highly substituted ester enolate. While further studies are required to understand ligand effects in the subsequent leaving group displacement, it is posited that the cationic ruthenium center must not be overly electron-withdrawing as the η^5-cyclohexadienyl ligand must retain nucleophilic character. To the best of our knowledge, transformation of a π-coordinated arene to a cycloheptatriene via an η^5-cyclohexadienyl intermediate is unprecedented in transition metal chemistry. In a related reaction, Rose-Munch previously reported the synthesis of $(\eta^5$-cyclohexadienyl$)Mn(CO)_3$ complexes derived from the addition of lithium enolates of α-chloro and α-bromo esters to $[(\eta^6\text{-}C_6H_6)Mn(CO)_3]PF_6$.[24] However, the isolated complexes from nucleophilic addition were not observed to undergo ring expansion to form a cycloheptatriene (Scheme 3B).

The reaction profile for the transformation of complex **2** to cycloheptatriene **3a** was computed using ORCA[25] at the DLPNO-CCSD(T1)//PBE0-D3 level of theory (Scheme 4). In complex **2**, the quaternary stereogenic carbon can adopt two possible reactive conformations wherein the C–Cl bond is primed to undergo backside attack by the cyclohexadienyl anion, either with a methyl substituent eclipsing the cyclohexadienyl ligand (as drawn in Scheme 4A) or an eclipsing ester substituent (as in the crystal structure of **2**). Pathways for intramolecular chloride displacement via both conformers of **2** were calculated,[26] and it was found that the



Scheme 4. (A) Computed pathways for the transformation of **2** to **3a**, and (B) associated Gibbs free energy profile. (C) Computed interatomic distances (Å) between the norcaradiene ligand and ruthenium center in **int–I**. ORCA at the DLPNO-CCSD(T1)//PBE0-D3 level of theory was used.

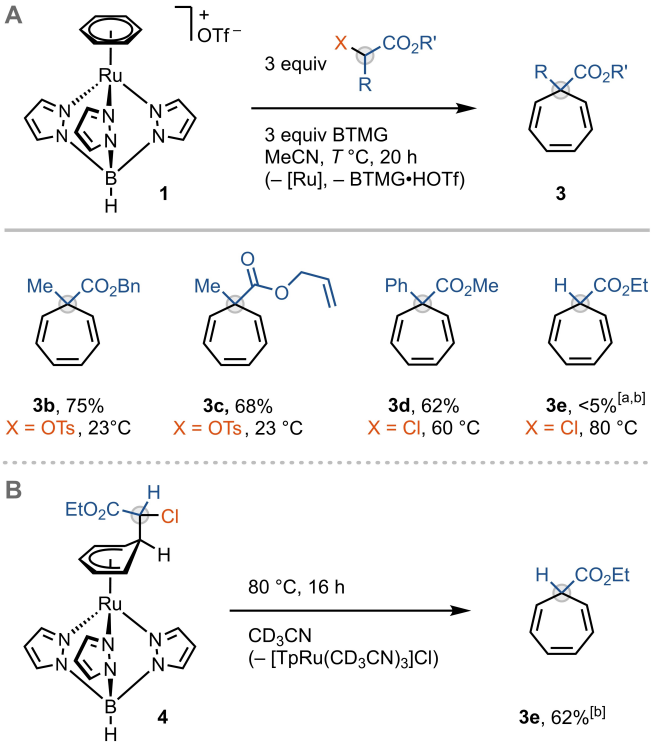
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kinetically and thermodynamically favored pathway occurs from the conformer with the eclipsing methyl group, resulting in an intermediate complex bearing a ruthenium-bound norcaradiene with *endo*-Me and *exo*-ester substituents (**int–I**). The activation free energy for chloride displacement (**TS–I**, 25.4 kcal/mol) is consistent with the experimental observation that **3a** is formed at 80 °C but not at 23 °C. Within **int–I**, the strained bridging C–C bond of the cyclopropane readily cleaves, giving a Ru(η^6-cycloheptatriene) complex (**int–II**; via **TS–II**, +3.9 kcal/mol relative to **int–I**). Replacement of either the norcaradiene or cycloheptatriene ligand by acetonitrile is exergonic (−14.5 and −7.2 kcal/mol, respectively), which liberates the organic product as equilibrating norcaradiene (**3a'**)[27] and cycloheptatriene (**3a**) forms. The lower calculated Gibbs free energy of **3a** relative to **3a'** (0.4 kcal/mol free energy difference) is in agreement with experimental low-temperature NMR studies showing that the equilibrium is shifted towards the cycloheptatriene form for compounds with geminal ester and alkyl substituents.[28] Based on the computed reaction pathway, the experimentally determined first-order decay for the thermolysis of **2** relates to a rate-limiting intramolecular chloride ion displacement step (computed **TS–I**). The lack of experimental observation of a ruthenium-bound cycloheptatriene intermediate (computed **int–II**) during the course of reaction is consistent with facile ligand substitution by acetonitrile solvent.

The geometry and electronic structure of **int–I** deserves further attention, as the bridging C–C bond of the norcaradiene ligand lies close to the Ru center, with Ru–C distances of only 2.391 and 2.392 Å, which are not significantly longer than the other four Ru–C bonds (average 2.152 Å, Scheme 4C). A natural bonding orbital (NBO) calculation indicates that the bridging σ(C–C) orbital is significantly bent towards the ruthenium center.[29] Second order perturbative estimates find a 44.1 kcal/mol energy contribution of the σ(C–C)→d(Ru) donation, which is smaller than those of the two π(C–C)→d(Ru) donations (224.3 and 225.5 kcal/mol, respectively) from the diene moiety of the bound norcaradiene. Therefore, **int–I** can be viewed as an η^4 complex with a σ(C–C)→d(Ru) agostic interaction.[30] Despite formally being a 16-electron complex, the ruthenium center of **int–I** was found *in silico* not to readily recombine with the chloride counteranion, which reflects a preference to maintain the C–C agostic interaction as part of a cationic complex rather than form a neutral complex containing a Ru–Cl bond.

To access a series of cycloheptatrienes by the ring expansion of π-coordinated benzene, the coupling partner was varied with different substituents (Scheme 5A). Whereas α-halo or α-(tosyloxy)esters promoted dearomatization in good yields, α-halo or α-(tosyloxy)nitriles gave low yields (0–40 % assay yields), and 1,3-dicarbonyl or amide-containing reagents did not promote ring expansion.[31] Reacting complex **1** with alkyl tosylate reagents containing benzyl or allyl ester groups provided cyclopheptatrienes **3b** and **3c** in 75 % and 68 % isolated yield, respectively, after 16 hours at 23 °C. A benzylic chloride was also competent in the reaction upon heating to 60 °C, providing phenyl-substituted



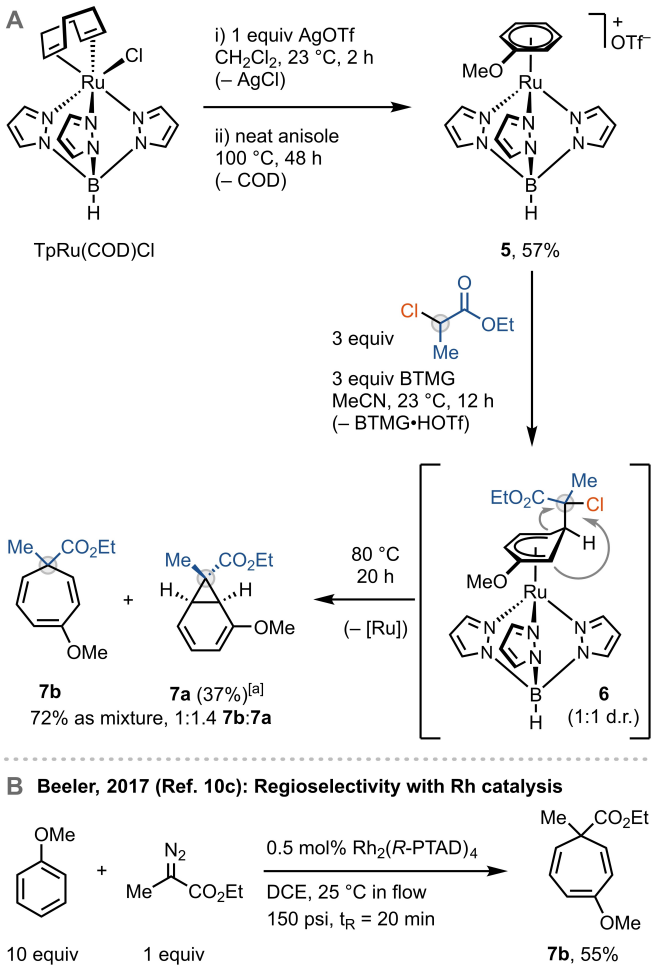
Scheme 5. (A) Variation of the ester coupling partner. (B) Thermolysis of ethyl 2-chloroacetate-derived complex **4**. Yields are of isolated products. [a] 6 equiv ethyl 2-chloroacetate used. [b] Yield determined by ^{1}H NMR spectroscopy using an internal standard.

product **3d** in 62 % yield. On the other hand, ethyl 2-chloroacetate, a reagent containing two enolizable protons, did not generate the corresponding cycloheptatriene **3e** (< 5 % yield after 16 hours at 80 °C). Analysis by ^{1}H NMR spectroscopy showed full conversion of complex **1** to a new organometallic complex formed in 70 % yield. It was deduced that, under the basic reaction conditions, the remaining enolizable proton in the product **3e** led to deprotonation and ligation to the ruthenium center, forming a cycloheptatrienyl-ligated ruthenium complex that was observed by high-resolution mass spectrometry.[32,33] Accordingly, to promote dearomatization in the absence of exogenous base, the Ru(η^5-cyclohexadienyl) intermediate derived from ethyl 2-chloroacetate (complex **4**) was synthesized, analogously to complex **2**. Thermolysis of **4** in acetonitrile-d_3 at 80 °C led to the formation of cycloheptatriene **3e** in 62 % yield, demonstrating the possibility to access the ring-expanded product using base-free conditions (Scheme 5B).

The regioselectivity of the dearomatization was investigated by targeting a ruthenium complex bearing a substituted arene. [TpRu(η^6-anisole)]OTf (**5**) was synthesized from TpRu(COD)Cl[34] by reaction with silver triflate followed by heating in neat anisole at 100 °C for 2 days (Scheme 6A). Complex **5** was isolated as a yellow solid in 57 % yield. Reaction of **5** with ethyl 2-chloropropanoate and BTMG in acetonitrile at 80 °C for 20 hours led to the formation of a 1.4:1 mixture of dearomatized products,

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Scheme 6. (A) Synthesis of [TpRu(η⁶-anisole)]OTf (**5**) and its reaction with ethyl 2-chloropropanoate. Yields are of isolated products. [a] Separation of **7a** by preparative thin-layer chromatography. Relative stereochemistry assigned by NMR spectroscopy at −40 °C. (B) Previously reported rhodium-carbene insertion into anisole.[10c] *R*-PTAD = (*R*)-(−)-(1-adamantyl)-(*N*-phthalimido)acetato; t_R = residence time.

norcaradiene **7a** (major) and cycloheptratriene **7b** (minor), in a combined yield of 72 % after chromatographic removal of the by-products and excess reagents. While both isomeric products are the result of carbon group insertion, it is established that the norcaradiene-cycloheptatriene equilibrium lies in favour of the norcaradiene when a substituent is vicinal to the cyclopropane, as in the case of **7a**.[11b] Norcaradiene **7a** was isolated as a pure compound by preparative thin-layer chromatography in 37 % yield. The minor constitutional isomer **7b** is the exclusive product of previously reported rhodium-catalyzed carbene insertion into anisole using an α-diazocarbonyl reagent (Scheme 6B),[10c,35] highlighting the utility of π-arene activation as a complementary synthetic approach to access alternative regioisomers through dearomatization. It is noted that attempts to synthesize a Ru(η⁶-arene) complex bearing an electron deficient arene were unsuccessful.[36]

To gain further insight, the reaction between complex **5** and ethyl 2-chloropropanoate was conducted in acetonitrile-d_3 at 23 °C. After 12 hours, full conversion of **5** to Ru(η⁵-cyclohexadienyl) intermediate **6** was observed (94 % yield by ^{1}H NMR spectroscopy, Scheme 6A). Inspection of the ^{1}H NMR spectrum of the reaction mixture revealed the formation of a single constitutional isomer from nucleophilic addition, wherein the ester enolate had selectively attacked the *meta* position. A 1:1 mixture of diastereomers of **6** formed as a consequence of the α-carbonyl stereocentre and planar chirality of the η⁵-cyclohexadienyl ligand.[37] On the basis of observing intermediate **6**, isomers **7a** and **7b** can thus be rationalized as the result of competing attack of the α-chloroester moiety in **6** by the 2- and 4-positions (relative to the methoxy group) of the cyclohexadienyl anion.

In conclusion, a dearomative ring expansion of arenes by ruthenium-mediated π-arene activation was discovered. The use of enolates derived from α-halo or α-(tosyloxy)esters enabled the nucleophilic attack, dearomatization, and liberation of the carbocyclic product under mild conditions with the formation of a defined solvent-coordinated ruthenium by-product. The departure from multistep dearomatization protocols that sequentially add nucleophiles, electrophiles, and oxidants to the reaction mixture lays the groundwork for expanding the scope and practicality of dearomatization reactions by π-arene complexes. Development of a catalytic dearomatization process is ongoing in our laboratory. Here, the outstanding challenge relates to the displacement of the dearomatized product from the ruthenium center by a molecule of arene substrate, rather than coordinating solvent, to reform the Ru(η⁶-arene) complex. Combined with the lessons learned in the effect of supporting ligands in the arene exchange kinetics of Ru(η⁶-arene) complexes,[22] guiding principles for the design of novel ruthenium complexes capable of catalytic dearomatization via π-arene activation have been established.

Supporting Information

Experimental and computational procedures, spectroscopic data, and NMR spectra of products are contained in the Supporting Information. Additional references are cited within the Supporting Information.[38,39]

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Conflict of Interest

The authors declare no conflict of interest.

Data Availability Statement

The data that support the findings of this study are available in the supplementary material of this article.

Keywords: dearomatization · ruthenium · π-arene

[1] a) M. F. Semmelhack, *Pure & App. Chem.* **1981**, *53*, 2379; b) A. R. Pape, K. P. Kaliappan, E. P. Kündig, *Chem. Rev.* **2000**, *100*, 2917; c) E. P. Kündig, A. Pape, *Topics Organomet. Chem.* **2004**, *7*, 71; d) L. J. Williams, Y. Bhonoah, L. A. Wilkinson, J. W. Walton, *Chem. Eur. J.* **2021**, *27*, 3650.

[2] a) W. D. Harman, *Topics Organomet. Chem.* **2004**, *7*, 95; b) F. Ding, W. D. Harman, *J. Am. Chem. Soc.* **2004**, *126*, 13752; c) B. K. Liebov, W. D. Harman, *Chem. Rev.* **2017**, *117*, 13721.

[3] a) F. Terrier, *Modern Nucleophilic Aromatic Substitution* VCH, Weinheim, **2013**; b) J. F. Bunnett, R. E. Zahler, *Chem. Rev.* **1951**, *49*, 273; c) D. G. Brown, J. Boström, *J. Med. Chem.* **2016**, *59*, 4443; d) *Arene Chemistry: Reaction Mechanisms and Methods for Aromatic Compounds* (Ed: J. Mortier), *Wiley*, Hoboken, **2016**, 131–298.

[4] a) C. Binnani, S. Kumar Singh, *Handbook of CH-Functionalization* (Ed.: D. Maiti), *Wiley-VCH*, **2023**, DOI: 10.1002/9783527834242.chf0039; b) J. F. Hartwig, *J. Am. Chem. Soc.* **2016**, *138*, 2; c) D. Kalyani, E. E. Marlier *Arene Chemistry: Reaction Mechanisms and Methods for Aromatic Compounds* (Ed: J. Mortier), *Wiley*, Hoboken, **2016**, pp. 675–713.

[5] a) C. Zheng, S.-L. You, *ACS Cent. Sci.* **2021**, *7*, 432; b) F. C. Pigge, *Arene Chemistry: Reaction Mechanisms and Methods for Aromatic Compounds* (Ed: J. Mortier), *Wiley*, Hoboken, **2016**, 399–423; c) W. C. Wertjes, E. H. Southgate, D. Sarlah, *Chem. Soc. Rev.* **2018**, *47*, 7996; d) C. J. Huck, D. Sarlah, *Chem* **2020**, *6*, 1589.

[6] a) L. N. Mander, *Synlett* **1991**, *1991*, 134; b) S. P. Roche, J. A. Porco Jr, *Angew. Chem. Int. Ed.* **2011**, *50*, 4068; c) C. J. Huck, Y. D. Boyko, D. Sarlah, *Nat. Prod. Rep.* **2022**, *39*, 2231.

[7] a) F. Lovering, J. Bikker, C. Humblet, *J. Med. Chem.* **2009**, *52*, 6752; b) F. Lovering, *MedChemComm* **2013**, *4*, 515.

[8] a) M. F. Semmelhack, J. J. Harrison, Y. Thebtaranonth, *J. Org. Chem.* **1979**, *44*, 3275; b) Y. K. Chung, H. S. Choi, D. A. Sweigart, *J. Am. Chem. Soc.* **1982**, *104*, 4245; c) F. Rose-Munch, V. Gagliardini, C. Renard, E. Rose, *Coord. Chem. Rev.* **1998**, *178–180*, 249; d) M. Rosillo, G. Domínguez, J. Pérez-Castells, *Chem. Soc. Rev.* **2007**, *36*, 1589; e) D. I. Bezuidenhout, B. van der Westhuizen, N. A. van Jaarsveld, S. Lotz, *J. Inorg. Organomet. Polym.* **2014**, *24*, 39.

[9] M.-Y. Wang, W.-L. Zeng, L. Chen, Y.-F. Yuan, W. Li, *Angew. Chem. Int. Ed.* **2024**, *63*, e202403917.

[10] a) T. Ye, A. McKervey, *Chem. Rev.* **1994**, *94*, 1091; b) S. E. Reisman, R. R. Nani, S. Levin, *Synlett* **2011**, *17*, 2437; c) G. S. Fleming, A. B. Beeler, *Org. Lett.* **2017**, *19*, 5268; d) Y. Guo, T. V. Nguyen, R. M. Koenigs, *Org. Lett.* **2019**, *21*, 8814; e) K. L. Smith, C. L. Padgett, W. D. Mackay, J. S. Johnson, *J. Am. Chem. Soc.* **2020**, *142*, 6449.

[11] a) G. Maier, *Angew. Chem. Int. Ed.* **1967**, *6*, 402; b) O. A. McNamara, A. R. Maguire, *Tetrahedron* **2011**, *67*, 9.

[12] C. A. Merlic, A. L. Zechman, M. M. Miller, *J. Am. Chem. Soc.* **2001**, *123*, 11101.

[13] A. Caballero, P. J. Pérez, *Chem. Eur. J.* **2017**, *23*, 14389.

[14] a) F. C. Pigge, J. J. Coniglio, *Curr. Org. Chem.* **2001**, *5*, 757; b) F. C. Pigge, J. J. Coniglio, R. Dalvi, *J. Am. Chem. Soc.* **2006**, *128*, 3498; c) F. C. Pigge, R. Dhanya, E. R. Hoefgen, *Angew. Chem. Int. Ed.* **2007**, *46*, 2887.

[15] a) S. Takemoto, H. Matsuzaka, *Tetrahedron Lett.* **2018**, *59*, 697; b) K. Chen, H. Shi, *Acc. Chem. Res.* **2024**, *57*, 2194.

[16] Synthesis of $[TpRu(\eta^6\text{-}C_6H_6)]PF_6$ previously reported: S. Bhambri, D. A. Tocher, *Polyhedron* **1996**, *15*, 2763.

[17] C. Slugovc, R. Schmid, K. Kirchner, *Coord. Chem. Rev.* **1999**, *185*(186), 109.

[18] S. Bhambri, A. Bishop, N. Kaltsoyannis, D. A. Tocher, *J. Chem. Soc. Dalton Trans.* **1998**, 3379.

[19] Deposition numbers 2379857 (for **1**) and 2379856 (for **2**) contain the supplementary crystallographic data for this paper. These data are provided free of charge by the joint Cambridge Crystallographic Data Centre and Fachinformationszentrum Karlsruhe Access Structures service.

[20] Synthesis of $[TpRu(MeCN)_3]PF_6$ previously reported: E. Rüba, W. Simanko, K. Mereiter, R. Schmid, K. Kirchner, *Inorg. Chem.* **2000**, *39*, 382.

[21] The identity of the ruthenium by-product was verified by conducting the thermolysis of **2** in protiated acetonitrile solvent and isolating $[TpRu(MeCN)_3]Cl$, with characterization by NMR spectroscopy and HRMS (Supporting Information, p. S13).

[22] T. Schulte, Z. Wang, C.-C. Li, A. Hamad, F. Waldbach, J. Pampel, R. Petzold, M. Leutzsch, F. Bahns, T. Ritter, *J. Am. Chem. Soc.* **2024**, *146*, 15825.

[23] a) D. M. Tellers, R. G. Bergman, *Organometallics* **2001**, *20*, 4819; b) T. J. Brunker, A. R. Cowley, D. O'Hare, *Organometallics* **2002**, *21*, 3123.

[24] F. Balssa, K. Aniss, F. Rose Munch, *Tetrahedron Lett.* **1992**, *33*, 1901.

[25] F. Neese, *WIREs Comput. Mol. Sci.* **2022**, *12*, e1606.

[26] Details of the calculated pathway for the reaction of **2** to **3a** via the alternative conformer of **2** (ester eclipsing cyclohexadienyl) are disclosed in the Supporting Information, p. S42.

[27] The alternative diastereomer of **3a'** having *endo*-ester and *exo*-methyl substituents on the cyclopropane was calculated to be higher in Gibbs free energy by 5.7 kcal/mol. See the Supporting Information, p. S42.

[28] a) F.-G. Klärner, S. Yaslak, M. Wette, *Chem. Ber.* **1977**, *110*, 107; b) H. Tsuruta, S. Mori, T. Mukai, *Chem. Lett.* **1974**, 1127.

[29] Visualizations of the calculated NBOs are found in the Supporting Information, p. S44.

[30] a) M. Etienne, A. S. Weller, *Chem. Soc. Rev.* **2014**, *43*, 242; b) B. G. Harvey, R. D. Ernst, *Eur. J. Inorg. Chem.* **2017**, 1205.

[31] Reaction of **1** with other coupling partners that led to low or zero yield of dearomatization products are reported in the Supporting Information, p. S36.

[32] M. L. H. Green, D. K. P. Ng, *Chem. Rev.* **1995**, *95*, 439.

[33] Reaction of **1** with ethyl 2-chloroacetate using 1 equivalent of BTMG generated **3e** in 42 % yield.

[34] a) C. Gemel, G. Trimmel, C. Slugovc, S. Kremel, K. Mereiter, R. Schmid, K. Kirchner, *Organometallics* **1996**, *15*, 3998; b) M. Jiménez-Tenorio, M. C. Puerta, P. Valerga, *Organometallics* **2015**, *34*, 1001.

[35] a) E. T. Crawford, K. L. Smith, J. S. Johnson, *Org. Lett.* **2022**, *24*, 1791; b) A. J. Anciaux, A. Demonceau, A. J. Hubert, A. F. Noels, N. Petiniot, P. Teyssié, *J. Chem. Soc. Chem. Commun.* **1980**, 765.

[36] An attempt to synthesize $[TpRu(\eta^6\text{-ethyl benzoate})]OTf$ from $[(\eta^6\text{-ethyl benzoate})RuCl_2]_2$ was unsuccessful. See the Supporting Information, p. S36. Alternative synthetic routes remain as part of ongoing investigations.

[37] F. Rose-Munch, E. Rose, *Org. Biomol. Chem.* **2011**, *9*, 4725.

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15213757, 2025, 6, Downloaded from https://onlinelibrary.wiley.com/doi/10.1002/ange.202421608 by Universitatsbibliothek RWTH Aachen University, Wiley Online Library on [03/07/2026]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

[38] Additional references from the Supporting Information for the synthesis or characterization data of reported compounds: a) B. M. Trost, C. M. Older, *Organometallics* **2002**, *21*, 2544; b) P. J. Fagan, M. D. Ward, J. C. Calabrese, *J. Am. Chem. Soc.* **1989**, *111*, 1698; c) D. Q. Tan, A. Younai, O. Pattawong, J. C. Fettinger, P. H.-Y. Cheong, J. T. Shaw, *Org. Lett.* **2013**, *15*, 5126; d) E. E. Galenko, V. A. Bodunov, M. A. Kryukova, M. S. Novikov, A. F. Khlebnikov, *J. Org. Chem.* **2021**, *86*, 4098.

[39] Additional computational references from the SI: a) C. Adamo, V. Barone, *J. Chem. Phys.* **1999**, *110*, 6158; b) S. Grimme, J. Antony, S. Ehrlich, H. Krieg, *J. Chem. Phys.* **2010**, *132*, 154104; c) S. Grimme, S. Ehrlich, L. Goerigk, *J. Comput. Chem.* **2011**, *32*, 1456; d) P. Pollak, F. Weigend, *J. Chem. Theory Comput.* **2017**, *13*, 3696; e) J. Zheng, X. Xu, D. G. Truhlar, *Theor. Chem. Acc.* **2011**, *128*, 295; f) F. Weigend, R. Ahlrichs, *Phys. Chem. Chem. Phys.* **2005**, *7*, 3297; g) Z. Li, Y. Xiao, W. Liu, *J. Chem. Phys.* **2014**, *141*, 054111; h) W. Liu, D. Peng, *J. Chem. Phys.* **2009**, *131*, 031104; i) Z. Li, Y. Xiao, W. Liu, *J. Chem. Phys.* **2012**, *137*, 154114; j) W. Kutzelnigg, W. Liu, *J. Chem. Phys.* **2005**, *123*, 241102; k) V. Barone, M. Cossi, *J. Phys. Chem. A* **1998**, *102*, 1995; l) M. Garcia-Ratés, F. Neese, *J. Comput. Chem.* **2020**, *41*, 922; m) Y. Guo, C. Riplinger, U. Becker, D. G. Liakos, Y. Minenkov, L. Cavallo, F. Neese, *J. Chem. Phys.* **2018**, *148*, 011101; n) C. Riplinger, B. Sandhoefer, A. Hansen, F. Neese, *J. Chem. Phys.* **2013**, *139*, 134101; o) C. Riplinger, P. Pinski, U. Becker, E. F. Valeev, F. Neese, *J. Chem. Phys.* **2016**, *144*, 024109; p) A. V. Marenich, C. J. Cramer, D. G. Truhlar, *J. Phys. Chem. B* **2009**, *113*, 6378; q) F. Neese, F. Wennmohs, A. Hansen, U. Becker, *Chem. Phys.* **2009**, *356*, 98; r) R. Izsák, F. Neese, *J. Chem. Phys.* **2011**, *135*, 144105; s) R. Izsák, F. Neese, W. Klopper, *J. Chem. Phys.* **2013**, *139*, 094111; t) B. Helmich-Paris, B. de Souza, F. Neese, R. Izsák, *J. Chem. Phys.* **2021**, *155*, 104109; u) P. Pollak, F. Weigend, *J. Chem. Theory Comput.* **2017**, *13*, 3696; v) Y. J. Franzke, R. Treß, T. M. Pazdera, F. Weigend, *Phys. Chem. Chem. Phys.* **2019**, *21*, 16658; w) C. Bannwarth, S. Ehlert, S. Grimme, *J. Chem. Theory Comput.* **2019**, *15*, 1652.

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