Activation and Functionalization of C–C σ-Bonds of Alkylidene Cyclopropanes at Main Group Centers

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Supporting Information Placeholder

ABSTRACT: Aluminum(I) and magnesium(I) compounds are reported for the C–C σ-bond activation of strained alkylidene cyclopropanes. These reactions result in the formal addition of the C–C σ-bond to main group center either at a single site (Al) or across a metal–metal bond (Mg–Mg). Mechanistic studies suggest that rather than occurring by a concerted oxidative addition, these reactions involve stepwise processes in which substrate binding to the main group metal acts as a precursor to α- or β-alkyl migration steps that break the C–C σ-bond. This mechanistic understanding is used to develop the magnesium-catalyzed hydrosilylation of the C–C σ-bonds of alkylidene cyclopropanes.

Reactions that break the strong C–C σ-bonds of hydrocarbons are essential for processing crude oil. The petrochemical industry relies on catalysis to crack long-chain hydrocarbons into shorter and more valuable building blocks. This transformation is challenging: C–C σ-bonds of hydrocarbons are strong, sterically congested, and surrounded by C–H bonds - which are often the first site to react. Common pathways for C–C σ-bond activation with transition metal complexes include oxidative addition[1] and β-alkyl elimination.[2] These two fundamental steps underpin numerous applications which involve the transition metal catalysed functionalization of C–C σ-bonds(Figure 1).[3–5]

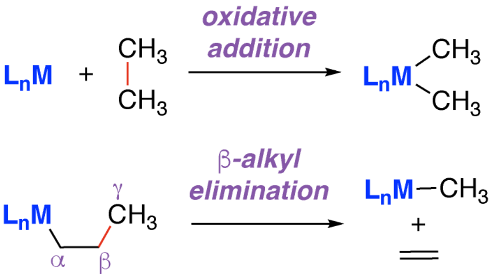
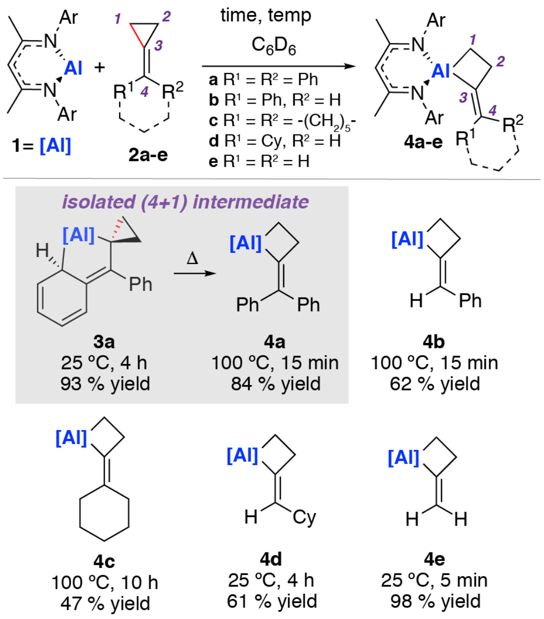


Figure 1. C–C σ-bond activation with transition metals.[6]

Examples of C–C σ-bond activation by main-group compounds are limited in comparison to transition metal complexes. For example, stoichiometric C–C σ-bond activation by β-alkyl elimination has been observed during the thermolysis of *tris*-neopentylaluminium at 200°C.[7] Low-valent main-group compounds including silylenes,[8] a phosphirene,[9] and an alumanyl anion[10] are known to insert into a C–C bond of benzene rings. While this reactivity could be described by a formal oxidative addition process, more precisely it involves a Büchner ring-expansion. The oxidative addition of the cyclobutene C–C σ-bond in biphenylene has also recently been observed at an anionic cyclic-alkylamino alumanyl complex.[11] Although these examples are yet to translate into new catalytic methods, Lewis acid catalysis has been applied to the functionalization of cyclopropanes through ring-opening reactions that break a C–C σ-bond.[12–14]

Herein we report C(sp^2)–C(sp^3) σ-bond activation within the coordination sphere of well-defined aluminium and magnesium compounds. A combination of DFT and experimental data show that while a redox reaction is involved in the formation of intermediates, the key C–C bond breaking step starts formally from an aluminum(III) or magnesium(II) species. α-Alkyl and β-alkyl migration mechanisms are in operation. The redox-neutral nature of the C–C σ-bond activation is leveraged to develop the first example of catalytic C–C σ-bond functionalization using magnesium-based catalysis.

Reaction of the aluminium(I) complex **1**[15,16] with the unsaturated cyclopropane **2a** at 25°C in C_6D_6 initially resulted in the formation of **3a** over the course of 4 hours (Scheme 1). This product is the result of a (4+1) cycloaddition.[17] Heating either crude or isolated samples of **3a** at 100°C in C_6D_6 for 15 minutes results in the formation of **4a**, a metallocyclobutane derived from C–C σ-bond activation. The reaction also proceeds slowly at 25°C over the course of several days. The relief of the ring strain and rearomatization provide a significant thermodynamic driving force this reaction. **3a** and **4a** have been characterized by single-crystal X-ray diffraction (Figure 2a). The reaction scope can be expanded to **2b-e**. The range of substrates demonstrates that aromatic substitution is not essential for C–C σ-bond activation, as alkyl-substituted substrates **2c** and **2d** react with **1** as does the parent methylidene cyclopropane **2e**. For trisubstituted alkenes **2b,d** a single stereoisomer of the product was observed. For **2c**, allylic C–H activation accompanies ring-opening.[18]



Scheme 1. Reaction of alkylidene cyclopropanes with **1**.

Kinetics measurements and DFT calculations were undertaken to better understand the key C–C σ-bond activation step. The transformation of **3a** → **4a** was found to be first-order with respect to **3a**. Eyring analysis over a 45-70°C range gave activation parameters: $\Delta H^{\ddagger} = 22.3 \pm 0.4$ kcal mol^{-1} and $\Delta S^{\ddagger} = 28.9 \pm 5.5$ cal K^{-1} mol^{-1}. The negative entropy of activation is consistent with an ordered transition state. The Gibbs activation energy is $\Delta G^{\ddagger}_{298K} = 24.4 \pm 2.1$ kcal mol^{-1}. The initial formation of the (4+1) cycloaddition intermediate **3a** was calculated to occur *via* a concerted pericyclic transition state, **TS-1**. The modest energy barrier of **TS-1**, $\Delta G^{\ddagger}_{298K} = 14.1$ kcal mol^{-1}, is consistent with the observation that formation of **3a** occurs at 25°C and is not the rate-determining step of the C–C σ-bond activation sequence. From the (4+1) cycloaddition intermediate **3a**, **TS-2** was located ($\Delta G^{\ddagger}_{298K} = 25.8$ kcal mol^{-1}) and connects directly to the product **4a**. This key step breaks the C–C σ-bond and involves an α-migration mechanism (Figure 2b). While substrates **2a-b** may both proceed through an intermediate derived from a (4+1) cycloaddition, this pathway is inaccessible for **2c-e**. Further calculations on the reaction of **1** with **2e** support the notation that a closely related reaction sequence involving a (2+1) cycloaddition and α-migration becomes accessible (supporting information). The direct oxidative addition of a C–C σ-bonds of strained three-membered rings to **1** was also considered.[19] A transition state that directly connects **1** and **2e** with **4e**, corresponding to an oxidative addition pathway, was found to be significantly higher in energy than the corresponding α-migration pathway ($\Delta G^{\ddagger}_{298K} = 35.3$ kcal mol^{-1}). Experimentally, **1** does not react with cyclopropylbenzene to form metallocyclobutane products even when heated at 100°C for one week in C_6D_6.

Curious as to whether the C–C σ-bond activation chemistry could be expanded to alternative main group reagents, we investigated the reaction of the magnesium(I) complex **6**[20–23] with alkylidene cyclopropanes. Addition of **6** to **2a** and **2b** resulted in the ring-opened 1,3-dimagnesio-3-butene products **7a** and **7b** after heating for 4h at 100°C and 1h at 25°C respectively (Figure 3a). No reaction is observed with either alkyl-substituted substrates **2c** or **2d**. Crystallization and isolation was amenable through the preparation of their DMAP (4-dimethylaminopyridine) adducts **7a•DMAP₂** and **7b•DMAP₂** (Figure 3b). **7b•DMAP₂** forms as a single stereoisomer. The mechanism for C–C σ-bond activation with **6** was again investigated using DFT calculations. Based on literature precedent and by analogy to the aluminum reagent **1**, it is highly likely that this reaction is initiated by the 1,2-addition of the Mg–Mg bond of **6** across the alkene to form a 1,2-dimagnesioethane intermediate.[24,25] In line with these expectations, **Int-1** was identified as an intermediate ($\Delta G^{\circ}_{298K} = -12.7$ kcal mol^{-1}) by computational methods. From **Int-1**, C–C σ-bond activation occurs by β-alkyl migration via **TS-3** to form **7a** ($\Delta G^{\ddagger}_{298K} = 12.7$ kcal mol^{-1}, Figure 3c).

The discrepancy between experimentally observed reaction conditions (4 h at 100°C) and calculated barriers ($\Delta G^{\ddagger}_{298K} = 12.7$ kcal mol^{-1}) suggest that in this case, breaking of the C–C bond is not rate limiting. While a transition state towards the formation of the 1,2-dimagnesioethane intermediate could not be located, the reaction proved sensitive to the steric demands of the magnesium reagent and did not proceed with bulkier analogues of **6**.

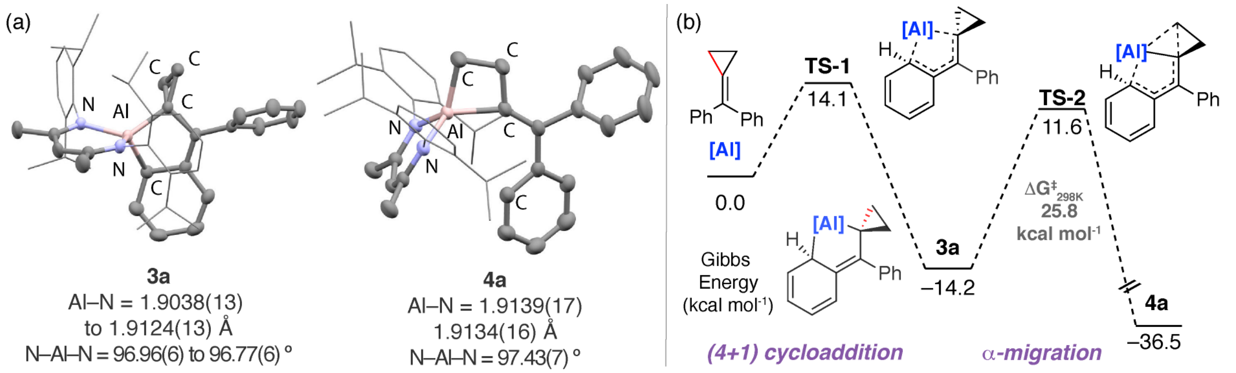


Figure 2. (a) Structures from single crystal Xray diffraction experiments on **3a** and **4a**. (b) DFT calculated pathway for C–C σ-bond activation *via* a (4+1) intermediate (for the analogous pathway via a (2+1) intermediate see the supporting information).

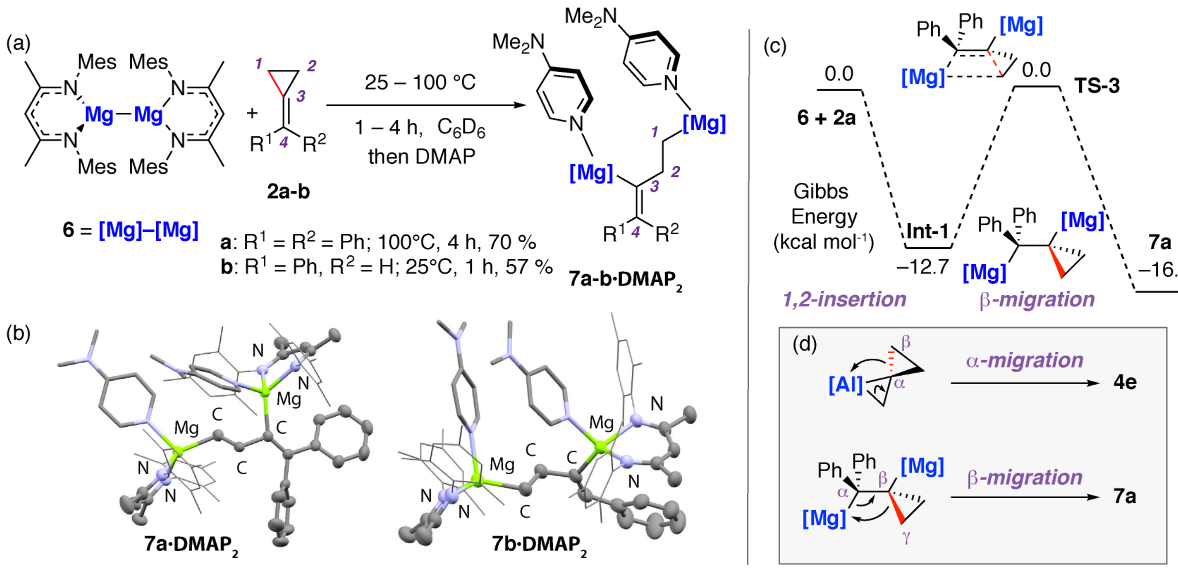


Figure 3. (a) C–C bond activation with magnesium(I) compound **6**. (b) Structures for **7a•DMAP₂** and **7b•DMAP₂** from single crystal X-ray diffraction experiments. (c) DFT calculated pathway for C–C bond activation *via* a 1,2-dimagnesioethane intermediate. (d) Comparison of α-migration and β-migration pathways.

The data show that the key factor for achieving C–C σ-bond activation is not the redox reactivity of the main group reagents **1** and **6** but being able to install electropositive Al or Mg atoms in the correct position of the hydrocarbon scaffold in order to promote an α- or β-alkyl migration mechanism. Further insight into the migratory mechanisms was provided by NBO calculations. Second-order perturbation analysis implicates the participation of the electrophilic main group site in C–C σ-bond activation in both mechanisms. Donor-acceptor interactions involving electron donation from the breaking C–C σ-bond into low-lying orbitals of aluminum(III) or magnesium(II) can be identified in both **TS-2** and **TS-3** (arrow-pushing - Figure 3d, see supporting information for details).

Based on the advancement of our understanding, we envisioned a new catalytic protocol for C–C σ-bond functionalization. By combining the new β-alkyl migration step with established σ-bond metathesis and alkene insertion chemistry of group 2 hydride catalysts the catalytic heterofunctionalization of C–C bonds should be accessible (Figure 4a).[26,27] Initially, each of the proposed steps of the catalytic cycle were investigated in stoichiometric reactions. The addition of the β-diketiminate stabilized magnesium hydride **8** to **2e** results in near quantitative formation of the ring-opened but-4-en-1-yl magnesium species **9** over 24 hours at 25°C. **9** results from the anti-Markovnikov insertion of the alkene into the Mg–H bond of **8** followed by facile β-migration involving C–C σ-bond activation. Subsequent addition of $PhSiH_3$ (2 equiv.) to a solution of **8** and heating the resultant mixture at 80°C for 3 hours afforded the known products **10a** and **10b** in a 5:3 ratio in 89% yield, along with reformation of **8**. The former silane is derived from a net hydrosilylation of the C–C σ-bond, the latter forms from a second intramolecular hydrosilylation of **10a** (Figure 4b).

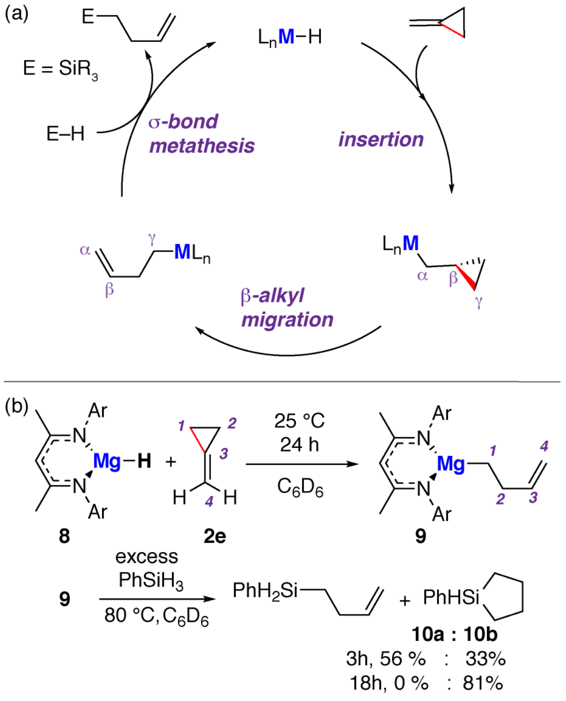


Figure 4. (a) Proposed catalytic cycle for C–C bond hydrosilylation. (b) Reaction of **8** with **2e** and **9** with $PhSiH_3$. Ar = 2,6-di-iso-propylphenyl.

A catalytic procedure involving the reaction of **2e**, $PhSiH_3$ (2 eq.) and 10 mol% **8** led to the formation of **10a:10b** in 73 % overall yield and a 4.6:1 ratio after 3h at 80°C. Further heating converted **10a** into **10b** in near quantitative yield. Similarly, the substituted alkylidene cyclopropanes **2a** and **2b** undergo catalytic C–C σ-bond hydrosilylation with **8**. In the case of **2b** a 1:1.1 mixture of *E:Z*-stereoisomers of the product was obtained (Figure 5). The reaction does not proceed in the absence of **8** at 80 °C.

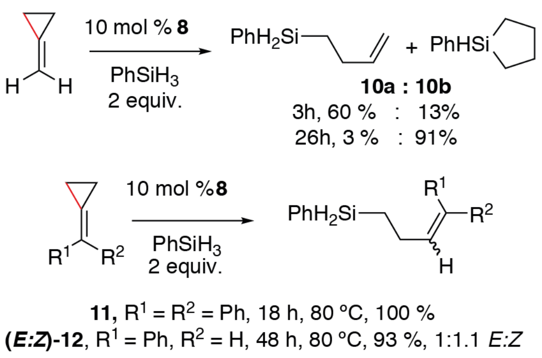


Figure 5. Catalytic C–C bond hydrosilylation with **8**.

In summary, we report the C–C σ-bond activation of strained alkylidene cyclopropanes by main group reagents. Analysis of the mechanism through isolation of intermediates, kinetics and DFT studies shows that C–C σ-bond activation at main group centers is possible by either α- or β-migration mechanisms. This understanding was used to develop a magnesium catalysed hydrosilylation of C–C bonds. We are continuing to expand the scope of this catalytic methodology and to explore the origin of stereochemistry.

ASSOCIATED CONTENT

The Supporting Information is available free of charge on the ACS Publications website. X-ray crystallographic data for**3a**, **4a-c**, **7a.DMAP$_2$**, **7b.DMAP$_2$**, and **9** are available from the Cambridge Crystallographic Data Centre (CCDC 1984848-1984854) and as a .cif file, full details of the experiments and calculations are available as a .pdf. NMR spectra and computational coordinates are available at DOI: 10.14469/hpc/7252.

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