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

Richard Y. Kong and Mark R. Crimmin\*

Department of Chemistry, Molecular Sciences Research Hub, Imperial College London, White City, London, W12 0BZ, UK. *Supporting Information Placeholder* 

ABSTRACT: Aluminum(I) and magnesium(I) compounds are reported for the C–C  $\sigma$ -bond activation of strained alkylidene cyclopropanes. These reactions result in the formal addition of the C–C  $\sigma$ -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  $\alpha$ - or  $\beta$ -alkyl migration steps that break the C–C  $\sigma$ -bond. This mechanistic understanding is used to develop the magnesium-catalyzed hydrosilylation of the C–C  $\sigma$ -bonds of alkylidene cyclopropanes.

Reactions that break the strong C–C  $\sigma$ -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  $\sigma$ -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  $\sigma$ -bond activation with transition metal complexes include oxidative addition<sup>1</sup> and  $\beta$ -alkyl elimination.<sup>2</sup> These two fundamental steps underpin numerous applications which involve the transition metal catalysed functionalization of C–C  $\sigma$ -bonds(Figure 1).<sup>3–5</sup>



Figure 1. C–C  $\sigma$ -bond activation with transition metals.<sup>6</sup>

Examples of C–C  $\sigma$ -bond activation by main-group compounds are limited in comparison to transition metal complexes. For example, stoichiometric C–C  $\sigma$ -bond activation by  $\beta$ -alkyl elimination has been observed during the thermolysis of *tris*-neopentylaluminium at 200°C.<sup>7</sup> Low-valent maingroup compounds including silylenes,<sup>8</sup> a phosphirene,<sup>9</sup> and an alumanyl anion<sup>10</sup> 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  $\sigma$ -bond in biphenylene has also recently been observed at an anionic cyclic-alkylamino alumanyl complex.<sup>11</sup> 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  $\sigma$ -bond.<sup>12–14</sup>

Herein we report  $C(sp^2)-C(sp^3) \sigma$ -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.  $\alpha$ -Alkyl and  $\beta$ -alkyl migration mechanisms are in operation. The redox-neutral nature of the C–C  $\sigma$ -bond activation is leveraged to develop the first example of catalytic C–C  $\sigma$ bond functionalization using magnesium-based catalysis.

Reaction of the aluminium(I) complex  $\mathbf{1}^{15,16}$  with the unsaturated cyclopropane 2a at 25°C in C<sub>6</sub>D<sub>6</sub> 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.<sup>17</sup> Heating either crude or isolated samples of **3a** at 100°C in C<sub>6</sub>D<sub>6</sub> 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

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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  $3a \rightarrow 4a$  was found to be first-order with respect to 3a. Eyring analysis over a 45-70°C range gave activation parameters:  $\Delta H^{\dagger} = 22.3 \pm 0.4$  kcal mol<sup>-1</sup> and  $\Delta S^{\dagger} = 28.9 \pm 5.5$  cal K<sup>-1</sup> mol<sup>-1</sup>. The negative entropy of activation is consistent with an ordered transition state. The Gibbs activation energy is  $\Delta G^{\dagger}_{298K} = 24.4 \pm 2.1$  kcal mol<sup>-1</sup>. 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**,  $\Delta G^{\dagger}_{298K} = 14.1$  kcal mol<sup>-1</sup>, is consistent with the observation that formation of **3a** occurs at 25°C and is not the rate-determining step of the C-C  $\sigma$ -bond activation sequence. From the (4+1) cycloaddition intermediate **3a**, **TS-2** was located ( $\Delta G^{\dagger}_{298K} = 25.8 \text{ kcal mol}^{-1}$ ) and connects directly to the product 4a. This key step breaks the C-C  $\sigma$ -bond and involves an  $\alpha$ -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  $\alpha$ -migration becomes accessible (supporting information). The direct oxidative addition of a C–C  $\sigma$ -bonds of strained threemembered rings to **1** was also considered.<sup>19</sup> 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  $\alpha$ -migration pathway ( $\Delta G^{\dagger}_{298K} = 35.3$  kcal mol<sup>-1</sup>). Experimentally, **1** does not react with cyclopropylbenzene to form metallocyclobutane products even when heated at 100°C for one week in C<sub>6</sub>D<sub>6</sub>.

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 alkylsubstituted substrates 2c or 2d. Crystallization and isolation was amenable through the preparation of their DMAP (4-dimethylaminopyridine) adducts 7a•DMAP<sub>2</sub> and 7b•DMAP<sub>2</sub> (Figure 3b). 7b•DMAP<sub>2</sub> forms as a single stereoisomer. The mechanism for C–C  $\sigma$ -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.<sup>24,25</sup> In line with these expectations, Int-1 was identified as an intermediate ( $\Delta G^{\circ}_{298K} = -12.7 \text{ kcal mol}^{-1}$ ) by computational methods. From Int-1, C–C  $\sigma$ -bond activation occurs by β-alkyl migration via **TS-3** to form **7a** ( $\Delta G^{\dagger}_{298K}$  = 12.7 kcal mol<sup>-1</sup>, Figure 3c).

The discrepancy between experimentally observed reaction conditions (4 h at 100°C) and calculated barriers ( $\Delta G^{\dagger}_{298K}$  = 12.7 kcal mol<sup>-1</sup>) 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  $\sigma$ -bond activation *via* a (4+1) intermediate (for the analogous pathway via a (2+1) intermediate see the supporting information).

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Figure 3. (a) C–C bond activation with magnesium(I) compound 6. (b) Structures for  $7a \cdot DMAP_2$  and  $7b \cdot DMAP_2$  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  $\alpha$ -migration and  $\beta$ -migration pathways.

The data show that the key factor for achieving C–C  $\sigma$ -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  $\alpha$ - or  $\beta$ -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  $\sigma$ -bond activation in both mechanisms. Donor-acceptor interactions involving electron donation from the breaking C–C  $\sigma$ -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  $\sigma$ -bond functionalization. By combining the new  $\beta$ -alkyl migration step with established  $\sigma$ -bond metathesis and alkene insertion chemistry of group 2 hydride catalysts the catalytic heterofunctionalization of C-C bonds should be accessible (Figure 4a).<sup>26,27</sup> Initially, each of the proposed steps of the catalytic cycle were investigated in stoichiometric reactions. The addition of the  $\beta$ 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  $\beta$ -migration involving C–C  $\sigma$ -bond activation. Subsequent addition of PhSiH<sub>3</sub> (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  $\sigma$ -bond, the latter forms from a second intramolecular hydrosilylation of 10a (Figure 4b).





A catalytic procedure involving the reaction of **2e**, PhSiH<sub>3</sub> (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  $\sigma$ -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  $\sigma$ -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  $\sigma$ -bond activation at main group centers is possible by either  $\alpha$ - or  $\beta$ -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**<sub>2</sub>, **7b.DMAP**<sub>2</sub>, 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.

## Corresponding Author

\*m.crimmin@imperial.ac.uk

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