



ORIGINAL ARTICLE

Theoretical study of the reactivity of $(\text{CH}_3)_2\text{AlCH}_2\text{I}$ promoted cyclopropanation reactions

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Received 12 March 2010; accepted 29 June 2010

Available online 10 July 2010

KEYWORDS

Density functional theory;
Aluminum carbenoid;
Methylene transfer;
Carbometalation

Abstract Density functional theory calculations are reported for the cyclopropanation reactions of $(\text{CH}_3)_2\text{AlCH}_2\text{I}$ with ethylene for two reaction channels: methylene transfer and carbometalation. These computational results suggest that the methylene transfer process is favored and the competition from the carbometalation pathway is negligible.

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1. Introduction

Cyclopropane moieties have been found in wide-range of natural and artificial compounds that exhibit important biological activities and in an array of substances used as starting materials and intermediates in organic synthesis (Rappoport, 1987; Fritsch et al., 1986; Evans et al., 1991; Rodriguez et al., 1993; Zhao et al., 1994; Nishiyama et al., 1994, 1995a,b; Doyle, 1995; Doyle et al., 1998; Boger et al., 1999; Salaun, 2000; Che et al., 2001; Rodriguez-Garcia et al., 2001). This has motivated a large number of research groups to develop new and wide-range methods to produce cyclo-propanated products. A reac-

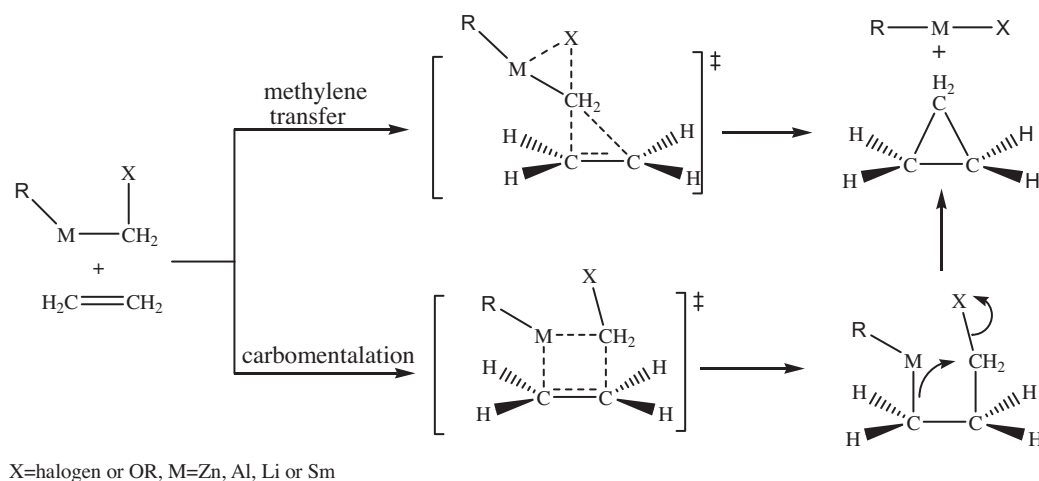
tion between iodomethylzinc iodide and an olefin that produces a cyclopropane compound was first reported by Simmons and Smith (1959) and Simmons et al. (1973) and is now called the Simmons–Smith (SS) reaction, which is the method for synthesizing cyclo-propanated products from olefins using a metallic carbenoid (SS) reagent. Following this a great deal of work have been done to improve and develop alternative methods to produce Simmons–Smith-type reagents. Many researchers have been trying to find more efficient and highly diastereoselective cyclo-propanating reagents. Metallic carbenoid is an important intermediate in organic synthesis for cyclopropanation reaction. In 1985, there were experimental reports that Al carbenoid is an efficient S–S reagent (Rubottom et al., 1985). The $\text{Al}/\text{CH}_2\text{I}_2$ carbenoid is believed to be one of the most efficient and highly diastereoselective cyclo-propanating reagents. The cyclopropanation reactions are usually performed at -40°C and high yields of cyclo-propanated products can be achieved.

It has been proposed that the carbenoid-promoted cyclopropanation reactions of interest proceed through two likely reaction pathways: methylene transfer and carbometalation (see Scheme 1). The reaction mechanism is system-dependent. For zinc carbenoids, it is thought that the methylene transfer mechanism represents the reaction reality (Rubottom et al.,

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Scheme 1

1985; Charette and Marcoux, 1995; Charette and Beauchemin, 2001; Furukawa et al., 1966; Wittig and Schwarzenbach, 1959; Denmark and Edwards, 1991; Closs and Moss, 1964; Molander et al., 1987; Molander and Harring, 1989; Maruoka et al., 1985, 1989; Bernardi et al., 1997; Dargel and Koch, 1996; Nakamura et al., 1998, 2003; Hermann et al., 2000; Boche and Lohrenz, 2001; Fang et al., 2002; Wang et al., 2002; Zhao et al., 2002). Samarium carbenoid cyclopropanation reactions are believed to have some competition between the methylene transfer mechanism and the carbometallation mechanism (Stiasny and Hoffman, 1995; Zhao et al., 2003; Wang et al., 2004). As for lithium carbenoids, Hoffmann (Stiasny and Hoffman, 1995) reported a possible alternative carbometallation/methylene transfer pathway. In this paper, aluminum carbenoid-promoted cyclopropanation reactions are investigated using theoretical methods. We found that the aluminum carbenoids have a “metal carbene complex” character similar to the classical Simmons–Smith carbenoids previously investigated using density functional theory (DFT) calculations. Our result for the aluminum carbenoids shows that the methylene transfer pathway is favored and competition from the carbometallation pathway is very small.

2. Computational details

The hybrid B3LYP density functional method (Becke, 1993, 1988; Lee et al., 1988) was used to investigate the cyclopropanation reaction mechanisms of the aluminum carbenoids with ethylene. The stationary structures of the potential energy surfaces were fully optimized at the B3LYP level of theory. Analytical frequency calculations at the same level of theory were performed in order to confirm the optimized structures to either a minimum or a first-order saddle-point as well as to obtain the zero-point energy correction. Furthermore, intrinsic reaction coordinate (IRC) calculations (Gonzalez and Schlegel, 1989, 1990) were performed to confirm that the optimized transition state correctly connects the relevant reactants and products. Geometry optimization for all of the reactants, intermediates, transition states and products as well as the frequency calculations were carried out with the 6-311G** basis set for all atoms of the reactions investigated (Glukhovtsev et al., 1995). All the calculations were carried out using the

Gaussian 98 and Gaussian 03 program suites (Frisch et al., 1998).

3. Results and discussion

3.1. Cyclopropanation reaction of the $(\text{CH}_3)_2\text{AlCH}_2\text{I}$ with ethylene

The optimized geometry for the Al carbenoid $(\text{CH}_3)_2\text{AlCH}_2\text{I}$ is shown in Fig. 1 along with the optimized geometry of the reactant complex (RC1) and the transition states (TS1, TS2) for cyclopropanations of ethylene through two different pathways to produce cyclopropane ($\text{c-C}_3\text{H}_6$) and $(\text{CH}_3)_2\text{AlI}$. The methylene transfer pathway involves a concerted $[2 + 1]$ addition through a transition state, TS1, in which the pseudotrigonal methylene group of the carbenoid adds to the ethylene π -bond to form new C–C bonds asynchronously. This process is accompanied by a 1,2-migration of the I anion from the carbon atom to the aluminum atom. According to the transition state proposed by Simmons and Smith (1959) and Moser (1969), this “butterfly” transition structure can explain the stereochemical features of this type of reaction. Another pathway named a carbometallation process, involves a $[2 + 2]$ addition of ethylene to the Al–C bond to form an intermediate (IM) through a four-centered transition state (TS2). A subsequent intramolecular substitution reaction of this intermediate produces the final cyclopropane product. In the methylene transfer pathway, the Al carbenoid $(\text{CH}_3)_2\text{AlCH}_2\text{I}$ approaches ethylene from above the molecular plane in an asymmetric manner; while in the carbometallation process, the ethylene molecule simultaneously moves to the Al carbenoid to form a π -complex which can be regarded as the reactant complex for both reaction pathways. In the transition structure TS1, the ethylene molecule has changed its planar structure with a significant pyramidalization of about 7.3° for C^2 , which indicates that the $\text{sp}^2 \rightarrow \text{sp}^3$ rehybridization is necessary for cyclopropane formation; whereas the pyramidalization of C^3 is only 0.8° . There is another significant piece of evidence for an asynchronous approach of the CH_2CH_2 molecule in the methylene transfer mechanism. The $\text{C}^1\text{--C}^2$ distance in TS1 is $2.224 \text{ \AA}$, which is $0.257 \text{ \AA}$ shorter than the $\text{C}^1\text{--C}^3$ distance. The interactions of the $(\text{CH}_3)_2\text{AlCH}_2\text{I}$ moiety with the π -olefin orbital are

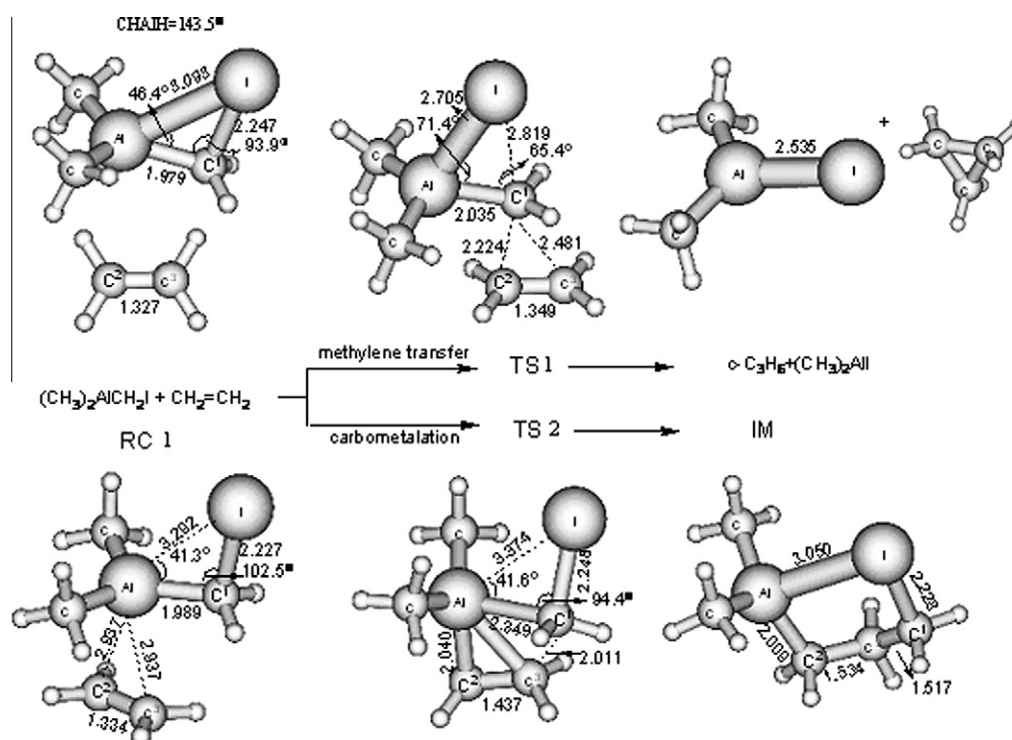


Figure 1 Schematic diagrams of the optimized geometry from the B3LYP/6-311G** level computations for the aluminum carbenoid $(\text{CH}_3)_2\text{AlCH}_2\text{I}$, reactant complex RC1, the intermediate IM as well as the transition state for the cyclopropanation with ethylene. TS1 = transition state for the methylene transfer for the reaction of $(\text{CH}_3)_2\text{AlCH}_2\text{I}$ with ethylene. TS2 = transition state for carbometalation for the reaction of $(\text{CH}_3)_2\text{AlCH}_2\text{I}$ with ethylene. Selected structural parameters are shown for each species with the bond lengths in Å and bond angles in degrees.

mainly responsible for the slight lengthening of $\text{C}^2=\text{C}^3$ bond and C^1-Al bond from the reactant complex (RC1) to the transition state (TS1) where the $\text{C}^2=\text{C}^3$ bond length is elongated by 0.015 Å and the C^1-Al bond length is elongated by 0.046 Å, respectively. Relatively large changes are associated with the $\angle \text{I}-\text{C}^1-\text{Al}$, the $\angle \text{I}-\text{Al}-\text{C}^1$, the C^1-I and $\text{Al}-\text{C}^1$ distances that vary from 102.5°, 41.31°, 2.227 Å, 1.989 Å in RC1, to 65.4°, 71.45°, 2.819 Å, 2.035 Å in TS1, respectively, as shown in Fig. 1. Notably, in the transition state TS1, the C^1-I bond becomes nearly broken and the electron-rich I atom is attracted by the metal center to almost result in a complete $\text{Al}-\text{I}$ bond. These changes in the bond lengths and angles are attributed to partial formation of the $(\text{CH}_3)_2\text{AlI}$ byproduct in the transition state. The $\text{Al}-\text{I}$ interaction is believed to give a sufficient compensation for the weakening of the $\text{Al}-\text{C}^1$ bond from RC1 to TS1. As shown in Fig. 1, the methylene transfer pathway has a barrier of 14.4 kcal/mol in $(\text{CH}_3)_2\text{AlCH}_2\text{I}$ and is exothermic by about 28.7 kcal/mol at the B3LYP level of theory. Vibrational analysis shows that the TS1 structure is a first-order saddle-point with only one imaginary frequency of $289i\text{ cm}^{-1}$ and the IRC calculations confirmed that TS1 connects the corresponding reactant RC1 and products ($\text{c}-\text{C}_3\text{H}_6$) and $(\text{CH}_3)_2\text{AlI}$. Thus, it is evident that TS1 is the transition state of the concerted reaction of $(\text{CH}_3)_2\text{AlCH}_2\text{I}$ with ethylene through the methylene transfer pathway.

With regard to the carbometalation pathway, there is an insertion reaction of the ethylene to the $\text{Al}-\text{C}^1$ bond to produce the intermediate IM through a four-centered TS2 transition state. Compared with the methylene transfer pathway, the carbometalation pathway has larger changes in the geometry

from the reaction complex to the transition state. The $\text{Al}-\text{C}^2$ interaction increases significantly from 2.937 Å in RC1 to 2.04 Å in TS2. The C^1-C^3 goes from a distance 3.296 Å in RC1 to 2.011 Å in TS2. This is accompanied by the weakening of the C^1-Al bonds from 1.989 Å in RC1 to 2.349 Å in TS2. It is interesting that the C^1-I bond length and the $\text{Al}-\text{I}$ interaction only change very slightly during the process from RC1 to TS2. This is different from the methylene transfer pathway and indicates that the $\text{Al}-\text{I}$ interaction contributes little to the weakening of the C^1-Al bonds of TS2 in the carbometalation process. Thus, more energy is needed to overcome the barrier in carbometalation pathway from RC1 to TS2. The reaction barrier height at the B3LYP/6-311G** level of theory for the reaction system of $(\text{CH}_3)_2\text{AlCH}_2\text{I} + \text{CH}_2\text{CH}_2$, is calculated to be 32.82 kcal/mol. The barrier height of 32.82 kcal/mol predicts that the reaction does not occur easily under room-temperature conditions. Vibrational analysis found that the optimized TS2 structure had one imaginary frequency of $391i\text{ cm}^{-1}$ and was confirmed to connect the corresponding reactants and products by IRC calculations.

4. Conclusions

In this paper we have studied, using a DFT approach, the potential energy surfaces for the reactions between ethylene and $(\text{CH}_3)_2\text{AlCH}_2\text{I}$ carbenoids which represent model systems for aluminum carbenoid-promoted cyclopropanation reactions. Two reaction channels were investigated: methylene transfer and carbometalation. The energy barriers for the methylene transfer pathway (14.4 kcal/mol) are significantly smaller than

those of the carbometallation pathway (about 32.82 kcal/mol). The methylene transfer process is favored and the competition from the carbometallation process is likely to be very small and this is consistent with experimental results. We have also demonstrated that the methylene transfer transition state corresponds to a three-centered structure similar to that originally suggested by Simmons and Smith (1959) and Moser (1969). The reactant complexes located on the reaction surface appear to form without any barrier. Our results are consistent with and can help explain the experimental observation that Al carbenoids can undergo efficient cyclopropanation reactions with olefins at $-40\text{ }^{\circ}\text{C}$.

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