

# Mechanistic competition variations due to the substituents in the lithium carbenoid promoted cyclopropanation reactions

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## Abstract

The cyclopropanation reactions of the  $\text{LiCH}_2\text{X}$  ( $\text{X} = \text{F}, \text{Cl}, \text{Br}$  and  $\text{I}$ ) carbenoids with ethylene were investigated at the CCSD(T)/6-311G\*\*//B3LYP/6-311G\*\* level of theory along two reaction pathways: methylene transfer and carbometalation. There exists a competition between these two reaction pathways for the different substituted lithium carbenoids. Interestingly, the substituent has different effect on the methylene transfer and carbometalation pathways. The trend of the activation energies for the methylene transfer pathway is  $\text{LiCH}_2\text{F}$  (9.8 kcal/mol) >  $\text{LiCH}_2\text{Cl}$  (7.6 kcal/mol)  $\approx$   $\text{LiCH}_2\text{Br}$  (7.4 kcal/mol)  $\approx$   $\text{LiCH}_2\text{I}$  (7.5 kcal/mol), whereas the activation energies for the carbometalation pathway increases in this order:  $\text{LiCH}_2\text{F}$  (6.1 kcal/mol) <  $\text{LiCH}_2\text{Cl}$  (7.1 kcal/mol) <  $\text{LiCH}_2\text{Br}$  (8.2 kcal/mol) <  $\text{LiCH}_2\text{I}$  (8.5 kcal/mol). The different effect mainly arises from that the substituent of the lithium carbenoid influences the hybridization character of the  $\text{C}^1$  atom. The mechanistic competition varies due to the different substituents of the lithium carbenoids during the cyclopropanation reactions. This result is revelatory for us to control mechanistic competition to obtain target product by modifying the substituents of the lithium carbenoids.

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## 1. Introduction

Cyclopropane-containing molecules are found in many natural and unnatural compounds exhibiting important biological activities and can be used as versatile synthetic starting materials or intermediates [1–9]. Carbenoid promoted cyclopropanation reaction is a very important method to produce cyclopropanes. Since the pioneering work by Simmons and Smith using diiodomethane and a Zn/Cu couple to react with olefins to form cyclopropanes [10,11], many efforts were invested to develop improvements or alternative techniques to form carbenoid reagents that can make cyclopropanes from olefins with high efficiency and stereoselectivity. In addition to zinc carbenoids such as the Simmons–Smith reagents, the Furukawa reagents [12], and

the Wittig–Denmark reagents [13,14], other powerful carbenoid reagents were also developed. In 1964, Closs and Moss [15] discovered the lithium carbenoids that can give the expected arylcyclopropanes in the presence of olefins at  $-10^\circ\text{C}$  with fair to good yields. In 1985, Yamamoto and co-workers [16,17] found that the dialkyl( $\alpha$ -iodoalkyl)-aluminum carbenoids can undergo cyclopropanations at  $-40^\circ\text{C}$  with high yields. In 1987, Molander [18,19] first reported the generation of samarium carbenoids by using a samarium/mercury amalgam in conjunction with  $\text{CH}_2\text{I}_2$ , which are new powerful supplement for the family of cyclopropanation carbenoids. Modifies of the structure of these carbenoids to improve the reactivity and stereoselectivity are still enthusiastically undergoing now [20–23].

Among these various carbenoids, lithium carbenoid is one of the most efficient cyclopropanation reagents, which can cyclopropanate olefins efficiently, even at  $-78^\circ\text{C}$  [24,15]. However, the debate of reaction mechanism for

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lithium carbenoids promoted cyclopropanations has lasted for a long time. It has been proposed that this kind of reaction of interest proceeds through two likely reaction pathways: methylene transfer and carbometalation (See Scheme 1). The methylene transfer pathway is a concerted transformation to produce cyclopropanes through a “butterfly-type” transition state ( $TS_M$ ). On the other hand, the carbometalation pathway is a two-step process involving a four-centered transition state ( $TS_C$ ) to form intermediate **1** followed by an intramolecular substitution to furnish the products. Hoberg first reported that carbometalation mechanism might operate, [25] whereas Burger thought carbometalation should be unreasonable for the addition of chloromethyl lithium to alkenes [26]. Although experimental and theoretical proof indicated that the methylene transfer pathway represents the reaction reality for the zinc carbenoids [27,28,13]. Hoffmann and Nakamura and their co-workers suggested in later publications that methylene transfer and carbometalation pathways might compete in the lithium carbenoid promoted cyclopropanations [27–29]. Hoffmann et al. suggested that Lewis-base assistance may render the carbometalation competitive with the methylene transfer pathway. The competition of these two pathways led to a mixture of two kinds of cyclopropanes. Nakamura and coworkers found that the transition state energies for the  $LiCH_2Cl + C_2H_4$  system at the B3LYP/6-31G\* level are 3.8 kcal/mol along the methylene transfer pathway and 2.1 kcal/mol along the carbometalation pathway. They also suggested that there was a competition between these two pathways. The influence of the substituents on the carbenoid character of the  $LiCH_2X$ , was ever theoretically studied by Boche [24]. They focused only on the methylene transfer mechanism. How the different substituents influence the competitive carbometalation pathway is not yet understood. In the light of the continuing interest on the carbenoid promoted cyclopropanation reactions [30–35], quantum mechanical studies are performed on cyclopropanations of the different substituted  $LiCH_2X$  ( $X = F, Cl, Br$  and  $I$ ) carbenoids with ethylene along the methylene transfer and carbometalation path-

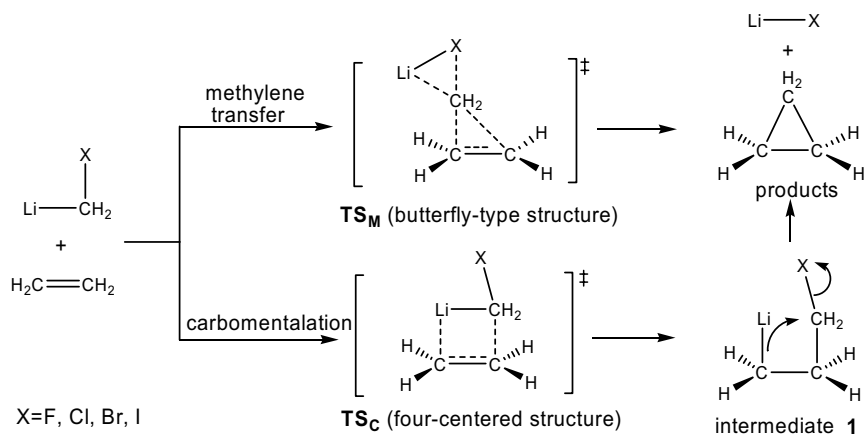
ways. We found the interesting mechanistic variations in competition due to the substituents. This result is revelatory for us to control mechanistic competition to obtain target product by modifying the substituents of the lithium carbenoids.

## 2. Computational methods

The lithium carbenoid promoted cyclopropanation reactions with ethylene were investigated with the density functional theory (DFT) using the hybrid B3LYP density functional [36,37]. Geometry optimization, frequency calculations and IRC calculations were carried out with the 6-311G\*\* basis set [38–40] for all the atoms of reactions, including 1 Atom [41]. Analytical frequency calculations at the same level were done in order to confirm the optimized structures to be either a minimum or a first-order saddle-point, as well as to obtain the zero-point energy (ZPE) correction. Intrinsic reaction coordinate (IRC) calculations [42,43] were performed to confirm the transition states connected the relevant reactants and products. Natural bond orbital (NBO) analysis was performed at the same level as the one used for geometry optimization [44]. Further single-point CCSD(T) [45,46] (coupled-cluster level with single and double excitations and with noniterative triples) calculations were performed on all B3LYP optimized structures, which are denoted as the CCSD(T)/6-311G\*\*//B3LYP/6-311G\*\* level of theory. The Boys localization procedure [47,48] was performed to obtain localized Kohn–Sham orbitals [49] (LOs). All the calculations were carried out using the GAUSSIAN 03 program [50].

## 3. Results

The optimized stationary structures on the potential energy surfaces of the reactions are depicted schematically in Fig. 1. The relative energies of optimized stationary structures relative to the starting materials (SM-X =  $LiCH_2X + C_2H_4$ ) with ZPE corrections are tabulated in Table 1. The investigated reactions of the lithium carbenoids



Scheme 1. The methylene transfer and carbometalation pathways for the lithium carbenoid promoted cyclopropanation with ethylene.

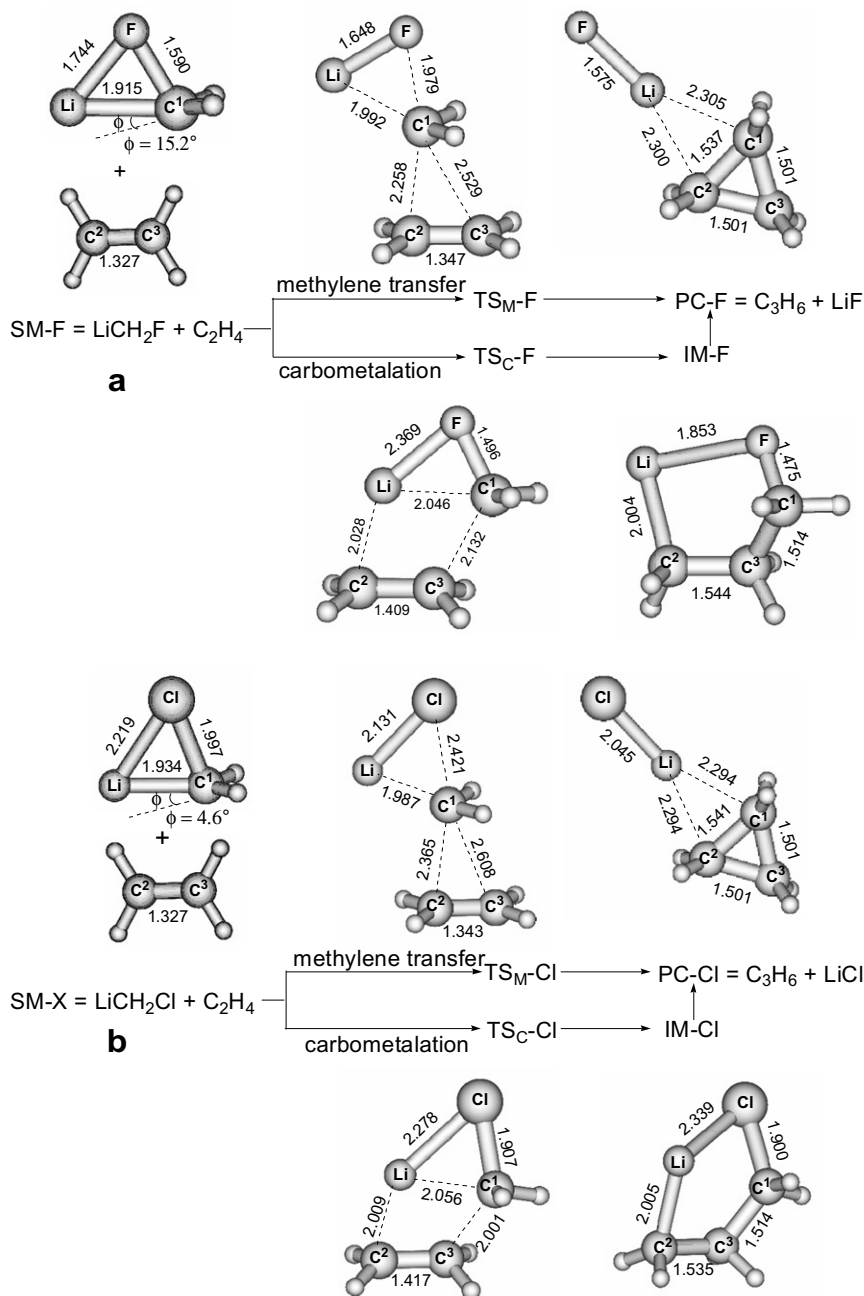


Fig. 1. Schematic diagrams of the optimized geometries for the cyclopropanation reactions of the lithium carbenoid  $\text{LiCH}_2\text{X}$  ((a)  $\text{X} = \text{F}$ , (b)  $\text{X} = \text{Cl}$ , (c)  $\text{X} = \text{Br}$ , (d)  $\text{X} = \text{I}$ ) with ethylene from the B3LYP/6-311G\*\* computations. Selected structural parameters are shown in angstroms.  $\phi$  is the angle between the  $\text{C}^1\text{HH}$  plane and the  $\text{Li}-\text{C}^1$  bond.

$\text{LiCH}_2\text{X}$  with ethylene produce cyclopropane ( $\text{c-C}_3\text{H}_6$ ) and  $\text{LiX}$  through two different pathways. The methylene transfer pathway involves a concerted [2+1] addition through the “butterfly-type” transition state,  $\text{TS}_\text{M-X}$ , in which the approximative planar methylene group of the carbenoid adds to the ethylene  $\pi$ -bond to form new C–C bonds asynchronously. This process is accompanied by a 1,2-migration of the X anion from the carbon atom to the lithium atom. According to the transition state proposed by Simmons [11], this “butterfly-type” transition structure can explain the stereochemical features of this type of reaction. Another

pathway named a carbometalation process involves a [2+2] addition of ethylene to the  $\text{Li}-\text{C}$  bond to form an intermediate ( $\text{IM-X}$ ) through a four-centered transition state ( $\text{TS}_\text{C-X}$ ). A subsequent intramolecular substitution reaction of this intermediate facily occurs to produce the final cyclopropane product. This intramolecular substitution process is not the rate-determining step of the carbometalation and will not be discussed further here [27,28,30].

As for the cyclopropanation of the fluorine substituted  $\text{LiCH}_2\text{F}$  carbenoid with ethylene along the methylene transfer pathway, the cycloaddition of the methylene of

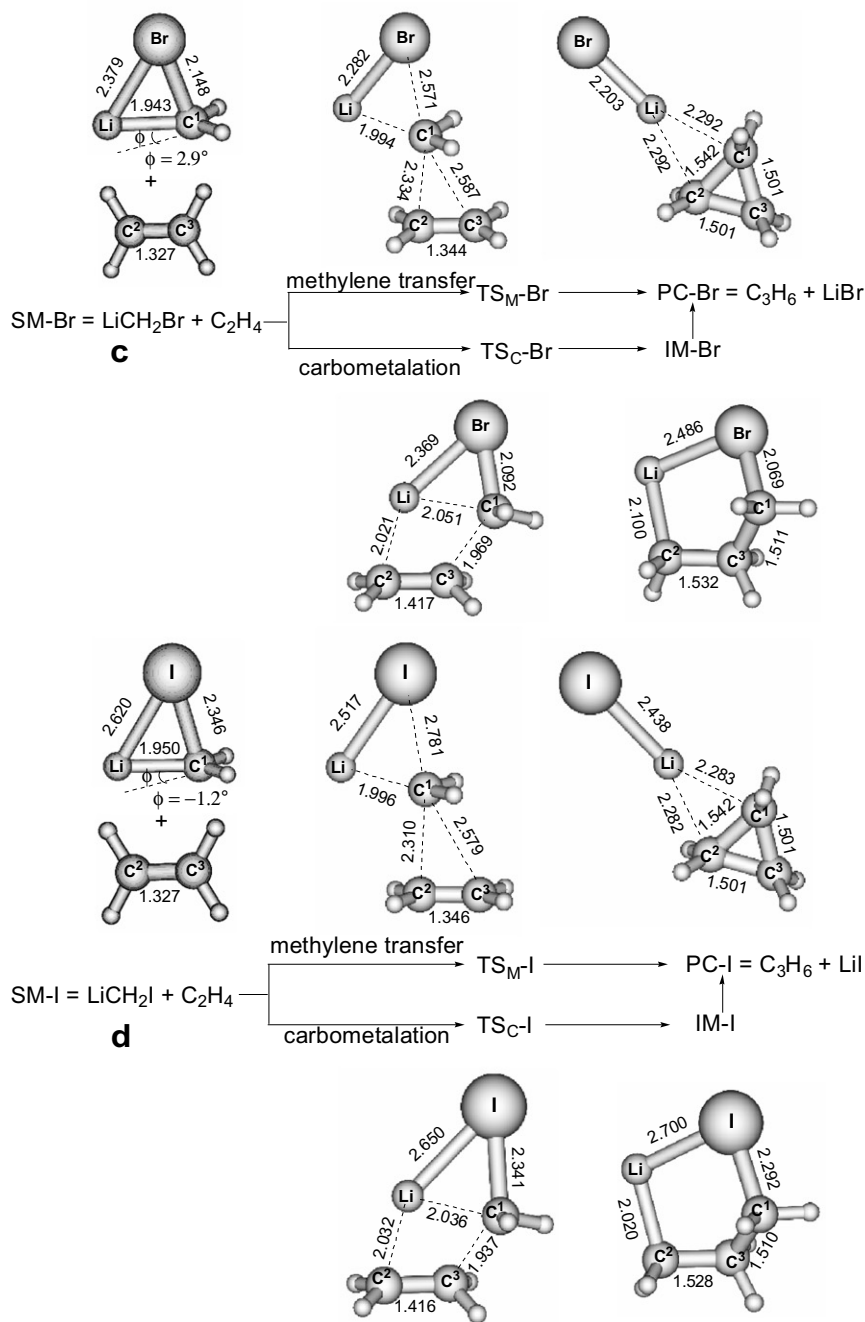


Fig 1. (continued)

the carbenoid to the ethylene has an asynchronous manner. The C<sup>1</sup>–C<sup>2</sup> distance in TS<sub>M</sub>-F is 2.258 Å, which is 0.271 Å shorter than the C<sup>1</sup>–C<sup>3</sup> distance, as shown in Fig. 1a. Evi-

dence can also be seen from the hybridization character of the carbon atoms of the ethylene in the transition state TS<sub>M</sub>-F. When approaching to the methylene, the ethylene

Table 1

CCSD(T)/6-311G\*\*//B3LYP/6-311G\*\* and B3LYP/6-311G\*\* calculated relative energies (kcal/mol) with ZPE correction relative to SM-X<sup>a</sup>

	F	Cl	Br	I
SM-X = LiCH <sub>2</sub> X + C <sub>2</sub> H <sub>4</sub>	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)
TS <sub>M</sub> -X	9.8 (7.8)	7.6 (5.9)	7.4 (6.2)	7.5 (6.8)
TS <sub>C</sub> -X	6.1 (4.3)	7.1 (7.5)	8.2 (7.8)	8.5 (7.7)
PC-X	-51.5 (-60.3)	-53.3 (-61.6)	-64.8 (-59.4)	-63.3 (-57.1)
IM-X	-28.2 (-23.2)	-20.2 (-14.0)	-17.6 (-12.5)	-15.6 (-11.1)

<sup>a</sup> The values are computed at the CCSD(T)/6-311G\*\*//B3LYP/6-311G\*\* level of theory with ZPE correction from the B3LYP/6-311G\*\* calculations. The values in parentheses are computed at the B3LYP/6-311G\*\* level of theory.

molecule has changed its planar structure with a significant pyramidalization of about  $10.7^\circ$  for  $C^2$  atom, which indicates that the  $sp^2 \rightarrow sp^3$  rehybridization is necessary for the cycloaddition, whereas the pyramidalization is only  $0.4^\circ$  for  $C^3$  atom. Notably, the  $C^1$ –F bond becomes nearly broken in the transition state  $TS_{M-F}$ , leading to a 1,2-migration of the electron-rich F atom to the metal center. The formation of an almost complete Li–F bond in the transition state is believed to give a sufficient compensation for the cleavage of the  $C^1$ –F bond [24]. As listed in Table 1, the methylene transfer pathway has an activation energy of 9.8 kcal/mol for the  $LiCH_2F + C_2H_4$  reaction system, and is exothermic by about 51.5 kcal/mol to form the PC-F, computed at the CCSD(T)/6-311G\*\*//B3LYP/6-311G\*\* level of theory. The calculated activation energy for  $LiCH_2F$  along the methylene transfer pathway at the B3LYP/6-311G\*\* level of theory is 7.8 kcal/mol, which is very close to the result calculated by Hermann et al. at the MP2/6-311++g\*\* level of theory [24].

The carbometalation pathway of the cyclopropanation of the lithium carbenoid with ethylene is similar to that of MeLi addition to ethylene [51,27]. The four-centered structure can be easily identified in  $TS_{C-F}$  of Fig. 1a. The  $C^2$ –Li distance is 2.028 Å, indicating the partial formation of  $C^2$ –Li bond. The  $C^1$ –Li bond have elongated from 1.915 Å in  $LiCH_2F$  to 2.046 Å in  $TS_{C-F}$ , accompanied with the strong interaction between  $C^1$  and  $C^3$  atoms. The  $C^1$ – $C^3$  distance is 2.132 Å, which is even shorted than that in  $TS_{M-F}$ . Although the  $C^2=C^3$  bond has been further weakened in  $TS_{C-F}$  (1.409 Å) than that in  $TS_{M-F}$  (1.347 Å), the relative energy for  $TS_{C-F}$  is still very low (6.1 kcal/mol at the CCSD(T)/6-311G\*\*//B3LYP/6-311G\*\* level of theory), since it needs not to cleave the  $C^1$ –F bond as compared with the case of  $TS_{M-F}$ . As listed in Table 1, the relative energy of the intermediate IM-F is  $-28.2$  kcal/mol. A subsequent intramolecular substitution reaction of this intermediate facily occurs to produce PC-F, as shown in Fig. 1a. The activation energy of the methylene transfer pathway (9.8 kcal/mol) is higher than that of the carbometalation pathway (6.1 kcal/mol) for the fluorine substituted  $LiCH_2F$  carbenoid.

The methylene transfer pathway of the cyclopropanation of the chlorine substituted  $LiCH_2Cl$  carbenoid with ethylene has a similar character to the  $LiCH_2F + C_2H_4$  system. As the ethylene approaches, the chlorine atom is also almost broken in the transition state  $TS_{M-Cl}$ . The  $C^1$ – $C^2$  (2.365 Å) and  $C^1$ – $C^3$  (2.608 Å) distances are relative longer than those of  $TS_{M-F}$ , as shown in Fig. 1b. This indicates that  $TS_{M-Cl}$  is a relative early transition state compared with  $TS_{M-F}$ . The activation energy of the methylene transfer pathway for the  $LiCH_2Cl$  carbenoid is calculated to be 7.6 kcal/mol at the CCSD(T)/6-311G\*\*//B3LYP/6-311G\*\* level of theory, which is lower by 2.2 kcal/mol than that for the  $LiCH_2F$  carbenoid. The methylene transfer pathway produces PC-Cl with an exotherm of 53.3 kcal/mol, which is slightly larger than the case of the  $LiCH_2F$  carbenoid. On the other hand, the activation energy of the car-

bometalation pathway for the  $LiCH_2Cl$  carbenoid is calculated to be 7.1 kcal/mol at the CCSD(T)/6-311G\*\*//B3LYP/6-311G\*\* level of theory, which is 1.0 kcal/mol higher than that for the  $LiCH_2F$  carbenoid. The formation of IM-Cl is exothermic by 20.2 kcal/mol relative to SM-Cl. As for the chlorine substituted carbenoid  $LiCH_2Cl$ , the methylene transfer and carbometalation pathways have rather similar activation energies (7.6 kcal/mol for the methylene transfer and 7.1 kcal/mol for the carbometalation).

With regard to the bromine substituted carbenoid  $LiCH_2Br$  and the iodine substituted carbenoid  $LiCH_2I$ , the structure changes along the methylene transfer and carbometalation pathways are very similar to those of the  $LiCH_2F$  and  $LiCH_2Cl$  carbenoids. The reaction schemes and selected geometric parameters are shown in Fig. 1c and d. The methylene transfer pathway of the  $LiCH_2Br + C_2H_4$  system has an activation energy of 7.4 kcal/mol and is exothermic by about 64.8 kcal/mol at the CCSD(T)/6-311G\*\*//B3LYP/6-311G\*\* level of theory. On the other hand, the carbometalation pathway has slightly higher activation energy of 8.2 kcal/mol at the same level. The activation energies of the methylene transfer and carbometalation pathways for the  $LiCH_2I + C_2H_4$  system are calculated to be 7.5 kcal/mol and 8.5 kcal/mol, respectively, at the CCSD(T)/6-311G\*\*//B3LYP/6-311G\*\* level of theory. The formation of PC-I and IM-I are exothermic by 63.3 kcal/mol and 15.6 kcal/mol, respectively.

#### 4. Discussion

Several points are noteworthy when analyzing the calculation results. (1) The methylene transfer and carbometalation pathways have comparative activation energies to each other for the  $LiCH_2X$  ( $X = F, Cl, Br$  and  $I$ ) carbenoids. The largest difference between the activation energies for these two reaction pathways is 3.7 kcal/mol for the  $LiCH_2F$  carbenoid. Other activation energy differences between these two pathways are 0.5 kcal/mol, 0.8 kcal/mol and 1.0 kcal/mol for the  $LiCH_2Cl$ ,  $LiCH_2Br$  and  $LiCH_2I$  carbenoids, respectively, as shown in Fig. 2. This indicates that the methylene transfer and carbometalation pathways compete with each other in the lithium carbenoid promoted cyclopropanations. Our results are in consistent with the experimental results by Hoffmann and coworkers [29], as well as with the calculation results by Nakamura et al. at the B3LYP/6-31G\* level of theory that the energies difference between these two pathways are 1.7 kcal/mol. (2) Although the activation energies are not significantly different from each other, we can clearly identify the approximate trend of them for different substituted carbenoids. The trend of the activation energies along the methylene transfer pathway is  $LiCH_2F$  (9.8 kcal/mol) >  $LiCH_2Cl$  (7.6 kcal/mol)  $\approx$   $LiCH_2Br$  (7.4 kcal/mol)  $\approx$   $LiCH_2I$  (7.5 kcal/mol), whereas the activation energies along the carbometalation pathway increased in this order:  $LiCH_2F$  (6.1 kcal/mol) <  $LiCH_2Cl$  (7.1 kcal/mol) <  $LiCH_2Br$  (8.2 kcal/mol) <

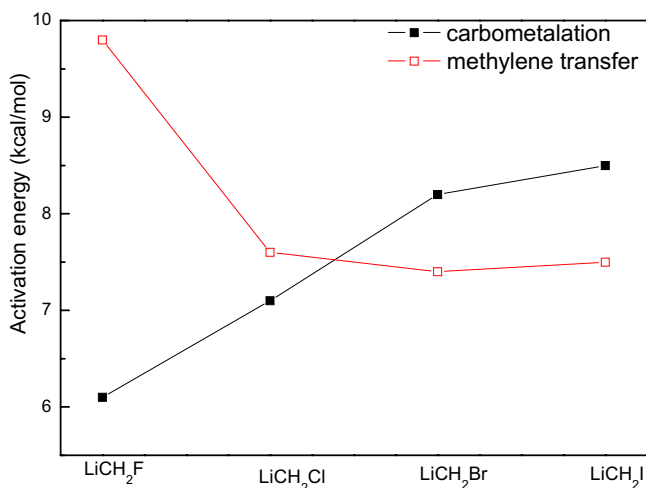


Fig. 2. Activation energies relative to starting materials for different substituted  $\text{LiCH}_2\text{X}$  carbenoid, X = F, Cl, Br, and I.

$\text{LiCH}_2\text{I}$  (8.5 kcal/mol), as shown in Table 1 and Fig. 2. This indicates that the substituent has different effect on the methylene transfer and carbometalation pathways. (3) Interestingly, the competition between these two pathways varies when changing the substituents of the lithium carbenoids. As for the fluorine substituted carbenoid  $\text{LiCH}_2\text{F}$ , the carbometalation pathway (6.1 kcal/mol) is more favored than the methylene transfer pathway (9.8 kcal/mol). The carbometalation pathway (7.1 kcal/mol) is still slightly more favored than the methylene transfer pathway (7.6 kcal/mol) for the chlorine substituted carbenoid  $\text{LiCH}_2\text{Cl}$ , though the activation energies of them are very similar. In contrast, when the substituents are bromine and iodine, the methylene transfer pathway (7.4 kcal/mol for the  $\text{LiCH}_2\text{Br}$  carbenoid and 7.5 kcal/mol for the  $\text{LiCH}_2\text{I}$  carbenoid) becomes more favored in the competition with the carbometalation pathway (8.2 kcal/mol for the  $\text{LiCH}_2\text{Br}$  carbenoid and 8.5 kcal/mol for the  $\text{LiCH}_2\text{I}$  carbenoid), as shown in Fig. 2.

It is necessary to further understand why the substituent has different effect on the methylene transfer and carbometalation pathways. Structural changes and other parameters of the lithium carbenoid from starting materials to transition states are summarized in Table 2. As for the methylene transfer pathway, the concerted step is strongly exothermic by 50–60 kcal/mol. The  $\text{TS}_M\text{-X}$  is a typical early transition state similar to the reactant complex. The transition state of  $\text{LiCH}_2\text{F}$  has the largest structural change among the investigated lithium carbenoids. The  $\text{C}^1\text{-Li}$  and  $\text{C}^1\text{-F}$  distances elongate 4.0% and 24.4%, and the  $\text{Li-F}$  distance shortens 5.5%. Therefore,  $\text{TS}_M\text{-F}$  is the least early transition state and has the highest activation energy. In the case of the  $\text{LiCH}_2\text{Cl}$ ,  $\text{LiCH}_2\text{Br}$  and  $\text{LiCH}_2\text{I}$  carbenoids, the structural changes are comparative to each other and smaller than that of the  $\text{LiCH}_2\text{F}$  carbenoid. The structural change of the  $\text{LiCH}_2\text{Cl}$  carbenoid is:  $\text{C}^1\text{-Li}$  (2.7%),  $\text{C}^1\text{-Cl}$  (21.2%) and  $\text{Li-Cl}$  (-4.0%); the structural change of the  $\text{LiCH}_2\text{Br}$  carbenoid is:  $\text{C}^1\text{-Li}$  (2.7%),  $\text{C}^1\text{-Br}$  (19.7%) and  $\text{Li-Br}$  (-4.1%); and the structural change of the  $\text{LiCH}_2\text{I}$  carbenoid is:  $\text{C}^1\text{-Li}$  (2.4%),  $\text{C}^1\text{-I}$  (18.6%) and  $\text{Li-I}$  (-3.9%). This is consistent with the trend of the activation energies along the methylene transfer pathway:  $\text{LiCH}_2\text{F}$  (9.8 kcal/mol) >  $\text{LiCH}_2\text{Cl}$  (7.6 kcal/mol)  $\approx$   $\text{LiCH}_2\text{Br}$  (7.4 kcal/mol)  $\approx$   $\text{LiCH}_2\text{I}$  (7.5 kcal/mol). In contrast with  $\text{TS}_M\text{-X}$ ,  $\text{TS}_C\text{-X}$  of the carbometalation pathway is not a very typical early transition state. The process  $\text{RC} \rightarrow \text{TS}_C\text{-X} \rightarrow \text{IM-X}$  is exothermic by about 20 kcal/mol and this is much lower than that of the process  $\text{RC} \rightarrow \text{TS}_M\text{-X} \rightarrow \text{PC}$ . As the transition state  $\text{TS}_C\text{-X}$  which is not very similar to  $\text{RC}$ , the trend of the activation energies can not be straightly interpreted by the structural changes of the lithium carbenoid from starting materials to transition states. The  $\text{LiCH}_2\text{F}$  carbenoid has the largest structural change among the investigated lithium carbenoids ( $\text{C}^1\text{-Li}$ , 6.8%;  $\text{C}^1\text{-F}$ , -5.9%;  $\text{Li-F}$ , 4.2%), but it has the lowest activation energy (6.1 kcal/mol) among them. On the other hand, the  $\text{LiCH}_2\text{I}$  carbenoid has the smallest structural change

Table 2

Calculated bond lengths, bond elongation (%)<sup>a</sup>, hybridization character of the  $\text{C}^1$  atom of the bond for the lithium carbenoid  $\text{LiCH}_2\text{X}$  (X = F, Cl, Br and I)

	$\text{C}^1\text{-Li}$		Hybr. $\text{C}^1$	$\text{C}^1\text{-X}$		Hybr. $\text{C}^1$	$\text{Li-X}$		$\phi^b$
	$r$ (Å)	Elong. (%) <sup>a</sup>		$r$ (Å)	Elong. (%) <sup>a</sup>		$r$ (Å)	Elong. (%) <sup>a</sup>	
$\text{LiCH}_2\text{F}$	1.915		$\text{sp}^{1.67}$	1.590		$\text{sp}^{10.17}$	1.744		15.2
$\text{TS}_M\text{-F}$	1.992	4.0		1.979	24.4		1.648	-5.5	
$\text{TS}_C\text{-F}$	2.046	6.8		1.496	-5.9		1.818	4.2	
$\text{LiCH}_2\text{Cl}$	1.934		$\text{sp}^{1.64}$	1.997		$\text{sp}^{11.98}$	2.219		4.6
$\text{TS}_M\text{-Cl}$	1.987	2.7		2.421	21.2		2.131	-4.0	
$\text{TS}_C\text{-Cl}$	2.056	6.3		1.907	-4.5		2.278	2.6	
$\text{LiCH}_2\text{Br}$	1.943		$\text{sp}^{1.57}$	2.148		$\text{sp}^{14.48}$	2.379		2.9
$\text{TS}_M\text{-Br}$	1.994	2.7		2.517	19.7		2.282	-4.1	
$\text{TS}_C\text{-Br}$	2.051	5.6		2.092	-2.6		2.431	2.2	
$\text{LiCH}_2\text{I}$	1.950		$\text{sp}^{1.53}$	2.346		$\text{sp}^{16.17}$	2.620		-1.2
$\text{TS}_M\text{-I}$	1.996	2.4		2.781	18.6		2.517	-3.9	
$\text{TS}_C\text{-I}$	2.036	4.4		2.341	-0.2		2.650	1.2	

<sup>a</sup> Bond elongation in the transition states as compared to the bond lengths of the  $\text{LiCH}_2\text{X}$  carbenoid, a negative change (%) means a shortening.

<sup>b</sup>  $\phi$  is the value of the angle between the  $\text{C}^1\text{HH}$  plane and the  $\text{Li-C}^1$  bond, as show in  $\text{SM-X}$  in Fig. 1.

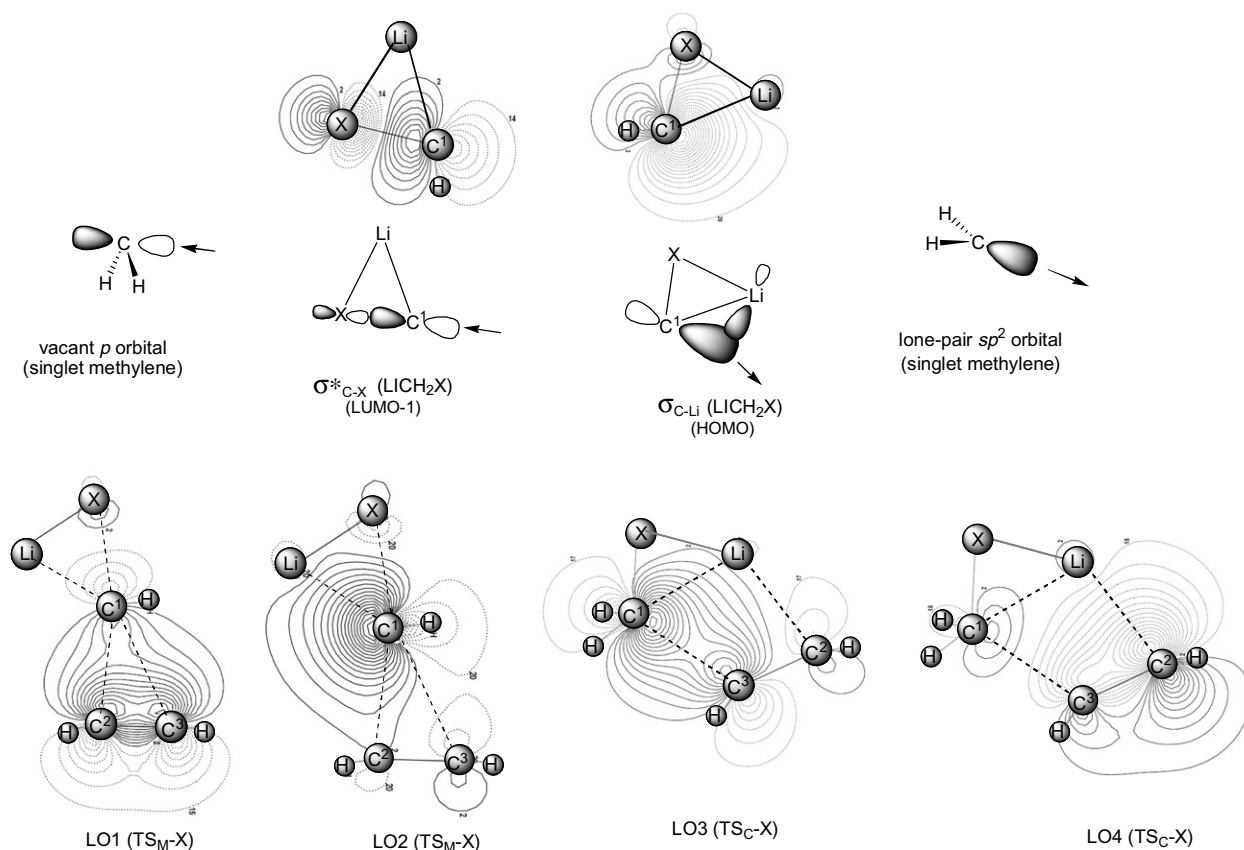


Fig. 3. Localized Kohn–Sham orbitals (LOs) of the lithium carbenoid  $\text{LiCH}_2\text{X}$  and the transition states are shown in contour plot type.

( $\text{C}^1\text{-Li}$ , 4.4%;  $\text{C}^1\text{-I}$ ,  $-0.2\%$ ;  $\text{Li-I}$ , 1.2%) but has the highest activation energy (8.5 kcal/mol). This may attribute to that the  $\text{C-X}$  bond is strengthened in the transition state instead of broken.

The analysis of the electronic structures of the carbenoids can help to understand the origin of the mechanistic dichotomy and the different substituent effect on them. With the aid of Boys' localized Kohn–Sham orbitals, one can see that the LUMO-1 of  $\text{LiCH}_2\text{X}$  represents the  $\text{C}^1\text{-X}$   $\sigma^*$  bond and the HOMO of  $\text{LiCH}_2\text{X}$  represents the  $\text{C}^1\text{-Li}$   $\sigma$  bond. The  $\text{C}^1\text{-X}$   $\sigma^*$  bond is quite close to the vacant  $p$  orbital of the singlet methylene (the simplest carbene) and the HOMO of  $\text{LiCH}_2\text{X}$  resembles quite closely the lone-pair  $sp^2$  orbital of the singlet methylene, as suggested by Houk et al. [52]. As shown in Fig. 3, the  $\text{C}^1\text{-X}$   $\sigma^*$  bond prefers to accept the  $\pi$  bond electrons of the ethylene in the arrow direction, leading to the formation of the “butterfly-type”  $\text{TS}_{\text{M-X}}$  on the methylene transfer pathway. On the other hand, the HOMO of  $\text{LiCH}_2\text{X}$  prefers to nucleophilically attack on the  $\pi^*$  ethylene orbital, which leads to the formation of the four-centered transition state  $\text{TS}_{\text{C-X}}$  along the carbometalation pathway.

As for  $\text{TS}_{\text{M-X}}$  of the methylene transfer pathway, as shown in Fig. 3, LO1 represents the interaction between the  $\text{C}^1\text{-X}$   $\sigma^*$  bond of the carbenoid and the  $\pi$  bond of the ethylene, accompanied with the cleavage of the  $\text{C}^1\text{-X}$   $\sigma$  bond. LO2 indicates that the  $\text{C}^1\text{-Li}$   $\sigma$  bond interacts with

the  $\pi^*$  ethylene orbital, assisting to break the  $\text{C}^2=\text{C}^3$  double bond to form cyclopropane. This leads to the partial formation of the  $\text{C}^1\text{-C}^2$   $\sigma$  bond in  $\text{TS}_{\text{M-X}}$  and indicates the asynchronous manner of the cycloaddition for the methylene transfer pathway [33]. As for  $\text{TS}_{\text{C-X}}$  of the carbometalation pathway, LO3 represents good overlap of the  $\text{C}^1\text{-Li}$   $\sigma$  bond with the polarized  $\pi^*$  orbital of ethylene, leading to the formation of the  $\text{C}^1\text{-C}^3$   $\sigma$  bond, as shown in Fig. 3. The  $\text{C}^2\text{-Li}$  bond incline to form synchronously leading to the four-centered transition state, which can be identified in LO4 that the  $\pi$  orbital is strongly polarized toward the  $\text{C}^2$  atom. The orbital analysis reveals that these two transition states have significant difference in the electronic character. The formation of  $\text{TS}_{\text{M-X}}$  for the methylene transfer pathway results mainly from the interaction between the electrophilic  $\text{C}^1\text{-X}$   $\sigma^*$  bond with the  $\pi$  bond of the ethylene, on the other hand, the formation of  $\text{TS}_{\text{C-X}}$  for the carbometalation pathway results mainly from the interaction between the nucleophilic  $\text{C}^1\text{-Li}$   $\sigma$  bond with the  $\pi^*$  bond of the ethylene. The diagrams of the key orbital interaction of the transition states are shown in Fig. 4. It is well-known that the stabilization energy of the bonding MO depends on the energy difference between the corresponding fragment molecular orbitals. As shown in Table 2, the hybridization character of the  $\text{C}^1$  atom in the  $\text{C}^1\text{-X}$  bond obtained from NBO analysis is  $sp^{10.17}$  for the  $\text{LiCH}_2\text{F}$  carbenoid,  $sp^{11.98}$  for the  $\text{LiCH}_2\text{Cl}$  carbenoid,  $sp^{14.48}$  for the  $\text{LiCH}_2\text{Br}$  carbenoid

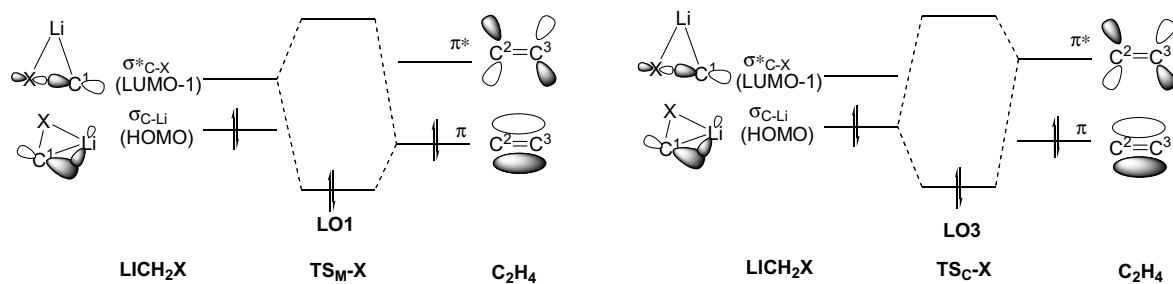


Fig. 4. Orbital interaction diagrams of the transition states  $TS_M-X$  and  $TS_C-X$ .

and  $sp^{17.17}$  for the  $LiCH_2I$  carbenoid. A higher  $p$  character of  $C^1$  atom in the  $C^1-X$  bond corresponds to a  $C-X$   $\sigma$  orbital with higher energy and a  $C-X$   $\sigma^*$  bond with lower energy, indicating a stronger electrophilic character of the carbenoids [7]. The lower energy of the  $C^1-X$   $\sigma^*$  bond of the lithium carbenoid, the smaller difference in energy between the  $C^1-X$   $\sigma^*$  bond and the  $\pi$  bond of the ethylene, and the more stabilization energy is obtained for the LO1 of the  $TS_M-X$ . This is in consistent with the appropriate decay trend of the activation energies along the methylene transfer pathway:  $LiCH_2F$  (9.8 kcal/mol) >  $LiCH_2Cl$  (7.6 kcal/mol)  $\approx$   $LiCH_2Br$  (7.4 kcal/mol)  $\approx$   $LiCH_2I$  (7.5 kcal/mol). As depicted in Fig. 4, if the  $C^1-Li$   $\sigma$  bond of the lithium carbenoid has a higher energy,  $C^1-Li$   $\sigma$  bond can donor to the  $\pi^*$  bond of the ethylene more easily to form the LO3 in the  $TS_C-X$  with more stabilization energy. As listed in Table 2, the hybridization character of the  $C^1$  atom in the  $C^1-Li$   $\sigma$  bond of the  $LiCH_2F$ ,  $LiCH_2Cl$ ,  $LiCH_2Br$  and  $LiCH_2I$  carbenoids are  $sp^{1.67}$ ,  $sp^{1.64}$ ,  $sp^{1.57}$  and  $sp^{1.53}$ , respectively. The lower  $s$  component in the hybridization character indicates a  $C^1-Li$   $\sigma$  bond with higher energy, leading to lower activation energy for the carbometalation. This reflects interestingly in the structure of the lithium carbenoid. The angle  $\phi$  between the  $C^1HH$  plane and the  $Li-C^1$  bond is larger as the lower  $s$  component in the hybridization character of the  $C^1$  atom in the  $C^1-Li$   $\sigma$  bond, making the  $C^1-Li$   $\sigma$  bond more exposed to interact with the ethylene, as shown in Fig. 1. The angle  $\phi$  decreases in the trend:  $LiCH_2F$  ( $15.2^\circ$ ) >  $LiCH_2Cl$  ( $4.6^\circ$ ) >  $LiCH_2Br$  ( $2.9^\circ$ ) >  $LiCH_2I$  ( $-1.2^\circ$ ), which is in good agreement with the trend of the activation energies along the carbometalation pathway:  $LiCH_2F$  (6.1 kcal/mol) <  $LiCH_2Cl$  (7.1 kcal/mol) <  $LiCH_2Br$  (8.2 kcal/mol) <  $LiCH_2I$  (8.5 kcal/mol). It is worthy of noting that the preferable orbital interaction possibly cause the large structural change.<sup>1</sup> This is why the  $TS_C-F$  has the largest structural change, whereas it has the lowest activation energy among the carbenoids investigated. Thus the substituent influences the hybridization character of the  $C^1$  atom leading to different effect on the methylene transfer and carbometalation pathways, which is revelatory for us that it may be a viable way to controlling mechanistic competition to obtain target product by modifying the substituents of the lithium carbenoids.

## 5. Conclusion

In this paper, we have studied the cyclopropanation reactions of the  $LiCH_2X$  ( $X = F, Cl, Br$  and  $I$ ) carbenoids with ethylene at the CCSD(T)/6-311G\*\*//B3LYP/6-311G\*\* level of theory along two reaction pathways: methylene transfer and carbometalation. The present studies revealed that the substituent of the lithium carbenoid has different effect on these two reaction pathways, leading to the mechanistic competition variations during the cyclopropanation reactions.

The methylene transfer and carbometalation pathways have comparative activation energies to each other for the different substituted lithium carbenoids. There exists an competition compete between these two reaction pathways, which agrees with the experimental results by Hoffmann and coworkers, [29] as well as the computational results by Nakamura et al. [27,28]. Interestingly, the substituent has different effect on the methylene transfer and carbometalation pathways. The trend of the activation energies along the methylene transfer pathway is  $LiCH_2F$  (9.8 kcal/mol) >  $LiCH_2Cl$  (7.6 kcal/mol)  $\approx$   $LiCH_2Br$  (7.4 kcal/mol)  $\approx$   $LiCH_2I$  (7.5 kcal/mol), whereas the activation energies along the carbometalation pathway increases in this order:  $LiCH_2F$  (6.1 kcal/mol) <  $LiCH_2Cl$  (7.1 kcal/mol) <  $LiCH_2Br$  (8.2 kcal/mol) <  $LiCH_2I$  (8.5 kcal/mol). Thus the competition between these two pathways varies interestingly when changing the substituents of the lithium carbenoids. The different effect mainly arises from that the substituent of the lithium carbenoid influences the hybridization character of the  $C^1$  atom. The result is revelatory for us that it is a potential way to control the mechanistic competition to obtain target product by modifying the substituents of the lithium carbenoids.

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## Appendix A. Supplementary material

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.jorganchem.2007.05.014.

<sup>1</sup> Helpful suggestion from referee's comments.



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