JOC Article

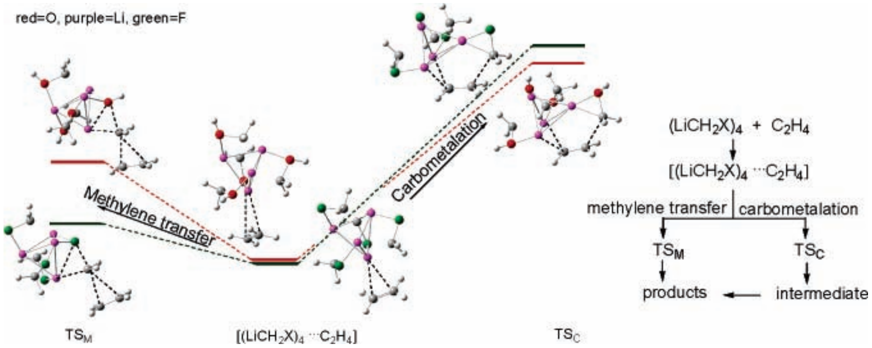
Methylene Transfer or Carbometalation? A Theoretical Study to Determine the Mechanism of Lithium Carbenoid-Promoted Cyclopropanation Reactions in Aggregation and Solvation States

Zhuofeng Ke,[†] Cunyuan Zhao,*[,†,‡] and David Lee Phillips[§]

School of Chemistry and Chemical Engineering, Sun Yat-Sen University, Guangzhou 510275, China, Ministry of Education Laboratory of Bioinorganic and Synthetic Chemistry, School of Chemistry and Chemical Engineering, Sun Yat-Sen University, Guangzhou 510275, China, and Department of Chemistry, The University of Hong Kong, Pokfulam Road, Hong Kong, China

ceszhcy@mail.sysu.edu.cn

Received October 14, 2006



Density functional theory calculations for the lithium carbenoid-promoted cyclopropanations in aggregation and solvation states are presented in order to investigate the controversy of the mechanistic dichotomy, that is, the methylene-transfer mechanism and the carbometalation mechanism. The methylene-transfer mechanism represents the reaction reality, whereas the carbometalation pathway does not appear to compete significantly with the methylene-transfer pathway and should be ruled out as a major factor. A simple model calculation for monomeric lithium carbenoid-promoted cyclopropanations with ethylene in the gas phase is not sufficient to reflect the reaction conditions accurately or to determine the reaction mechanism since its result is inconsistent with the experimental facts. The aggregated lithium carbenoids are the most probable reactive species in the reaction system. The calculated reaction barriers of the methylene-transfer pathways are 10.1 and 8.0 kcal/mol for the dimeric $(LiCH_2F)_2$ and tetrameric $(LiCH_2F)_4$ species, respectively, compared with the reaction barrier of 16.0 kcal/mol for the monomeric $LiCH_2F$ species. In contrast, the reaction barriers of the carbometalation pathways are 26.8 kcal/mol for the dimeric $(LiCH_2F)_2$ and 33.9 kcal/mol for the tetrameric $(LiCH_2F)_4$ species, compared with the reaction barrier of 12.5 kcal/mol for the monomeric $LiCH_2F$ species. The effects of solvation were investigated by explicit coordination of the solvent molecules to the lithium centers. This solvation effect is found to enhance the methylene-transfer pathway, while it is found to impede the carbometalation pathway instead. The combined effects of the aggregation and solvation lead to barriers to reaction in the range of 7.2−9.0 kcal/mol for lithium carbenoid-promoted cyclopropanation reactions along the methylene-transfer pathway. Our computational results are in good agreement with the experimental observations.

Introduction

Carbenoid-promoted cyclopropanation reactions are a very important method to produce cyclopropanes. Since the pioneering work by Simmons and Smith[1,2] using $IZnCH_2I$ reacted with olefins to form cyclopropanes, many efforts have been invested in this field not only for synthetical utilities[3−8] but also for

---

* To whom correspondence may be addressed. Fax: 86-20-8411-0696. Phone: 86-20-8411-0696.

[†] School of Chemistry and Chemical Engineering, Sun Yat-Sen University.

[‡] Ministry of Education Laboratory of Bioinorganic and Synthetic Chemistry, Sun Yat-Sen University.

[§] The University of Hong Kong.

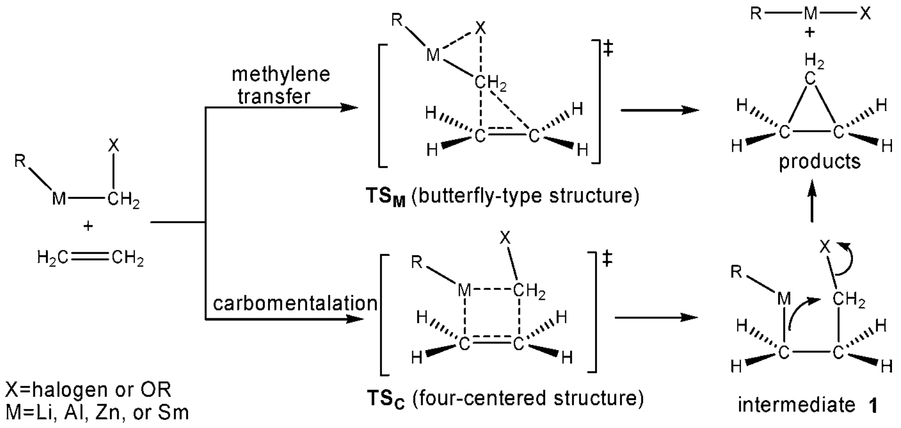
(1) Simmons, H. E.; Smith, R. D. *J. Am. Chem. Soc.* **1958**, *80*, 5323−5324.

(2) Simmons, H. E.; Smith, R. D. *J. Am. Chem. Soc.* **1959**, *81*, 4256−4265.

(3) Boche, G.; Lohrenz, J. C. W. *Chem. Rev.* **2001**, *101*, 697−756.

10.1021/jo062129i CCC: $37.00

SCHEME 1. The Methylene-Transfer Mechanism and Carbometalation Mechanism for Carbenoid-Promoted Cyclopropanation Reactions



theoretical interest.[9−16] There has long been a mechanistic discussion about these cyclopropanation reactions, that is, a methylene-transfer pathway and a carbometalation pathway (see Scheme 1).[10,11,13,17,18] The methylene-transfer mechanism was originally proposed by Simmons and Smith[2] and is a concerted [1 + 2] addition through a butterfly-type transition state (TS_M), accompanied by a migration of the halide anion from the carbon atom to the metal atom. On the other hand, the two-step carbometalation mechanism involves a four-centered transition state (TS_C) to give intermediate **1** followed by an intramolecular substitution to furnish the cyclopropane.[11,17−19]

The mechanistic dichotomy for carbenoid-promoted cyclopropanation reactions is suggested to be metal dependent. For zinc carbenoids, Wittig reported an experimental proof for the methylene-transfer pathway,[17] and theoretical comparison[11,13] also suggests that the methylene-transfer pathway represents the reaction reality. Aluminum carbenoid-promoted cyclopropanations were first found experimentally by Yamamoto and coworkers,[20] and recent calculations suggested that the methylene-transfer pathway is predominantly favored and that the competition from the carbometalation pathway is negligible.[21] Lithium carbenoids were found early in the 1960s to give the expected arylcyclopropanes in the presence of olefins at −10 °C with the yields ranging from fair to good.[22] However, the controversy of the mechanistic dichotomy for lithium carbenoid-promoted cyclopropanations has not yet been resolved. Hoberg reported that carbometalation might operate,[19] whereas Burger has thought carbometalation should be unreasonable.[23] Hoffmann and Nakamura suggested in later publications that methylene-transfer and carbometalation pathways might compete in lithium carbenoid-promoted cyclopropanations.[11,13,18] Nakamura and co-workers calculated the cyclopropanation reaction of $LiCH_2Cl$ with C_2H_4 at the B3LYP/6-31G* level and found that the transition-state energy for the methylene-transfer pathway is 3.8 kcal/mol and that for the carbometalation is 2.1 kcal/mol. They suggested that there was a competition between these two pathways. Samarium carbenoids,[24,25] having similar properties to the lithium carbenoids, may also have this mechanistic dichotomy.[14,15] Experimental evidence is still not available to determine this mechanistic controversy. Which pathway represents the reaction reality? Does competition between them exist in the reaction reality? Further investigation is necessary to settle this fundamental mechanistic question.

It has been experimentally documented that the $LiCH_2-$halogen carbenoids are much more reactive than the $LiCH_2-$OR for cyclopropanation reactions.[12,26−28] From experimental experience, it is evident that the $LiCH_2-$halogen can cyclopropanate olefins efficiently even at −78 °C.[12,22] However, the low tendency of the $LiCH_2OR$ carbenoids for cyclopropanations was reported by Schöllkopf et al. They found that the reactions of LiCH(Ph)−OPh with olefins only give cyclopropanes in very low yields. The influence of the leaving groups, X (X = F, Cl, Br, I, and OH), on the carbenoid character of the $LiCH_2X$ was

---

(4) Charette, A. B.; Marcoux, J. F. *Synlett* **1995**, 1197−1207.

(5) Lebel, H.; Marcoux, J. F.; Molinaro, C.; Charette, A. B. *Chem. Rev.* **2003**, *103*, 977−1050.

(6) Lautens, M.; Klute, W.; Tam, W. *Chem. Rev.* **1996**, *96*, 49−92.

(7) DelMonte, A. J.; Dowdy, E. D.; Watson, D. J. *Top. Organomet. Chem.* **2004**, *6*, 97−122.

(8) Charette, A. B.; Beauchemin, A. *Org. React.* **2001**, *58*, 1−415.

(9) (a) Mareda, J.; Rondan, N. G.; Houk, K. N.; Clark, T.; Schleyer, P. v. R. *J. Am. Chem. Soc.* **1983**, *105*, 6997−6999. (b) Rohde, C.; Clark, T.; Kaufmann, E.; Schleyer, P. v. R. *J. Chem. Soc., Chem. Commun.* **1982**, 882−884.

(10) Bernardi, F.; Bottoni, A.; Miscione, G. P. *J. Am. Chem. Soc.* **1997**, *119*, 12300−12305. Bernardi et al. also proposed another reaction pathway related to the Simmons−Smith reaction, the C−H insertion pathway to form propene.

(11) Hirai, A.; Nakamura, M.; Nakamura, E. *Chem. Lett.* **1998**, 927−928.

(12) Hermann, H.; Lohrenz, J. C. W.; Kuhn, A.; Boche, G. *Tetrahedron* **2000**, *56*, 4109−4115.

(13) Nakamura, M.; Hirai, A.; Nakamura, E. *J. Am. Chem. Soc.* **2003**, *125*, 2341−2350.

(14) Zhao, C. Y.; Wang, D. Q.; Phillips, D. L. *J. Am. Chem. Soc.* **2003**, *125*, 15200−15209.

(15) Wang, D. Q.; Zhao, C. Y.; Phillips, D. L. *J. Org. Chem.* **2004**, *69*, 5512−5515.

(16) Zhao, C. Y.; Wang, D. Q.; Phillips, D. L. *J. Am. Chem. Soc.* **2002**, *124*, 12903−12914.

(17) Wittig, G.; Wingler, F. *Chem. Ber.* **1964**, *97*, 2146−2164.

(18) Stiasny, H. C.; Hoffmann, R. W. *Chem.−Eur. J.* **1995**, *1*, 619−624.

(19) Hoberg, H. *Liebigs Ann. Chem.* **1962**, *656*, 1−14.

(20) Maruoka, K.; Fukutani, Y.; Yamamoto, H. *J. Org. Chem.* **1985**, *50*, 4412−4414.

(21) Li, Z.-H.; Ke, Z. F.; Zhao, C. Y.; Geng, Z.-Y.; Wang, Y.-C.; Phillips, D. L. *Organometallics* **2006**, *25*, 3735−3742.

(22) Closs, G. L.; Moss, R. A. *J. Am. Chem. Soc.* **1964**, *86*, 4042−4053.

(23) Burger, U.; Huisgen, R. *Tetrahedron Lett.* **1970**, *11*, 3049−3051.

(24) Molander, G. A.; Etter, J. B.; Zinke, P. W. *J. Am. Chem. Soc.* **1987**, *109*, 453−463.

(25) Imamoto, T.; Takiyama, N. *Tetrahedron Lett.* **1987**, *28*, 1307−1308.

(26) Boche, G.; Opel, A.; Marsch, M.; Harms, K.; Haller, F.; Lohrenz, J. C. W.; Thiimmler, C.; Koch, W. *Chem. Ber.* **1992**, *125*, 2265−2273.

(27) Bosold, F.; Zulauf, P.; Marsch, M.; Harms, K.; Lohrenz, J.; Boche, G. *Angew. Chem., Int. Ed. Engl.* **1991**, *30*, 1455−1457.

(28) Schöllkopf, U.; Eisert, M. *Liebigs Ann. Chem.* **1963**, *664*, 76−88.

studied theoretically by Boche and co-workers.[12] They focused only on the methylene-transfer mechanism and found that different $LiCH_2$−halogen carbenoids have rather similar low transition-state energies, but the $LiCH_2$−OH has a roughly 2.5 times higher transition-state energy than that of the $LiCH_2$−halogen. The different influences of the X substituents on the mechanistic dichotomy of the lithium carbenoid-promoted cyclopropanations, however, have not yet been examined further. In the light of our continuing interest on carbenoid-promoted cyclopropanation reactions,[14−16,21,29] we have performed quantum mechanical studies on cyclopropanations of the $LiCH_2X$ (X = halogen and OR) carbenoids with ethylene along the methylene-transfer and carbometalation pathways to help determine the reaction mechanism.

Organolithium compounds are often depicted as mononuclear species. However, such compounds are, in fact, aggregated species (see a review by van Koten et al. and reference therein[30]). The different aggregation states may exhibit different properties and reactivities.[31] For instance, *n*-BuLi itself is a hexamer (*n*-Bu_6Li_6) in the solid state, and this aggregation state is at least partially retained in solution in apolar media; however, in solvents such as diethyl ether, the presence of tetramers and dimers becomes predominant.[32] A NMR study revealed that the TMEDA solvate of 2-lithiobenzofuran and 2-lithiobenzothiophene is dimeric in toluene, similar to the calculated dimeric structures for fluoromethyllithium and chloromethyllithium.[31,33] A recent computational study of mixed aggregates of chloromethyllithium with lithium dialkylamides was reported by Pratt.[34] All of these results might be expected to have some resemblance to the $LiCH_2X$ carbenoids. Some early reports suggested that the thermodynamics of dissociation of carbenoids to produce free carbene depends on the states of aggregation.[3,9b] These aggregated species are important for the interpretation of the reaction properties and the information related to mechanism(s) of the cyclopropanations. To our knowledge, there have been no studies examining how the aggregated lithium carbenoids influence the reactivities of the lithium carbenoid-promoted cyclopropanations. Here, we are pleased to report a computational study of the cyclopropanations of the aggregated lithium carbenoid species with ethylene on both methylene-transfer and carbometalation pathways. Our results show that the methylene-transfer pathway is highly favored over the carbometalation pathway in the aggregation states. Comparison of different substituted lithium carbenoid ($LiCH_2$−halogen and $LiCH_2OR$)-promoted cyclopropanations in aggregation states strongly supports our results and is in good agreement with the experimental observations.

Solvent molecules may be strongly coordinated, and it is essential to include this effect in realistic models of the structures and reactivity of reactive species in the solution phase.[31] Persistent coordination of polar solvent molecules to organolithium in the liquid solution phase has been well-documented by NMR spectroscopy, kinetics, and computational methods, as well X-ray crystal structural characterization.[36−42] Recently, Pratt and co-workers reported structural studies on lithium carbenoids in ethereal solvent.[31,43] In the study of the reaction of the analogous organolithium compound MeLi with formaldehyde, Hæffner showed that the solvent has a pronounced effect on these reactions and results in mechanism variations.[35] A recent study by Zhao et al. also revealed that solvation has a different effect on the mechanistic dichotomy for cyclopropanations of a samarium carbenoid with ethylene.[14] However, to our knowledge, the explicit solvation effect on the lithium carbenoid-promoted cyclopropanations has not been considered in previous theoretical studies. Here, we have investigated how solvation affects the mechanism by explicitly coordinating solvent molecules to the monomeric and aggregated lithium carbenoids. Explicit solvation has substantially different effects on the mechanistic dichotomy. Explicit solvation enhances the methylene-transfer pathway but impedes the carbometalation pathway. The combined aggregation and solvation effects make the reaction barrier of the methylene transfer decrease to the 7.2−9.0 kcal/mol range, whereas the reaction barrier of the carbometalation pathway is predicted to be much higher. Our study indicates that calculations simply with the monomeric species in the gas phase cannot accurately reflect the real reaction. The investigation shows how both aggregation and solvation influence the reaction mechanism(s) for lithium carbenoid-promoted cyclopropanation reactions and also offers insight into the reaction mechanisms of many aggregated organometallic compounds in polar solvents.

Computational Methods

All molecules and transition states were fully optimized with the density functional theory (DFT) using the hybrid B3LYP density functional.[44,45] 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[46,47] were performed to confirm the transition states connecting the relevant reactants and products. All geometry optimizations, frequency calculations, and IRC calculations were carried out with the 6-311G** basis set[48−50] for all of the atoms of

---

(29) Wang, D. Q.; Phillips, D. L.; Fang, W. H. *Organometallics* **2002**, *21*, 5901−5910.

(30) Gossage, R. A.; Jastrzebski, J. T. B. H.; van Koten, G. *Angew. Chem., Int. Ed.* **2005**, *44*, 1448−1454.

(31) Pratt, L. M.; Ramachandran, B.; Xidos, J. D.; Cramer, C. J.; Truhlar, D. G. *J. Org. Chem.* **2002**, *67*, 7607−7612.

(32) Kottke, T.; Stalke, D. *Angew. Chem., Int. Ed. Engl.* **1993**, *32*, 580−582.

(33) Harden, S.; Boersma, J.; Brandsma, L.; Kanters, J. A.; Bauer, W.; Pi, R.; Schleyer, P. v. R.; Scholhorn, H.; Thewalt, U. *Organometallics* **1989**, *8*, 1688−1696.

(34) Pratt, L. M.; Le, L. T.; Truong, T. N. *J. Org. Chem.* **2005**, *70*, 8298−8302.

(35) Hæffner, F.; Sun, C.; Williard, P. G. *J. Am. Chem. Soc.* **2000**, *122*, 12542−12546.

(36) Fraenkel, G.; Chow, A.; Winchester, W. R. *J. Am. Chem. Soc.* **1990**, *112*, 2582−2585.

(37) Fraenkel, G.; Duncan, J. H.; Wang, J. H. *J. Am. Chem. Soc.* **1999**, *121*, 432−443.

(38) Fraenkel, G.; Duncan, J. H.; Martin, K.; Wang, J. *J. Am. Chem. Soc.* **1999**, *121*, 10538−10544.

(39) Sun, X.; Collum, D. B. *J. Am. Chem. Soc.* **2000**, *122*, 2452−2458.

(40) Sun, X.; Collum, D. B. *J. Am. Chem. Soc.* **2000**, *122*, 2459−2463.

(41) Chadwick, S. T.; Rennels, R. A.; Rutherford, J. L.; Collum, D. B. *J. Am. Chem. Soc.* **2000**, *122*, 8640−8647.

(42) Rutherford, J. L.; Collum, D. B. *J. Am. Chem. Soc.* **2001**, *123*, 199−202.

(43) Pratt, L. M.; Nguyen, N. V.; Le, L. T. *J. Org. Chem.* **2005**, *70*, 2294−2298.

(44) Lee, C. T.; Yang, W. T.; Parr, R. G. *Phys. Rev. B* **1988**, *37*, 785−789.

(45) Niecke, E.; Becker, P.; Nieger, M.; Stalke, D.; Schoeller, W. W. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 1849−1852.

(46) Gonzalez, C.; Schlegel, H. B. *J. Phys. Chem.* **1990**, *94*, 5523−5527.

(47) Gonzalez, C.; Schlegel, H. B. *J. Chem. Phys.* **1989**, *90*, 2154−2161.

(48) Krishnan, R.; Binkley, J. S.; Seeger, R.; Pople, J. A. *J. Chem. Phys.* **1980**, *72*, 650−654.

(49) Curtiss, L. A.; McGrath, M. P.; Blaudeau, J.-P.; Davis, N. E.; Binning, R. C., Jr.; Radom, L. *J. Chem. Phys.* **1995**, *103*, 6104−6113.

(50) Blaudeau, J.-P.; McGrath, M. P.; Curtiss, L. A.; Radom, L. *J. Chem. Phys.* **1997**, *107*, 5016−5021.

reactions. The Boys localization procedure[51,52] was performed to obtain localized Kohn−Sham orbitals[53] (LOs). Natural bond orbital (NBO) analysis was performed at the same level as the one used for geometry optimization.[54] All of the calculations were carried out using the Gaussian 03 program.[55] For the computational facility, $LiCH_2F$ was selected as an example for the $LiCH_2$−halogen carbenoids commonly used in experiments. A previous study showed that different $LiCH_2$−halogen carbenoids have rather similar reactivities during cyclopropanations.[12] $LiCH_2OH$ was selected as the model for the $LiCH_2OR$ carbenoids, which has a low tendency for cyclopropanations, as documented experimentally. These reactions usually take place in ether solvent. The aggregation states for the carbenoid $LiCH_2X$ are denoted as $(LiCH_2X)_2$ and $(LiCH_2X)_4$ for the dimer and tetramer, respectively, in all of the figures and tables presented here. To estimate the solvation effect, we added dimethylether (DME) molecules explicitly coordinated to the lithium centers of the lithium carbenoids. The lithium carbenoids coordinated with DME molecules are denoted as $(LiCH_2X)_m/(DME)_n$ ($m = 1, 2,$ and 4; $n = 0, 1, 2,$ and 4) in all of the figures and tables presented here. The polarized continuum model (PCM)[56] for ether solvent ($\epsilon = 4.335$) was also applied to estimate reaction barriers using Bondi's set of atomic radii.[57]

According to previous studies,[9,11,12] these cyclopropanation reactions begin with the starting materials [SM = $(LiCH_2X)_m/(DME)_n + C_2H_4$; $m = 1, 2,$ and 4; $n = 0, 1, 2,$ and 4]. The SM first forms the reactant complex (RC). On the methylene-transfer pathway, the formed RC furnishes cyclopropane in a concerted way through the butterfly-type transition state (TS_M). On the carbometalation pathway, the RC goes upon the four-centered transition state (TS_C) to form the intermediate (IM), which then gives the products by a subsequent intramolecular substitution reaction. According to the previous studies of the mechanism dichotomy, the intramolecular substitution process to produce the cyclopropanes will not be discussed further in this paper.[11,13,14]

Results and Discussion

A. Cyclopropanations of the Monomeric $LiCH_2X$ (X = F and OH) Carbenoids with Ethylene. The calculation results of cyclopropanations of the monomeric $LiCH_2X$ (X = F and OH) with ethylene along methylene-transfer and carbometalation pathways are shown in Figure 1.[58] The carbenoid character of $LiCH_2X$ (X = halogen and OR) has attracted experimental and theoretical attentions for some time. The most stable isomer of the monomer $LiCH_2X$ is the one that has a X-bridged, carbon−lithium bond,[3,9,31,59] as shown in SM in Figure 1. Study of the electronic structures of carbenoids helps to understand the origin of the mechanistic dichotomy. With the aid of Boys' localized Kohn−Sham orbitals, we found that the LO1 of $LiCH_2F$ represents the C^1−X σ^* bond, which is quite close to the empty p orbital of the simplest carbene, singlet methylene. This orbital prefers a reaction with nucleophiles in the direction indicated by the arrow in Figure 2.[9a] The electrophilic attack of the C^1−X σ^* bond on the π bond of the ethylene leads to the formation of the butterfly-type TS_M1 on the methylene-transfer pathway. On the other hand, LO2 is responsible for the strong nucleophilic C^1−Li σ bond of $LiCH_2F$, which is quite close to the filled sp^2 orbital of the simplest carbene methylene and prefers a nucleophilic attack in the arrow direction, as shown in Figure 2. The donor of the C^1−Li σ bond to the π^* ethylene orbital leads to the formation of the four-centered transition state TS_C1 along the carbometalation pathway. There is a significant difference between the electronic features of these two transition states. As shown in Figure 2, LO3 of TS_M1 represents the interaction between the C^1−X σ^* bond of the carbenoid $LiCH_2F$ and the π bond of the ethylene. The donor of the π electrons assists to cleave the C^1−X σ bond. One can also see that the C^1−Li σ bond interacts with the π^* ethylene orbital, leading to the partial formation of the C^1−C^2 σ bond and the weakening of the C^1−Li σ bond in LO4. Therefore, it is reasonable to describe the TS_M as a carbenoid $LiCH_2X$ with decomplexed LiX, approaching C_2H_4.[12] As for carbometalation, the π orbital is polarized toward the C^2 atom, leading to the interaction between the C^2 atom and the Li atom, as shown in LO5. LO6 of TS_C1 represents good overlap of the C^1−Li σ bond and the polarized π^* orbital of ethylene in the four-centered transition state, which leads to the strong interaction between the C^1 and C^3 atoms to form the C^1−C^3 σ bond. Therefore, the TS_C can be viewed as the simultaneous addition of the methylene nucleophile and the metal electrophile in a push−pull manner.[60]

SM1 first forms a π-type reactant complex, RC1, which is lower in energy by 8.2 kcal/mol. The formed RC1 then goes upon the transition state TS_M1 along the methylene-transfer pathway or upon the TS_C1 along the carbometalation pathway. The transition-state energies (relative to SM) of TS_M1 and TS_C1 are calculated to be 7.8 and 4.3 kcal/mol, respectively. The calculated transition-state energy of the methylene-transfer pathway is very similar to that obtained by Boche at the MP2/6-311G** level (7.4 kcal/mol). Energy analysis shows that the transition-state energy for the carbometalation pathway is lower than that for the methylene-transfer pathway. A similar result was reported by Nakamura and co-workers for the cyclopropanation reaction of $LiCH_2Cl$ with ethylene at the B3LYP/6-31G* level. They found that the energy of the transition state for the methylene-transfer pathway is 3.8 kcal/mol and that for the carbometalation is 2.1 kcal/mol. They suggested that there may be competition between these two pathways.[11,13] Only judging by the relative energies for the transition states in the

---

(51) Boys, S. F. *Quantum Theory of Atoms, Molecules, and the Solid State*; Academic Press: New York, 1968.

(52) Haddon, R. C.; Williams, G. R. J. *Chem. Phys. Lett.* **1976**, *42*, 453−455.

(53) Kohn, W.; Sham, L. J. *Phys. Rev. A* **1965**, *140*, 1133−1138.

(54) Reed, A. E.; Curtiss, L. A.; Weinhold, F. *Chem. Rev.* **1988**, *88*, 899−926.

(55) Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Montgomery, J. A., Jr.; Vreven, T.; Kudin, K. N.; Burant, J. C.; Millam, J. M.; Iyengar, S. S.; Tomasi, J.; Barone, V.; Mennucci, B.; Cossi, M.; Scalmani, G.; Rega, N.; Petersson, G. A.; Nakatsuji, H.; Hada, M.; Ehara, M.; Toyota, K.; Fukuda, R.; Hasegawa, J.; Ishida, M.; Nakajima, T.; Honda, Y.; Kitao, O.; Nakai, H.; Klene, M.; Li, X.; Knox, J. E.; Hratchian, H. P.; Cross, J. B.; Bakken, V.; Adamo, C.; Jaramillo, J.; Gomperts, R.; Stratmann, R. E.; Yazyev, O.; Austin, A. J.; Cammi, R.; Pomelli, C.; Ochterski, J. W.; Ayala, P. Y.; Morokuma, K.; Voth, G. A.; Salvador, P.; Dannenberg, J. J.; Zakrzewski, V. G.; Dapprich, S.; Daniels, A. D.; Strain, M. C.; Farkas, O.; Malick, D. K.; Rabuck, A. D.; Raghavachari, K.; Foresman, J. B.; Ortiz, J. V.; Cui, Q.; Baboul, A. G.; Clifford, S.; Cioslowski, J.; Stefanov, B. B.; Liu, G.; Liashenko, A.; Piskorz, P.; Komaromi, I.; Martin, R. L.; Fox, D. J.; Keith, T.; Al-Laham, M. A.; Peng, C. Y.; Nanayakkara, A.; Challacombe, M.; Gill, P. M. W.; Johnson, B.; Chen, W.; Wong, M. W.; Gonzalez, C.; Pople, J. A. *Gaussian 03*, revision D.01; Gaussian, Inc.: Wallingford, CT, 2004.

(56) Cossi, M.; Scalmani, G.; Rega, N.; Barone, V. *J. Chem. Phys.* **2002**, *117*, 43−54.

(57) Bondi, A. *J. Phys. Chem.* **1964**, *68*, 441−451.

(58) There may exist another concurrent reaction, the C−H insertion to form propene. We have located the transition state for it, and the structure of this transition state has been added to the Supporting Information. This transition state is similar to those reported by Bernardi et al. (ref 10) and has a relatively high reaction barrier (27.0 kcal/mol at the B3LYP/6-311.G** level of theory). Considering that we are mainly concerned with the mechanisms that produce cyclopropanes for the lithium carbenoids, we didn't discuss it further in this paper.

(59) Qiu, H.; Deng, C. *Chem. Phys. Lett.* **1996**, *249*, 279−283.

(60) Nakamura, E.; Nakamura, M.; Miyachi, Y.; Koga, N.; Morokuma, K. *J. Am. Chem. Soc.* **1993**, *115*, 99−106.

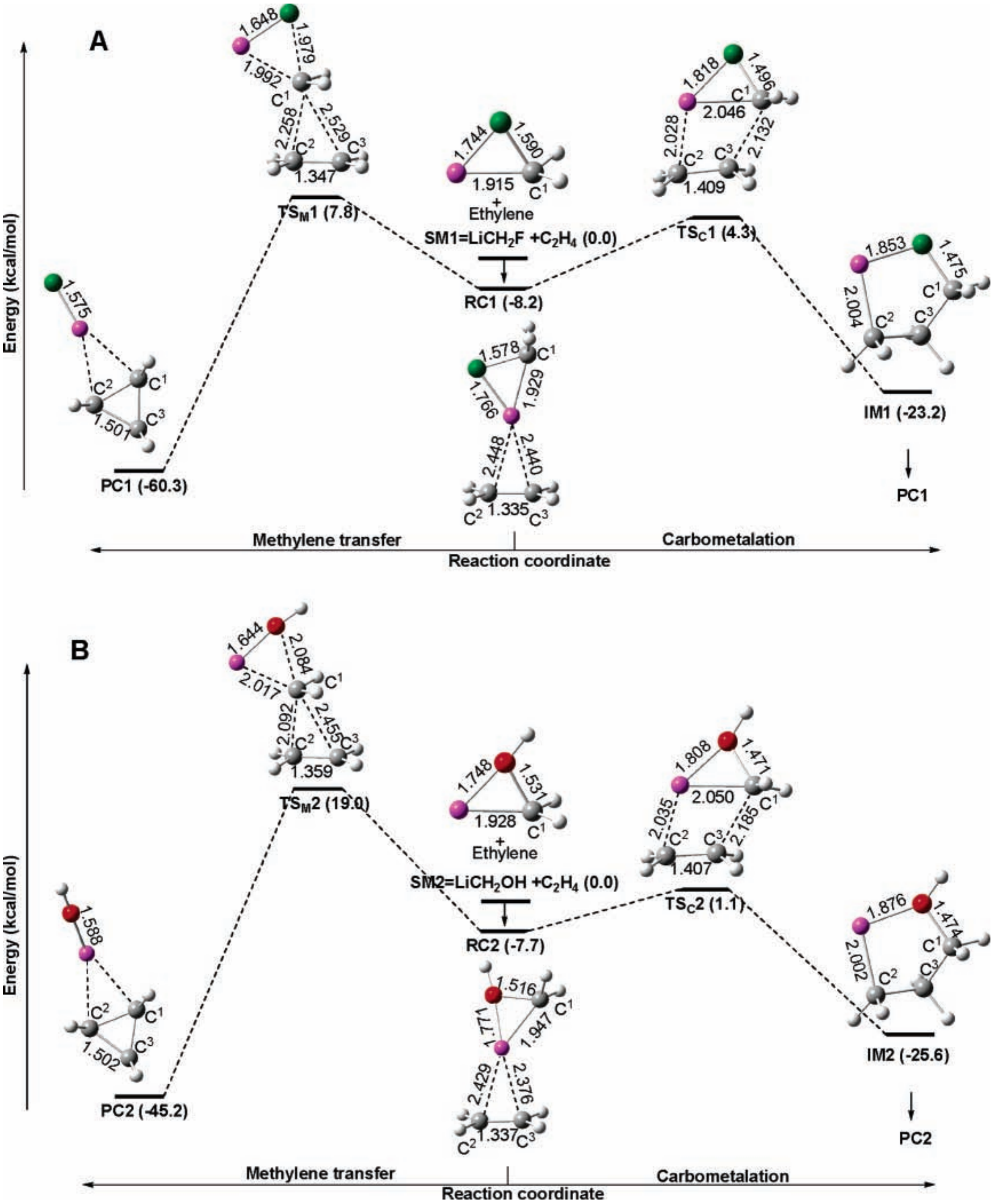


FIGURE 1. Reaction profiles of the monomeric lithium carbenoid LiCH$_2$X (A, X = F and B, X = OH)-promoted cyclopropanations of ethylene along the methylene-transfer and carbometalation pathways (B3LYP/6-311G** level). Selected parameters are given in Å. Energies relative to the starting materials (SM = LiCH$_2$X + ethylene) are shown in kcal/mol in the parentheses. Lithium is shown in purple, oxygen is shown in red, and fluorine is shown in green.

calculation for the cyclopropanations of the monomeric LiCH$_2$F with ethylene in the gas phase, the carbometalation pathway can compete with and even be more favored than the methylene-transfer pathway.

The calculation result of the cyclopropanation of LiCH$_2$OH with ethylene was depicted in Figure 1B. Changing the substituent F to OH, one can see that the distances of the Li−C^1 (2.084 Å) in TS$_M$2 is 36.1% longer than that of the SM2 (1.531 Å), whereas the distances of the Li−C^1 (2.084 Å) in TS$_M$1 is only 24.5% longer than that of the SM1 (1.590 Å). The elongation of O−C^1 bonds from SM2 to TS$_M$2 is 4.6%, which is also more than that of the F−C^1 from SM1 to TS$_M$1 (4.0%). The distances of the C^1−C^2 and C^1−C^3 bonds (C^1−C^2, 2.092 Å; C^1−C^3, 2.455 Å) in TS$_M$2 are smaller than those in TS$_M$1 (C^1−C$^{2!}$, 2.258 Å; C^1−C$^{3!,}$ 2.529 Å). These suggest that TS$_M$2 is a later transition state compared to TS$_M$1 with a much higher transition-state energy of 19.0 kcal/mol. As for the carbometalation pathway, the distances of Li−C^2 (2.035 Å) and C^1−C^3 (2.185 Å), the key geometric parameters for the transition state TS$_C$2, are longer than those of the TS$_C$1 (values of 2.028 and 2.132 Å, respectively), indicating that TS$_C$2 is an earlier transition state compared to TS$_C$1. The transition-state

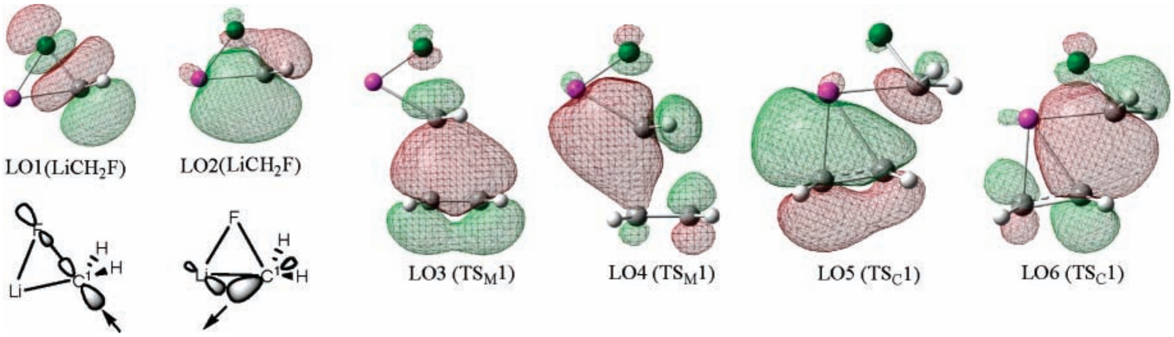


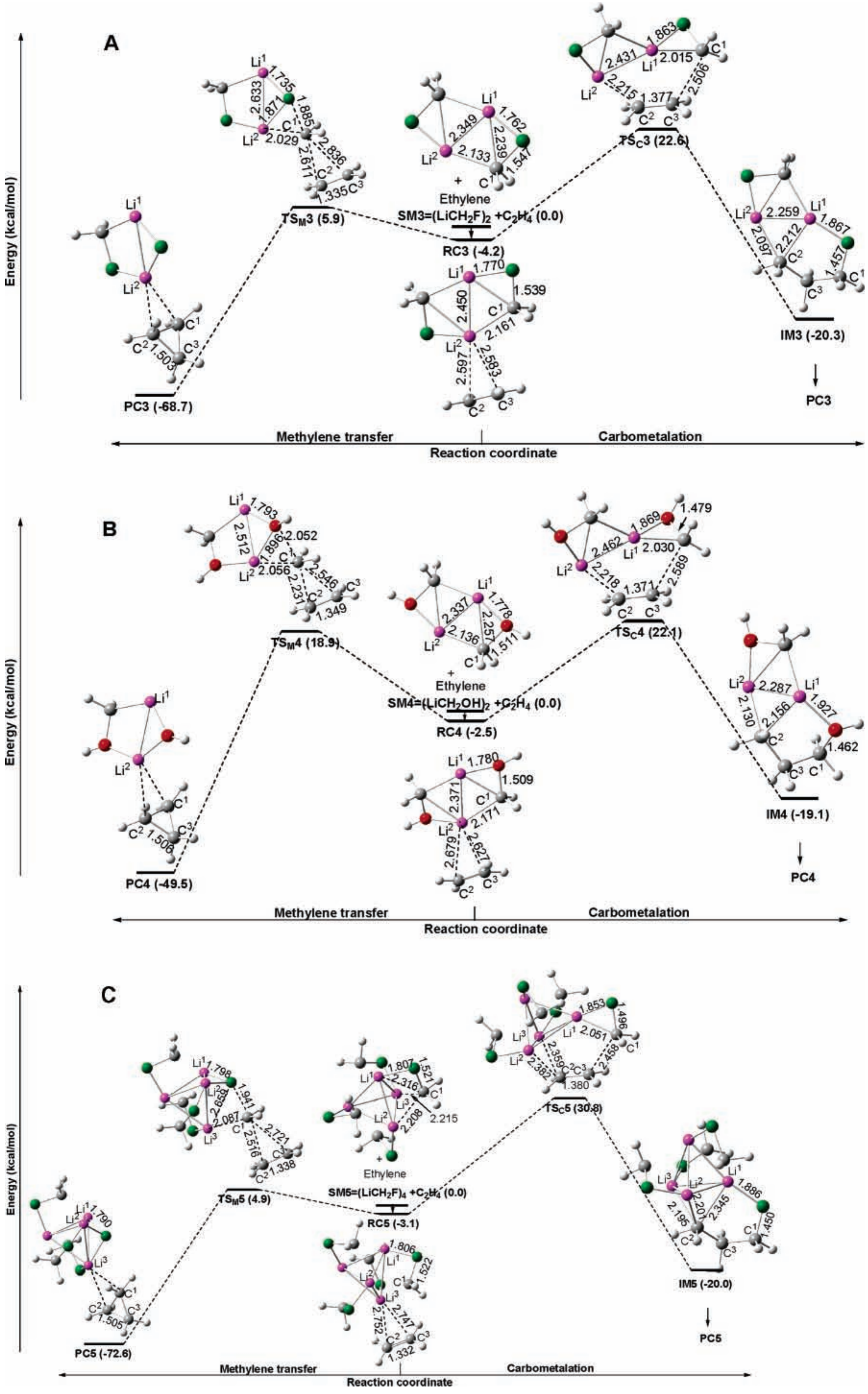
FIGURE 2. Localized Kohn−Sham orbitals (LOs) of $LiCH_2F$, TS_M1, and TS_C1. All of the LOs (0.02 isovalue) were obtained at the B3LYP/STO-3G level for the B3LYP/6-311G** geometries.

energy of TS_C2 for the carbometalation pathway is only 1.1 kcal/mol. This is much lower than that of TS_M2 for the methylene-transfer pathway (19.0 kcal/mol).

These results are surprising in that the methylene-transfer pathway cannot compete with the carbometalation pathway in the cyclopropanation of $LiCH_2OH$ with ethylene. However, does the carbometalation pathway represent the reaction reality or really compete with the methylene-transfer pathway in experiments? This question still remains unsettled when considering the experimental facts that the $LiCH_2$−halogen carbenoids are much more reactive than the $LiCH_2$−OR for cyclopropanation reactions.[12,26−28] The $LiCH_2$−halogen can cyclopropanate olefins efficiently even at −78 °C, but the reactions of the $LiCH_2OR$ carbenoids with olefins only give cyclopropanes in very low yields. The reaction barrier (relative to RC) for $LiCH_2OH$ along the carbometalation pathway is 8.8 kcal/mol, lower than that for $LiCH_2F$ (12.5 kcal/mol). This obviously contradicts the experimental observation that the $LiCH_2$−halogen carbenoids are much more reactive than the $LiCH_2$−OR. The reaction barrier for $LiCH_2OH$ along the methylene-transfer pathway is 26.7 kcal/mol, which is much higher than that for $LiCH_2F$ with the value of 16.0 kcal/mol. This is, on the contrary, in qualitative agreement with experimental results. Although the calculation results show that the reaction barriers for the carbometalation pathways are lower than those for the methylene-transfer pathways, the carbometalation may not operate due to their inconsistency with the experimental observations. These simple model calculations for cyclopropanations of monomeric $LiCH_2X$ with ethylene in the gas phase are not sufficient to reflect the reaction reality or to determine the reaction mechanism. The carbenoid is undoubtedly solvated and aggregated in the reaction solution.[9a] We will discuss the cyclopropanations of the lithium carbenoids with ethylene in aggregation and solvation states so as to determine a better description of the reaction mechanism.

B. Cyclopropanations of $LiCH_2X$ (X = F and OH) Carbenoids with Ethylene in Aggregation States. Organolithium compounds are, in fact, aggregated species in the reaction systems.[30] The different aggregation states exhibit different properties and reactivities.[31] As reported in previous studies, dimers and tetramers are the most stable aggregation states for organolithium compounds in a polar solvent.[32] Here, we investigate the dimeric and tetrameric $LiCH_2X$ (X = F and OH) carbenoids and their cyclopropanation reactions with ethylene to estimate the effect of aggregation on the reaction reactivities and to determine the most likely reaction mechanism. The reaction profiles and the optimized geometries are shown in Figure 3.

The optimized geometries of the dimeric $LiCH_2X$ (X = F and OH) carbenoids have C_{2h} symmetry, as shown in Figure 3A and B. These structures are very similar to those of the dimeric $LiCH_2F$ and $LiCH_2Cl$ previously studied by Pratt et al.[31] The methylene group is stabilized by the lithium−lithium bond (2.349 Å) in the dimeric $(LiCH_2F)_2$ species (see SM3 in Figure 3A) where the distances of the C^1−Li^1 and C^1−Li^2 bonds are 2.239 and 2.133 Å, respectively. The aggregation of two monomeric $LiCH_2F$ to form the dimeric $(LiCH_2F)_2$ is strongly exothermic by −44.6 kcal/mol in the gas phase. As depicted in Figure 3A, the dimeric $(LiCH_2F)_2$ species first forms a reactant complex, RC3, with ethylene. Because of the aggregation, the stabilization energy of this π-type interaction decreases to 4.2 kcal/mol, from 8.2 kcal/mol for the monomeric $LiCH_2F$ case. As the reaction goes along the methylene-transfer or the carbometalation pathways, there are significant differences attributed to the aggregation of the carbenoids. The most interesting result is that the transition-state energy of TS_M3 for the methylene-transfer pathway decreases to 5.9 kcal/mol, whereas the transition-state energy of TS_C3 for the carbometalation pathway increases significantly to 22.6 kcal/mol, compared to the monomeric $LiCH_2F$ + ethylene system. Considering the lesser stabilization of the reactant complex, the reaction barrier for the methylene-transfer pathway is 10.1 kcal/mol, which is 5.9 kcal/mol lower than that of the monomeric case. In contrast, the reaction barrier for the carbometalation pathway is 26.8 kcal/mol, which is much higher than that of the monomeric case (12.6 kcal/mol). The enhancement of the reactivity for the methylene-transfer pathway can be understood by structural analysis of the transition state. As the ethylene approaches the methylene, the leaving fluorine atom strongly interacts with both of the two lithium ions. The lengths of the Li^1−F and Li^2−F bonds are 1.735 and 1.871 Å, respectively, as shown in Figure 3A. As discussed in section A, the character of TS_M can be described as a carbenoid species with decomplexed LiX, approaching C_2H_4. The formation of the Li−X bond can compensate for other structural changes in the transition state.[12] The interaction of two lithium ions with the leaving fluorine in the TS_M3 compensates much more than that of the TS_M1, which has only one formed Li−F bond. This leads to a lower transition-state energy for the TS_M3. On the other hand, the geometry of the TS_C1 for the carbometalation changes in a very different manner. As depicted in Figure 3A, the Li^2−C^1 bond in the TS_C3 has been completely cleaved compared to that in RC3 and SM3. Moreover, there is no compensation for the interaction of the lithium ions and the fluorine atom because the Li^1−F bond (1.863 Å) is longer than that of the RC3 (1.770


A
Energy (kcal/mol)
PC3 (-68.7)
TS$_M$3 (5.9)
SM3=(LiCH$_2$F)$_2$ +C$_2$H$_4$ (0.0)
+ Ethylene
RC3 (-4.2)
TS$_C$3 (22.6)
IM3 (-20.3)
PC3
Li^1
Li^2
C^1
C^2
C^3
1.503
1.735
2.633
1.871
1.885
2.029
2.611
2.836
1.335
2.349
1.762
2.133
2.239
1.547
1.770
2.450
1.539
2.161
2.597
2.583
2.431
1.863
2.015
2.215
1.377
2.506
2.259
1.867
2.097
2.212
1.457
Methylene transfer
Carbometalation
Reaction coordinate
B
Energy (kcal/mol)
PC4 (-49.5)
TS$_M$4 (18.9)
SM4=(LiCH$_2$OH)$_2$ +C$_2$H$_4$ (0.0)
+ Ethylene
RC4 (-2.5)
TS$_C$4 (22.1)
IM4 (-19.1)
PC4
1.506
1.793
2.512
1.896
2.052
2.056
2.231
2.546
1.349
2.337
1.778
2.136
2.257
1.511
1.780
2.371
1.509
2.171
2.679
2.627
2.462
1.869
1.479
2.030
2.218
1.371
2.589
2.287
1.927
2.130
2.156
1.462
Methylene transfer
Carbometalation
Reaction coordinate
C
Energy (kcal/mol)
PC5 (-72.6)
TS$_M$5 (4.9)
SM5=(LiCH$_2$F)$_4$ +C$_2$H$_4$ (0.0)
+ Ethylene
RC5 (-3.1)
TS$_C$5 (30.8)
IM5 (-20.0)
PC5
Li^3
1.790
1.505
1.798
2.659
1.941
2.087
2.516
2.721
1.338
1.807
1.521
2.316
2.208
2.215
1.806
1.522
2.752
2.747
1.332
1.853
1.496
2.051
2.359
2.458
2.382
1.380
1.886
1.450
2.195
2.201
2.345
Methylene transfer
Carbometalation
Reaction coordinate

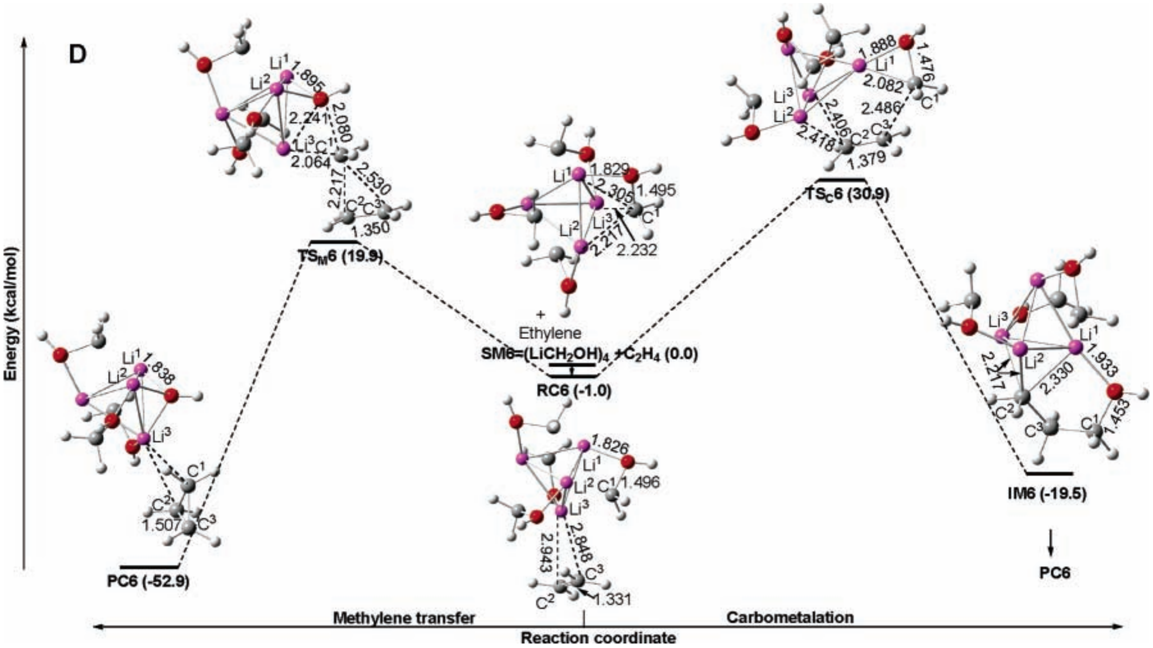


FIGURE 3. Reaction profiles of the aggregated lithium carbenoid $(LiCH_2X)_m$ (A, X = F and m = 2; B, X = OH and m = 4; C, X = F and m = 4; D, X = OH and m = 4)-promoted cyclopropanations of ethylene along the methylene-transfer and carbometalation pathways (B3LYP/6-311G** level). Selected parameters are given in Å. Energies relative to the starting materials [SM = $(LiCH_2X)_m$ + ethylene] are shown in kcal/mol in the parentheses. Lithium is shown in purple, oxygen is shown in red, and fluorine is shown in green.

Å) and the Li^2 atom and F atom have no interaction with each other. Furthermore, the less positive natural charge distribution on the lithium ion (0.847) of the $(LiCH_2F)_2$ than that (0.889) of the $LiCH_2F$ makes the lithium electrophile addition in the transition state relatively more difficult. Thus, the carbometalation pathway has a much higher reaction barrier of 26.8 kcal/mol and cannot compete with the methylene-transfer pathway, of which the reaction barrier is only 10.1 kcal/mol.

The most stable isomer of the tetrameric $(LiCH_2F)_4$ species is S_4 symmetric, as shown in Figure 3C. The four lithium ions interact with each other to form a tetrahedral structure in the $(LiCH_2F)_4$ species, where each of the methylene groups is stabilized by a three-lithium ring. The aggregation of two dimeric $(LiCH_2F)_2$ to form the tetrameric $(LiCH_2F)_4$ is also strongly exothermic by −31.2 kcal/mol in the gas phase. The stabilization energy of the reactant complex RC5 relative to SM5 is slightly lower by 1.1 kcal/mol compared to that of the RC3 due to the multiple aggregation of the tetrameric $(LiCH_2F)_4$ species compared to that of the dimeric $(LiCH_2F)_4$ species. As for the methylene-transfer pathway, the transition-state energy of TS_M5 is decreased slightly by 1.0 kcal/mol compared to that of the TS_M3. One can see that, except for the formation of Li^1-F and Li^2-F bonds, there also exists a certain interaction between the Li^3 and F atoms to compensate for other structural changes in TS_M5. The distance between the Li^3 and F atoms is 2.659 Å, which is closer than the sum of their van der Waals radii. This further decreases the reaction barrier of the methylene-transfer pathway to 8.0 kcal/mol. With regard to the carbometalation pathway, larger structural changes from the SM5 and RC5 to the transition state TS_C5 can easily be identified compared to that of the $(LiCH_2F)_2$ case. The Li^2-C^1 and Li^3-C^1 bonds are both completely cleaved in the TS_C5, indicating the reaction needs to overcome a higher barrier. It is also disadvantageous for the carbometalation that the natural charge distribution in the lithium ion further decreases from 0.847 for $(LiCH_2F)_2$ to 0.828 for $(LiCH_2F)_4$. In the tetrameric aggregation case, the reaction barrier of the carbometalation pathway (33.9 kcal/mol) increases even further from that of the methylene-transfer pathway (8.0 kcal/mol).

Because it has been experimentally documented that the $LiCH_2-$halogen carbenoids are much more reactive than the $LiCH_2-OR$ for cyclopropanation reactions,[12,26−28] a study of the $LiCH_2OH$ carbenoids with ethylene in their aggregation states was also carried out here to estimate the different reactivities between these two kinds of lithium carbenoids. The reaction profiles and the geometries are shown in Figure 3B and D. The dimeric $(LiCH_2OH)_2$ species is exothermic by 47.7 kcal/mol relative to the two monomeric $LiCH_2OH$ species, and the tetrameric $(LiCH_2OH)_4$ species is exothermic by 32.0 kcal/mol relative to the two dimeric $(LiCH_2OH)_2$ in the gas phase. Similar to the aggregated $LiCH_2F$ carbenoids, the aggregated $LiCH_2OH$ carbenoids can also lower the reaction barrier of the methylene-transfer pathway from 26.7 kcal/mol for monomeric $LiCH_2OH$ to 21.4 kcal/mol for dimeric $(LiCH_2OH)_2$ and to 20.9 kcal/mol for tetrameric $(LiCH_2OH)_4$. On the other hand, the reaction barrier of the carbometalation pathway increases from 8.8 kcal/mol for monomeric $LiCH_2OH$ to 24.6 kcal/mol for dimeric $(LiCH_2OH)_2$ and to 31.9 kcal/mol for tetrameric $(LiCH_2OH)_4$ due to the large structural changes occurring from RC4 to TS_C4 and from RC6 to TS_C6, similar to the case of the $LiCH_2F$ carbenoids in their aggregation states. These results are much different than those for the monomeric $LiCH_2OH$ carbenoid, where the reaction barrier for the methylene-transfer pathway (26.7 kcal/mol) is much higher than that of the carbometalation pathway (8.8 kcal/mol). The methylene-transfer pathway is obviously much more favored in the aggregation states. The reaction barriers of the methylene pathway are 21.4 kcal/mol for the dimeric $(LiCH_2OH)_2$ and 20.9 kcal/mol for the tetrameric $(LiCH_2OH)_4$, which are much higher than those for the dimeric $(LiCH_2F)_2$ (10.1 kcal/mol) and tetrameric $(LiCH_2F)_4$ (8.0 kcal/mol). This is in good agreement with the experimental observations that the $LiCH_2-$halogen carbenoids are much more reactive than the $LiCH_2-OR$ for cyclopropanation reactions, and it provides an explanation for the experimental reactivity of these lithium carbenoids.[12,26−28]

The above calculation of cyclopropanations of the lithium carbenoids with ethylene in their aggregation states reveals that the reaction barrier of the methylene-transfer pathway decreases from 16.0 kcal/mol for the monomeric $LiCH_2F$ carbenoid to 10.1 kcal/mol for the dimeric $(LiCH_2F)_2$ carbenoid and then to 8.0 kcal/mol for the tetrameric $(LiCH_2F)_4$ carbenoid. The aggregated lithium carbenoids are more stable species than the monomeric ones in the gas phase and exhibit different properties and reactivities. The clustering lithium ions in the aggregation states can compensate the transition states more for the methylene-transfer pathway than for the monomeric lithium carbenoid case. This makes the cyclopropanation of lithium carbenoids with ethylene more efficient and indicates that the aggregated lithium carbenoids are the most probable reactive species in the reaction systems. In the aggregation states, the carbometalation reaction pathway needs to overcome large structural changes from the reactant complex to the transition state. The reaction barriers for the carbometalation pathway in aggregation states are so high [26.8 kcal/mol for the dimeric $(LiCH_2F)_2$ carbenoid and 33.9 kcal/mol for the tetrameric $(LiCH_2F)_4$ carbenoid] that the carbometalation pathway cannot compete with the methylene-transfer pathway and should not contribute significantly to the cyclopropanation reactions. The comparison of different influences of substituents X on the reaction mechanisms shows that the calculation results for the aggregation states are in good agreement with the experimental observations. These computed results for the aggregation states more accurately reflect the reaction realities.

C. The Explicit Solvation Effect on the Reaction Mechanism of Lithium Carbenoid-Promoted Cyclopropanations with Ethylene. Cyclopropanation reactions are usually carried out in polar organic solvents for various carbenoid reagents. Polar solvent molecules may be strongly coordinated. The solvent effect can be very important in realistic models of the structures and reactivity of carbenoids in the solution phase.[31] The lithium carbenoids usually promote cyclopropanations in ether solvent. Here, we present a detailed computational study to investigate the solvation effect on the mechanistic dichotomy, that is, the methylene-transfer and the carbometalation, for the lithium carbenoid-promoted cyclopropanation reactions by explicitly coordinating one and two DME molecules to the lithium center. The reaction profiles and the optimized geometries for the explicitly solvated $LiCH_2F$ carbenoid along the methylene-transfer and the carbometalation pathways are shown in Figure 4.

The coordination of one solvent molecule to $LiCH_2F$ to form a $LiCH_2F$/DME species is exothermic by 19.2 kcal/mol. The $LiCH_2F$/DME species has a carbenoid moiety similar to that of the unsolvated $LiCH_2F$. The $Li-C^1$ and $Li-F$ bond lengths are elongated slightly from 1.744 and 1.915 Å in the unsolvated $LiCH_2F$ to 1.784 and 1.945 Å in the $LiCH_2F$/DME species. A reactant complex RC7 can also be formed by the π-type interaction between the ethylene and the lithium center. Because of the coordinated solvent molecule, the stabilization energy of this π-type interaction is only 3.7 kcal/mol, lower by 4.5 kcal/mol than that of the unsolvated $LiCH_2F$ with ethylene. The transition-state energy of TS_M7 increases by only 0.9 kcal/mol due to the explicit coordination of one solvent molecule to the lithium center, as shown in Figures 1A and 4A. On the other hand, the transition-state energy of TS_C7 is 7.8 kcal/mol, increased by 3.5 kcal/mol due to the explicit coordination of one DME to the lithium center. The reaction barrier for the carbometalation pathway is similar to that of the unsolvated $LiCH_2F + C_2H_4$ system, attributed to the increase of the transition-state energy and the decrease of the stabilization energy of the π-type reactant complex. The reaction barrier for the methylene-transfer pathway decreases to 12.4 kcal/mol, lower by 3.6 kcal/mol compared to that of the corresponding unsolvated case. This enhanced reactivity should be the composite effect of the stabilization of the solvated $LiCH_2F$/DME species and the decreasing stabilization of the reactant complex between the solvated $LiCH_2F$/DME species with ethylene, which come from the incorporation of the solvent molecule. The strong interaction (19.2 kcal/mol for one DME) between the oxygen atom of the solvent molecule and the lithium center weakens the interaction of the reactive species with ethylene. The increased reactivity for this pathway can also be readily understood by an increase in the electrophilic character of the methylene in the $LiCH_2F$/DME species. NBO analysis revealed that the natural charge of the C^1 atom, which is supposed to be responsible for the reactivity of the carbenoid species along the methylene-transfer mechanism, increases from −0.602 in $LiCH_2F$ to −0.565 in $LiCH_2F$/DME. This makes the methylene accept the π electrons of the olefin more readily. On the contrary, the transition state of the carbometalation pathway should be described as the simultaneous addition of the methylene nucleophile and the metal electrophile in a push−pull manner, as discussed in section A. Because of the coordination of solvent molecule to the $LiCH_2F$, the natural charge of the lithium ion becomes less positive and goes from 0.889 in $LiCH_2F$ to 0.842 in $LiCH_2F$/DME and is accompanied by the less negative charge distribution in the C^1 atom. This makes the addition of the methylene nucleophile and the metal electrophile relatively difficult, leading to a higher transition-state energy for the carbometalation pathway.

The coordination of a second solvent molecule to $LiCH_2F$/DME to form a $LiCH_2F/(DME)_2$ species is exothermic by 12.1 kcal/mol. As shown in Figure 4B, the stabilization energy between the $LiCH_2F/(DME)_2$ and ethylene for RC8 is only 1.4 kcal/mol, which is further decreased by 2.3 kcal/mol compared to that for RC7. As for the methylene-transfer pathway, the transition-state energy of TS_M8 (8.1 kcal/mol) decreases slightly by 0.6 kcal/mol due to the explicit coordination of the second solvent molecule to the $LiCH_2F$/DME species. Considering the decreasing stabilization for the reactant complex RC8, the reaction barrier of the methylene-transfer pathway becomes 9.5 kcal/mol, and this is decreased by another 2.9 kcal/mol compared to that for the $LiCH_2F$/DME system (12.4 kcal/mol). Evidence can also be seen from the natural charge distribution on the C^1 atom, which becomes a lesser negative value (−0.556) compared with those of the $LiCH_2F$/DME (−0.565) and $LiCH_2F$ (−0.602) species. On the other hand, the transition energy of TS_C8 for the carbometalation pathway increases to 12.6 kcal/mol when a second solvent molecule is explicitly coordinated to the system. This makes the carbometalation pathway have a higher reaction barrier of 14.0 kcal/mol, despite the lower stabilization for the reactant complex RC8. One can see that the natural charge distribution on the lithium ion becomes lower and lower [going from 0.889 for the $LiCH_2F$ species to 0.842 for the $LiCH_2F$/DME species and then to 0.830 for the $LiCH_2F/(DME)_2$ species]. On the basis of the character of the transition

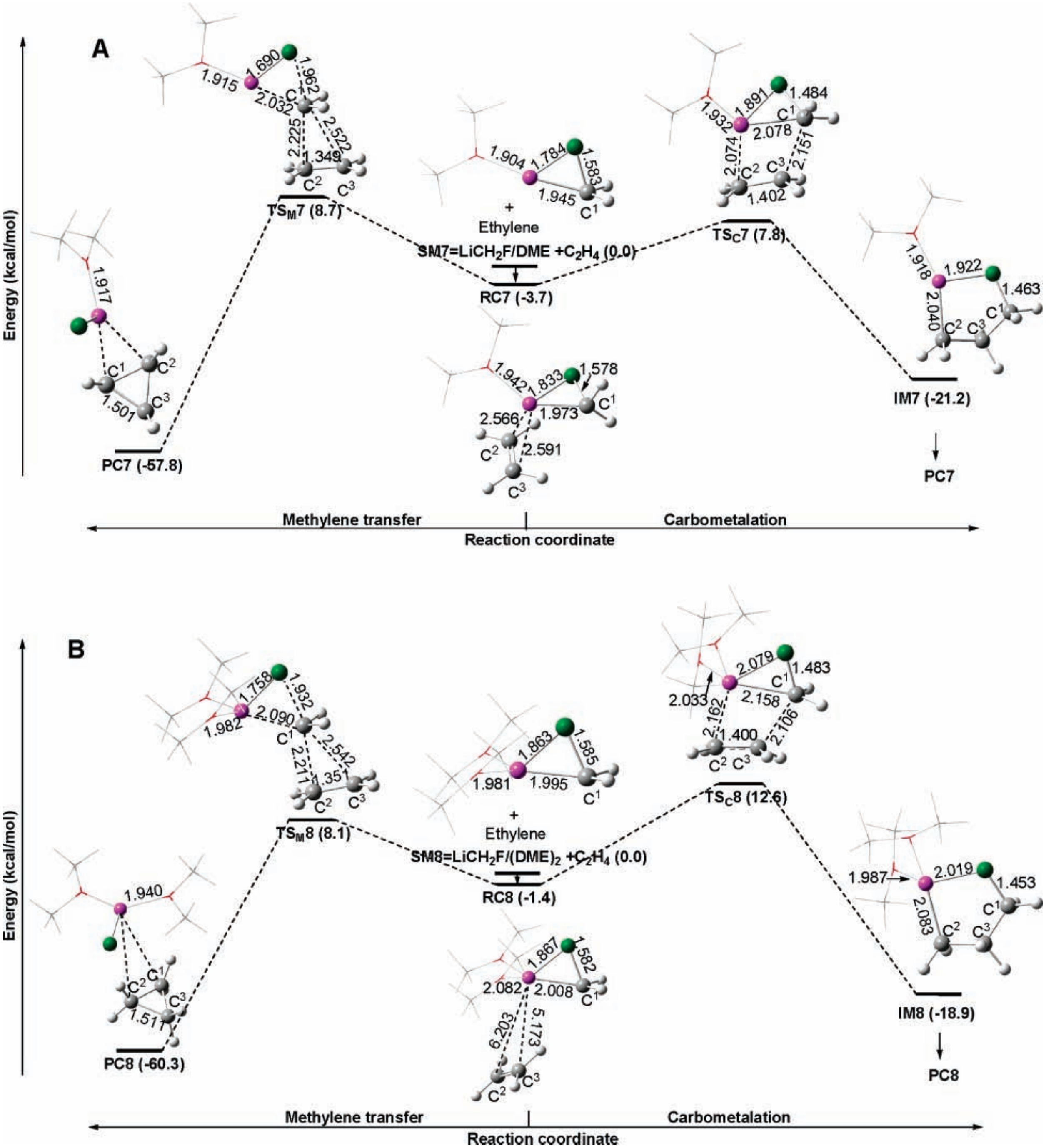


FIGURE 4. Reaction profiles of the explicit solvated lithium carbenoid $LiCH_2F/(DME)_n$ (A, $n = 1$; B, $n = 2$)-promoted cyclopropanations of ethylene along the methylene-transfer and carbometalation pathways (B3LYP/6-311G** level). Selected parameters are given in Å. Energies relative to the starting materials [SM = $LiCH_2F/(DME)_n$ + ethylene] are shown in kcal/mol in the parentheses. Lithium is shown in purple, oxygen is shown in red, and fluorine is shown in green. The coordinated solvent molecules are shown in the wireframe type for conciseness.

state of the carbometalation pathway, the lesser negative natural charge distribution on the C^1 atom and the lesser positive natural charge distribution on the lithium ion obviously make the carbometalation pathway more difficult.

The above calculations of the cyclopropanations of the lithium carbenoids with ethylene by explicitly coordinating solvent molecules to the lithium center exhibit an interesting trend for the methylene-transfer pathway. The strong interaction of the solvent molecules with the lithium center weakens the interaction of the lithium carbenoid species with ethylene. The reactant complexes were found to be lower and lower in stability (going from −8.2 kcal/mol for RC1 to −3.7 kcal/mol for RC7 and then to −1.4 kcal/mol for RC8) relative to their starting materials. It is expected that the interaction of the carbenoid species with ethylene becomes very weak and can be negligible in a fully solvated system. The reaction barriers for the methylene-transfer mechanism systematically decrease as more solvent molecules are added to the species (going from 16.0 kcal/mol for no DME solvent added to 12.4 kcal/mol for one DME added and to 9.5 kcal/mol for two DME added). The reaction barriers for the methylene-transfer pathway can be reasonably described as an exponential decay process as the

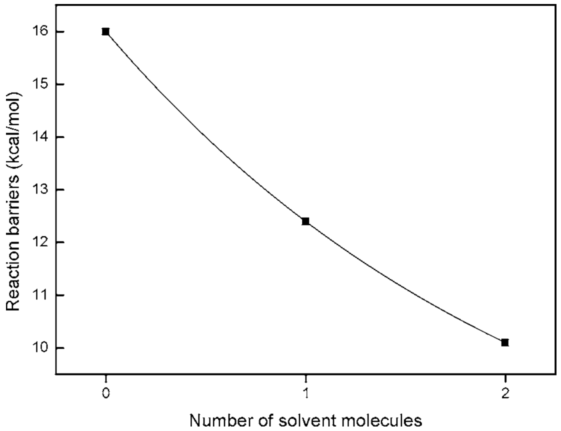


FIGURE 5. Reaction barriers (B3LYP/6-311G**, kcal/mol) of the methylene-transfer pathway for the $LiCH_2F/(DME)_n$ + ethylene system as a function of the number of DME molecules ($n = 0$, 1, and 2).

number of DME molecules goes from $n = 0$ to $n = 2$, as shown in Figure 5. To further consider the bulk solvation effects, the PCM model was utilized for ether solvent ($\epsilon = 4.335$) to the $LiCH_2F/(DME)_2$ + ethylene system at the B3LYP/6-311G** level of theory. The computed reaction barrier with ZPE correction included for the methylene-transfer pathway is 9.4 kcal/mol. This is almost the same as in the case of the reaction system explicitly coordinated with two DME molecules (9.5 kcal/mol), indicating that the explicit coordination of two DME molecules to the lithium center is sufficient to reflect the effect of solvation. This can be regarded as a best limit as two more DME molecules are coordinated to the lithium carbenoid. In contrast, the transition-state energies for the carbometalation pathway become noticeably higher and range from 4.3 kcal/mol for no DME added to 7.8 kcal/mol for one DME added and then to 12.6 kcal/mol for two DME added. Considering the decreasing stabilization of the π-type reactant complexes, the reaction barriers remain higher at 14.0 kcal/mol due to the explicit coordination of two solvent molecules to the lithium center. In combination with the continuum solvation model PCM (ether solvent, $\epsilon = 4.335$), the computed reaction barrier of the carbometalation pathway with ZPE correction included is 16.2 kcal/mol for the $LiCH_2F/(DME)_2$ + ethylene system at the B3LYP/6-311G** level of theory. This barrier is obviously higher than that (12.5 kcal/mol) of the $LiCH_2F$ + ethylene system in the gas phase. The coordination of solvent molecules makes the lithium ion have a lesser positive charge distribution and the C^1 atom have a lesser negative charge distribution. This leads the reaction barriers of the carbometalation pathway for $LiCH_2F$ to remain higher. These results suggest that the solvation effect helps make the methylene-transfer pathway more favorable than the carbometalation pathway and that the strong interaction between the lithium ion and the solvent molecules appears to impede the carbometalation pathways.

D. Combined Effects of Aggregation and Solvation on the Reaction Barrier for Lithium Carbenoid-Promoted Cyclopropanation Reactions. We have clarified in the previous sections that the calculations based on the monomeric lithium carbenoid in the gas phase are not sufficient to accurately reflect the experimental observations of the cyclopropanation reactions or to determine the reaction mechanism. We also showed that the methylene-transfer pathway is more favored than the carbometalation pathway and that the latter cannot compete effectively with the former and should be ruled out in aggregation states. The solvation effect can enhance the methylene-transfer pathway; however, it impedes the carbometalation

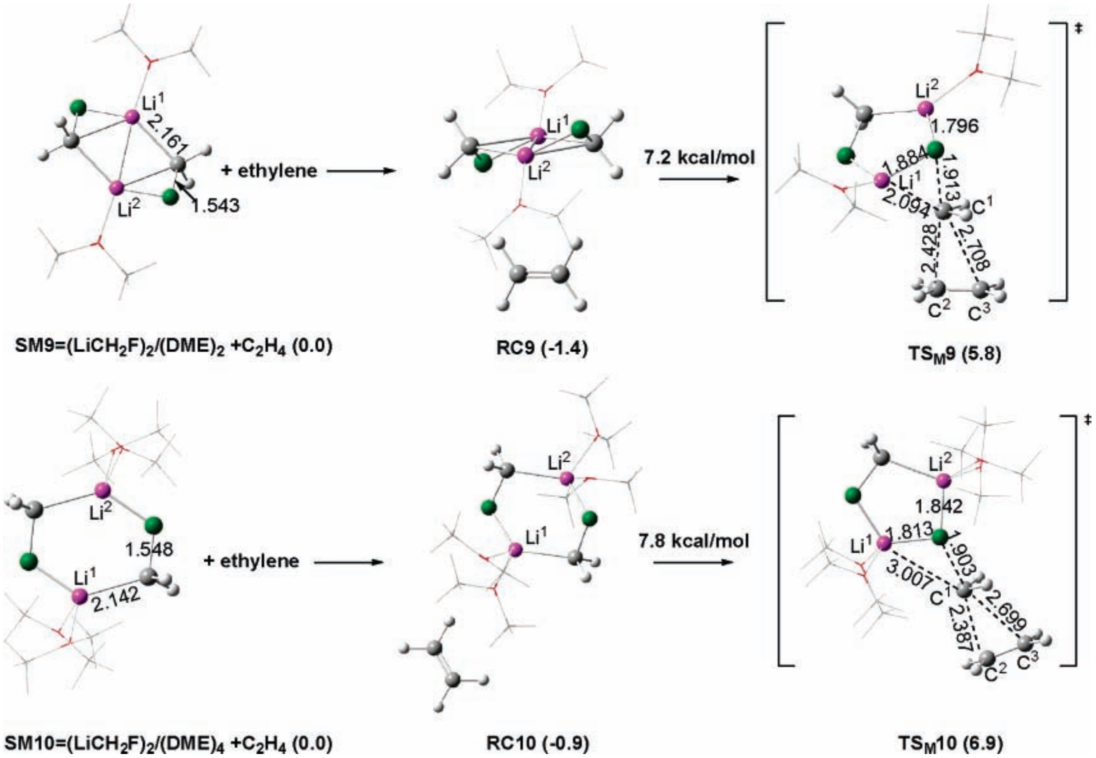


FIGURE 6. Models of cyclopropanations of the $(LiCH_2F)_2/(DME)_n$ ($n = 2$ and 4) carbenoids with ethylene along the methylene-transfer pathway (B3LYP/6-311G** level). Selected parameters are given in Å. Energies relative to the starting materials [SM = $(LiCH_2F)_2/(DME)_n$ + ethylene] are shown in kcal/mol in the parentheses. Lithium is shown in purple, oxygen is shown in red, and fluorine atom is shown in green. The coordinated solvent molecules are shown in the wireframe type for conciseness.

TABLE 1. Reaction Barriers (kcal/mol) Computed at the B3LYP/6-311G Level for the Cyclopropanations of the Lithium Carbenoids with Ethylene**

	Monomer $LiCH_2X/(DME)_n$			Dimer $(LiCH_2X)_2/(DME)_n$			Tetramer $(LiCH_2X)_4/PCM^a$	
	$n = 0$	$n = 1$	$n = 2$	$n = 0$	$n = 2$	$n = 4$	$(LiCH_2X)_4$	$(LiCH_2F)_4/PCM^a$
barrier-M[b] (X = F)	16.0	12.4	9.5	10.1	7.2	7.8	8.0	7.2
barrier-C[c] (X = F)	12.5	11.5	14.0	26.8			33.9	
barrier-M (X = OH)	26.7	22.7	21.5	21.4			20.9	
barrier-C (X = OH)	8.8			24.6			31.9	

[a] The reaction barrier with the ZPE correction included was calculated using the PCM model for the tetrameric $(LiCH_2F)_4 + C_2H_4$ system. [b] Barrier-M are the reaction barriers of the methylene-transfer pathway. [c] Barrier-C are the reaction barriers of the carbometalation pathway.

pathway. Considering that the solvation effect impedes the carbometalation pathway, the carbometalation pathway is predicted to be more unfavored in the aggregation and solvation states. Calculations were carried out here to estimate enhancement of the cyclopropanation reaction along the methylene-transfer pathway in the aggregation and solvation states. As shown in Figure 6, the $(LiCH_2F)_2/(DME)_2$ species is a dimeric $(LiCH_2F)_2$ carbenoid explicitly coordinated by one DME on each of the lithium centers. The $(LiCH_2F)_2/(DME)_2$ species can be considered as a solvated dimeric carbenoid formed by two solvated $LiCH_2F$/DME species, of which the dimerization energy is predicted to be −33.8 kcal/mol at the B3LYP/6-311G** level of theory. Furthermore, the dimerization energy of $(LiCH_2F)_2/(DME)_4$, formed by two corresponding $LiCH_2F/(DME)_2$ species, is predicted to be −22.5 kcal/mol at the same level, indicating that the aggregated lithium carbenoid species are stable in their solvation states. The reaction barrier decreases to 7.2 kcal/mol due to the explicit coordination of one DME to each of the lithium centers, compared to the reaction barrier of 10.1 kcal/mol for the unsolvated dimeric $(LiCH_2F)_2$ carbenoid. This enhanced reactivity is mainly attributed to the lesser stabilization of the reactant complex. As shown in Figures 3A and 6, the stabilization of the RC9 relative to SM9 is 1.4 kcal/mol, which is lower by 2.8 kcal/mol than that of the RC3, whereas the transition-state energy of TS_M9 (5.8 kcal/mol) is similar to that of TS_M3 (5.9 kcal/mol). The coordination of a second solvent molecule to each of the lithium centers in the $(LiCH_2F)_2/(DME)_2$ forms the $(LiCH_2F)_2/(DME)_4$ species, as shown in Figure 6. The reaction barrier for the $(LiCH_2F)_2/(DME)_4$ species, on the other hand, increases slightly to 7.8 kcal/mol due to a second coordinated solvent molecule, indicating the saturation of the reactivity enhancement of the solvent effect. One can see in the TS_M10 of Figure 6 that the Li^1-C^1 (3.007 Å) bond is almost broken due to the bulk coordination of the DMEs to the Li^1 atom. The distances of the C^1-C^2 (2.387 Å) and C^1-C^3 (2.699 Å) are slightly shorter than those of the TS_M9 (C^1-C^2, 2.428 Å; C^1-C^3, 2.708 Å), indicating that TS_M10 is a relatively late transition state compared to TS_M9. The larger structural change from RC10 to TS_M10, compared with those from RC9 to TS_M9, makes the transition-state energy slightly higher (6.9 kcal/mol). This suggests that a decrease of the exposure of the centers in the aggregation states may somewhat reduce the reactivity enhancement of the solvation effect. The reaction barrier using the PCM model for ether solvent ($\epsilon = 4.335$) to the $(LiCH_2F)_2/(DME)_4 + C_2H_4$ system is calculated to be 9.0 kcal/mol, at the same level with ZPE correction included. This is consistent with the barriers calculated by the explicit solvation model and can be considered as the average effect of the solvation on the reaction barrier. The reaction barrier for the tetrameric $(LiCH_2F)_4$ carbenoid in its solvation states can also be predicted to be 7.2 kcal/mol using the PCM model, which is slightly lower than that of the unsolvated case (8.0 kcal/mol). Thus, the reaction barriers of the methylene transfer for the $LiCH_2F$ carbenoid in its aggregation and solvation states are calculated to be in the 7.2−9.0 kcal/mol range. These values are in good agreement with the experimental condition for a variety of carbenoid species that have also been studied theoretically; the $LiCH_2$−halogen can cyclopropanate olefins efficiently even at −78 °C. The samarium carbenoids (8.8 kcal/mol barrier estimated from calculations) can also cyclopropanate olefins efficiently at −78 °C;[14] the aluminum carbenoids (12.8 kcal/mol barrier estimated from calculations) can cyclopropanate olefins at about −40 °C,[21] and the zinc carbenoids (21.2 kcal/mol barrier estimated from calculations) usually cyclopropanate olefins at room temperature. This also indicates that our results calculated for aggregation and solvation states reflect the reaction reality of the lithium carbenoid-promoted cyclopropanations very well.

Summary and Concluding Remarks

Density functional theory calculations for selected lithium carbenoid-promoted cyclopropanations in aggregation and solvation states were presented to examine the mechanistic dichotomy, that is, the methylene-transfer and carbometalation mechanisms. The methylene-transfer mechanism represents the reaction reality more accurately, whereas the carbometalation pathway cannot compete with the methylene-transfer pathway and does not appear to make a significant contribution. Our results also indicate that calculations simply with the monomeric species in the gas phase, usually used in previous studies, are not sufficient to reflect the reaction reality or even lead to false results. The more accurate reaction mechanism modeling should be carried out in aggregation and solvation states. This work may provide a helpful hint to the solution of the reaction mechanisms of many aggregated organometallic compounds in polar solvents.

The simple model calculations for the monomeric lithium carbenoid-promoted cyclopropanations with ethylene in the gas phase are not sufficient to reflect the reaction reality or to determine the reaction mechanism. These calculations reveal that monomeric $LiCH_2F$ has a barrier of 16.0 kcal/mol for the methylene-transfer pathway and a barrier of 12.0 kcal/mol for the carbometalation pathway. The monomeric $LiCH_2OH$, on the other hand, has a barrier of 26.7 kcal/mol for the methylene-transfer pathway and a barrier 8.8 kcal/mol for the carbometalation pathway, as listed in Table 1. The reaction barrier for the $LiCH_2OH$ along the carbometalation pathway is the lowest one among them. This obviously contradicts the experimental observations that the $LiCH_2$−halogen carbenoids are much more reactive than the $LiCH_2$−OR for cyclopropanation reactions.[12,26−28]

The calculations of the cyclopropanations of the lithium carbenoids with ethylene in aggregation states reveal that the reaction barrier of the methylene-transfer pathway decreases from 16.0 kcal/mol for the monomeric $LiCH_2F$ carbenoid to 10.1 kcal/mol for the dimeric $(LiCH_2F)_2$ carbenoid and to 8.0 kcal/mol for the tetrameric $(LiCH_2F)_4$ carbenoid, as summarized in Table 1. In the aggregation states, the clustering lithium ions can compensate more for the structural changes in the transition states of the methylene-transfer pathway compared to that in the monomeric lithium carbenoid case. This makes the cyclopropanation of lithium carbenoids with ethylene more efficient and indicates that the aggregated lithium carbenoids are the most likely reactive species in the reaction systems. In contrast, the reaction barrier for the carbometalation pathway in the aggregation states increases significantly from 12.5 kcal/mol for the monomeric $LiCH_2F$ carbenoid to 26.8 kcal/mol for the dimeric $(LiCH_2F)_2$ carbenoid and to 33.9 kcal/mol for the tetrameric $(LiCH_2F)_2$ carbenoid, as listed in Table 1. The carbometalation pathway cannot compete with the methylene-transfer pathway and should be ruled out in the aggregation states. The reaction barriers of the methylene pathway are 21.4 kcal/mol for dimeric $(LiCH_2OH)_2$ and 20.9 kcal/mol for tetrameric $(LiCH_2OH)_4$. The reaction barriers of the carbometalation for aggregated $LiCH_2$-OH are higher (24.6 and 31.9 kcal/mol for the dimer and the tetramer, respectively) than the reaction barriers of the methylene-transfer pathway in their aggregation states. Comparison of the differently substituted lithium carbenoid ($LiCH_2X$ and $LiCH_2$−halogen)-promoted cyclopropanations in aggregation states strongly supports our results and is in good agreement with the experimental observations.

The solvation effect on the cyclopropanations of the lithium carbenoids with ethylene was investigated by explicitly coordinating solvent molecules to the lithium ion of $LiCH_2F$. The solvation effect helps make the methylene-transfer pathway more favored than the carbometalation pathway. The reaction barrier for the methylene-transfer mechanism decreases systematically from 16.0 kcal/mol for no DME solvent added to 12.4 kcal/mol for one DME added and to 9.5 kcal/mol for two DME molecules added, as listed in Table 1. In contrast, the transition-state energy for the carbometalation pathway becomes systematically higher, leading to a higher reaction barrier (about 14.0 kcal/mol). The coordination of the solvent molecules to the lithium center impedes the carbometalation pathways.

In summary, in the experimental reaction systems, the carbometalation pathway should not make a significant contribution because of its higher reaction barrier in the aggregation state and the impediment effect of the solvation for this pathway; the reaction barriers of the methylene-transfer mechanism fall in the range of 7.2−9.0 kcal/mol, as listed in Table 1. These results for the methylene-transfer pathway agree well with the experiments that show that the $LiCH_2$−halogen carbenoids can cyclopropanate olefins efficiently even at −78 °C, indicating that the calculation results in the aggregation and solvation states more accurately reflect the reaction reality of the lithium carbenoid-promoted cyclopropanations.

Acknowledgment. This research has been supported by the National Natural Science Foundation of China (Grant No. 20673149), the Scientific Research Foundation for the Returned Overseas Chinese Scholars, State Education Ministry and grants from the Sun Yat-Sen University to C.Y.Z., and the Research Grants Council of Hong Kong (HKU-7021/03P) to D.L.P. All of these are gratefully acknowledged.

Supporting Information Available: Cartesian coordinates and the sum of electronic and zero-point energies for transition and ground states from DFT calculations. This material is available free of charge via the Internet at http://pubs.acs.org.

JO062129I