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The Electrophilic Nature of Carbenoids, Nitrenoids, and Oxenoids

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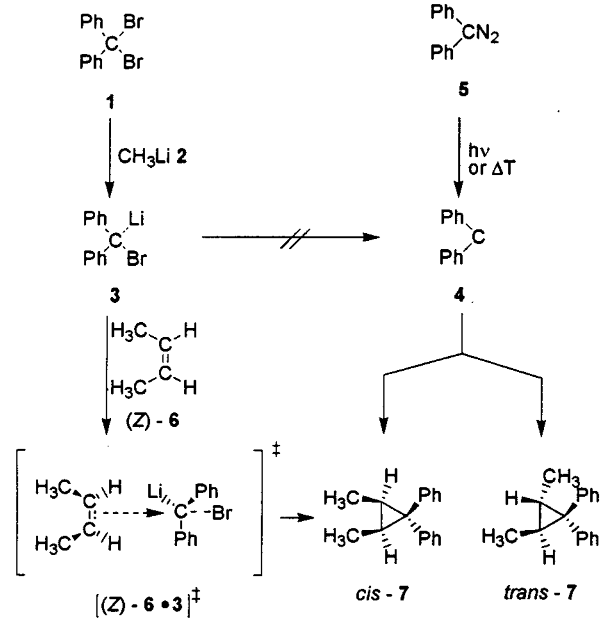
1. Carbenoids

1.1. Introduction

Carbenes such as **4**, which were first prepared from the corresponding diazo compounds **5** either photochemically or thermally (Scheme 1), received their name “collaboratively by W.v.E. Doering, S. Winstein and R.B. Woodward in a nocturnal Chicago taxi” in 1954.[1]

Scheme 1. Carbenes and Carbenoids



The genius loci apparently was again at work when G. L. Closs and L. E. Closs[2a] proposed in 1962 for the first time the term “carbenoid molecule” in the course of studies actually aimed at the finding of new carbene precursors.[2b] When they reacted diphenyldibromomethane **1** with methyllithium **2** in the presence of olefins such as, e.g., (*Z*)-**6**, the formation of the corresponding cyclopropane *cis*-**7** occurred completely stereoselectively. Since *cis*- and *trans*-**7** were formed when diphenyldiazomethane **5** was photolyzed in the presence of (*Z*)-**6**, the same triplet carbene, which according to Skell et al.[3] is the reactive intermediate in the photolysis of **5**, could not be the product determining intermediate in the reaction of **1** with **2**, followed by the addition to (*Z*)-**6**. Rather, the “carbenoid molecule **3**, a more stable complex of diphenylcarbene **4** with lithium bromide” was proposed to react with (*Z*)-**6** to give the cyclopropane *cis*-**7** “via a transition state that corresponds closely to that of an S_N2 reaction ([(*Z*)-**6·3**]‡)”.[2a] In 1964, Closs and Moss[4] proposed “the use of the term “carbenoid” (as a noun) for the description of the intermediates which exhibit reactions qualitatively similar to those of carbenes without necessarily being

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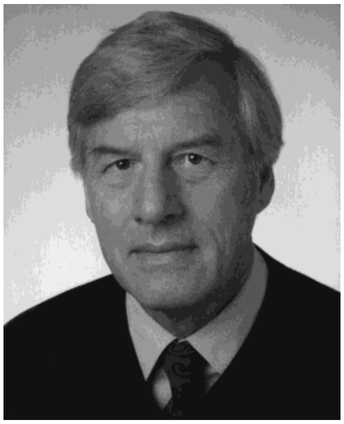
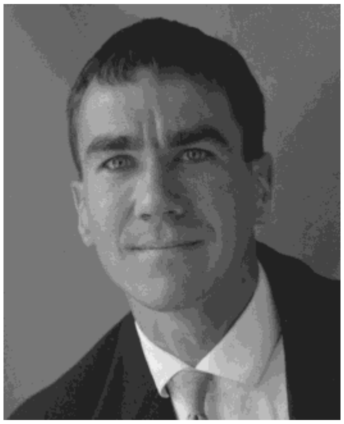


Gernot Boche studied chemistry at Stuttgart, Germany, and Vienna, Austria. His master thesis was directed by Prof. Theodor Förster at the Technical University in Stuttgart and his Ph.D. thesis (1967) by Prof. Rolf Huisgen in München. After postdoctoral activities in München and with Prof. E.E. van Tamelen at Stanford University, he started his own research program at the University in München. In 1979 he became full professor at the University in Marburg. His research interests include organometallic (especially lithium) compounds, their structures and reactions, quantum chemical calculations of such species, and investigation of mutagenic and cancerogenic aromatic amines and nitro compounds, most importantly their transformation into harmless species of that type by small structural variations. Besides chemistry, he enjoys family life with his wife, three children, and six grandchildren, reading, photography, and his garden.



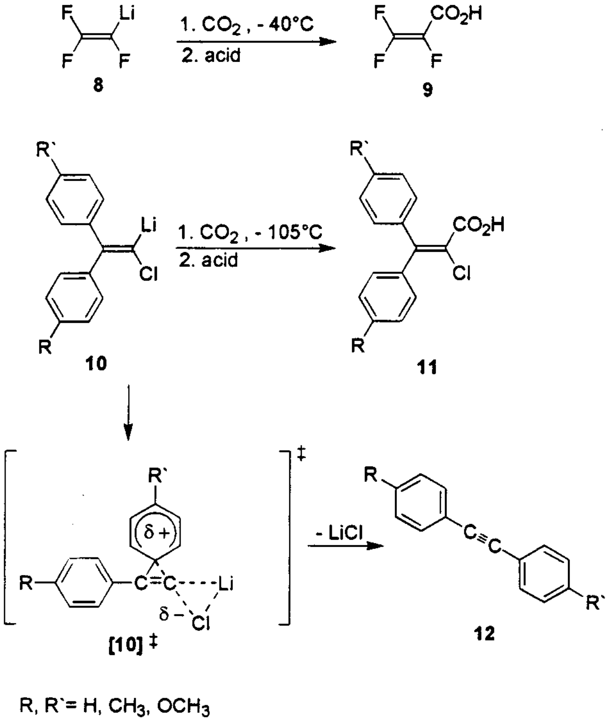
John C. W. Lohrenz has studied chemistry at the Philipps University in Marburg and at the University of Bristol. After taking his Ph.D. in Prof. Gernot Boche's group in Marburg 1993, he spent 15 months as a postdoc with Prof. Tom Ziegler in Calgary, Canada, and 8 months in Prof. Walter Thiel's group in Zürich, Switzerland. He joined the computational chemistry group at BAYER AG, Central Research, in 1996, where he was mostly concerned with the investigation of homogeneous and heterogeneous catalysis with quantum chemical methods. In 1999 he took over the responsibility for the HTS (high throughput screening) data management in the crop protection business unit. His research interests include organometallic chemistry, computational studies of catalytic reactions, data mining, and molecular modeling techniques at different levels of theory.

free divalent carbon species".[5] Immediately the question arose about the structure of carbenoids such as **3** and their amazing electrophilicity— after all being organolithium compounds or, less precisely, "anions".[6] In the "Outlook" of his review article on "Intermediates of the α-Elimination", Kirmse[6b] described the situation in early 1965 as follows: "The transformation of olefins into cyclopropanes, originally thought to be characteristic for carbenes, is increasingly recognized as a reaction of organometallic (carbanion) intermediates". He continues, "A reliable criterion for carbene reactivity is at the moment only the (intramolecular) C−H insertion reaction."

The following examples illustrate important aspects of carbenoid chemistry in its early years. The reader will notice soon that the above-mentioned paradigm concerning the C−H insertion reaction exclusively of carbenes survived only very shortly.

The first intermolecular trapping reaction clearly proving the *anionic* nature of carbenoids was performed by Seyferth et al.[7] when they reacted trifluorovinyllithium **8** with carbon dioxide at −40 °C, followed by protonation to give the acid **9**; see Scheme 2.

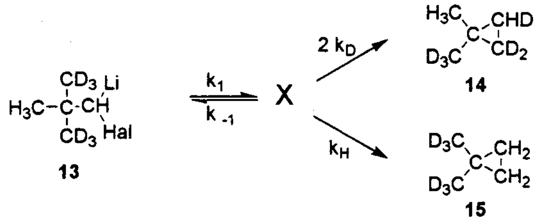
Scheme 2. Trapping Reactions of Carbenoids with CO_2, and the Fritsch−Buttenberg−Wiechell Rearrangement



The vinylic Li/F carbenoid **8** is of exceptional thermal stability due to the β-fluoro substituents, as shown by a comparison with a "normal" vinylic Li/Hal carbenoid of the type **10** (Scheme 2). The reaction of **10** with carbon dioxide to give **11** has to be performed at −105 °C, as Köbrich and Trapp reported[8] (see also the review article of Köbrich on "Eliminations at Olefins" published in early 1965[6c]). Furthermore, these authors came to the conclusion that the Fritsch−Buttenberg−Wiechell rearrangement[9] of β-aryl-substituted vinylic halides, treated with a strong base, should not proceed via the corresponding vinylidene formed by α-elimination of, e.g., LiCl from **10** (Scheme 2). Instead the migrating (R′-substituted) aryl group is thought to substitute the vinylic (!) chloride of **10** via a transition state [**10**]‡, corresponding to an intramolecular trapping reaction of a carbenoid by a nucleophile finally leading to **12**. With donor substituents R and R′, the reaction is fast even at −90 °C. These findings are in perfect agreement with earlier studies of Bothner-By,[10] Curtin,[11] and Simonetta[12] who showed that it is the aryl group *trans* to the halide that undergoes the 1,2-migration. Such a stereoselectivity would not be observed with a vinylidene as the reactive intermediate. In a historical perspective, the Fritsch–Buttenberg–Wiechell rearrangement, discovered in 1894,[9] is the first reaction of a carbenoid, the first to demonstrate the electrophilic nature of such species, and the first to give information on the stereochemistry of the reaction of a nucleophile at a carbenoid carbon atom although the details of this rearrangment were disclosed and understood only more than 60 years later.[10–12]

The question of whether it is the carbenoid RCH-LiHal or the carbene RCH, formed by α-elimination of LiHal, that undergoes C–H(D) insertion reactions, was the topic of a study of Goldstein and Dolbier.[13] They found that the intramolecular insertion reactions of the partially deuterated haloneopentyllithiums **13** into C–H and C–D bonds, respectively, to give the cyclopropanes **14** and **15**, respectively, are halide dependent (Scheme 3). This demands "the presence of the halide in the transition state for hydrogen transfer, most probably still (at least in part) bonded to its original carbon atom. The plausible, more detailed hypothesis, that hydrogen transfer be concerted with carbon–halogen cleavage, though *not required* by the data, finds comforting analogy in the Fritsch–Buttenberg–Wiechell rearrangement".[13]

Scheme 3. Intramolecular H/D Kinetic Isotope Effects of Carbenoid C–H(D) Insertion Reactions



halide	temp. [°C]	k_H / k_D
I	- 30 ± 1	2.76 ± 0.09
I	- 44 ± 1	2.43 ± 0.02
Br	- 44 ± 1	2.06 ± 0.10
Cl	- 68 ± 3	1.71 ± 0.06

"A superficially acceptible alternative would require carbenes of varying excess energy to have been generated, although unprecedented in such an environment and unlikely for other reasons. Intramolecular C–H(D) insertion thus becomes another "diagnostic carbene reaction" now shown to be characteristic, instead, of a precursor."[13]

That the C–H(D) insertion reaction indeed is not a "reliable criterium for carbene reactivity", as supposed one year earlier,[6b] was independently proven by Kirmse and Wächtershäuser in 1966.[14a] They compared the competition of the cyclopropane forming intramolecular C–H insertion reactions into tertiary (3°), secondary (2°), and primary (1°) C–H bonds of the carbenoids R-CHNaCl **16a–f**, formed from the corresponding halides R-CH_2Cl and $NaNH_2$, with those of the carbenes R-CH **17a–f**, prepared from the corresponding diazo species R-CH-N_2. The competition constants (Table 1) refer to the insertion into one respective C–H bond.

Table 1. Competition Constants of C–H Insertion Reactions of the Carbenoids R-CHNaCl 16a–f (Formed from R-CH$_2$Cl + NaNH$_2$) and the Carbenes R-CH 17a–f (Formed by Thermolysis of R-CHN$_2$) into Tertiary (3°) and Secondary (2°) versus Primary (1°) C–H Bonds[a]

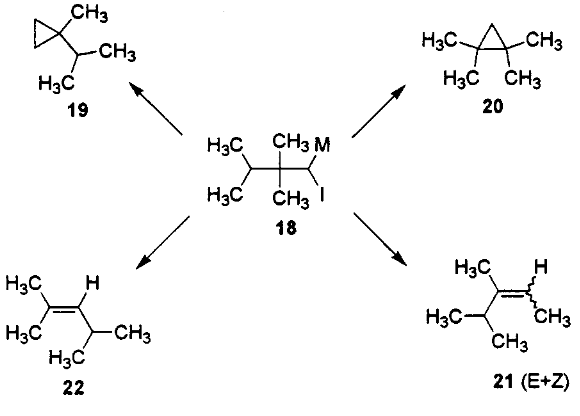
compds **16**, **17**	R	competition	competition constants R-CH(Na)Cl **16**	 R-CH **17**
a	2-butyl	2°trans/1°	2.77	1.60
		2°cis/1°	0.69	0.49
		cis/trans	0.25	0.30
b	3-pentyl	cis/trans	0.09	0.18
c	2-(2-methyl butyl)	2°/1°	1.59	0.78
d	2-(2,4-dimethyl butyl)	2°/1°	1.69	0.96
e	2-(3-methyl butyl)	3°/1°	1.80	0.83
f	2-(2,3-dimethyl butyl)	3°/1°	1.06	0.38

[a] The data refer to one respective C–H bond.

It is quite clear from Table 1 that the competition constants of the carbenoid insertion reactions (**16a–f**) are generally higher than those of the carbene insertion reactions (**17a–f**), indicating a higher selectivity of the carbenoid insertions. It was—and still is—indeed remarkable that not only carbenes but also carbenoids ("anions") are electrophilic enough to react with the rather weakly nucleophilic C–H bonds![14b]

In the same publication,[14a] Kirmse and Wächtershäuser reported not only on C–H insertion reactions but also on 1,2-alkyl migrations of neo-alkyl-type carbenoids to give olefins. An example is given by the carbenoids 1-metallo-1-iodo-2,2,3-trimethylbutane **18** which on warming led not only to the cyclopropanes **19** and **20** (C–H insertion) but also to the olefins **21** and **22** (alkyl migration); see Scheme 4.

Scheme 4. Product Distribution, Olefin (21 + 22) versus Cyclopropane (19 + 20) Formation, and Competition of Insertion into Tertiary (3°) versus Primary (1°) C–H Bonds in the Reactions of Carbenoids 18



compound	M= Na	Li	Mg	Zn	Cu
19	88	87.5	69.5	3.0	3.3
20	11	8.5	20.0	2.0	2.0
21	1	3.7	10.0	94.5	92.0
22	-	0.3	0.5	0.5	3.7
(21+22) / (19+20)	0.01	0.04	0.17	19	22
3° / 1°	0.74	0.60	1.74	4.0	5.2

While the carbenoids **18** with M = Na, Li, and Mg gave mostly cyclopropanes **19** and **20**, the alkyl migration reactions to give the olefins **21** and **22** dominated in the cases of Zn and Cu. Furthermore, the tendency for alkyl migration (olefin formation) paralleled the selectivity for insertion into tertiary (3°) versus primary (1°) C−H bonds. Most importantly, the formation of **19**, **20**, **21**, and **22** is clearly a function of the metal M, which is not agreeable with a common metal-free intermediate (carbene), however, with carbenoids of different properties. The alkyl-1,2-rearrangement therefore is not restricted to cations and carbenes, but rather it is also observed with carbenoids, as similarly shown earlier by the 1,2-aryl migrations in the Fritsch−Buttenberg−Wiechell rearrangement (Scheme 2).

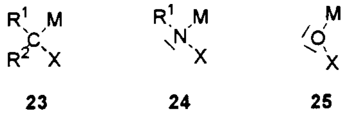
Thus, within a short period of time the existence of carbenoids was firmly established in reactions with electrophiles, as e.g. carbon dioxide (Scheme 2) or by protonation (deuteration), *but also in reactions typical for carbenes* like additions to C=C bonds (Scheme 1), 1,2-alkyl(aryl) migrations (Schemes 2 and 4), and C−H(D) insertions reactions (Schemes 3 and 4). The exchange of lithium (more rarely of sodium and potassium) with other metals, especially magnesium[6q,u,15] and zinc ("Simmons−Smith reagents"),[6r,v;16] led to carbenoids which were thermally more stable and reacted more selectively than the alkali metal species (see Scheme 4).[17]

Not surprisingly, all the carbenoids became preferred subjects of physical organic studies and especially for synthetic applications. A CAS online search (May 2000) revealed 302 different compounds of only the type $R_2C(Li)Hal$ and 1451 references containing the term "carbenoid(s)". A comprehensive treatment of all aspects of carbenoids within the framework of this review was therefore a apriori impossible. A logical selection, however, is indicated by the ambiphilic behavior of carbenoids. First, as being normal for carbenoids, they react with electrophiles. In his review article "Lithium-Halocarbenoids - Carbanions of High Synthetic Value", Siegel surveyed in 1982[6l] the reactions of carbenoids with electrophiles rather comprehensively, and Braun summarized in 1998 the chemistry of "α-Heteroatom-Substituted 1-Alkenyllithium Reagents: Carbanions and Carbenoids for C−C Bond Forming Reactions",[6w] again concentrating on the nucleophilic properties of carbenoids. In his final remarks, Siegel[6l] came to the following conclusions: "Some characteristics of the chemistry of carbenoids are still not well understood as for example the nucleophilic substitution on the carbenoid center. Another still unsolved problem is the structure of (halo) carbenoids." Since both aspects are quite well understood in the meantime, we will concentrate in this review on the structure of carbenoids and on their reactions as electrophiles with emphasis on experimental as well as theoretical investigations. It is then shown that the insights gained in the case of the intensively studied carbenoids (see, e.g., **23** in Scheme 5) analogously apply for nitrenoids **24** and oxenoids **25** (Scheme 5).

1.2. Stereochemistry of the Reactions of Li/Hal Carbenoids with Nucleophiles

The first point of interest is the stereochemistry of carbenoid reactions with nucleophiles. The S_N2-type substitution of the halide by the migrating aryl substituent in the Fritsch−Buttenberg−Wiechell rearrangement has been mentioned (see Scheme 2). How is the situation in other carbenoid reactions with nucleophiles?

Scheme 5. Carbenoids 23, Nitrenoids 24, and Oxenoids 25

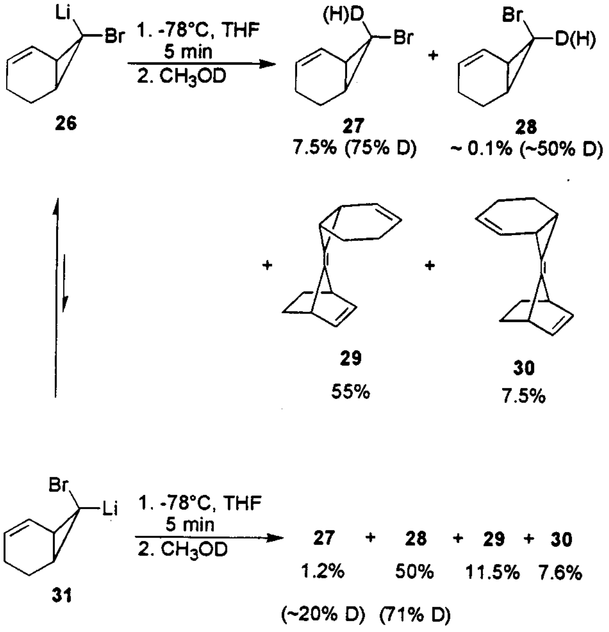


M = Li, Na, K, MgX, ZnX etc.
X= F, Cl, Br, I, OR and other leaving groups
R^1, R^2 = H, alkyl and aryl substituents

1.2.1. Reactions with C=C Bonds

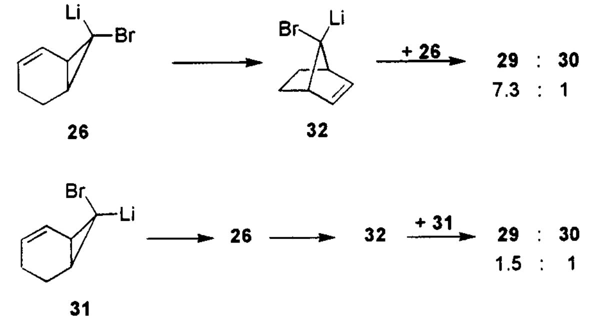
The reactions of Li/Hal carbenoids[18,19] with olefins[2a,4,6d,20−26] were among the first reactions of carbenoids studied comprehensively. Similar studies were performed with the Simmons−Smith reagent in which zinc is the key metal.[6r,v,16] First indications concerning the stereochemistry of the reaction of a Li/Hal carbenoid with a C=C bond came from investigations of Skattebøl-type rearrangements.[27] Thus, Warner and Herold[28] were able to prepare stereoselectively the carbenoids **26** and **31** with **26** being the thermodynamically more stable species; see Scheme 6.

Scheme 6. Intramolecular Reactions of Cyclopropyl Carbenoids with a C=C Bond: The Skattebøl Rearrangement, and "Eliminative Dimerization" of Two Carbenoids



From the results shown in Scheme 6, one can conclude that the more stable **26** rearranges ~15 times faster (first to give **32**, see Scheme 7, and then **29** and **30**, respectively) than **31**. The only reasonable explanation is that the double bond participates effectively in **26**, but not in **31**, supporting the ionization of bromine in **26** in an S_N2-type fashion

Scheme 7. "Eliminative Dimerization" of Carbenoid 32 with Carbenoids 26 and 31, Respectively



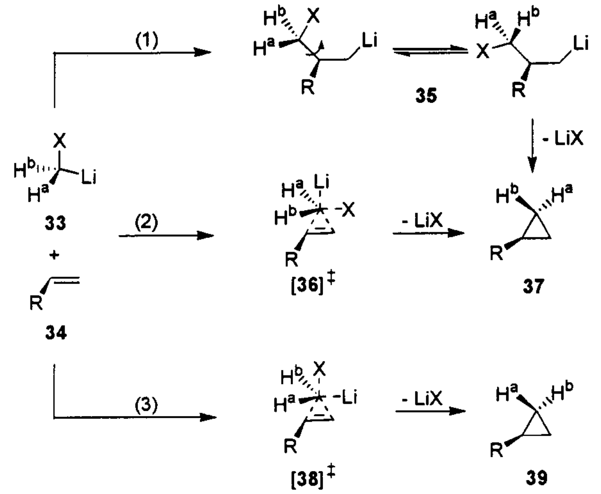
from the rear side finally to give the rearranged **32** (Scheme 7).

In the case of the isomeric **31**, such a double bond participation is impossible, and the carbenoid isomerization **31** → **26** becomes the rate-limiting step.[29]

Another point is of interest: if the olefinic "dimers" **29** and **30** would be formed from intermediate carbenes, the ratio **29**:**30** should be the same in the reaction starting with **26** as well as with **31**. Since this is clearly not the case (see Scheme 7), **32** most likely reacts with **26** (if formed from **26**) and with **31** (if formed from **31**), finally giving **29** and **30**. We shall return to such "eliminative dimerizations" of carbenoids in section 1.2.4.

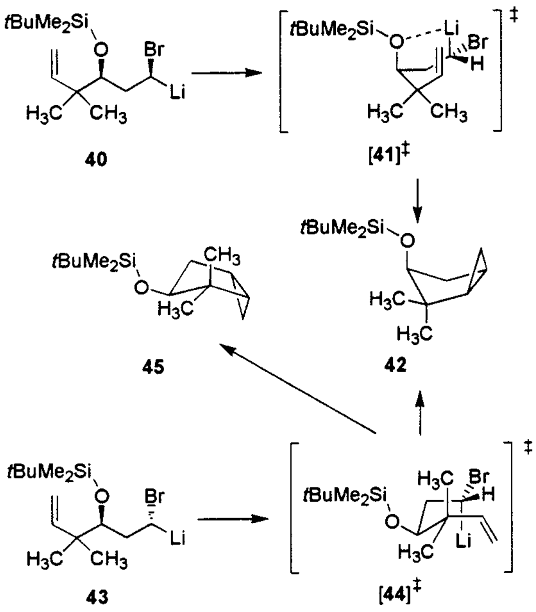
The proof of the stereochemistry of the carbenoid cyclopropanation reaction with olefins was provided recently. From the possible pathways (Scheme 8), namely, carbolithiation of the olefin **34** by the carbenoid **33** to give **35** followed by rotation around the C−C bond and ring closure to the cyclopropane **37** (1) (which is topologically identical with a concerted process via transition state [**36**]‡ (2)) and the concerted carbenoid reaction via the transition state [**38**]‡ to give the isomeric cyclopropane **39** (3), the two-step carbolithiation process (1) was ruled out by Huisgen and Burger in 1970[30] at least for the addition of chloromethyllithium to olefins. Obviously, the carbolithiation process (1) (Scheme 8) corresponds to a nucleophilic reactivity of the carbenoid **33** with an olefin which is unfavorable.

Scheme 8. Stereochemistry of Cyclopropane Formation from Carbenoids and Olefins: Expectations



In 1995 Stiasny and Hoffmann[31] investigated the intramolecular cyclopropanations of the diastereomeric carbenoids **40** and **43**. As one can see from Scheme 9, **40** is perfectly set up for an S$_N$2-type transition state [**41**]‡ with backside attack of the C=C bond at the C−Br bond to give cyclopropane **42**. Correspondingly, the half-life of this reaction is less than 5 min at −110 °C.

Scheme 9. Stereochemistry of Cyclopropane Formation from Carbenoids and Olefins: Experiments



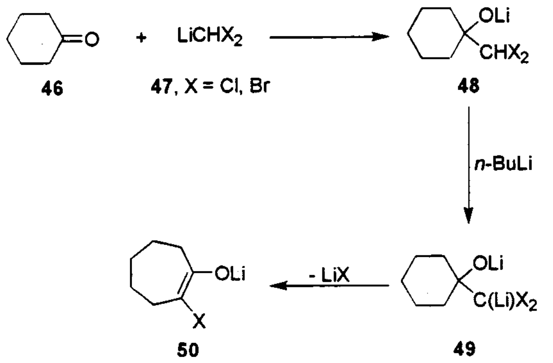
Reaction of the diastereomeric carbenoid **43** is much slower, giving the two products **42** and **45** (the different behavior of **40** and **43** also rules out the reaction of carbenes). Compound **45** should be formed in a concerted, S$_N$2-type pathway via [**44**]‡, which however is not stabilized by a Lewis base−Li$^+$ interaction as is the case for [**41**]‡. Compound **42** could be formed via a transition state analogous to [**36**]‡ in Scheme 8. Alternatively, **42** may be traced back to a carbolithiation process assisted by an internal Lewis base (which facilitates such reactions).

In conclusion, the reactions of carbenoids with C=C bonds proceed favorably as suggested by Closs and Closs[2a] and Closs and Moss[4]. The experimental findings are in agreement with quantum chemical calculations of Mareda, Rondan, Houk, Clark, and Schleyer,[32] theoretical considerations of Hoveyda, Evans, and Fu,[33] and a recent DFT study of the Simmons−Smith reaction by Bernardi, Bottoni, and Miscione.[34] Details of the theoretical work are discussed in section 1.4.1.3.

1.2.2. Reactions with C−C Bonds

In the early 1970s, several groups[35−38] reported on the reactions of carbonyl compounds such as **46** with dichloro(dibromo)-methylithium **47** to give adducts of the type **48**; see Scheme 10. Further treatment with base led, via the carbenoid **49** and migration of a substituent from the β-carbon atom to the carbenoid

Scheme 10. Homologation of a Cyclic Ketone with $LiCHX_2$ Carbenoids

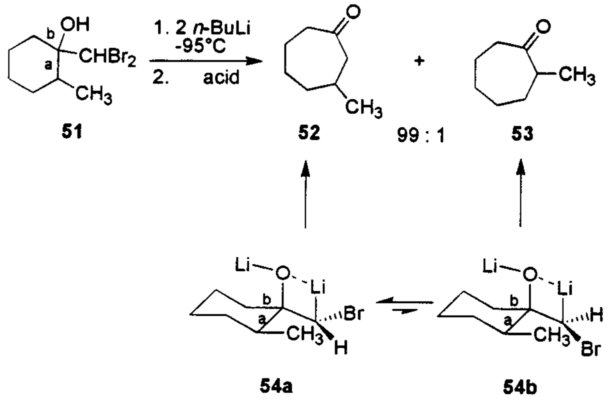


carbon together with the elimination of LiCl(Br), to the ring-enlarged **50**.

Undoubtedly the rearrangement **49** → **50** profits from the formation of the enolate **50**. While the carbenoid **47** acts as a nucleophile, it is the electrophilic nature of the carbenoid **49** which determines the course of the reaction. Rearrangements of carbenoids to give olefins without the support of a LiO-substituent at the *β*-C-atom were described earlier; see Scheme 4.

Nozaki et al.[39] studied the regioselectivity in the reaction of dibromomethyl-2-methylcyclohexanol **51** with 2 equiv of *n*-butyllithium in tetrahydrofuran at −95 °C and found the two ketones, **52** and **53**, in a 99:1 ratio; see Scheme 11.

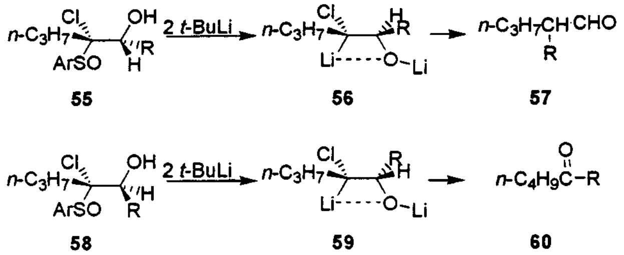
Scheme 11. Regioselectivity in C−C Bond Migration to a Carbenoid Carbon Atom



The reason for the strongly preferred migration of bond a as compared to bond b was explained with the preference of diastereomer **54a** in equilibrium with **54b** as a result of the repulsion between Br and the CH_3 group in **54b**, and the migration of the alkyl group anti to the departing bromide leading to the observed regiospecificity of the rearrangement. Vedejs and Shephard[40] confirmed the regioselectivity of the ring enlargement; however, Murray[41] reported on nonspecific rearrangements.[42]

A new method for preparing *β*-oxido carbenoids, recently reported by Satoh,[43a] is more detailed here because of its interesting stereochemical information. Reaction of α-chloro-*β*-hydroxy sulfoxides such as **55**, and its diastereoisomer **58**, with 2 equiv of *tert*-butyllithium[43b] led to two diastereomeric *β*-oxido carbenoids **56** and **59**, respectively, with the preferred conformations shown in Scheme 12.

Scheme 12. Configuration-Dependent Chemoselective Rearrangements of the *β*-Oxido Carbenoids 56 and 59



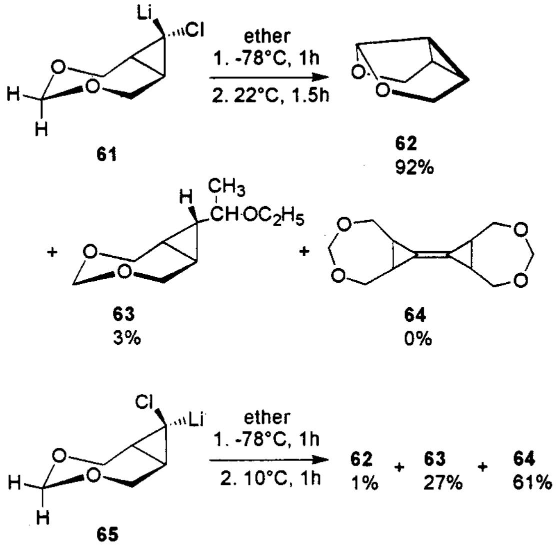
Intramolecular S_N2-type interaction with the carbenoid C−Cl bond in the case of **56** is only possible with the C−C bond of group R finally migrating to the carbenoid carbon atom. Elimination of LiCl leads to the aldehyde **57**. Indeed, **57** is formed 99 times more favorably than the ketone **60**, a product of migration of the *β*-H atom. On the other hand, migration of hydrogen to the carbenoid carbon atom is strongly preferred (99:1) if the reaction is started from **58**. In the most favorable conformation of the carbenoid **59**, the *β*-C−H bond is now set up for an anti-interaction with the carbenoid C−Cl bond leading to the ketone **60**. Both reactions clearly show the stereoselective reactivity of carbenoids as compared to that of carbenes. In both cases—C−C and C−H bonds, respectively, being the nucleophiles—the preferred geometry is of the S_N2-type. The C−H bond insertion (H-migration) in the case of the carbenoid **59** is an example of reactions dealt with in more detail in the following section 1.2.3.

1.2.3. Reaction with C–H Bonds

We have mentioned the first C−H bond insertions (H-migrations) in the chemistry of carbenoids in the Introduction (see Schemes 3 and 4). For further reactions of this type, the reader is referred to review articles; see ref 6. A first example of such a reaction supporting the S_N2-type anti stereochemistry was shown in Scheme 12; see the transformations **58** → **59** → **60**. Another example of stereoselectivity in carbenoid C−H insertion reactions was provided by Taylor;[44,6i,6m] see Scheme 13.

Thus, diastereoisomer **61** is perfectly arranged for an S_N2-type interaction of the remote C−H bond (in the “boat” conformation of **61**) with the carbenoid C−Cl bond to give predominantly **62**. The ether insertion product **63** is formed in low yields (3%). It is worth mentioning that these S_N2-substitutions occur at carbenoid cyclopropane (!) C−Cl bonds. Normal cyclopropyl chlorides are extremely reluctant toward S_N2-type substitutions.[6s] In the diastereoisomer **65**, an intramolecular S_N2-type insertion into the C−Cl bond to give **62** is obviously unfavorable. Correspondingly, **62** is the least formed species (1%), and insertion into ether C−H bonds competes successfully (**63**, 27%). The olefin **64**, not observed starting from **61**, is mostly formed (61%). As indicated in Scheme 6 and detailed in section 1.2.4, **64** is the

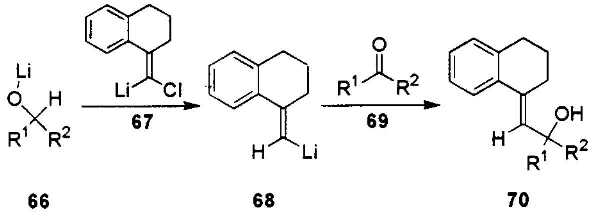
Scheme 13. Different Reactivity of the Two Diastereomeric Li/Cl Carbenoids 61 and 65



result of an “eliminative dimerization” of two carbenoids **65** and not of a carbene dimerization.

Finally, Oku, Harada, et al.[45] concluded from their studies of hydride transfer from alkoxides onto carbenoids that these reactions occur with inversion of configuration, the stereoselectivity being 74−100%. The sequence **66** + **67** → **68** + **69** → **70** as shown in Scheme 14 illustrates the case.

Scheme 14. Stereoselective Substitution with a Hydride at a Vinylic Carbenoid Carbon Atom



In conclusion, C−H bond insertions of carbenoids as well as carbenoid reactions with hydride occur—like reactions with C=C and C−C bonds—in an S$_N$2-type mode.

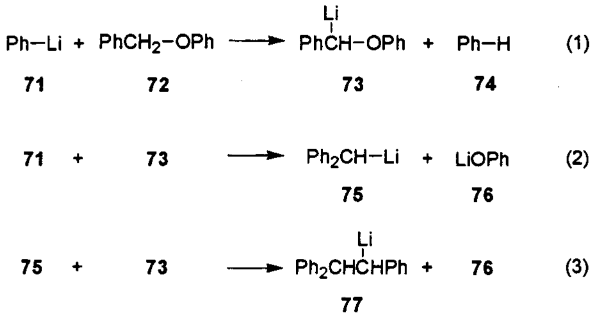
The hydride transfer leads directly to the reaction of “carbanions” and other anionic nucleophiles with carbenoids.

1.2.4. Reactions with (Carb)anionic Nucleophiles Including “Eliminative Dimerizations” of Two Carbenoids

Since carbenoids have been shown to react with rather weak nucleophiles such as C=C or even C−C and C−H bonds, it is not surprising that they react rather fast with (carb)anionic nucleophiles. An example of a reaction with hydride H$^-$ was given in the previous chapter (Scheme 14). In the following we will concentrate on reactions with “carbanions”, which are often present due to the preparation of carbenoids either by deprotonation or by halogen-(metalloid)−lithium exchange with, e.g., RLi compounds. Furthermore carbenoids themselves are “carbanions”.

Homologation of RLi by means of a carbenoid was among the first reactions of a carbenoid with a carbon nucleophile (although the first example of such a reaction was not recognized for a long time as such, especially since a Li/OR carbenoid was involved). In 1938, Lüttringhaus and Sääf[46] reported the reaction of phenyllithium **71** with benzyl phenyl ether **72** to give the α-lithiated benzyl phenyl ether **73** and benzene **74** (Scheme 15, reaction 1).

Scheme 15. Homologation Reactions of the Li/OR Carbenoid 73



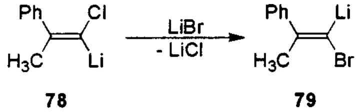
However the reaction did not stop at that stage: phenyllithium **71** not only reacted as a base with ether **72** but also as a nucleophile with the α-lithiated benzyl phenyl ether **73** to give diphenylmethyllithium **75** and lithium phenoxide **76** (reaction 2 in Scheme 15). In a further reaction of this type (3), **75** reacted with **73** to give **77** and **76**. On protonation, **75** led to diphenylmethane (14%) and **77** to 1,1,2-triphenylmethane (33%). Thus, the lithiated ether clearly behaved as a Li/OR carbenoid. Wittig and Löhmann[47] confirmed this sequence and noticed the “higher mobility” (“grössere Beweglichkeit”)[18] of the phenolate group in the carbenoid **73** as compared to the phenolate group in the ether **72**. A similar homologation sequence was found by Ziegler and Gellert[19] in the reaction of *n*-butyllithium with dimethyl ether.[48]

In the Li/Hal carbenoid series Kirmse and Wedel[49] observed a homologation when they reacted methyllithium with 1,1-dibromomethane in ether to give ethyl bromide (48%) and propyl bromide (13%). When Huisgen and Burger[30] reacted *n*-butyllithium with CH_2Br_2 or CH_2BrCl “even under conditions which we have described as optimal for the conversion of alkenes to cyclopropanes, the formation of homologous alkyl bromides remained the major reaction pathway”. The homologous alkyl bromides are formed from the first formed homologous alkyllithium species (^{n}BuLi + $LiCH_2Br(Cl)$ → *n*-pentyllithium + LiBr(Cl)) by Li−Br exchange with CH_2Br_2 or CH_2BrCl.

The stereochemistry of the reaction of (carbon) nucleophiles with a carbenoid carbon atom again was determined with cyclopropyl and vinyl carbenoids because of their higher configurational stability (see also Schemes 13 and 14). Seminal information was provided by the halide exchange (Br$^-$ versus Cl$^-$) in the reaction of the vinylic Li/Cl carbenoid **78** with LiBr to give preferentially the Li/Br carbenoid **79**,[50] see Scheme 16.

The stereochemistry implies an S$_N$2-type substitution at a vinylic C−Cl bond which is not observed in nonlithiated vinyl chlorides. A related reaction could

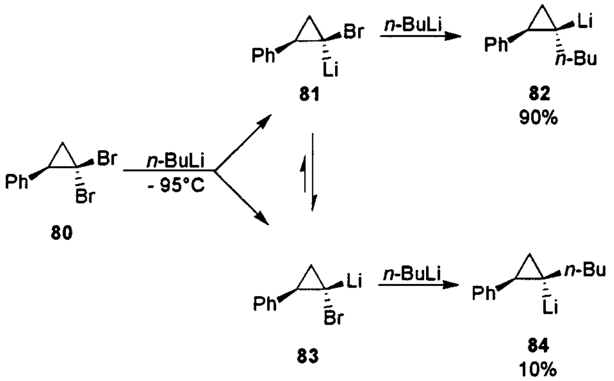
Scheme 16. Stereoselective Cl−/Br− Exchange of the Vinylic Li/Cl Carbenoid 78



be responsible for the isomerization of vinyl carbenoids (in the case of **78**, LiCl instead of LiBr) and of other carbenoids.[50]

Kitatani, Yamamoto, Hiyama, and Nozaki[51] observed stereoselective substitution at a cyclopropyl carbenoid in the reaction with *n*-butyllithium; see Scheme 17.

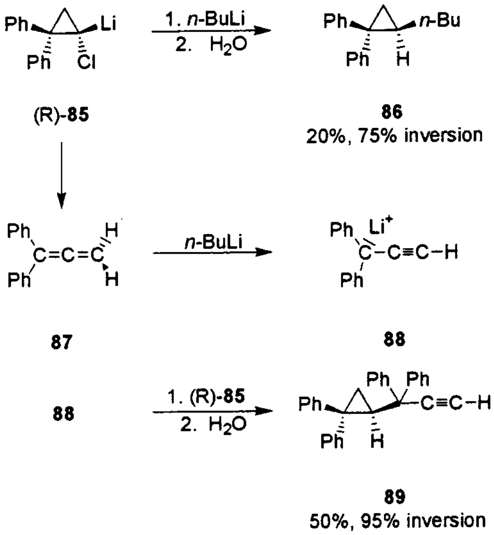
Scheme 17. Stereoselective Substitution with *n*-Butyllithium at the Cyclopropyl Carbenoid Carbon Atoms of 81 and 83



In the reaction of the dibromide **80** with excess ^{n}BuLi at −95 °C, the *trans*-Li isomer **81** is predominantly formed and not the thermodynamically more stable **83**. Further reaction of **81** and **83** with ^{n}BuLi leads to substitution of Br^- by $^nBu^-$ with inversion of configuration at the carbenoid carbon atom to give the cyclopropyllithium compounds **82** and **84**, respectively. The stereoselectivity as shown by trapping reactions of **82** and **84** with electrophiles amounts to 90−100%.

The stereochemical course of substitution reactions of chiral cyclopropyl- and vinyl-carbenoids with RLi compounds as nucleophiles was studied by Walborsky et al.[52] The cyclopropyl case is shown in Scheme 18.

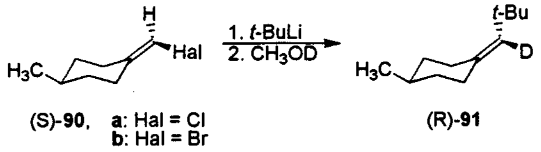
Scheme 18. Stereoselective Substitution with RLi at the Carbenoid Carbon Atom of (*R*)-85



Reaction of (*R*)-**85** with *n*-butyllithium leads to the substitution products **86** and **89**. Compound **86** (20%, 75% inversion) was formed by reaction of ^{n}BuLi with (*R*)-**85**. The major product **89** (50%, 95% inversion) results from a sequence of reactions starting with the well-known cyclopropyl carbenoid → allene transformation[6] to give **87**. Then **87** is deprotonated by ^{n}BuLi to give **88** which acts as a nucleophile in the reaction with (*R*)-**85** finally to give **89**.

The substitution reaction of RLi at a vinylic carbenoid carbon is shown in Scheme 19.

Scheme 19. Stereoselective Substitution with ^{t}BuLi at a Vinylic Carbenoid Carbon Atom

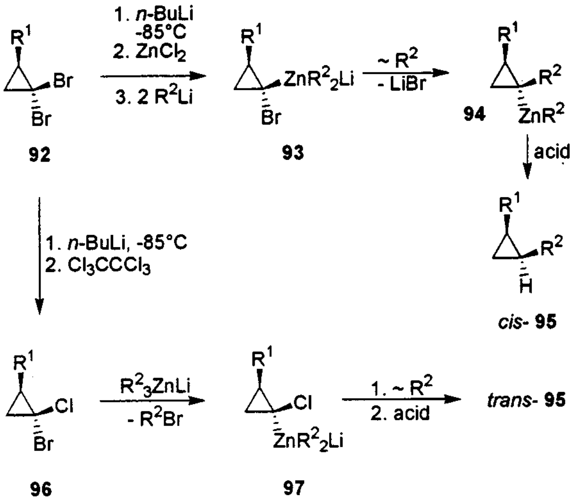


90	solvent	T [°C]	yield of 91 [%]	inversion [%]
a	ether	- 75	36	65
a	THF	- 75	70	69
b	ether	- 90	17	69
b	THF	- 90	5	76

Reaction of (*S*)-**90a** with ^{t}BuLi in diethyl ether (THF) gave, after deuteration with CH_3OD, (*R*)-**91** with 65 (69)% inversion; the corresponding bromide (*S*)-**90b** led to (*R*)-**91** with 69 (76)% inversion. Compound (*R*)-**91** is formed via deprotonation of (*S*)-**90** by ^{t}BuLi to give the corresponding carbenoid, which then reacts with another ^{t}BuLi under predominant inversion of configuration to give a vinyllithium species which is deuterated to give (*R*)-**91**. In the case of (*S*)-**90b**, bromine−lithium exchange is the predominant reaction (58 and 90%, respectively).

Stereoselective formation of *cis*- and *trans*-substituted cyclopropanes, respectively, by means of zincate carbenoids have been performed by Harada and Oku et al.[53] on a preparative scale. The important steps of the procedure are outlined in Scheme 20.

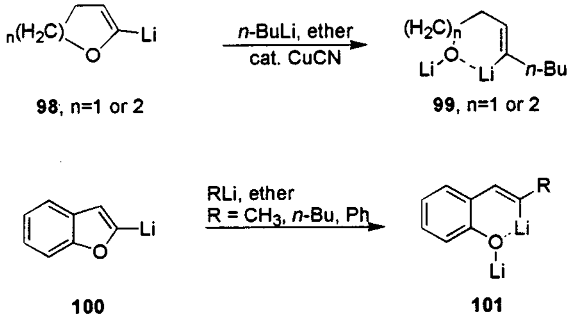
Scheme 20. Stereoselective Synthesis of *cis*- and *trans*-Substituted Cyclopropanes via Zinc-ate Carbenoids 93 and 97



Reaction of the dibromocyclopropane **92** with ^{n}BuLi, followed by $ZnCl_2$ and 2 equiv of R^2Li, provides the zinc-ate **93**. Intramolecular substitution at the carbenoid carbon atom by R^2 led to **94** which after protonation gave the *cis*-cyclopropane *cis*-**95** with a selectivity of >10:1. The route from **92** to the *trans*-isomer *trans*-**95** involves chlorination of the Li/Br carbenoid to give **96**, zincation of the C–Br bond (**97**), intramolecular R^2-migration as in the case of **93**, and protonation to *trans*-**95**. In both cases, S_N2-type substitutions at the carbenoid C-atoms by R^2 of the zinc-ates **93** and **97**, respectively, are relevant for the observed stereoselectivities which in the *trans*-**97** case are also generally >10:1. In principle, the same routes have been used for the stereoselective syntheses of (*Z*) and (*E*) alkenes, respectively,[53] which is not outlined here.

S_N2-type substitution reactions have also been observed in the case of the cyclic vinylic Li/OR carbenoids **98** and **100** (although there is not really a choice of stereochemistry because of the ring systems); see Scheme 21.

Scheme 21. Reaction of the Vinylic Li/OR Carbenoids 98 and 100 with RLi Nucleophiles

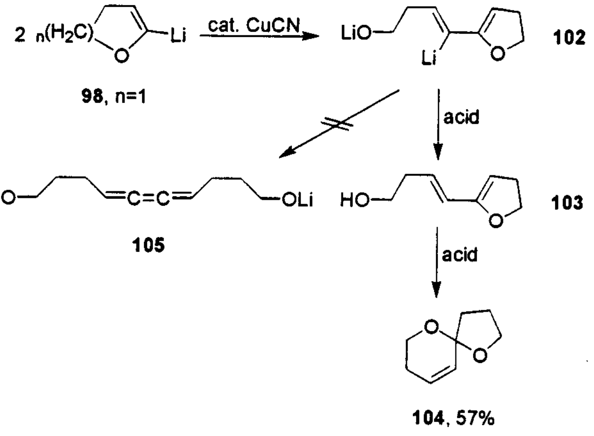


Thus the α-lithiated vinyl ethers **98** react with ^{n}BuLi, catalyzed by CuCN, to give the vinyllithium species **99** stereoselectively.[54] Similarly, lithiated benzofuran **100** gives with RLi stereoselectively compounds **101**.[55] Nucleophilic substitution by an S_N2 mechanism at a nonlithiated enolether α-carbon atom was never observed. This is indeed remarkable about the transformations **98** → **99** and **100** → **101**.[56]

An interesting observation was made when **98** ($n = 1$) was reacted with 0.17 mol. equiv of CuCN without adding another RLi; see Scheme 22.[54a] Then one molecule of **98** acts as a nucleophile and another one as an electrophile to give, after protonation, **104** in 57% yield.[54a]

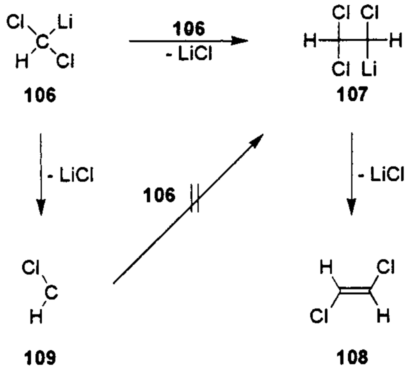
Dimerization of carbenes to give olefins is a well-known reaction,[6e,f,i,j,k] as is the "dimerization" of carbenoids although the latter is more difficult to prove. This example, however, is a very rare case of an "eliminative dimerization" of two carbenoids, because here the first formed intermediate **102** could be trapped before 1,2-elimination of MX had occurred. Obviously the 1,2-elimination of lithium alkoxide to give the olefin **105** is not very favorable. Protonation of **102** gives the enol ether **103** which finally leads to the spiroketal **104**.

Scheme 22. "Eliminative Dimerization" of Two Carbenoids 98



How is the situation of "eliminative dimerizations" in the case of Li/Hal carbenoids? As observed by Köbrich and Merkle, dichloromethyllithium **106** forms easily 1,2-dichloroethene **108**; see Scheme 23.[57a]

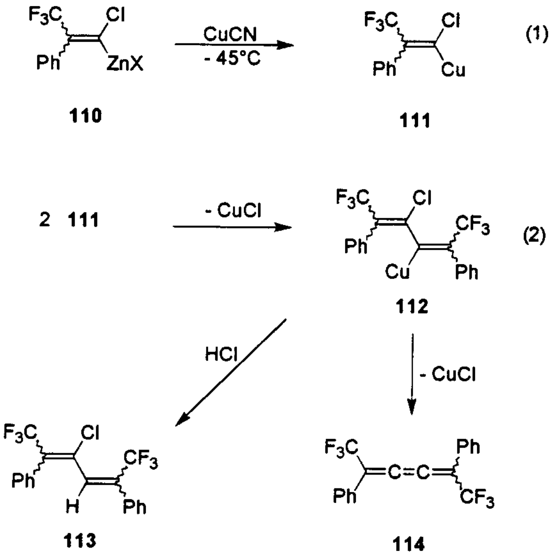
Scheme 23. "Eliminative Dimerization" of Dichloromethyllithium 106



If this reaction would occur via nucleophilic addition of the carbenoid **106** to the chlorocarbene **109** to give **107** which is transformed into **108** by β-elimination of LiCl, the reaction should be first order in **106** (dimerization of **109** is excluded). The concentration-dependent half-life of **106** excludes the reaction of **106** with **109**. Therefore the reaction should proceed such that two carbenoids **106** react with each other, one being the electrophile and the other one the nucleophile, to give **107** and then **108**. Since **106** is less nucleophilic than, e.g., *n*-butyllithium, the reaction of **106** with **106** is slower than with ^{n}BuLi. That carbenes similarly should not be involved in the formation of the olefins **29** and **30** from the carbenoids **26** and **31**, respectively, as discussed by Warner,[28] was shown earlier; see Scheme 6. The intermediate **102**, Scheme 22, which undergoes rather slow 1,2-elimination of LiOR, indeed proves the formation of such intermediates in the carbenoid "eliminative dimerization" at least in this particular case. In "dimerizations" of "normal" Li/Hal carbenoids, the corresponding 1,2-elimination of LiHal is very fast. However, if the alkali metal is replaced by Zn or Cu, the first product of the "eliminative dimerization" is also detectable as recently shown by Burton et al.;[58] see Scheme 24.

Reaction of the ZnX/Cl carbenoid **110** with 1 equiv of CuCN leads to a Cu-carbenoid **111** (reaction 1),

Scheme 24. Interception of the Intermediate 112 in the "Eliminative Dimerization" of the Cu/Cl Carbenoid 111



which acts as a nucleophile *and* an electrophile to give the intermediate **112** (reaction 2). Compound **112** was detected by F NMR spectroscopy as well as trapped with HCl to give **113**. Elimination of CuCl gives the olefin **114**.

In conclusion, the examples outlined in chapter 1.2 clearly demonstrate that all the reactions with nucleophiles (C=C, C−C, C−H bonds, and (carbon) nucleophiles), which are typical for carbenes, are also performed by carbenoids which underlines their strong electrophilic nature. Before the reasons for the strong electrophilic nature of carbenoids are discussed, the question is investigated whether it is always the carbenoid which reacts in what might be a carbenoid reaction, or whether in some cases it is the carbene instead.

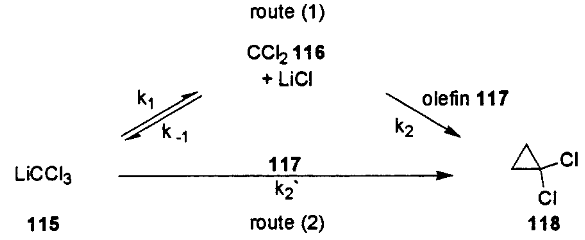
1.3. Carbenes Formed from Carbenoids

The formation of carbenes from carbenoids was first shown by J. Hine in his classical work on the alkaline hydrolysis of haloforms (HCX_3, X = Cl, Br, I, respectively).[6a] These studies led also to the introduction of the concept of dihalocarbenes as reactive intermediates in solution.[59] We will concentrate in this section on investigations in solutions without water because of their comparability with reactions discussed in sections 1.1. and 1.2.

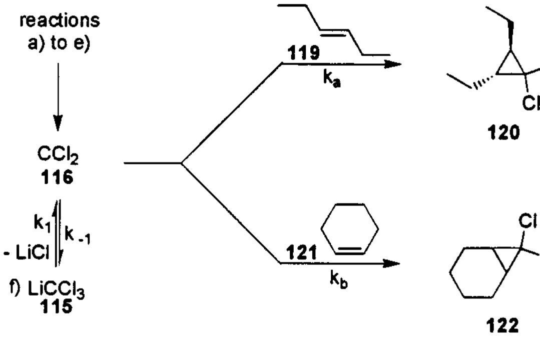
Trichloromethyllithium **115** was one of the first carbenoids studied intensively in etheral solvents; however, it has been uncertain for a long time whether it is the dichlorocarbene CCl_2 **116** that undergoes the reaction with an olefin **117** to give the cyclopropane **118** (route 1 in Scheme 25) or the carbenoid $LiCCl_3$ **115** (route 2).

Compared with other carbenoids, $LiCCl_3$ **115** showed strong electrophilic character,[6d] less thermal stability than dichloromethyllithium $LiCHCl_2$ **106**,[23,60] intermolecular insertion of the CCl_2-moiety into the α-CH-bonds of tetrahydrofuran,[23] and high yields of cyclopropanes in reactions with olefins.[21−26,61] A comparison of the competition constants k_a/k_b of the dichlorocyclopropane-forming reactions a−e with (*E*)-3-hexene **119** to give **120**, and with cyclohexene **121** to give **122**, in which dichlorocarbene **116** is known to be formed from different precursors, with the competition constant k_a/k_b starting with $LiCCl_3$ **115** (reaction f) revealed the carbene CCl_2 **116** as the reacting species also in that case; see Scheme 26.[62,63]

Scheme 25. Carbene or Carbenoid Reaction of $LiCCl_3$ 115 with an Olefin?



Scheme 26. Competition Constants k_a/k_b in the Dichlorocyclopropane Forming Reactions a to e, and f with $LiCCl_3$ 115

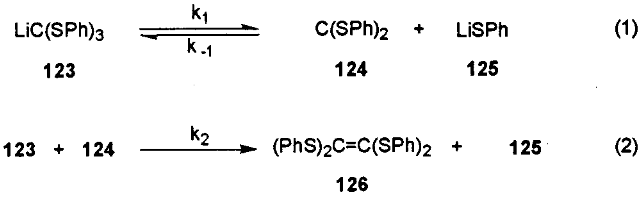


		k_a / k_b
a)	$PhHgCCl_2Br$, 80°C	0.52
b)	CCl_3CO_2Na, 80°C	0.52
c)	$PhHgCCl_3$, NaI, 80°C	0.54
d)	$PhHgCCl_2Br$, NaI, -15°C	0.44
e)	$HCCl_3$ + KO*t*-Bu, -15°C	0.44
f)	$LiCCl_3$ **115**, -73°C	0.40

It was also shown that cyclohexene **121** accelerates the decomposition of the carbenoid $LiCCl_3$ **115**.[62] These results led to the conclusion that $LiCCl_3$ **115** reacts with olefins via route 1 in Scheme 25 with k_2 being the rate determining step (k_1, $k_{-1} \gg k_2$), and not via route 2.

The carbenoid/carbene problem was also the subject of a study performed by Seebach and Beck.[64] They showed that the carbene bis(phenylthio)methylene **124** (together with lithium thiophenolate **125**) is easily formed from the carbenoid lithium-tris(thiophenyl)methane **123** (reaction 1 in Scheme 27) and that the reaction of the carbenoid **123** with the

Scheme 27. Formation of the Carbene 124 from the Carbenoid 123

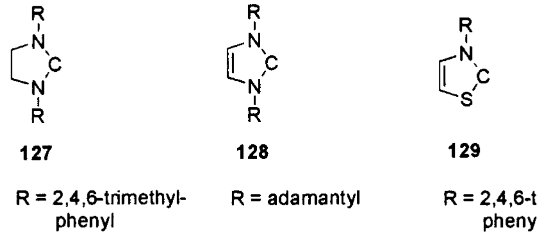


carbene **124** to give the olefin **126** and the thiophenolate **125** (reaction 2 in Scheme 27) is the rate determining step.

What is the reason for the facile formation of the carbenes CCl_2 **116** and $C(SPh)_2$ **124** from the corresponding carbenoids $LiCCl_3$ **115** and $LiC(SPh)_3$ **123**, respectively? Interestingly, if *one* chlorine atom in $LiCCl_3$ **115** is substituted by hydrogen to give $LiCHCl_2$ **106**, reactions of the corresponding monochloro-carbene CHCl **109** formed by α-elimination of LiCl from $LiCHCl_2$ **106** were never observed, as Köbrich and Merkle reported.[57a] Only the carbenoid $LiCHCl_2$ **106** underwent reactions with nucleophiles.

The difference between the pairs $LiCCl_3$ **115**/CCl_2 **116** (+LiCl), $LiC(SPh)_3$ **123**/$C(SPh)_2$ **124** (+LiSPh), and $LiCHCl_2$ **106**/CHCl **109** (+LiCl) is due to the different stabilities of the carbenes formed in each case. Paulino and Squires[65] determined the heats of formation of various singlet carbenes: CF_2 −39.4 kcal/mol; CCl_2 52.1 kcal/mol; CH_2 92.9 kcal/mol. Thus the stability of a carbene increases strongly with the donor qualities of its substituents. One can conclude from these results that CHCl **109** is less stable than CCl_2 **116** and that $C(SPh)_2$ **124** should also be well stabilized.[6g,i,j,k] Not surprisingly, since Scheibler's struggle to find an organic derivative of carbon monoxide in the 1930s,[66] there have been numerous attempts to find evidence, or even to isolate, of stable carbenes of the type CX_2 with X being Hal, NR_2, SR, OR, etc. In the 1960s Wanzlick[67] was very close to isolating such species, but it was only until 1991 that Arduengo et al. were able to crystallize first **128**[68a] (and many others of that type) and then **127** and **129**; see Scheme 28.[68]

Scheme 28. Stable Crystalline Carbenes



127 R = 2,4,6-trimethylphenyl

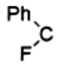
128 R = adamantyl

129 R = 2,4,6-trimethylphenyl

It will be seen in section 1.4.1.1 how the stability of the respective carbene determines the structure of the corresponding carbenoid.

Finally it should be mentioned that the rate constants k_{-1} of the reactions of a carbene (CFPh, **130**) with various salts (compare Schemes 25−27) have recently been measured by Moss et al.,[69]; see Table 2.

Table 2. Rate Constants k_{-1} of the Reactions of the Carbene CFPh 130 with Various Salts in Acetonitrile at 20 °C



130

entry	salt	k_{-1} [$M^{-1}s^{-1}$]
1	LiBr	$3.9 \pm 0.2 \times 10^7$
2	$^nBu_4NBr$	$1.3 \pm 0.03 \times 10^7$
3	LiI	$2.6 \pm 0.07 \times 10^7$
4	$^nBu_4NI$	$1.5 \pm 0.04 \times 10^7$
5	$^nBu_4NCl$	$2.0 \pm 0.04 \times 10^8$
6	$^nBu_4NN_3$	$2.8 \pm 0.4 \times 10^8$
7	$LiClO_4$	$4.7 \pm 0.3 \times 10^6$
8	$LiBF_4$	$4.8 \pm 0.2 \times 10^6$
9	$^nBu_4NClO_4$	

First of all, and in agreement with the conclusions drawn by Köbrich et al.[62] from the reactions of $LiCCl_3$ **115** with olefins and by Seebach from his studies of $LiC(SPh)_3$ **123**,[64] the reactions of the carbene **130** with all sorts of salts are very fast except for $^nBu_4NClO_4$ (entry 9, Table 2), in the case of which no reaction is observed. Next it is interesting to look at the differences between the various k_{-1} values. From entries 1 and 2 it is indicated that both, Li^+ and Br^-, contribute to the kinetics of the quenching of **130** with LiBr since the rate constant k_{-1} for the reaction of **130** with $^nBu_4NBr$ is only one-third of that with LiBr. It seems that Br^- and Li^+ attack **130** simultaneously: Br^- at the empty p-orbital and Li^+ at the sp^2-orbital containing two electrons. A related metal assistance has also been invoked for the cleavage of carbenoid C−X bonds.[6c,d,e,18,52] It is therefore not surprising that $^nBu_4NClO_4$ does not react with the carbene **130**.

The results of chapters 1.1 and 1.2 can be summarized as follows: carbenoids react as electrophiles with many types of nucleophiles. Only comparatively stable, donor-substituted carbenes CX_2 are formed from carbenoids by α-elimination of MX. The carbene (in equilibrium with the carbenoid) may be the better electrophile and react with a nucleophile (which could be the carbenoid, see Scheme 27).

We now turn to the question of the structure of carbenoids and the reason for their strong electrophilicity even though they are written as "anions".

1.4. Structural Investigations of Carbenoids

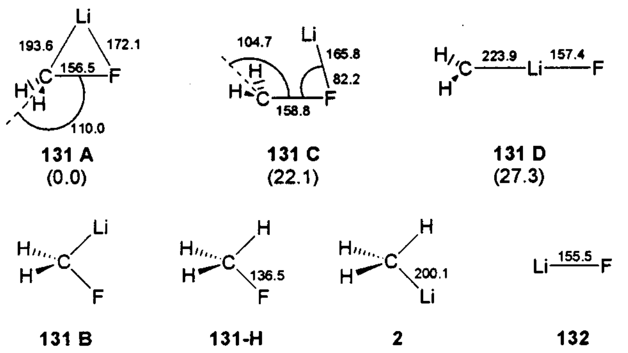
1.4.1. Quantum Chemical Calculations of Carbenoids

1.4.1.1. Structures of Carbenoids. In 1979 the first structural investigations of carbenoids were published: D. Seebach et al. reported on NMR investigations of carbenoids, which will be dealt with in detail in section 1.4.2, and P.v.R. Schleyer et al. provided insights into carbenoids by means of quantum chemical calculations, the theme of this section. It is perhaps interesting to mention that the first crystal structure determination of a carbenoid was published by G. Boche et al. only in 1993; see section 1.4.3.

1.4.1.1.1. $LiCH_2F$. The subject of the first theoretical calculations by the Schleyer group was the simplest model carbenoid $LiCH_2F$ **131**.[70−74] The results of the MP4SDTQ/6-31G(d)//6-31G(d)+ZPE calculations are summarized in Scheme 29.[72]

The most stable $LiCH_2F$ isomer is the lithium-bridged **131A** with Li^+ binding both to carbon and fluorine. The most striking features of **131A** are (i) the strongly elongated C−F bond from 136.5 pm in the nonlithiated **131-H** to 156.5 pm (20.0 pm, 14.7%) and (ii) all four ligands lying in a single hemisphere. In agreement with the calculations, the elongation of the bond between carbon and the leaving group X

Scheme 29. MP4SDTQ/6-31G(d)//6-31G(d)+ZPE Structures of $LiCH_2F$ 131; Bond Lengths [pm]; Bond Angles [deg]; Relative Energies [kcal mol^{-1}, in parentheses][a,b]



[a] The C−Li and Li−F bond lengths in CH_3Li **2** and Li−F **132** are given for comparison. [b] The numbering **131-H** and **131A**−**D** as shown in Scheme 29 is used throughout this work for ease of comparing related structures of different carbenoids. Thus, the nonlithiated compound is **131-H**, the Li-bridged species **131A**, the tetrahedral one **131B**, the carbene-donor complex **131C**, and the carbene-acceptor complex **131D**.

was later shown in crystal structure investigations (section 1.4.3) to be characteristic of carbenoids. It also agrees with weakened C−X bonds as postulated from the NMR investigations of carbenoids (section 1.4.2) and with the enhanced electrophilic reactivity of carbenoids outlined in sections 1.1 and 1.2. The Li−F distance in **131A** measures 172.1 pm as compared to 155.5 pm in LiF **132**.

The less stable structures **131C** (22.1 kcal mol^{-1}, C−F 158.8 pm (22.3 pm, 16.3%)) and **131D** (27.3 kcal mol^{-1}, C−F bond broken!) can be regarded as singlet methylene-lithium fluoride complexes in which the carbene acts as an acceptor and a donor, respectively. Compounds **131C** and **131D** are unstable with respect to **131A** because lithium is bonded only to one atom (F and C, respectively) as compared to both atoms in **131A**. Thus, **131C** and **131D** are at best suggested to be metastable species. Interestingly, a classical tetrahedral structure **131B** could not be located on the potential surface probably because of the favorable interaction of Li^+ with fluorine.

It was also pointed out[70] that, at least when isolated in the gas phase (to which conditions the calculations refer), the carbenoid $LiCH_2F$ **131** should be a rather stable species, both thermodynamically and toward all possible unimolecular dissociation pathways. The isodesmic bond separation reaction (eq 1) (MP4SDTQ/6-31G(d)//6-31G(d)+ZPE)[72] shows a large net stabilization.

$$\underset{\textbf{131-H}}{CH_3F} + \underset{\textbf{2}}{CH_3Li} \xrightarrow{-15.0\ [\mathrm{kcal\ mol^{-1}}]} \underset{\textbf{131}}{LiCH_2F} + CH_4 \qquad (1)$$

$LiCH_2F$ **131** was studied at various levels of theory[32,71−76] including electron correlation and zero-point energy corrections; see Scheme 29 (in ref 72, 13 different levels are listed). The relevant differences are summarized as follows. The bent structure **131D** (HF/4-31G) is linear (C−Li−F 180°) at all higher levels; **131C** becomes more favorable than **131D** (e.g., E_{rel} [MP4SDTQ/6-31G(d)//6-31G(d) + ZPE]: **131C** 22.1 kcal mol^{-1} and **131D** 27.3 kcal mol^{-1}). In addition, the activation energies for the rearrangements of **131C** to **131A** (5.0 kcal mol^{-1}) and **131D** to **131A** (1.5 kcal mol^{-1}) clearly indicate that the higher energy isomers are metastable with respect to **131A**.[72,74]

Of special interest are the reaction energies (MP4SDTQ/6-31G(d)//6-31G(d) + ZPE) shown in eqs 2−4.[72]

$$LiCH_2F\ \textbf{131 A} \longrightarrow CH_2\ (^1A_1) + LiF \qquad 49.3\ \mathrm{kcal\ mol^{-1}} \qquad (2)$$

$$2\ \textbf{131 A} \longrightarrow H_2C{=}CH_2 + 2\ LiF \qquad -98.0\ \mathrm{kcal\ mol^{-1}} \qquad (3)$$

$$\textbf{131 A} + CH_2{=}CH_2 \longrightarrow C_3H_6 + LiF \qquad -59.0\ \mathrm{kcal\ mol^{-1}} \qquad (4)$$

Thus, eq 2 clearly shows that from a thermodynamic point of view α-elimination of LiF from the carbenoid $LiCH_2F$ **131A** to give the carbene CH_2 and LiF is very unfavorable in the gas phase (49.3 kcal mol^{-1}). This agrees nicely with the results in solution outlined in sections 1.2 and 1.3: the experimental observations indicated that only carbenes with two donor substituents are formed by α-elimination of LiX from the corresponding carbenoids. In all other cases it is the carbenoid that reacts. In contrast to eq 2, the "eliminative dimerization" of two carbenoids $LiCH_2F$ **131A** to give ethene and 2 LiF (−98.0 kcal mol^{-1}, eq 3), and the reaction of $LiCH_2F$ **131A** with ethene to give cyclopropane C_3H_6 and LiF (−59.0 kcal mol^{-1}, eq 4), are highly exothermic in the gas phase, again in excellent agreement with the situation observed in solution.

"Other than direct reaction of $LiCH_2F$ **131A**, the most likely carbene-like reaction of **131A** involves separation of the ion pair to give $LiCH_2^+$. The frontier orbitals of $LiCH_2^+$ are very similar to those of singlet CH_2 so that the two species may be expected to exhibit similar electrophilic reactivity".[70] To this date the ion $LiCH_2^+$, however, has not been shown to exist, not even in equilibrium with $LiCH_2F$ **131A**. Köbrich[6d] considered the metallocarbenium ion−halide anion form (e.g. **131′**) to be a contributor to the structure of lithium carbenoids (besides **131″**).

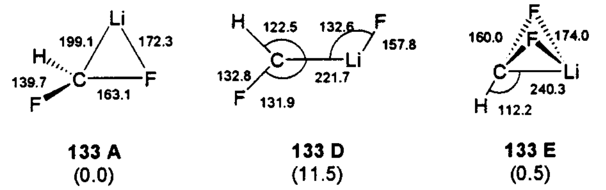
$$\underset{\textbf{131'}}{LiCH_2^+F^-} \longleftrightarrow \underset{\textbf{131}}{LiCH_2F} \longleftrightarrow \underset{\textbf{131''}}{Li^+CH_2F^-}$$

It thus seems that the strongly elongated C−F bonds in **131A** and **131C** are reason enough for the high electrophilicity of such carbenoids. The formation of an ion pair like $LiCH_2^+F^-$ apparently is not a prerequisite. A "metal assisted ionization" of carbenoids in reactions with nucleophiles, as suggested by Köbrich[6d] and Walborsky,[52] is also evident from the structures **131A** and **131C**: Li^+ is directly bonded to the leaving group F^-.

1.4.1.1.2. $LiCHF_2$. The first disubstituted model carbenoid, $LiCHF_2$ **133**, was also investigated by the Erlangen group;[77] see Scheme 30.

Again, the global minimum **133A** is characterized by a lithium-bridged C−F bond which is strongly elongated (163.1 pm (23.4 pm; 16.8%)) as compared to the nonbridged one (139.7 pm). The structure of **133A** strongly resembles the structure of $LiCH_2F$

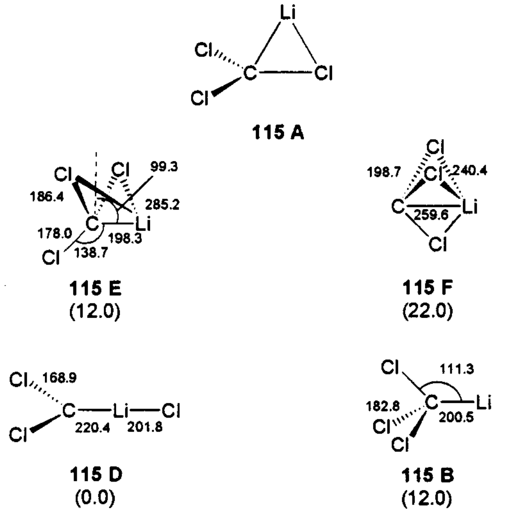
Scheme 30. MP2/4-31G//4-31G Structures of $LiCHF_2$ 133; Bond Lengths [pm]; Bond Angles [deg]; Relative Energies [kcal mol^{-1}, in parentheses]



131A; see Scheme 29. In **133E** a new structural type emerges: Li^+ is bonded to two fluorine atoms, and the C−Li bond is elongated to 240.3 pm. The two C−F bonds again are very long (160.0 pm). This structure is also strongly stabilized, which is reflected in the low energy relative to **133A** (0.5 kcal mol^{-1}). Compound **133D** closely resembles the CH_2·LiF complex **131D** (Scheme 29): one C−F bond is broken. Of special interest is the difference in the relative energies between $LiCHF_2$ **133D** (11.5 kcal mol^{-1}) and $LiCH_2F$ **131D** (28.7 kcal mol^{-1}, also MP2/4-31G//4-31G).[70] Apparently the second F atom in **133D** stabilizes the carbene part of the carbene complex **133D** strongly. These data agree nicely with the experimental findings outlined in section 1.3 according to which the formation of carbenes from carbenoids is strongly related to the stabilization of the respective carbene by donor substituents. Again, a classical tetrahedral structure **133B** was not found.

1.4.1.1.3. $LiCCl_3$. The first carbenoid with three substituents X studied by theoretical methods was $LiCCl_3$ **115**. Scheme 31 summarizes the calculations.[74,78]

Scheme 31. 6-31G(d)//3-21G(d) Structures of $LiCCl_3$ 115; Bond Lengths [pm]; Bond Angles [deg]; Relative Energies [kcal mol^{-1}, in parentheses]

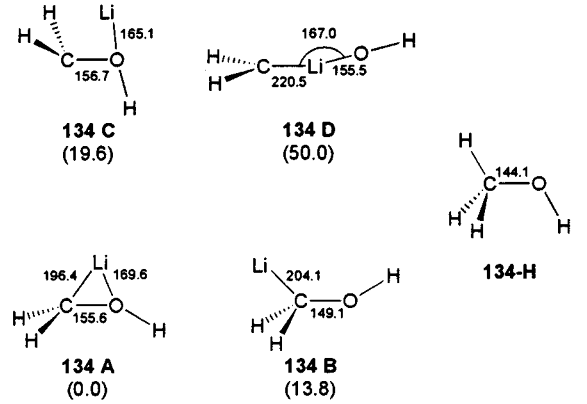


Out of the five structures, **115A** collapses without activation energy to **115D**, the CCl_2·LiCl complex. As already indicated by the increased stability of $LiCHF_2$ **133D**, the dichloro-carbene complex **115D** is strongly stabilized by the two chlorine donor substituents, resulting in the most stable isomer. It is thus not surprising that $LiCCl_3$ **115** was the first carbenoid known to form the corresponding carbene CCl_2 **116** (see section 1.3). The tetrahedral structure **115B** is 12.0 kcal mol^{-1} higher in energy than **115D**, as is **115E** in which Li^+ bridges two C−Cl bonds. The C−Cl bonds in **115B** are elongated (182.8 pm) as compared, e.g., to those in **115D** (168.9 pm). This holds as well for the two C−Cl bonds in **115E** which are bridged by lithium (186.4 pm). Structure **115F** is very remarkable: it is best described as a CCl_3^- Li^+ ion pair. Again the C−Cl bonds are very long (198.7 pm).

Interestingly, the infrared spectrum of matrix-isolated $LiCCl_3$ **115** suggested the presence of (at least) two isomers.[79] The principal form has been assigned to possess C_3 (and possibly C_{3v}) symmetry. Additionally, frequences corresponding to a weakened C−Cl bond and to a Li−Cl linkage have been assigned. These findings could be attributed to an equilibrium between a carbenoid $LiCCl_3$ **115B**, **E**, or **F** and the very stable carbene (complex) CCl_2·LiCl **115D**.

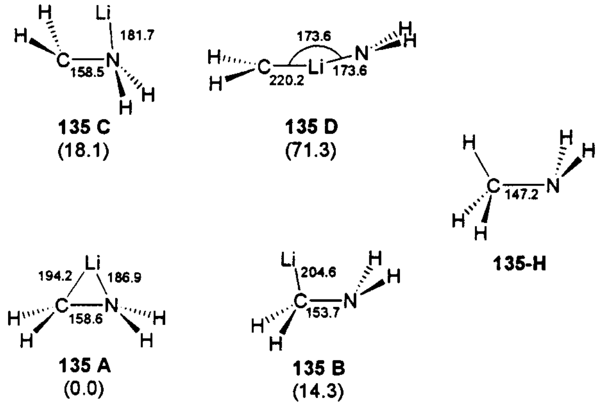
1.4.1.1.4. $LiCH_2OH$. As pointed out in chapter 1.2, α-lithiated ethers $LiCH_2OR$ turned out to be Li/OR carbenoids if the reaction of such species with an organolithium nucleophile R′Li to give $LiCH_2R'$ and LiOR, or with $LiCH_2OR$, is a criterium for being a carbenoid. It was therefore of great interest to see whether these experimental findings would be supported by calculations or not. Scheme 32[80] clearly shows that $LiCH_2OH$ **134** is a good model for Li/OR carbenoids.[55,73,74,80−82]

Scheme 32. MP2/6-31G(d)//3-21G Structures of $LiCH_2OH$ 134; Bond Lengths [pm]; Bond Angles [deg]; Relative Energies [kcal mol^{-1}, in parentheses]



The calculated structures of $LiCH_2OH$ **134** correspond closely to those calculated for $LiCH_2F$ **131**; see Scheme 29. The bridged structure **134A** is the most stable one with a C−O bond being 11.5 pm (8.0%) longer than in methanol CH_3OH (144.1 pm). In the case of $LiCH_2F$ **131A**, the C−F bond lengthening, however, was clearly more pronounced (14.7%). Interestingly, Li/F carbenoids have never been observed experimentally while lithiated ethers are useful reagents in synthesis (see section 1.2.4). The pseudo-tetrahedral **134B** is 13.8 kcal mol^{-1} less stable than **134A**, while the CH_2·OH(Li) carbene complex **134C** lies 19.6 kcal mol^{-1} and the CH_2·LiOH carbene complex **134D** 50.0 kcal mol^{-1} higher in energy than **134A**. In the latter complex, the C−O

Scheme 33. MP2/6-31G(d)//3-21G Structures of $LiCH_2NH_2$ 135; Bond Lengths [pm]; Relative Energies [kcal mol^{-1}, in parentheses]



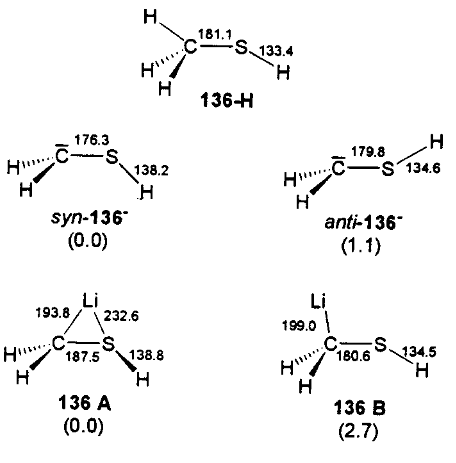
bond is broken. Like **134A**, the isomers **134B** and **134C** have longer C–O bonds than methanol CH_3–OH (144.1 pm).

1.4.1.1.5. $LiCH_2NH_2$. Scheme 33 shows the situation in the case of $LiCH_2NH_2$ **135** as a model for α-lithiated amines: are these compounds also carbenoids?[73,80,82]

As one can see from Scheme 33,[80] the situation in the case of $LiCH_2NH_2$ **135** is similar to that of $LiCH_2$-OH **134** except that the bond lengthening of the C–X bond in the case of $LiCH_2NH_2$ **135** is even less pronounced than there: in the bridged **135A** the C–N bond is only 11.4 pm (7.8%) longer than in CH_3-NH_2 (147.2 pm). As shown in more detail in chapter 1.4.3, α-lithiated amines indeed should not be regarded as carbenoids: a substitution reaction of the type $LiCH_2NR^1R^2 + LiR' \rightarrow LiCH_2R' + LiNR^1R^2$ was never observed, and crystal structures show only marginal C–N bond lengthening.

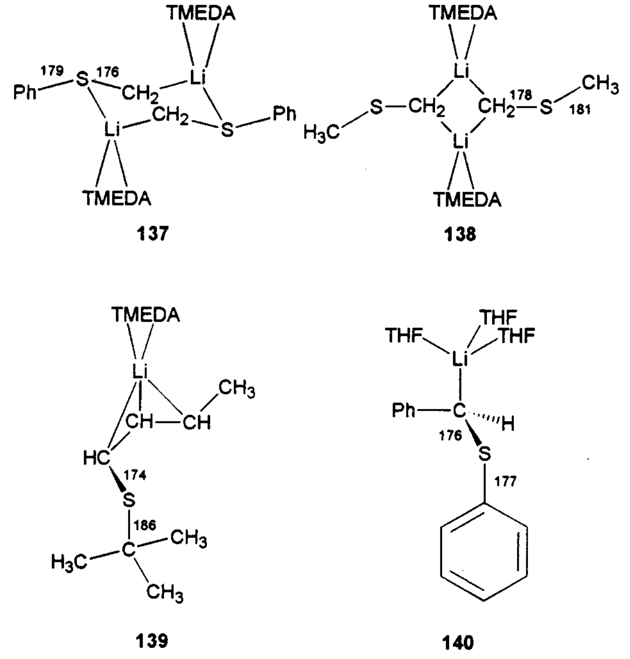
1.4.1.1.6. $LiCH_2SH$. At this point it is interesting to discuss briefly a case which is completely different from $LiCH_2F$ **131**, $LiCHF_2$ **133**, $LiCCl_3$ **115**, $LiCH_2$-OH **134**, and even $LiCH_2NH_2$ **135**, namely that of $LiCH_2SH$ **136**, a model for α-lithiated thioethers; see Scheme 34.[73,83,84,85]

Scheme 34. MP2/6-311++G(d,p)//MP2/6-311++G(d,p) Structures of $LiCH_2SH$ 136; Bond Lengths [pm]; Relative Energies [kcal mol^{-1}, in parentheses]



A first important outcome is the small energy difference between the bridged isomer **136A** and the pseudo-tetrahedral structure **136B** (2.7 kcal mol^{-1}), the only two structures that were found. Although the C–S bond in **136A** (187.5 pm) is lengthened as compared to that in **136-H** (181.1 pm), it is slightly *shortened* in **136B** (180.6 pm). C–S bond shortening is even more pronounced in the two anions CH_2-SH^- syn-**136**$^-$ (176.3 pm) and anti-**136**$^-$ (179.8 pm). Thus if one assumes that the marginally stabilizing Li–S bond in **136A** is broken by solvation of Li^+, e.g. by ether molecules, leading to a pseudo-tetrahedral structure as in **136B**, the C–S bond in α-lithiated thioethers should be slightly shortened. This is exactly the case, as shown by the solid state structures of **137**,[86] **138**,[86] **139**,[87] and **140**;[85,88,89] see Scheme 35.

Scheme 35. Tetrahedral Structures and Shortening of the C–S Bond in the Solid State Structures of α-Lithiated Thioethers; Bond Lengths [pm]

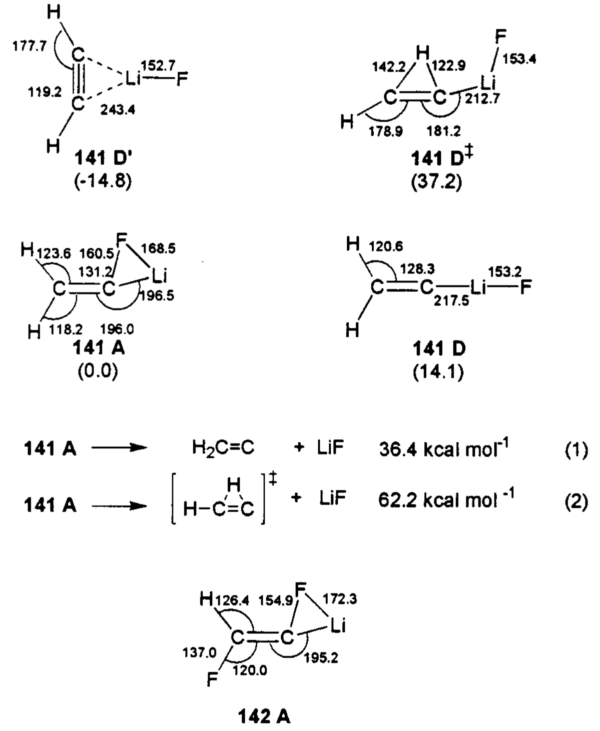


The solid state structures document also the low tendency of second-row elements to be Li^+-bridged.[73,83,84,85] Furthermore, there is no example of an α-lithiated thioether reported in the literature in which such a species behaves like a carbenoid. $LiC(SPh)_3$ **123** (Scheme 27) is a different case: here even the carbene $C(SPh)_2$ **124** is formed very easily because of the stabilization of **124** by two donor substituents. Therefore, $LiC(SPh)_3$ **123** is a carbenoid.

1.4.1.1.7. $H_2C{=}CLiF$. The first calculations of carbenoids of the type HXC=CLiF with X = H and F, respectively, were reported by Wang and Deng.[90] The results of $H_2C{=}CLiF$ **141** are shown in Scheme 36.

Once again the most stable structure is the Li^+-bridged **141A** with both substituents at the carbenoid carbon atom on one side of the olefin. Thus, the structure of **141A** is analogous to that of $LiCH_2F$ **131A** with all substitutents in one hemisphere (see Scheme 29). The carbene complex $H_2C{=}C{\cdot}LiF$ **141D** lies 14.1 kcal mol^{-1} higher in energy, while the acetylene•LiF complex **141D′** is 14.8 kcal mol^{-1} more stable than **141A**. This agrees with the long known

Scheme 36. 3-21G//3-21G Structures of $H_2C{=}CLiF$ 141 and HFC=CLiF 142A; Bond Lengths [pm]; Bond Angles [deg]; Relative Energies [kcal mol^{-1}, in parentheses]



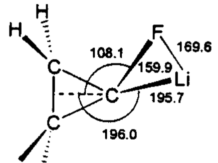
tendency of carbenoids of the type RR′C=CLiX to undergo the Fritsch−Buttenberg−Wiechell rearrangement giving R-C≡C-R′ + LiX with the substituent R (or R′) trans to the leaving group X undergoing the migration; see Scheme 2. The calculations show also that the rearrangement does not occur at the carbene stage: the decomposition of **141A** to give $H_2C{=}C$ + LiF requires 36.4 kcal mol^{-1} (eq 1, Scheme 36), and the energy of the transition state of the 1,2-hydrogen shift within the carbene + LiF is 62.2 kcal mol^{-1} above **141A** (eq 2, Scheme 36). In contrast, the transition state of the Fritsch−Buttenberg−Wiechell rearrangement **141D**‡ amounts to 37.2 kcal mol^{-1}. The authors[90] are not sure about the question which hydrogen in **141A** undergoes the rearrangement, and assume "the hydrogen at the same side of the C=C bond with F may migrate in favor".[90] As pointed out earlier, this would disagree with the experimental observation at least in the bis-aryl-substituted cases (Scheme 2). Interestingly, structure **141A** shows that the angle H−C=C of the hydrogen trans to the C−F bond is smaller than 120°, namely 118.2°, while it is 123.6° for the hydrogen cis to the C−F bond; see Scheme 36, **141A**. This indicates that the hydrogen trans to the C−F bond is "on its way" to the neighboring C atom, while the other hydrogen "moves down" toward its position in the acetylene, exactly as observed in the Fritsch−Buttenberg−Wiechell rearrangement. The calculations of the transition state **141D**‡, however, are possibly based on the assumption that the *cis*-hydrogen migrates.

It is also interesting to compare the relative energies of the $H_2C{=}C{\cdot}LiF$ complex **141D** (14.1 kcal mol^{-1}, Scheme 36) and the dissociation energy **141A** → $H_2C{=}C$ + LiF (36.4 kcal mol^{-1}, eq 1, Scheme 36) with the related values (also 3-21G//3-21G) of the carbenoid $LiCH_2F$ **131**. There the complex $H_2C{\cdot}LiF$ **131D** is 28.4 kcal mol^{-1} higher in energy than **131A**, and the reaction **131A** → CH_2 + LiF requires 56 kcal mol^{-1}.[74] Consequently, according to these calculations, vinylidene $H_2C{=}C$ is more easily formed from its Li/F carbenoid **141A** than methylene H_2C from **131A**.

Since the calculations of the carbenoid HFC=CLiF **142** do not reveal any new insights into the structures of vinylic carbenoids, the reader is referred to the original literature.[90] It is only mentioned here that the carbenoid C−F bond is considerably longer (154.9 pm) than the noncarbenoid C−F bond (137.0 pm); see **142A** in Scheme 36. The bond angles at the noncarbenoid C atom F−C=C (120.0°) and H−C=C (126.4°) are in agreement with the data discussed in the case of **141A**. The same applies for the geometry at the carbenoid carbon atom.

1.4.1.1.8. C_3H_4LiF. Wang, Deng et al. also calculated the structure of the cyclopropyliden-Li/F carbenoid **143**, in which case only one minimum structure (**143A**) was found; see Scheme 37.[91]

Scheme 37. 3-21G Structure of the Cyclopropylidene-Li/F Carbenoid 143A; Bond Lengths [pm]; Bond Angles [deg]



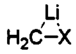
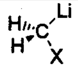
143 A

The data show that Li as well as F are positioned on one side of the cyclopropane ring plane, a situation which is comparable to that found for $H_2C{=}CLiF$ **141A**, Scheme 36, as well as for **131A**, Scheme 29. Furthermore the C−F bond is strongly elongated to 159.9 pm as compared to 140.4 pm in CH_3F.

In summary, the calculations of various Li/Hal and Li/OR compounds at all sorts of calculational levels are in agreement with these compounds being carbenoids. The most stable structure (except for $LiCCl_3$ **115**, Scheme 31) is **A** with Li^+ bridging the C−X bond, which is elongated as compared to the nonlithiated compounds. Higher energy structures (**B**, **C**, **D**, etc.) should only be favored, e.g., by solvation of Li^+ (see section 1.4.1.2) or other more special reasons (see, e.g., $LiCCl_3$ **115** in section 1.4.1.1.3). The bond lengthening of the C−N bond in α-lithiated amines **135** (Scheme 33) is less pronounced than in the cases of Li/Hal and Li/OR carbenoids. In α-lithiated thioethers **136**, the C−S bond is even shorter than in the corresponding thioethers (Scheme 34). Not surprisingly, **135** and **136** were never observed to undergo reactions with nucleophiles which is characteristic for carbenoids.

1.4.1.1.9. A Systematic Study of $LiCH_2X$, X = H, F, Cl, Br, I, OH, NH_2, SH; $LiCHX_2$, X = F, Cl, Br, I, OH; $LiCX_3$, X = F, Cl, Br, I; Cyclopropyl Carbenoids (C_3H_4LiX), X = F, Cl, OH, NH_2, SH; and Vinyl Carbenoids ($H_2C{=}CLiX$), X = F, Cl, OH, NH_2, SH. What is the Influence of the Different Halides X on

Table 3. MP2(full)/6-311++G(d,p)+ZPE Relative Energies [kcal mol^{-1}] and Bond Lengths [pm] of Compounds of the Type CH_3X and $LiCH_2X$, X = F, Cl, Br, I, OH, NH_2, SH

X		E_{rel} [kcal mol^{-1}] r [pm]	H_3C-X **H**	 **A**	 **B**	H_2C-XLi **C**	H_2C-LiX **D**
H	**2**	C-Li	-		198.2		
F	**131**	E_{rel}	-	0.0	n.f.	21.5	27.1
		C-F	138.7	155.8	n.f.	155.0	-
		F-Li	-	178.5	n.f.	171.4	161.9
		C-Li	-	192.4	n.f.	-	221.0
Cl	**144**	E_{rel}	-	0.0	n.f.	22.8	29.7
		C-Cl	177.5	190.0	n.f.	186.7	-
		Cl-Li	-	219.7	n.f.	211.0	204.3
		C-Li	-	194.7	n.f.	-	217.8
Br $^{c)}$	**145**	E_{rel}	-	0.0	n.f.	22.9	30.0
		C-Br	193.6	206.6	n.f.	203.8	-
		Br-Li	-	238.1	n.f.	228.0	222.0
		C-Li	-	196.7	n.f.	-	218.7
I $^{c)}$	**146**	E_{rel}	-	0.0	n.f.	24.5	30.8
		C-I	214.7	226.6	n.f.	223.9	-
		I-Li	-	261.9	n.f.	250.7	244.0
		C-Li	-	196.6	n.f.	-	217.1
OH	**134**	E_{rel}	-	0.0	13.6	16.4	44.4
		C-OH	142.1	152.3	146.7	151.4	-
		OH-Li	-	177.5	-	171.7	162.6
		C-Li	-	194.1	201.8	-	221.0
NH_2	**135**	E_{rel}	-	0.0	13.7	15.0	65.4
		C-NH_2	146.3	154.5	150.8	152.7	-
		NH_2-Li	-	190.9	-	184.6	177.8
		C-Li	-	192.9	203.9	-	219.0
SH	**136**	E_{rel}	-	0.0	3.5 $^{a)}$	2.7	49.8
		C-SH	181.1	187.5	181.3	180.6	-
		SH-Li	-	232.6	-	- $^{b)}$	216.3
		C-Li	-	193.8	193.8	199.0	217.2

[a] This structure is a transition state. [b] No bonding interaction between S and Li could be found. [c] MP2 optimized structures using 6-311++G(d,p) basis sets for all atoms except for Br and I where effective core potentials together with (4111/4111/1) basis sets were used.[93] n.f.: not found.

the "Carbenoid Character"? In the following Tables 3−7,[92] high level calculations of the above-mentioned species are summarized for the following reasons: (1) The calculations discussed so far in this chapter deal with different carbenoids in a nonsystematical manner at all sorts of theoretical levels. It is thus difficult, e.g., to compare related structures of carbenoids (**A**, **B**, **C**, **D**, etc.) only differing in the substituent X. (2) In section 1.4.2, NMR investigations of carbenoids will be discussed, and the unusual chemical shifts of carbenoid carbon atoms are compared with ab initio IGLO NMR calculations. This requires highly reliable geometries since the calculated shieldings have been shown to depend strongly on the geometry. (3) Because of the computational effort, Li/Br and Li/I carbenoids have not been studied by theoretical means in the earlier calculations. However, since exactly these carbenoids are among the most widely used in synthesis, it is desirable to get some insight into the structures of these species. It was also of interest to look at the differences within the Li/Hal series, Hal = F, Cl, Br, I. Is it possible to answer the question: "Which carbenoid $LiCH_2Hal$ has the "strongest" carbenoid character?"

Table 3 summarizes MP2(full)/6-311++G(d,p)+ZPE relative energies and main structural features of compounds of the type $LiCH_2X$, X = F, Cl, Br, I, OH, NH_2, SH.

The following trends can be observed: (1) In the halide series $LiCH_2Hal$ (Hal = F **131**; Cl **144**; Br **145**; I **146**), the carbene complexes H_2C-XLi **C** are between 21.5 and 24.5 kcal mol^{-1}, and the carbene complexes H_2C-LiX **D** between 27.1 and 30.8 kcal mol^{-1} higher in energy than the bridged structures **A**. (2) In the case of $LiCH_2OH$ **134** and $LiCH_2NH_2$ **135**, structures **C** are destabilized by 16.4 and 15.0 kcal mol^{-1}, and **D** by 44.4 and 65.4 kcal mol^{-1}, respectively. The classical structures **B** are also less stable than **A** (13.6 and 13.7 kcal mol^{-1}, respectively). (3) $LiCH_2SH$ **136** is different from the other species: structure **B** (3.5 kcal mol^{-1}), which is a transition state, and structure **C** (2.7 kcal mol^{-1}) are only slightly higher in energy than **A**, while **D** lies 49.8 kcal mol^{-1} above **A**. Thus, there is strong preference for the Li^+-bridged structures **A** in all cases except for $LiCH_2SH$ **136**. (4) The C−X bonds in the bridged structures **A** are strongly elongated with the elongation ratio r_A/r_H decreasing from X = F (12.3%) to Cl (7.0%), Br (6.7%), and I (5.5%), and from F (12.3%) to OH (7.2%) and NH_2 (5.6%). The C−S bond is only 3.5% longer.

Considering the above raised question as to the "carbenoid character" within the $LiCH_2Hal$ series, the elongation of the C−Hal bonds *as compared to the nonlithiated CH_3−Hal* bonds indicates decreasing "carbenoid character" from $LiCH_2F$ **131A** via $LiCH_2Cl$ **144A** and $LiCH_2Br$ **145A** to $LiCH_2I$ **146A**. The degree of "carbenoid character" is, however, not easy to define. A calculation of the *transition states of the reactions of the $LiCH_2Hal$ carbenoids with ethene* to give cyclopropane and LiHal reveals a different situation: the transition state energies (and thus the electrophilicities) of $LiCH_2Hal$, Hal = F, Cl, Br, I, are essentially the same; see section 1.4.1.3, Table 8. The reasons for this result are outlined there.

In earlier studies Schleyer, Houk et al. have analyzed the structures and stabilities of α-hetero-substituted organolithium and organosodium compounds as well as of the corresponding anions.[73] They came to the following conclusions: the first-row $LiCH_2X$ species, X = NH_2, OH, F, are better stabilized (−6.0, −8.5, −13.0 kcal mol^{-1}) than their anions (0.0, −5.3, −9.3 kcal mol^{-1}) due to Li-bridging, as observed in structures **A**. Sodium has a diminished tendency for bridging. The second-row $Li(Na)CH_2Cl$ carbenoids are stabilized to the same extent as the corresponding anions. The presence of metals in MCH_2X, X = SH, PH_2, SiH_3, cancels much of the α-substituent stabilizing effects in the anions. The second-row elements stabilize more than the first-row elements (CH_2SH^- −20.9, CH_2Cl^- −13.8; $LiCH_2SH$ −7.4, $LiCH_2Cl$ −16.5 kcal mol^{-1}) due to the more electropositive character (Cl > F, S > O, etc.), the more effective hyperconjugation (S−H > O−H, etc.), and the greater polarizability. d-Orbitals do not contribute significantly to the stabilization, although to the geometry.

Bernardi et al., who investigated the stabilization of α-substituted oxy- and thio-carbanions,[84] came to the following conclusion: the C−X bond weakening associated with the removal of a proton in the CH_3 fragment of CH_3-X (X = OH, SH) is more significant for X = OH than X = SH, and this differential bond weakening effect is the source of the relative stabilities of the anions. This observation is also related to the question why α-lithiated ethers are carbenoids, and α-lithiated thioethers are not.

From the analyses made by Schleyer, Houk et al.,[73] Bernardi et al.,[84] and the data summarized in Table 3, one can furthermore conclude that the difference between the Li/Cl carbenoid $LiCH_2Cl$ **144** and the "non-carbenoid" $LiCH_2SH$ **136** should mainly result from the hyperconjugation of the negatively charged carbon with the S−H bond in **136**. In the case of chlorine, a similar effect is excluded which leads to an elongated and thus less stable $LiCH_2$−Cl bond in **144**. Furthermore, the rather strong elongation of the C−F bond in $LiCH_2F$ **131** as compared to that of the C−Cl bond in $LiCH_2Cl$ **144** (see Table 3) parallels the situation of $LiCH_2OH$ **134** and $LiCH_2SH$ **136** (see above).

Table 4 summarizes relative energies and main structural features of compounds of the type $LiCHX_2$, X = F, Cl, Br, I, OH.[92]

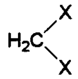
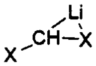
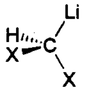
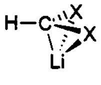
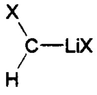
An important feature is the outcome of isomer **E** with lithium bridging two C−X bonds. The relative energy of **E** compared to isomer **A** varies between 4.7 kcal mol^{-1} (**149E**, X = OH) and −0.7 kcal mol^{-1} (**147E**, X = Br). In the case of **148**, X = I, isomer **A** could not be localized. In general, a higher stability of the HXC·LiX complexes **D** is noticed as compared to the H_2C·LiX complexes **D** (Table 3). The relative energies range from 11.9 to 21.1 kcal mol^{-1} while it is 27.1 to 44.4 kcal mol^{-1} in the latter case. Obviously, a donor substituent X at the carbene carbon atom stabilizes the carbene (complex) markedly. The C−X bond elongation in the Li-bridged isomers **A** is even more pronounced than in the case of the $LiCH_2X$ isomers **A** (compare with Table 3): **133A**, X = F, 14.9%; **106A**, X = Cl, 8.2%; **147A**, X = Br, 7.4%; **149A**, X = OH, 8.9%. Interestingly, it is only the Li-bridged C−X bond which is strongly elongated; the nonbridged C−X bond is only marginally longer than the C−X bond in the corresponding H species: **133A**, X = F, 1.6%; **106A**, X = Cl, 1.3%; **147A**, X = Br, 2.2%; **149A**, X = OH, 0.9%. This emphasizes the importance of Li^+-bridging of C−X bonds, and of the donor qualities of the nonbridging substituent X, for the removal of the leaving group X^- (or of LiX) in carbenoids. In isomers **E**, the two C−X bonds are elongated as compared to the H species, but not as much as this is the case for the one Li^+-bridged C−X bond in isomer **A**. The equal elongation of *two* C−X bonds in **E** is responsible for this result (see, e.g., **106E**, X = Cl, 5.4%; **148E**, X = I, 4.7%).

Finally, we would like to stress the importance of correlation effects in structures such as those shown in Table 4. In the HF/4-31G structure of $LiCHF_2$ **133E** discussed earlier (Scheme 30), only a very weak C−Li bond (240.3 pm) was found which led to the conclusion that it is best described as a CHF_2-Li^+ complex.[77] The MP2(full)/6-311++G(d,p) results (Table 4), on the other hand, led also in the case of isomers **E** to rather short C−Li bonds (e.g., **133E**, 188.2 pm). Thus, compounds **E** are better described as isomers with both C−X bonds being Li^+-bridged.[92]

Table 5 summarizes relative energies and main structural features of compounds of the type $LiCX_3$, X = F, Cl, Br, I.

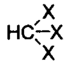
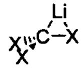
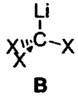
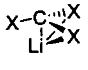
In the case of the carbenoids $LiCX_3$ structures **A** are again the global minima. The Li^+-bridged C−X bonds are even more elongated than in the cases of $LiCH_2X$ **A** (Table 3) and $LiCHX_2$ **A** (Table 4): $LiCF_3$ **150A** 21.0%; $LiCCl_3$ **115A** 10.6%; $LiCBr_3$ **151A** 9.9%; and $LiCI_3$ **152A** 7.5% (Table 5). This table also shows that in the **A** isomers the other, non-Li^+-bridged C−X bonds are hardly longer than in the nonlithiated species HCX_3. Not surprisingly, the potential surface of all carbenoids $LiCX_3$ is rather flat: the energy difference between the most and least stable isomers were calculated to be in the case of $LiCF_3$ **150** 4.4 kcal mol^{-1}, $LiCCl_3$ **115** 8.6 kcal mol^{-1}, $LiCBr_3$ **151** 7.1 kcal mol^{-1}, and $LiCI_3$ **152** 12.0 kcal mol^{-1} (Table 5). This might explain why $LiCCl_3$ **115 A** was not found on the Hartree−Fock level.[74,78] From the above findings it is also clear why all dihalo-carbenes (and their LiX complexes) are so easily formed from the carbenoid precursors (see chapter 1.3). Only in the case of $LiCF_3$ **150** the classical structure **B** is a minimum. The weakly elongated C−F bonds in **150B** (138.9 pm) as compared to HCF_3 **150-H** (133.7 pm) show that tetrahedral **150B** is rather different from

Table 4. MP2(full)/6-311++G(d,p)+ZPE Relative Energies [kcal mol^{-1}] and Bond Lengths [pm] of Compounds of the Type CH_2X_2 and $LiCHX_2$, X = F, Cl, Br, I, OH; Values in Parentheses Refer to C–X Bonds without Li^+-Bridge

X	E_{rel} [kcal mol^{-1}] r [pm]	 H	 A	 B	 E	 D
F	E_{rel}	-	0.0	n.f.	2.7	15.1
133	C-F	135.9	156.2	n.f.	148.6	-
	(C-F')		(138.1)			(129.1)
	F-Li	-	179.0	n.f.	196.4	161.5
	C-Li	-	194.2	n.f.	188.2	223.0
Cl	E_{rel}	-	0.0	n.f.	-0.4	14.7
106	C-Cl	176.6	191.1	n.f.	186.2	-
	(C-Cl')		(179.0)			(165.4)
	Cl-Li	-	221.6	n.f.	238.4	204.2
	C-Li	-	195.3	n.f.	189.4	222.9
Br[b]	E_{rel}	-	0.0	n.f.	-0.7	16.7
147	C-Br	193.0	207.2	n.f.	203.3	-
	(C-Br')		(197.3)			(180.9)
	Br-Li	-	241.6	n.f.	256.9	221.3
	C-Li	-	195.0	n.f.	191.4	216.1
I[b]	E_{rel}	-	n.f.	n.f.	0.0	21.1
148	C-I	214.8	n.f.	n.f.	224.9	-
	(C-I')					(201.3)
	I-Li	-	n.f.	n.f.	280.1	244.3
	C-Li	-	n.f.	n.f.	192.5	213.4
OH	E_{rel}	-	0.0	13.9[a]	4.7	11.9
149	C-OH	140.6	153.1	144.9[a]	153.1	-
	(C-OH')		(141.8)			(129.7)
	OH-Li	-	176.5	-	181.5	163.0
	C-Li	-	196.9	203.3	229.8	219.9

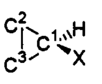
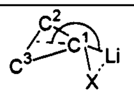
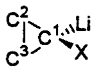
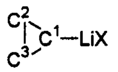
[a] This structure is a transition state. [b] MP2 optimized structures using 6-311++G(d,p) basis sets for all atoms except for Br and I where effective core potentials together with (4111/4111/1) basis sets were used.[93] n.f.: not found.

Table 5. MP2(full)/6–311++G(d,p)+ZPE Relative Energies [kcal mol^{-1}] and Bond Lengths [pm] of Compounds of the Type CHX_3 and $LiCX_3$, X = F, Cl, Br, I; Values in Parentheses Refer to C–X Bonds without Li^+-Bridge

X	E_{rel} [kcal mol^{-1}] r [pm]	 H	 A	 B	 E	 F	$X_2C–LiX$ D
F	E_{rel}	-	0.0	4.4	3.3	3.5	3.1
150	C-F	133.7	161.8	138.9	157.4	146.9	
	(C-F')		(134.2)		(132.1)		(128.4)
	F-Li	-	177.8	-	176.9	190.1	160.9
	C-Li	-	196.7	201.5	242.8	218.8	226.6
Cl	E_{rel}	-	0.0	4.5[a]	8.6[a]	3.3	2.8
115	C-Cl	176.5	195.2	181.0	199.8	190.0	
	(C-Cl')		(177.7)		(177.0)		(167.9)
	Cl-Li	-	221.8	-	215.3	225.0	203.9
	C-Li	-	196.6	197.7	275.9	232.6	216.9
Br[b]	E_{rel}	-	0.0	3.7[a]	7.1	1.2	6.2
151	C-Br	193.2	213.3	198.4	217.1	208.5	
	(C-Br')		(195.4)		(195.9)		(184.2)
	Br-Li	-	239.9	-	232.6	243.5	221.0
	C-Li	-	198.0	197.2	290.7	248.1	217.4
I[b]	E_{rel}	-	0.0	2.4[a]	-0.8	1.4	11.2
152	C-I	215.9	232.2	221.2	229.2	232.3	
	(C-I')		(219.0)		(215.5)		(205.7)
	I-Li	-	264.9	-	277.1	266.1	243.9
	C-Li	-	197.9	196.2	195.8	260.0	214.8

[a] This structure is a transition state. [b] MP2 optimized structures using 6-311++G(d,p) basis sets for all atoms except for Br and I where effective core potentials together with (4111/4111/1) basis sets were used.[93] n.f.: not found.

Table 6. HF/6-311++G(d,p) Relative Energies (kcal mol^{-1}), Bond Lengths [pm], and Bond Angles [deg] of Cyclopropyl Compounds C_3H_5X and LiC_3H_4X, X = F, Cl, OH, NH_2, SH

X	E_{rel} [kcal mol^{-1}] r [pm]	 **H**	 **A**	 **B**	 **D**
H	C-Li	-		196.3	
153	C^1-C^2	150.0		152.6	
	C^2-C^3	150.0		149.4	
	∡ (C^2-C^3)-C-Li	-		130.2	
F	E_{rel}	-	0.0	n.f.	2.2
143	C-F	135.4	161.5	n.f.	-
	F-Li	-	174.1	n.f.	160.3
	C-Li	-	191.9	n.f.	222.0
	C^1-C^2	148.1	149.8	n.f.	148.0
	C^2-C^3	151.6	149.7	n.f.	148.3
	∡ (C^2-C^3)-C-Li	-	194.1	n.f.	180.0
Cl	C-Cl	177.0	n.f.	n.f.	-
154	Cl-Li	-	n.f.	n.f.	207.6
	C-Li	-	n.f.	n.f.	216.7
	C^1-C^2	148.9	n.f.	n.f.	147.9
	C^2-C^3	150.7	n.f.	n.f.	148.3
OH	E_{rel}	-	0.0	n.c.	16.5
155	C-OH	138.4	149.3	n.c.	-
	HO-Li	-	178.7	n.c.	161.8
	C-Li	-	192.0	n.c.	221.1
	C^1-C^2	148.9	150.0	n.c.	148.1
	C^2-C^3	151.8	150.9	n.c.	148.3
	∡ (C^2-C^3)-C-Li	-	181.7	n.c.	180.0
NH_2	E_{rel}	-	0.0	n.c.	37.9
156	C-NH_2	143.7	151.9	n.c.	-
	H_2N-Li	-	192.5	n.c.	177.2
	C-Li	-	196.2	n.c.	220.0
	C^1-C^2	149.8	150.6	n.c.	148.1
	C^2-C^3	150.3	150.0	n.c.	148.3
	∡ (C^2-C^3)-C-Li	-	173.7	n.c.	180.0
SH	E_{rel}	-	n.f.	0.0	15.5
157	C-SH	180.0	n.f.	181.7	-
	HS-Li	-	n.f.	n.b.	209.5
	C-Li	-	n.f.	198.0	215.5
	C^1-C^2	149.4	n.f.	151.0	147.9
	C^2-C^3	150.7	n.f.	150.3	148.4
	∡ (C^2-C^3)-C-Li	-	n.f.	133.9	180.0

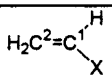
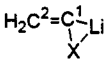
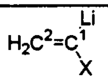
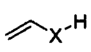
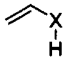
n.b.: no bond. n.c.: not calculated. n.f.: not found.

the other carbenoid species. This holds also for **115B**, **151B**, and **152B**, although these structures are transition states (Table 5). Isomers **F**, in which Li^+ is bonded exclusively to the three X atoms, show intermediate elongations of all three C−X bonds (C−F: from 133.7 to 146.9 pm in **150E**; C−Cl: from 176.5 to 190.0 pm in **115E**; C−Br: from 193.2 to 208.5 pm in **151E**; C−I: from 215.9 to 232.3 pm in **152E**). Two rather long Li^+-bridged C−X bonds, on the other hand, are observed in isomers **E** (see Table 5). In summary, the very flat potential surfaces as found for compounds $LiCHal_3$ are in excellent agreement with the facile interplay between carbenoid and carbene (complex) structures in this series.

Table 6 summarizes relative energies and main structural features of cyclopropyl carbenoids C_3H_4-LiX, X = F, Cl, OH, NH_2, SH together with those of cyclopropyllithium (X = H).[92]

In the case of the Li/F carbenoid **143**, the most stable isomer is the Li^+-bridged **143A**; however, the carbene·LiF complex **143D** is only 2.2 kcal mol^{-1} higher in energy. The bond elongation of C−F from 135.4 (**143-H**) to 161.5 pm (**143A**; 26.1 pm; 19.3%) is quite remarkable. It is in agreement with the facile formation of the carbene·LiF complex **143D** (2.2 kcal mol^{-1}) and underlines the problem to detect such a Li/F carbenoid. One can also see from Table 6, that lithium is in the same hemisphere as fluoride (see also Scheme 37).[91] The most stable Li/Cl "carbenoid" is the carbene complex with LiCl **154D**. In fact, neither **154A** nor **154B** could be found. The hydroxy species **155** is most stable in its Li^+-bridged form **155A**. The C−O bond elongation (10.9 pm; 7.9%) is clearly less than in the Li/F case **143A**. Correspondingly, the carbene·LiOH complex **155D** is 16.5 kcal mol^{-1} higher in energy than **155A**. Even less is the

Table 7. HF/6-311++G(d,p) Relative Energies (kcal mol^{-1}), Bond Lengths [pm], and Bond Angles [deg] of Vinylic Compounds $H_2C{=}CHX$ and $H_2C{=}CLiX$, X = F, Cl, Br, OH, NH_2, SH

X	E_{rel} [kcal mol^{-1}] r [pm]	 **H**		 **A**	 **B**	$H_2C^2{=}C^1{-}LiX$ **D**
H	C-Li	-			196.3	
158	$C^1{=}C^2$	131.8			134.0	
	∡ $C^1{=}C^2$-Li	-			121.4	
F	E_{rel}	-		0.0	n.f.	1.3
141	C-F	132.6		159.8	n.f.	-
	F-Li	-		174.1	n.f.	159.8
	C-Li	-		192.5	n.f.	221.8
	$C^1{=}C^2$	130.8		131.1	n.f.	128.2
	∡ $C^1{=}C^2$-Li	-		193.3	n.f.	180.0
Cl	C-Cl	174.0		n.f.	n.f.	-
159	Cl-Li	-		n.f.	n.f.	206.9
	C-Li	-		n.f.	n.f.	218.7
	$C^1{=}C^2$	131.1		n.f.	n.f.	128.1
Br [a]	C-Br	189.4		n.f.	n.f.	-
160	Br-Li	-		n.f.	n.f.	222.7
	C-Li	-		n.f.	n.f.	218.0
	$C^1{=}C^2$	131.1		n.f.	n.f.	128.1
		 **anti-H**	 **syn-H**			
OH	E_{rel}	0.0	-1.6	0.0	4.1	18.8
161	C-OH	135.1	134.5	145.4	135.6	-
	HO-Li	-	-	180.7	-	161.3
	C-Li	-	-	191.9	187.7	222.7
	$C^1{=}C^2$	131.5	131.9	132.5	134.8	128.2
	∡ $C^1{=}C^2$-Li	-	-	180.9	82.2	180.0
NH_2	E_{rel}	n.f.	-	0.0	n.f.	35.9
162	C-NH_2	n.f.	137.2	148.3	n.f.	-
	H_2N-Li	n.f.	-	196.8	n.f.	176.7
	C-Li	n.f.	-	191.1	n.f.	222.9
	$C^1{=}C^2$	n.f.	132.6	132.9	n.f.	128.2
	∡ $C^1{=}C^2$-Li	n.f.	-	142.9	n.f.	180.0
SH	E_{rel}	n.f.	-	0.0	0.7	8.7
163	C-Sh	n.f.	176.6	194.0	178.3	-
	HS-Li	n.f.	-	237.9	n.b.	219.6
	C-Li	n.f.	-	191.9	197.5	218.5
	$C^1{=}C^2$	n.f.	131.8	132.4	133.4	128.0
	∡ $C^1{=}C^2$-Li	n.f.	-	167.8	122.0	178.5

[a] HF optimized structures using 6-311++G(d,p) basis sets for C, Li, and H and ECP for Br with a (4111/4111/1) splitting.[93] n.f.: not found. n.b.: no bond.

C−N bond elongation in the Li/NH_2 compound **156A** (8.2 pm; 5.7%), which for that reason is 37.9 kcal mol^{-1} more stable than the carbene·$LiNH_2$ complex **156D**. In the Li/SH species, the nonbridged classical isomer **157B** has the lowest energy, and the C−S bond is elongated by only 1.7 pm (0.9%). As discussed earlier (Scheme 34), such compounds behave like normal "carbanions".

Finally, Table 7 summarizes relative energies and main structural features of vinyl carbenoids $H_2C{=}CLiX$, X = F, Cl, Br, OH, NH_2, SH together with those of vinyllithium, X = H.[92]

The results of the Li/F carbenoid **141** agree in many aspects with those discussed in more length in section 1.4.1.1.7 (Scheme 36). A major difference is the energy of the carbene complex $H_2C{=}C{\cdot}LiF$ **141D** which is only 1.3 kcal mol^{-1} higher in energy than the most stable **141A**. Again, the C−F bond elongation from 132.6 pm in **141-H** to 159.8 in **141A** (27.2 pm; 20.5%) is remarkable. After all, it is a *vinylic C−F bond* which is so strongly elongated and thus weakened. Li and F, as found earlier (see Scheme 36), are on the same side of isomer **A** preforming complex **D**. According to the calculations of Table 7, the Li/Cl (**159**) and the Li/Br carbenoid **160** exist only as carbene complexes **159D** and **160D**, respectively. As in the case of the vinylic Li/F carbenoid **141**, the most stable isomer found is **A** for X = OH (**161A**), X = NH_2 (**162A**), and X = SH (**163A**). Similar to the C−F case also these C−X bonds are strongly elongated in the vinylic isomers **A**: **161A** (10.9 pm; 8.1%); **162A** (11.1 pm; 8.1%); **163A** (17.4 pm; 9.8%). The classical isomer **B** is found to be slightly higher in energy in the cases of **161B** (4.1

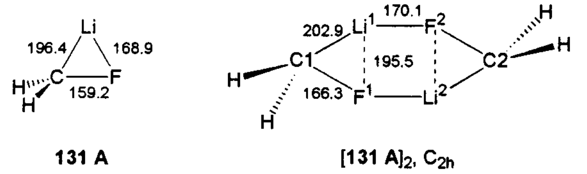
kcal mol^{-1}) and **163B** (0.7 kcal mol^{-1}), while the carbene complexes $H_2C{=}C{\cdot}LiX$ are 18.8 kcal mol^{-1} (**161D**), 35.9 kcal mol^{-1} (**162D**), and 8.7 kcal mol^{-1} (**163D**) higher in energy than isomers **A**.

All of these calculations refer to unsolvated compounds (gas phase). The influence of aggregation and solvation on the structures of carbenoids is dealt with in the following chapter.

1.4.1.2. Aggregation and Solvation of Carbenoids.

The first calculations of a carbenoid dimer ($[LiCH_2F]_2$ [**131**]$_2$) were published by Rohde, Clark, Kaufmann, and Schleyer.[71] The question of whether carbenoids are monomers or aggregated species in solution was of interest after Seebach's findings that the ^{13}C signal of carbenoids is split up by ^6Li into a triplet which shows that only one ^6Li is attached to each carbon atom.[94] This, however, does not mean necessarily that the solution contains only monomors. Optimization of $LiCH_2F$ **131** and [**131**]$_2$ at the HF/3-21G level with C_{2h} symmetry constraint for the dimer led to **131A** and [**131A**]$_2$; see Scheme 38.

Scheme 38. 3-21G Structures of $LiCH_2F$ 131A and [131A]$_2$; Bond Lengths [pm]



"Previous experience indicated that [**131A**]$_2$ would be the most stable dimer structure; the size of the system discouraged consideration of other alternatives".[71] Thus, if the particular "Li–F"-dimer [**131A**]$_2$ is formed, each ^{13}C atom is connected to *one* ^6Li which would also be in agreement with the triplet signal of ^{13}C in carbenoids.[94] [**131A**]$_2$ is 56.2 kcal mol^{-1} more stable than two monomers **131A**, which indicates that dimer formation is very favorable and therefore very likely. The geometry of the monomer **131A** is essentially retained in the dimer [**131A**]$_2$ except for the Li1–F1 (Li2–F2) bonds which are strongly lengthened (168.9 → 195.5 pm). The Li1–F2 (Li2–F1) distance (170.1 pm) is close to that calculated for $[LiF]_2$ (168.4 pm). An interesting result of the dimer formation is shown in eqs 5 and 6.

$$\underset{\textbf{131 A}}{LiCH_2F} \longrightarrow CH_2\ (^1A_1) + LiF \qquad 55.9\ \text{kcal mol}^{-1} \qquad (5)$$

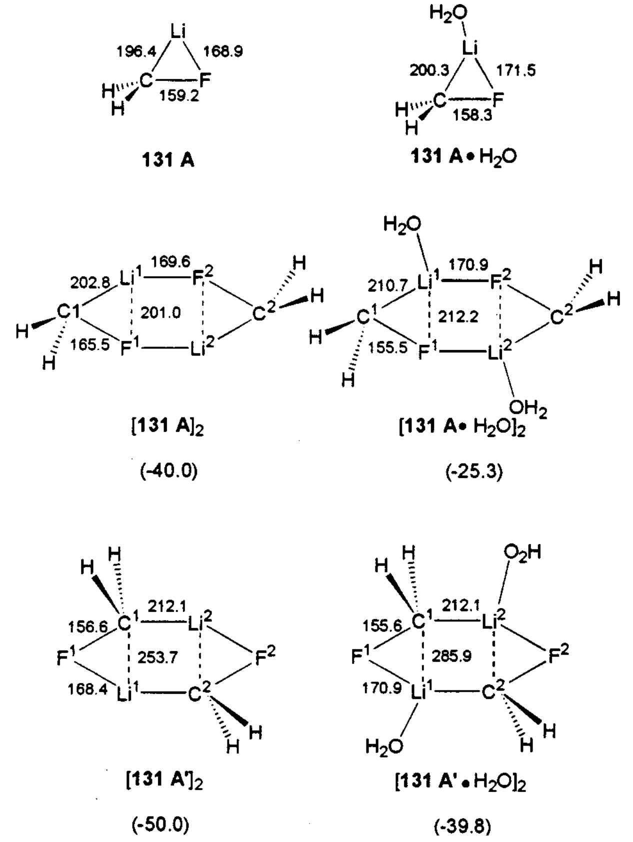
$$\underset{\textbf{[131 A]}_2}{[LiCH_2F]_2} \longrightarrow CH_2\ (^1A_1) + LiCH_2F{\bullet}LiF \qquad 34.0\ \text{kcal mol}^{-1} \qquad (6)$$

Thus, the formation of the carbene CH_2 ($^1A_1$) should be facilitated from the dimer [**131A**]$_2$ as compared to the monomer **131A** by 21.9 kcal mol^{-1}.

Besides [**131A**]$_2$, a further and even more stable dimer [**131A′**]$_2$ was found in MP2/6-31G(d)//3-21G calculations;[92] see Scheme 39.

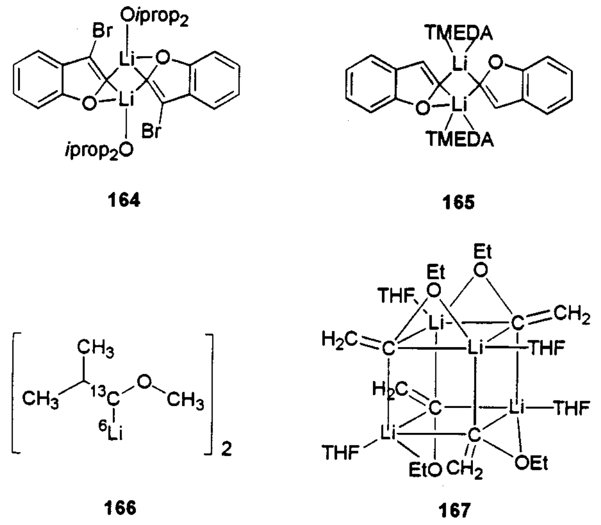
The "Li-F"-dimer [**131A**]$_2$ is also much more stable than two monomers **131A** (−40 kcal mol^{-1}; see Scheme 39); however, the "Li-C"-dimer [**131A′**]$_2$ is 50 kcal mol^{-1} more stable than 2 **131A**. In the "Li-C"-dimer [**131A′**]$_2$ the C–F bond is much less elongated (156.6 pm) than in the "Li-F"-dimer [**131A**]$_2$ (165.5 pm), and even less so than in the monomer **131A** (159.2 pm). Although rather long, a second Li–C bond (Li1–C1 (Li2–C2) 253.7 pm) is found in [**131A′**]$_2$ besides the C1–Li2 (C2–Li1) bond (212.1 pm). The long Li–C bonds disappear if each lithium is *solvated* by one H_2O molecule, as shown by [**131A′**·H_2O]$_2$ in Scheme 39: Li1–C1 (Li2–C2) elongates to 285.9 pm which is considered to be much too long (>250 pm) for a C–Li bond. Consequently, if [**131A′**·H_2O]$_2$ is a model for the dimer in solution, only *one* lithium should be bonded to each carbon which is also in agreement with the triplet structure of the ^{13}C signal in ^6Li/Hal carbenoids.[94] The triplet nature of the ^{13}C–^6Li coupling in Li/Hal-carbenoids therefore seems not to be a reliable tool to determine the aggregation state of carbenoids. Solvated dimers are much more likely than monomers, even if the energy of dimerization decreases to −25.3 and −39.8 kcal mol^{-1}, respectively, on solvation of each Li^+ with one H_2O molecule (Scheme 39).

Scheme 39. MP2/6-31G(d)//3-21G Calculations of $LiCH_2F$ 131A, 131A·H_2O, and Their Dimers; Energies of Aggregation [kcal mol^{-1}, in parentheses]; Bond Lengths [pm]



An experimentally supported situation with regard to aggregation is given in the case of the model Li/OH carbenoid $LiCH_2OH$ **134**. It was found that Li/OR carbenoids have a high tendency for aggregation which is apparent from cryoscopic measurements, ^{13}C–^6Li coupling constants and especially their multiplicities, and crystal structure determinations (for details of the latter; see section 1.4.3). Thus (see Scheme 40), **164**[55,81,82] and **165**[95] are dimers in the

Scheme 40. Aggregated Li/OR Carbenoids



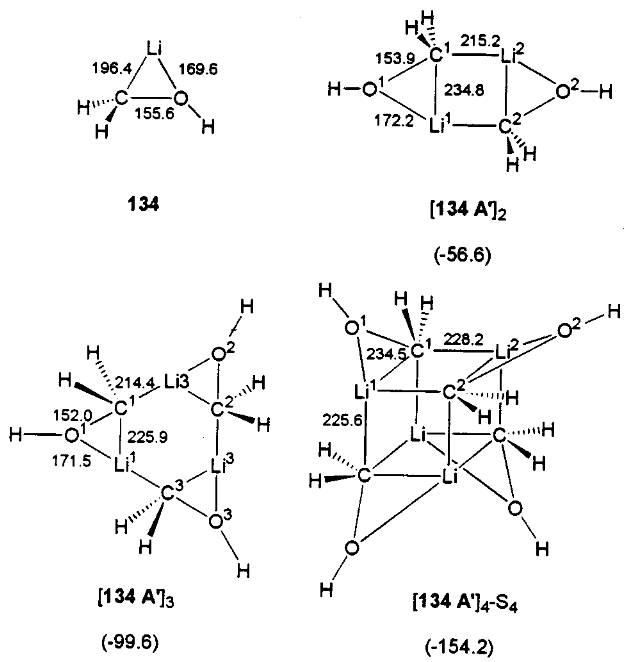
solid state. The quintuplet nature of the carbenoid ^{13}C atom of **165**[95] and of the ^{6}Li-isobutyl methyl ether **166**[55] in solution indicates also the contact of two ^{6}Li to each ^{13}C atom, and cryoscopic determinations of the aggregation of **166** in THF at −108 °C led to $n = 2.2-2.9$.[96] Furthermore, α-ethoxyvinyllithium **167**, a polymer in the solid state, shows a seven-line-multiplet in THF at −90 °C, indicating a tetramer structure (Scheme 40) with three lithiums at each carbon, which is confirmed by ^{6}Li-^{1}H HOESY experiments.[97]

These results are nicely in agreement with the calculated structures of LiCH$_2$OH **134** and its aggregates; see Scheme 41.

First, the high aggregation energies emphasize the preference of Li/OR carbenoids for aggregation. A closer look at the geometry of the "Li-C"-dimer [**134A′**]$_2$ reveals similarities with the "Li-C"-dimer [**131A′**]$_2$ in the LiCH$_2$F case (Scheme 39), however, with one major difference: the "intramolecular" C1−Li1 (C2−Li2) bond length (234.8 pm) is within the normal range of C−Li bond lengths. Together with the even shorter C1−Li2 (C2−Li1) bond (215.2 pm), the structure thus is in agreement with the quintuplet nature of the above-mentioned ^{13}C−^{6}Li couplings. Two lithiums interact also with one carbon atom in the trimer [**134A′**]$_3$. Since monomers, dimers, and tetramers are the dominant species in the case of organolithium compounds, the trimer [**134A′**]$_3$ is less likely to exist. In the tetramer [**134A′**]$_4$-S$_4$ (a tetramer with D_2 symmetry of equal energy and similar bond lengths was also found) each carbon is connected with three Li$^+$, the bond lengths of which are "normal" (225.6, 228.2, and 234.5 pm). This is in agreement with the seven-line signal in the ^{13}C-^{6}Li NMR spectrum of **167**. The model calculations with LiCH$_2$OH **134** (Scheme 41) therefore give reasonable insight into the situation as found experimentally in the case of Li/OR carbenoids (Scheme 40). Finally, it should be mentioned that a "Li-O"-dimer [**134A**]$_2$ corresponding to the "Li-F"-dimer [**131A**]$_2$ (Scheme 39) was not found.[92]

Let us now return to the effect of solvation on the structures of carbenoids. In all of the solvated

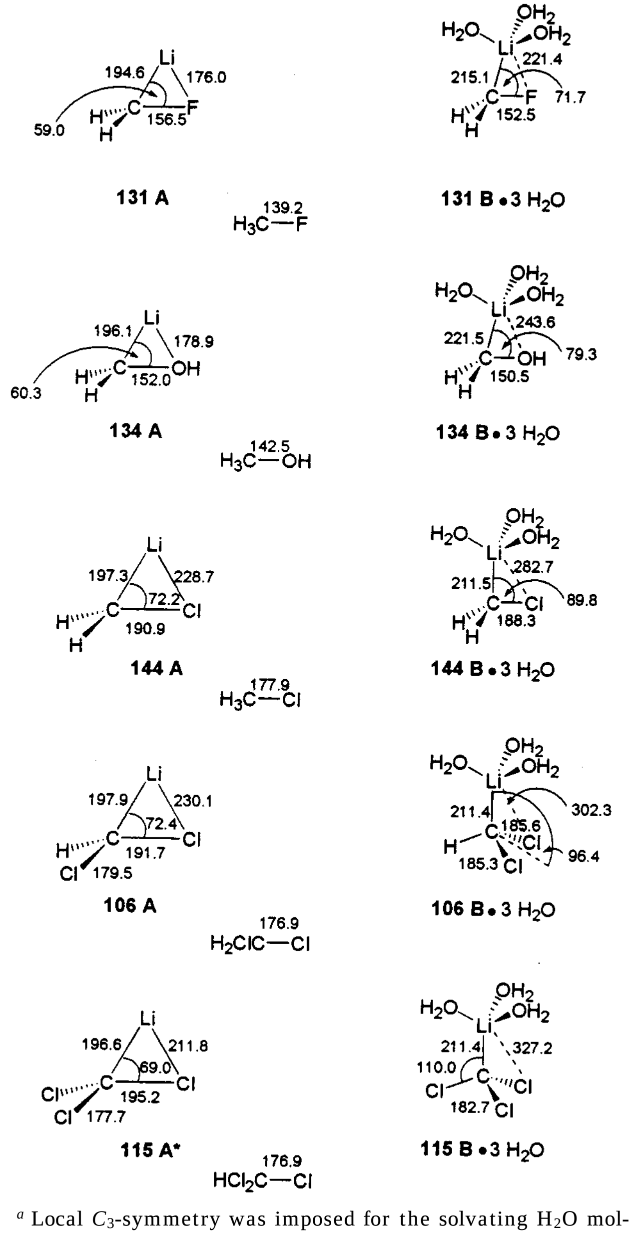
Scheme 41. MP2/6-31G(d)//3-21G Structures of LiCH$_2$OH 134 and Some Aggregates; Energies of Aggregation [kcal mol^{-1}, in parentheses]; Bond Lengths [pm]



structures—**131A**·H$_2$O, [**131A**·H$_2$O]$_2$, as well as [**131A′**·H$_2$O]$_2$ (Scheme 39)—parallel to the *lengthening* of the Li−F bonds, the corresponding C−F bonds are *shortened* if compared to the unsolvated species. If the C−X bond lengthening is a significant criterion for the carbenoid nature of a carbenoid, which is strongly indicated by all the calculations of carbenoids discussed so far, then solvation should stabilize a carbenoid. The experimental observation related to this result of the calculations was first made by Köbrich[6d] who found Li/Hal carbenoids to be markedly more stable in the better solvating THF than in diethyl ether. The following calculations (Scheme 42) provide evidence that the weakening (breaking) of (bridging) Li$^+$ bonds and the shortening of C−X bonds in carbenoids by solvation is a general phenomenon.

As one can see from Scheme 42, in the tris-solvated Li/F-carbenoid **131B**·3H$_2$O the C−F bond is shortened to 152.5 pm while both the C−Li (215.1 pm) and the Li−F (221.4 pm) distances increase considerably. Consequently, the angle F−C−Li increases from 59.0 to 71.7° which altogether leads from a bridged structure with all bonds in one hemisphere (**131A**) to one approaching a tetrahedron at carbon (**131B**·3H$_2$O). This trend becomes even more pronounced in the other species outlined in Scheme 42 in which the tendency of Li$^+$ binding to X is less pronounced than in LiCH$_2$F **131**. The solvated Li/OH carbenoid **134B**·3H$_2$O has a slightly shorter C−O bond (150.5 pm), a longer C−Li bond (221.5 pm), and a long Li−O distance (243.6 pm) which again results in a larger O−C−Li angle (79.3°). In the Li/Cl carbenoid **144B**·3H$_2$O, the Cl−C−Li angle reaches 89.8°, going via 96.4° in LiCHCl$_2$ **106B**·3H$_2$O to 110 °C in LiCCl$_3$ **115B**·3H$_2$O. In all cases, the bridging of C−X bonds by Li$^+$ is more or less broken up by the solvent molecules. Concomitantly, the C−X bonds are short-

Scheme 42. MP2(fc)/6-31G(d) Structures of Unsolvated and Solvated (3H_2O) Carbenoids; Bond Lengths [pm]; Bond Angles [deg][a]



[a] Local C_3-symmetry was imposed for the solvating H_2O molecules. The asterisk (*) indicates MP2/6-311++G(d,p) geometry; at the MP2/6-31G(d) level, **115A** rearranged to **115D** without activation energy.

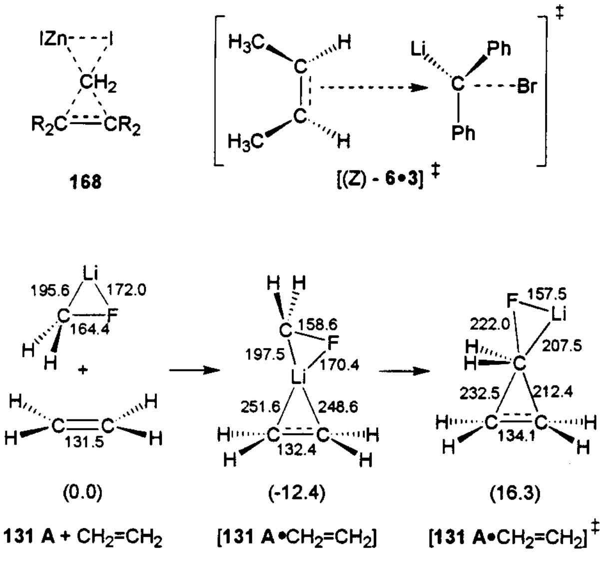
ened which is more so the case in the trichloro species **115B**·3H_2O than in the dichloro compound **106B**·3H_2O and the monochloro species **144B**·3H_2O; see Scheme 42. This sequence results from the C−Cl bond elongation now being equally distributed over three (**115B**·3H_2O) and two (**106B**·3H_2O) C−Cl bonds instead of one C−Cl bond in **144B**·3H_2O.

In related investigations, Tonachini et al. came to similar conclusions.[98] They studied the monomer ⇌ dimer equilibrium of $LiCHF_2$ and $LiC(CH{=}CH_2)F_2$ as well as of the sodium species. In all cases, the dimer is more stable than the monomer (compare Schemes 39 and 41). Furthermore, the solvated (H_2O) dimer is less favored than the unsolvated one[98a] (see Scheme 39). In the corresponding Li(Na)$CHCl_2$ and Li(Na)$C(CH{=}CH_2)Cl_2$ compounds, the dimers are also favored but to a much lesser extent than in the analogous difluoro systems. This makes sense especially if only "Li(Na)-F" and "Li(Na)-Cl" dimers are considered. As a consequence, in the solvated (H_2O) species, the $LiCH(CH{=}CH_2)Cl_2{\cdot}3H_2O$ monomers are more stable than both the di- and tetrahydrated dimers. In the sodium case, solvated monomers and dimers are of comparable energy with the monomers being slightly favored.[98b]

In summary, the interplay of aggregation and solvation has strong effects on carbenoids and their properties as, e.g., C−Li and C−X bond lengths, breaking of the Li^+-bridging of the C−X bond, multiplicity of the $^{13}C{-}^{6}Li$ coupling. The influences on the various bonds determine the carbenoid character and thus the "stability" and reactivity of carbenoids. The influences of solvation on ^{13}C chemical shifts and the calculations of these shifts are detailed in section 1.4.2.

1.4.1.3. Transition States of Reactions of Carbenoids. The first computational investigation of the reaction of a carbenoid, namely, that of $LiCH_2F$ **131** with ethene to give cyclopropane, was published by Houk, Schleyer et al. in 1983.[32] It was of great interest to see whether the calculations are in agreement with the many earlier mechanistic proposals and experimental investigations of such a reaction, especially with regard to the electrophilic nature of the carbenoid.[2a,4,6g,16a,b,24,99−101] For the Simmons−Smith reaction[16] in which the carbenoid is $IZnCH_2I$ (or a solvated or aggregated version thereof), a "butterfly" transition state structure **168** (Scheme 43) has been suggested.[16a,b,101] A similar transition state was proposed by Köbrich for the reaction of $LiCCl_3$ **115** with an olefin.[100] As pointed out earlier in section 1.1, Closs[2a] discussed the transition state structure [(*Z*)-**6·3**]‡ (Scheme 43) for the reaction of aryl carbenoids with alkenes, in which the π bond acts as a nucleophile causing an S_N2-like displacement of the

Scheme 43. Proposed Transition States 168 and [(Z)-6·3]‡ of Reactions of a Carbenoid with an Olefin To Give a Cyclopropane, and the Calculated (HF/3-21G) Pathway (131A + $CH_2{=}CH_2$); Relative Energies [kcal mol^{-1}, in parentheses]; Bond Lengths [pm]



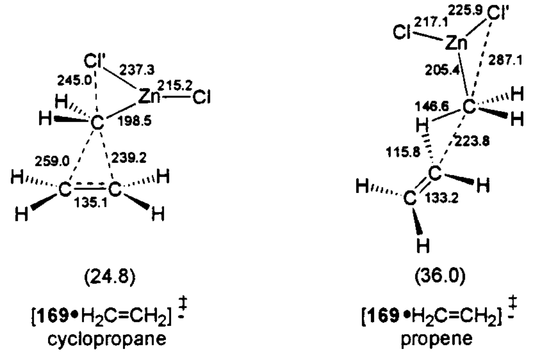
leaving group Hal from the electrophilic carbenoid carbon atom. The stereochemistry of such reactions was outlined in detail in section 1.2.1.

The HF/3-21G computational results[32] led to the conclusion that the transition state structure corresponds well to the one proposed by Closs ([(*Z*)-**6·3**]‡). The LUMO of the carbenoid LiCH$_2$F **131A** is the $\sigma^*_{\mathrm{C-F}}$ orbital, which is attacked by nucleophiles as in an S$_N$2-type reaction. The HOMO of the carbenoid is more or less a carbanion-type lone pair orbital, or a strongly polarized $\sigma_{\mathrm{C-Li}}$ orbital. Some of the significant bond lengths are summarized in Scheme 43. LiCH$_2$F **131A** and ethene first form a complex [**131A**·H$_2$C=CH$_2$] (−12.4 kcal mol^{-1}) which has only slight distortions from reactand geometries, together with rather long bonds from lithium to the ethene carbon atoms (248.6 and 251.6 pm, respectively). The transition state structure [**131A**·H$_2$C=CH$_2$]‡ is only slightly related to the “butterfly” **168** (Scheme 43) because the CH$_2$ group in [**131A**·H$_2$C=CH$_2$]‡ is in a plane nearly parallel to the ethene plane as this is similarly the case in the structure [(*Z*)-**6·3**]‡ proposed by Closs.[2a] The LiCH$_2$F-LUMO can interact in an electrophilic sense with the ethene HOMO on one side of the carbenoid carbon atom, and simultaneously with a fluorine lone pair on the other side. Li$^+$ is loosely associated with the lone pair HOMO on CH$_2$ and bonded more strongly to the departing fluorine. The C−F bond is significantly stretched by 58 pm (35%), while the C−Li bond is elongated by 12 pm (6%). The Li−F bond is shortened by 14 pm (8%). In contrast to these data, the C−C bonds are still very long (212.4 and 232.5 pm). Thus, LiF is strongly “decomplexed” which increases the carbene character of the CH$_2$ moiety. It is therefore not surprising that [**131A**·H$_2$C=CH$_2$]‡ resembles the transition state structures for free halocarbene cycloadditions.[102] A comparison with experimental results (see Schemes 6, 7, 8, and especially 9 in section 1.2.1) shows that the calculated transition state structure is in perfect agreement with the stereochemistry of the reaction of a carbenoid with an olefin to give a cyclopropane.

More recently, a DFT study of the Simmons−Smith cyclopropanation reaction of ClZnCH$_2$Cl **169** with ethene (transition state structure [**169**·H$_2$C=CH$_2$]‡-cyclopropane); see Scheme 44, was published by Bernardi et al.[34] Interestingly, a second reaction channel was found leading to propene CH$_2$=CH-CH$_3$ (transition state structure [**169**·H$_2$C=CH$_2$]‡-propene); see Scheme 44. The latter corresponds to the insertion of the carbenoid into a C−H bond (see section 1.2.3).

The cyclopropane forming transition state structure [**169**·CH$_2$=CH$_2$]‡-cyclopropane is similar to the one shown in Scheme 43 of the LiCH$_2$F **131A** addition to ethene. The newly formed C−C bonds amount to 259.0 and 239.2 pm. The C−Cl′ bond is strongly elongated (34.1%), but the C−Zn bond is only slightly loosened (1.5%). The “carbene character” of a Simmons−Smith reaction is thus less pronounced than in the reaction of LiCH$_2$F **131A** with H$_2$C=CH$_2$, or, in other words, Zn-carbenoids such as ClZnCH$_2$Cl (and others of this type) are “weaker carbenoids” than Li/Hal carbenoids. This is in agreement with all experimental observations. A detailed comparison of the transition state structures [**131A**·H$_2$C=CH$_2$]‡ involving LiCH$_2$F (Scheme 43) and [**169**·H$_2$C=CH$_2$]‡-cyclopropane with ClZnCH$_2$Cl (Scheme 44), however, is not appropriate because of the rather different levels used in the calculations.

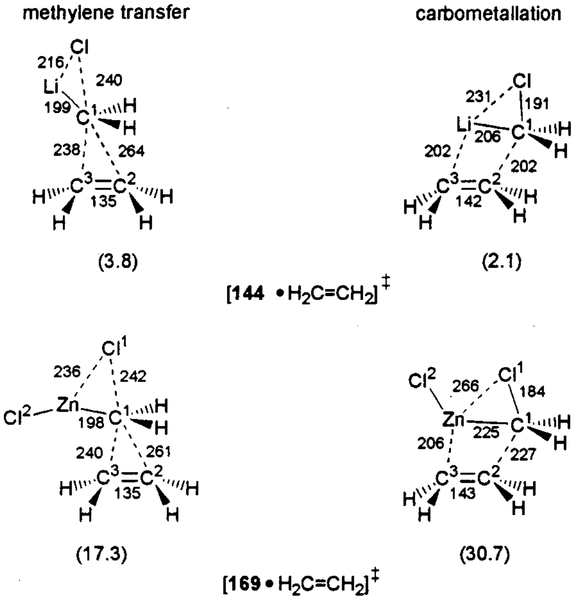
Scheme 44. Transition State Structures (B3LYP/6-311G(d,p)//B3LYP/DZVP) of the Reaction of ClZnCH$_2$Cl 169 with H$_2$C=CH$_2$ To Give Cyclopropane ([169·H$_2$C=CH$_2$]‡-cyclopropane) and Propene ([169·H$_2$C=CH$_2$]‡-propene), Respectively; Bond Lengths [pm]; Relative Energies [kcal mol^{-1}, in parentheses]



This is not the case if one compares the transition state structures of the cyclopropane and the propene formation, respectively, in Scheme 44. In the propene forming reaction, CH$_2$ inserts into a vinylic C−H bond. The three atoms involved in the process are arranged in a three-centered structure, in which the C−H ethene bond is breaking while two new bonds are simultaneously formed, one between the ethene H atom and the carbenoid CH$_2$ carbon atom (C−H 146.6 pm), and the other one between the ethene carbon atom and the methylene carbon atom (C−C 223.8 pm). The insertion process is again responsible for strong structural changes in the Zn-carbenoid, which are similar to those in the cyclopropane forming transition state. The chlorine atom Cl′ is moving away from the CH$_2$ carbon atom (C−Cl′ 287.1 pm) to form a new bond with Zn (Zn−Cl′ 225.9 pm), and the C−Zn bond is lengthened (C−Zn 205.4 pm). Not unexpectedly, the activation energy for the cyclopropane forming reaction is much smaller (24.8 kcal mol^{-1}) than for the C−H insertion (36.0 kcal mol^{-1}). This agrees perfectly with experimental results: in the Simmons−Smith reaction, olefins are very selectively cyclopropanated while C−H insertion reactions are unknown.[16] As pointed out in sections 1.1 and 1.2.3, this is not so in the reactions of Li/Hal carbenoids with olefins.

A recent study of Nakamura et al.[103] of the reactions of LiCH$_2$Cl **144** and ClZnCH$_2$Cl **169**, respectively, with ethene by means of DFT methods (see Scheme 45) allows a direct comparison of different reaction channels: the two carbenoids behaving as electrophiles and nucleophiles, respectively, to give cyclopropane. The activation energy for the cyclopropanation with LiCH$_2$Cl **144** *via methylene transfer* (electrophilic pathway) amounts only to 3.8 kcal mol^{-1}, while the value for the reaction with ClZnCH$_2$Cl **169** is considerably higher (17.3 kcal mol^{-1}). The alternative transition states for the cyclopropana-

Scheme 45. Transition State Structures of the Methylene Transfer and Carbometalation Pathways, Respectively, of the Cyclopropanation of Ethene with $LiCH_2Cl$ 144 (B3LYP/6-31G(d)) and $ClZnCH_2Cl$ 169 (B3LYP/6-31G(d)/SVP(Zn)), Respectively; Bond Lengths [pm]; Relative Energies [kcal mol^{-1}, in parentheses]



tions, namely *via carbometalation* of the ethene double bond followed by intramolecular $LiCl(ZnCl_2)$ elimination (nucleophilic pathway), are also outlined in Scheme 45. In the case of the $LiCH_2Cl$ (**144**) reaction, this pathway has also a very low activation barrier (2.1 kcal mol^{-1}). As shown in Scheme 9, investigations of the stereochemistry of such reactions showed the preference for the methylene transfer pathway and, thus, for the electrophilic character of the carbenoid carbon atom. The carbometalation with $ClZnCH_2Cl$ **169** has a rather high activation energy (30.7 kcal mol^{-1}) which clearly excludes this route as a pathway to cyclopropanes. Again it is evident from these calculations that Li/Cl (and other Li/Hal) carbenoids have a much more pronounced "carbenoid character" than ClZn/Cl carbenoids (and other Simmons–Smith reagents of this type).

At this point it is of interest to mention briefly the situation in the case of olefins reacting with a *carbene*. In an ab initio study of the reaction of singlet methylene with the C–H bond of ethene,[104] no activation energy was found if electron correlation is included. Similarly, no activation energy was found for the addition of a carbene to a double bond.[102,105] It is well-known that the insertion of singlet methylene into vinylic C–H bonds indeed can compete successfully with the addition process to the double bond, although the latter is faster.[106,107]

The difference between *lithium* and *zinc* carbenoids, $LiCH_2Hal$ and $HalZnCH_2Hal$, respectively, is quite clear from the above-discussed calculations and the experimental findings. The reason for the difference is the more covalent character of the C–ZnHal bond as compared to the almost completely ionic C–Li bond. Due to this difference, both the nucleophilicity as well as the electrophilic character of zinc carbenoids is reduced compared to lithium carbenoids (see the discussion of the structures of the 2-*lithiated* thiazole **205**, the 2-*ZnBr*-thiazole **206**, and the 2-ZnCl-benzoxazole **207** (Scheme 57) in section 1.4.3.2).[108] What is the influence *of different leaving groups X* (especially X = Hal) on the nature of, e.g., lithium carbenoids $LiCH_2X$, X = F, Cl, Br, I, OH—a question which was first raised in section 1.4.1.1.9. In the literature dealing with carbenoids[6] (mostly with Li/Hal carbenoids), significant differences are not discussed in the *Li/Hal* series. In analogy to the cyclopropanation reactions detailed in Schemes 43–45, we calculated the reactions of the carbenoids $LiCH_2F$ **131A**, $LiCH_2Cl$ **144A**, $LiCH_2Br$ **145A**, $LiCH_2I$ **146A**, and $LiCH_2OH$ **134A** with ethene on various levels of theory.[109] The results are summarized in Table 8.

Table 8. Calculated Transition State Energies [kcal mol^{-1}] of the Reactions of the Carbenoids $LiCH_2X$ (X = F, Cl, Br, I, OH) + $H_2C{=}CH_2$ to Give Cyclopropane + LiX[a]

	F	Cl	Br	I	OH
basis set[b]	**131A**	**144A**	**145A**	**146A**	**134A**
1	7.4(10.1)	6.9(7.9)	6.6(7.7)	6.1(7.4)	19.2(19.8)
2	7.4	8.1			
3	3.8	3.9			
4	5.0	6.2			

[a] The energies are related to the energies of $LiCH_2X$ + $H_2C{=}CH_2$; MP2 (full) with different basis sets. [b] Basis set 1: H, C, Li, F, O: 6-311 ++G(d,p); Cl, Br, I: Stuttgarter ECP's (4111/4111/1).[93] Basis set 2: H, C, Li, F, Cl: 6-311 ++G(d, p). Basis set 3: H, C, F, Cl: AUG-cc-pVDZ; Li: 6-311 ++G(d,p). Basis set 4: geometries optimized with basis set 2, single-point calculations with basis set 3; H, C, F, Cl: AUG-cc-pVDZ; Li: 6-311 ++G(d,p). Values in parentheses indicate those with ZPE correction.

First it is evident that the energies of the transition states of the Li/Hal carbenoids, Hal = F, Cl, Br, I, do not vary significantly. Calculated with basis set 1, a small continuous decrease is observed from the Li/F compound to the Li/I species. Basis sets 2–4 indicate a slightly smaller activation energy for the Li/F as compared to the Li/Cl carbenoid. In contrast to these results, one finds a much higher activation energy for the reaction of $LiCH_2OH$ **134A** with $H_2C{=}CH_2$. Indeed, Li/OR carbenoids are only poor reagents for cyclopropanation reactions. The results of a study of Schöllkopf[110] are outlined in Scheme 46.

In the reaction of the Li/OR carbenoid **73** with the olefins **170** and **171**, respectively, only poor yields of cyclopropanes **172** (0.5%) and **173** (2%), respectively, are detected. Apparently the reaction of **73** with the better nucleophile *n*-butyllithium, or with itself, are the more successful pathways (see Schemes 15, 21, 22).

What is the reason for the almost equal transition state energies in the reactions of the Li/Hal carbenoids **131A**, **144A**, **145A**, and **146A** with ethene? After all, the cleavage of a C–F bond as in **131A** requires much more energy than the cleavage of a C–I bond (**146A**). On the other hand, as pointed out in the discussion of the reaction of $LiCH_2F$ **131A** with ethene (Scheme 43), *LiF is strongly decomplexed in the transition state [**131A**·$H_2C{=}CH_2$]‡*. This is also the

Scheme 46. Cyclopropanation Reactions of the Li/OR Carbenoid 73 with the Olefins 170 and 171 To Give 172 and 173

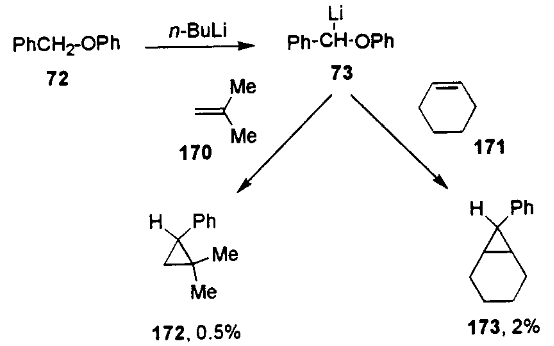


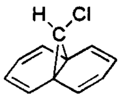
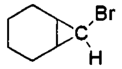
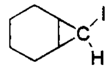
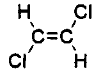
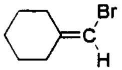
Table 9. Bond Dissociation Energies of $LiCH_2X$ and LiX, X = F, Cl, Br, I, OH, and Reaction Energies $LiCH_2X + Li^+ \rightarrow LiCH_2^+ + LiX$ [kcal mol^{-1}]; Calculated with Basis Set 1, Table 8

X	$LiCH_2X \rightarrow LiCH_2^+ + X^-$	$LiX \rightarrow Li^+ + X^-$	$LiCH_2X + Li^+ \rightarrow LiCH_2^+ + LiX$
F	194.8	183.1	11.7
Cl	170.1	154.8	15.3
Br	164.1	147.5	16.6
I	156.3	137.3	19.0
OH	217.9	189.2	28.7

case for LiHal, Hal = Cl, Br, I, and LiOH, in the transition state structures of the reactions of **144A**, **145A**, **146A**, and **134A**, respectively, with ethene. The bond dissociation energies $LiCH_2X \rightarrow LiCH_2^+ + X^-$ and $LiX \rightarrow Li^+ + X^-$, X = F, Cl, Br, I, and OH, calculated with basis set 1, Table 8, are outlined in Table 9.

It can be seen from Table 9 that the dissociation energies of $LiCH_2X$ into $LiCH_2^+ + X^-$ decrease strongly from X = F (194.8 kcal mol^{-1}) to 156.3 kcal mol^{-1} with X = I, the energy difference being 38.5 kcal mol^{-1}. A similar trend is observed in the case of the dissociation energies of LiHal to give $Li^+ + Hal^-$ with X = F amounting to 183.1 kcal mol^{-1} and X = I being 137.3 kcal mol^{-1}. The energy difference between these two cases is 45.8 kcal mol^{-1}. In the last column of Table 9 are listed the reaction energies $LiCH_2X + Li^+ \rightarrow LiCH_2^+ + LiX$, which increase from 11.7 kcal mol^{-1} (X = F) to 19.0 kcal mol^{-1} (X = I). The difference between these energies amounts only to 7.3 kcal mol^{-1}. These data suggest the reason for the similar transition state energies of the Li/Hal carbenoids with ethene (Table 8): the energy required for the C−X bond cleavage is essentially compensated by the Li−X bond formation. One can also see from Table 9 that the reaction energy $LiCH_2OH + Li^+ \rightarrow LiCH_2^+ + LiOH$ is much higher (28.7 kcal mol^{-1}) than in the case of the Li/Hal carbenoids. This is in agreement with the higher transition state energy of the reaction of $LiCH_2OH$ **131A** with ethene (19.2 kcal mol^{-1}) (see Table 8) and the experimental findings (see Scheme 46). In conclusion, the transition state energies of the reactions of carbenoids $LiCH_2X$ with ethene provide a reasonable criterion for their "carbenoid character". The Simmons−Smith reagents fit into this picture; see Schemes 44 and 45.

Table 10. ^{13}C Chemical Shifts δ [ppm] and $^{13}C-^6Li$ Coupling Constants *J* [Hz] of Li/Hal Carbenoids

entry	compound	δ[ppm]	Li-carbenoid δ[ppm]	Δδ(H, Li) [ppm]	$^1J(^{13}C^6Li)$ [Hz] triplet
1	CH_2Cl_2	55.5	105.5	50.0	16.3
2	CH_2Br	22.5	101.3	78.8	16.3
3	CH_2I_2	-55.0	61.0	126.0	16.3
4	$CHCl_3$	80.0	145.9	65.9	17.0
5	$CHBr_3$	9.7	152.2	142.5	16.3
6	CHI_3	-138.0	142.0	280.0	17.0
7	CH_2CBr_2H	42.6	148.1	105.5	17.0
8		43.5	86.0	42.5	17.0
9		24.4	79.9	55.5	-
10		-7.9	83.2	91.1	17.0
11		121.3	189.4	68.1	-
12		99.2	200.8	101.6	16.8

Two further publications deal with cyclopropanation reactions of carbenoids. Density functional studies of the Simmons−Smith reaction including relativistic effects were published by Koch and Dargel.[111] The results, which are related to earlier mentioned ones (Schemes 44 and 45), lead to activation energies of 11.5 to 14.6 kcal mol^{-1} (depending on the method). Nakamura et al. recently calculated how Simmons−Smith reactions of $ClZnCH_2Cl$ **169** with an olefin ($H_2C{=}CH_2$) can be accelerated by Lewis acids ($ZnCl_2$).[112] They also calculated a model case for the reaction of the Simmons−Smith reagent with allylic alcohols. Reactions of this type are used for enantioface selective cyclopropanations of allylic alcohols.[113]

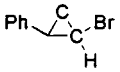
1.4.2. NMR Studies and ^{13}C Chemical Shift Calculations

1.4.2.1. Experimental NMR Investigations. The pioneering work in this area was performed by the Seebach group.[94] It was found that in Li/Hal carbenoids the carbenoid ^{13}C atom is strongly deshielded up to 280 ppm, the coupling constants with ^1H and ^{13}C nuclei attached to the carbenoid C atom are strongly decreased, and the $^{13}C-^6Li$ coupling constant, structurally independent, is almost constant and large (~17 Hz). Some examples of the deshielding of the carbenoid carbon atom and of $^{13}C-^6Li$ coupling constants are given in Table 10.

The coupling constants ^1J ($^{13}C-^6Li$) are all around 17 Hz. In "normal" organolithium compounds ^1J ($^{13}C-^6Li$) is between 8 and 10 Hz. Entries 1 to 3 show that Δ*δ* (H, Li) in $LiCHX_2$ (X = Cl, Br, I) increases from 50.0 to 126.0 ppm. A similar trend is observed for $LiCX_3$ (X = Cl, Br, I); see entries 4−6 (Δ*δ* = 65.9 to 280.0 ppm). In the cyclopropyl carbenoid series (entries 8−10), Δ*δ* also increases from X = Cl to X = I (Δ*δ* = 42.5 to 91.1 ppm), as is similarly the case for the vinylic species (entries 11 and 12).

Some $^1H-^{13}C$ and $^{13}C-^{13}C$ coupling constants with the lithiated ^{13}C atom are summarized in Table 11. In CH_2Cl_2 (entry 1) the $^1H-^{13}C$ coupling constant decreases on lithiation from 178 to 110 Hz; CH_2I_2 (entry 2) shows a similar trend. Similarly $^{13}C-^{13}C$ coupling constants decrease on lithiation as shown

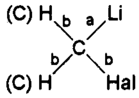
Table 11. Comparison of ^{1}H−^{13}C and ^{13}C−^{13}C Coupling Constants *J* [Hz] in Nonlithiated and Lithiated Organo-halides

entry	compound	$J_{H\text{-}C}$ H-C-H	 H-C-Li	$\Delta J_{H\text{-}C}$
1	CH_2Cl_2	178	110	-68
2	CH_2I_2	173	95	-78
		$J_{C\text{-}C}$ C-C-H	 C-C-Li	$\Delta J_{C\text{-}C}$
3	CH_3CBr_2H	37	8	-29
4		13	<0.1	-13

from entries 3 and 4. In "normal" organolithium compounds related effects are also observed albeit somewhat smaller.

Seebach et al. came to the following conclusions concerning the ^{13}C NMR data outlined above; see Scheme 47.

Scheme 47. Carbenoid Carbon Atom of Li/Hal Carbenoids in the ^{13}C NMR Spectrum, and Conclusions Thereof



bond a: high s-character, therefore large ^{13}C-^{6}Li coupling constant

bonds b: due to the higher s-character in bond a, there is a higher p-character in bonds b, which leads to

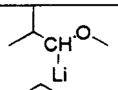
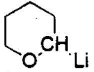
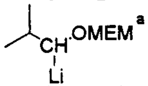
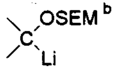
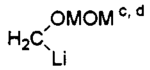
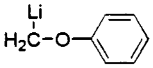
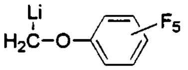
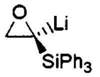
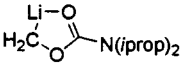
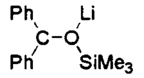
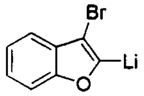
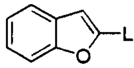
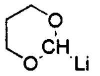
1. stronger polarizations of the C-Hal bonds, resulting in a deshielding of the carbenoid C atom, and
2. reduced ^{1}H-^{13}C and ^{13}C-^{13}C coupling constants with the carbenoid C atom

Scheme 47 needs no further comment. The explanation for the strong deshielding of the carbenoid ^{13}C atom ("stronger polarization of the C−X bonds"), however, is a rather general one. Therefore we shall return to this point in section 1.4.2.2.

In Schemes 15, 21, and 22 it was shown that α-lithiated ethers are Li/OR carbenoids. Calculations (Schemes 32, 41, 42; Tables 3, 4, 6, 7) support the experimental findings according to which species of the type LiC(R^1,R^2)OR are electrophilic and react quite well at least with nucleophiles R^3Li to give $LiCR^1R^2R^3$ + LiOR. Thus the question arises whether the carbenoid ^{13}C atom in α-lithiated ethers is also deshielded. Table 12 shows that this is clearly the case.[55]

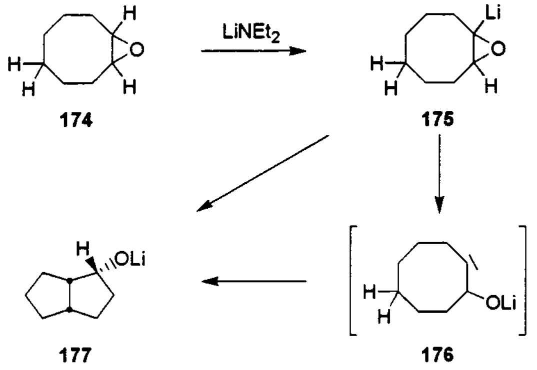
First the reader is reminded of the chemical shifts of three Li/Cl carbenoids (entries 14−16). They show also the influence of the number of the Cl atoms on the chemical shifts. α-Lithiated ethers $LiCH_2OR$ thus should be compared with the deshielding of the carbenoid carbon atom in $LiCH_2Cl$ (32.3 ppm, entry 14). As indicated by the entries 1−8, in α-lithiated ethers the deshielding of the lithiated ^{13}C atom is almost as strong as in $LiCH_2Cl$ which consequently characterizes these compounds as Li/OR carbenoids. In agreement with $LiCHCl_2$ (50.0 ppm, entry 15), the deshielding in a lithiated acetal is stronger (40.0 ppm, entry 13) than in α-lithiated ethers (entries 1−8). The chelate (dipole)-stabilized species (entry 9, 7.0 ppm) shows a much smaller effect, while the lithiated ether with Li only bonded to oxygen (entry 10, 34.8 ppm) has an even smaller downfield shift than the model system diphenylmethan/diphenylmethyllithium (38.7 ppm).[94d] In such compounds the deshielding is due to rehybridization at the anionic carbon atom; an additional "carbenoid" effect (entry 10) is thus not observed. This is in agreement with experimental observations according to which the lithiated diphenylmethyl-trimethylsilyl ether is not electrophilic.[55] A comparison of entries 6 and 7 indicates stronger carbenoid character in the lithiated methyl pentafluorophenyl ether (29.9 ppm) than in the lithiated methyl phenyl ether (19.7 ppm) which again agrees with the experimental observations: pentafluorophenolate is the better leaving group than phenolate.[55] The ^{13}C data of the α-lithiated oxirane (entry 8) are also of interest: the Δδ-value (36.9 ppm) is even higher than that of $LiCH_2Cl$ (32.3 ppm, entry 14). Experimental evidence for the strong electrophilicity of α-lithiated oxiranes is found in the literature. Cope[115] discovered the reaction of the oxirane **174**

Table 12. ^{13}C Chemical Shifts [ppm] of the Carbenoid Carbon Atoms in Li/OR Carbenoids; Comparison with Some Li/Cl Carbenoids

entry	carbenoid	δ [ppm]	Δδ (H, Li) [ppm]
1		106.4	26.4
2		95.7	26.2
3		102.4	27.8
4		96.7	28.0
5		74.0	19.0
6		74.5	19.7
7		92.2	29.9
8		79.0	36.9
9		67.3	7.0
10		111.2	34.8
11		218.4	73.7
12		215.6	70.8
13		134.8	40.0
14	$LiCH_2Cl$	57.9	32.3
15	$LiCHCl_2$[f]	105.5	50.0
16	$LiCCl_3$[f]	145.9	65.9

[a] MEM = (2-methoxyethoxy) methyl. [b] SEM = [2-(trimethylsilyl) ethoxy] methyl. [c] MOM = methoxymethyl. [d] Reference 114. [e] Reference 95. [f] Reference 94d.

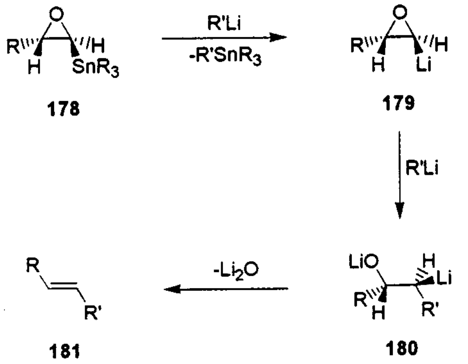
Scheme 48. Insertion of the Carbenoid 175 (or the Carbene 176) into a C−H Bond To Give 177



with lithiumdiethylamide to give the C−H insertion product **177**; see Scheme 48. The reaction proceeds through the α-lithiated oxirane **175** which could directly (or via the intermediate carbene **176**) lead to **177**.

The reactions of α-lithiated oxiranes such as **175** take advantage of the loss of strain in the three-membered ring. Another example is the "reductive alkylation";[116] see Scheme 49.

Scheme 49. "Reductive Alkylation" of α-Lithiated Oxiranes 179



Sn/Li exchange in **178** gives the α-lithiated oxirane **179**, which reacts as an electrophile with R′Li leading to **180**. β-Elimination of Li_2O results in the olefin **181**.[117]

A MP2/6-311++G(d,p) calculation shows the strong elongation of the C−O bond in oxirane **182** (143.3 pm) on lithiation to give **183** (160.0 pm); see Scheme 50.[55]

Scheme 50. MP2/6-311++G(d,p) Calculated Structures of 182 and 183; Bond Lengths [pm]

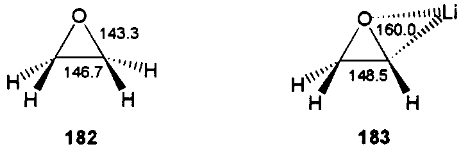
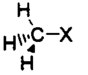
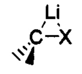
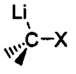


Table 13. IGLO/II+sp//MP2/6-311++G(d,p) Calculated ^{13}C NMR Chemical Shifts δ (Triple-ζ Basis[118a]), Relative Chemical Shifts $\Delta\delta = \delta_{C-Li} - \delta_{C-H}$ (in Italics), and, in Part, Experimental δ-Values [ppm] (in Parentheses) of H_3C-X and $LiCH_2X$ Isomers A, B, and C, X = H, F, Cl, OH, SH, and NH_2[a]

entry	X			 A	 B	 C
1	H		-2.3 (-2.3)	-	-23.1 (2) *-20.8*	-
2	F	131	67.6 (71.6)	143.3 *75.7*	-	158.2 *90.6*
3	Cl	144	28.1 (25.6)	74.7 *46.6*	-	72.4 *44.3*
4	OH	134	49.3 (49.9)	79.0 *29.7*	55.6 *6.3*	82.6 *33.3*
5	SH	136	10.0 (6.5)	11.7 *1.7*	-3.7 *-13.7*	-
6	NH_2	135	29.9 (28.3)	37.4 *7.5*	29.2 *-0.7*	53.8 *23.9*

[a] The calculated δ-values are related to the δ-system (tetramethylsilane) with CH_4 (δ −2.3 ppm) as the standard. The geometries correspond to those in Table 3.

For the "vinylic" Li/OR carbenoids (entries 11 and 12 in Table 12) large Δδ values are observed: 73.7 and 70.8 ppm, respectively. This is a general phenomenon of lithiated, sp^2-hybridized carbon atoms.[94d] The values of monomeric phenyllithium (68.1 ppm), its dimer (60.3 ppm), or the tetramer of vinyllithium (54.4 ppm) show, however, that the α-lithiated vinyl ethers are even stronger deshielded, which is in agreement with their carbenoid nature (for the electrophilic reactivity of such compounds, see, e.g., Schemes 21 and 22).

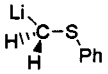
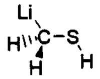
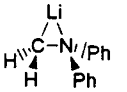
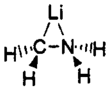
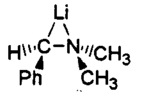
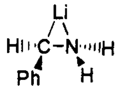
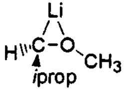
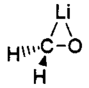
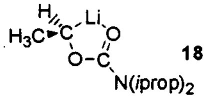
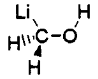
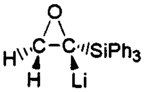
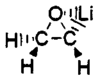
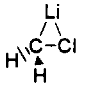
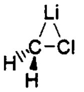
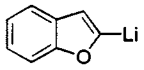
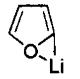
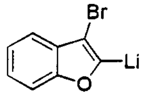
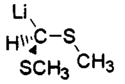
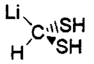
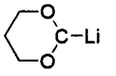
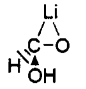
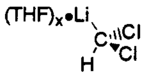
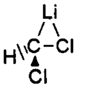
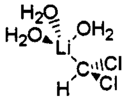
1.4.2.2. IGLO Calculations of Chemical Shifts; a Comparison with Experimental Results. The IGLO method for the calculation of chemical shifts has been introduced by Kutzelnigg et al.[118] It was used by Schleyer and Kutzelnigg et al. for the calculation of ^{13}C chemical shifts of organolithium compounds.[119] We calculated the chemical shifts of the compounds H_3C-X, X = H, F, Cl, OH, NH_2, SH, and their Li-isomers, $LiCH_2X$ **A**, **B**, and **C**; see Table 13.[55,82,92] A *positive* Δδ-value in Table 13 corresponds to a *deshielded* ^{13}C atom.

First, and in agreement with the calculations of "normal" organolithium compounds,[119] methyllithium **2**, entry 1, is shielded (−20.8 ppm). The experimental value amounts to −13.0 ppm, and the calculated one for $[CH_3Li{\cdot}H_2O]_4$ is −13.3 ppm;[119] see Table 14 (which summarizes experimental and calculated data), entry 1.

A shielding is also calculated for the tetrahedral $LiCH_2SH$ species **136B** (−13.7 ppm, Table 13, entry 5). The experimental value of (phenylthio)methyllithium **137** is −10.8 ppm;[94e] see Table 14, entry 2. This could be indicative of a tetrahedral structure of **137** *in solution*, which would agree with the tetrahedral structure of (phenylthio)methyllithium **137** in a crystalline complex; see Scheme 35. The Li-bridged structure **136A**, which was never observed in solid state structures of α-lithiated thioethers (see Scheme 35), was calculated to have a Δδ value of 1.7 ppm (Table 13, entry 5). As mentioned before, and in agreement with the (calculated) chemical shifts, α-lithiated thioethers are not known to behave like carbenoids.

The situation is rather similar in the case of α-lithiated amines (Table 13, entry 6). The Li-bridged isomer **135A** is weakly deshielded (7.5 ppm), while the tetrahedral **135B** shows even a minor shielding (−0.7 ppm). The value of **135A** (7.5 ppm) corresponds nicely to the experimentally determined value of 8.1

Table 14. Comparison of Some IGLO Calculated and Experimentally Determined ^{13}C Chemical Shifts

Entry	experiment		Δδ [ppm]	Δδ [ppm]	calculations	
1	$(^{13}CH_3Li)_4$	$(2)_4$	-13.0	-13.3	$(2\bullet OH_2)_4$[119]	$(^{13}CH_3Li\bullet OH_2)_4$
2		**137** [94e]	-10.8	-13.7	**136 B** [a]	
3		**184** [120]	8.1	7.5	**135 A** [a]	
4		**185** [121]	19.9	20.9	**186 A** [b]	
5		**166** [120]	26.4	29.7	**134 A** [a]	
6		**187** [120]	7.0	6.3	**134 B** [a]	
7		**188**[120]	36.9	54.8	**183 A** [a]	
8		**144** [82]	33.7	46.6	**144 A** [a,c]	
9		**165** [95]	73.7	76.8	**189 A** [d]	
		**164** [82]	70.8			
10		**190** [94e]	-7.0	-11.3	**191B** [e]	
11		**192** [82]	40.0	43.3	**193 A** [e]	
12		**106•xTHF** [94d]	50.0	62.8	**106 A** [f]	
				49.5	**106 B•3H₂O** [f, 124]	

[a] MP2/6-311++G(d,p) geometry. [b] The calculated value was approximated through the addition of the experimental shift of benzyllithium (13.4 ppm)[94d] to the calculated shift of **135A**. [c] For the tris-hydrated **144B**·3H$_2$O one calculates Δδ = 27.3 (compare with **106A** and **106B**·3H$_2$O, entry 12). [d] HF/6-31G(d) geometry. [e] HF/6-311++G(d,p) geometry. [f] MP2/6-31 G(d) geometry.

ppm as measured for *N*,*N*′-diphenylamino-methyllithium LiCH$_2$NPh$_2$ **184**[120] (Table 14, entry 3), which suggests a Li-bridged structure of **184** *in solution*. In the case of *N*,*N*′-(dimethylamino)-benzyllithium LiCH(Ph)NMe$_2$ **185** Δδ is 19.9 ppm;[121] see Table 14, entry 4. With the experimental Δδ value of benzyllithium[94d] (13.4 ppm) and the calculated value of **135A** (7.5 ppm), a "theoretical" value Δδ 20.9 ppm is determined for an α-amino-benzyllithium compound (**186A**), which is in excellent agreement with Δδ 19.9 ppm of **185**. The Li-bridging in the solution structure of LiCH(Ph)NMe$_2$ **185**, which is suggested by the NMR results, is supported by the solid state structure of **185**; see section 1.4.3.1.

In contrast to the compounds discussed above, α-lithiated ethers were demonstrated to be Li/OR carbenoids; see sections 1.2.4 and 1.4.1.1.4. According to Table 13, entry 4, the bridged LiCH$_2$OH **134A** is calculated to have Δδ 29.7 ppm, and the tetrahedral **134B** 6.3 ppm, which is in good agreement with the carbenoid character of α-lithiated ethers. Entry 5 in Table 14 reveals the experimentally determined Δδ-value of the lithiated isobutyl methyl ether **166** (26.4 ppm)[120] which is very close to that of **134A** (29.7 ppm). It thus seems that **166** has a Li-bridged structure in solution, which is similarly observed in the solid state structures of the α-lithiated benzofurans **164** and **165**; see section 1.4.3.2. Entry 6 in Table 14 shows the Δδ value of the α-lithiated carbamate **187** to amount to 7.0 ppm which is very close to 6.3 ppm as calculated for the tetrahedral **134B**. Indeed, Li-carbamates of the type **187** are known to have a chelate structure[122,123] which leads to a **134B**-type arrangement around the carbenoid carbon atom. A comparison of $\Delta\delta$ as determined by ^{13}C NMR spectroscopy in solution with $\Delta\delta$ values calculated for structural isomers of carbenoids thus gives useful hints on the structure of such carbenoids in solution.

The strong carbenoid character of α-lithiated oxiranes was discussed in detail in section 1.4.2.1. This property agrees nicely with the strong IGLO shift in **183A** (54.8 ppm, Table 14, entry 7). Experimentally it was only possible to determine the ^{13}C NMR spectrum of the Ph_3Si-substituted, α-lithiated oxirane **188**. Even in that case the strongest deshielding of an α-lithiated ether (36.9 ppm, Table 14, entry 7) was measured.[120]

The strongest deshielding of all compounds of interest are calculated for the Li/Cl (**144A**, 46.6 ppm) and Li/F carbenoids (**131A**, 75.7 ppm, entries 3 and 2, Table 13). The value of **131A** (75.7 ppm) indicates a very strong carbenoid nature of Li/F carbenoids if compared to the nonlithiated species which corresponds to the lengthening of the C−F bond as dicussed in section 1.4.1.1.9. Unfortunately, a ^{13}C NMR spectrum of $LiCH_2F$ **131** so far has not been measured: even at −120 °C only the product of "eliminative dimerization", $H_2C{=}CH_2$, was observed in the NMR spectrum.[120] The experimental value of $LiCH_2Cl$ **144** ($\Delta\delta$ 33.7 ppm)[82] is in fair agreement with the calculated number of **144A** (46.6 ppm); see Table 14, entry 8.

In Table 13 are also listed the IGLO values of the carbene-donor complexes **C** CH_2-XLi. The values are rather close to those of the bridged isomers **A**. The existence of isomers **C**, however, is very unlikely, at least in most carbenoids of the type $LiCH_2X$, because of the instability with regard to isomers **A** (see Table 3 in section 1.4.1.1.9). Isomers **D** of the type H_2C-LiX (carbene-acceptor complexes) have been omitted from Table 13. The $\Delta\delta$ values are calculated to be in the range of 900−1000 ppm. We assume that in the case of these compounds electron correlation plays a major role because of the small HOMO−LUMO gaps. Thus electron correlation should be included in the calculations, which is not the case in the IGLO method.

The agreement between experimentally determined ^{13}C NMR values and IGLO calculated ones is also observed in other cases. In Table 14, entry 9, are listed the lithiated benzofurans **165** and **164** (73.7 and 70.8 ppm, respectively). The ^{13}C values correspond nicely to 76.8 ppm as calculated for α-lithiofuran **189A**. The ^{13}C atom in the lithiated thioacetal **190** is shielded (−7.0 ppm)[94e] (Table 14, entry 10), as is the ^{13}C atom in the IGLO model $LiCH(SH)_2$ **191B** (−11.3 ppm). In contrast, one observes a strongly deshielded ^{13}C atom in the lithiathed acetal **192** (40.0 ppm),[82] which is in excellent agreement with the calculated model $LiCH(OH)_2$ **193A** (43.3 ppm); see Table 14, entry 11.

The calculation of chemical shifts of carbenoids by means of the IGLO method *with and without solvent molecules* gives hints of the structure of carbenoids in different solvents. Thus, for the unsolvated, Li-bridged $LiCHCl_2$ **106A**, $\Delta\delta$ is calculated to be 62.8 ppm[124] (see Table 14, entry 12), while the tri-solvated $LiCHCl_2{\cdot}3H_2O$, which is of the structural type **B** (**106B**·$3H_2O$), has $\Delta\delta$ 49.5 ppm[124] (Table 14, entry 12). In good donor solvents such as THF, the normally favorable bridging of the C−Cl bond by Li^+ (structural type **A**) should therefore be less favorable than a nonbridged species with tri-solvated lithium (**106B**·$3H_2O$), which is in agreement with the experimental findings: $\Delta\delta$ of $LiCHCl_2$ **106** in THF (**106**·*x*THF) amounts to 50.0 ppm. In solvents with lower donor qualities the bridged structure **106A** should dominate.

Table 15. Mullikan, Natural Population Analysis (NPA), and Bader Partial Charges of H_3CF 131-H and $LiCH_2F$ 131A

	method	C	H	Li	F
H_3CF **131-H**	Mulliken	−0.217	0.140		−0.204
	NPA	−0.051	0.146		−0.386
	Bader	0.546	0.029		−0.634
$LiCH_2F$ **131 A**	Mulliken	−0.512	0.117	0.548	−0.271
	NPA	−0.605	0.126	0.896	−0.542
	Bader	−0.220	−0.014	0.914	−0.666

1.4.2.3.1. The Deshielding of the Carbenoid ^{13}C Atom from a Theoretical Point of View. The deshielding of the ^{13}C carbenoid atom is not due to the charge at this atom. Table 15 summarizes the results of different calculations of the partial charges[125−127] at the various atoms of CH_3F **131-H** and $LiCH_2F$ **131A**.

Although the methods vary strongly, it is evident that in all cases the carbenoid carbon atom of $LiCH_2F$ **131A** bears a partial *negative* charge. Since this charge is ca. 0.5 ± 0.2 electrons higher than in the nonlithiated CH_3F **131-H**, a *shielding* of the carbenoid carbon atom in $LiCH_2F$ could have been expected. This is clearly not the case as detailed in sections 1.4.2.1 and 1.4.2.2. The numbers in Table 15 also exclude a "partical positive charge at the carbenoid C atom of $LiCH_2F$ **131A** due to the polarization of the C−X bond" as the reason for the *deshielding*.

What is responsible for the deshielding of the carbenoid ^{13}C atom in the NMR spectra of carbenoids? The IGLO method allows the localization of the molecular orbitals of a molecule to give core, bond, and lone pair orbitals, respectively. Thus, not only the isotropic chemical shifts σ but also the dia- or paramagnetic contributions of the various localized molecular orbitals (LMOs) can be calculated. In Table 16 are summarized the contributions of the LMOs C_{1s}, σ_{C-H}, σ_{C-X}, σ_{C-Li}, and the sum of the others (Σ_{others}) to the total isotropic chemical shift σ of various compounds. The $\Delta\delta$ value of the chemical shift is also added. Antibonding orbitals are not given explicitly by the IGLO calculations.

Table 16 shows an almost constant diamagnetic contribution (∼200.9 ppm) of the carbon 1s orbital in all the compounds. The most striking differences between the various species are calculated for the σ_{C-Li} orbitals. In the "carbanion" CH_3Li **2** and in $LiCH_2SH$ **136B** (which is not a carbenoid), the positive value indicates a diamagnetic (shielding) contribution, in agreement with experimental results

Table 16. LMO Contributions to the Isotropic Chemical Shift σ [ppm] of Various Compounds (Negative Values: Paramagnetic Contributions; Positive Values: Diamagnetic Contributions); Δδ [ppm] Is Also Given; δ_{C-H} Corresponds to One C−H Bond

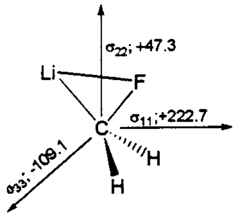
compound		C_{1s}	σ_{C-H}	σ_{C-X}	σ_{C-Li}	Σ_{other}	σ_{total}	Δδ
CH_3Li	**2**	200.89	3.64		8.26	−0.03	220.03	−20.8
$LiCH_2SH$	**136A**	200.92	−6.47	5.80	−8.00	−0.52	185.25	1.7
	136B	200.90	−1.64	3.99	0.48	−1.35	200.74	−13.7
$LiCH_2NH_2$	**135A**	200.91	−8.38	−3.96	−20.34	−0.36	159.50	7.5
	135B	200.91	−6.52	−6.30	−12.48	−1.41	167.69	−0.7
$LiCH_2OH$	**134A**	200.93	−18.96	−5.62	−39.59	0.16	117.96	27.7
	134B	200.93	−12.54	−9.22	−24.51	−0.78	141.35	6.3
$LiCH_2Cl$	**144A**	200.94	−21.38	3.42	−40.47	1.07	122.20	46.6
$LiCH_2F$	**131A**	200.95	−35.03	−5.04	−72.70	0.48	53.63	75.7

(Table 14). In contrast, from $LiCH_2NH_2$ **135** via $LiCH_2OH$ **134** and $LiCH_2Cl$ **144** to $LiCH_2F$ **131** the paramagnetic (deshielding) contribution of σ_{C-Li} increases. Since the absolute values of these contributions are the largest, it is the C−Li bond which makes an important contribution to the deshielding of a carbenoid ^{13}C atom. In the tetrahedral isomers **B**, the contribution of the C−Li bond is smaller than in the Li-bridged isomers **A**. This is in agreement with longer (weaker) C−X bonds in the Li^+-bridged isomers **A** than in isomers **B** (see, e.g., Table 3 and Scheme 42), corresponding to a higher energy σ_{C-X} orbital (and a lower energy σ^*_{C-X} orbital) in isomers **A** than in isomers **B**. The energy of the σ^*_{C-X} orbitals are of special significance because they are the partners of the σ_{C-Li} orbitals for the deshielding effect (see below).

The contributions of the σ_{C-H} orbitals to the deshielding increase similarly in the series CH_3Li **2** < $LiCH_2SH$ **136** < $LiCH_2NH_2$ **135** < $LiCH_2OH$ **134** < $LiCH_2Cl$ **144** < $LiCH_2F$ **131**, which indicates, as in the case of the C−Li bond, an interaction of σ_{C-H} with the σ^*_{C-X} orbital of the respective compound.

The importance of the σ^*_{C-X} orbital is evident from a calculation of the anisotropic contributions to the chemical shift in a carbenoid. In Scheme 51 are shown the axes of the anisotropic chemical shifts and their values in the case of $LiCH_2F$ **131A**. Negative values of σ correspond to paramagnetic, deshielding contributions. The axes are numbered according to increasing paramagnetic contributions.

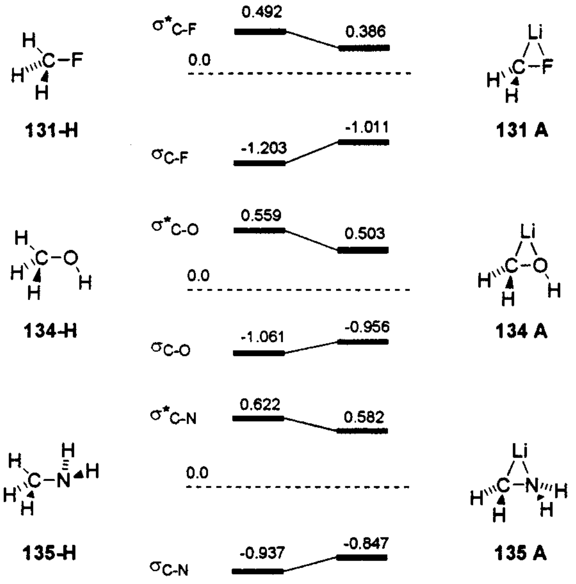
Scheme 51. Axes of the Anisotropic Chemical Shifts σ and Their Values [ppm] in $LiCH_2F$



The strong paramagnetic contribution, σ_{33} −109.1 ppm, is oriented perpendicular to the plane of the atoms C, F, and Li. The σ_{33} value thus results from an interaction in the C, F, Li-plane of the σ_{C-Li} orbital with the σ^*_{C-F} orbital. The high energy σ_{C-Li} orbital and the low energy σ^*_{C-X} orbital thus determine to a large extent the deshielding of a carbenoid carbon atom in a compound of the type $LiCH_2X$ (and in other carbenoids).

1.4.2.3.2. The Energies of σ_{C-X} and σ^*_{C-X} Orbitals in Various Compounds $LiCH_2X$ and Their Significance for the Carbenoid Character. In section 1.4.2.3.1, it became evident that the energy of the σ^*_{C-X} orbital is of major importance for the deshielding of the ^{13}C atom of a carbenoid. A low lying σ^*_{C-X} orbital would also agree with the facile S_N2-type substitutions induced by nucleophiles at the carbenoid carbon atom as described in detail in the Introduction. Thus the question arises whether in carbenoids the energies of the σ_{C-X} orbitals indeed are raised, and those of the σ^*_{C-X} orbitals simultaneously lowered, if compared with the nonlithiated compounds. We have analyzed the energies of the respective σ_{C-X} and σ^*_{C-X} orbitals by means of the natural bond analysis (NBO)[126] in various compounds; see Scheme 52.[92]

Scheme 52. HF/6-311++G(d,p) Energies [au] of σ_{C-X} and σ^*_{C-X} Orbitals



It is immediately evident from Scheme 52 that lithiation leads to higher energy σ_{C-X} and lower energy σ^*_{C-X} orbitals. The strongest effect is observed in the case of the Li/F carbenoid **131A**, and the weakest with X = NH_2 (**135-H** and **135A**): σ_{C-F} is destabilized by 0.192 au, and σ^*_{C-F} is lowered by 0.106 au, while it is 0.090 au (σ_{C-N}) and 0.040 au (σ^*_{C-N}) in the Li/NH_2 species. The energies of the σ^*_{C-X} orbitals are also in agreement with the electrophilicities of the corresponding species: σ^*_{C-F} 0.386 au, σ^*_{C-O} 0.503 au, σ^*_{C-N} 0.582 au. As pointed out earlier, and in agreement with a high-energy

σ^*_{C-N} orbital, compounds of the type $LiCR^1R^2NR_2$ do not react with nucleophiles. The σ^*_{C-X} orbital energies, furthermore, are in good agreement with the significance of these orbitals in determining the amount of deshielding of the carbenoid ^{13}C atom; see section 1.4.2.3.1. In conclusion, the NBO analysis of the orbital energies of the σ_{C-X} and σ^*_{C-X} orbitals of $LiCH_2X$ compounds supports (the amount of) the carbenoid character as shown in reactions with nucleophiles and by the ^{13}C NMR spectra.

1.4.3. Crystal Structures of Carbenoids

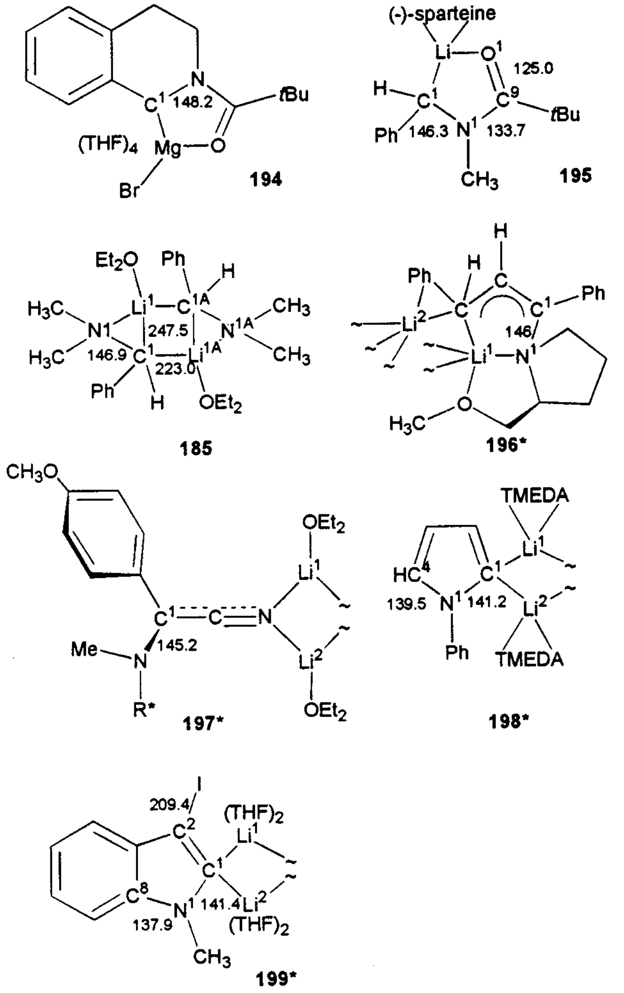
1.4.3.1. The Li/NR$_2$ Case. Besides the electrophilic nature as observed in reactions with nucleophiles (see the Introduction 1.1 and section 1.2) and the deshielding of the ^{13}C atom in the NMR spectrum (see section 1.4.2), the C−X bond length in the solid state structures of compounds of the type $Li(MgX)\,CR^1R^2X$ ($X = Hal, OR, NR_2, SR$) should correlate with their carbenoid character (see section 1.4.1). It was shown in Scheme 35 that α-lithiated thioethers $LiCR^1R^2(SR)$ have *shortened* C−S bonds, which perfectly agrees with their noncarbenoid nature: they do not react with nucleophiles, and the ^{13}C atom is rather shielded than deshielded.

How is the situation of α-lithiated amines, which also do not react with nucleophiles but show a weak deshielding of the ^{13}C atom (see Tables 13 and 14)? The significant parts of the solid state structures of α-lithiathed amines are shown in Scheme 53 together with the pertinent bond lengths.

The first solid state structure of an α-metalated amine has been reported by Seebach et al., namely that of **194**.[128] The bond of interest, C1−N, is 148.2(13) pm long. In a nonmetalated compound with an sp^3-hybridized carbon atom used for comparison, the corresponding C−N bond measures 147.2(4) pm. The almost negligible elongation of C1−N in **194**, however, needs to be related to the hybridization of the anionic C1 atom in this species, which unfortunately is unknown because the position of the H atom at C1 could not be determined. Any hybridization of the anionic C1 atom with an s-character higher than sp^3 corresponds to a more pronounced lengthening of C1−N in **194** than indicated by the bond length given above: the mean bond length of C_{sp^2}-NMe_2 in enamines is 140.0 pm.[129] The five-membered ring chelation in **194** agrees well with the chelation in related α-lithiated oxygen compounds (see section 1.4.3.2, Table 14, compound **187**, and compound **200** in Scheme 55) and with that of **195** (Scheme 53).

(*S*)-α-(Methylpivaloylamino)-benzyllithium-(−)-sparteine **195** shows the characteristics of a dipole-stabilized, chelated lithiated amine (slight shortening of N1−C9 from 135.3 to 133.7 pm, and slight lengthening of C9−O1 from 123.4 to 125.0 pm as compared to the nonlithiated species).[130] The sum of the bond angles at the benzyl-anion-type C1 atom adds up to 341° (sp^3: 328.5°; sp^2: 360°), which is indicative of pyramidalization. In comparison with the calculated bond length in a neutral species with the same hybridization at C1, the C1−N1 bond (146.3 pm) in **195** is marginally elongated. In CH_3-NH_2, the C−N bond is 146.5 pm long.[131]

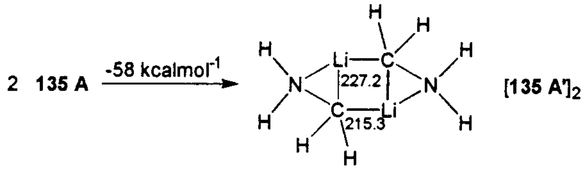
Scheme 53. Crystal Structures of α-Lithiated "Amines": Essential Features; Bond Lengths [pm][a]



[a] The asterisk (*) indicates that only part of the dimer structure is shown.

In the crystal structure of [α-(dimethylamino)-benzyllithium·diethyl ether]$_2$ **185**, the anionic carbon C1 and N1 are bridged by Li1, and a dimer is formed along the C−Li bonds. A molecule of diethyl ether occupies the fourth coordination site at Li1. The distance of C1 to the bridging Li (247.5 pm) is longer than C1−Li1A (223.0 pm). This result corresponds to the calculated unsolvated model [**135A′**]$_2$, Scheme 54[130] (see also section 1.4.1.2 on aggregation and solvation of carbenoids).

Scheme 54. MP2/6-31G(d)//3-21G Calculated Dimerization of 135A To Give [135A′]$_2$; Bond Lengths [pm]



In **185**, the benzylic carbon atom C1 is also pyramidalized: the sum of the bond angles at C1 amounts to 341°. The C1−N1 bond (146.9 pm) corresponds exactly to the mean value of C−N bonds in C_{sp^3}-hybridized Ph-CH(R)-NMe_2 compounds (146.8 ppm).[132]

An estimation of the C−N bond length in a neutral compound with the carbon atom having the same hybridization as in **185** leads to the conclusion that C1−N1 in **185** is slightly elongated (∼3 pm). Marginally longer C1−N1 bond lengths are also found in (3*S*)-3-lithio-1-[(*S*)-2-(methoxymethyl)pyrrolidino]-1,3-diphenylpropene **196**[133] and (4*S*,5*S*)-*N*-lithio-[*N*′-(2,2-dimethyl-4-phenyl-[1,3]dioxan-5-yl)-*N*′-methylamino]-4-methoxyphenylketene imine **197**[134]—146 and 145.2 pm, respectively. Because of the planarity of the anionic C1 atoms in **196** and **197**, one has to compare the C1−N1 bond lengths in these compounds with the earlier mentioned C−N bond length in enamines (140.0 pm).

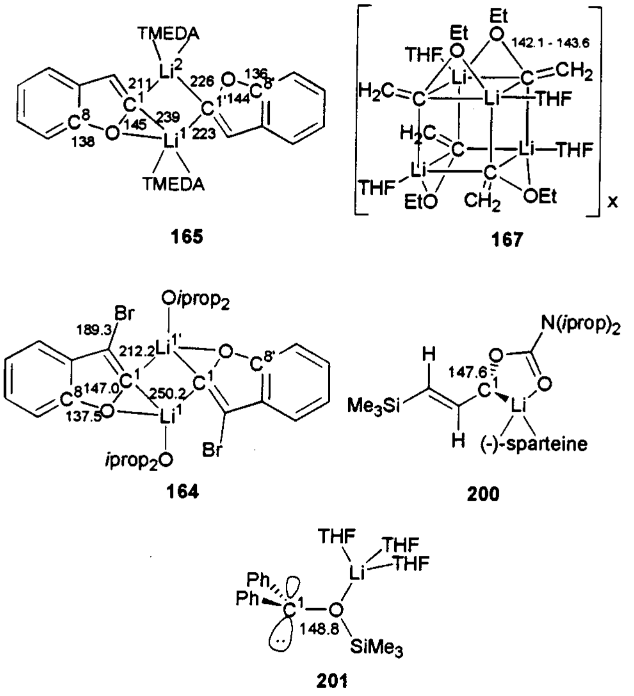
The crystal structure of the dimeric [2-lithio-1-phenyl-pyrrole·TMEDA]$_2$ **198**[135] offers the advantage of an intramolecular comparison of the C−N bond lengths: C1−N1 is slightly longer (141.2 pm) than C4−N1 (139.5 pm), a result which is perfectly in line with the situation in the other α-lithiated amines.

Not unexpectedly, the solid state structure of [3-iodo-2-lithio-1-methylindole·2THF]$_2$ **199** agrees with these results.[130] It is remarkable that Li does not bridge the C1−N1 bond, as this is also not the case in **198**. On the other hand, such a bridging is observed in **185** (the intramolecular chelation in **194**, **195**, and **196** is more favorable than a Li−C−N-bridging as in **185**; the same holds for the coordination of Li at the N-atoms of the cyano groups in **197**, which also prevents a Li−C−N bridge). Undoubtedly, the difference between the Li-bridged **185**, and **198** as well as **199**, is strongly influenced by the different donor qualities of the solvent (complexing) molecules in the two different cases: in **185**, diethyl ether cannot compete successfully with the Li−C−N bridge, while this is the case with TMEDA and THF, respectively, in **198** and **199**. These solid state structures thus nicely demonstrate how the most favorable bridged isomer **135A** of LiCH$_2$NH$_2$ (and of others of that structural type) are transformed by "solvent" molecules into the tetrahedral isomer **B** with less carbenoid character. These findings perfectly agree with the results of the calculations outlined in section 1.4.1.2.

The C1−N1 bond length in **199** (141.4 pm) is slightly longer than the mean value of the corresponding bond in indoles (139.0 pm).[132] C8−N1 is slightly shorter (137.9 pm). Finally it should be mentioned that **199** contains an iodine atom at C2 in *β*-position to the Li atom at C1, which normally leads to fast elimination of LiI. In the case of five-membered rings as in **199**, however, elimination does not occur because of the strain which would be induced in the five-membered ring by the triple bond formed.[130,136] The stability toward elimination is corroborated by the bond length C2−I (209.4 pm) which corresponds almost exactly to the mean value of C$_{sp^2}$−I bonds (209.5 pm).[132] A similar situation holds for the C−Br bond length in **164**; see section 1.4.3.2, Scheme 55.

In summary, the C1−N1 bond lengths in α-lithiated amines are slightly (2−5 pm) elongated if compared to appropriate nonlithiated reference compounds. A related elongation was predicted in model calculations of LiCH$_2$NH$_2$ **135**; see Scheme 33 and Table 3. The model structure **135A**, respectively its "Li−C"-dimer [**135A′**]$_2$, as well as the tetrahedral **135B**, are verified in the solid state structures. The modest bond elongation of the C−N bonds is in agreement with the NMR investigations of compounds of the type LiCR^{1}R^2(NR$_2$) which show only small deshielding of the anionic ^{13}C atom. Since reactions of LiCR^{1}R^2(NR$_2$) with nucleophiles, as, e.g., Nu$^-$Li$^+$, to give LiCR^{1}R^{2}Nu + LiNR$_2$, are not known to date—in contrast to Li/Hal and Li/OR carbenoids—α-lithiated amines are not carbenoids. They behave like normal "carbanions".

Scheme 55. Crystal Structures of Li/OR Carbenoids: Essential Features; Bond Lengths [pm]



1.4.3.2. Li/OR Carbenoids.

As outlined in the Introduction, Li/OR carbenoids behave as electrophiles in the presence of strong nucleophiles as, e.g., organolithium compounds. Furthermore, model calculations with LiCH$_2$OH **134** show significant elongation of the C−O bond especially in the Li-bridged isomer **134A**, but also in **134B**; see section 1.4.1.1.4. In addition, ^{13}C NMR investigations of α-lithiated ethers reveal a strong deshielding of the anionic ^{13}C atom, which altogether characterizes these compounds as carbenoids (see section 1.4.2). Solid state structure investigations agree fully with this characterization. Scheme 55 summarizes the solid state structures of α-lithiated ethers together with the pertinent bond lengths.

The first solid state structure of an α-lithiated ether was published by Harder, Brandsma, Schleyer, Thewalt et al.,[95] although the Li/OR carbenoid character in the structure of 2-lithiobenzofuran **165** was not discussed. It is quite clear from Scheme 55, that the C1−O and C1′−O bonds (145 and 144 pm, respectively) are elongated with respect to the C8−O and C8′−O bonds (138 and 136 pm, respectively). A related structure, namely that of 2-lithio-3-bromobenzofuran **164**, shows similar features.[55,81,82,137] The carbenoid bond C1−O measures 147.0 pm, while the “normal” C8−O bond amounts only to 137.5 pm. Some other aspects of **164** and **165** are of interest. In the diisopropyl ether complexed **164**, *both* carbenoid C−O bonds are bridged by lithium; while in the TMEDA-complexed **165**, *one* C−O bond is Li-bridged. The Li^+-bridging is remarkable in that case because Li(1) adopts a pentacoordinate structure, although lithium is normally tetracoordinated. Furthermore, a dimer across the *C−Li* bonds is formed in both cases, which perfectly agrees with the theoretical model (see section 1.4.1.2 on aggregation and solvation of carbenoids). The different bond lengths of C1−Li1 (250.2 pm) and C1−Li1′ (212.2 pm) also support the theoretical model [**134A′**]$_2$. In addition it is interesting to compare the two lithiated benzofurans **164** and **165** with the lithiated benzoindole **199** (Scheme 53). First, the two C−N bond lengths in **199** differ less than the corresponding C−O bond lengths in **164** and **165**, in agreement with the carbenoid nature of the latter two compounds. Second, in the lithiated indole **199** (as in **198**), Scheme 53, no Li-bridging of the C−N bond is observed. The electron pair at the N atom in such compounds indeed should not have very good donor qualities, while the O atom in lithiated benzofurans has a second electron pair for complexation with lithium. In **164** a bromo atom is in the position β to lithium, a situation corresponding to that in **199**, Scheme 53. LiBr-elimination in **164** is excluded for the same reasons as outlined for LiI-elimination from **199**. Correspondingly the C−Br bond is as long (189.3) as the one in bromoarenes (189.7 pm).[132]

α-Ethoxyvinyllithium **167** crystallizes in tetramer units as a polymer complexed with THF; see Scheme 55.[97] Most significantly the C1−O bonds (142.1−143.6 pm, mean value 142.8 pm) are remarkably elongated as compared to those in vinyl ethers (∼136 pm).[138] Furthermore, all carbenoid C−O bonds are bridged by lithium. Not unexpectedly, the carbenoid nature of **167** is also documented by the ^{13}C NMR spectrum of the carbenoid carbon atom: $\Delta\delta = 60.7$ ppm, as compared to $\Delta\delta = 54.4$ ppm of the tetrameric vinyllithium.[97]

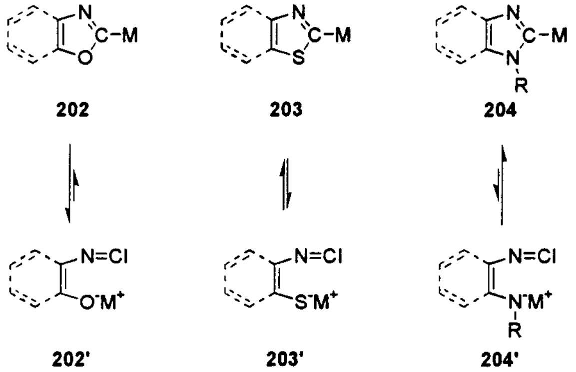
The general features of the crystal structure of the sparteine-complexed carbamoyloxy-3-trimethylsilylallyllithium (−)-sparteine **200**[123] (Scheme 55) correspond closely to those of **194** and **195** (Scheme 53). Lithium in **200** is not bridging the C1−O bond because a more favorable dipole-stabilized five-membered ring chelate is formed which overcomes the energy diffence between the most stable calculated Li-bridged isomer **134A** and the tetrahedral **134B** (13.6 kcal mol^{-1}; see section 1.4.1.1.4). Once again, C1−O is elongated (147.6 pm); for comparison, the mean value of 11 C_{sp^3} (6 C_{sp^2})−OCb bonds is 143.6 (139.9) pm.[132]

Diphenyl(trimethylsilyloxy)methyllithium·3THF **201** (Scheme 55) fulfils the structural requirements corresponding to the theoretical model **134C** (see section 1.4.1.1.4): it is of the carbene-donor complex type H_2C-XLi.[81] The stabilization of the negative charge at the anionic C1 atom by delocalization into the two phenyl rings is the prerequisite for the removal of lithium from this carbon atom (Li−C1 280.7 pm). It is noteworthy that the two phenyl rings at C1 are slightly bent toward lithium, exactly as predicted by the model **134C**. The C1−O bond is strongly elongated to 148.8 pm. The mean (maximum) value for the C−O bond in 135 C_{sp3}−$OSiMe_3$ groups amounts to 140.2 (146.1) pm; in 24 C_{sp2}−$OSiMe_3$ cases the values are 137.5 (142.8) pm. Since the hybridization at C1 is much closer to sp^2 than to sp^3, the elongation of C1−O in **201** roughly amounts to 10 pm.

With regard to the structure of **201**, it is interesting to mention that Paulino and Squires investigated the anion F_2C-Cl^- in the gas phase.[139] The C−Cl bond is very weak and, according to calculations, very long. Thus, this compound is called a carbene-anion complex. Quite similarly **201** can be understood as a carbene-$[OSiMe_3]^-$ complex (with $Li^+\cdot$3THF attached to the oxygen atom).

It is also interesting to mention briefly the tendency for α-elimination in the case of 2-metalated (benz)oxazoles **202** and the related (benzo)thiazoles **203** and (benz)imidazoles **204**. The situation of the 2-lithiated species is summarized in Scheme 56.[140,141]

Scheme 56. Tendency for α-Elimination of 2-Metallated (Benz)oxazoles 202, (Benz)thiazoles 203, and (Benz)imidazoles (204); M = Li

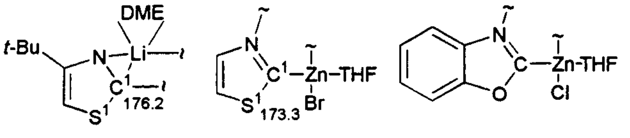


Compounds **202**, **203**, and **204** can be regarded as carbenoids which on α-elimination lead to the isomers **202′**, **203′**, and **204′**, respectively. The isocyanide which is formed in each case is, at least formally, a very stable carbene. Most importantly, the tendency toward α-elimination corresponds in the cases of **202** and **204**, respectively, perfectly to the carbenoid character of Li/OR carbenoids as desribed in this section and to the behavior of Li/NR_2 compounds as detailed in section 1.4.3.1. Thus, a ring opening starting from **204** to give **204′** with nitrogen being the leaving group was never observed. On the other hand, 2-lithiated (benz)oxazoles **202** rearrange even at low temperatures (−78 °C) very fast to the ring-opened isomers **202′**. 2-Lithiated (benzo)thiazoles **203** are in equilibrium with their ring-opened isomers **203′**, with the equilibrium depending on the detailed structure of these compounds.

In the crystal structure of 2-*lithiated* 4-*tert*-butylthiazole **205**, C1−S1 is 176.2 pm long;[140] see Scheme 57.

The crystal structure of *2-ZnBr*-thiazole **206** (Scheme 57) shows a shorter C1−S1 bond (173.3

Scheme 57. Crystal Structures of 2-Lithium- (205) and 2-ZnBr-thiazole 206 and 2-ZnCl-benzoxazole 207: Essential Features; Bond Lengths [pm][a]



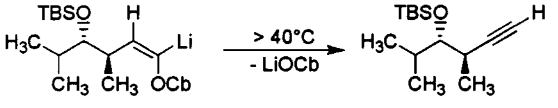
205* **206*** **207***

[a] The asterisk (*) indicates that only part of the dimer is shown.

pm)[140] which is in agreement with the less pronounced carbenoid character of Zn-carbenoids as compared to Li-carbenoids.[108] This is also the reason why it is possible to crystallize *2-ZnCl*-benzoxazole **207** (Scheme 57).[108] Due to the higher p-character of the C−Zn bond ($sp^{1.9}$) in such compounds, the C−O bond has a comparatively large s-character ($sp^{2.5}$), as shown by model calculations. In contrast, in 2-lithiated oxazoles C−Li has $sp^{1.0}$- and C−O $sp^{3.6}$-hybridization, which is in line with the facile C−O bond cleavage of 2-Li-oxazoles.

In conclusion, the solid state structures of α-lithiated ethers and related compounds are fully in agreement with the carbenoid character of these compounds, as also documented by ^{13}C NMR investigations, theoretical studies, and reactions with nucleophiles. The Fritsch−Buttenberg−Wiechell rearrangement **208** → **209** is a final documentation of the carbenoid reactivity of such species;[54b] see Scheme 58.

Scheme 58. Fritsch−Buttenberg−Wiechell Rearrangement of the Vinylic α-Lithiated 208



208 **209**

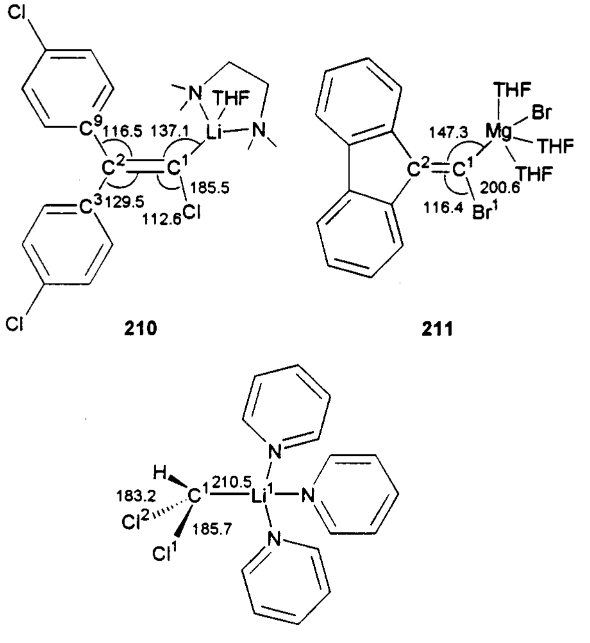
$$\mathrm{Cb} = \overset{\mathrm{O}}{\overset{\|}{\mathrm{C}}}\mathrm{-N}(i\mathrm{prop})_2$$

1.4.3.3. Li/Hal Carbenoids. It was not before 1993 that the first crystal structure of a Li/Hal carbenoid was obtained by Boche, Marsch, Müller, and Harms, namely that of 1-chloro-2,2-bis(4-chlorophenyl)-1-lithioethene·TMEDA·2THF **210**,[142] Scheme 59.

In accordance with the characteristics of a carbenoid, the C1−Cl bond is strongly elongated (12.6 pm) from 172.9 pm (mean value of 63 vinylic $C_{sp}2$−Cl bonds)[132] to 185.5 pm in **210**. Because of the excellent solvation of Li by TMEDA and THF, Li is not bridging C1−Cl (Li−Cl 325.4 pm). Model calculations led to the result that a Li-bridged C−Cl bond should be even longer (Tables 3 and 7). The elongated C1−Cl bond in **210** is in agreement with the stereoselective substitution of the alkylidene carbenoid **67** by hydride (Scheme 14), of **78** by bromide (Scheme 16), and of vinylic Li/Cl and Li/Br carbenoids by ^{t}BuLi as outlined in Scheme 19.

The bond angles at C1 and C2 reveal further interesting structural features of an alkylidene carbenoid. At C1, the angle Cl−C1−C2 amounts to 112.6° which is smaller than the 120° angle at an sp^2-hybridized carbon atom. On the other hand, Li−C1−C2 (137.1°) is much larger. This situation indicates the reaction path of the α-elimination to give the corresponding vinylidene: the C1−Cl bond develops into the empty p-orbital, while the C1−Li orbital becomes the filled sp-orbital.

Scheme 59. Crystal Structures of the Li/Cl Carbenoids 210 and 212 and the MgBr/Br Carbenoid 211: Essential Features; Bond Lengths [pm]; Bond Angles [deg]



210 **211** **212**

Furthermore, together with the bond angles at C1 those at C2 are in excellent agreement with the beginning of a Fritsch−Buttenberg−Wiechell rearrangement. As shown in Scheme 2, it is always the aryl group trans to the leaving group X which migrates. In the case of **210** it should be C9 that moves to C1. Indeed, the angle C1−C2−C9 (116.5°) is clearly smaller than C1−C2−C3 (129.5°). The latter angle indicates that in the course of such a rearrangement C3 moves toward the axis C1−C2.

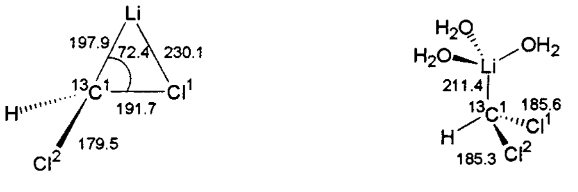
In 9-bromo-9-[(bromomagnesium)methylene]fluorene·4THF **211**,[143] one observes a similar situation at C1 as in **210**. The C1−Br1 bond is 10.3 pm longer (200.6 pm) than the mean value of 63 C_{sp2}−Br bonds (190.3 pm).[132] This elongation amounts to 5.4% as compared to 7.3% of the C−Cl bond in the case of **210**, which is in agreement with the tendency as expected from calculations of Li/Cl and Li/Br carbenoids (see Tables 3 and 7). Furthermore, the angle Br1−C1−C2 is smaller (116.4°) and the angle Mg−C1−C2 much larger (147.3°) than the normal 120° angles at sp^2-carbon atoms. The widened angle Mg−C1−C2 leads to a distance Mg−Br1 of 312.9 pm which is close to the van der Waals contact of Mg and Br (301 pm). This scenario supports the beginning of the α-elimination of $MgBr_2$ by means of a metal assisted ionization of the C1−Br1 bond. Correspondingly, C1−Mg (219.0 pm) is longer than in other cases of C_{sp2}−MgBr bonds (mean value of five C_{sp2}−MgBr bonds: 213.4 pm).[132]

The only carbenoid with a tetrahedral carbon atom so far characterized by X-ray crystallography is

$LiCHCl_2$·3pyridine **212**;[124] see Scheme 59. Li1 is bonded to C1(C1−Li1 210.5 pm) and to the N-atoms of three pyridine molecules (Li1−N1(N2)(N3) 207.7 (201.7) (203.3) pm). Of special interest are the C1−Cl1 and C1−Cl2 distances which amount to 185.7 and 183.2 pm. Consequently, these carbenoid C−Cl bonds are ca. 10 pm longer than those in CH_2Cl_2 (174.6 pm). The sum of the bond angles at C1 Cl2−C1−Cl1 (105.3°), Cl1−C1−H1 (96°), and Cl2−C1−H1 (107°) amounts to 308° which is remarkably smaller than the value of a normal tetrahedral carbon atom (328°). Thus, both the smaller sum of these bond angles as well as the elongated C−Cl bonds are in agreement with a higher p-character in the C−H and C−Cl bonds resulting from the higher s-character in the C−Li bond (see Scheme 47).

To obtain information on the significance of the solvation, the structures of $LiCHCl_2$ **106A** and the tris-hydrated **106B**·$3H_2O$ were used as models;[124] see Scheme 60.

Scheme 60. MP2(fc)/6-31G(d) Structure of 106A and 106B·3H$_2$O

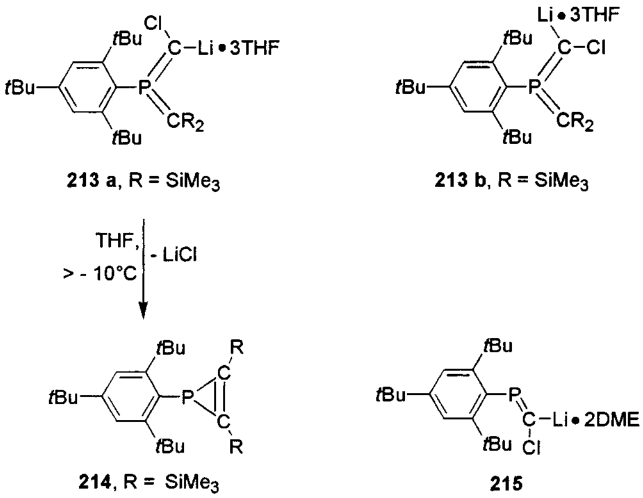


106 A **106 B•3H$_2$O**

In **106A**, the Li-bridged C1−Cl1 bond amounts to 191.7 (+14.8) pm, while C1−Cl2 is only slightly elongated (179.5 (+2.6) pm) if compared to C−Cl in CH_2Cl_2 (176.9 pm, MP2(fc)/6-31G(d) calculation). Poor solvation of Li^+ by solvent molecules promotes bridging of the C−Cl bond by Li^+ which leads to high reactivity of the bridged C−Cl bond. This agrees with experimental observations according to which carbenoids are “less stable” in *diethyl ether* than in the better solvating *THF*, as mentioned earlier. Therefore, the tris-solvated **106B**·$3H_2O$ is a better model for the latter case and for the solid state structure **212**: due to the solvent molecules there is no contact between Li^+ and a Cl atom, and the C−Cl bonds are shorter (185.3 and 185.6 pm) than C1−Cl1 in **106A**. Most importantly, these calculated bond lengths agree nicely with the experimentally observed ones: 183.2 and 185.7 pm. The significance of the models **106A** and **106B**·$3H_2O$ for IGLO calculations and the structure of **106** in solution was pointed out in section 1.4.2.2 and Table 14.

A special kind of a carbenoid was recently described by Niecke et al., namely the methylene-phosphoranylidene carbenoid **213**;[144] see Scheme 61.

Scheme 61. Phosphavinylidine Carbenoids



213 a, R = SiMe$_3$ **213 b**, R = SiMe$_3$ **214**, R = SiMe$_3$ **215**

Depending on the preparation, either a 1:6 mixture of **213a**:**213b** or **213a** alone is received. A crystal structure determination of **213a** reveals the following data: the angle P−C−Li is strongly widened to 155.7°, the angle P−C−Cl is narrowed to 109.4°, and the C−Cl bond is lengthened from 171.2 pm in the protonated species to 181.6 pm in **213a**. Model calculations are in agreement with these structural features. Qualitatively, the situation in **213a** thus corresponds to that of the carbenoids **210** and **211**. Warming of **213a** in THF above −10 °C results in the formation of **214** and LiCl.

Niecke et al. investigated also the “phosphavinylidene carbenoid” **215**.[145] Remarkably, in **215** the angle P−C−Li amounts only to 122.4°, while it is 120.5° for P−C−Cl. Similarly C−Cl is (only) 177.8 pm long, a value which compares well with that of a species in which Li is replaced by PCl_2. From the structural features of **215**, the carbenoid character is therefore not evident. Calculations of the model compounds *E*/*Z* H_3C-P=C(Cl)Li·2DME, *E*/*Z* H_3C-P=C(Cl)$^-$, and *E*/*Z* H_3C-P=C(Cl)H reveal much smaller P−C−Cl angles in the Li compounds and the anions (108.4 to 117.2°) than in the protonated species (122.9 and 130.7°). Similarly, the C−Cl bonds in the Li compounds and the anions (186.1 to 191.5 pm) are clearly longer than in the protonated species (174.6 and 175.0 pm). The discrepancies between experiment and theory have to be worked out.

1.5. Carbenoids: Conclusions

The strong electrophilic nature of Li/OR and Li/Hal carbenoids as observed in reactions with all sorts of nucleophiles is now well understood by a combination of theoretical studies with NMR and crystal structure investigations. The high s-character of the C−M bond causes a higher p-character of the C−X bond which corresponds to a σ_{C-X} orbital of higher energy and a σ^*_{C-X} orbital of lower energy. Solid state structures reveal the longer C−X bonds. The elongated carbenoid C−X bond is in agreement with facile reactions of carbenoids, even having vinylic C−X bonds, with nucleophiles. IGLO calculations lead to an understanding of the deshielding of the carbenoid ^{13}C atom, which is strongly related to the situation of the σ_{C-M} and the σ^*_{C-X} orbitals. In contrast, compounds of the Li/NR_2 and Li/SR type cannot be regarded as carbenoids.

2. Nitrenoids

2.1. Introduction

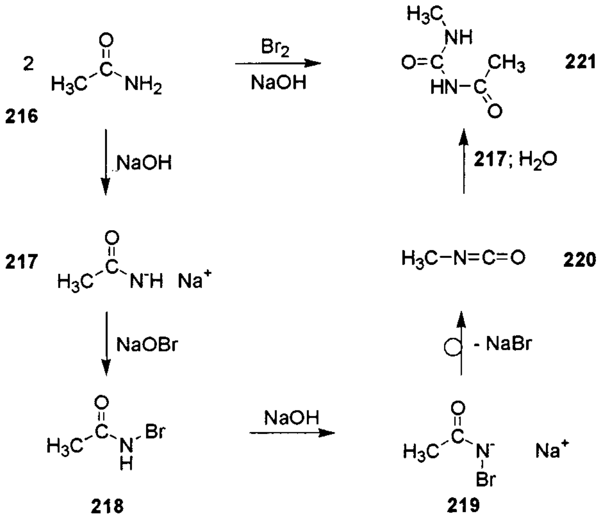
Nitrenoids **24** have a long history in organic chemistry although their nitrenoid properties have been recognized only in recent years.

24

M = Li, Na, K, MgX, ZnX etc.
X = Hal, OR and other leaving groups
R = alkyl, aryl and other substituents

In 1881, A. W. Hofmann reported “Über die Einwirkung des Broms in alkalischer Lösung auf Amide” (“On the reaction of bromine in alkaline solution with amides”) and discoverd the well-known rearrangement **216** → **221**; see Scheme 62.[146]

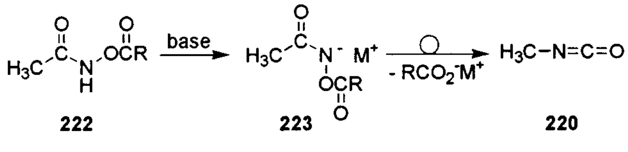
Scheme 62. Hofmann Rearrangement



Reaction of the acetic acid amide **216** (and of others) with bromine occurs only in the presence of sodium hydroxide and leads to the urea derivative **221**. Undoubtedly, **216** is first deprotonated to give **217**. Bromination with NaOBr, formed from Br_2 and NaOH, gives the even more acidic N-bromoamide **218** which is deprotonated with NaOH to the nitrenoid **219**. Compound **219**, however, is not isolated under the reaction conditions. It rather undergoes a 1,2-migration of the methyl group to the nitrenoid nitrogen atom with elimination of NaBr leading to the isocyanate **220**. Addition of the nucleophile **217** to **220** and protonation gives the isolated product **221**. Although it seems clear from the literature[147] that it is not the nitrene,[148] formed by α-elimination of NaBr from **219**, which undergoes the rearrangement, the evidence is also not conclusive for rearrangement concerted with loss of the N-attached leaving group (Br^-Na^+ in the case of **219**).

The related Lossen rearrangement of O-acylated hydroxylamine derivatives of the type **222**, which on treatment with base also give isocyanates such as **220** (and their follow-up products) via nitrenoids of the type **223**, was discovered already in 1872 (Scheme 63).[149]

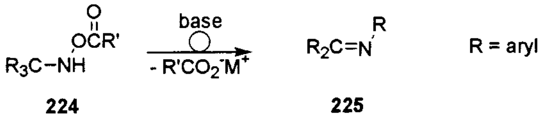
Scheme 63. Lossen Rearrangement



Again, the concerted rearrangement of the methyl group and loss of RCO_2-M^+ was not shown definitively.[147]

In the Stieglitz rearrangment[150] **224** → **225** the leaving group at nitrogen is the same as in the Lossen rearrangment; see Scheme 64.

Scheme 64. Stieglitz Rearrangement



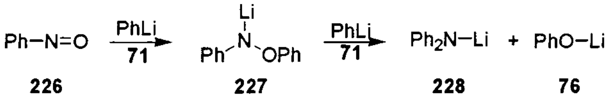
The mechanism of this rearrangement—nitrene or nitrenoid—is likewise not clear.[147] This situation marks the difference between nitrenoid and carbenoid rearrangements: in the latter case the carbene or carbenoid nature, respectively, was shown quite clearly in many cases; see sections 1.1. to 1.3. Reactions other than rearrangements of nitrenoids are shown in the following.

2.2. Amination Reactions of (Anionic) Nucleophiles with Nitrenoids

In this section we will concentrate on reactions which are likely to occur through a nitrenoid although this is not definitively proven in most of the cases.

The term “nitrenoid” was coined by Köbrich in 1967[151] when he studied reactions of phenyllithium **71** with nitrosobenzene **226**; see Scheme 65.

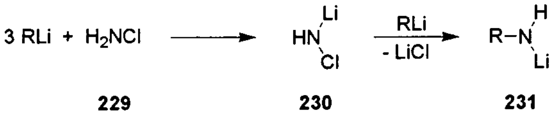
Scheme 65. Reaction of Phenyllithium with Nitrosobenzene via a Nitrenoid (227)



On protonation, diphenylamine and phenol are formed, which are due to the lithiated precursors **228** and **76**. Most likely, **228** and **76** result from the reaction of the nucleophile phenyllithium **71** with the electrophilic **227**, which thus should be called a nitrenoid. The sequence is analogous to the reaction of the carbenoid **73** with phenyllithium **71** to give diphenylmethyllithium **75** and phenolate **76** as outlined in Scheme 15.

“Electrophilic aminations of carbanions”[152] of the type **227** + **71** → **228** (Scheme 65) are well-known reactions. Coleman and co-workers first studied the reactions of N-haloamines with Grignard[153] and then with organolithium reagents.[154] Most significantly, in the reactions with the latter, 3 equiv of RLi led to the highest yields of amines in the reactions with N-chloroamine **229**; see Scheme 66.

Scheme 66. Amination of RLi with *N*-Chloroamine 229

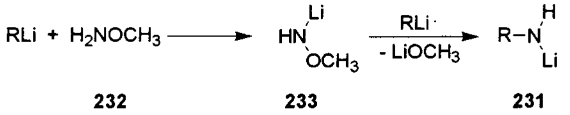


This strongly suggests that H_2NCl **229** is first deprotonated by RLi to give the nitrenoid **230** which then reacts with a second equivalent of RLi to give **231**, and on protonation the corresponding amine.

This sequence is of synthetic significance because it allows the formation of a C—N bond with a nucleophilic carbon atom.

The related amination of "carbanions" RLi (and of others) with *O*-methylhydroxylamine **232** is known as the Schewerdina—Kotscheschkow amination reaction;[155,152] see Scheme 67.

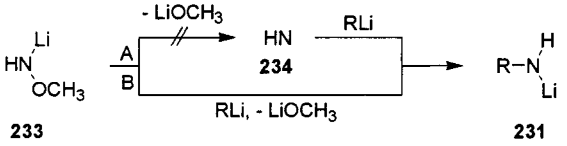
Scheme 67. Amination of RLi with *O*-Methylhydroxylamine 232



As in the case of *N*-chloroamine **229** (Scheme 66), deprotonation takes place first to give the nitrenoid **233**, which then reacts with a second RLi to give the N-lithiated amine **231**. Compound **231** is protonated to form the respective amine. To overcome the problem of using (at least) 2 equiv of the organometallic reagent (e.g., RLi), it was suggested to use an expendable RLi in the deprotonation step **232** → **233** and only then employ the lithium reagent to be aminated (**233** → **231**).[156]

The mechanism of the electrophilic amination of "carbanions" with *O*-alkylhydroxylamines was studied experimentally by Beak et al.[157] There are two possible pathways. (1) The nitrenoid **233** could undergo an α-elimination of $LiOCH_3$ to give the nitrene **234** which then adds RLi to produce **231** (pathway A in Scheme 68). (2) In pathway B a nucleophilic substitution reaction takes place at the nitrenoid nitrogen atom of **233** to give **231** directly. The authors[157] demonstrated conclusively that it is pathway B which takes place. As in the case of the carbenoids in which the α-elimination to give carbenes occurs only under special conditions (see sections 1.1 to 1.3), the formation of nitrenes from nitrenoids is also not a very favorable reaction. This is an especially unlikely pathway with the poor leaving group $CH_3O^-Li^+$ at the nitrogen atom of **233**. In contrast, with better leaving groups such as RSO_3—Li^+, the formation of the nitrene from the corresponding nitrenoid is a very fast reaction; see section 2.3, **272** → **267**. The S_N2-type substitution reaction as shown in pathway B of Scheme 68 is further supported by theoretical calculations; see section 2.4.

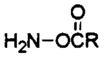
Scheme 68. Electrophilic Amination with Nitrenoids: Mechanistic Alternatives



Amination reactions of organolithium compounds were also performed with *O*-arylhydroxylamines (e.g., **235**),[158] *O*-acylhydroxylamines (e.g., **236**),[158] *O*-sulfonyl-hydroxyl-amines (e.g., **237**),[159] and *O*-phosphinylhydroxylamines (e.g., **238**).[160]

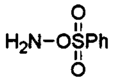
$H_2N\text{-}OPh$

235



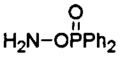
$H_2N\text{-}O\overset{O}{\overset{\|}{C}}R$

236



$H_2N\text{-}O\overset{O}{\overset{\|}{\underset{\underset{O}{\|}}{S}}}Ph$

237



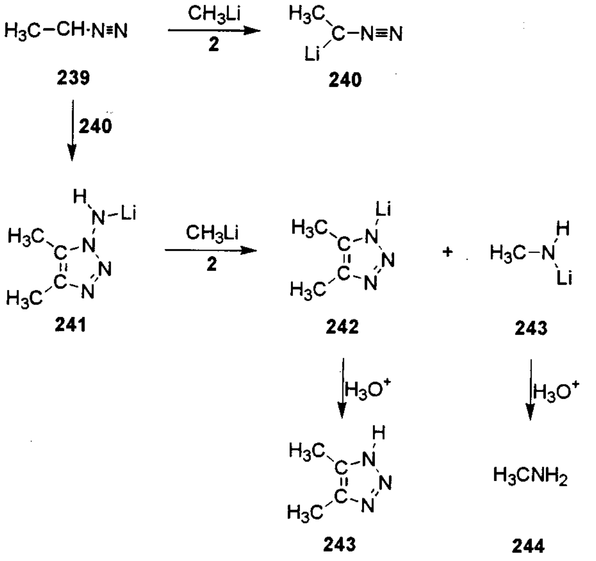
$H_2N\text{-}O\overset{O}{\overset{\|}{P}}Ph_2$

238

It was, however, not investigated whether the aminations occurred (1) via direct reaction of RLi with **235**—**238**, (2) through a nitrene intermediate (see Scheme 68, pathway A) or (3) via the corresponding nitrenoid (see reaction B, Scheme 68), although the latter seems plausible.

The latter pathway is also suggested for a reaction which at first sight seems rather puzzling. In a series of papers E. Müller et al. investigated the reactions of diazomethane CH_2N_2 and monosubstituted diazomethanes as, e.g., methyl-diazomethane CH_3-CHN_2 **239** with organolithium compounds such as methyllithium **2**. In the latter reaction, 4,5-dimethyl-1,2,3-triazole **243** and methylamine **244** are formed on protonation; see Scheme 69.[161]

Scheme 69. Reaction of Monosubstituted Diazomethanes (239) with CH_3Li 2

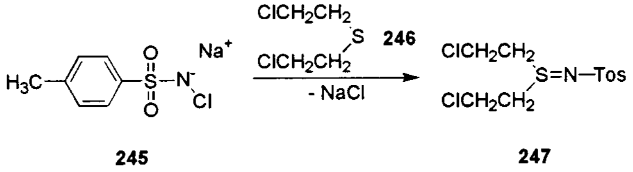


Structural and quantum chemical investigations by Boche et al.[162] led to the conclusion that the first formed lithiated methyldiazomethane **240** undergoes a cycloaddition with **239** to give **241** which is a nitrenoid. Therefore it reacts with CH_3Li **2** to give the lithiated triazole **242** and lithiated methylamine **243** which on protonation lead to the isolated products **243** and **244**. Undoubtedly, the lithiated triazole **242** is a comparatively good leaving group.

Chloramine T **245** and related *N*-halogeno-*N*-metallo reagents[163] are a well-known class of nitrenoids which—among other reactions—undergo electrophilic aminations of nucleophiles such as sulfides, selenides, sulfoxides, or sulfimides. Interestingly, the reaction with sulfides was discovered during World War I when mustard gas **246** was destroyed with **245** to give the sulfimide **247**; see Scheme 70.[164]

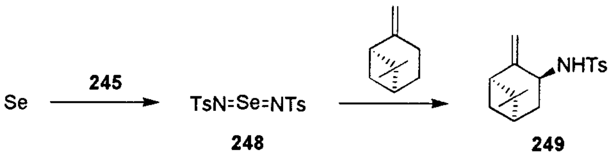
The reactions with the other nucleophiles mentioned above occur analogously.[163] Their use in electrophilic amination reactions, however, is limited because chloramine T **245**-type species act also as a

Scheme 70. Reaction of Chloramine T with an S-nucleophile



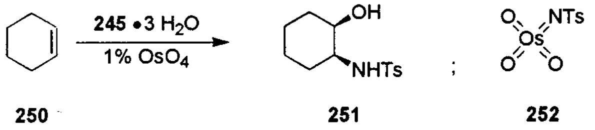
source of halonium cations and nitrogen anions.[163] An important new development for chloramine T **245** based reagents (and *N*-halogeno-*N*-metallo carbamidates such as MeOC(O)NNaCl) came about after Sharpless' discovery of the formation of the imido selenium species **248**, formed from Se and **245**, and the allylic amination with **248**, e.g., to give **249**; see Scheme 71.[165]

Scheme 71. Reaction of 245-based 248 with Olefins



Also in 1976, a vicinal hydroxyamination process was developed in the Sharpless group on the basis of chloramine T **245**·3H_2O; see Scheme 72.

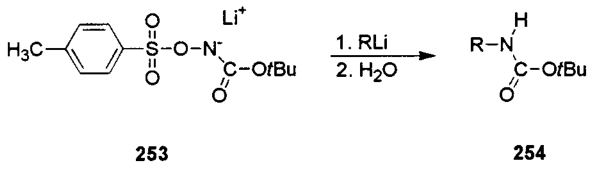
Scheme 72. Vicinal Hydroxyamination Involving 245·3H$_2$O



Reaction of cyclohexene **250** with **245**·3H_2O in the presence of 1% OsO_4 led to the N-tosylated 1,2-hydroxyamine **251**. It is assumed that **252** is the effective reagent.[166] These findings started an avalanche of studies involving nitrenoids and transition metal catalysts to perform (stereo)selective reactions with the formation of C−N bonds. Since the details of the reactions of nitrenoids with the catalysts are not known exactly this topic is not discussed further. The interested reader is referred to some recent references.[167−170]

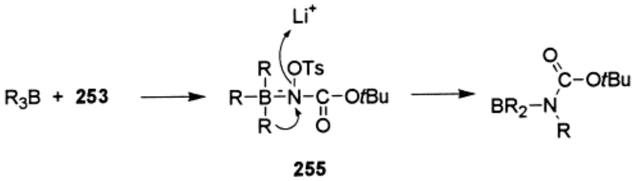
The transfer of the NHBoc group in electrophilic amination reactions of organolithium compounds by means of a nitrenoid was achieved by Genet et al.[171] Thus, deprotonation of the corresponding N−H species with 1 equiv of RLi led to lithium *tert*-butyl-*N*-tosyloxycarbamate **253** which on reaction with all sorts of organolithium species gave directly the Boc-protected amines **254**; see Scheme 73. N-Protected compounds of the type **254** are often useful in organic syntheses.

Scheme 73. Electrophilic Amination of RLi with the Nitrenoid 253



In some cases, CuI has to be used as a catalyst.[171] A second publication describes the amination of organoboranes with **253** which probably proceeds as outlined in Scheme 74.[172]

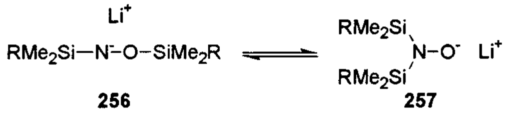
Scheme 74. Amination of Boranes with 253



Addition of the nitrenoid **253** to R_3B should give the intermediate **255** which is perfectly suited for an intramolecular migration of R to N and loss of LiOTs. There is ample precedence for related aminations of boranes in the literature.[173]

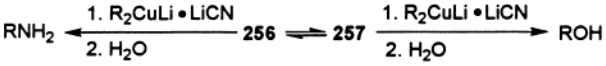
An extraordinarily interesting system was discovered by West and Boudjouk[174] because it provides potentially a *nitrenoid* as well as an *oxenoid*: the lithium bis(organosilyl)hydroxylamines **256** and **257**; see Scheme 75.

Scheme 75. Nitrenoid−Oxenoid Equilibrium



The authors were able to show that **256** is in equilibrium with **257**, with the position of the equilibrium being a function of R. They also trapped both the nitrenoid **256** as well as the oxenoid **257** with electrophiles such as CH_3I. Reactions of nucleophiles with **256** ⇌ **257** were performed by Ricci et al.[175] They used cyano-Gilman cuprates of the type $R_2CuLi·LiCN$ which gave, besides the amines RNH_2, the alcohols ROH on hydrolysis. Some of the reactions are summarized in Table 17.

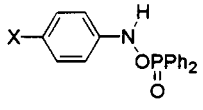
Table 17. Amination and Hydroxylation of Cyano-Gilman Cuprates by the Nitrenoid 256 and the Oxenoid 257, Repectively



$R_2CuLi·LiCN$, R =	R-NH_2 [%]	R-OH [%]
^{n}Bu	48	18
^{s}Bu	60	5
^{t}Bu	80	10

The formation of ROH clearly shows that **257** behaves like an electrophilic oxenoid of the general structure M−O−X **25**; see Scheme 5. Compound **256** gives the nitrenoid reaction with the cuprates. It would be very interesting to tune the properties of the equilibrium **256** ⇌ **257** and of the nucleophiles such that only nitrenoid or oxenoid reactivity is observed. More details about oxenoids are found in section 3.

Table 18. Starting Materials 258a–d and 259–261



258

	X	σ_p^-
a	$-COCH_3$	0.84
b	$-CN$	0.88
c	$-SO_2CH_3$	0.98
d	$-NO_2$	1.24

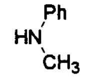
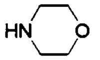
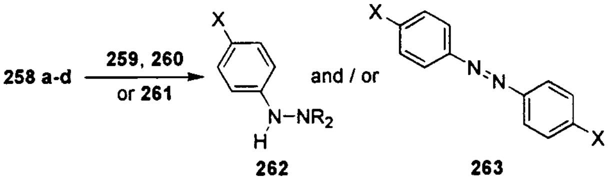
	amines	pk_B
259		9.15
260		5.70
261	$HN(nC_3H_7)_2$	3.09

Table 19. Yields [%] of 262 and/or 263 in the Reactions of 258a–d with 259–261



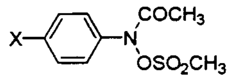
258	259–261	262 [%]	263 [%]
a	259	71	
	260	23	70
	261		91
b	259	75	
	260	20	70
	261		93
c	259	77	
	260	15	80
	261		92
d	259	95	
	260	8	80
	261		90

2.3. "Eliminative Dimerization" and Nitrene Formation of Nitrenoids

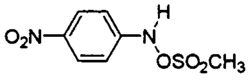
The difference between nitrenoid and nitrene reactivity as a result of different leaving group qualities is illustrated in the following examples. Reaction of the p-substituted *O*-diphenylphosphinoylhydroxylamines **258a**–**d** with the amines **259**–**261** (Table 18) leads to the hydrazines **262** and/or symmetrical azo compounds **263**; see Table 19.[176]

The hydrazines **262** are formed by amination of the amines **259** and **260** with **258**; see Scheme 76. The decreasing yields of hydrazines **262** together with the increasing amounts of azo compounds **263** on going from **258a** to **d**, with the latter having the best acceptor substituent, and from **259** to **261**, with **261** being the strongest base (see Tables 18 and 19), suggests a competition between the nucleophilic attack of the amines **259**–**261** at **258** to give the hydrazines **262**, and a reaction channel starting with deprotonation of **258** to give the nitrenoids **264** which lead to the azo compounds **263**; see Scheme 76.

Table 20. Yields [%] of 270, 271, and 263 from 268a–d and 269d in the Reactions with *n*-Butylamine

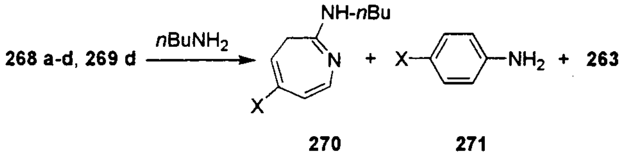


268



269 d

a: X = $-COOCH_3$
b: X = $-COCH_3$
c: X = $-CN$
d: X = $-NO_2$

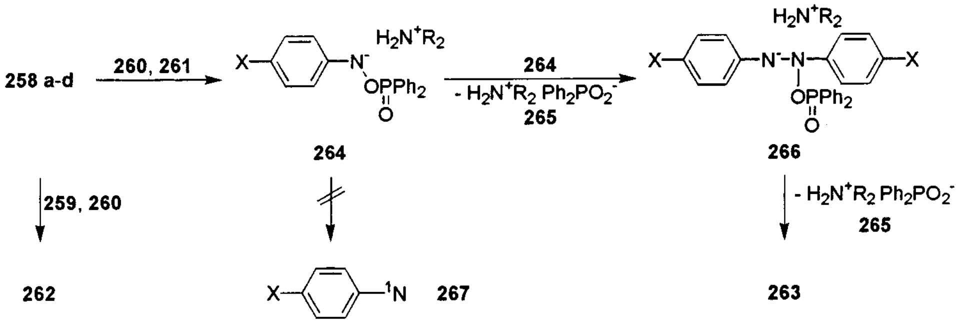


268a–d, 269d	*T* [deg]	**270** [%]	**271** [%]	**263** [%]
268a	20	93		
268b	20	8	44	25
	78	47	15	20
268c	−30	9	49	23
	20	30	3	67
	78	51	2	44
268d	−30		90	7
	78		94	2
269d	−30		60	30
	78		15	22

To form the azo compounds **263**, the nitrenoids **264** behave as an electrophile and a nucleophile (as this is also known from carbenoids, see section 1.2.4) to give the intermediate **266** which finally loses $H_2N^+R_2$ $Ph_2PO_2^-$ **265**. Thus, the azo compounds **263** are formed via "eliminative dimerization". The independently prepared potassium salt of **258d** gives exclusively **263d**. A nitrene **267**, formed by α-elimination of $H_2N^+R_2$ $Ph_2PO_2^-$ **265** from the nitrenoid **264**, is clearly not present, as shown by the following investigations. They demonstrate that the leaving group qualities in **265** are not good enough, while a nitrenoid → nitrene transformation determines the reactions of the acceptor-substituted *O*-(methylsulfonyl)-phenylhydroxamic acids **268a**–**d** and of *p*-nitrophenyl-*O*-(methylsulfonyl)-hydroxylamin **269d** with *n*-butylamine; see Table 20.[177]

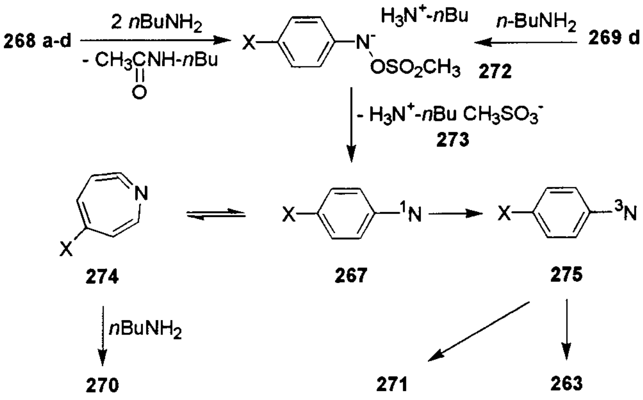
In this case hydrazines **262** are not formed at all—in contrast to the reactions of **258a**–**d** with amines

Scheme 76. "Eliminative Dimerization" of Two Nitrenoids 264



(Table 19)—however, one finds the 3-H-azepines **270** and the anilines **271** together with the azo compounds **263**; see Table 20. These products are typical for nitrene intermediates as shown in a plethora of investigations on the photolysis and thermolysis of aryl azides in the presence of amines.[148] In the present case, the reaction starts with the deacetylation of **268a**−**d** by ^{n}BuNH$_2$, or the deprotonation of **269d**, to give the nitrenoid **272**; see Scheme 77.

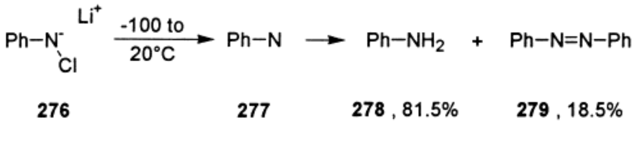
Scheme 77. α-Elimination of the Nitrenoids 272 To Give the Nitrenes 267 (and Their Follow-Up Products)



In comparison to the nitrenoid **264** (Scheme 76), **272** has the much better leaving group H$_3$N$^+$-^{n}Bu-H$_3$CSO$_3$ $^-$ **273** which leads rapidly to the singlet nitrene **267**. Compound **267** is in equilibrium with **274** which is trapped by ^{n}BuNH$_2$ to give **270**.[148] Intersystem crossing of **267** results in the triplet nitrene **275** which is known to form anilines **271** and azo compounds **263** under these reaction conditions.[148] The very facile intersystem crossing reaction of the nitro-substituted nitrene **267d** to give the triplet nitrene **275d** is also known.[148]

Not unexpectedly, the elimination of LiCl from *N*-chloro-*N*-lithio-aniline **276** was also observed.[178] Compound **276**, prepared from *N*-chloro-aniline and ^{n}BuLi, "decomposed" on warming from −100 °C to room temperature to give aniline **278** and azobenzene **279**; see Scheme 78.

Scheme 78. Formation of the Nitrene 277 from the Nitrenoid 276



Since thermal or photochemical decomposition of phenyl azide gave the same products **278** and **279**, the same aryl nitrene intermediate **277** is also formed by α-elimination from **276**.

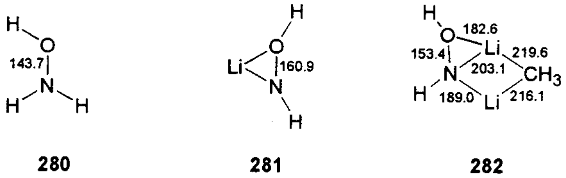
The results as documented in Schemes 77 and 78 thus indicate that nitrenoids are able to undergo α-elimination faster than other reactions to lead to the corresponding nitrenes. This, however, is the more rare case of nitrenoid reactivity (as this is similarly the case in carbenoid chemistry) (see section 1.3).

2.4. Structural Investigations

2.4.1. Quantum Chemical Calculations

2.4.1.1. LiNHOH. A first theoretical study of the model nitrenoid LiNHOH **281** was published by Boche and Wagner in 1984.[179] The significant features of the HF/4-31G structures of hydroxylamine H$_2$NOH **280** and LiNHOH **281** are listed in Scheme 79.

Scheme 79. HF/4-31G Bond Lengths [pm] of 280 and 281, and the HF/6-31G Structure of the complex 282



Thus, besides the bridged structure of **281**, the main difference between **280** and **281** is the much longer N−O bond in **281** (160.9 pm) than in **280** (143.7 pm). This goes along with a raising of the HOMO from −11.24 eV in **280** to −6.97 eV in **281** and a lowering of the LUMO from 6.32 eV in **280** to 0.50 eV in **281**. Such a situation corresponds exactly to that found in carbenoids (see section 1.4.1.1). It is therefore in agreement with the strong electrophilic nature of nitrenoids although being "anions". The strong tendency for electrophilic reactivity of nitrenoids is further supported by the following isodesmic reactions; see Table 21.

Table 21. ΔΔ*E* [kcal mol^{-1}] for the Isodesmic Reactions a−c; Energy//Geometry Optimization

$$NH_2^+ + LiNH_2 \rightleftharpoons NH_3 + LiNH^+ \quad (a)$$

$$NH_2^+ + LiNHOH \rightleftharpoons NH_2OH + LiNH^+ \quad (b)$$

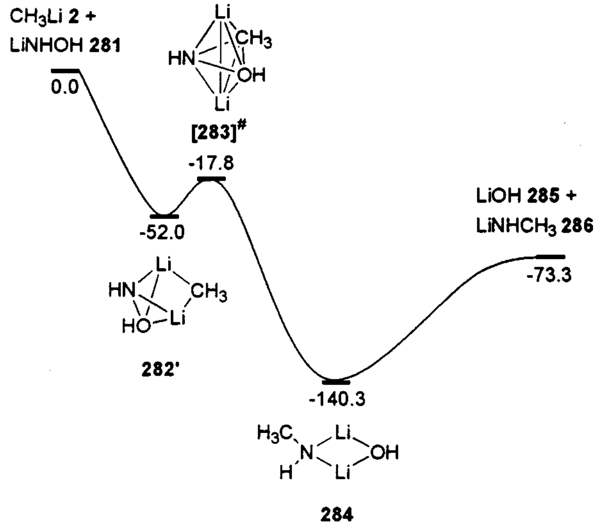
$$CH_3^+ + LiCH_3 \rightleftharpoons CH_4 + LiCH_2^+ \quad (c)$$

	MNDO// MNDO	4-31G// MNDO	4-31G// 4-31G	6-31G(d)// 4-31G
a	−74.1	−92.1	−95.1	−88.4
b	−72.9	−97.8	−79.7	−82.8
c	−63.2	−77.9	−77.6	−78.1

As shown in Table 21a,b, LiNH$^+$ is strongly stabilized compared to NH$_2$$^+$. The calculations also indicate a stronger stabilization of LiNH$^+$ (a and b) as compared to LiCH$_2$$^+$ (c) (for LiCH$_2$$^+$, see also section 1.4.1.1.1). In further work on the same subject,[180a] essentially the same structures of **280** and **281** were calculated (6-31G). In addition, the structure of a possible intermediate in the reaction of **281** with CH$_3$Li, the model complex LiNHOH·LiCH$_3$ **282**, was calculated; see Scheme 79. Not surprisingly, the N−O-bridged structure of LiNHOH **281** is retained in the complex **282**. The nitrenoid LiNHOH **281** is 17.7 kcal mol^{-1} less stable than the isomeric, also N−O-bridged oxenoid H$_2$N-OLi, which is of interest with respect to the nitrenoid−oxenoid equilibrium **256** ⇌ **257**; see Scheme 75.[180b]

The amination of organolithium compounds by N-lithio alkoxy amides was also studied by McKee.[181] He calculated the reaction profile of the reaction of LiNHOH **281** with CH_3Li **2** finally to give LiOH **285** and $LiNHCH_3$ **286**; see Scheme 80.

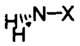
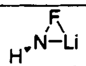
Scheme 80. 3-21+G Potential Energy Surface for the Amination of CH_3Li 2 with LiNHOH 281

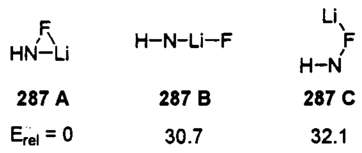


First, the complex **282′** is formed which is 52.0 kcal mol^{-1} more stable than the starting materials. From **282′** a trigonal bipyramidal-like transition state [**283**]‡ is reached (34.2 kcal mol^{-1}) which leads to the product complex **284** (88.3 kcal mol^{-1} more stable than **282′**). The products LiOH **285** + $LiNHCH_3$ **286** are 67.0 kcal mol^{-1} higher in energy than **284**. The propensity of Li^+ for bridging (and thus for promoting the reaction of **281** with **2**) is clearly seen as the transition state [**283**]‡ contains two lithiums capping CH_3O^-, CH_3^-, and NH in a bipyramidal-type arrangement.

2.4.1.2. LiNHF. The lengthening of the N−X bonds in nitrenoids LiHNX, X = F, OH, NH_2, as compared to those in H_2NX, is shown from quantum chemical calculations;[92] see Scheme 81.

Scheme 81. MP2/6-311++G(d,p) Bond Lengths [pm] in H_2NX and LiHNX Together with HF/3-21G Structures of LiNHF 287 (E_{rel} in kcal mol^{-1})

X			Δ_{N-X}
F	141.8	155.7	+ 13.9
OH	143.8	153.1	+ 9.3
NH_2	143.9	146.7	+ 2.8



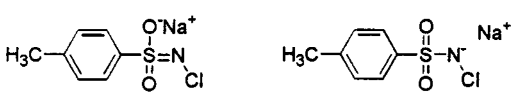
As in the case of the carbenoids (see Table 3), the bond to X = F is more stretched than the bonds to X = OH and NH_2. Furthermore, the N−X bond lengthening is less pronounced than the C−X bond lengthening.

Recently, various structures of LiNHF **287** were calculated.[182] Not unexpectedly, and as found before,[92] the bridged structure **287A** is much more stable than the linear **287B** and the bent **287C**; see Scheme 81.

2.4.2. Crystal Structures of Nitrenoids

2.4.2.1. Chloramine T·3H$_2$O. The first solid state structure of a nitrenoid was published by Olmstead and Power in 1986, namely that of chloramine T trihydrate **245**·$3H_2O$.[183] Since "the crystal structure of chloramine T is complex and cannot easily be described by the usual packing of molecular species",[183] we refer here only to the most significant aspects. The first is the absence of a Na−N bond: the closest Na···N interaction amounts to 409.5 pm. Na^+ is rather bonded to the oxygen atom of a sulfonyl group and to oxygen atoms of water molecules. Most interestingly with respect to the solid state structures of carbenoids (see section 1.4.3), the calculations of N−X bond lengths in nitrenoids (see section 2.4.1), and the solid state structure of [(**288**)$_2$·3 THF] (see section 2.4.2.2), the N−Cl bond length (172.0 pm) equals the mean distance in NCl_3 and is the same as one of the N−Cl distances in $[PtCl(NH_3)_3(NCl_2)_2]Cl$ (175 and 166 pm), or, in other words, the N−Cl bond in **245**·$3H_2O$ is not elongated. From their data the authors conclude that **245** is best described as **245A** and not as **245B**; see Scheme 82.

Scheme 82. Bonding Descriptions of 245



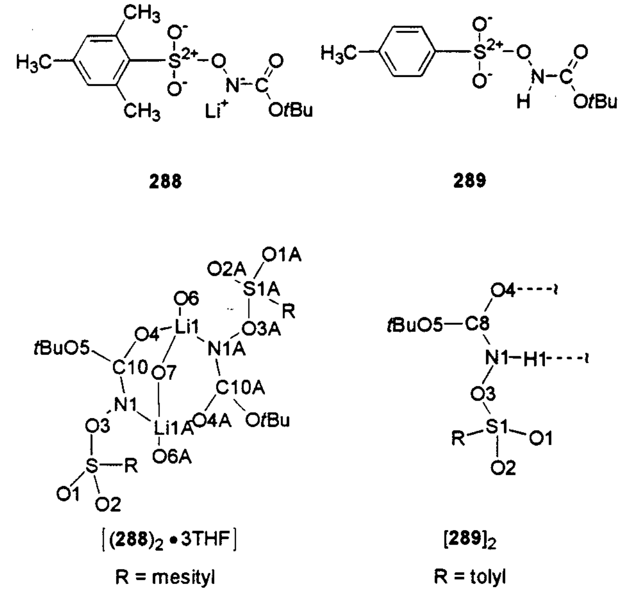
245 A **245 B**

Most likely both descriptions are not correct: quantum chemical calculations of sulfoxides and sulfones indicate quite clearly that sulfur−oxygen bonds in these compounds are polar (S^+−O^-) and not π-type double bonds,[85] which should similarly apply for sulfur−nitrogen bonds. So far the structure of **245** has not been studied quantum chemically. It would be interesting to find out whether the not elongated N−Cl bond is related to **245** also being a halonium cation donor.

2.4.2.2. [*N*-Lithio-*N*-mesitylsulfonyloxy-*tert*-butylcarbamate)$_2$·3THF]. To compare the structure of a nitrenoid with that of the corresponding N−H compound, Boche et al. investigated the solid state structures of **288** and **289**; see Scheme 83.[184] Compound **288** corresponds essentially to the nitrenoid **253** which was used by Genet[171,172] for electrophilic aminations of RLi compounds; see Scheme 73.

In [(**288**)$_2$·3THF] the two anions are linked by two Li^+ such that Li1 (Li1A) is bound to N1A (N1) and O4 (O4A). Furthermore each Li^+ interacts with one terminal (O6; O6A) and one shared THF molecule (O7). Interestingly, the two oxygen atoms of the sulfonoxy group, O1 (O1A) and O2(O2A), are not bound to Li^+ despite their excellent donor quali-

Scheme 83. Part of the Crystal Structures of [(288)$_2$·3THF] and [289]$_2$; the C Atoms of the THF Molecules in the Nitrenoid [(288)$_2$·3THF] Are Omitted for Clarity[a]



[a] In [**289**]$_2$ only part of the dimer structure is shown.

ties.[89,185] The dimer [**289**]$_2$ is held together by two hydrogen bonds.

The following changes in bond lengths are relevant for the nitrenoid character of **288**: (1) C10−O5 in [(**288**)$_2$·3THF] is 5 pm longer than C8−O5 in (**289**)$_2$ (134.7 and 129.7 pm). Thus **288** should eliminate LiO^{t}Bu rather easily to give the corresponding isocyanate. Similarly, in Li-ester enolates, which give easily ketenes, the C−OR bond is elongated.[186] (2) The lengthening of the N1−O3 bond in the nitrenoid [(**288**)$_2$·3THF] as compared to the neutral species [**289**]$_2$ from 142.3 to 148.5 pm is perfectly in agreement with the nitrenoid character of species such as **288** or **253**.[171,172] It is also in agreement with quantum chemical calculations of N−O bond lengths in nitrenoids (see section 2.4.1).

In conclusion, reactivities and quantum chemical as well as experimental structural studies support the nitrenoid character of compounds of the type LiNRX (X = leaving group). As in the case of carbenoids, their electrophilic nature is especially noteworthy. Furthermore, only if X is an excellent leaving group are nitrenoids transformed into nitrenes.

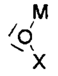
3. Oxenoids

3.1. Introduction

The term “oxenoid”, either as an adjective or a noun, was not very well defined until recently. Hamilton[187] suggested in 1964 that enzymes as well as their chemical models, which accomplish transfer of an oxygen atom, be termed “oxenoids”. As a result different classes of compounds, which were able to transfer an oxygen atom to some substrate under various conditions, were investigated with regard to their “oxenoid” properties.[188] In this review article, we restrict ourselves to a logical extension of the term oxenoid MOX **25** from carbenoids MCR^{1}R^{2}X **23** and nitrenoids MNRX **24**, as independently proposed by Julia, Saint-Jalmes, and Verpeaux,[189a] and Boche, Bosold, and Lohrenz,[190] in 1993/94.


23

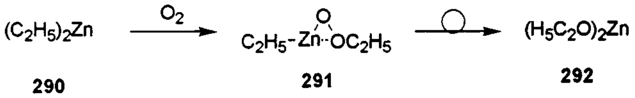

24


25

Thus oxenoids **25** are compounds which bear a metal M and a leaving group X at the oxygen atom. Hydrogen peroxide, peracids, dioxirans, metal oxo compounds, etc., therefore do not fall into this category. Correspondingly, typical properties of oxenoids **25** should be related to those of carbenoids **23** (see section 1) and nitrenoids **24** (see section 2), as, e.g., their electrophilic nature. As we will show in this section, this is exactly the case.

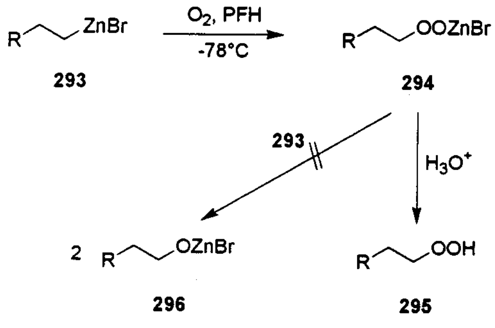
Historically it is interesting to mention that the first oxenoid (**291**) was prepared in Marburg by Frankland in 1853[191] although he neither isolated nor postulated **291** as an intermediate; see Scheme 84.

Scheme 84. Reaction of Diethylzinc with O$_2$



Frankland reacted diethylzinc **290** with dioxygen O$_2$ and received zinc diethylate **292**. In 1890 Demuth and Meyer proposed **291** as a likely intermediate which should be formed by “insertion” of an O$_2$ molecule into the Zn−C bond.[192] Fast intramolecular rearrangement of the zinc-bonded ethyl group to the anionic oxygen atom and cleavage of the O−O bond should give **292**. Thus **291** is an oxenoid. It is also interesting that the first preparation of peroxides RCH$_2$CH$_2$OOH **295** from ZnBr-hydroperoxides **294** was likewise performed in Marburg (142 years after Frankland's work) when Knochel and Klement reacted alkylzinc bromides **293** with high concentrations of O$_2$ dissolved in perfluorohexanes (PFH) at −78 °C; see Scheme 85.[193]

Scheme 85. Hydroperoxides from Alkyl Zinc Bromides with O$_2$



Because of the high O$_2$ concentrations, **293** reacts essentially only with O$_2$ to form the ZnBr-peroxide **294** and not with the just-formed oxenoid **294** to form the alcoholate **296** in an undesired side reaction because **296** would finally give the alcohol RCH$_2$CH$_2$-OH. In the case of **291** (Scheme 84) the *intra*molecular formation of the alcoholate **292** via oxenoid reaction is more difficult to avoid.

The “autoxidation side reaction” of Grignard reagents and organolithium species analogous to the reaction sequence **293** → **294** → **296** (Scheme 85) was noticed in the chemistry of these compounds also from the very beginning.[194] Thus, Bodroux[195] and Wuyts[196] detected the formation of phenols in the oxidation of arylmagnesium halides, while Porter and Steel studied this reaction in more detail.[197] Porter and Steel also proposed that phenylmagnesium bromide **297** should first react with O_2 to the peroxide **298**, which in a consecutive reaction with **297** should lead to the phenolate **299** which is protonated to give phenol; see Scheme 86.

Scheme 86. Oxidation of a Grignard Reagent with O_2 and an Oxenoid, Respectively

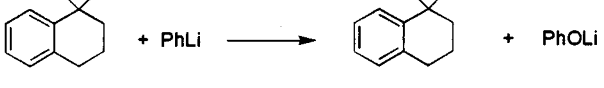
$$\underset{\mathbf{297}}{C_6H_5MgBr} + O_2 \longrightarrow \underset{\mathbf{298}}{C_6H_5OOMgBr}$$

$$\underset{\mathbf{298}}{C_6H_5OOMgBr} + \mathbf{297} \longrightarrow \underset{\mathbf{299}}{2\ C_6H_5OMgBr}$$

The reaction of the electrophilic MgBr-peroxide **298** with the nucleophilic Grignard reagent **297** reveals the oxenoid character of **298**. Not unexpectedly, Grignard also noticed the oxidation of “his” compounds: in 1928 he reported on the oxidation of $C_6H_5C{\equiv}C\text{-}MgBr$ to give $Ph\text{-}C{\equiv}C\text{-}OH$ and its follow-up products.[198] MgBr salts of peroxides of the general type **298** were first isolated by Walling and Buckler in 1955,[199] who thus verified the Porter–Steel reaction path (Scheme 86). The aliphatic oxenoids ROOMgBr were accessible by using excess dioxygen, which similarly allowed the isolation of the zinc bromide peroxides **294**; see Scheme 85. Lawesson and Yang (1959) studied the oxidation of Grignard reagents RMgX with various oxidants, among them *tert*-butyl hydroperoxide.[200] After deprotonation of the peroxide with 1 mol. equiv of RMgX, the reaction follows the sequence outlined in Scheme 86 (ROOMgX + RMgX → 2 ROMgX).

In the organolithium series, the oxidation of RLi with ROOLi was experimentally proven in 1939 by Müller and Töpel.[201] They reacted the independently synthesized lithium peroxide **300** with phenyllithium **71** and isolated the alcoholate **301** and the phenolate **76** (respectively the corresponding alcohol and phenol); see Scheme 87.

Scheme 87. Oxidation of Phenyllithium 71 with the Lithium Oxenoid 300



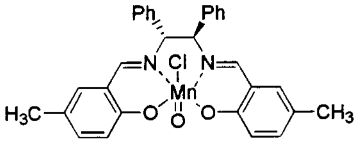
300 **71** **301** **76**

This important discovery indicates the generality of the reaction of organolithium reagents with lithiated peroxides (oxenoids) to give alcoholates *without the simultaneous involvement of dioxygen O_2*; see section 3.2.1.

The most widely used and most “simple” oxenoid—although generally not known as such—should also be mentioned in this Introduction: sodium hypochloride NaOCl **302**.

Na-O-Cl

302



303

Compound **302** is well-known because of its antimicrobial[202a] and bleaching[202b] properties. More recent significance comes from its use in the preparation of biomimetic oxidation catalysts.[202c] Jacobsen et al.[202d,e] and Katsuki et al.[202f,g] used it for the preparation of manganese oxo complexes of the type **303** which are important catalysts for the stereoselective synthesis of epoxides from olefins. Since neither the solid state structure[202h] nor quantum chemical studies of **302** are known, and since the details of the reactions of transition metal compounds with **302** are also not detailed in the literature, it is hoped that future investigations shed more light on **302** and other oxenoids of that type like LiOCl, KOCl, or $Ca(OCl)_2$.[202i]

3.2. Oxidation Reactions of (Anionic) Nucleophiles with Oxenoids

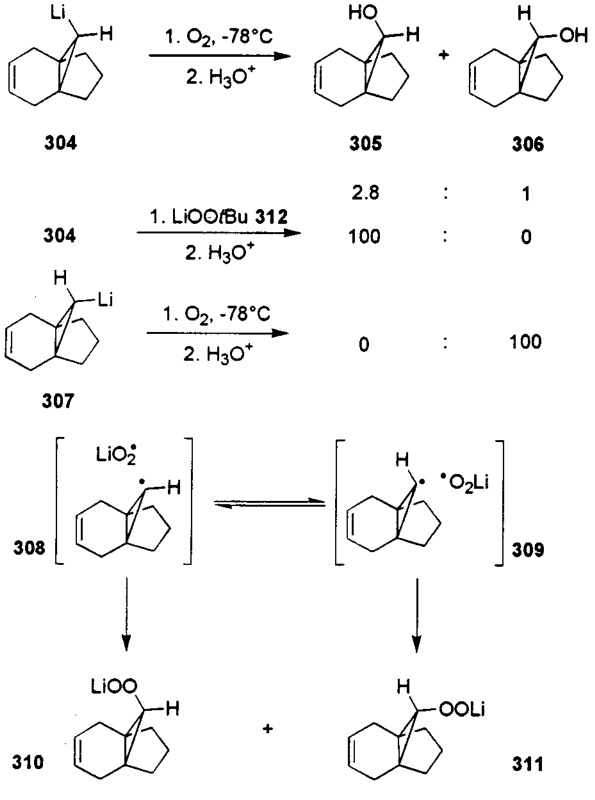
3.2.1. LiOOR Oxenoids

After Müller’s discovery[201] of lithiated peroxides such as **300** being oxidants for organolithium compounds such as PhLi **71** (see Scheme 87), it was of interest to know more about the details of such reactions and to compare them with oxidations in which dioxygen O_2 was involved (see Scheme 86). The first pertinent investigation was published by Warner and Lu.[203] When they stereoselectively prepared the configurationally stable cyclopropyllithium compound **304**, and reacted it with dioxygen O_2, on protonation the two isomeric alcohols **305** and **306** were isolated in a ratio of 2.8:1; see Scheme 88.

In the reaction of the isomeric **307** with O_2, only the cyclopropanol **306** was found. The authors[203] explained these results with the intermediate formation of the radical pairs **308** and **309** which allow fast epimerization at the cyclopropyl radical center. Recombination of the radical pairs results in the isomeric Li-peroxides **310** and **311**. These oxenoids react with further **304** or **307** to give finally the alcohols **305** and **306**.

The important question was whether the stereochemistry of the first step—the formation of the oxenoids **310** and **311** via O_2-oxidation—determines the observed stereochemistry. An answer provided the reaction of the cyclopropyllithium compound **304** with lithiated *tert*-butylperoxide $LiOO^tBu$ **312**, which led exclusively to the alcohol **305** (and *tert*-butyl alcohol)—in contrast to the reaction of **304** with O_2; see Scheme 88. “Thus the carbanionic reduction of lithium hydroperoxides indeed appears to be an S_N2 reaction, although an electron-transfer process within

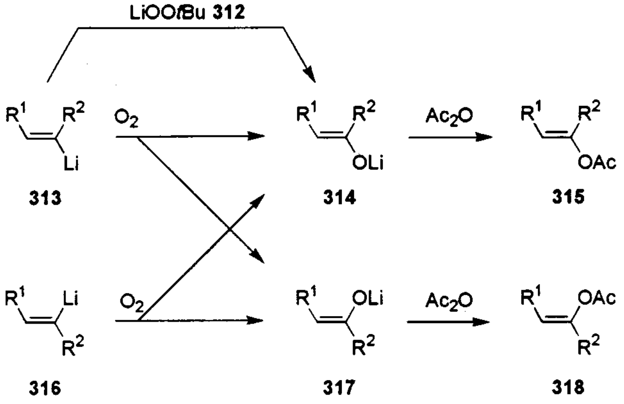
Scheme 88. Oxidation of Isomeric Cyclopropyllithium Compounds with O_2 and LiOO^{t}Bu, Respectively



a cage too tight to allow epimerization is, of course, not excludable".[203]

Similar observations were made by Whitesides et al.[204a] in studies of the oxidation of vinyllithium reagents to lithium enolates with dioxygen and LiOO^{t}Bu **312**, respectively. Thus, reaction of the isomeric vinyllithium reagents **313** and **316** with O_2 led via the enolates **314** and **317** to the esters **315** and **318**; see Scheme 89.

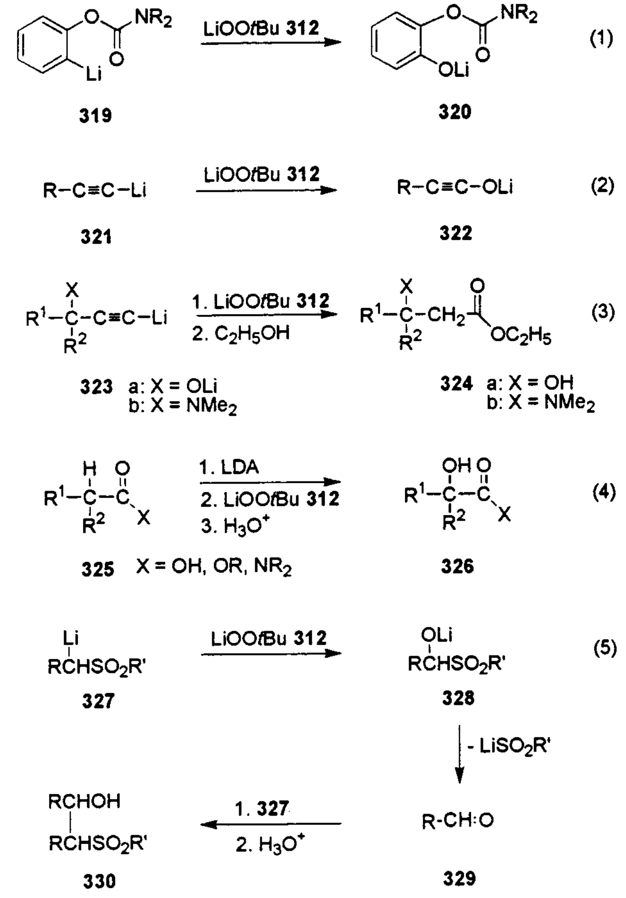
Scheme 89. Oxidation of Vinyllithium Compounds with O_2 and LiOO^{t}Bu, Respectively



In contrast, reaction of the vinyllithium species **313** with LiOO^{t}Bu **312** gives only the enolate **314** (and then the ester **315**). These stereochemical observations implicate vinyl radicals in reactions of vinylic lithium reagents with dioxygen and exclude them (at least as long living species) in reactions with the oxenoid LiOO^{t}Bu **312**. The transfer of an oxygen atom from oxenoids of the type LiOOR thus occurs with retention of configuration at nucleophiles of the type RLi although RLi compounds have a high tendency for electron-transfer reactions as shown by the "autoxidation" with O_2. LiOOR oxenoids such as **312** therefore can be used in stereoselective oxidations of RLi species, a reaction which indeed might occur via an S_N2-type reaction.[204b]

After Julia et al.[189] had realized the analogy of oxenoids LiOOR with carbenoids $LiCH_2OR$ and nitrenoids LiNHOR they performed oxidation reactions of various organolithium compounds with LiOO^{t}Bu **312**. Following ortho-metalation to **319**, reaction of **319** with **312** gave the phenolate **320** (respectively the corresponding phenol) in 80% yield (reaction 1, Scheme 90).[205]

Scheme 90. Oxidation of RLi Compounds with LiOO^{t}Bu



They also developed the oxidation of lithium acetylides **321** with LiOO^{t}Bu **312** to give inolates **322** into a synthetically interesting method; see Scheme 90, reaction 2. This reaction corresponds to that reported by Grignard[198] as mentioned in the Introduction 3.1.

Husemann showed that α-hydroxylated and α-aminated alkines such as **323a** and **b** can also be oxidized with **312**.[206] After reaction with ethanol the β-hydroxy and β-amino carboxylic acid esters **324a** and **b**, respectively, are isolated; see Scheme 90, reaction 3. If an enantiomerically pure α-hydroxy alkine is used, the chirality is completely transferred into the β-hydroxy carboxylic acid ester.[206]

Table 22. Yields of ROH [%] from the Oxidations of the Respective Organometallic Compounds with $LiOOCMe_2Ph$ 331

R	RLi	RCu(CN)Li	$R_2Cu(CN)Li_2$
^{n}Bu	85	84	82
^{t}Bu	81	89	90
Ph	85	83	78

Furthermore, carboxylic acid (derivatives) **325** can be α-hydroxylated with LiOO^{t}Bu **312** to form **326**; see Scheme 90, reaction 4.[189] Finally, α-lithiated sulfones **327** were oxidized with **312**.[189] In agreement with the other reactions of Scheme 90, the alcoholate **328** is first formed which eliminates $LiSO_2R'$ to give the aldehyde **329**. Its reaction with the starting material **327** leads to the isolated product **330**, a *β*-hydroxy sulfone; see reactions 5 in Scheme 90. The yields of the isolated compounds of the reactions listed in Scheme 90 are in the range of 60−90%.

In the first publication by Boche et al. on oxidation with oxenoids[190] it was shown that not only organolithium compounds RLi and Grignard species RMgBr could be oxidized with oxenoids LiOOR to the corresponding alcoholates ROLi(MgBr) but also lower order cyano cuprates RCu(CN)Li and cyano-Gilman cuprates $R_2Cu(CN)Li_2$. In these oxidations lithiated cumyl hydroperoxide $LiOOCMe_2Ph$ **331** was used as the oxenoid. Table 22 lists the oxidations of some RLi compounds and the corresponding cuprates. Oxidation with LiOO^{t}Bu **312** leads to similar results. Most importantly, alcohols (phenols) are formed in high yields.

The transformation of RCu(CN)Li and $R_2Cu(CN)Li_2$ with LiOO^{t}Bu **312** into alcohols (phenols) ROH deserves some interest because cuprates of this type, especially $R_2Cu(CN)Li_2$ and R_2CuLi, undergo with dioxygen O_2 fast electron transfer which mainly leads to dimers R−R. Whitesides et al. oxidized **332** with O_2 at −78 °C and received mainly the coupling product **333** (83%) besides some 1-butene **334** (13%) and little butanol **335** (4%); see Scheme 91.[207]

Scheme 91. Oxidation of the Cuprate 332 with O_2

$$(n\text{-}C_4H_9)_2CuLi \xrightarrow[-78\,°C]{O_2} n\text{-}C_8H_{18} + n\text{-}C_4H_8 + n\text{-}C_4H_9OH$$

332 **333**, 83% **334**, 13% **335**, 4%

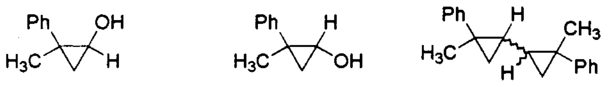
Of synthetic interest is the coupling of different aryl groups R^1 and R^2 in R^1R^2CuLi with O_2 at −125 °C to give $R^1{-}R^2$ (biphenyl compounds).[208]

To know more about the oxidation of cuprates with LiOO^{t}Bu **312**, Husemann, Möller, and Boche studied the question of whether radicals are involved in these oxidations by means of a cyclopropyl radical clock.[209a] For that purpose the cyclopropyl cuprates *cis*-**336a**−**c** and *trans*-**336a**−**c** were oxidized with LiOO^{t}Bu **312**, and with O_2, respectively, and the reactions analyzed with regard to the formation of the corresponding alcohols *cis*-**337** and *trans*-**337**, as well as the non-separated mixture of the stereoisomeric dimers **338**; see Table 23.

Table 23. Oxidation of Cuprates with O_2 and LiOO^{t}Bu, Respectively

cis-336 a-c **trans-336 a-c**

a: M = $CuR(CN)Li_2$; b: M = Cu(CN)Li; c: M = CuRLi
R = 2-methyl-2-phenyl-cyclopropyl



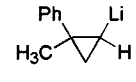
cis-337 **trans-337** **338**

cuprates	O_2 yield [%] of *cis*-**337**	*trans*-**337**	**338**
cis-**336a**	19	8	60
trans-**336a**	9	33	26
cis-**336b**	16	38	35
trans-**336b**	15	18	25
cis-**336c**	1	5	59
trans-**336c**	2	14	42

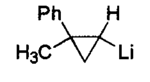
cuprates	LiOO^{t}Bu **312** yield [%] of *cis*-**337**	*trans*-**337**	**338**
cis-**336a**	77	0	0
trans-**336a**	5	58	3
cis-**336b**	86	0	0
trans-**336b**	0	76	3
cis-**336c**	46	0	4
trans-**336c**	4	39	3

Table 23 reveals that the reactions of the cyclopropyl cuprates **336** with dioxygen O_2 involve radical species $R^\bullet$ which isomerize before they probably recombine with $^\bullet$OOLi (see Scheme 88). Furthermore, dimerization to give **338** is observed, as known from other cuprate oxidations with O_2; see Scheme 91. The situation in the oxidation of the cyclopropyl cuprates **336** with the oxenoid LiOO^{t}Bu **312** is rather different from the O_2 oxidations: mostly the alcohols **337** are formed with a high degree of retention of configuration. In some reactions, small amounts of the isomeric alcohols **337** (4 and 5%, respectively) as well as of the dimers **338** (3 and 4%) are found; see Table 23. At the moment one cannot decide whether these latter products are due to some dioxygen present, or—more likely—whether the oxenoid **312** undergoes, in addition to the preferred S_N2-substitution with cuprates, some electron transfer from the cuprates. In the oxidations of the lithium (*cis*(*trans*)-**339**) as well as the Grignard compounds (*cis*(*trans*)-**340**), corresponding to the cuprates *cis*- and *trans*-**336**, with LiOO^{t}Bu **312**, not unexpectedly neither isomeric alcohols **337** nor dimers **338** are found.[209a] This result is perfectly in agreement with the results outlined in Scheme 88. It further indicates also for the reactions of Grignard compounds with oxenoids LiOOR an S_N2-type mechanism. Oxenoids of the X_3-TiOOR-type (see section 3.2.2) oxidize *cis*(*trans*)-**339** and *cis*(*trans*)-**340** also with complete retention of configuration.[209a]

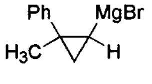
In conclusion, RLi and RMgX species are oxidized by oxenoids LiOOR to the corresponding alcoholates. This is similarly the case for various cuprates. The former compounds undergo an S_N2-type substitution



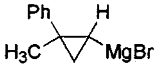
cis-339



trans-339



cis-340



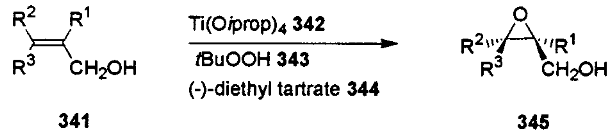
trans-340

at the oxenoid O atom with retention of configuration at the anionic carbon atoms of RLi and RMgX, at least if they are of the vinyl and cyclopropyl type as is the case in the examples shown here. With cuprates (some) electron-transfer might be involved, which is indicated by some stereoisomerization and dimerization.[209b]

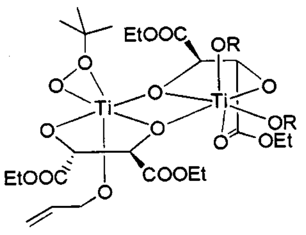
3.2.2. X_3TiOOR Oxenoids

The enantioselective formation of epoxides **345** from allylic alcohols **341**, Ti(O^{i}prop)$_4$ **342**, *tert*-butyl hydroperoxide **343**, and (−)- or (+)-diethyl tartrate **344** became one of the mostly used catalyzed stereoselective reactions in organic synthesis. Scheme 92 shows the reaction with (−)-diethyl tartrate **344**.[210]

Scheme 92. Sharpless Epoxidation Reaction



Sharpless proposed a mechanism via the dimer complex **346** with the bridged structural element TiOOR next to the carbon−carbon double bond.[210] A similar structure is part of a mechanistic proposal by Corey.[211] This epoxide forming reaction thus corresponds exactly to the cyclopropanation of an olefin with a carbenoid; see section 1.2.1.

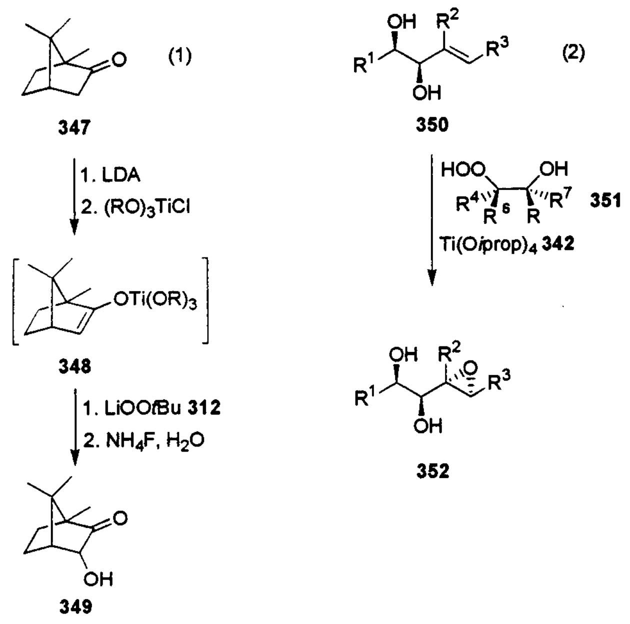


346

The oxygen bridged structure of the TiOOR oxenoid part was later shown by Boche et al. to exist in the solid state structure of a Ti-peroxide complex; see section 3.3. It is also the result of calculations; see section 3.3. Kagan,[212a,b] Modena, Nugent,[212c] and Uemura[212d] used the Sharpless system for the enantioselective oxidation of sulfides to sulfoxides R^1-S*-(O)-R^2. In that case the nucleophile R^1-S-R^2 reacts instead of the C=C bond with the X_3TiOO^{t}Bu oxenoid part of the complex.

Oxenoids of the structural type X_3TiOO^{t}Bu should play the relevant part in a diastereoselective oxidation reaction developed by Schulz; see Scheme 93, reaction 1.[213]

Scheme 93. Further Oxidations with Ti-peroxides



Reaction, for instance, of camphor **347** with LDA and (RO)$_3$TiCl should lead to the Ti-enolate **348**. Addition of LiOO^{t}Bu **312** should then provide the structural element TiOO^{t}Bu which oxidizes the enolate to the hydroxy compound **349** in 94% yield, de >95%. A reaction similar to the Sharpless epoxidation (Scheme 92), in which also a Ti-oxenoid should be the important structural element, was published by Adam;[214] see reaction 2, Scheme 93. Enediols such as **350** are reacted with the hydroperoxide **351** and Ti(O^{i}prop)$_4$ **342** giving epoxides such as **352** in high yields (>95%) and similar stereoselectivity.

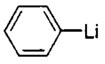
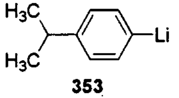
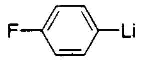
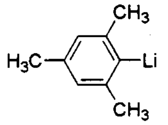
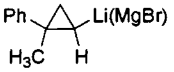
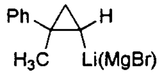
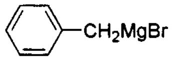
Most interestingly, the Sharpless system Ti(O^{i}prop)$_4$ **342** and ^{t}BuOOH **343**, more precisely, the resulting Ti-peroxide (oxenoid) part TiOO^{t}Bu, can also be used for the oxidation of organometallic compounds RLi and RMgBr. Husemann[206,209a] found that e.g. aryllithium species **71** and **353**−**355** give good yields of the corresponding phenols in this Ti-(O^{i}prop)$_4$-mediated reaction. Some examples are given in Table 24.

Aliphatic RLi and RMgBr compounds are oxidized to ROH in yields ranging between 69 and 96% with the ^{t}Bu species being the only exception (38 and 14%, respectively).[209a] It is important that RLi and RMgBr are not protonated to a remarkable extent under the reaction conditions, although ^{t}BuOOH **343** and not LiOO^{t}Bu **312** or LiOOCMe$_2$Ph **331** (Table 22) are used for oxidation. Boche et al. studied the stereochemistry of this oxidation reaction by means of the isomeric cyclopropyllithium (Grignard) compounds *cis*(*trans*)-**339** and *cis*(*trans*)-**340** (Table 24): in both cases only the cyclopropanol **337** was formed with retention of configuration. Dimers **338** (Table 23) were not detected.[209a] Therefore, intermediate radicals formed by electron transfer from RLi or RMgX onto the Ti-oxenoid structural element should not occur: the TiOOR oxenoid part oxidizes lithium and Grignard compounds, like LiOOR, very likely by an S_N2-type reaction. This corresponds to the observation that the benzyl Grignard **356** is oxidized to benzyl alcohol without the formation of bibenzyl.[215]

Table 24. Oxidation of RLi(MgBr) in a Ti(O^{i}prop)$_4$-Mediated Reaction with ^{t}BuOOH

$$\text{R-M} \xrightarrow[\text{-70° to -58°C, THF, 1h}]{\text{Ti(O}i\text{prop)}_{\text{R}}\text{-RM}} \xrightarrow[\text{-78° to 20°C}]{\text{1.1 }t\text{BuOOH R-R}} \xrightarrow{\text{H}_3\text{O}^+} \text{R-OH}$$

M = Li, MgBr

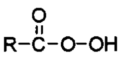
R-M	ROH [%]	R-M	ROH [%]
 **71**	87	 **353**	80
 **354**	84	 **355**	78
 **cis-339 (340)**	68 (79)	 **trans-339 (340)**	43 (60)
 **356**	71		

A final reaction in solution which is discussed here and in which the structural element TiOOR should be involved is the Ti(O^{t}Bu)$_4$ (**357**)-catalyzed "decomposition" of ^{t}BuOOH **343** to give singlet dioxygen $^1O_2$ **358** and ^{t}BuOH; see Scheme 94, reaction 1.[216]

Reaction 1 is finished after 20 min at 25 °C as shown by the luminescence/time diagram of $^1O_2$ **358**.[216] *m*-Chloroperbenzoic acid **259** forms $^1O_2$ **358** even faster: reaction 2, Scheme 94, takes only 50 s at 10 °C. Besides the detection in the luminescence/time diagram, $^1O_2$ **358** was trapped by 9,10-dimethylanthracene **360** to give the adduct **361** in yields between 30 and 50%; see Scheme 94, reaction 3. The formation of $^1O_2$ **358** from ^{t}BuOOH **343**,[217] hydrogen peroxide HOOH **362**,[218] and peracids **363**[219] catalyzed by (transition) metals has been reported before.[220]

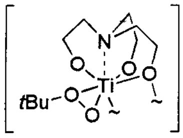
H-O-O-H

362

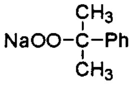


$$\text{R-}\overset{\text{O}}{\overset{\|}{\text{C}}}\text{-O-OH}$$

363



364



$$\text{NaOO-}\overset{\text{CH}_3}{\underset{\text{CH}_3}{\text{C}}}\text{-Ph}$$

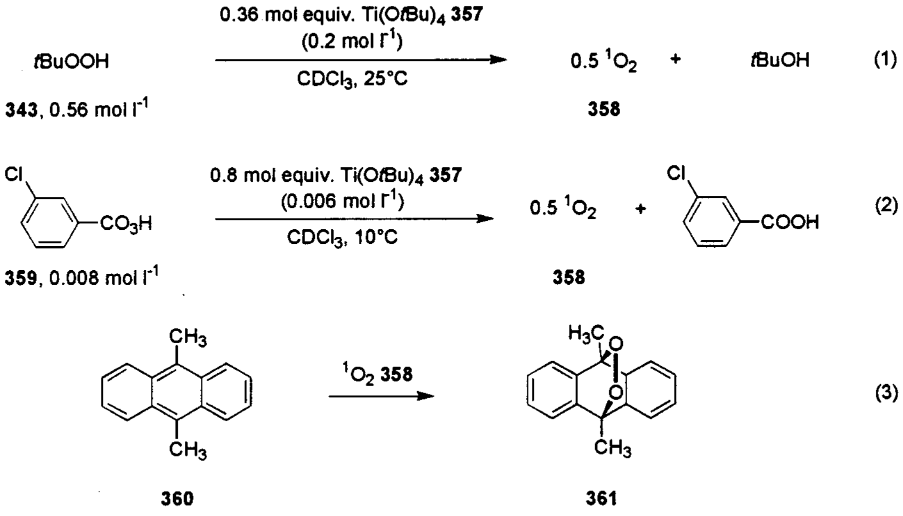
365

The interesting question is the following: Are the two oxygen atoms of $^1O_2$ **358** produced from *one* such molecule, with *two* oxygen atoms next to each other, or from the reaction of two of these molecules with each other, each providing one oxygen atom? LiOO^{t}Bu **312** "decomposes" only above 100 °C; see section 3.3. Similarly, the Ti-peroxide **364**, which can be isolated, does not give $^1O_2$ **358** on heating; see section 3.3. The sodium salt of cumene hydroperoxide **365** slowly forms $^1O_2$ **358** at 70 °C, with the $^1O_2$-formation being described by the kinetic equation of a *second-order reaction*.[221] This may implicate the "eliminative dimerization" of two oxenoids to give $^1O_2$; see section 3.3. The reaction is about 50 times faster if an equimolar amount of cumene hydroperoxide is present.[221] Similarly, the rate of the $^1O_2$-formation from H_2O_2 **362** as well as from peracids **363** is fastest with equal amounts of "acid" and the corresponding metal salt.[218,219] These results could indicate that in the Ti(O^{t}Bu)$_4$-catalyzed formation of $^1O_2$ from ^{t}BuOOH **343** the Ti-peroxide ^{t}BuOOTi(O^{t}Bu)$_3$ **366**, formed from ^{t}BuOOH **343** and Ti(O^{t}Bu)$_4$ **357**, transfers an oxygen atom onto ^{t}BuOOH **343** to give the trioxide **367**; see Scheme 95, reactions 1 and 2.

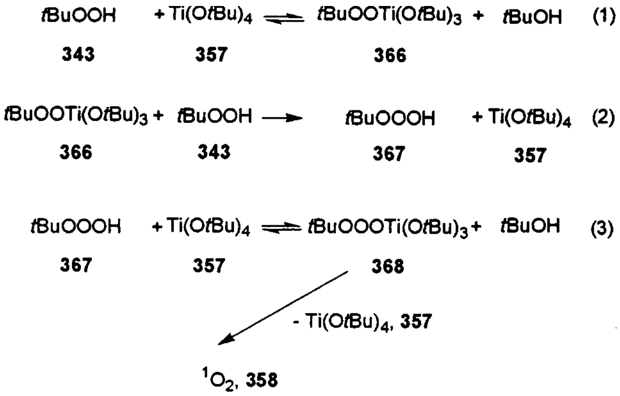
Then **367** is deprotonated by **357** to give the Ti-trioxide **368** (reaction 3) which undergoes a fast 1,2-elimination of **357** to form $^1O_2$ **358**. Similar reaction sequences could be responsible for the $^1O_2$-formation from H_2O_2 **362**[218] and peracids **363**[219], catalyzed by (transition) metal compounds, and for the $^1O_2$ formation from ^{t}BuOOH **343** with other catalysts than **357**.[217]

Labeling studies suggest that one oxygen atom in $^1O_2$, formed from Caro's acid **369**** and the salt **370** (as well as from other peracids RCO$_3$H **363**** and their salts **371**), comes from the acid and

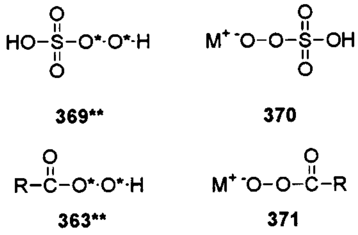
Scheme 94. Ti(O^{t}Bu)$_4$-Catalyzed Formation of $^1O_2$ from ^{t}BuOOH and *m*-Chloro-perbenzoic Acid, Respectively



Scheme 95. Possible Mechanism for the Formation of $^1O_2$ from 343 and 357



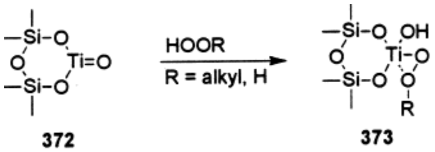
one from the salt, respectively, to give ^{1}O−*O **358***.[219c,222,219a,219d,223]



These findings are in agreement with the formation of **367** from **366** and **343**, Scheme 95 (reaction 2) (although they do not prove it). The titanated trioxide derivative **368**, formed from **367** and **357**, should easily eliminate **357** to give $^1O_2$ **358**, as known from other trioxide compounds.[224,225] Future investigations will have to clarify whether the structural element TiOO^{t}Bu indeed acts as an oxenoid in the Ti(O^{t}Bu)$_4$-catalyzed facile formation of $^1O_2$ **358** from ^{t}BuOOH **343**. In the case of the meta-chloro-perbenzoic acid **359**, a similar sequence as outlined in Scheme 95 leads to the structural element TiOOC(O)aryl which should be a "super oxenoid" because of the much better leaving group aryl-CO_2^-. A mechanism for the $^1O_2$ formation in which the dimerization of two singlet oxygen atoms ^{1}O, formed by α-elimination of MX from an oxenoid MOX, should be responsible for the product $^1O_2$ **358**, is clearly excluded for energetic reasons; see section 3.3.

Finally, oxenoids with the structural element TiOOR(H) play an important role in heterogeneous catalysis. Shell[226] developed a titanium silicate **372** which reacts with ROOH (R = alkyl, H[227]) to form, as suggested,[228] an oxenoid of the type **373**; see Scheme 96.

Scheme 96. TiOOR-Type Oxenoids in Heterogeneous Catalysis


372
373

The catalyst is used, e.g., for the oxidation of propene to give propene oxide. The intermediate formation and the reaction of **373** is in agreement with the strong electrophilic nature of such Ti-peroxides both in heterogeneous as well as homogeneous reactions.

3.2.3. Further Transition Metal Oxenoids

The Sharpless expoxidation reaction of allylic alcohols **341** with Ti(O^{i}prop)$_4$ **342**, ^{t}BuOOH **343**, and (+)- or (−)-diethyl tartrate **344** to give epoxides **345** with high enantioselectivity (see Scheme 92) was also studied with zirconium and hafnium compounds as, e.g., Zr(O^{i}prop)$_4$ and Hf(OEt)$_4$.[229] The product yields, however, cannot compete with those in the Ti-catalyzed reaction. Most likely, peroxides (oxenoids) with the structural elements **374** and **375** are involved in the oxygen transfer step.


374
375

Epoxidations of allylic alcohols were similarly observed when compounds of the type (^{t}Bu$_3$C-O)$_3$M-CH$_3$, M = Zr, Hf, were reacted with dioxygen O_2. It is reasonable to assume that O_2 inserts first into the M−CH$_3$ bond to give peroxides (^{t}Bu$_3$C-O)$_3$M-OOCH$_3$, M = Zr, Hf. These oxenoids, which correspond to **374** and **375**, react then with the allylic C=C bond to give the epoxides.[230]

Indeed, if tetrabenzylzirconium is reacted with dioxygen in toluene at −74 °C, one finds 14.5% benzylhydroperoxide on hydrolysis.[230] Even more stable is the di-peroxide **377** formed on reaction of tetrabenzylhafnium **376** with dioxygen at −78 °C; see Scheme 97.[231]

Scheme 97. Formation of the Hafnium Diperoxide 377 from 376 and O_2

$$\underset{\mathbf{376}}{(PhCH_2)_4Hf} \xrightarrow[\text{toluene, -78°C}]{O_2} \underset{\mathbf{377}}{(PhCH_2OO)_2Hf(CH_2Ph)_2}$$

The solid state structure of a hafnium peroxide and the intramolecular oxenoid reaction of this species is documented in section 3.3.

The stability of these Zr- and Hf-peroxides is in strong contrast to that of the corresponding Ti species: **378**, e.g., reacts with O_2 directly to the corresponding tetra-alkoxide **379**; see Scheme 98.[232] A peroxide intermediate cannot be isolated.

Scheme 98. "Autoxidation" of Tetraalkyltitanium Compounds

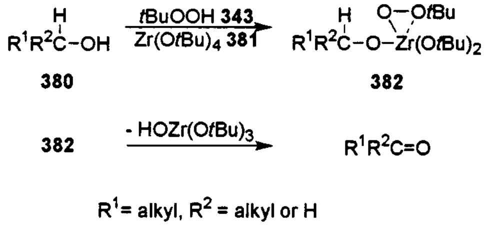
$$\underset{\mathbf{378}}{TiR_4} \xrightarrow[\text{toluene}]{O_2} \underset{\mathbf{379}}{Ti(OR)_4}$$

a: R = $CH_2{}^t$Bu; b: R = CH_2SiMe_3

This indicates comparatively strong oxenoid character of Ti-peroxides.

Krohn used Zr(O^{t}Bu)$_4$ **381** and ^{t}BuOOH **343** for the oxidation of primary and secondary alcohols **380** to aldehydes and ketones, respectively.[233] In this case an intermediate of the type **382** should be formed from the alcohol **380**, ^{t}BuOOH **343**, and Zr(O^{t}Bu)$_4$ **381**; see Scheme 99.

Scheme 99. Zr(O^{t}Bu)$_4$-Catalyzed Oxidation of Alcohols to Aldehydes (Ketones)

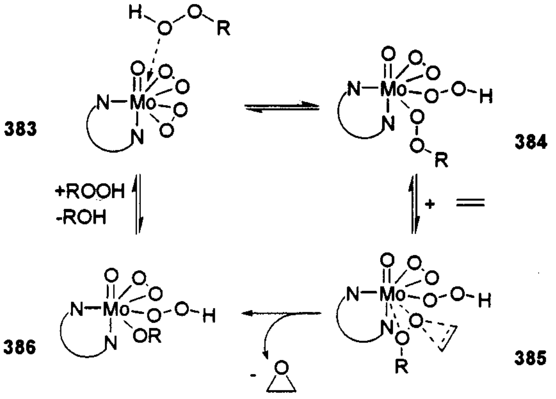


Although the details of the mechanism of the oxygen transfer steps are not known, the reaction corresponds to an insertion of the oxenoid oxygen atom into a β-C−H bond. The analogous formation of acetone from Ti(O^{i}prop)$_4$ **342** and ^{t}BuOOH **343** at temperatures >0 °C has been reported before by Sharpless.[210d] For that reason the epoxidation of allylic alcohols with Ti(O^{i}prop)$_4$ is performed at −20 °C. The analogous insertion of carbenoid carbons into C−H bonds is discussed in section 1.2.3.

Vanadium catalysts are also of interest in epoxidation reactions.[234−238] The intermediate formation of V^V-peroxides (oxenoids) is nicely supported by a solid state structure in which the oxygen atoms of the peroxide group are η^2-bridged by the cation; see section 3.3.

The industrially very important HALCON process[239] in which propene is oxidized to propene-oxide by ^{t}BuOOH and molybdenum peroxo complexes (L−L)MoO(O$_2$)$_2$ proceeds through oxenoids too, as recently discovered by Thiel.[240] The mechanism is shown in Scheme 100.

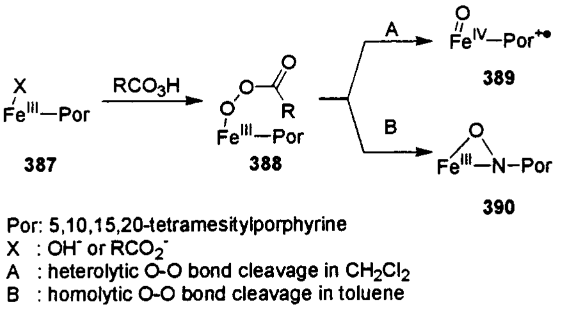
Scheme 100. (L−L)MoO(O$_2$)$_2$ Catalyzed Oxidation of an Olefin



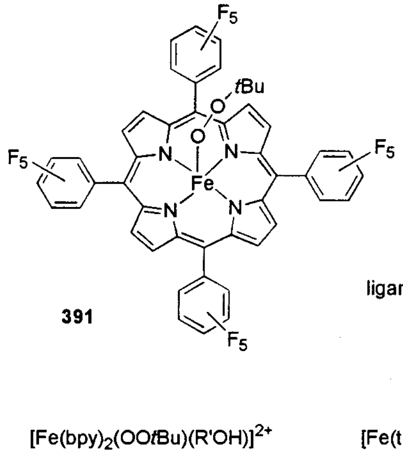
In the first step ROOH (^{t}BuOOH; HOOH) coordinates with the Lewis acidic Mo^{VI} center of **383**. Then ROOH protonates one of the peroxo ligands of **383** to give **384**. η^2-Coordination of the alkyl peroxide ligand leads to activation for the oxygen transfer from the oxenoid onto the olefin (**385**), giving the epoxide and **386**. Elimination of ROH and renewed addition of ROOH leads back to **383** + ROOH. The oxenoid transition state **385** is essentially equal to the transition state as formulated for the Sharpless epoxidation reaction (see formula **346**). A similar mechanism as outlined in Scheme 100 was recently found by Sundermeyer et al. for peroxomolybdenum complexes as epoxidation catalysts in biphasic hydrogen peroxide activation.[241]

Although it is not the purpose of this review article to discuss oxidation reactions catalyzed by iron^{III} prophyrins in detail (see the Introduction 3.1 and ref 188a−d), one has to mention that it is not only the oxo-ferryl porphyrin π-cation radical (TMP$^{+\bullet}$)Fe^{IV}=O **389** that undergoes oxidation reactions e.g. of olefins, but also the first formed acylperoxoiron(III) porphyrin complex [(TMP)Fe^{III}(OOC(O)R)] **388**, if, e.g., the 5,10,15,20-tetramesitylporphinato iron(III) [(TMP)Fe^{III}(X), X = HO$^-$ or RCO$_2$$^-$] **387** is reacted with a peracid RCO$_3$H; see Scheme 101.

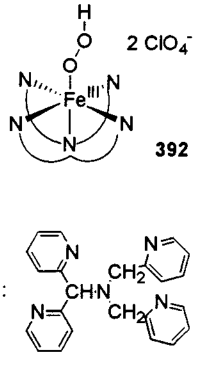
Scheme 101. Formation and Decay of the Acylperoxoiron(III) Porphyrin Complex 388



Machii, Watanabe, and Morishima[242] recently showed the dependence of the oxidation reactions on the peracid RCOOH used, which would not be the case if the oxo-ferryl π-cation radical **389** was the only oxidant. Besides, the formation of the porphyrin oxidation product **390** in toluene also depends on the acylperoxo-unit present in **388**. Iron(III) peroxo species related to **388** similarly are formed if compounds of the type **387** are reacted with peroxides ROOH, hydrogen peroxide HOOH, and even with dioxygen. Correspondingly, Bold[243a] recently prepared *tert*-butylperoxo-5,10,15,20-tetra((pentafluoro)phenyl)porphinato-iron(III) **391** and proved its existence by means of MS, ESR, and UV spectroscopy as well as its oxenoid reactivity.



391



392

[Fe(bpy)$_2$(OO*t*Bu)(R'OH)]$^{2+}$

393

bpy: 2,2'-bipyridine

[Fe(tpa)(OO*t*Bu)(R'OH)]$^{2+}$

394

tpa: tris(2-pyrimidylmethyl)amine

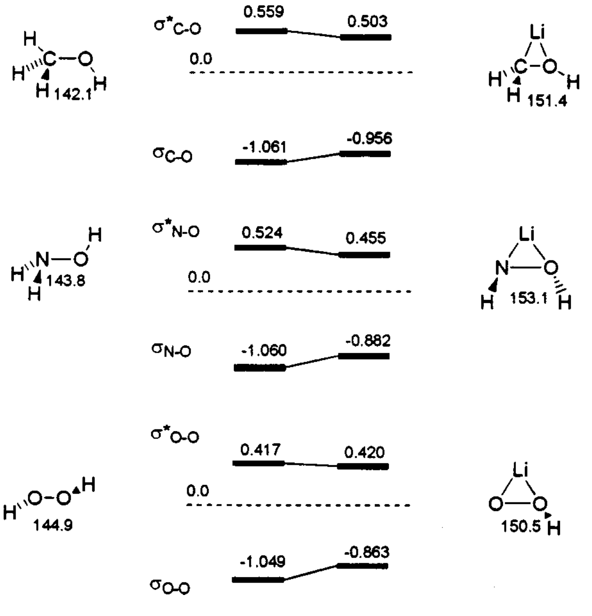
Feringa and Que, Jr., et al. demonstrated the existence of the non-heme model compound for "activated bleomycin" **392** by MS spectroscopy and showed that it oxidizes cyclohexane to cyclohexanol.[243b] The alkylperoxoiron intermediates **393** and **394**, respectively, were synthesized and characterized as oxidants by Que, Jr., et al.[243c,d] It thus turns out that oxenoids of the type Fe^{III}-O-OR(H) play also an important role in the rather complex chemistry of iron-catalyzed oxidation reactions. Very recently relevant work along these lines was published by Nam et al.[243e,f]

3.3. Structural and Theoretical Studies of Oxenoids

3.3.1. Lithium Oxenoids

In sections 2 and 3, respectively, it was shown that nitrenoids LiNROR and oxenoids MOOR, M = Li$^+$, Ti^{IV}, Zr^{IV}, Hf^{IV}, V^V, Mo^{VI}, Fe^{III}, are strongly electrophilic. Therefore, they react with all sorts of nucleophiles, which documents their relationship to carbenoids (see section 1). Are these common properties also observed in quantum chemical calculations and in structural investigations? In Scheme 102 are shown the C(N,O)−OH bond lengths and the energies of the $\sigma(\sigma^*)$ orbitals of H_3C-OH, H_2N-OH, and HO-OH, together with those of the lithiated model carbenoid $LiCH_2$-OH, nitrenoid LiNH-OH, and oxenoid LiO-OH, respectively.[190]

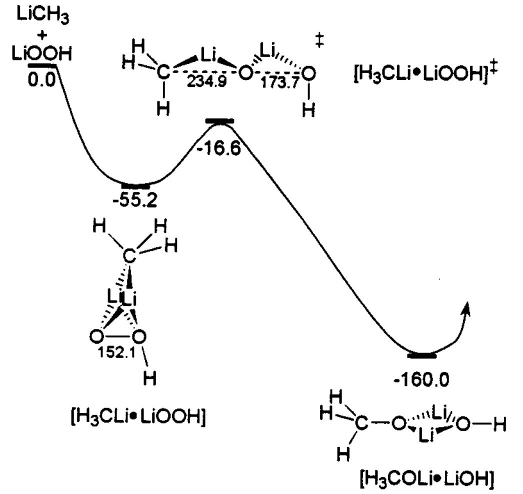
Scheme 102. MP2/6-311++G(d,p) Calculated C(N,O)−OH Bond Lengths [pm] and σ (σ^*) Orbital Energies [au] (HF/6-311++G(d,p)) of These Bonds in $H_3C(H_2N,HO)$-OH and $LiCH_2((NH,O)$-OH



In the carbenoid case the C−O bond is lengthened on lithiation from 142.1 to 151.4 pm (Δ = 9.3 pm), which is in agreement with the structures of carbenoids (see section 1.4.3). Concomitantly, σ_{C-O} is raised from −1.061 to −0.956 au (Δ = 0.105 au) and σ^*_{C-O} is lowered from 0.559 to 0.503 au (Δ = 0.056 au). The formation of the nitrenoid is accompanied by a bond lengthening of the N−O bond from 143.8 to 153.1 pm (Δ = 9.3 pm), a raising of σ_{N-O} by 0.178 au and a lowering of σ^*_{N-O} by 0.069 au. In the oxenoid case the O−O bond is lengthened by 5.6 pm and the σ_{O-O} orbital is raised by 0.186 au, while the already low σ^*_{O-O} orbital (0.417 au) stays essentially at the same level (0.420 au). The quantum chemical results as shown in Scheme 102 are therefore in good agreement with the experimental results so far reported.

The S_N2-type transition state in reactions, e.g., of organolithium (Grignard) reagents with oxenoids (see, e.g., Schemes 88 and 89 and Table 24) is also nicely supported by quantum chemical studies.[244−247] The model reaction of H_3CLi with LiOOH is outlined in Scheme 103.[247]

Scheme 103. MP2(fc)/6-31G(d) Calculations of the Reaction of H_3CLi with the Model Oxenoid LiOOH; Relative Energies [kcal mol^{-1}]; Bond Lengths [pm]

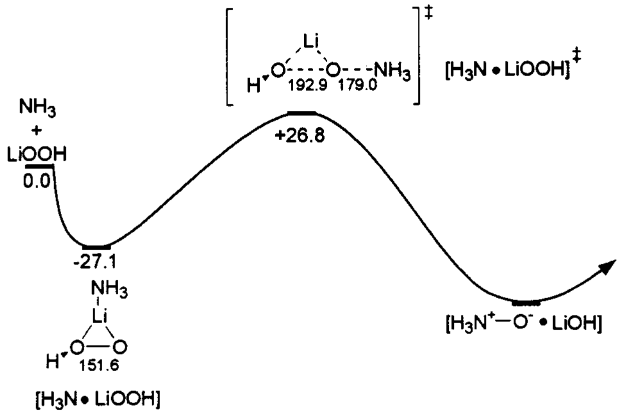


$LiCH_3$ and LiOOH first form the complex $H_3CLi\cdot LiOOH$ in which both Li$^+$ bridge the O−O bond (152.1 pm). This bond is only slightly longer (0.3 pm) than in the Li$^+$-bridged oxenoid LiOOH. The situation changes strongly in the transition state $[H_3CLi\cdot LiOOH]^‡$. Now the O−O bond is elongated to 173.7 pm. Most significantly, the nucleophile H_3C^- is oriented linearly to the O−O bond, as expected for an S_N2 reaction. One of the Li cations connects the anionic C atom of H_3C^- with the electrophilic oxygen atom of the oxenoid, while the other one is perfectly placed for a metal assisted ionization of the leaving group HO$^-$. From the transition state the product complex $H_3COLi\cdot LiOH$ is reached.

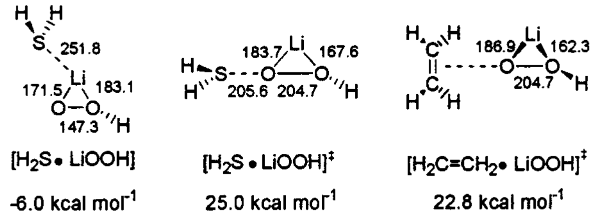
A similar profile was calculated for the reaction of H_3N with LiOOH; see Scheme 104.[244]

The initially formed complex $H_3N\cdot LiOOH$ is not as stable as $H_3CLi\cdot LiOOH$ (Scheme 103), and the transition state $[H_3N\cdot LiOOH]^‡$ is much higher in energy than $[H_3CLi\cdot LiOOH]^‡$ (Scheme 103). These data are in agreement with experimental results: the oxidation of organometallic compounds RM with oxenoids LiOOR is a fast reaction even at −78 °C (see section 3.2.1), while amines are oxidized reluctantly by LiOOR. The geometry of the transition state is again of the S_N2-type. The oxidation of H_2S by the model oxenoid LiOOH follows the same characteristics.[245]

Scheme 104. MP2/6-31G(d) Profile of the Reaction of H_3N with LiOOH; Relative Energies [kcal mol^{-1}]; Bond Lengths [pm]



Scheme 105. CISD/6-31G(d) Calculations of the Complex $H_2S{\cdot}LiOOH$ and the Transition State $[H_2S{\cdot}LiOOH]^‡$; the Transition State Structure of $[H_2C{=}CH_2{\cdot}LiOOH]^‡$ Is Also Shown; Bond Lengths [pm]



The complex $H_2S{\cdot}LiOOH$ and the S_N2-type transition state $[H_2S{\cdot}LiOOH]^‡$ are outlined in Scheme 105.

The transition state of the oxidation of a model olefin with the model oxenoid LiOOH, $[H_2C{=}CH_2{\cdot}LiOOH]^‡$,[246] see also Scheme 105, fits into the overall picture.

In conclusion, quantum chemical calculations are in agreement with the changes which occur on formation of an oxenoid LiOOR from HOOR, and with the S_N2-type reactions of LiOOR with nucleophiles.

The first solid state structure of an alkali (earth) peroxide was published by Boche et al.[247] Lithium *tert*-butylperoxide, which was prepared from *tert*-butylhydroperoxide and lithium diisopropylamide, crystallized as a dodecamer; see Figure 1A. LDA was used as the base in order to avoid oxidation reactions by $LiOO^tBu$ of, e.g., *n*-butyllithium.

$[LiOO^tBu]_{12}$ has a polar center with 12 lithium and 24 oxygen atoms, and a hydrophobic shell resulting from the 12 *tert*-butyl groups. Both O—O bonds of the asymmetric unit are bridged by Li^+; see Figure 1B (O1—Li1B 210.9(5) pm, O2—Li1B 190.9(5) pm, O3—Li2E 196.1(5) pm, O4—Li2E 199.3.(5) pm). Furthermore, each anionic oxygen atom is bonded to two further Li^+: O2—Li1 185.2(5) pm, O2—Li2D 190.2(5) pm; and O3—Li1 191.3(5) pm, O3—Li2 186.9(5) pm. The O—O bonds are essentially of equal length (O1—O2 147.5(3), O3—O4 147.7(3) pm). They are only slightly longer than the mean value of O—O bonds in 12 crystals containing HO—OH (145.3 pm) and in 29 crystals with HO—OR units (146.5 pm).[132] What is the reason for the marginal O—O bond lengthening in the dodecamer $[LiOO^tBu]_{12}$? According to quantum chemical calculations, the aggregation plays a major role for the O—O bond lengths in oxenoids; see Scheme 106.

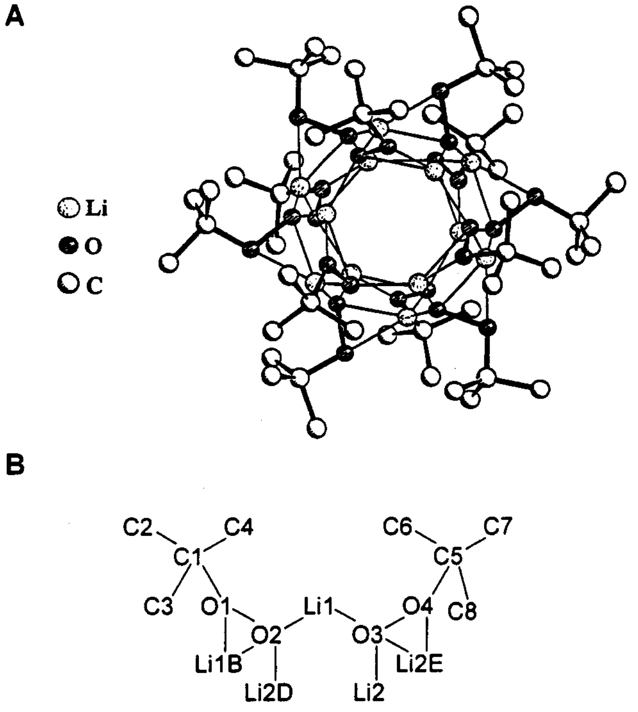
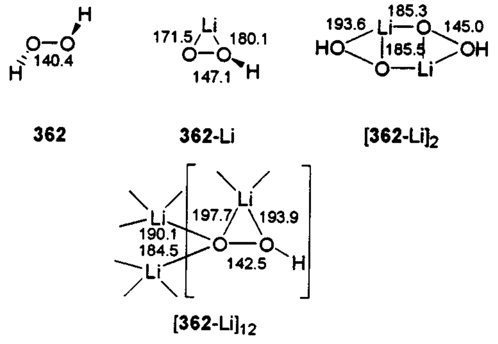


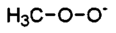
Figure 1. (A) Crystal structure of $[LiOO^tBu]_{12}$ (hydrogen atoms are omitted for clarity). (B) Asymmetric unit of $[LiOO^tBu]_{12}$ with the bonds to the Li^+ neighbors. Significant bond lengths: O1—O2, 147.5(3) pm; O3—O4, 147.7(3) pm. (Reprinted with permission from ref 247. Copyright 1996 Wiley-VCH Verlag GmbH.)

Scheme 106. HF/6-31+G(d) 5D Bond Lengths [pm] of 362 and the Lithiated 362-Li, [362-Li]$_2$, and [362-Li]$_{12}$



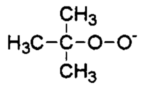
To also include the whole model dodecamer [**362**-Li]$_{12}$ into the calculations, a comparatively low theoretical level (HF/6-31+G(d)5D) had to be used.[247] The O—O bond length in the nonlithiated HO—OH **362** amounts to 140.4 pm. In the lithiated monomer **362**—Li, LiO—OH elongates to 147.1 pm, while it is reduced to 145.0 pm in the dimer [**362**—Li]$_2$ and to 142.5 pm in the dodecamer [**362**—Li]$_{12}$; see Scheme 106. Almost equal O—O bond lengths were also found experimentally in the dodecamer $[LiOO^tBu]_{12}$ (147.5(3) and 147.7(3) pm) and for the mean value of HO—OR bonds in crystals (146.5 pm).[132] These results suggest that the additional stabilization of the negative charge at the anionic oxygen atoms of [**362**-Li]$_2$ and [**362**-Li]$_{12}$ ([LiOO^{t}Bu]$_{12}$) by the lithium cation(s) of one (two) further LiO−OH (LiOO^{t}Bu) molecules is responsible for the O−O bond length reduction in the aggregates as compared to the monomer. It would be interesting to prove experimentally the longer O−O bond in a monomeric LiOO^{t}Bu.

The behavior of [LiOO^{t}Bu]$_{12}$ was also studied in the mass spectrometer.[248] It shows signals of mixed oligomeric (^{t}BuOLi)$_m$(^{t}BuOOLi)$_n$Li$^+$ ($m + n = 1{-}8$) cluster ions, which are due to formal losses of oxygen atoms from (^{t}BuOOLi)$_{m+n}$Li$^+$ ions. Therefore it was of interest to know about the mechanistic origin of the formal O atom expulsion. Does it reflect the oxenoid character of LiOO^{t}Bu within the cluster ions? The loss of an oxygen atom is rather endothermic (ca. 94 kcal mol^{-1}) for the model reaction $HOO^- \rightarrow HO^- + {}^1O$, and it is still quite unfavorable ($\Delta H_r = 49$ kcal mol^{-1}) if a spin-forbidden generation of triplet oxygen atoms (^{3}O) is assumed.[249] Thus the question arises as to whether a unimolecular gas-phase reaction is feasible. Does the metal ion support the elimination of oxygen atoms? If the formal loss of oxygen atoms does not occur as a unimolecular gas-phase reaction, how are the corresponding ions formed? To answer these questions, first the decomposition of the metastable methylperoxy anion **395** and the *tert*-butylperoxy anion **396** were studied. They did not give an indication for the oxenoid character in the metastable and the collision induced fragmentations of these base anions.



$H_3C{-}O{-}O^-$

395

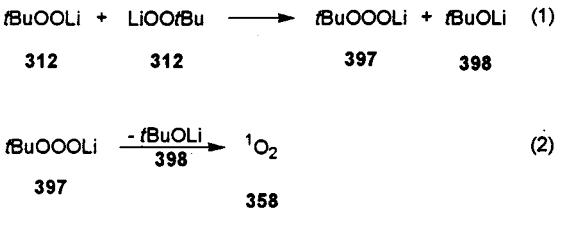


$H_3C{-}C(CH_3)_2{-}O{-}O^-$

396

Loss of oxygen atoms was also excluded for the formation of the cluster ions from [LiOOtBu]$_{12}$. Rather, the cluster ions must be due to thermal decomposition of the solid [LiOOtBu]$_{12}$ crystals, and this makes it plausible to assume that molecular oxygen is generated instead of oxygen atoms. The mechanism would correspond to an "eliminative dimerization" (see Scheme 107), as similarly observed in the case of two carbenoids (see section 1.2.4) and two nitrenoids (see section 2.3).

Scheme 107. "Eliminative Dimerization" of Two Lithium-*tert*-butylperoxides 312 To Give $^1O_2$ 358



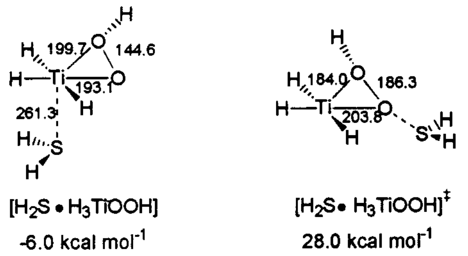
In reaction 1, two molecules of **312** form *tert*-butyltrioxyllithium **397** and lithium *tert*-butanolate **398**; in the second step, **397** eliminates **398** and forms $^1O_2$ **358**. The latter reaction would be analogous to the facile formation of $^1O_2$ **358** from Ti(O^{t}Bu)$_4$ **357** and ^{t}BuOOH **343** via the trioxide **368**; see Scheme 95. The pathways outlined in Scheme 107 are also in agreement with thermochemical results. As mentioned above, the model reaction $H{-}O{-}O^- \rightarrow OH^- + {}^1O$ is endothermic by 94 kcal mol^{-1}. In contrast, formation of $^1O_2$ from 2 HOO$^-$ is essentially thermoneutral: 1.4 kcal mol^{-1}. For the reaction $LiOOH \rightarrow LiOH + {}^1O$, ΔH_r amounts to 84.1 kcal mol^{-1}, while the reaction of 2 LiOOH to give 2 LiOH + $^1O_2$ is even exothermic ($\Delta H_r = -16.3$ kcal mol^{-1}).[248]

In conclusion, the α-elimination of oxenoids to give oxygen atoms is energetically very unfavorable, as is the formation of nonstabilized carbenes from carbenoids (see section 1.3). At higher temperatures (130 °C in the mass spectrometer), however, two LiOOR oxenoid molecules react with each other to give $^1O_2$ in a bimolecular reaction ("eliminative dimerization"). This is also the case for NaOOR and X$_3$TiOOR oxenoids, as indicated earlier.

3.3.2. Ti-, Hf-, V-, Fe-Oxenoids

Because of the importance of the Sharpless epoxidation it is not surprising that titanium peroxides and their reaction with olefins quickly became the subject of theoretical investigations. Jørgensen, Hoffmann et al. performed an extended Hückel study of the Sharpless reaction and came to the conclusion that a spiro approach of the alkene part of the allylic alcohol at the η^2-bridged peroxygen is most favorable,[250] as proposed by Finn and Sharpless; see formula **346** in section 3.2.2.[210,251] More recently, Wu et al.[252] performed density functional studies on the stereocontrol of the Sharpless expoxidation which led to a slightly modified Sharpless model. Jørgensen also calculated the reaction of H$_2$S with H$_3$TiOOH first to the complex H$_2$S·H$_3$TiOOH and then via the transition state [H$_2$S·H$_3$TiOOH]‡ to the product complex H$_2$SO·H$_3$TiOH. The structures of the complex H$_2$S·H$_3$TiOOH and of the transtion state [H$_2$S·H$_3$TiOOH]‡ together with the energies relative to H$_2$S + H$_3$TiOOH are shown in Scheme 108.[245]

Scheme 108. MP2/6-32G(d) Relative Energies [kcal mol^{-1}] and Bond Lengths [pm] of H$_2$S·H$_3$TiOOH and [H$_2$S·H$_3$TiOOH]‡



As in the case of the oxidation of H$_2$S with LiOOH (Scheme 105), H$_2$S migrates in the transition state [H$_2$S·H$_3$TiOOH]‡ into the O−O axis of H$_3$TiOOH, thereby lengthening O−O from 144.6 to 186.3 pm and shortening the bridging Ti−O bond from 199.7 to 184.0 pm.

Finally, a theoretical study has to be mentioned in which the authors investigated the reaction of *each of the two* hydroperoxide oxygen atoms O^1 and O^2 of (R$_3$Si-O-)$_3$Ti-O^1-O^2-H·CH$_3$OH with ethene.[253] The calculations are of interest because it was proposed that it is O^2 which attacks the olefin in such reactions and

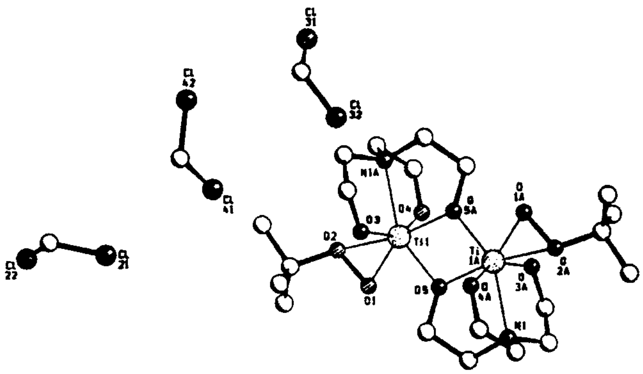


Figure 2. Crystal structure of [((η^2-*tert*-butylperoxo)-titanatrane)$_2$·3dichloromethane] (**399**)$_2$·3CH$_2$Cl$_2$. (Reprinted with permission from ref 255. Copyright 1996 American Chemical Society.)

not the oxenoid O^1 atom.[254] The calculations give a straightforward answer: the transition state energy for the transfer of O^1 amounts to $\Delta E = 11.9$ kcal mol^{-1}, while it is $\Delta E = 32.0$ kcal mol^{-1} for O^2. It would have been highly surprising if a titanium peroxide (and any other metal peroxide) would not react preferentially in an *oxenoid* manner, i.e., with transfer of *O1* onto a nucleophile.

The first solid state structure of a titanium peroxide was published by Boche et al.:[255] [((η^2-*tert*-butylperoxo)titanatrane)$_2$·3dichloromethane] (**399**)$_2$·3CH$_2$Cl$_2$; see Figure 2.

The CH$_2$Cl$_2$ molecules are independent of the (η^2-*tert*-butylperoxo)titanatrane dimers (**399**)$_2$.

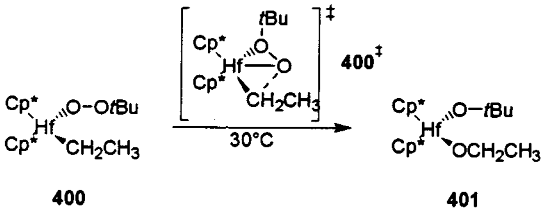
The bonding around Ti1 shows the η^2-coordination of the anionic O1 (Ti1−O1 191.3(3) pm) and the neutral O2 (Ti1−O2 226.9(2) pm) peroxide oxygen atoms. The bond to N1A amounts to 229.9(3) pm, while the bonds to O3 (185.0(3) pm) and O4 (188.2(3) pm) are shorter than those to the bridging O5 (199.4(2) pm) and O5A (204.8(2) pm). The O−O bond length (146.9(3) pm) is close to the mean value of the O−O bonds in 29 HOOR (146.5 pm) and 14 HOOH (145.3 pm) molecules in crystals.[132] The mean value of the O−O bond length in 18 species of the type η^1-MOOR is 146.7 pm.[132]

The η^2-coordination of Ti by the peroxide oxygen atoms as found in (**399**)$_2$·3CH$_2$Cl$_2$ supports the theoretical investigations mentioned above. The O−O bond length, however, is usually calculated to be longer than that in the crystals of (**399**)$_2$·3CH$_2$Cl$_2$: (Ti(OCH$_2$)$_2$(η^2-OOCH$_3$)(OCH$_2$CH=CH$_2$)(OH$_2$), 156.6 pm;[252a] Ti(η^2-OOH)(OH)$_3$, 156.2 (149.3) pm;[252b] Ti(η^2-OOH)(OH)$_3$, 149.2 pm.[190] The O−O bond is only calculated to be "short" in the complex H$_2$S·H$_3$TiOOH (144.6 pm); see Scheme 108. The formation of the *dimer* (**399**)$_2$·3CH$_2$Cl$_2$ in the crystals could explain its relatively short O−O bond if compared to the calculations of the O−O bond lengths in most of the monomers as outlined above, a situation which corresponds to monomeric LiOOH and its aggregates; see Scheme 106.

(**399**)$_2$·3CH$_2$Cl$_2$ is an excellent oxidant: it transforms organolithium compounds RLi into the corresponding alcoholates (phenolates) ROLi (compare with Table 24 in section 3.2.2), sulfides to sulfoxides, and amines to hydroxylamines.[255]

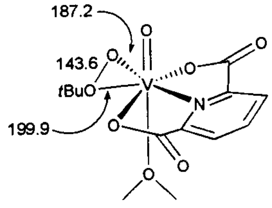
The crystal structure of a hafnium-alkyl peroxide, namely that of di-(pentamethylcyclopentadienyl)-(ethyl)-hafnium-*tert*-butyl peroxide **400**, was published by Bercaw et al.;[256] see Scheme 109.

Scheme 109. Transformation of the Hafnium Peroxide 400 at 30 °C in the Dialkoxide 401



Compound **400** does not show η^2-coordination of the peroxide oxygen atoms at the metal, probably because of sterical hindrance. This could be (one of) the reason(s) why the ethyl group in **400** is not oxidized, at least not at 0 °C in acetone. Warming to 30 °C, however, leads to migration of the ethyl group toward the peroxide oxygen atom and formation of the dialkoxide **401**. The η^2-coordination as found in the case of titanium as well as lithium peroxides (Figures 1 and 2) suggests a similar "metal assistance" of the oxidation also in the case of **400** (see the likely transition state **400**‡).

Vanadium^V compounds are also excellent catalysts for oxidation reactions.[228] It is therefore not surprising that it was a V^V-compound which first disclosed the η^2-structure of the peroxide moiety: vanadium-dipicolinato-*tert*-butylperoxide **402**.[257]



402

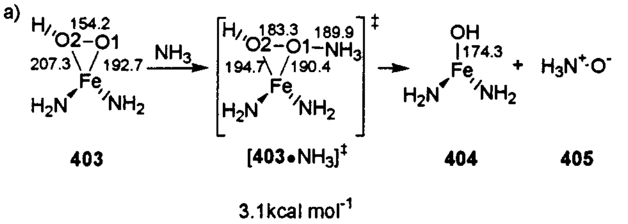
The anionic oxygen has a V−O bond length of 187.2 pm, while the other peroxide oxygen atom is 199.9 pm away from vanadium. The O−O bond is comparatively short (143.6 pm).

The mechanism of the oxygen atom transfer to ammonia from a diamidoiron(III) hydroperoxide (**403**) was calculated by Bach, Schlegel et al.;[244] see Scheme 110.

The calculations show first that a bridged structure **403** is also, in the case of iron(III)-peroxides, the most favorable one. As expected from earlier calculations of related transition states, the O−O bond is lengthened in [**403**·NH$_3$]‡. The intrinsic reactivity of **403** toward NH$_3$ is greater than that of LiOOH (see also Scheme 104) and of a peracid.[244] Thus, compounds of the type **403** (and not only iron-oxo compounds) are excellent oxygen donors which is in agreement with the results outlined in Scheme 101.

In conclusion, oxenoids of the type M−O−X, M = various metal ions, X = mainly OH(OR), behave as compounds which are related to carbenoids M−CH$_2$−X and nitrenoids M−NH−X. Calculations show a favorable bridging of the O−X bond by M which is in

Scheme 110. Optimized Geometries of 403 and the Transition State Structure [403·NH$_3$]‡ for Oxygen Atom Transfer from 403 to Ammonia NH$_3$: (a) Optimized Geometries and Energies at the MP2/3-21G Level; (b) Geometries Optimized at MP2/WH and CASSCF(7,7)/3-21G (in Parentheses) and Energy of the Transition State [403·NH$_3$]‡ at the MP2/WH Level; Energies [kcal mol^{-1}]; Bond Lengths [pm]



b)

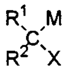
	Fe-O1	Fe-O2	O-O	N-O	[403 • NH$_3$]‡
403	189.2	214.8	150.0	-	15.6
	(192.1)	(206.1)	(163.1)	-	-

agreement with a metal assistance of the O−X bond cleavage. The O−X bond is weakened by metalation. The bridging of O−X is found in the crystal structures of the Li-, Ti-, and V-peroxides [**362**−Li]$_{12}$, (**399**)$_2$·3CH$_2$Cl$_2$, and **402**, respectively. Calculation of reactions with nucleophiles are in agreement with the electrophilic character of the anionic (oxenoid) peroxide oxygen atom (and not with the transfer of the neutral oxygen atom!). The reaction occurs in an S$_N$2-type fashion with retention of configuration at the nucleophile (e.g., RLi), and without electron transfer. α-Elimination of MX from M−O−X to give singlet (as well as triplet) oxygen atoms (^{1}O and ^{3}O, respectively) seems impossible for energetic reasons. The reaction of two molecules M−O−X with each other to give $^1O_2$ and 2 MX, however, is energetically feasable, which is in agreement with the formation of $^1O_2$ in the presence of metal compounds and peroxides (hydrogen peroxide) or from Li(Na)OOR at elevated temperatures. Such "eliminative dimerizations" are also known from carbenoids and nitrenoids.

4. Final Conclusions

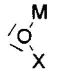
It is evident from the sections on carbenoids **23**, nitrenoids **24**, and oxenoids **25** that these "anions" have many properties in common, e.g., they are very electrophilic. Carbenoids **23** react with nucleophiles as, e.g., C−H, C−C, and C═C bonds, and all of them react with a wide range of organometallic compounds RM. Especially noteworthy is the "eliminative dimerization" of two carbenoids **23** (nitrenoids **24**, oxenoids **25**) in which case one molecule of each species reacts as a nucleophile and the other one as an electrophile followed by a second elimination of MX. α-Elimination of MX to give carbenes from **23** and nitrenes from **24** is only observed if the respective carbene or nitrene is stabilized by donor substituents, and/or MX is an excellent leaving group. In the case of the oxenoids **25**, α-elimination to give ^{1}O (or ^{3}O) is unknown.

Quantum chemical calculations support the electrophilic nature of **23**−**25**. In comparison to the nonmetalated species, **23**−**25** have an elongated C(N,O)−X bond, and the nucleophiles approach the central atom along the C(N,O)−X axis in an S$_N$2-type geometry. In most of the cases the C(N,O)−X bond is bridged by M$^+$ which leads to a metal assisted ionization of the C−X bond. The bond elongation, especially in the cases of the carbenoid C−X and the nitrenoid N−X bonds, is well documented by X-ray crystal structure investigations. A natural bond analysis shows that the σ-orbitals of the C(N,O)−X bonds are energetically raised and the corresponding σ* orbitals lowered if compared with those in the protonated compounds, both in agreement with the facile reactions of **23**−**25** with nucleophiles. Furthermore, the lowered σ^*_{C-X} orbital energies in the carbenoids **23** lead to an understanding of the deshielding of the carbenoid carbon atoms in the ^{13}C NMR spectra of **23**, which result mainly from the energetically very favorable interaction of the high lying C−M bond orbital (with large coefficients at the carbon atom) with the lowered σ^*_{C-X} orbital (also with larger coefficients at the carbon atom).

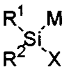


23

24



25



404

M = metal; X = leaving group

Thus, a metal *and* a leaving group, bonded simultaneously to a C, N, or O atom, gives rise to the characteristic properties of carbenoids **23**, nitrenoids **24**, and oxenoids **25**. In a simple picture, this is due to the high s-character of the C(N,O) atomic orbital in the C(N,O)−M bond, as a consequence of which the C(N,O) atomic orbital in the C(N,O)−X bond adopts high p-character.

Not surprisingly, similar properties as shown for **23**−**25** have recently been found in silenyloids of the structural type **404**.[258]

5. Acknowlegdments

The basis for this article was laid in the investigations on carbenoids, nitrenoids, and oxenoids of my co-workers C. Boie, M. Bold, F. Bosold, F. Haller, K. Harms, H. Hermann, C. Hilf, M. Husemann, W. Kleemiss, A. Kühn, B. Ledig, J. C. W. Lohrenz, M. Marsch, C. Meier, K. Möbus, M. Möller, A. Müller, A. Opel, M. Schimeczek, N. Schmiedeberg, F. Schubert, and P. Zulauf and in the cooperations with colleagues H. Ahlbrecht, Universität Giessen, J. Cioslowski, Florida State University, Tallahassee, W. Koch, Technische Universität Berlin, and H.-U. Wagner, Universität München. It has been a great pleasure and honor for me to be involved in these common scientific studies. The drawings were made by Sven Kannenberg. The text was written by Mrs. Ingrid Bublys, who did not always have an easy job. I am very grateful to all of them. Special thanks go to the Deutsche Forschungsgemeinschaft, Sonderforschungsbereich 260, and to the Fonds der Chemischen Industrie. Without their continuous financial support, the insights revealed here could not have been gained.

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