

Reactivity of 13,13-Dibromo-2,4,9,11-tetraoxadispiro[5.0.5.1]tridecane toward Organolithiums: Remarkable Resistance to the DMS Rearrangement[†]

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Reactions of dibromocyclopropane **2a**, containing two spiro-fused 1,3-dioxane rings, with MeLi gave only the methylation products **8** and **9** even at elevated temperatures. In contrast, the cyclohexane analogue **2b** treated with MeLi underwent a smooth rearrangement to bicyclo[1.1.0]butane **11b** at -78 , -10 , or $+35$ °C. Treatment of **2a** with PhLi gave the α -Ph anion **13** as the only product, which underwent smooth methylation with MeI to give **14**. Under the same conditions, **2b** with PhLi gave bicyclo[1.1.0]butane **11b** accompanied by bromophenyl derivative **8b**. Treatment of either dibromide with *t*-BuLi gave a mixture of products including debrominated cyclopropanes **12**. Experimental results were augmented with DFT calculations for salts **23** and MP2//DFT-level calculations for carbenes **22**. They demonstrated a higher stability of the dioxane α -bromo anion with respect to α -elimination by 4.8 kcal/mol and also a lower tendency of the carbene **22a** to undergo rearrangement by 4.0 kcal/mol than the cyclohexane analogues. These differences have been attributed to the inductive effect of the four oxygen atoms, which results in lower LUMO energy, the higher positive charge at the carbenic center, and the overall more electrophilic character of carbene **22a** as compared to the cyclohexane derivative **22b**. The rearrangement of carbenes **22** to the corresponding allenes **1**, the thermodynamic products, requires a higher activation energy ΔG^\ddagger_{298} by 4.2 kcal/mol for dioxane and 6.4 kcal/mol for cyclohexane derivatives than for the formation of the bicyclo[1.1.0]butanes **11**. The ΔG^\ddagger_{298} for intramolecular insertions to the C–H bond is low and calculated as 6.0 kcal/mol for dioxane **22a** and 2.0 kcal/mol for the formation of cyclohexane **22b**.

Introduction

The Doering–Moore–Skattebøl (DMS) method^{1–3} represents a general and convenient route to substituted allenes **I** (Figure 1).^{4,5} The reaction involves a rearrangement of cyclopropylidene **II**, which typically is generated from the corresponding dibromocyclopropane **III** by lithium–halogen exchange followed by α -elimination of the bromide ion from **IV**.⁶ The rearrangement of the parent carbene has been the subject of detailed experi-

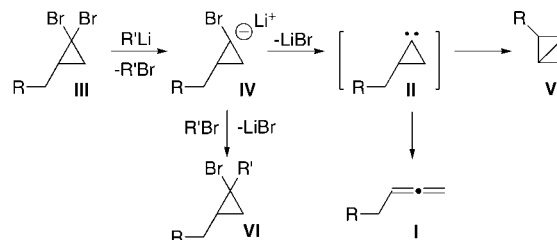


FIGURE 1. General reaction pathways for transformation of *gem*-dibromocyclopropanes.

mental and theoretical investigations,^{7–9} which conclude that the reaction is generally characterized by a low activation energy. The formation of allenes **I** from dibromocyclopropanes **III** often competes with the formation of bicyclo[1.1.0]butanes

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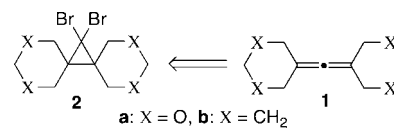
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(BCB) **V**, which are formed in quantities ranging from traces to exclusive products.^{10–14} This competition between the two pathways for rearrangement of **II** is governed by the substituents, which exert steric strain,^{8,15} conformational change,¹⁶ or rarely electronic effects.^{13,15,17}

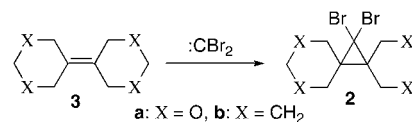
The formation of carbene **II** (or a carbenoid) by α -elimination from the initial α -bromo anion **IV** is generally fast at temperatures above $-50\text{ }^\circ\text{C}$,¹⁸ which are typical conditions for the DMS rearrangement.³ In rare cases, the α -elimination step is slow and the anion is alkylated by an alkyl halide generated in a lithium–halogen exchange reaction to form **VI** in quantities ranging from 2 to 13%.^{19–22} An electron-withdrawing heteroatom is usually present in these cases, and the alkylation has been attributed to the stability of the bromolithium intermediate **IV** resulting from intramolecular coordination with oxygen^{21,23,24} or sulfur.²⁰ In other cases, an alkyl halide was added to the reaction mixture at temperatures $< -70\text{ }^\circ\text{C}$ to avoid the DMS rearrangement and to obtain the desired alkylation product.^{25,26}

In the course of our work on functionalized spirocyclic systems, we focused on protected tertakis(hydroxymethyl)allene **1a** and envisioned its formation by the DMS rearrangement of the corresponding dibromocyclopropane **2a** (Scheme 1). This expectation was based on the reported efficient rearrangements of the cyclopropyl²⁷ and cyclobutyl²⁸ analogues of **2a** to the

SCHEME 1



SCHEME 2



corresponding allenes. Surprisingly, the precursor **2a** demonstrated a significant resistance to the rearrangement, and neither desired allene **1a** nor other products of rearrangement could be detected directly. For a better understanding of this result, we also investigated a similar reaction with the cyclohexane analogue **2b**.

Here, we report the preparation of cyclopropanes **2a** and **2b** and their reactions with MeLi, PhLi, and *t*-BuLi. The experimental data presented in the Results were augmented with computational analysis and constitute the basis for mechanistic considerations presented in the Discussion.

Results

Synthesis of Dibromocyclopropanes 2. The synthesis of dibromide **2** was accomplished by dibromocarbene addition to the corresponding alkene **3** (Scheme 2). Cyclopropanation of 5,5'-bi[1,3-dioxanylidene] (**3a**) under PTC conditions²⁹ overnight resulted in a mixture of starting material and dibromide **2a** in a 2:3 ratio (determined by ¹H NMR), and the product was isolated in 19% yield. A prolonged reaction time did not change the ratio. However, nearly complete conversion of **3a** was achieved after several additions of more base and catalyst, and the product was isolated in about 35% yield after 3 days of stirring. In contrast, the cyclopropanation reaction of olefin **3b** under identical conditions went to completion overnight, and dibromide **2b** was obtained in 55% yield. In an attempt to improve the yield of **2a**, PhHgCBr₃ was used as the source of dibromocarbene recommended for weakly nucleophilic olefins.³⁰ Thus, a reaction of **3a** with 1.5 equiv of PhHgCBr₃ proceeded to about 50% conversion, and cyclopropane **2a** was isolated in 28% yield.

The preparation of olefin **3a** was reported in the literature as a component of a mixture or a sole product of a reaction between 5-bromo-5-nitro[1,3]dioxane (**4**) and EtSnA³¹ or the lithium salt of 5-nitro[1,3]dioxane³² (**5**) in DMSO (Scheme 3). The reported 80% yield of **3a** could not be reproduced despite our efforts. Numerous reactions closely following the literature procedure³¹ and using either carefully dried reagents under strictly anaerobic atmosphere or just reagent grade DMSO gave the same and

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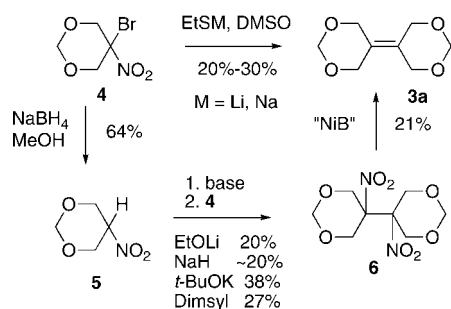
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SCHEME 3



consistent results of 20%–30% yield. We noticed, however, low mass recovery from the reaction mixture, which was presumably due to partial water solubility of olefin **3a** or products of dioxane ring opening. Most organic material was recovered from the aqueous workup in the first three extractions with benzene, and additional extractions or even continuous extraction gave only traces of organic products. Reducing the volume of originally³¹ used DMSO by substituting approximately 50% of it with benzene did not affect the yield of **3a**.

While optimizing the single-step preparation of **3a**, we were simultaneously searching for an alternative method for its preparation. In particular, we focused on reduction of vicinal dinitroalkanes with "NiB", which was reported to give good yields for similar dioxane derivatives.³³ Unfortunately, the reduction of the dinitro derivative **6** under these conditions³³ gave consistently low yields of about 20% of the desired olefin **3a**. The preparation of **6** followed a modified literature procedure³² and involved a reaction of nitrodioxane **5** and bromide **4**. Thus, a lithium salt of **5**³² was reacted with **4** to give the coupling product **6** in a 20% isolated yield, while 75% yield was reported in the literature.³² Using the sodium salt of **5**, prepared in situ with NaH, did not improve the yield of **6**. Higher yields were obtained using either *t*-BuOK in DMSO³⁴ (38%) or Li Dimsyl³⁵ (27%) as bases. The K₂CO₃/PTC method, reported for coupling of nitropropane,³⁶ gave only traces (<5% by GC) of the coupling product **6** and the unreacted starting material.

Bicyclohexylidene (**3b**) was initially obtained according to a literature procedure for McMurry coupling of cyclohexanone.³⁷ Since this method proved to be difficult and impractical for multigram scale preparations, sufficient amounts of **3b** were obtained in four straightforward steps and 35% overall yield from cyclohexanone according to a literature procedure.³⁸

Reactions with Organolithiums. Dibromocyclopropanes **2** were treated with 1.1–6 equiv of MeLi, *t*-BuLi, or PhLi at –78, –10, or 35 °C (boiling ether). After 2 h at the same or elevated temperature, the reaction mixtures were quenched with water and the resulting crude mixtures of products were investigated by NMR and MS techniques. Some of the mixtures were partially separated, and several products were isolated in the pure form and analyzed. The collected analytical data supported

with DFT calculations (vide infra) allowed for structural assignments of the individual products. Results for individual reactions and distribution of products are shown in Table 1.

The dioxane derivative **2a** showed limited solubility in ether at the temperatures below 0 °C, and most of its reactions were run at –10 °C at low concentrations (~10 mM). For instance, **2a** partially precipitated from 8 mM solutions at –78 °C. Experiments with both dibromides demonstrated that the lithium-halogen exchange reactions with 1.1 equiv of MeLi were inefficient for the 10 mM solutions of **2**, and most (~90%) of the starting material was recovered contaminated with <5% of mono bromide **7**.

Reactions of dioxane derivative **2a** with 2.2 equiv of MeLi at –10 °C gave the monobromo derivative **7a** as the main product accompanied by small amounts of the bromomethyl product **8a** (R = Me), both isolated in a combined yield of ~95% (entry 1). The same reaction run in hot ether (entry 2) did not give the protonated product **7a**, and instead the dimethyl derivative **9a** and bromo methyl **8a** (R = Me) were formed in equal amounts as the sole products. This suggests that the α -bromocarbanion derived from **2a** in part reacts slowly with MeBr at ambient temperature and, in part, is protonated during workup. Some support for this scenario was provided by the next experiment (entry 3) in which **2a** was treated first with 2.2 equiv of MeLi, and after 5 min excess MeI was added at –10 °C. No protonation product **7a** was detected, and the bromo methyl **8a** (R = Me) and dimethyl **9a** were the main products formed in a 3:2 ratio. The reaction mixture also contained about 20% of unreacted dibromide **2a**, which suggests that 5 min is insufficient time for complete lithium–halogen exchange and that a reaction between MeLi and MeI is faster than lithiation of **2a**. With higher MeLi to **2a** ratios, the dimethylated product **9a** dominated and traces of another product, presumably **10a** (R = Me), were occasionally detected.

Attempts at separation of the complex mixtures into individual components by either chromatographic methods or recrystallization were largely unsuccessful. Instead, reaction products were identified by NMR and MS techniques, and the formation of **1a** or possible bicyclo[1.1.0]butane **11a** in quantities >1% can be excluded. NMR analysis showed that all products have high molecular symmetry, and the olefinic ¹H or ¹³C signals were completely absent in either crude or chromatographically isolated mixtures of products.

Initial experiments with MeLi indicated that methylation with MeBr of the transient α -bromocarbanion derived from **2a** is faster than the loss of bromide ion and rearrangement. To avoid the presence of the strongly electrophilic MeBr in the reaction mixture, we investigated reactions of **2a** with PhLi and *t*-BuLi. The first reagent generates the nonelectrophilic PhBr in the lithium–halogen exchange with **2a**, while *t*-BuLi gives *t*-BuBr, which is quickly destroyed by excess *t*-BuLi.³⁹

Reactions of **2a** with PhLi gave an unexpected result. At a low PhLi/**2a** ratio (entry 4), half of the starting dibromide reacted giving equal amounts of the protonated anion (**7a**) and the product of phenylation (!) **10a** (R = Ph), according to GC/MS analysis. When 5 equiv of PhLi was used (entry 5), the sole product was **10a** (R = Ph) isolated in 63% yield. GC/MS analysis demonstrated that the reaction was complete after 10 min at –10 °C, and no intermediates were observed. Addition of PhLi to **2a** in boiling ether (35 °C) had little effect on the reaction outcome, and **10a** (R = Ph) was formed cleanly as the

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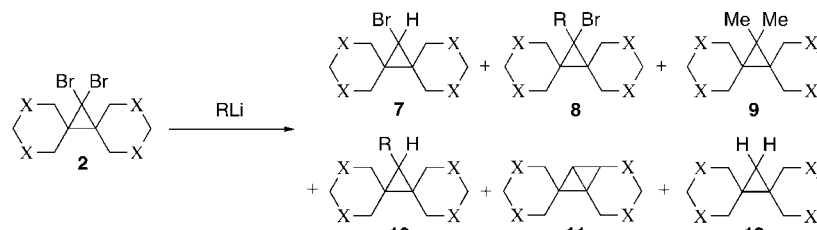
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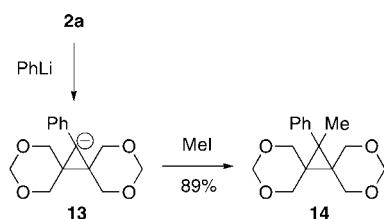
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TABLE 1. Product Distribution in Reactions of Dibromocyclopropanes **2** with RLi


entry	R	R-Li (equiv)	T (°C)	2	7	8	9	10	11	12
1	2a	Me	2.2	-10 → rt		85 ^a	10 ^a			
2	X = O	Me	2.2	35			45 ^b			
3		Me	2.2 + MeI	-10 → rt	20 ^a		45 ^a			
4		Ph	2.5	-10 → rt	55 ^b	20 ^b		20 ^b		
5		Ph	5	-10 → rt or 36				100 or 63 ^c		
6		<i>t</i> -Bu	1.1	-80 → -10	50 ^b	50 ^b				
7		<i>t</i> -Bu	5	-10				7 ^c		30 ^c
8	2b	Me	5.3	-80 → -10, or -10 → rt, or 35					~100 ^c	
9	X = CH ₂	Ph	2.5	-10 → rt			60 ^a			40 ^a
10		Ph	2.5	35			40 ^{b,d}			60 ^b
11		<i>t</i> -Bu	2.5	-80 → -10		30 ^{a,e}	10 ^b			80 ^b
12		<i>t</i> -Bu	2.5	-80		50 ^{a,e}				60 ^a
13		<i>t</i> -Bu	5	-80 → -10						25 ^a
										80 ^a
										20 ^a

^a From NMR ratio of products in isolated mixture. ^b From GC/MS ratio of products in the crude mixture. ^c Isolated yield. ^d Diene **19** was isolated in 37% yield and 90% purity. ^e No **7a** was observed at 3× higher concentration of **2b** in ether.

SCHEME 4



sole product. To demonstrate that α -phenylcarbanion **13** is involved in the formation of **10a** (R = Ph), MeI was added to the reaction mixture before quenching with water. In this case, the methyl derivative **14** was formed as the only product, which was isolated in 89% yield (Scheme 4).

Reactions of **2a** with *t*-BuLi were generally less clean than those with MeLi or PhLi. Thus, a reaction of **2a** with 1.1 equiv of *t*-BuLi gave a mixture consisting mostly of the starting material and monobromide **7a** in a 1:1 ratio (entry 6). When **2a** was treated with 5 equiv of *t*-BuLi at -10°C , all starting dibromide **2a** was consumed, and the isolated reaction mixture (>70% of the theoretical amount) consisted of three main products (entry 7). Two of them were identified as *tert*-butyl derivative **10a** (R = *t*-Bu) and the debrominated product **12a** in a ratio of about 2:5 by GC/MS or 1:4 by NMR. The mixture was partially separated giving the first fraction containing mainly **10a** (R = *t*-Bu), the second fraction containing mainly **12a**, and the third fraction as a mixture of **12a** and the unknown component(s) in a 2:1 ratio. Analysis of the NMR spectra of the last fraction revealed that the unknown component(s) had olefinic signals in the range of 111–114 and about 142 ppm, in addition to the aliphatic signals in the high field. The olefinic byproduct could be formed by attack of *t*-BuLi on the acetal group of the dioxane ring. However, their formation by a reaction of *t*-BuLi with the transient bicyclo[1.1.0]butane **11a** cannot be excluded. Monobromide **8a** (R = *t*-Bu) was never observed in these reactions by GC/MS or by NMR methods.

When the same reaction was conducted at -80°C instead of -10°C using a total of 6 equiv of *t*-BuLi, GC/MS and NMR analysis showed significantly less of the unidentified byproduct. Both **10a** and **12a** were isolated chromatographically in 6% and 27% yields, respectively, and independently characterized.

In all reactions of **2a** with RLi, mass recovery of organic products was high, often close to the theoretical amount. No cyclopropylidene rearrangement products, neither allene **1a** nor bicyclo[1.1.0]butane **11a**, were observed directly among the reaction products. Only in reactions with *t*-BuLi at -10°C could **2a** form **11a** as a transient species.

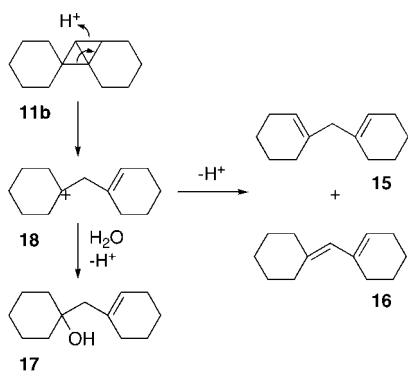
In contrast to the reactivity of **2a**, treatment of the cyclohexane analogue **2b** with organolithium reagents gave bicyclo[1.1.0]butane **11b** as either the exclusive (reactions with MeLi, entry 8) or a significant (reactions with PhLi and *t*-BuLi) product. Also, many of the products observed in reactions of dioxane **2a** with organolithium reagents were not detected in the analogous reactions of **2b**. The ¹³C NMR spectrum of crude freshly prepared **11b** showed no molecular symmetry and no olefinic signals. During chromatographic separation, attempted distillation, or even storage at ambient temperature for over 1 day, **11b** decomposed to form two isomeric olefinic products in a ratio of about 4:1 (NMR). This ratio changed to 9:1 (NMR) upon further chromatographic purification (SiO₂, hexanes). On the basis of NMR and MS analysis, the two olefins were assigned structures **15** (major) and **16** (minor), respectively (Scheme 5). Further support for the assignment was provided by a close match of the NMR spectra with those reported for the two olefins prepared by other routes.^{40,41}

The proposed mechanism for proton-catalyzed ring opening in bicyclo[1.1.0]butane **11b** and the formation of the dienes

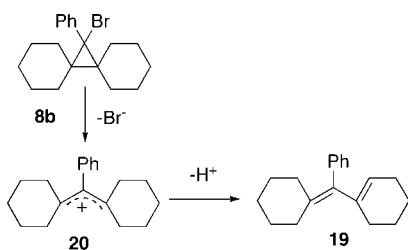
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SCHEME 5



SCHEME 6



shown in Scheme 5 is consistent with literature data for other bicyclo[1.1.0]butanes and the pathways for their ring-opening processes.^{10,42–44} Support for the proposed mechanism is also provided by the occasional isolation of cyclohexanol **17** apparently formed by the hydration of the intermediate cation **18** (Scheme 5).

The reaction of **2b** with PhLi at -10°C (Table 1, entry 9) gave the expected bicyclo[1.1.0]butane **11b** and, surprisingly, phenyl derivative **8b** ($\text{R} = \text{Ph}$) in approximately 2:3 ratio (NMR). The ratio was temperature sensitive, and at higher temperatures more bicyclo[1.1.0]butane **11b** was formed. Thus, the same reaction run at 35°C (Table 1, entry 10) was completed after 10 min, and the **11b/8b** ratio was $\sim 8:1$. Upon attempted chromatographic separation of the crude reaction mixture, the bromide completely rearranged to diene **19**, which was isolated in 37% yield. The observed facile ionization of **8b** ($\text{R} = \text{Ph}$) and the formation of diene **19** is consistent with a recent report of rearrangement of 1-bromo-2,2,3,3-tetramethyl-1-phenylcyclopropane in warm methanol.⁴⁵ An independent experiment demonstrated that bicyclo[1.1.0]butane **11b** is stable to PhLi at ambient temperatures for at least several hours. The ionization of the formally cumylyc bromide **8b** ($\text{R} = \text{Ph}$) permits a 2π electrocyclic cyclopropane ring opening to form the allyl cation **20**, which upon the subsequent elimination of a proton gives the diene **19** (Scheme 6).

Reactions of **2b** with $t\text{-BuLi}$ gave bicyclo[1.1.0]butane **11b** and smaller amounts of debrominated product **12b**. In reactions with low $t\text{-BuLi}/2\text{b}$ ratios, monobromide **7b** was also observed in addition to **11b** and **12b**. The proportions of the products depended on the amounts of the organolithium and reaction temperature, and also varied somewhat from run to run. In one

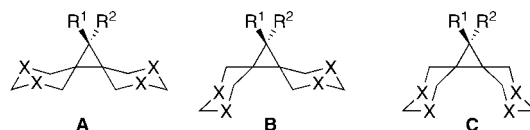


FIGURE 2. Three main conformers of the dioxane and cyclohexane derivatives with $\text{R}^1, \text{R}^2 = \text{H, Me, } t\text{-Bu, Ph}$.

set of experiments with 2.5 equiv of $t\text{-BuLi}$, less bicyclo[1.1.0]butane **11b** was produced and lower **11b/12b** ratio was observed at -80°C (entry 11) than when the reaction was run at -10°C (entry 12). When 5 equiv of $t\text{-BuLi}$ was used (Table 1, entry 13), monobromide **7b** was completely absent, and the mixture contained bicyclo[1.1.0]butane **11b** and debrominated product **12b** as the sole products in about 4:1 ratio. The ratio was practically the same whether the reaction mixture was quenched with cold EtOH at -78°C or poured into EtOH or water at ambient temperature.

Finally, a competition experiment was conducted in which a 1:1 equimolar mixture of dibromocyclopropanes **2a** and **2b** was reacted with 1.1 equiv of MeLi . GC/MS analysis showed that dioxane dibromide **2a** was completely consumed forming the monobromide **7a**, while only about 10% of the cyclohexyl dibromide **2b** was converted to **11b** as evident from GC/MS and ^1H NMR of the crude reaction mixture.

Theoretical Analysis. To better understand the experimental results and to support structural assignment of the observed products, we investigated the formation and rearrangement of several relevant carbenes, and calculated the NMR chemical shifts for selected products at the B3LYP level of theory.

Conformational Analysis. The dioxane and cyclohexane dispiro derivatives can exist in three main conformational forms shown in Figure 2. Calculations at the B3LYP/6-31+G(d,p) level for the dioxane derivatives revealed that thermodynamic stability of the conformers follows the order $\text{B} > \text{A} > \text{C}$, which parallels the trend in their net molecular dipole moments. Conformers of type **A** are less stable than those of type **B** by about 1.0–1.5 kcal/mol, while conformers of type **C** are still less stable by an additional ~ 1 kcal/mol.

Conformers **A** and **B** of the cyclohexane derivatives appear to have similar thermodynamic stability with a conformer of type **A** being slightly favored, e.g., by 0.2 kcal/mol for **12b**. On the basis of these results, calculations of carbene formation and subsequent rearrangement to either **1** or **11** typically involved conformers of type **B** for dioxane derivatives and conformers of type **A** for the cyclohexane analogues. NMR calculations (vide infra) use the relative stability of the conformers to calculate weighted average chemical shifts of selected products. Detailed numerical information is given in the Supporting Information.

Carbene Formation. Gas-phase calculations for anions **21** show that the loss of Br^- ion and the formation of the corresponding carbene **22** is endothermic. For the parent cyclopropylidene **22c**, the endotherm is about 20 kcal/mol (Table 2), and this energy increases by about 3.5 kcal/mol per added cyclohexane unit to 26.8 kcal/mol for **22b**.⁴⁶ In contrast, α -elimination from anion **21d** containing one dioxane ring is more endothermic by about 12 kcal/mol relative to the parent **21c** and by nearly 20 kcal/mol from anion **21a** containing two

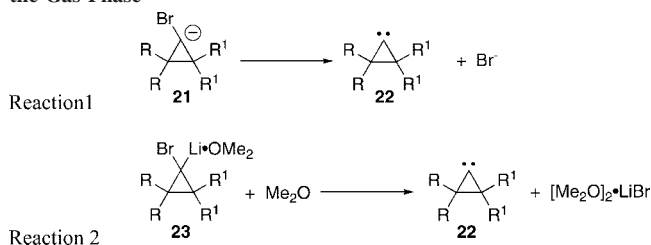
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TABLE 2. Calculated Energies for the Formation of Carbenes in the Gas Phase^a

R	R	R'	R'	Reaction 1		Reaction 2	
				ΔH kcal/mol	ΔG_{298} kcal/mol	ΔH kcal/mol	ΔG_{298} kcal/mol
a				39.3	29.9	26.0 ^b	22.5 ^b
b				26.8	17.9	19.4	17.7
c	H	H	H	19.8	12.1	15.6	15.9
d		H	H	31.7	22.9	21.0 ^b	18.1 ^b
						20.3 ^c	19.6 ^c
e		H	H	23.3	14.4	16.9	15.5

^a B3LYP/6-31+G(d,p) level of theory. ^b The Li⁺ interacts with the ring's oxygen atoms. ^c The Li⁺ does not interact with the ring's oxygen atoms.

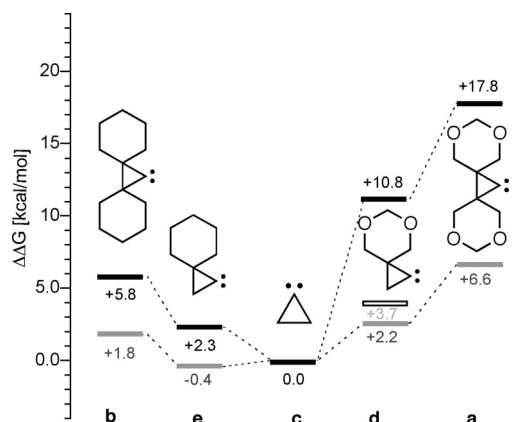
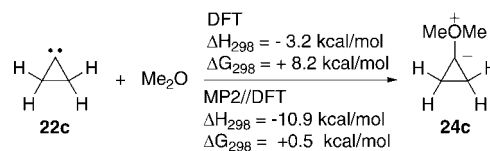


FIGURE 3. Relative energies for the formation of carbene **22** from anion **21** (black, reaction 1) and from salt **23** (gray, reaction 2). The empty bar represents data for **23d** in which Li⁺ is not coordinated to the dioxane ring. For reaction schemes, see Table 2.

dioxane rings. The entropy change in the reaction is about 30 cal/mol·K, which lowers the free energy change by almost 9 kcal/mol. The graphical representation of free energy change in the process is shown in Figure 3.

Salts of the anions **23** in which the lithium ion is coordinated to a molecule of Me₂O are more realistic models for solution processes. Calculations for the formation of carbenes **22b** from **23** revealed a smaller endotherm for the LiBr·2Me₂O complex elimination as compared to the elimination of Br⁻ from **21** (Table 2). The enthalpy of the elimination reaction increases for each added cyclohexane ring relative to the parent **23c** and for **23b** the energy is higher by 3.8 kcal/mol.

SCHEME 7

Addition of dioxane rings to **23c** has a more pronounced effect on the enthalpy of elimination. Thus, the first dioxane ring increases the enthalpy of complex elimination by nearly 5 kcal/mol in **23d**. Intramolecular coordination of the Li⁺ ion by the ring's oxygen atoms in **23d** moderately stabilizes the salt, and consequently, the enthalpy of elimination increases by 0.7 kcal/mol. Addition of the second dioxane ring increases this enthalpy by 5 kcal/mol in **23a** in which the Li⁺ ion is internally coordinated. Free energy change for these reactions is shown graphically in Figure 3. Interestingly, coordination of the Li⁺ ion to dioxane's oxygen atoms decreases the endergonicity of the complex elimination in spite of increased endotherm of the reaction. This is due to lowering of entropy of **23d** by 7 cal/mol·K upon intramolecular coordination of the Li⁺ ion.

The results demonstrate that the dioxane salt **23a** is more stable toward elimination and carbene formation than the cyclohexane analogue **23b** by about 5 kcal/mol.

Stabilization of carbenes by coordination to a molecule of ether appears to be modestly exothermic for cyclopropylidene **22c** forming **24c**, but due to the significant entropy decrease (-38 cal/mol·K) the process is still endergonic at this level of theory (Scheme 7). This small energy gain in stabilization of **22c** is insufficient to offset the 15.6 kcal/mol endotherm of the elimination of the LiBr complex from **23c**, and the whole process is significantly endergonic due to the net negative entropy change. Calculations at the MP2/6-31+G(d,p)//B3LYP/6-31+G(d,p) level with the DFT thermodynamic corrections lower this energy by 7.7 kcal/mol, and the resulting free energy change for the formation of **24c** from carbene **22c** is nearly zero.⁴⁷ This suggests that complex **24c** is in equilibrium with carbene **22c**, and the calculations for the free carbene in gas phase provide a reasonable approximation of the solution reactivity.

The optimized geometry of the parent salt **23c** converged at the C_s point group symmetry (Figure 4). The Me₂O, Li, and Br lie in the symmetry plane, which is orthogonal to the cyclopropane ring. The Me₂O and cyclopropane fragments are connected by the Li⁺ ion, which is also coordinated to the Br atom. The resulting C—Li···OMe₂ and C—Li···Br angles are 171° and 130°, respectively. The Li···OMe₂ and Li—C distances (1.89 Å and 1.96 Å, respectively) found in the parent salt **23c** are approximately constant in the series of salts **23**, while the Br—C and Br···Li distances vary in response to the structural changes.

The C—Br distance, d_{C-Br} , in the parent salt **23c** (2.22 Å) is practically unchanged, and the Br···Li separation (2.44 Å) is shortened by 0.01 Å upon appending the cyclohexane rings. In contrast, the d_{C-Br} decreases by 0.06 Å with simultaneous increase of the Br···Li distance by 0.03 Å upon appending the first dioxane ring in **23d**. Moving the lithium atom toward the dioxane oxygen atoms in **23d** trades the coordination of the cation by the bromine atom ($d_{Li-Br} = 2.94$ Å) for the ring oxygen atom ($d_{Li-O} = 2.14$ Å) and leads to the contraction of

(47) A reliable theoretical description of the stability of a dative bond such as that in **24c** is provided by the MP2 method.

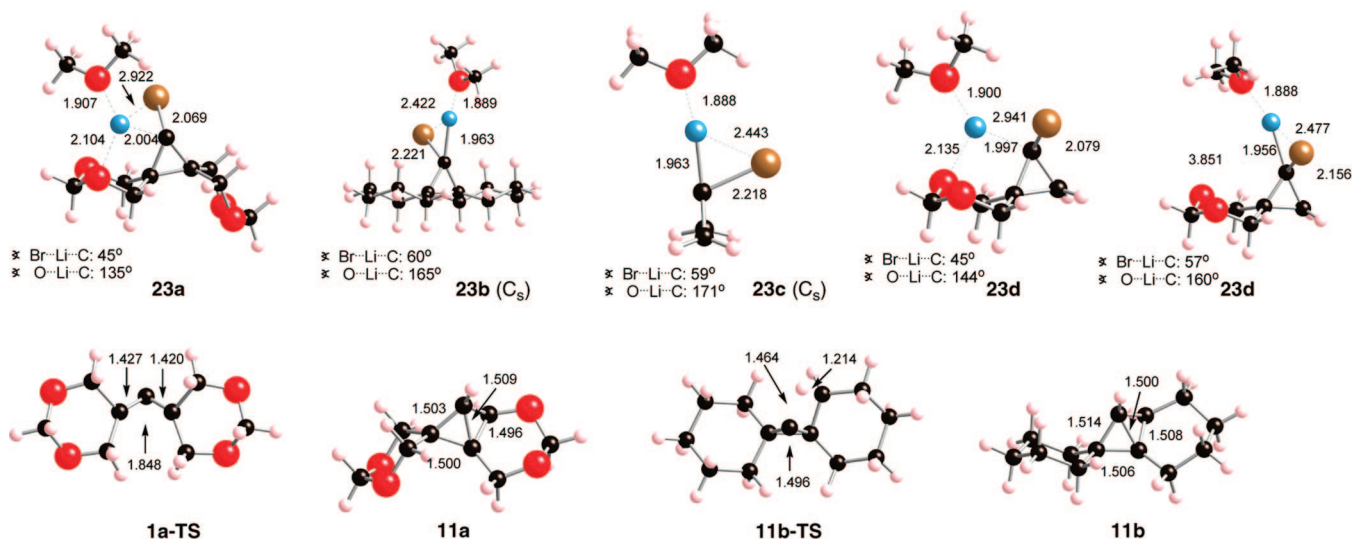


FIGURE 4. Optimized (B3LYP/6-31+G(d,p)) geometries of ground- and transition-state structures for selected molecules with indicated selected interatomic distances and angles.

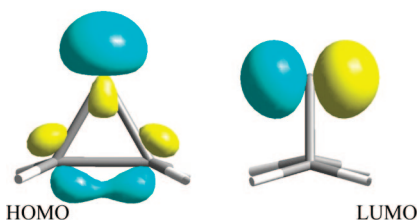


FIGURE 5. Representation of the FMO contours obtained at the B3LYP/6-31+G(d,p) level of theory for the cyclopropylidene (**22c**).

the C–Br distance by 0.08 Å. In the bisdioxane salt **23a** in which the Li⁺ ion is also internally coordinated, the C–Br distance is further reduced by 0.01 Å and the Li–C separation is slightly enlarged to 2.00 Å. Overall, the C–Br distance in **23a** is shorter by 0.15 Å than that in cyclohexane analogue **23b**. A similar trend in the shortening of the C–Br distance, d_{C-Br} , upon addition of dioxane rings in salts **23** is also found for the bromo anions **21d** and **21a**. Thus, in **21d** the d_{C-Br} decreases by 0.04 Å relative to the parent **21c** and by an additional 0.03 Å (to 2.09 Å) in **21a**. For the cyclohexane analogues **21e** and **21b** the d_{C-Br} decreases by about 0.01 Å per added ring.

The observed trends in the Br–C bond lengths in both series of compounds **21** and **23** parallel the trends in the energetics of the carbene formation from the two substrates.

Carbene Electronic Properties. Analysis of NBO wave functions for the series of carbenes **22** shows that the HOMO involves an $sp^{0.5}$ hybridized orbital of the carbenic atom, while the LUMO is essentially a pure p orbital orthogonal to the cyclopropylidene ring (Figure 5). The energies of the LUMO and HOMO orbitals are gradually increasing upon substitution with the cyclohexane rings. In contrast, the LUMO, which is responsible for the electrophilic properties, gradually decreases in the series of dioxane analogues, while the HOMO remains practically unchanged (Figure 6). Thus, addition of the cyclohexane rings increases nucleophilic properties of the carbene, while dioxane rings enhance its electrophilic properties, which is consistent with the general trend in philicity of carbenes and their reactivity with alkenes.⁴⁸ This conclusion for carbenes **22** is further supported by an analysis of the charge density, which demonstrated that the carbenic center retains approximately the same charge for the cyclohexane derivatives, **22b** and **22e**, and

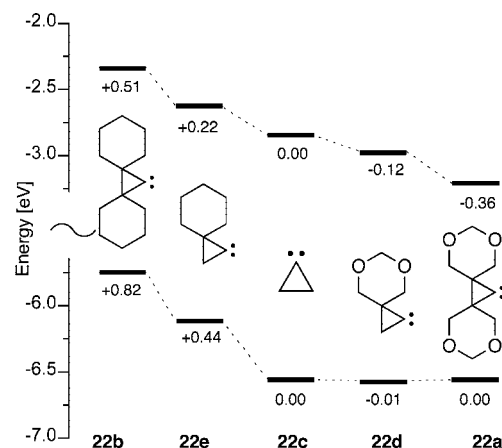
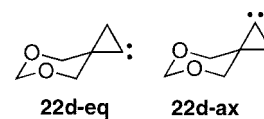


FIGURE 6. Absolute and relative energies of the LUMO and HOMO obtained at the B3LYP/6-31+G(d,p) level of theory for a series of carbenes. For **22c**, $E_{HOMO} = -6.56$ eV and $E_{LUMO} = -2.85$ eV.

the parent **22c** (+0.19), while in the dioxane analogues **22d** and **22a** the charge is higher (+0.21). Interestingly, the orientation of the cyclopropylidene with respect to the dioxane ring has a significant effect on the properties of the carbene. For the equatorial orientation of the carbenic center in **22d-eq**, the LUMO is lower by 0.19 eV than in the axial conformer **22d-ax**, while the enthalpy difference between the two conformers is only 0.15 kcal/mol. This suggests that stereoelectronic interactions (such as those in the anomeric or gauche effects) exist between the oxygen atoms and the carbenic center.

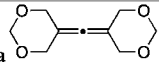
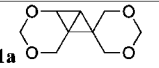
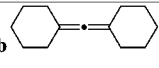
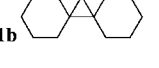
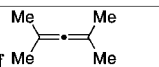
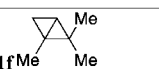


Carbene Rearrangement. Investigation of the rearrangement of two singlet carbenes **22a** and **22b** revealed that the formation of either the corresponding allenes **1** or bicyclo[1.1.0]butanes **11** is a highly exothermic process characterized by a relatively

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TABLE 3. Calculated Thermodynamic Parameters for Rearrangement of Cyclopropylidene^a

R^1
 R R
11 \longleftrightarrow R R
 R R **22** \longrightarrow R R
 R R **1**

Compound	Transition State			Product		
	symmetry	ΔH_{298}^\ddagger kcal/mol	ΔG_{298}^\ddagger kcal/mol	symmetry	ΔH_{298} kcal/mol	ΔG_{298} kcal/mol
 1a	C ₁	11.0	11.2	C ₂	-68.0	-68.2
 11a	C ₁	4.6	6.0	C ₁	-61.4	-59.9
 1b	C _s	9.2	8.4	C ₂	-68.7	-69.3
 11b	C ₁	1.0	2.0	C ₁	-58.8	-57.7
1c $\text{C}=\text{C}=\text{C}$	C ₁	3.9 ^b	3.6	D _{2d}	-66.9	-66.6
 1f	C _s	8.9	8.2	D _{2d}	-69.0	-70.0
 11f	C ₁	1.8	2.7	C ₁	-59.0	-58.0

^a MP2/6-31+G(d,p)//B3LYP/6-31+G(d,p) level of theory with DFT thermodynamic corrections. Symmetry of the starting carbenes: **22a**-C_s, **22b**-C₂, **22c**-C_{2v}, **22f**-C₂. ^b This value is consistent with that obtained with the CCSD//CASSCF (3.6 kcal/mol) or CCSD//CISD (4.2 kcal/mol) methods (ref9) and is lower by 1.3 kcal/mol than that calculated at the DFT//DFT level of theory.

low ≤ 11 kcal/mol activation energy (Table 3). The calculated ΔG_{298}^\ddagger values are greater for the dioxane carbene **22a** than for the analogous transformations of the cyclohexane analog **22b**. A comparison of the calculated activation energies with those for two model carbenes, the parent cyclopropylidene (**22c**) and tetramethylcyclopropylidene (**22f**), is particularly informative (Table 3). Thus, activation energies for the rearrangement of the cyclohexane and tetramethyl carbenes, **22b** and **22f**, to the corresponding allenes are similar and nearly 5 kcal/mol higher than that obtained for the transformation of the parent cyclopropylidene (**22c**) to allene **1c**. This significant increase of ΔG_{298}^\ddagger for **22b** and **22f** and also **22a** (about 7 kcal/mol) is contrary to expectations based on results for *cis*-2,3-dimethylcyclopropylidene⁸ and is presumably related to steric interaction of the four substituents in the ring opening TS.

Further inspection of the computational results for both carbenes **22a** and **22b** shows that the formation of bicyclo[1.1.0]butanes **11** is significantly easier (kinetic products) than the rearrangement to the corresponding allenes **1**, which are the thermodynamic products. The calculated activation enthalpy for the C-H insertion process in all three carbenes **22** is in the range of 1–4.6 kcal/mol, which is consistent with activation energies calculated for the insertion of methylene to methane and ethane at a similar level of theory.⁴⁹ The order of the calculated ΔH^\ddagger values, **22b** < **22f** < **22a**, appears to reflect the

electronic effects of the group adjacent to the $-\text{CH}_2-$ in the carbene **22**. Thus, replacement of a hydrogen atom in the methyl of **22f** with alkyl in **22b** lowers the ΔH^\ddagger by 0.8 kcal/mol, while the substitution of an alkoxy for hydrogen in **22a** increases the ΔH^\ddagger by 2.8 kcal/mol.

The difference between the free energies of activation ΔG^\ddagger for the two competing rearrangements of carbenes **22** is >4 kcal/mol, which suggests that bicyclo[1.1.0]butanes **11** are practically the only expected products. The calculated low activation energies for the C-H insertion process (<6.0 kcal/mol) further suggests that the rearrangement of **22** to **11** should be observed even at low temperatures. The fact that only rearrangements of **22b** to **11b** and **22f** to **11f**^{10,11} are observed experimentally indicates the difficulties with the formation of the dioxane carbene **22a**, which is consistent with the computational results for anions **21** and **23**.

Analysis of the transition-state geometry for the allene rearrangement revealed that the tetramethyl and cyclohexane structures **1f-TS** and **1b-TS** have the C_s symmetry and the shortest in the series C(2)⋯C(3) distances of 1.778 and 1.834 Å (Figure 4), respectively. In contrast, transition states **1c-TS** and **1a-TS** are asymmetric, and the degree of deviation from the C_s geometry follows the trend in the C(2)⋯C(3) separation. Thus, for **1a-TS** with the C(2)⋯C(3) distance of 1.848 Å the parameters⁵⁰ δ_1 and δ_2 are small (6° and 12°) and they increase to 12° and 17° for **1c-TS** for which the C(2)⋯C(3) is the longest (1.995 Å). This is consistent with the extensive analysis

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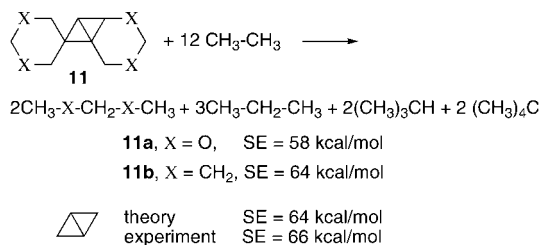


FIGURE 7. Strain energy (SE) calculated from SCF energies at the B3LYP/6-31+G(d,p) level of theory using a homodesmotic reaction. Experimental SE for the parent bicyclo[1.1.0]butane taken from ref 52

for the parent cyclopropylidene,⁹ according to which the ring opening process initially follows the disrotatory symmetric motion of the two CR₂ groups characteristic for a 2e concerted process. In the vicinity of the TS one of the CR₂ groups begin to rotate faster destroying the C_s symmetry. For the parent cyclopropylidene **1c**, this asymmetric motion begins at about 1.85 Å,⁹ which is consistent with the observed symmetric TS for cyclohexane **1b-TS** (1.834 Å) and asymmetric TS for dioxane **1a-TS** (1.848 Å).

The intramolecular insertion of carbene into the C–H bond and the formation of the bicyclo[1.1.0]butane derivative **11** is a concerted process⁴⁹ in which the vacant p orbital interacts with the C–H bond, while the hydrogen moves to the carbenic sp^{0.5}-hybridized orbital. In the transition state for rearrangement of both **22a** and **22b**, the C–H is elongated by about 0.15 Å and the H⋯C(1) distance is about 1.5 Å. The C(1)⋯C distance is about 1.95 Å. The C–C bond formation and the hydrogen transfer are both more advanced in the cyclohexane **11b-TS** by about 0.04 Å than in the dioxane **11a-TS**.

Strain Energy (SE). Strain energies (SEs) for the two bicyclo[1.1.0]butanes, the expected **11a** and the observed **11b**, were obtained using a homodesmotic reaction⁵¹ and compared to that of the parent bicyclo[1.1.0]butane. The results shown in Figure 7 demonstrate that the SE for the cyclohexane derivative **11b** is identical to that obtained for the parent, which in turn is close to that obtained from experimental heats of formation.⁵² The SE for the dioxane derivative **11a** is lower by 6 kcal/mol than that of **11b**. However, considering that analogous calculations for [1,3]dioxane give SE of –2 kcal/mol, the overall strain of **11a** is similar to that of the cyclohexane derivative **11b**.

Analysis of the molecular geometry for the three bicyclo[1.1.0]butanes showed no unusual differences, except for the length of central C–C bond. It is longer for **11a** (1.509 Å) than for cyclohexane **11b** (1.500 Å) and for the parent (1.494 Å).

NMR Structural Assignment. Among 10 primary and 5 secondary products of reactions of **2a** and **2b** with RLi, 5 were isolated in their pure forms. The remaining compounds were analyzed as mixtures, and their structural assignment was based on MS and NMR spectra, comparison with literature NMR spectra (**12b**, **15**, and **16**), or close match with analogous cyclopropane derivatives^{53–56} (bromine-containing derivatives, **2**, **7**, **8**, and also **9a**; details in the Supporting Information). Further support for the structural assignment to the observed products that do not contain bromine (**9a**, **10a** (R = Me, Ph, *t*-Bu), **11**, and **12**) was provided by comparison of the DFT-

calculated and experimental ¹H and ¹³C NMR chemical shifts (Figure 8). The theoretical chemical shifts used for the correlation were obtained as weighted averages of chemical shifts for 2–4 major conformers for each compound. For dioxane derivatives, the predominant conformers are of type **B** (Figure 2), while for the cyclohexane analogues both conformers of type **A** and **B** are populated to a similar degree.

Structural assignment of the experimental ¹H and ¹³C NMR data for the comparison with the theoretical values was made on the basis of general trends in chemical shifts, coupling constant values (¹H data), relative intensities of the signals, and DEPT results (**11b**). For the two cyclohexane derivatives **11b** and **12b**, the ambiguous ¹³C data for CH₂ groups was compared to the best matching theoretical values. Most of the ¹H NMR data for **11b** and **12b** could not be unambiguously matched with the calculated values, and therefore, only a few distinct signals were used for the correlation. Thus, only the cyclopropane CH₂ signal of **12b** was used in Figure 8a, although the position of the maximum of the overlapping multiplets at 1.43 ppm is in excellent agreement with the weighted average for the calculated ¹H chemical shifts (1.44 ppm). The results are shown in Figure 8, and numerical data is provided in the Supporting Information.

Correlations presented in Figure 8 generally show good agreement between the theoretical and experimental values. The biggest differences between the two sets of data are observed for the cyclopropane ring. Thus, the results show that the ¹H signals of the cyclopropane CH group in dioxane derivatives are systematically underestimated by about 0.2 ppm with a maximum of 0.28 ppm for **12a**. Calculations also systematically overestimated the ¹³C chemical shifts for the spiro C atoms of the dioxane derivatives by about 3 ppm, and for the other cyclopropane ring C atom a substantial overestimation by –4.6 ppm was found for **9a**. Chemical shifts of both carbon atoms of the cyclopropane ring in **12b** are underestimated by 6.5 and 2.5 ppm.

Discussion

Experimental results show that dibromocyclopropane **2b** reacts with alkyllithiums as expected giving the rearrangement product **11b**, while the dioxane derivative **2a** gives only substitution products and no rearrangement. Reaction pathways observed for both substrates are summarized in Scheme 8.

The cyclohexane derivative **2b** smoothly forms the lithium salt **23b** upon treatment with MeLi, which subsequently undergoes elimination of LiBr. The resulting carbene **22b** (or carbenoid) rearranges to bicyclo[1.1.0]butane **11b** in a nearly quantitative yield. The step of LiBr elimination is fast even at low temperature, and no methylation products are observed. This indicates that reaction rates for elimination are greater than alkylation ($k_{2b} \gg k_{5b}$ and $k_{2b} \gg k_{6b}$ in Scheme 8) and also that the rate for C–H insertion is greater than rearrangement to allene **1b** ($k_{4b} \gg k_{3b}$). The latter is consistent with the computed lower free energy of activation for the formation of **11b** than for the formation of allene **1b** by 6.4 kcal/mol (Table 3) and with reports of the preferential formation of bicyclo[1.1.0]butanes by some other tetrasubstituted *gem*-dibromocyclopropanes.^{10,11,14}

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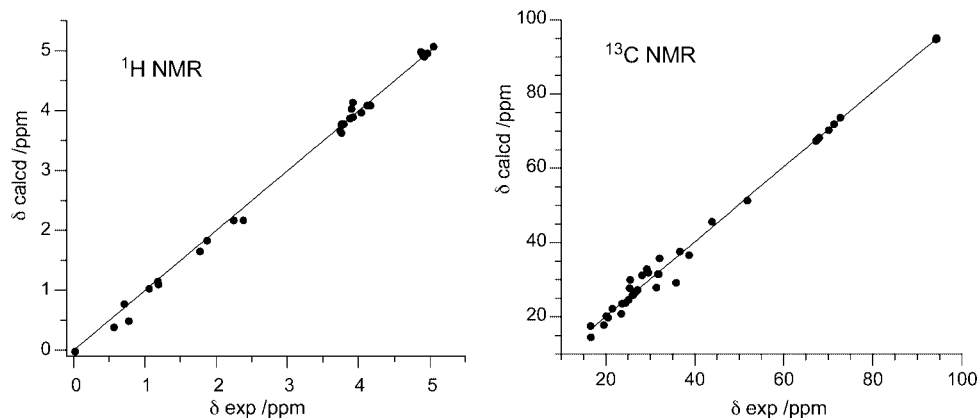
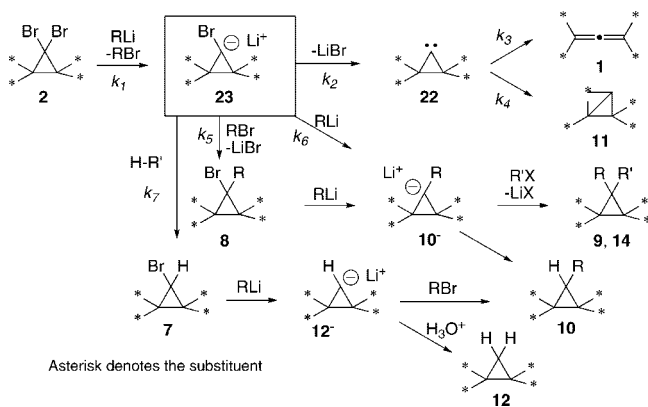
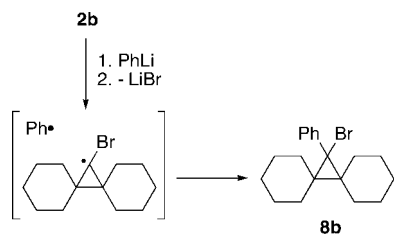


FIGURE 8. Correlation between calculated (B3LYP/6-311+G(2d,p)//B3LYP/6-31G(d,p)) and experimental ^1H (a) and ^{13}C NMR (b) chemical shifts δ for selected compounds. Best fit functions: $\delta_{\text{calcd}} = 0.999(5) \times \delta_{\text{exp}}$ ($r^2 = 0.996$) and (b) $\delta_{\text{calcd}} = 1.007(7) \times \delta_{\text{exp}}$ ($r^2 = 0.994$).

SCHEME 8



SCHEME 9



In contrast, salt **23a** derived from dioxane derivative **2a** and MeLi undergoes efficient methylation with MeBr to yield **8a**. This indicates that $k_{2a} \ll k_{5a}$ for the dioxane derivative and also that the activation energy for LiBr elimination is significantly higher than that for methylation of the anion. Assuming that the rates of methylation of either anion **23a** or **23b** are similar ($k_{5a} \sim k_{5b}$), the rate of LiBr elimination from the former is significantly lower than that from the cyclohexyl derivative **23b** ($k_{2a} \ll k_{2b}$). This is consistent with the computed higher endergonicity for the formation of carbene **22a** by nearly 5 kcal/mol than the formation of **22b** from the respective salts **23** (Table 2). In the presence of excess MeLi, bromide **8a** undergoes Li-halogen exchange, and the resulting anion **10a⁻** is methylated again giving the dimethyl derivative **9a**.

Reactions of dibromides **2a** and **2b** with PhLi gave surprising results highlighting again the differences in the reactivity of the two compounds. Thus, reactions of the cyclohexane dibromide **2b** with PhLi gave the expected bicyclo[1.1.0]butane derivative **11b**, but, surprisingly also the bromide **8b** (R = Ph) was formed as the only byproduct. The formation of **8b** can be

explained as a coupling of a caged radical pair⁵⁷ that is formed during the metal-halogen exchange (MHE) process in accordance with a general mechanism⁵⁸ involving a single electron transfer (SET) process (Scheme 9). The proposed mechanism for the formation of **8b** is consistent with the observations that (i) the amount of **8b** appears to be greater at lower temperatures and at lower concentrations and (ii) no other byproduct are observed in significant amounts.

A reaction of the dioxane dibromide **2a** with PhLi proceeds differently than that of the cyclohexane analog. In this case, the initially formed bromoanion **23a** apparently undergoes a facile nucleophilic substitution with excess PhLi to give salt **10a-Li**, which is either protonated to give **10a** or methylated with MeI to give **14** as the exclusive products. This indicates again that the rate for LiBr elimination from **23a** is significantly lower than those for the competing processes, including a reaction of the anion with PhLi ($k_{6a} \gg k_{2a}$, Scheme 8). It may appear that the observed product **10a-Li** is formed according to a metal-assisted ionization (MAI) of the C-Br bond in the anion **23a** as it was postulated for vinyl α -haloanions⁵⁹ and later for some cyclopropyl α -haloanions.^{26,60} The computational results show however, that there is no significant loosening of the C-Br bond in the dioxane derivative **23a** as postulated in MAI and experimentally observed for some carbenoids.¹⁸ Instead, the C-Br bond in **23a** is shorter by 0.15 Å than that in the cyclohexane analogue **23b**. Moreover, the Li⁺ ion is coordinated to the ring's oxygen atoms, which opens the carbon center for nucleophilic attack. Therefore, a more appropriate description for the process observed in **2a** should be coordination-assisted nucleophilic substitution (CANS) as shown in Figure 9. Interestingly, this mechanism does not seem to operate for reactions of **2a** with MeLi, presumably due to the presence of MeBr. The observation of bromide **8a** (R = Me) in reactions with MeLi (Table 1) as the primary product indicates that in this case $k_{5a} > k_{6a}$. The formation of methylation byproduct (analogues of **8-10**) and also bicyclopentadienes (products of self-condensation) in reactions of some dibromocyclohexanes

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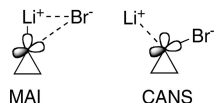
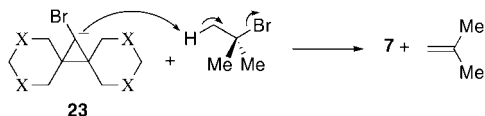


FIGURE 9. Proposed configuration for metal-assisted ionization (MAI)⁵⁹ and coordination-assisted nucleophilic substitution (CANS). See the text for details.

SCHEME 10



clopropanes with MeLi has been reported in the literature,^{2,22,61–63} but always as minor components of mixtures of products.

Results for reactions of dibromides **2a** and **2b** with *t*-BuLi are consistent with those obtained with MeLi and PhLi, although they are complicated by the presence of *t*-BuBr formed in the metal–halogen exchange process. In the reactions of dibromide **2b** with *t*-BuLi, the bicyclo[1.1.0]butane **11b** is still the dominant product, but is accompanied by debrominated product **12b** formed regardless of the reaction and quenching process temperatures. The formation of **12b** can be rationalized as a competition between the α -bromo anion **23b** and *t*-BuLi for the proton from *t*-BuBr (Scheme 10) on one hand, and Br[−] elimination and the formation of carbene (carbenoid) **22b** on the other. Since the lithium–halogen exchange is a fast process, the *t*-BuLi that is being added dropwise to **2b** is rapidly consumed leaving anion **23b** and *t*-BuBr. Thus, at the beginning of *t*-BuLi addition the concentration of anion **23b** is greater than that of *t*-BuLi, and **23b** may effectively compete for the proton from *t*-BuBr. At low temperature, the elimination of Br[−] and the formation of carbene **22b** is slow, and less bicyclo[1.1.0]butane **11b** is formed in favor of **7b** (Table 1, entry 12). At higher temperatures (−10 °C), the formation of carbene (carbenoid) and its subsequent rearrangement to bicyclo[1.1.0]butane **11b** is the dominant process, and less monobromide **7b** is generated (Table 1, entry 11). With the low *t*-BuLi/**2b** ratio, the excess *t*-BuLi is never achieved and monobromide **7b** is formed in significant quantities. For the high *t*-BuLi/**2b** ratio, the generated monobromide **7b** is lithiated with excess *t*-BuLi that is built up at the end of the addition process, and the resulting anion **12b**[−] is protonated during the workup. Thus, on the basis of the product distribution (Table 1), it can be postulated that at low temperatures $k_{2b} < k_{7b}$ (entry 12) and at higher temperatures $k_{2b} > k_{7b}$ (entry 11). At high *t*-BuLi/**2b** ratio, excess *t*-BuLi completely transforms **7b** to anion **12b**[−], which subsequently gives **12b**. Better understanding and support of this proposed mechanism require further detailed experimental studies.

Reaction of dibromide **2a** and *t*-BuLi also gives the debrominated product **12a** among unidentified product(s) arising presumably from the low stability of the [1,3]dioxane ring toward the base. The formation of **12a** can be envisioned to occur in a way analogous to that of the generation of **12b** from **2b**. The initially formed anion **23a** is protonated with *t*-BuBr to form **7a**, which is further converted to **12a**. In addition, some of the anion **23a** apparently undergoes substitution reaction (CANS) with *t*-BuLi giving **10a** (R = *t*-Bu). The distribution

of these two products, **10a** and **12a**, indicates that $k_{7a} > k_{6a}$. There is no clear evidence for the generation of carbene **22a**, although it cannot be excluded that some of the unidentified byproduct(s) are derived from a reaction of *t*-BuLi with the transient bicyclo[1.1.0]butane **11a**.

Overall, elimination of LiBr from anion **23a** and the formation of carbene **22a** (or a carbenoid) appears to be the slowest process among all possible pathways in the transformation of **2a**, at least with MeLi and PhLi. The lithium salt **23a** is stabilized by nearly 5 kcal/mol over salt **23b** and appears to exhibit dual philicity: it reacts with electrophiles such as MeBr or, in their absence, with nucleophiles such as PhLi.

The origin of the observed difference in reactivity of the two cyclopropanes **2a** and **2b** lies primarily in the electronic structure of the carbenes **22a** and **22b** and, to some extent, in the ability of the dioxane rings to chelate the Li⁺ ion. Analysis of the three carbenes **22a–c** shows significantly more electrophilic character of the dioxane carbene **22a** due to the inductive effect of the −CH₂O− groups. This is evident from the higher positive charge of the carbenic center and lower energy of the LUMO. This in turn, results in tighter bonding to an electron donor Br[−], as evident from the C–Br bond length in the anions **21** and Li salts **23**, and less favorable α -elimination process in **21a** and **23a**. Consistent with this view is the observed slow addition of: CBr₂ to olefin **3a**, and also fast reactions of dibromide **2a** with RLi ($k_{1a} > k_{1b}$), as compared to the cyclohexane analogues.

The rigidity of the molecular skeleton and the orientation of oxygen atoms relative to the carbenic center are not optimal for the effective chelation of Li⁺ in **23a**. Therefore, this internal coordination provides only a modest additional enthalpic stabilization of **23a**, which is compensated by the entropy decrease. It results, however, in moving the Li⁺ ion away from the carbanion center and exposing it to both electrophiles and nucleophiles. In other dibromocyclopropanes, containing either flexible or better aligned substituents, such as methoxy,²³ alkoxymethyl,^{17,64} acetal,^{21,24,65–67} alkylthiomethyl,^{20,68} and dialkylaminomethyl,^{69,70} the heteroatom can effectively chelate the Li⁺ ion increasing the overall stability of the salt and directing the insertion reaction.⁷¹ These single substituents, however, do not significantly affect the carbenic center, and the formation of carbenes (carbenoids) and their subsequent reactions (insertion or rearrangement) are the dominant processes. This is in sharp contrast to our results for **2a**, and, to our knowledge, there is no other dibromocyclopropane that is resistant to the carbene formation. In this sense dibromocyclopropane **2a** is an exceptional compound.

Conclusions

The reactions of two dibromocyclopropanes **2a** and **2b** with three different organolithium reagents revealed several mechanistic pathways, which depend on the substrate and the

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organolithium. The cyclohexane derivative **2b** reacts as expected to form carbene **22** (or carbenoid), which undergoes rearrangement to **11b**. In contrast, the anion derived from **2a** is unusually stable and undergoes either alkylation with MeBr (electrophilic substitution) or arylation with PhLi (nucleophilic substitution) as the main or exclusive reaction pathways. This significant resistance to the α -elimination process in anion **23a** is ascribed to the cumulative effect of four $-\text{CH}_2\text{O}-$ groups, rather than to the intramolecular coordination of the Li^+ ion by the ring oxygen atoms. Calculations for a series of anions indicate that the dioxane ring increases the electrophilic character of the cyclopropylidene by lowering the LUMO, which retards the α -elimination process. The effect is approximately additive for each dioxane group. A comparative analysis of the literature data indicates that a single $-\text{CH}_2\text{O}-$ or $-\text{CH}_2\text{N}<$ substituent does not noticeably impact the reactivity of dibromocyclopropanes and their intermediates.

Overall, the electron withdrawing effect of the four $-\text{CH}_2\text{O}-$ groups results in the enhanced electrophilicity of carbene **22a** and manifests itself in (i) the resistance of the anion **23a** to the elimination of LiBr, (ii) slow addition of $:\text{CBr}_2$ to olefin **3a**, and (iii) in fast reactions of dibromide **2a** with RLi ($k_{1a} > k_{1b}$), as compared to the cyclohexane analogues.

Future studies of carbene **22a** and its rearrangement to **1a** and **11a** will require a different precursor such as the appropriate diazo derivative.

Computational Details

Quantum-mechanical calculations were carried out with the B3LYP^{72,73} and MP2(fc)⁷⁴ methods using the Gaussian 98 package.⁷⁵ Geometry optimizations were performed with the DFT method using either the 6-31+G(d,p) or 6-31G(d,p) (for NMR analysis) basis sets, appropriate symmetry constraints, and default convergence limits. Transition states were located using the QST3 keyword. The guess for the TS geometry was generated by optimizing the geometry with the C2–C3 distance frozen at 1.85 Å for allene formation, and C1–C α , C1–H α , and C α –H α distances frozen at 1.95 Å, 1.33 Å, and 1.32 Å, respectively. Carbenes were considered in their singlet states.

Vibrational frequencies obtained with the DFT method were used to characterize the nature of the stationary points and to obtain thermodynamic parameters. Zero-point energy (ZPE) corrections were scaled by 0.9806.⁷⁶ Population analysis was obtained using the NBO algorithm⁷⁷ supplied in the Gaussian package. For rearrangement of carbenes, single-point energies were calculated with the MP2 method without the BSSE correction. Following general recommendations,⁷⁸ isotropic magnetic shielding tensors were calculated for major conformers of each compound with the GIAO method at the B3LYP/6-311+G(2d,p)//B3LYP/6-31G(d,p) level of theory. Population of each conformer was established from the calculated differences

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in free energy and used to calculate weighted shielding tensor for each nucleus, which was converted to NMR chemical shifts using cyclohexane as the reference. More details are listed in the Supporting Information.

Experimental Details

Melting points are uncorrected. NMR spectra were recorded at either 300 MHz (^1H) and 75 or 100 MHz (^{13}C), respectively, in CDCl_3 , unless otherwise specified. Chemical shifts were referenced to TMS (^1H) or solvent (^{13}C).

13,13-Dibromo-2,4,9,11-tetraoxadispiro[5.0.5.1]tridecane (2a). **Method A.** A 50% aq solution of NaOH (10 g, 125 mmol) was added dropwise at room temperature to a vigorously stirred solution of olefin **3a** (3.45 g, 20 mmol), CHBr_3 (5.5 mL, 60 mmol), and TEBA (50 mg, 0.2 mmol) in CH_2Cl_2 (25 mL). After 12 h, no more progress was observed by GC/MS, and additional portions of CHBr_3 (5 mL) and TEBA (50 mg) were added. The stirring was continued for 3 days during which two additional portions of CHBr_3 and TEBA were added. The reaction mixture was filtered through Celite, which was washed with CH_2Cl_2 (200 mL). The organic layer was separated, dried (NaSO_4), and concentrated. Excess CHBr_3 was distilled off under reduced pressure. The resulting mixture of starting material and product (1:4 ratio by ^1H NMR) was separated by column chromatography ($\text{CH}_2\text{Cl}_2/\text{EtOAc}$, 10:1). The isolated product (2.5 g) was recrystallized from EtOH, giving 1.80 g (33% yield) of **2a** as colorless crystals (mp 162–166 °C). Alternatively, dibromide **2a** was dried in vacuum (P_2O_5) and then sublimed at 125 °C/1.0 Torr giving a white solid: mp 163.5–164 °C; ^1H NMR δ 3.99 and 4.04 (AB, $J = 12.0$ Hz, 8H), 4.90 and 4.92 (AB, $J = 6.2$ Hz, 4H); ^{13}C NMR δ 32.0, 40.7, 68.9, 94.1; IR (neat) 1147 (C–O) cm^{-1} ; MS m/z 235 and 233 (1:1, 1), 86 (63), 65 (100); HRMS calcd for $\text{C}_9\text{H}_{13}\text{Br}_2\text{O}_4$ 342.9181, found 342.9199. Anal. Calcd for $\text{C}_9\text{H}_{12}\text{Br}_2\text{O}_4$: C, 31.42; H, 3.52. Found: C, 31.63; H, 3.50.

Method B. Following a general procedure,³⁰ PhHgCBr_3 (13.7 g, 26 mmol) was added in one portion to a stirred solution of olefin **3a** (3.0 g, 17 mmol) in dry benzene (30 mL) under nitrogen. The reaction mixture was heated to 85 °C for 5 h. The solid precipitate was filtered, and the filtrate was concentrated. The resulting mixture of starting material **3a** and product **2a** (1:1 by ^1H NMR) was separated as above giving 1.60 g (28% yield) of **2a**.

13,13-Dibromodispiro[5.0.5.1]tridecane (2b). The dibromide was obtained from olefin **3b** as described for **2a** in method A without additional portions of CHBr_3 , base or catalysts. The crude product was passed through a silica gel plug, recrystallized (isooctane), and sublimed (70 °C at 1.5 Torr) giving 71% yield of the dibromide **2b** as colorless crystals: mp 101–102 °C; ^1H NMR δ 1.37–1.74 (m); ^{13}C NMR δ 24.9, 25.8, 30.9, 35.3, 56.8; MS m/z 256 and 254 (M – Br, 1:1, 31), 175 (M – 2 Br, 100). Anal. Calcd for $\text{C}_{13}\text{H}_{20}\text{Br}_2$: C, 46.46; H, 6.00. Found: C, 46.51; H, 6.07.

Reaction of 2 with Organolithium. General Method. To a stirred solution of dibromide **2** (typically 0.7 mmol) in dry ether (50–70 mL), the appropriate amount of 1.2 M MeLi in ether, 2.0 M PhLi in dibutyl ether, or 1.7 M *t*-BuLi in pentane was added dropwise at –78, –10, or 36 °C under argon. After the addition was complete, the reaction mixture was placed in an ice–salt bath (–10 °C) or allowed to warm to ambient temperature. Alternatively, MeLi or PhLi were added to a solution of **2** in boiling ether. After 2 h, the reaction mixture was quenched with degassed water

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(0.25–0.5 mL), the aqueous layer was separated, and the organic layer was concentrated. ^1H NMR, ^{13}C NMR, and GC/MS were taken of the crude mixture. Products were purified and partially separated by column chromatography and/or sublimation. Detailed procedures and analytical data are provided in the Supporting Information.

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Supporting Information Available: Full experimental details for **3–12**, NMR spectra for reaction products, and computational results. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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