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# Stereochemistry in Carbenoid Formation by Bromine/Lithium and Bromine/Zinc Exchange Reactions of *gem*-Dibromo Compounds

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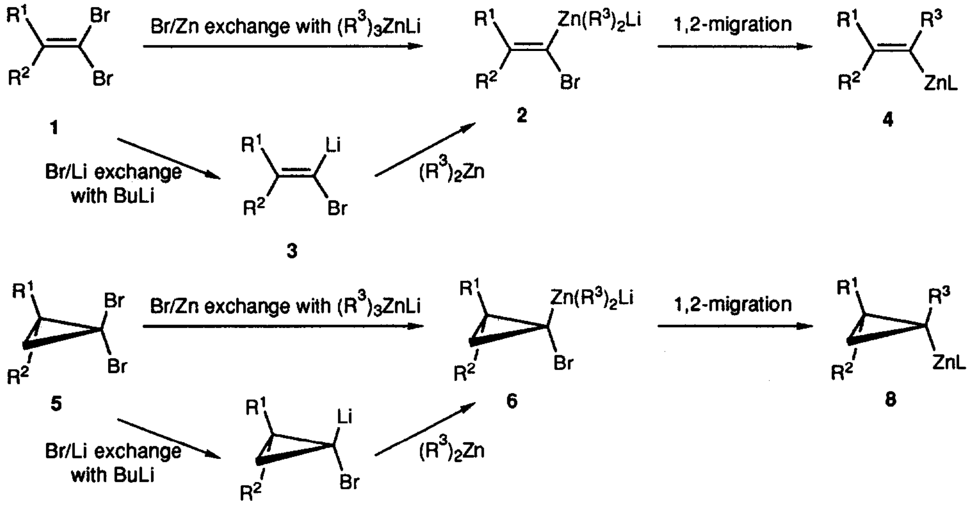
***Abstract:*** Stereochemistry in generation of lithium and zincate carbenoids by bromine/metal exchange reactions of *gem*-dibromo compounds with BuLi and lithium triorganozincates, respectively, has been investigated. Both lithium and zincate carbenoids derived from 1,1-dibromoalkenes are demonstrated to be configurationally stable at low temperatures whereas, in the presence of the unreacted starting dibromoalkenes, the lithium carbenoids, but not the zincate carbenoids, undergo facile isomerization at the carbenoid carbons. Zincate carbenoids derived from 1,1-dibromocyclopropanes undergo isomerization slowly at the carbenoid carbons in the presence of the starting dibromocyclopropanes. The isomerization reactions of the lithium and zincate carbenoids are proved to proceed through a mechanism involving a bromine/metal exchange between the carbenoids and the starting dirbromo compounds. Highly stereoselective formation of the lithium carbenoids is observed in the reaction of 1,1-dibromoalkenes under the thermodynamic conditions. Under kinetically controlled conditions, both the bromine/lithium and bromine/zinc exchange reactions take place preferentially at the sterically more hindered bromine atom of the starting *gem*-dibromo compounds. The observation is rationalized by an exchange mechanism involving a linear transition state of either an ate complex formation or an $S_N2$ reaction at the more hindered bromine atom where strain relief due to the elongation of the carbon-bromine bond is expected.

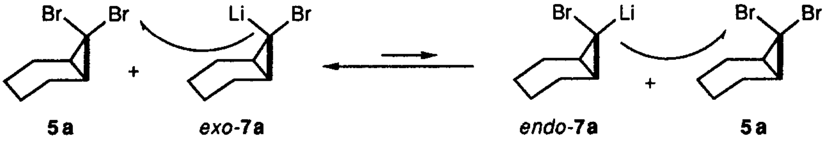
α-Haloorganometallic compounds (so-called carbenoids) possessing both nucleophilic and electrophilic reactivities are versatile intermediates in carbon-carbon bond forming reactions.[1,2] Tetravalent nature of carbenoids, if their stereochemistry is properly controlled, may endow these reactions with a high level of stereoselectivity, which is difficult to be attainable by using divalent free carbenes.[2d,3]

We have recently reported that zincate carbenoids such as (1-bromoalkenyl)zincate 2 and (1-bromocyclopropyl)zincate 6 undergo a smooth intramolecular nucleophilic substitution reaction, or a 1,2-migration reaction, to give synthetically versatile organozinc species 4 and 8, respectively (Scheme 1).[4] The requisite zincate carbenoids can be prepared either by a direct bromine/zinc exchange of the corresponding *gem*-dibromo compounds with triorganozincate or by a bromine/lithium exchange followed by ate complex formation of the resulting lithium carbenoids (3 and 7). Because the 1,2-migration takes place with inversion of configuration at the carbenoid carbon in the absence of unfavorable steric constraints, stereocontrol in generation of zincate carbenoids is indispensable for the stereoselective reactions.[4a,b]

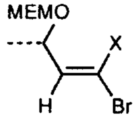
The halogen/metal exchange reaction of *gem*-dihalo compounds is one of the most efficient and frequently employed methods of generating carbenoids.[1] However, factors governing the stereochemistry of the reaction have not been fully elucidated.[5] A few reports have appeared on the stereoselective formation of lithium carbenoids under thermodynamic conditions. Seyferth and co-workers studied stereochemistry in generation of bromonorcaranyllithium **7a**.[5a] They demonstrated that, in the presence of dibromonorcarane **5a**, a precursor of the carbenoid, **7a** undergoes a very facile stereoisomerization through a mechanism involving a bromine/lithium exchange with **5a** (eq 1). As a result, one can generate thermodynamically more stable carbenoid *exo*-**7a** with high stereoselectivity (>99:1) by using a slight excess of **5a**.[4b,5d] More recently, Braun and Mahler reported similar isomerization behavior of 1-bromoalkenyllithium **10**.[6] They noted that lithium carbenoid *E*-**10** can be generated almost exclusively when dibromoalkene **9** was allowed to react with 0.95 equiv of BuLi at -105 °C. In comparison with the stereoselectivity under the thermodynamic conditions, much less attention has been focused on the kinetic stereoselectivity in generation of carbenoids.



**Scheme1**



(1)



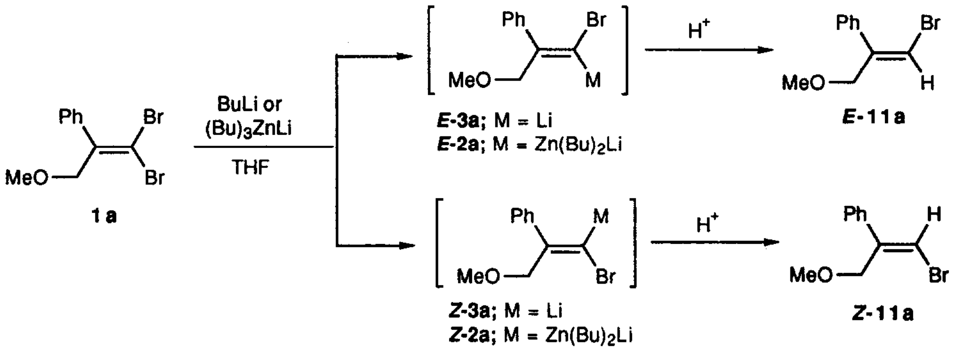
MEM = $MeOCH_2CH_2OCH_2$
**9**; X = Br
*E*-**10**; X = Li

Herein, we report the results of our stereochemical study on carbenoid formation by halogen/metal exchange reaction.[7] Stereoselectivities were investigated for the reactions of 1,1-dibromoalkenes and 1,1-dibromocyclopropanes with butyllithium and triorganozincates both under kinetic and thermodynamic conditions. The study not only discloses several controlling factors valuable for the stereoselective generation of the carbenoids but also provides valuable information concerning the mechanism of carbenoid formation by the halogen/metal exchange reactions.

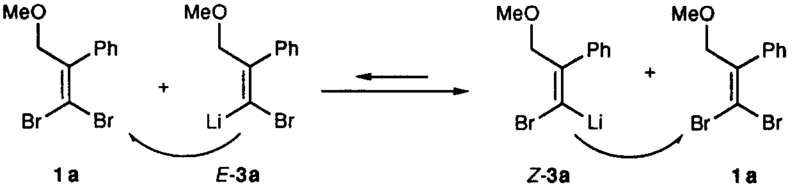
## RESULTS AND DISCUSSION

### *Generation of 1-Bromoalkenyllithiums by Bromine/Lithium Exchange Reaction of 1,1-Dibromoalkenes*

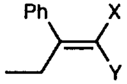
Addition of a THF solution of dibromoalkene **1a** to a THF/hexane solution of BuLi (2 equiv) at -94 °C during a 90-sec period followed by immediate treatment of the resulting lithium carbenoid **3a** with AcOH/THF gave a 73:27 mixture of bromoalkenes *E*- and *Z*-**11a** in 84% yield (eq 2). Carbenoid **3a** was found to be configurationally stable under these conditions; the *E*/*Z* ratio did not change when the above reaction mixture was allowed to stand for 30 min at -94 °C before protonation (*E*:*Z* = 73:27, 83% yield).[8]



(2)



(3)

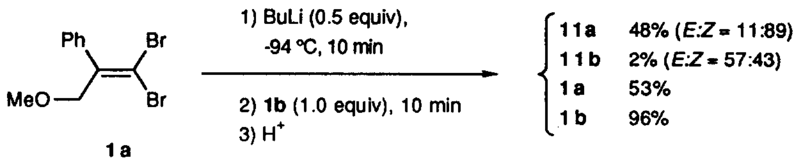


**1b**; X, Y = Br
*E*-**3b**; X = Li, Y = Br
*Z*-**3b**; X = Br, Y = Li
*E*-**11b**; X = H, Y = Br
*Z*-**11b**; X = Br, Y = H

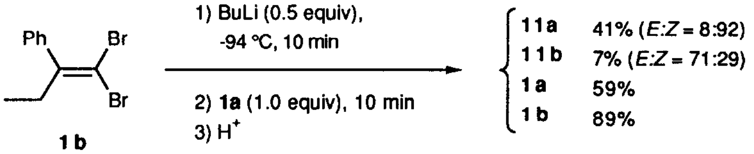
Interestingly, the ratio was reversed when BuLi was added to a THF solution of **1a**. Thus, generation of carbenoid **3a** by the addition of BuLi (1.1 equiv) at -94 °C during a 90-sec period followed by immediate protonation afforded *Z*-**11a** stereoselectively (*Z*:*E* = 77:23) in quantitative yield. The reversal of the stereoselectivity implies that lithium carbenoid **3a** undergoes a rapid *E*/*Z* isomerization during addition of BuLi through a bromine/lithium exchange with the unreacted dibromoalkene (eq 3).[5a,6] Indeed, addition of BuLi to a solution of **1a** (2 equiv) during a 90-sec period followed by standing the resulting mixture for 0, 10, and 30 min at -94 °C gave 87:13 (97%), 90:10 (102%), and 89:11 (97%) mixtures of *Z*- and *E*-**11a**, respectively.

Analogous results were obtained for 1,1-dibromo-2-phenylbutene (**1b**). When **1b** was added to a solution of BuLi (2 equiv), a 60:40 mixture of *Z*- and *E*-**11b** was produced in 78% yield. On the other hand, addition of BuLi to **1b** (2 equiv) followed by immediate protonation resulted in the formation of *E*- and *Z*-**11b** in the ratio of 77:23 (98% yield). Carbenoid **3b** also underwent isomerization, under these conditions, to attain equilibrium within 10 min; upon standing the above reaction mixture for 3, 10, and 30 min at -94 °C, the *E*/*Z* ratio of **11b** varied to 93:7, 97:3, and 97:3, respectively.

To gain support for the isomerization mechanism, following crossover experiments were carried out. Lithium carbenoid **3a**, generated by adding BuLi to **1a** (2 equiv), was treated with dibromoalkene **1b** at -94 °C for 10 min and then quenched with AcOH/THF. The procedure was repeated, but with the order of introduction of the two dibromoalkens interchanged. The results of these experiments shown in eqs 4 and 5 verify the isomerization mechanism involving intermolecular exchange with the unreacted dibromoalkene.



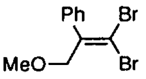
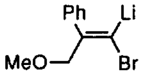
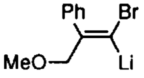
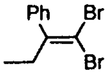
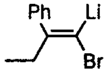
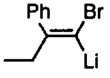
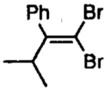
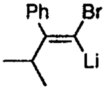
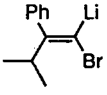
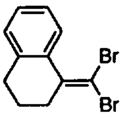
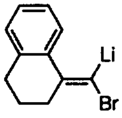
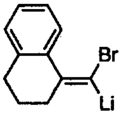
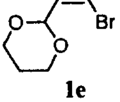
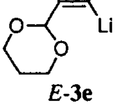
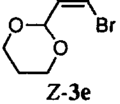
(4)



(5)

Under the thermodynamic conditions, where dibromoalkenes were used in excess, carbenoids *E*-**3a** and *Z*-**3b** were formed preferentially. The opposite selectivites in the reactions where **1a,b** were added to BuLi are therefore deduced to be controlled kinetically. With methods in hand for generation of 1-bromoalkenyllithium either under the thermodynamic or under the kinetic conditions, stereochemistry of bromine/lithium exchange was

Table 1 Reaction of 1,1-Dibromoalkenes **1a-e** with BuLi under Thermodynamic Conditions[a]

| Entry | Dihaloalknes | Lithium Carbenoids | | Ratio[b] | Yield (%)[c] |
|---|---|---|---|---|---|
| | | Major isomer | Minor isomer | | |
| 1 | <br>**1a** | <br>*Z*-**3a** | <br>*E*- **3a** | 89:11 | 97 |
| 2 | <br>**1b** | <br>*E*-**3b** | <br>*Z*- **3b** | 97:3 | 100 |
| 3[d] | <br>**1c** | <br>*Z*-**3c** | <br>*E*-**3c** | 76:24 | 96 |
| 4[d] | <br>**1d** | <br>*E*- **3d** | <br>*Z*-**3d** | 97:3 | 91 |
| 5 | <br>**1e** | <br>*E*-**3e** | <br>*Z*-**3e** | 99:1 | 102 |

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[a] Unless otherwise noted, bromine/lithium exchange reaction was performed at -94 °C by adding BuLi to a THF solution of **1** (2.0 equiv) during a 90-sec period followed by standing the mixture at the same temperature for 0.5 h before protonation with AcOH/THF. [b] Ratio of the geometrical isomers of the corresponding bromoalkene determined by capillary GC (PEG 20M) analysis. [c] GC yield of the corresponding bromoalkene. [d] The reaction was performed at -116 °C in a mixed solvent of THF and $Et_2O$ (45:55).

Table 2 Reaction of 1,1-Dibromoalkenes **1a-i** with BuLi and Trialkylzincates under Kinetic Conditions[a]

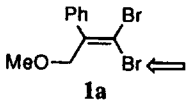
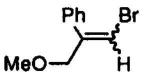
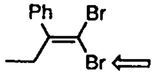
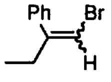
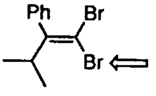
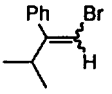
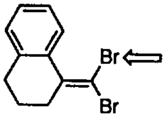
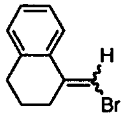
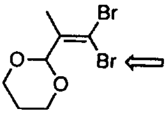
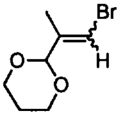
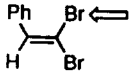
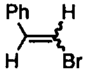
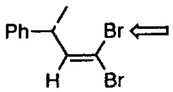
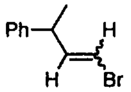
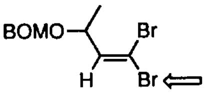
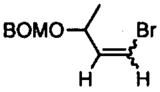
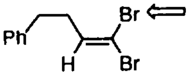
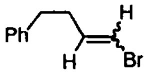
| Entry | Dibromoalkene | Reagent | Products | Ratio[b] | Yield[c] |
|---|---|---|---|---|---|
| 1 |  **1a** | BuLi |  *E*- and *Z*-**11a** | 73:27 | 84 |
| 2[4a] | | (Bu)$_3$ZnLi | | 95:5 | 83 (17) |
| 3[4a] | | ($^s$Bu)$_3$ZnLi | | 95:5 | 86 (16) |
| 4[4a] | | ($^t$Bu)$_3$ZnLi | | 92:8 | 29 (68) |
| 5 |  **1b** | BuLi |  *Z*- and *E*-**11b** | 60:40 | 78 |
| 6[4a] | | (Bu)$_3$ZnLi | | 80:20 | 30 (67) |
| 7[d] |  **1c** | BuLi |  *Z*- and *E*-**11c** | 81:19 | 54 (14) |
| 8 | | (Bu)$_3$ZnLi | | 96:4 | 24 (74) |
| 9[e] | | | | 96:4 | 94 |
| 10[d] |  **1d** | BuLi |  *E*- and *Z*-**11d** | 82:18 | 66 (16) |
| 11 | | (Bu)$_3$ZnLi | | 89:11 | 62 (37) |
| 12[f] | | | | 89:11 | 99 |
| 13 |  **1e** | BuLi |  *E*- and *Z*-**11e** | 71:29 | 96 |
| 14[4a] | | (Bu)$_3$ZnLi | | 95:5 | 96 |
| 15 | | ($^s$Bu)$_3$ZnLi | | 88:12 | 97 |
| 16 | | ($^t$Bu)$_3$ZnLi | | 98:2 | 72 (28) |
| 17[4a] |  **1f** | (Bu)$_3$ZnLi |  *E*- and *Z*-**11f** | 77:23 | 98 (2) |
| 18[4a] |  **1g** | (Bu)$_3$ZnLi |  *E*- and *Z*-**11g** | 69:31 | 61 (35) |
| 19[4a] | | ($^s$Bu)$_3$ZnLi | | 48:52 | 86 (5) |
| 20[4a] |  **1h** | (Bu)$_3$ZnLi |  *Z*- and *E*-**11h** | 55:45 | 93 (9) |
| 21[4a] | | ($^s$Bu)$_3$ZnLi | | 71:29 | 99 |
| 22[4a] | | ($^t$Bu)$_3$ZnLi | | 56:44 | 19 (83) |
| 23[4a] |  **1i** | (Bu)$_3$ZnLi |  *E*- and *Z*-**11i** | 52:48 | 66 |

Table 2 (continued)

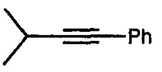
[a]Unless otherwise noted, bromine/lithium exchange reaction was performed at -94 °C by adding a THF solution of **1** to a THF solution of BuLi (2.0 equiv) during a 90-sec period followed by immediate protonation with AcOH/THF. Unless otherwise noted, bromine/zinc exchange reaction was carried out by adding a THF solution of **1** to a THF solution of a lithium trialkylzincate (1.3 equiv) at -85 °C followed by protonation with AcOH/THF after 5 min. [b]Ratio of the geometrical isomers of the corresponding bromoalkenes were determined by capillary GC (PEG 20M) analysis. Major isomers are those derived from the reaction at bromine atoms indicated by arrows in the structures of **1a-i**. [c]GC yield of the corresponding bromoalkene. Recovery of the starting material is shown in parenthesis. [d]The reaction was performed at -116 °C in a mixed solvent of THF and $Et_2O$ (45:55). [e]The reaction was performed for 20 h. [f]The reaction was performed for 24 h.

investigated for other dibromoalkenes **1c-e** The results obtained under the thermodynamic and kinetic conditions are summarized in Tables 1 and 2, respectively.

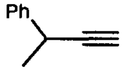
In comparison with **3a,b**, carbenoid **3c** was less stable undergoing, to some extent, Fritsh Buttenberg Wiechel (F-B-W) rearrangement[9] to alkyne **12c** (31% yield) at -94 °C.[10] The rearrangement was retarded considerably when the reaction was carried out at -116 °C in a mixed solvent of THF and $Et_2O$ (45:55 by volume). Reaction of **1d** was also performed at -116 °C due to the formation of several byproducts of higher boiling points at -94 °C. It is known that lithium carbenoids derived from monosubstituted dibromoalkenes are much less stable than those derived from disubstituted dibromoalkenes undergoing a facile F-B-W rearrangement by hydrogen migration.[9] Indeed, reaction of dibromoalkene **1f** resulted in the formation of alkyne **12f** in 79% yield.

Carbenoid formation proceeded with high stereoselectivity under the thermodynamic conditions (Table 1). Levels of the selectivities are generally higher than kinetic ones. We have recently demonstrated that chlorination of the stereoselectively generated lithium carbenoids followed by bromine/metal exchange of the resulting *gem*-bromochloro compounds furnishes the isomeric carbenoids with the opposite stereochemistry (eq 6).[4a] Although the reversal in stereoselectivities were not observed between the thermodynamically controlled and kinetically controlled reactions of **1c-e**, the highly stereoselective reactions under the thermodynamic conditions is of synthetic importance for the stereocontrol in the carbenoid generation.

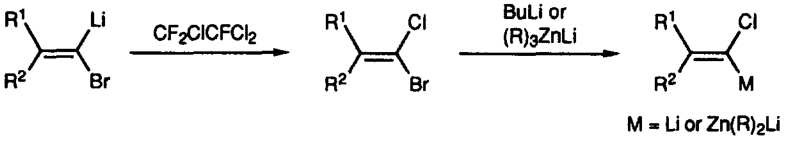
Judging from the thermodynamic selectivity for *Z*-**3a** in which the lithium atom is *anti* to the methoxymethyl group, directing effect by chelation is not significant in the thermodynamically controlled reactions.[11] Nevertheless, such effect might be responsible for the slightly lower selectivity of *Z*-**3a**, comparing with that of *E*-**3b**, and for the exclusive formation of *E*-**3e** with the 1,3-dioxa-2-yl group.



**12c**



**12f**

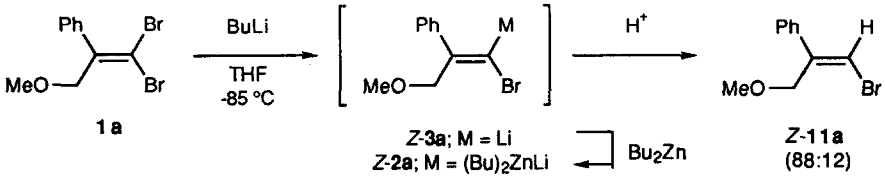


(6)

*Generation of 1-Bromoalkenylzincates by Bromine/Zinc Exchange Reaction of 1,1-Dibromoalkenes*

Addition of dibromoalkene **1a** to a THF solution of lithium tributylzincate ($(Bu)_3ZnLi$)[12] (1.3 equiv) at -85 °C followed by quenching with AcOH/THF after 5 min gave **3a** (83%) with high *E* selectivity (*E*:*Z* = 95:5) (eq 2). The *E*:*Z* ratio did not change either when a similar reaction was performed by using 2 equiv of **1a** for 24 h (*E*:*Z* = 95:5; 98%) or when $(Bu)_3ZnLi$ was added to a THF solution of 2 equiv of **1a** (-85 °C, 30 min) (*E*:*Z* = 94:6; 100%). Analogous results were obtained with other 2,2-disubstituted dibromoalkenes **1b-e**.

There are two plausible interpretations of these results. The intermediate zincate carbenoid **2** would be configurationally stable irrespective of the presence of unreacted dibromoalkene **1** exhibiting a constant kinetic ratio. Alternatively, **2** would undergo a very rapid isomerization exhibiting a constant thermodynamic ratio. In order to discriminate these possibilities, minor zincate carbenoid *Z*-**2a** was prepared separately via lithium carbenoid *Z*-**3a** and its configurational stability was examined (eq 7). Thus, a 89:11 mixture of lithium carbenoids *Z*- and *E*-**3a**, prepared by adding BuLi to a THF solution of **1a** (2 equiv) at -94 °C, was treated with $Bu_2Zn$ (1.1 equiv) and the resulting mixture of zincate carbenoid **2a** was standing, in the presence of unreacted **1a**, at -85 °C for 30 min. Hydrolysis of the mixture yielded a 87:13 mixture of *Z*- and *E*-**11a** (96%). The result clearly showed that zincate carbenoid **2a** is configurationally stable and the observed stereoselectivity was controlled kinetically.



(7)

*Kinetic stereoselectivities in generation of zincate carbenoids from a series of dibromoalkenes* **1a-i** are summarized in Table 2. Bromine/zinc exchange reaction of disubstituted dibromoalkenes **1a-e** exhibited stereoselectivities similar to those observed in the bromine/lithium exchange reactions but the levels of the selectivity was generally higher. Stereoselectivities in the bromine/lithium exchange reactions of monosubstituted dibromoalkenes **1f-i** were unclear due to the thermal lability of the resulting lithium carbenoids. On the other hand, the corresponding zincate carbenoids are stable at -85 °C affording stereochemical information on the bromine/metal exchange of monosubstituted dibromoalkenes. Reactions were moderately *E*-selective for **1f,g** but nonselective for **1h,i**. Stereochemical outcomes similar to that with $(Bu)_3ZnLi$ were observed in the reactions with $(^sBu)_3ZnLi$ and $(^tBu)_3ZnLi$. $(^tBu)_3ZnLi$ was found to be considerably less reactive while exhibiting slightly higher stereoselectivities.

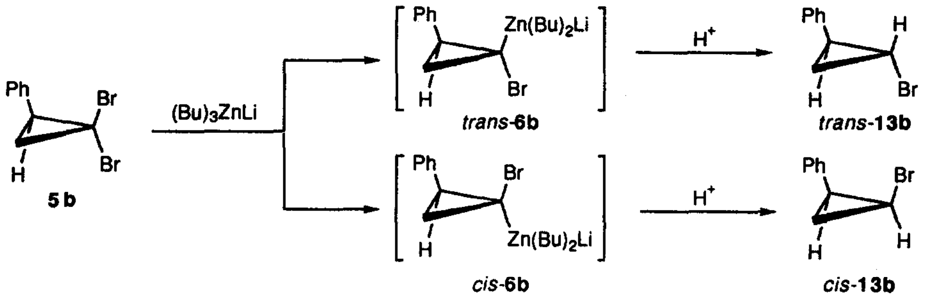
### *Generation of 1-Bromocyclopropylzincates by Bromine/Zinc Exchange Reaction of 1,1-Dibromocyclopropanes*

Stereochemistry in generation of 1-bromocyclopropylzincates was investigated by using 1,1-dibromo-2-phenylcyclopropane (**5b**) and 7,7-dibromonorcarane (**5a**) as substrates (eqs 8 and 9, Table 3). Reactions were carried out by adding **5a,b** to a solution of $(Bu)_3ZnLi$ at low temperatures. The resulting bromocyclopropylzincates **6a,b** were trapped with AcOH/THF and analyzed in the form of bromocyclopropane **13a,b**.

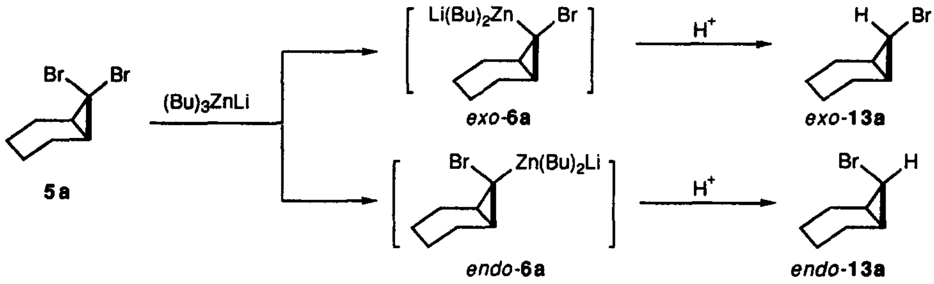
Table 3 Reaction of 1,1-Dibromocyclopropanes **5a,b** with $(Bu)_3ZnLi$

| Entry | Substrate | Molar Ratio **5**:$Bu_3ZnLi$ | Temp (°C) | Time (h) | Yield (%)[a] | *trans:cis* or *exo:endo*[b] |
|---|---|---|---|---|---|---|
| 1 | **5b** | 1:1.3 | -85 | 1 | 82 (15) | 64:36 |
| 2 | | 1:1.3 | -85 | 23 | 95 | 62:38 |
| 3 | | 2.0:1 | -85 | 23 | 112 | 36:64 |
| 4 | | 2.0:1 | -85 | 43 | 113 | 33:67 |
| 5 | **5a** | 1:1.3 | -85 | 1 | <2 | - |
| 6 | | 1:1.3 | -60 | 1 | 33 (50) | 58:42 |
| 7 | | 2.0:1 | -60 | 24 | 61 (8) | 56:44 |

[a] GC yield of the corresponding bromocyclopropanes. Recovery of the starting material is shown in parenthesis.
[b] Ratio of the stereoisomers of the corresponding bromocyclopropane determined by capillary GC (PEG 20M) analysis.

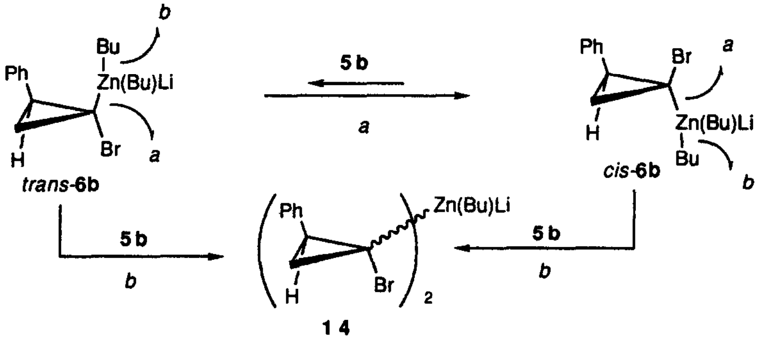


(8)



(9)

Reaction of **5b** with $(Bu)_3ZnLi$ (1.3 equiv) at -85°C for 1 h afforded a 64:36 mixture of *trans*- and *cis*-**13b** (82% yield) together with the recovery of **5b** (15%) (entry 1). The *trans*/*cis* ratio did not alter significantly when the above reaction attained to completion after 23 h (entry 2). In sharp contrast to the geometrical stability of 1-bromoalkenylzincate, carbenoid **6b** underwent isomerization at the carbenoid carbon in the presence of **5b**. Thus, the stereoselectivity was reversed when the reaction was carried out by using 2 equiv of **5b** for a longer period (entries 3 and 4). The isomerization is a relatively slow process provided **5b** was not used in excess. Formation of the *trans* isomer of the zincate was preferable under the kinetic conditions. It has been reported that the *trans* isomer of the lithium carbenoid is produced with high stereoselectivity in the reaction of **5b** with BuLi under the thermodynamic conditions.[5a] By contrast, our result showed that the *cis* isomer of zincate carbenoid **6b** is thermodynamically more stable. This implies that the $(Bu)_2ZnLi$ group is sterically more demanding than a bromine atom.

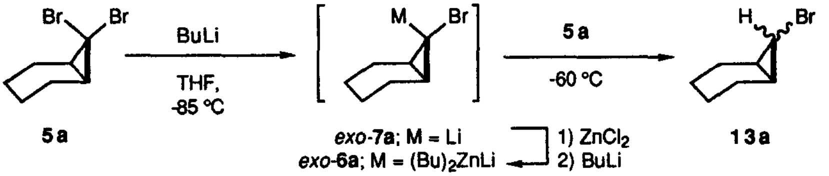


**Scheme 2**

The isomerization of zincate carbenoid **6b** proceeds most probably through a mechanism similar to that of lithium carbenoids (Scheme 2). Zincate carbenoid **6b** may undergo an exchange reaction with **5b** either to regenerate dibromide **5b** (isomerization process, path a) or to form bromobutane and zincate carbenoid **14** (path b). In entries 3 and 4, yields of **13b**, based on $(Bu)_3ZnLi$, exceeded 100%. The result indicates that the later pathway also takes place partially in these reactions.[13]

The reaction of **5a** with $(Bu)_3ZnLi$ proceeded rather slowly at -85 °C; only trace amount of bromonorcarane **13a** (<2%) was produced (eq 9, entry 5). When the reaction was carried out at -60 °C for 1 h, **13a** was obtained in 33% yield with *exo/endo* ratio of 58:42 (entry 6).[14] The ratio did not change remarkably in the reaction using 2 equiv of **5a** at -60 °C for 24 h (entry 7).

These results suggest that isomerization of **6a** is a very slow process and, therefore, the observed ratios are the result of kinetic control. The notion was verified by a following experiment. Treatment of lithium carbenoid *exo*-**7a**, prepared stereoselectively (98:2) by the reaction of **5a** with BuLi at -85 °C,[5b] with $ZnCl_2$ and BuLi (2 equiv) afforded *exo*-**6a** (eq 10). Upon standing at -60 °C with 1 equiv of **5a** for 1 h and with 5 equiv of **5a** for 24 h, *exo*-**6a** underwent isomerization slowly to give, by hydrolysis, **13a** with the *exo/endo* ratio of 93:7 and 89:11, respectively. In the absence of **5a**, *exo*-**7a** was configurationally stable, judging from the formation of a 98:2 mixture of *exo*- and *endo*-**6a** in the reaction for 1 h at -60 °C.



(10)

*Kinetic Stereoselectivities in Bromine/Metal Exchange Reactions*

It has sometimes been quoted that halogen/metal exchange takes place at the sterically less hindered halogen atom of *gem*-dihalo compounds.[5h,15,16] However, inspection of the kinetic selectivites in Table 1 revealed a general trend of a preferential reaction at the sterically more constrained bromine atom of 1,1-dibromoalkenes. For example, dibromoalkene **1d**, whose Z-bromine atom is considerably congested by the neighboring benzene ring, underwent the exchange stereoselectively at the Z-bromine atom to give the *E*-carbenoids (Table 2, entries 10 and 11). Similarly, in the reaction of **1c**, the bromine/zinc exchange took place at the bromine atom syn to the strically demanding isopropyl group with high selectivity (entries 7 and 8). In the reactions of monosubstituted dibromoalkenes **1f,g**, the zincate carbenoids with *E*-geometry were generated predominantly (entries 16-18).

It is somewhat less clear which bromine atom is more hindered in **1a** and **1b**. Semiempirical calculations (AM1)[17] were carried out to gain insight into their structures.[18] For the stable conformers of **1a,b**, the distances between allylic proton $H_a$ and $Br_a$ were found to be uniformly shorter than those between ortho proton $H_b$ and $Br_b$, suggesting that $Br_a$ is more hindered (Fig. 1). Values of torsional angles between the phenyl and alkenyl groups were calculated to be 63-71° and 90° for the stable conformers of **1a,b** and **1c**, respectively. Judging from the torsional angle of 50° for the stable conformer of **1f**, substitution of the alkyl group at the geminal position seems to render the phenyl group to rotate further, resulting in the reduction of its effective size against the syn bromine atom.

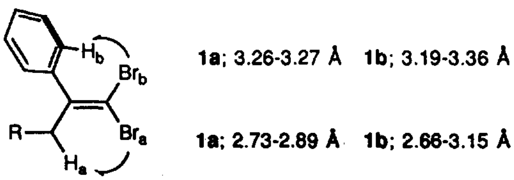
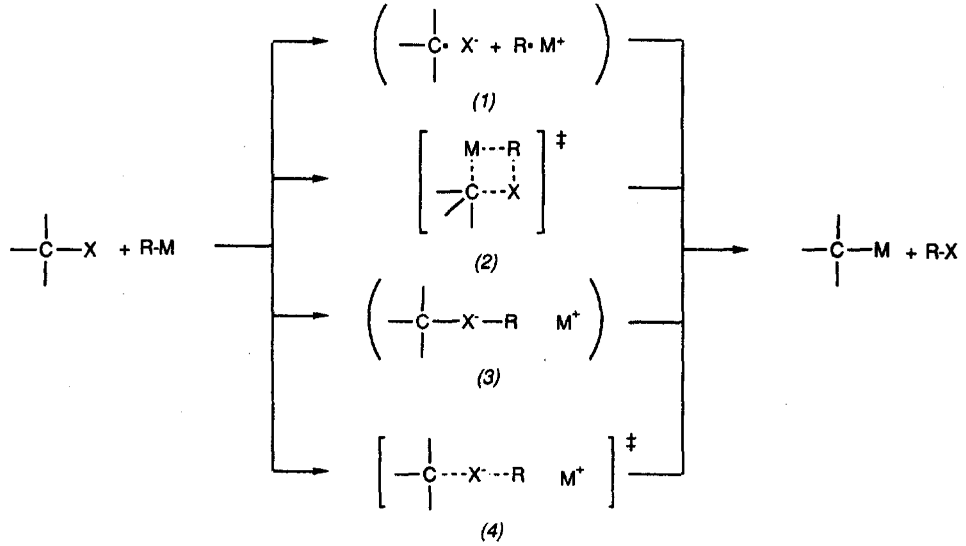


Fig. 1

Levels of kinetic selectivities depend on the extent of steric constraint of the bromine atoms. Of monosubstituted dibromoalkenes, **1f,g** with the sterically more demanding substituents exhibited moderate selectivity for the reaction at the bromine atom syn to the substituents. Of disubstituted dibromoalkenes, higher selectivities were observed in the reactions of **1c-e** with a more congested bromine atom than **1b**.

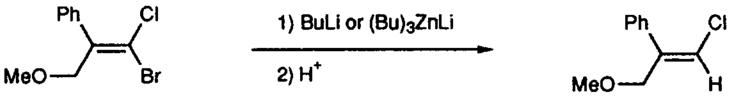
The bromine/zinc exchange of dibromocyclopropanes **5a,b** also proceeded preferentially at the sterically more constrained bromine atoms under the kinetically controlled conditions (Table 3). Results suggesting similar stereochemical bias has been reported in bromine/lithium exchange reaction of **5a**, carried out presumably under the kinetic conditions. Thus, Seyferth and co-workers noted the stereoselective formation of *exo*-**7a** (81:19) when **5a** was added to a solution of BuLi.[5a]. Similar stereoselectivity was also reported by Nozaki and Hiyama in the methylation of the carbenoid; addition of BuLi to a mixed solution of **5a** and iodomethane in THF-HMPA at -95 °C afforded a 80:20 mixture of *exo*- and *endo*-7-bromo-7-methylnorcarane in 86% yield.[22]

Halogen/lithium exchange reaction is a principal method for the preparation of a variety of organolithium compounds and much effort has been made to elucidate the mechanism. Four different mechanisms have been suggested for the reaction; (1) a stepwise process initiated by a single electron transfer; (2) a four-centered concerted process; (3) formation of an intermediate 10-X-2 ate complex, and (4) a concerted $S_N2$ displacement (Scheme 3). Recently, Bailey and Patricia have reviewed these mechanistic studies and they noted that the pathway followed may be dependent on the reactants and the reaction conditions.[23] More recently, Beak and Allen demonstrated, by using an approach based on endocyclic restriction test, that aryl bromide/alkyllithium exchange reaction proceeds through an ate complex or an $S_N2$ mechanism which involves geometrically restricted linear transition state.[23] Although halogen/metal exchange reaction of *gem*-dihalo compounds is frequently used in preparation of carbenoids, the mechanism of the exchange reaction has not been addressed previously. Elucidation of the mechanism is of significant importance for the stereocontrol in carbenoid generation.



**Scheme 3**

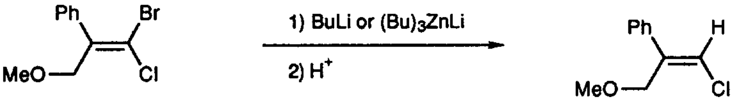
Single electron transfer (SET) has been claimed in bromine/lithium exchange for a number of systems.[25] Observation of loss of configuration of radical intermediates, involved in the mechanism, as well as their rearrangement has often been adopted as an experimental proof of the SET mechanism.[23,26] Alkenyl radicals are known to undergo a rapid geometrical isomerization.[26,27] Although the isomerization is known to be retarded in cage processes,[28] one can expect a partial loss of stereochemical integrity in the bromine/metal exchange involving a SET mechanism. In order to evaluate the stereospecificity, bromine/lithium and bromine/zinc exchange reactions of bromochloroalkenes *E*- and *Z*-**15** were examined. The results shown in eqs 11 and 12 clearly demonstrate that the exchange reaction takes place stereospecifically with retention of the configuration of the carbenoid carbon. In the exchange reaction involving SET mechanism, formation of several minor products by hydrogen abstraction, combination, and disproportionation of the radical intermediates is often observed.[23] The exchange reaction of the *gem*-dibromo compounds proceeded cleanly without formation of such byproducts. In addition, (${}^t$Bu)$_3$ZnLi which should be a better electron donor, in comparison with (Bu)$_3$ZnLi, exhibited a lower reactivity in the bromine/zinc exchange reaction (Table 2, entries 4, 15, and 21). Judging from these results, the SET mechanism is less likely for the present carbenoid formation .



(11)

**Z-15** (*Z*:*E* =91:9)

*E*-**16**
BuLi; 83%, *E*:*Z*=91:9
(Bu)$_3$ZnLi; 92%, *E*:*Z*=92:8

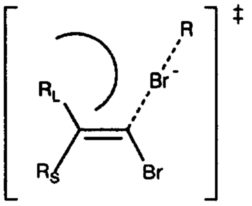


(12)

*E*-**15** (*E*:*Z* = 67:33)

*Z*-**16**
BuLi; 90%, *Z*:*E*=63:37
(Bu)$_3$ZnLi; 97%, *Z*:*E*=67:33

The observation of the higher reactivities of the more hindered bromine atom is not compatible with a sterically demanding four-centered transition state model. The X-ray structure of a lithium bis(pentafluorophenyl)iodinanide-TMEDA complex has been determined by Franham and Calabrese.[29] This species has a nearly linear C-I-C arrangement (∠C-I-C = 175 °C) with long carbon-iodine bond distances (2.331(5), 2.403 (6)). The selectivities observed in the present study are most reasonably explained by a linear transition state (**17**) of either an ate complex[30] or S$_N$2[31] reaction where strain relief due to elongation of the carbon-bromine bond is expected in the reaction at the more hindered bromine atom. Because metal cations (Li$^+$, (R)$_2$ZnLi$^+$) may locate out of the plane in **17**, a directing effect of metal chelation could not be expected according to this mechanism. Indeed, similar levels of stereoselectivity in the bromine/lithium exchange reaction of **1a** and **1b** as well as the nonselective reaction of the benzyloxymethyl (BOM) derivatives **1f** indicates that such effect is not responsible in kinetically controlled reactions.



**17**

## CONCLUSION

We have shown that the lithium carbenoids, generated by the reaction of 1,1-dibromoalkenes with BuLi, are configurationally stable at low temperatures but, in the presence of unreacted dibromoalkenes, they undergo a facile isomerization at the carbenoid carbons. It has also been shown that the zincate carbenoids generated from 1,1-dibromoalkenes are configurationally stable irrespective of the stoichiometry of the reaction. By contrast, the zincate carbenoid derived from 1,1-dibromocyclopropanes are found to undergo isomerization in the presence of the excess dibromocyclopropanes. These isomerization reactions have been proved to proceed through a mechanism involving bromine/metal exchange between the carbenoids and unreacted dibromo compounds. Highly stereoselective formation of the lithium carbenoids was observed in the reaction of 1,1-dibromoalkenes under the thermodynamic conditions. Under the kinetically controlled conditions, both the bromine/lithium and bromine/zinc exchange reactions took place preferentially at the sterically more hindered bromine atom of the dibromoalkenes and dibromocyclopropanes. The trends in stereoselectivites are most reasonably explained by a linear transition state of either an ate complex or $S_N2$ displacement mechanism where strain relief due to elongation of the carbon-bromine bond is expected in the reaction at the more hindered bromine atom.

## EXPERIMENTAL

$^1$H- and $^{13}$C-NMR spectra were recorded in $CDCl_3$ at 300 MHz and 75.6 MHz, respectively. Microanalyses were performed by the Microanalysis Center of Kyoto University. GC analyses were performed with 20 m PEG-20M and 30 m OV-1 capillary columns. Wakogel C-300 was used for flash chromatography. Unless otherwise specified, all organic extracts were dried over $Na_2SO_4$. THF was distilled from sodium benzophenone ketyl. Commercial anhydrous $ZnCl_2$ was dried in vacuo at 100 °C for 10 h over $P_2O_5$. All the reactions were performed under a nitrogen or argon atmosphere. Reactions at -85, -94, and -116 °C were carried out by using a Neslab Cryo Cool immersion cooler, liquid nitrogen/toluene bath, and liquid nitrogen/ether bath, respectively.

The following starting materials were prepared according to literature; dibromoalkenes **1a,b,e-i**[4a], dibromocyclopropanes **4a,b**[32], and bromochloroalkenes *Z*- and *E*-**15**.[4a] Characterization of reaction products **11a,b,e-i**, **12f**, and **16** were reported previously.[4a]

### *1,1-Dibromo-3-methyl-2-phenylbut-1-ene* (**1c**)

The compound was prepared in 75% yield by the reaction of isobutyrophenone with diethyl dibromolithiomethanephosphonate (1.2 equiv).[32] **1c**: $^1$H-NMR δ 0.97 (6H, d, *J* = 6.9 Hz), 3.32 (1H, sept, *J* = 6.9 Hz), 7.04 (2H, m), 7.31-7.41 (3H,m); $^{13}$C-NMR δ 20.41, 35.63, 88.30, 127.51, 128.10, 128.49, 138.74, 152.28; IR (KBr) 1600 (m), 1465 (s), 1455 (s), 1435 (s), 1115 (s), 890 (s), 790 (s), 780 (s), 765 (s), 730 (s), 700 (s), 620 (s), 530 (s) cm$^{-1}$; mass spectrum, m/z (relative intensity) 306, 304, 302 ($M^+$, 9, 17, 9), 225, 223 (19), 182, 180 (10), 144 (100), 143 (75), 129 (71), 128 (79); exact mass calcd for $C_{11}H_{12}{}^{79}Br_2$; 301.9306, found; 301.9341, calcd for $C_{11}H_{12}{}^{79}Br^{81}Br$; 303.9286, found; 303.9309, calcd for $C_{11}H_{12}{}^{81}Br_2$; 305.9266, found; 305.9304. Anal. Calcd for $C_{11}H_{12}Br_2$: C, 43.46; H, 3.98. Found C, 43.69; H, 4.07.

### *(2,3-Benzo-2-cyclohexenylidene)dibromomethane* (**1d**)

The compound was prepared in 95% by the reaction of 3,4-dihydro-1(2*H*)-naphthalenone with diethyl dibromo-lithiomethanephosphonate (2.0 equiv).[32] **1d**: bp 84-85 °C/ 0.05 mmHg ; $^1$H-NMR δ 1.76-1.85 (6H, m), 2.65 (2H, t, *J* = 6.5 Hz), 2.68 (2H, t, *J* = 6.9 Hz), 7.14-7.28 (3H, m), 7.877 (1H, m); $^{13}$C-NMR δ 22.88, 30.10, 34.12, 86.62, 125.14, 127.56, 128.22, 128.93, 134.46, 140.35, 140.60; IR (liquid film) 1600 (w), 1480 (s), 1450 (s), 795 (s), 755 (s), 745 (s) cm$^{-1}$; mass spectrum, m/z (relative intensity) 304, 302, 300 ($M^+$, 25, 50, 25), 223, 221 (12), 142 (89), 141 (100); exact mass calcd for $C_{11}H_{10}{}^{79}Br_2$; 299.9149, found; 299.9148, calcd for $C_{11}H_{10}{}^{79}Br^{81}Br$; 301.9129, found; 301.9135, calcd for $C_{11}H_{10}{}^{81}Br_2$; 303.9109, found; 303.9113. Anal. Calcd for $C_{11}H_{10}Br_2$: C, 43.75; H, 3.34. Found C, 44.02; H, 3.33.

### *General Procedure for Br/Li Exchange Reaction of Dibromoalkenes* **1a-e** *with BuLi under Kinetic Conditions*

To a stirred solution of BuLi (0.5 mmol, 1.62 N in hexane) in THF (1.5 mL) at -94 °C was added a THF (0.25 mL) solution of dibromoalkene **1** (0.25 mmol) during a 90-sec period. Reaction was quenched immediately by adding 1 M solution of AcOH in THF. The mixture was poured into brine and extracted three times with ether. The dried organic layer was analyzed by capillary GC (PEG-20M) using the internal standard method.

*General Procedure for Br/Li Exchange Reaction of Dibromoalkenes* **1a-e** *with BuLi under Thermodynamic Conditions*

To a stirred solution of dibromoalkene **1** (0.5 mmol) in THF (0.75 mL) at -94 °C was added BuLi (0.25 mmol, 1.62 N in hexane) during a 90-sec period. After being stirred at -94 °C for 10-30 min, the mixture was quenched by adding 1 M solution of AcOH in THF. The mixture was poured into brine and extracted three times with ether. The dried organic layer was analyzed by capillary GC (PEG-20M) using the internal standard method. Spectral data of new compounds are as follows.

*(E)-1-Bromo-3-methyl-2-phenylbutene* (*E*-**11c**):[33] $^1$H-NMR δ 1.04 (6H, d, *J* = 7.0 Hz), 3.31 (1H, sept, *J* = 7.0 Hz), 6.03 (1H, s), 7.13 (2H, m), 7.28-7.33 (3H, m); IR (liquid film) 1600 (s), 1490 (s), 1455 (s), 1440 (s), 1210 (s), 770 (s), 715 (s), 700 (s), 670 (s) cm$^{-1}$; MS, m/z (relative intensity) 226, 224 (M$^+$, 18, 18), 145 (100), 130 (29), 129 (39), 128 (26), 117 (26), 102 (32), 91 (38); HRMS cacd for $C_{11}H_{17}{}^{79}B$: 224.0201, found 224.0183, calcd for $C_{11}H_{13}{}^{81}Br$: 226.0181, found 226.0227. Anal. Calcd for $C_{11}H_{13}Br$ (mixture of *E* and *Z* isomers): C, 58.69; H, 5.82. Found C, 58.81; H, 5.76.

*(Z)-1-Bromo-3-methyl-2-phenylbutene* (Z-**11c**):[33] $^1$H-NMR δ 1.07 (6H, d, *J* = 6.8 Hz), 2.70 (1H, d sept, *J* = 1.2 and 6.8 Hz), 6.24 (1H, d, *J* = 1.2 Hz), 7.15 (2H, m), 7.30-7.42 (3H, m); IR (liquid film) 1595 (s), 1490 (s), 1465 (s), 1460 (s), 1440 (s), 1290 (s), 790 (s), 770 (s), 755 (s), 730 (s), 695 (s) cm$^{-1}$; MS, m/z (relative intensity) 226, 224 (M$^+$, 20, 20), 145 (100), 130 (31), 129 (47), 128 (29), 117 (28), 102 (40), 91 (49); HRMS cacd for $C_{11}H_{17}{}^{79}B$: 224.0201, found 224.0191, calcd for $C_{11}H_{13}{}^{81}Br$: 226.0181, found 226.0196.

*(E)-(2,3-Benzo-2-cyclohexenylidene)bromomethane* (*E*-**11d**):[33] $^1$H-NMR δ 1.87 (2H, quint, *J* = 6.3 Hz), 2.66 (2H, dt, *J* = 2.1 and 6.3 Hz), 2.77 (2H, t, *J* = 6.3 Hz), 6.75 (1H, t, *J* = 2.1 Hz), 7.14-7.25 (3H, m), 7.48 (1H, dd, *J* = 1.8 and 7.2 Hz); IR (liquid film) 1610 (s), 1585 (s), 1565 (s), 1480 (s), 1450 (s), 1435 (s), 1210 (s), 745 (s), 715 (s), 700 (s) cm$^{-1}$; mass spectrum, m/z (relative intensity) 224, 222 (M$^+$, 60), 143 (50), 128 (100), 115 (66); exact mass calcd for $C_{11}H_{11}{}^{79}Br$; 222.0044, found; 222.0051, calcd for $C_{11}H_{11}{}^{81}Br$; 224.0024, found; 224.0012; Anal. Calcd for $C_{11}H_{11}Br$ (mixture of *E* and *Z* isomers): C, 59.22; H, 4.97. Found C, 59.42; H, 4.85.

*(Z)-(2,3-Benzo-2-cyclohexenylidene)bromomethane* (Z-**11d**):[33] $^1$H-NMR δ 1.90-1.99 (2H, m), 2.50-2.54 (2H, m), 2.87 (2H, t, *J* = 6.6 Hz), 6.23 (1H, t, *J* = 1.2 Hz), 7.14-7.28 (3H, m), 8.21 (1H, dd, *J* = 2, 7 Hz); IR (liquid film) 1600 (m), 1480 (s), 1450 (s), 1445 (s), 1430 (s), 1325 (s), 1265 (s), 1100 (s), 775 (s), 760 (s), 740 (s), 720 (s), 675 (s) cm$^{-1}$; mass spectrum, m/z (relative intensity) 224, 222 (M$^+$, 59), 143 (51), 128 (100), 115 (66); exact mass calcd for $C_{11}H_{11}{}^{79}Br$; 222.0044, found; 222.0047, calcd for $C_{11}H_{11}{}^{81}Br$; 224.0024, found; 224.0004.

*Reaction of Lithium Carbenoid* **3a** *with Dibromoalkene* **1b** *(eq 4)*

To a stirred solution of dibromoalkene **1a** (153 mg, 0.5 mmol) in THF (0.8 mL) at -94 °C was added BuLi (0.15 mL, 0.25 mmol, 1.62 N in hexane) during a 90-sec period and the mixture was stirred at -94 °C for 10 min. Dibromoalkene **1b** (145 mg, 0.5 mmol) was added to the resulting solution of lithium carbenoid **2a** at the same temperature. After being stirred for 10 min, the mixture was quenched by adding 1 M solution of AcOH in THF. The mixture was poured into brine and extracted three times with ether. The dried organic layer was analyzed by capillary GC (PEG-20M) using an internal standard method. The analysis showed the presence of **11a** (0.24 mmol, 48% yield based on **1a** used, *E*:*Z* = 11:89), **11b** (0.01 mmol, 2% yield based on **1b** used, *E*:*Z* = 57:43), **1a** (0.26 mmol, 53% yield), **1b** (0.48 mmol, 96% yield).

The reaction of lithium carbenoid **2a** with **1b** (eq 6) was carried out by a procedure identical to that described above except that the order of addition of dibromoalkenes **1a** and **1b** was interchanged. The capillary GC (PEG-20M) analysis showed the presence of **11a** (0.21 mmol, 41% yield based on **1a** used, *E*:*Z* = 8:92), **11b** (0.04 mmol, 7% yield based on **1b** used, *E*:*Z* = 71:29), **1a** (0.29 mmol, 59% yield), **1b** (0.45 mmol, 89% yield).

*Bromine/Zinc Exchange Reaction of Dibromoalkenes* **1c,d** *(Table 2, entries 8, 9, 11, and 12) and Dibromocyclopropane* **5a,b** *(Table 3) with (Bu)$_3$ZnLi*

The reaction of **1c** for 5 min (Table 2, entry 8) is given as a representative example. To a solution of anhydrous $ZnCl_2$ (1.25 mmol) in THF (3.8 mL) at 0 °C was added a solution of BuLi (2.31 mL, 3.75 mmol, 1.62 M in hexane) and the mixture was stirred for 15 min. To the resulting solution of (Bu)$_3$ZnLi at -85 °C was added a THF (1.5 mL) solution of 1,1-dibromoalkene **1c** (136 mg, 1.0 mmol) and the mixture was stirred for 5 min. Reaction was quenched by adding 1 M solution of AcOH in THF at -85 °C. The mixture was poured into aq HCl (1 N) and was extracted three times with ether. The combined extracts were washed with aq $NaHCO_3$ solution. The analysis of the dried organic layer by capillary GC (PEG-20M) using an internal standard method showed the presence of bromoalkene **11c** (0.24 mmol, 24%, *E*:*Z* = 4:96) and **1c** (0.74 mmol, 74%).

*Attempted Isomerization of Zincate Carbenoid Z-***2a** *in the Presence of Dibromoalkene* **1a**

Lithium carbenoid **3a** (*Z*:*E* = 89:11) was prepared by the reaction of dibromoalkene **1a** (153 mg, 0.5 mmol) with BuLi (0.15mL, 0.25 mmol, 1.62 M in hexane) in THF (1.5 mL) under the thermodynamic conditions as described before. A solution of $Bu_2Zn$, prepared by the reaction of $ZnCl_2$ (38 mg, 0.28 mmol) with BuLi (0.35 mL, 0.56 mmol, 1.62 M in hexane) in THF (0.3 mL), was slowly added to the solution of **3a** at -94 °C. After being stirred at -85 °C for 30 min, the reaction mixture was quenched by adding 1 M solution of AcOH in THF. The mixture was poured into aq HCl (1 N) and was extracted three times with ether. The combined extracts were washed with aq $NaHCO_3$ solution. The analysis of the dried organic layer by capillary GC (PEG-20M) using an internal standard method showed the presence of bromoalkene **11a** (0.23 mmol, 96% (based on **1c** consumed), *Z*:*E* = 87:13) and **1c** (0.26 mmol).

*Isomerization of Zincate Carbenoid exo-***6a** *in the Presence of Dibromo-cyclopropane* **5a** *(eq 10)*

To a stirred solution of dibromocyclopropane **5a** (152 mg, 0.6 mmol) in THF (2.1 mL) at -85 °C was added BuLi (0.37 mL, 0.6 mmol, 1.62 N in hexane) during a 90-sec period and the mixture was stirred at the same temperature for 15 min. To the resulting solution of lithium carbenoid *exo*-**7a**[34] at -85 °C was then added successively a THF (1.5 mL) solution of $ZnCl_2$ (82 mg, 0.6 mmol), BuLi (0.74 mL, 1.2 mmol, 1.62 N in hexane), and a THF (1.5 mL) solution of **5a** (152 mg, 0.6 mmol). After being stirred for 1 h at -60 °C, the mixture was quenched by adding 1 M solution of AcOH in THF. The mixture was poured into aq HCl (1 N) and was extracted three times with ether. The combined extracts were washed with aq $NaHCO_3$ solution. Analysis of the dried organic layer by capillary GC (OV-1) using an internal standard method showed the presence of bromonocarane **13a** (0.46 mmol, 77% *exo*:*endo* = 93:7) and **5a** (0.52 mmol, 87% recovered). The reaction was also carried out identical to that described above except that the solution of the zincate carbenoid was stirred for 24 h and that additional 5 equiv of **5a** was used. Analysis of the reaction mixture showed the presence of bromonocarane **13a** (87% *exo*:*endo* = 89:11) and **5a** (91% recovered).

*Reactions of Bromochloroalkenes* **E- and Z-15** *with BuLi and (Bu)$_3$ZnLi*

To a solution of bromochloroalkene *Z*-**15** (*Z*:*E* = 91:9) (73 mg, 0.28 mmol) in THF (0.84 mL) at -94 °C was added BuLi (0.19 mL, 0.31 mmol, 1.62 M in hexane) during a 90-sec period. Reaction was quenched by adding 1 M solution of AcOH in THF. The mixture was poured into brine and extracted three times with ether. The dried and concentrated organic extract was purified by flash chromatography (silicagel, eluting with 5% ether in pentane) to give a 91:9 mixture of *E*- and *Z*-**16**[4a] (42 mg, 83% yield).

A THF (2.1 mL) solution of (Bu)$_3$ZnLi was parepared by the reaction of $ZnCl_2$ (94 mg, 0.69 mmol) and BuLi (1.3 mL, 2.1 mmol, 1.62 M in hexane). To this solution at -85 °C was added a THF (0.8 mL) solution of *Z*-15 (*Z*:*E* = 91:9) (76 mg, 0.29 mmol), and the mixture was stirred for 8 h at the same temperature. Reaction was quenched by adding 1 M solution of AcOH in THF. The mixture was poured into aq HCl (1 N) and was extracted three times with ether. The combined extracts were washed with aq $NaHCO_3$ solution. The dried ($Na_2SO_4$) and concentrated organic layer was purified by flash chromatography (5% ether in pentane) to give a 67:33 mixture of *E*- and *Z*-**16**[4a] (51 mg, 97% yield).

Reactions of *E*-**15** ($E/Z$ = 67/33) were carried out by a procedure similar to that described above. The reaction time for $(Bu)_3ZnLi$ was 12 h.

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13. Zincate carbenoid **2e** exhibited a similar reactivity.[4a]
14. At the higher temperatures, 1,2-alkyl migration of the intermediate zincate carbenoid took place concomitantly, making the stereochemical analysis of the initial bromine/zinc exchange difficult.

15. Braun and Mahrler reported that reaction of dibromoalkene **9** with 1.2 equiv BuLi at -105 °C afforded a ca. 1:2 mixture of *E*- and *Z*-**10**.[6]

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18 The initial structures were obtained by a torsion-angle tree-search method[19] by using MacroModel (MM2 force field).[20,21] Optimization of these structures by AM1 semiempirical MO method revealed that **1a** and **1b** have two and five stable conformers, respectively, within 2.0 kcal/mol of the corresponding lowest energy conformers. Heat of formation (kcal/mol) and the torsional angel (degree, the value in parentheses) for each conformer are as follows: **1a**, 35.34 (68), 35.70 (67), **1b**, 2.90 (71), 2.99 (65), 3.75 (63), 3.81 (69), 4.16 (68).

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33. Stereochemical determination of these compounds is based on NOESY analyses.

34. In a separate experiment, the lithium carbenoid generated under similar conditions was hydrolyzed with AcOH/THF to give a 98:2 mixture of *exo*- and *endo*-**13a**.

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