J. Org. Chem. **1995**, *60*, 663−672 **663**

A Mechanistic Study of the Reactions of Geminal Dihalides with LDA. Evidence for a Single Electron Transfer Pathway in the Reaction of Geminal Diiodides[†]

E. C. Ashby,* Abhay K. Deshpande, and Girish S. Patil[‡]

School of Chemistry and Biochemistry, Georgia Institute of Technology, Atlanta, Georgia 30332

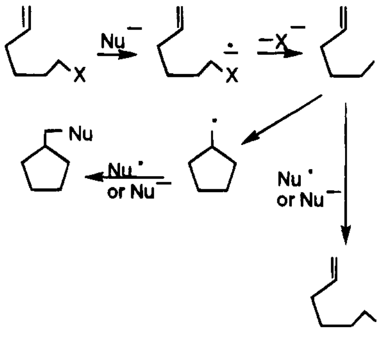
Received August 26, 1994[⊗]

While the reaction of the geminal dichloride, 6,6-dichloro-5,5-dimethyl-1-hexene (**8a**) with LDA afforded only one product, which was derived from a chlorocarbene intermediate, the reaction of the corresponding geminal diiodide **8b** resulted in the formation of a number of products that were accounted for by a single electron transfer (SET) initiated reaction. This difference in the reactivity patterns of the two substrates shows that the reduction potential of **8b** is more favorable than that of **8a** and that LDA can function as a one-electron donor. Additionally, **8a** was more reactive toward LDA than the already studied monochloro substrate (**1a**) with the same carbon skeleton. This enhanced reactivity is attributed to the increased acidity of the hydrogen atom attached to the carbon bearing the two chlorine atoms in **8a**. The observation that **8b** reacted with LDA at a faster rate, not only relative to **8a** but also to the corresponding monoiodo compound **1c**, indicates that the reduction potential of **8b** is more favorable than that of **1c** for SET reduction by LDA. Based on the nature of the products formed in the reactions of **8a** and **8b** with LDA, evidence is presented that supports the notion that, in addition to funtioning as a strong base, LDA can also function as a one-electron donor toward the geminal diiodide **8b**.

Introduction

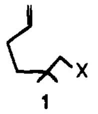
The reaction between an aliphatic halide and a nucleophile is one of the most fundamental reactions in organic chemistry. Extensive studies carried out by various workers over a number of years have revealed that these reactions frequently afford products that cannot be accounted for by a simple S_N1 or S_N2 process.[1−3] It is now well established that, depending upon the nature of the halide substrate, the nucleophile, and the solvent, nucleophilic aliphatic substitution can lead to products that are derived from radical intermediates.

Alkyl halides have been extensively used as typical substrates to study mechanistic features of nucleophilic aliphatic substitution. In order to establish radical intermediacy, it has been found very convenient to incorporate in these studies alkyl halides that can function as "cyclizable radical probes". The basis for this methodology stems from the fact that a nucleophile of favorable oxidation potential can serve as a one-electron donor toward a substrate of favorable reduction potential which can result in the formation of a radical intermediate. This intermediate can then react further by a number of pathways, e.g. undergo cyclization, an $S_{RN}1$ pathway, an atom-transfer radical chain cyclization, etc., to form the same products produced by both S_N1 and S_N2 pathways. Since the 5-hexenyl radical has been reported to cyclize,[4] at a rate of 10^5/s, to the methylcyclopentyl radical (eq 1), this type of radical probe has proven to be quite useful for the mechanistic studies of specific reactions.



(1)

Employing the sterically hindered neopentyl type halides has proven to be an excellent strategy to detect SET in a reaction. The neopentyl type system **1** has several advantages in the sense that being hindered, the possibility of a S_N2 pathway is decreased, by being a primary halide the likelihood of a S_N1 pathway is also decreased, and by not having a β-hydrogen atom, dehydrohalogenation is eliminated. These factors make the SET pathway more easily observable, if indeed it is at all possible.



1

1a: X=Cl, **1b**: X=Br
1c: X=I

Work in this group has dealt primarily with mechanistic studies concerning reactions of suitable "cyclizable" alkyl halides with a variety of nucleophiles such as cuprates,[5] enolates,[6] trimethyltin anion,[7] thiolates,[8] lithium diisopropylamide (LDA),[9] lithium aluminum hydride

---

[†] This paper is dedicated to the memory of Dr. Kenneth G. Hancock, former Director of Dynamics for the National Science Foundation. He was a gentleman and a scholar. He was also an excellent administrator, a tireless and dedicated worker for the advancement of chemistry, and a much loved, respected and appreciated colleague.

[‡] Present address: Systran Corp., Dayton, OH 45432.

[⊗] Abstract published in *Advance ACS Abstracts*, January 1, 1995.

(1) Kornblum, N.; Michel, R. E.; Kerber, R. C. *J. Am. Chem. Soc.* **1966**, *88*, 5662.

(2) Russell, G. A.; Dannen, W. C. *J. Am. Chem. Soc.* **1966**, *88*, 5663.

(3) Bunnett, J. F.; Kim, J. K. *J. Am. Chem. Soc.* **1970**, *92*, 7463.

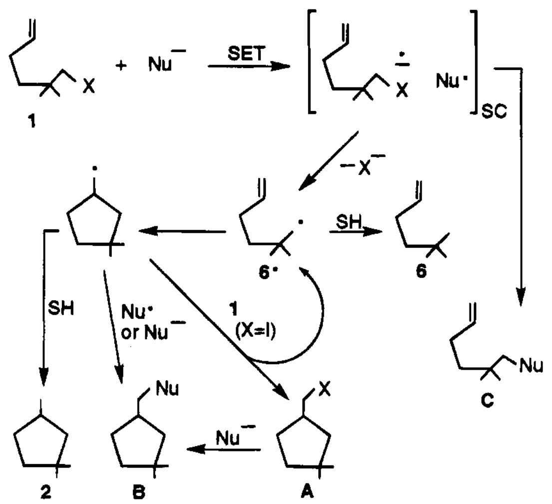
(4) (a) Arai, S.; Sato, S.; Shida, S. *J. Chem. Phys.* **1960**, *33*, 1277. (b) Ingold, K. U.; Chatgilialoglu, C.; Scaiano, J. C. *J. Am. Chem. Soc.* **1981**, *103*, 7739.

(5) Ashby, E. C.; DePriest, R. N.; Tuncay, A.; Srivastava, S. *Tetrahedron Lett.* **1982**, *23*, 5251.

(6) Ashby, E. C.; Argyropoulos, J. *J. Org. Chem.* **1985**, *50*, 3274.

0022-3263/95/1960-0663$09.00/0

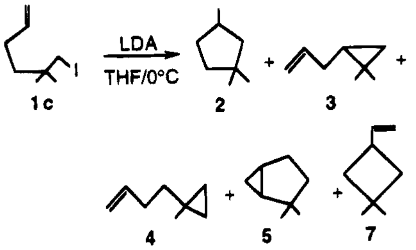
Scheme 1



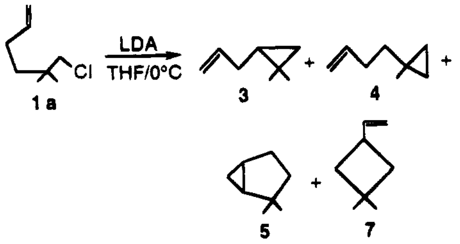
(LiAlH$_4$),[10] and diphenylphosphide anion.[11] Although considered to be a strong base, LDA has been shown to act as a one-electron donor in reactions with heterocycles,[12] α-bromo imines,[13] and conjugated acetylenes.[14] Recent work by this group aimed at a mechanistic evaluation of the reaction of LDA with the cyclizable probe 6-iodo-5,5-dimethyl-1-hexene (**1c**) has shown that, in such a reaction, there is involvement of carbene, carbanion, and free radical intermediates that lead to the formation of several products.[9] Based on the results of this study, it was observed that the extent of SET was the highest with the iodo substrate **1c** and that no evidence for SET was observed with the chloro substrate **1a**. The detailed electron transfer pathway involving substrate **1** and a nucleophile that leads to all radical derived products (in addition to the normal substitution products, eq 1) is shown in Scheme 1.

As seen in Scheme 1, the formation of hydrocarbons **2** and **6** is preceded by the radical **6•** which differs from the 5-hexenyl radical only in having a *gem*-dimethyl group on the carbon adjacent to the radical center. The introduction of such a group has been found to enhance the rate of cyclization of the resulting radical ($k_c = 3.6 \times 10^6$/s),[15] and this enhancement has been attributed to what is referred to as the Thorpe–Ingold or "*gem*-dimethyl" effect.[16–18] This ring closure has also been found to be far more regiospecific than the corresponding ring closure of the 5-hexenyl radical, in that with the 5-hexenyl radical, 2% of the six-membered ring was observed whereas with the *gem*-dimethyl substituted radical, exclusive formation of the five-membered ring was observed.[19] Experiments have shown that the ratio of the relative rate constant for the cyclization of the *gem*-dimethyl substituted 5-hexenyl radical (to the (dimethylcyclopentyl)methyl radical) to hydrogen atom abstraction by the radical (from n-Bu$_3$SnH) is 1.50 mol/L at 25 °C in benzene ($k_{1,5}/k_H = 1.50$ mol/L).[15] This favorable rate of cyclization compared to abstraction of a hydrogen atom has served as a useful criterion to detect the presence of radical intermediates in a particular reaction. Indeed, quite significant, or at times just detectable, yields of cyclized substitution products or hydrocarbons from open chain substrates are good indications that radicals are involved in the mechanistic pathway.

It is well known that alkyl iodides have a more favorable reduction potential, compared to alkyl bromides and alkyl chlorides and therefore more easily undergo reduction by an electron transfer pathway. This was indeed observed to be the case when the results of the reaction of **1c** with LDA were compared to those of **1a**.[9] While the reaction of **1c** led to the formation of the radical derived hydrocarbon **2**, as the major product (eq 2) and carbene-derived products **3–5** and **7** (which can also arise from a carbanion), the reaction of **1a** with LDA (eq 3) gave products **3–5** and **7**, but no **2**.



(2)



(3)

Although a considerable amount of work has been carried out with alkyl halides as the substrates in nucleophilic aliphatic substitution, the alkyl geminal dihalides have been relatively unexplored (except for photochemical studies[20]). It was therefore decided to study the reactions of aliphatic geminal dihalides with LDA with the primary objective directed toward determining how the reactivity of the geminal dihalide substrate toward LDA changes with the number and type

---

[7] (a) Ashby, E. C.; DePriest, R. N. *J. Am. Chem. Soc.* **1982**, *104*, 6144. (b) Ashby, E. C.; DePriest, R. N.; Su, W.-Y. *Organometallics* **1984**, *3*, 1718. (c) Ashby, E. C.; Su, W.-Y.; Pham, T. N. *Organometallics* **1985**, *4*, 1493.

[8] Ashby, E. C.; Park, W.-S.; Su, W.-Y. *J. Org. Chem.* **1985**, *50*, 5184.

[9] (a) Ashby, E. C.; Park, B. *Acta Chem. Scand.* **1990**, *44*, 291. (b) Ashby, E. C.; Park, B.; Patil, G. S.; Gadru, K.; Gurumurthy, R. *J. Org. Chem.* **1993**, *58*, 424.

[10] (a) Ashby, E. C.; DePriest, R. N.; Goel, A. B. *Tetrahedron Lett.* **1981**, *22*, 1763. (b) Ashby, E. C.; DePriest, R. N.; Goel, A. B. *Tetrahedron Lett.* **1981**, *22*, 3729. (c) Ashby, E. C.; DePriest, R. N.; Pham, T. N. *Tetrahedron Lett.* **1983**, *24*, 2825. (d) Ashby, E. C.; DePriest, R. N.; Goel, A. B.; Wenderoth, B; Pham, T. N. *J. Org. Chem.* **1984**, *49*, 3545. (e) Ashby, E. C.; Pham, T. N. *J. Org. Chem.* **1986**, *51*, 3598. (f) Ashby, E. C.; Wenderoth, B.; Pham, T. N.; Park, W.-S. *J. Org. Chem.* **1984**, *49*, 4505. (g) Ashby, E. C.; Pham, T. N.; Madjdabadi, A. A. *J. Org. Chem.* **1988**, *53*, 6156.

[11] Ashby, E. C.; Gurumurthy, R. G.; Ridlehuber, R. W. *J. Org. Chem.* **1993**, *58*, 4205.

[12] Newkome, G. R.; Hager, D. C. *J. Org. Chem.* **1982**, *47*, 599.

[13] Kimpe, N. D.; Yao, Z. P.; Schamp, N. *Tetrahedron Lett.* **1986**, *27*, 1707.

[14] Shen, C.; Ainsworth, C. *Tetrahedron Lett.* **1979**, *20*, 89.

[15] Beckwith, A. L. J.; Easton, C. J.; Lawrence, T.; Serelis, A. K. *Aust. J. Chem.* **1983**, *36*, 545.

[16] Allinger, N. L.; Zalkow, V. *J. Org. Chem.* **1960**, *25*, 701.

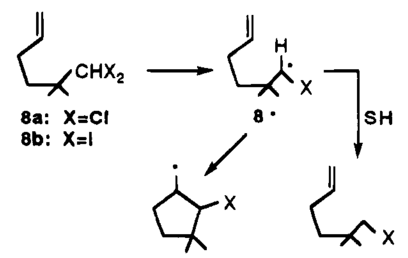
[17] Eliel, E. L.; Allinger, N. L.; Angyal, S. J.; Morrison, G. A. *Conformational Analysis*; Wiley: New York, 1965; p 191.

[18] Gream, G. E.; Serelis, A. K. *Aust. J. Chem.* **1978**, *31*, 863 and the references therein.

[19] Beckwith, A. L. J.; Lawrence, T. *J. Chem. Soc., Perkin Trans. 2* **1979**, 1535.

[20] (a) Meijs, G. F. *J. Org. Chem.* **1984**, *49*, 3863. (b) Rossi, R. A.; Santiago, A. N. *J. Chem. Res. (S)* **1988**, 172. (c) Meijs, G. F. *J. Org. Chem.* **1986**, *51*, 606. (d) Kropp, P. J.; Pienta, N. J. *J. Org. Chem.* **1983**, *48*, 2084 and the references therein. (e) Jones, C. R.; Moret, E.; Grant, B. *J. Org. Chem.* **1983**, *48*, 2090 and the references therein.

Scheme 2



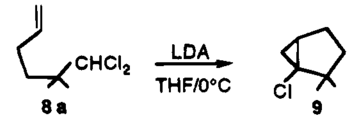
8a: X=Cl
8b: X=I

of halogen atoms attached to the same carbon atom and how this influences the mechanistic course of the reaction compared to what is already known about reactions involving alkyl monohalides.

The geminal dihalides that were chosen for this study have the general structure **8**, so that this substrate can function as a "cyclizable radical probe". If **8** receives an electron from a nucleophile, it would lead to the formation of the haloalkyl radical **8**$^\bullet$ which would be expected to abstract a hydrogen atom as well as cyclize (Scheme 2). This would mean that once the haloalkyl radical is formed, hydrogen atom abstraction would compete with cyclization. We have recently reported the calculated rates of cyclization of **8**$^\bullet$ as being 7.4 × 10^5/s with X = Cl, and 5.5 × 10^5/s with X = I.[21] An attempt was also made to determine the values of the reduction potentials of **8a** and **8b**. But despite careful experimental conditions, we were unsuccessful.

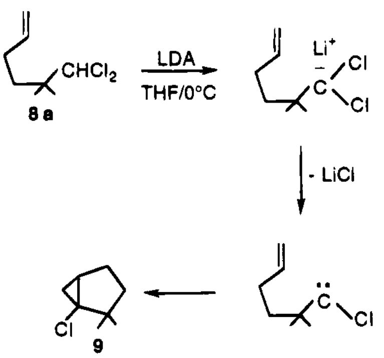
Results and Discussion

Reaction of 6,6-Dichloro-5,5-dimethyl-1-hexene (8a) with LDA. When 6,6-dichloro-5,5-dimethyl-1-hexene (**8a**) was allowed to react with LDA in THF at 0 °C, no reaction was observed at a molar ratio of 1:1 after 2 h; however, at 1:3 ratio, there was partial consumption of **8a** after 2 h. On the other hand, when the ratio of **8a** to LDA was increased to 1:5, all of the substrate reacted in about 2 h. Only one product (**9**) was obtained in this reaction (87% yield), and **9** (eq 4) was stable to LDA for 24 h at 0 °C (eq 4). Lack of formation of any other products in the reaction suggests that the reaction between **8a** and LDA, under the conditions employed, involves only one mechanistic pathway. The sole formation of **9** does not provide any basis for suggesting an electron transfer mechanism. The presence of two chlorine atoms on the same carbon atom has strongly enhanced the acidity of the proton attached to the carbon holding the chlorine atoms compared to the enhancement of the reduction potential of the molecule (Scheme 3). Therefore, since LDA is a very strong base, deprotonation should be a highly favorable process, even if the reduction potential of **8a** were more favorable for an ET reaction compared to that of **1a**, where only one chlorine atom is present. Indeed, the acidity increase in **8a** is very significant since earlier work with **1a** had shown[9] that its reaction with LDA (**1a**:LDA = 1:5) was very slow, and that even after 120 h at 0 °C, 53% of **1a** was recovered.



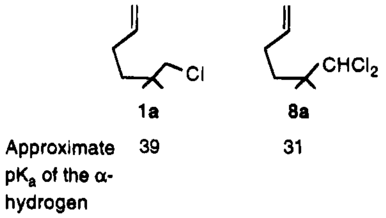
8a **9** (4)

Scheme 3



8a **9**

On the other hand, the introduction of an additional chlorine atom allowed the reaction of **8a** with LDA to proceed to completion in about 2 h. It would be reasonable to assume that in **1a**, the pK_a of the α-hydrogens would be approximately 39 since the pK_a of the hydrogens in CH_3Cl is reported to be 39.[22] For the dichloro substrate, **8a**, the pK_a of the α-hydrogen is expected to be approximately 31, since the reported pK_a for the protons in CH_2Cl_2 is 31.[22] This increase in the acidity of the protons in **8a** compared to **1a** of 8 pK_a units, is sufficient to account for the large increase in the rate of the reaction of **8a** compared to **1a** and is strong evidence that deprotonation is involved as the initial step of the reaction.



The fact that only intramolecular addition of the chlorocarbene across the C=C bond was observed to the exclusion of intramolecular insertion into a C—H bond, is easily explainable on the basis of what is known about the reactivity of halocarbenes.[23] The halocarbenes are classified as electrophilic carbenes, and the electronegativity of the halogen atom involved influences the electrophilicity of the halocarbene. Such an electrophilic carbene is known to prefer addition across an electron rich C=C bond.[24] This is exactly what is observed in the case of the chlorocarbene generated in the reaction of **8a** with LDA. Neither radical (pathway a) nor carbanion (pathway b) intermediates lead to the formation of **9** (Scheme 4).

Reaction of 6,6-Diiodo-5,5-dimethyl-1-hexene (8b) with LDA. Although the number of products formed, and their corresponding yields, in the reaction of **8b** with LDA were both influenced by the molar ratio of **8b** to LDA, a typical reaction between the two can be represented by eq 5.

Effect of Stoichiometry. When 6,6-diiodo-5,5-dimethyl-1-hexene (**8b**) was allowed to react with LDA in THF at 0 °C, the product composition and product yields

---

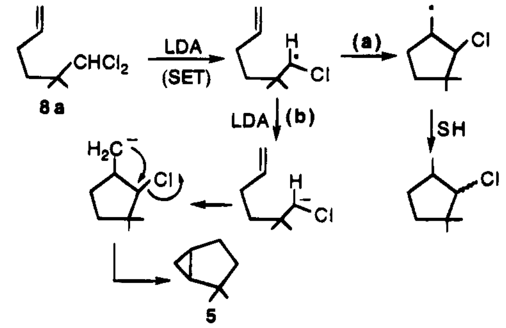
[21] Ashby, E. C.; Deshpande, A. K. *J. Org. Chem.* **1994**, *59*, 3798.

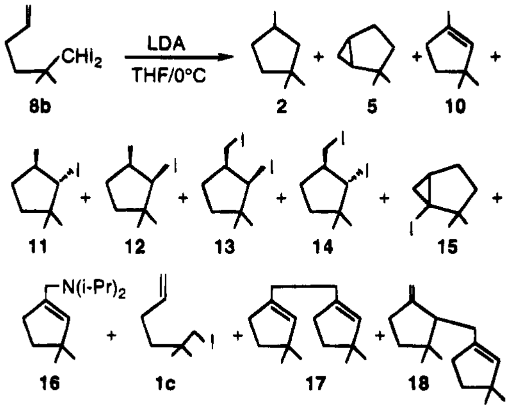
[22] Benderskii, V. A.; Krivenko, A. G.; Simbirtseva, G. V. *Elektrokhimiia* **1987**, *23*, 748.

[23] Kostikov, R. R.; Molchanov, A. P.; Khlebnikov, A. F. *Upsekhi Khimii* **1989**, *58*, 1122 and the references therein.

[24] (a) Skell, P. S.; Garner, A. Y. *J. Am. Chem. Soc.* **1956**, *78*, 5430. (b) Doering, W. v. E.; Henderson, W. A., Jr. *J. Am. Chem. Soc.* **1958**, *80*, 5274.

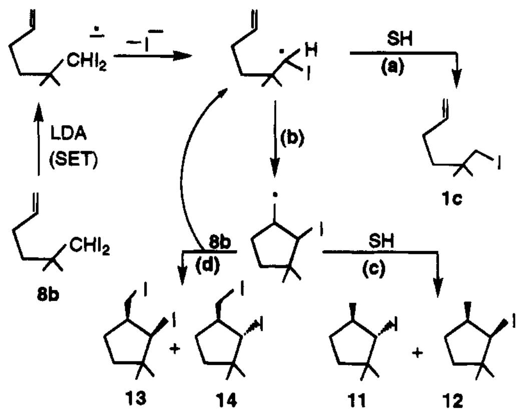
Scheme 4





(5)

Scheme 5

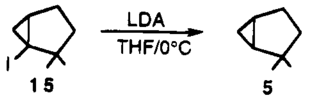


were found to be governed by the molar ratio of **8b** to LDA. The reaction was carried out at three different ratios, and the results obtained are summarized in Table 1 (exps 1−4). The products shown in the first three experiments are those that were formed, in less than a minute, on adding **8b** to LDA. At the lowest ratio of 1:1, 30% of unreacted **8b** was recovered (exp 1), even after 4 h at 0 °C. At an intermediate ratio of 1:3 (exp 2), no unreacted **8b** was recovered after 1 min; however, three additional products (**16**, **17**, and **18**) were observed. At the highest ratio employed (1:5, exp 3), nine products were detected initially; however, after 20 h (exp 4), products **11**, **12**, and **15** disappeared completely and the amount of product **5** increased dramatically.

The formation of a number of cyclized products in the reaction of **8b** with LDA strongly indicates the presence of free radicals as precursors to these products. Also, dimer formation suggests the involvement of radicals. Of all the products that were detected, only **15** appeared to be derived from an iodocarbene intermediate and is formed by the same pathway that was suggested for the formation of **9** from **8a**, except that proton abstraction from **8a** is much easier than **8b**. Thus **9** turns out to be the sole product from **8a**. Also, **8b** has a much more favorable reduction potential than **8a** so that the reaction of LDA with **8b** results in SET competition with carbene formation.

The formation of the iodo compounds **1c** and **11**−**14** in exps 1 and 2 can be accounted for by considering a SET pathway (LDA transfers an electron to **8b**), that leads to an open chain iodo radical, which serves as the precursor to all five iodo compounds (Scheme 5). As shown, if this iodo radical abstracts a hydrogen atom (pathway a), it would form **1c**.

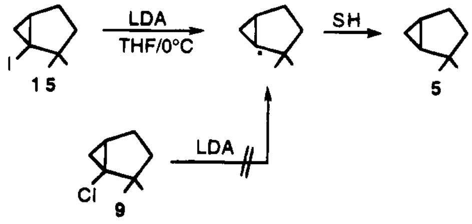
Cyclization of the radical (pathway b), followed by hydrogen atom abstraction (pathway c) leads to the two isomers **11** and **12**. Once the cyclized radical forms, in addition to abstracting a hydrogen atom, it could also abstract an iodine atom from **8b** (pathway d), resulting in the formation of the cyclized diiodo isomeric compounds **13** and **14** via a radical chain process. It was observed that the product distribution and product yields that were obtained in the reaction of **8b** with LDA at the three ratios employed were influenced by the amount of LDA present. With an increase in the amount of the base, the amount of **15** that was formed also increased, as expected. At 1:1 ratio, **15** was formed in 13% yield, at 1:3 ratio, 20% yield, and at 1:5 ratio, **15** was formed (initially) in 25% yield. However, as shown in Table 1 (exp 4), **15** was completely consumed by LDA after 20 h, resulting in the formation of **5** from 11 to 28%. These results show that **15** reacted with LDA to produce **5** (eq 6).



(6)

It is interesting that although **9** did not react with LDA, **15** did. This result can be interpreted as being indicative of a SET pathway in the reaction of the alkyl iodide **15** with LDA (Scheme 6), since **15** is expected to have a more favorable reduction potential than the alkyl chloride **9**.

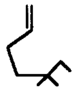
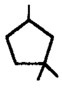
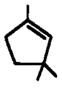
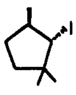
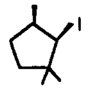
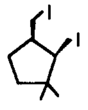
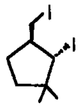
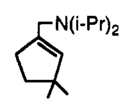
Scheme 6



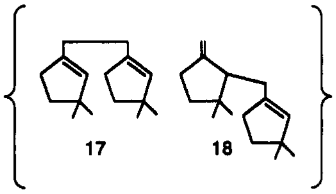
The diisopropylamino-substituted product **16** was detected in 2% yield in exp 2 and in 5% yield in exp 3. It was not detected at the lowest ratio of 1:1 (exp 1). A possible mode of formation of **16** involves the coupling of the cyclized radical generated from **8b** with a diisopropylamino radical (pathway a) or the diisopropylamino anion (pathway b), followed by dehydrohalogenation (Scheme 7).

The observation that **1c**, found in 10% yield (exp 2), was not detected when the reaction of **8b** with LDA was carried out at a 1:5 ratio (exp 3) suggests that **1c** reacts with the excess LDA. In fact, earlier work by this group has shown that **1c**, on reaction with LDA, affords **2** as the main product (~50%).[9] This means that in the

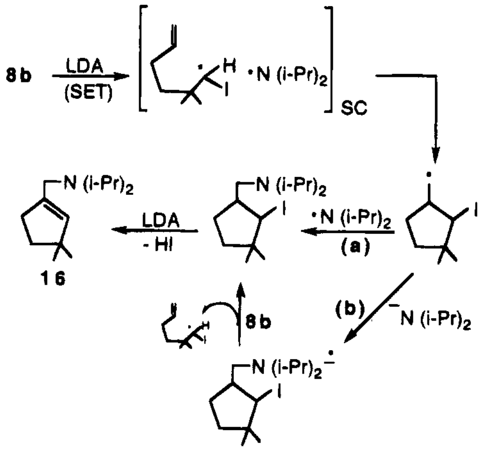
Table 1. Reactions of 6,6-Diiodo-5,5-dimethyl-1-hexene (8b) with LDA in THF at 0 °C

Exp. No.	Ratio 8b : LDA	% 8b Recovered	% Yields of Products[a]									
			 1c	 2	 5	 10	 11	 12	 13	 14	 15	 16
1	1 : 1[b]	30	5	0	2	1	2	3	25	12	13	0
2	1 : 3[b]	0	10	1	6	2	4	4	0	10	20	2
3	1: 5[b, c]	0	0	5	11	10	6	2	0	0	25	5
4	1 : 5[d]	0	0	7	28	14	0	0	0	0	0	5

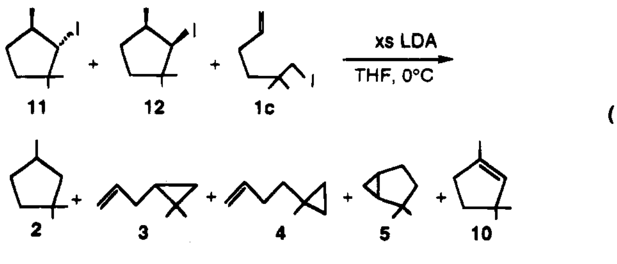
[a] In exp. 2, the dimers 17 and 18 were also formed in yields of 3% and 2%, respectively, and in exp. 3, they were formed in yields of 5% and 4%, respectively. [b] Product composition and yields within a minute after adding 8b to LDA. [c] This reaction was also carried out in the dark, but absence of light did not reduce the rate of formation of products (which is very fast in laboratory light) appreciably. [d] Product composition and yields after 20 hours at 0°C. Among the products were also 17 and 18, formed in yields of 5% and 4%, respectively.



Scheme 7



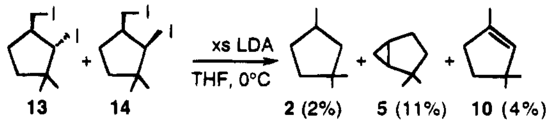
reaction of **8b** with LDA, at least some of **2** is a result of a reaction between **1c** and LDA. However, **2** can also be envisioned as being the product of the reaction of **11**/**12** with LDA (reduction). Additionally, reaction of **11**/**12** with LDA would also be expected to produce **10** by dehydrohalogenation. When a mixture of **1c**, **11**, and **12** (in a 2:1:1 ratio) was allowed to react with excess LDA at 0 °C, in THF (eq 7), the products detected were **2**–**5**



(7)

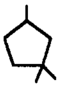
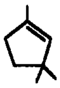
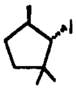
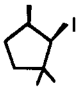
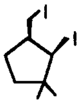
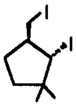
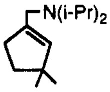
and **10**. It has already been shown that **3**–**5** are derived from the carbene formed from **1c**.[9] The products **2**–**5** and **10** were found in the ratio of 10:1:2:1:9. Of the two cyclized monoiodo isomers **11** and **12**, the loss of a molecule of HI, to form **10**, is more likely to take place from the *cis* isomer **12**, since the iodine and hydrogen atoms are *anti* to each other, making an easy *anti* elimination of HI. This explanation is supported by the fact that **12** decreases 3-fold in concentration compared to **11** when the ratio of **8b** to LDA proceeds from 1:3 to 1:5.

Observation of the product composition of the reaction of **8b** with LDA shows that the two cyclized diiodo isomers (**13** and **14**) were detected in yields of 25 and 12%, respectively, in exp 1 (1:1 ratio). However, on increasing the amount of LDA (exp 2 and exp 3), not only did the yields of **13** and **14** decrease, but the overall material balance of the reaction decreased. Lowering of the yields indicates that **13** and **14** reacted further with the excess LDA. Therefore, it was decided to allow an isolated mixture of **13** and **14** to react with exess LDA, in THF, at 0 °C (eq 8). The analysis of the products formed revealed that these products accounted for the consumption of only a small portion of the original mixture (no unreacted **13** or **14** was recovered). Plausible pathways that can lead to the three observed products are shown later in this section in Scheme 11. It was concluded that both **13** and **14** reacted with LDA, not only to afford **2**, **5**, and **10**, but also to produce, in relatively larger quantities, higher boiling products that could not be detected by GLC analysis even under a variety of temperature programming conditions up to 275 °C. It is, therefore, quite possible that the low material balance at the higher ratios (1:3 and 1:5) was due to a reaction of **13**/**14** with LDA.

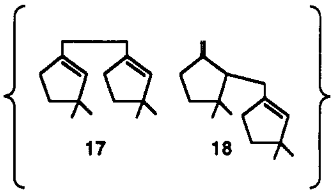


(8)

Table 2. Comparison of the Reactions of 6,6-Diiodo-5,5-dimethyl-1-hexene (8b) with LDA in THF at 0 °C in the Presence and Absence of DBNO

EXP. No.	Ratio 8b : LDA	% 8b Recovered	% Yields of Products[a]									
			 1c	 2	 5	 10	 11	 12	 13	 14	 15	 16
2[b]	1 : 3	0	10	1	6	2	4	4	0	10	20	2
5[c]	1 : 3[d]	4	5	<1	4	1	4	4	0	0	34	0

[a] Product composition and yields within a minute after adding 8b to LDA. [b] In exp. 2, the dimers 17 and 18 were also formed in yields of 3% and 2%, respectively, and in exp. 5, they were formed in yields of 1% and 0.5%, respectively. [c] The reaction employed 50 mol% DBNO. [d] This reaction also afforded two additional products, each with a molecular weight of 381 (thought to be Nitroxide Radical Trapped products derived from the iodo radicals).

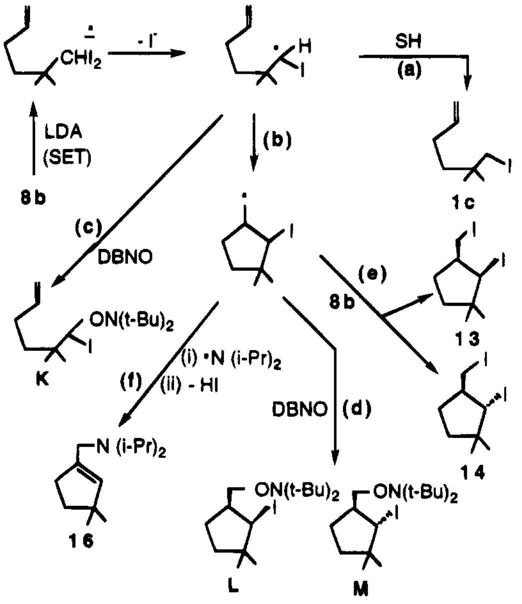


17 18

Effect of Radical Traps. In order to provide more information concerning radical involvement in the reaction of **8b** with LDA, and support the mechanisms proposed in Schemes 5 and 7, it was decided to carry out the reaction in the presence of a suitable radical (or radical anion) trap. Earlier work by this group had shown that dicyclohexylphosphine (DCPH) cannot be used as a radical trap since it readily reacts with LDA to yield DCP$^-$ which, in turn, is capable of reacting with an alkyl halide substrate.[9] It was also found during the course of these studies that *p*-dinitrobenzene (PDNB), which is a very useful radical anion trap, reacted quite rapidly with LDA at 0 °C in THF. The decision to use di-*tert*-butyl nitroxide radical (DBNO) as a radical trap in these studies was based on the observation that, although it reacted with LDA at 0 °C, the rate at which it was consumed was much slower than the rate at which **8b** reacted with LDA. The use of DBNO proved to be successful. When the reaction of **8b** and LDA was carried out at a molar ratio of 1:3 in the presence of 50 mol % DBNO in THF at 0 °C, interesting results (Table 2, exp 5) were obtained which could be directly compared with the results of the reaction without DBNO (exp 2).

In the presence of DBNO, 4% of **8b** was recovered after 1 min while in the absence of DBNO (exp 2), no unreacted **8b** was recovered after the same time period. It is important to note the complete absence of **14** and **16** in the reaction that employed DBNO, the lowering of the yield of the open chain monoiodo compound **1c**, and the large increase in the yield of **15**. These observations indicate that the reaction of **8b** with LDA involved a radical pathway and that DBNO must have trapped the intermediate iodo radicals that were precursors to **1c**, **14**, and **16** (Scheme 8).

Scheme 8



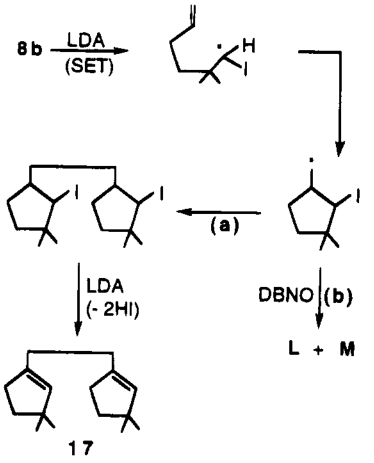
An interesting result involving the use of DBNO (exp 5) was the formation of two products in 4% yield each, that are believed to be the nitroxide radical trapped (NRT) products. The two compounds showed similar MS fragmentation patterns with a molecular ion peak at *m/e* of 381. This molecular weight corresponds to the products that would be derived when the DBNO radical couples with an iodo radical (open chain or cyclized) formed in the reaction (Scheme 8). Possible structures of the NRT products are shown as **K**, **L**, and **M**; however, since the MS patterns of the two compounds were similar, the two NRT products are believed to be **L** and **M**.

The yield of **15**, the iodocarbene-derived product, increased from 20% in the absence of DBNO to 34% in the presence of DBNO. This result shows that in the presence of DBNO, the pathway leading to **15** via the iodocarbene is a predominant one, since the other pathways which involve radical intermediates are inhibited by DBNO.

As proposed in Scheme 8, the trapping of the initially generated open chain iodo radical (from **8b**) by DBNO (pathway c), influences the formation of **1c** (pathway a) as well as the cyclization of the radical (pathway b). This results in the lowering of the yield of **1c** in exp 5 (5%) compared to the yield in exp 2 (10%). Similarly, once the iodo radical cyclizes, it appears to be trapped by DBNO (pathway d). This lessens the possibility of the cyclized radical undergoing transformations shown by pathways e (to form **13** and **14**) and f (to form **16**). It can be argued that in the presence of DBNO, the open-chain NRT product **K** should be formed, in addition to **L** and **M**. However, the absence of **K** possibly indicates that in the presence of DBNO, the radical cyclizes at a rate faster than at which it is trapped by DBNO. This does not rule out the possibility that in the presence of a larger excess of DBNO, the radical may be trapped by DBNO to form **K**.

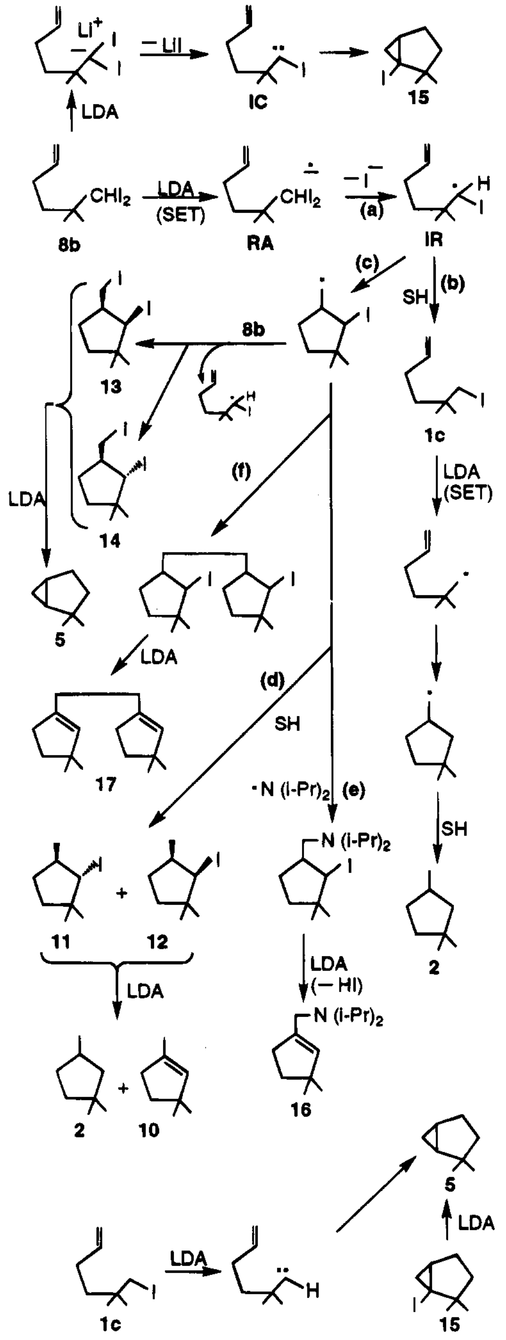
It was also noticed that the yield of the dimer **17** in the presence of DBNO (exp 5) was 1% whereas the dimer was detected in 3% yield in the absence of DBNO (exp 2). This suggests that DBNO interferes in the formation of **17**, most probably by scavenging the precursor radical to **17**. A likely pathway to **17** involves the dimerization of the cyclized radical, formed by cyclization of the open chain iodo radical, followed by elimination of two molecules of HI as shown in Scheme 9 (the mechanism of formation of **18** will be described later). Apparently, DBNO traps the cyclized radical to form NRT products and thus affects the yield of **17** in exp 5.

Scheme 9



The comparison of the results of exp 5 and exp 2, in addition to the observation that a number of cyclized products are formed in the reaction of **8b** with LDA, support a mechanism involving radical intermediates. The mechanistic pathways involved in the reaction, that are consistent with the observations made, are outlined in Scheme 10. As shown, an electron transfer from LDA to the geminal diiodo substrate **8b** generates the radical anion of **8b** (**RA**). Loss of an iodide ion forms the open chain iodo radical (**IR**), which then serves as the precursor to all the products, except **15** (**5** can also be formed via a carbene intermediate, as shown at the bottom of Scheme 10). The formation of **15** involves the generation of the iodocarbene (**IC**) which undergoes an intramolecular addition across the C=C bond.

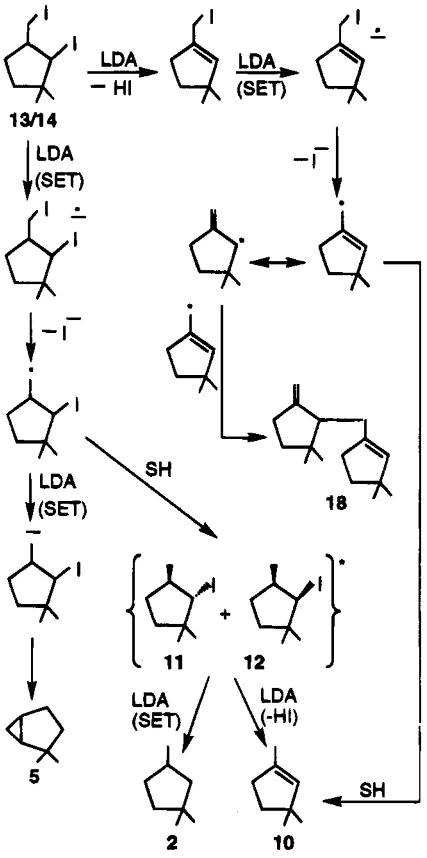
Scheme 10



Not shown in Scheme 10 is the mode of formation of the dimer **18**, detected in yields of 2 and 4% (exps 2 and 3). This dimer could have been formed by the pathways proposed in Scheme 11. Formation of **18**, as a result of a reaction of **13**/**14** with LDA, could be proposed; however, on allowing a mixture of **13** and **14** to react with LDA, at 0 °C, **18** was *not detected* (see eq 8). We believe that the lack of formation of **18** in eq 8 is due to the effect of the large excess of LDA used in the experiment. It is reasonable to suggest that the lack of formation of **18** in eq 8 and the low material balances experienced in those experiments in which LDA was used in excess (eq 8, exps 3 and 4, Table 1) are due to polymerization of **18**. It can be seen in Scheme 11 that the formation of **10** could also be preceded by a radical.

The mechanistic pathways proposed in Scheme 10 for the reaction of **8b** with LDA, involve hydrogen atom abstraction by intermediate radicals to afford the observed products. An ideal source of hydrogen atoms in a reaction that involves radicals, is usually the solvent (THF in this case). To test the hypothesis that THF may be the hydrogen atom donor, a reaction between **8b** and LDA was carried out in THF-d_8. In this experiment, the

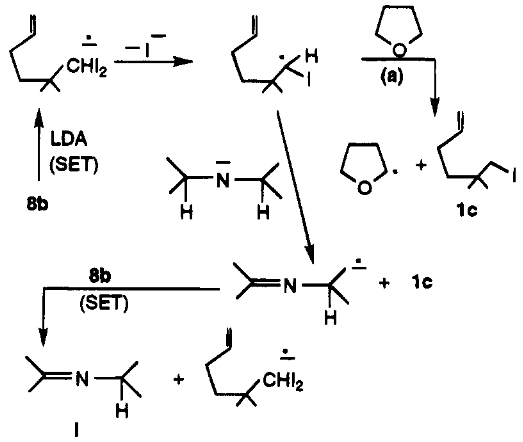
Scheme 11



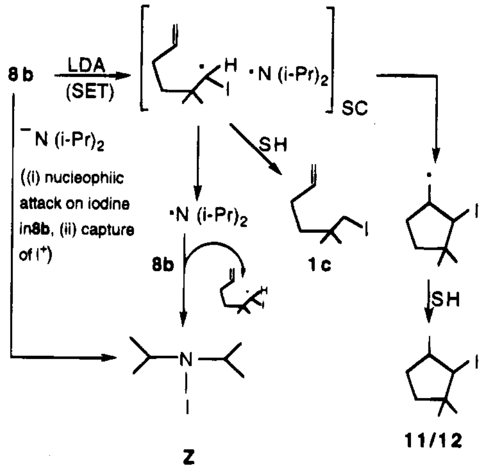
*Compounds **11** and **12** were not detected in the reaction of **13** and **14** with LDA. It is possible that they were formed and reacted rapidly with LDA to afford **2** and **10**.

deuterium content in products that were suspected to be a result of hydrogen atom abstraction by radicals (**1c**, **11**, and **12**) was determined. It was found that the deuterium incorporation in these products was very low. This means that the radicals (if present) had abstracted hydrogen atoms from another source in the reaction system. Based on the results that were obtained from studies carried out by this group on the reaction of 6-iodo-5,5-dimethyl-1-hexene (**1c**) with LDA-d_2,[9b] it seems likely that the radicals formed in the reaction of **8b** with LDA (Scheme 10) abstracted the α-hydrogen atoms from LDA. Thus, we allowed **8b** to react with LDA-d_2 (the hydrogen atoms on the α-carbon were replaced by deuterium)[25] in THF. Analysis of the deuterium content in **1c** (detected in 12% yield) revealed 15% d_1 incorporation. This showed that in the reaction of **8b** with LDA, once the iodo radical is formed, it does abstract a hydrogen atom from LDA. A similar mechanism was proposed by Bunnett concerning the dehalogenation of aryl halides by lithium 2,6-dimethylpiperidide.[26] It was then decided to carry out the reaction of **8b** with LDA-d_2 in THF-d_8. It was found that the deuterium content in **1c** had risen to 38%. The results of the two reactions, involving LDA-d_2, confirm the hypothesis that the open chain iodo radical that is generated from **8b** by SET from LDA leads to the formation of **1c** as a result of hydrogen atom abstraction from the solvent THF as well as the hydrogen atom on the carbon that is α to the nitrogen in LDA (Scheme 12).

Scheme 12



Scheme 13



If THF and LDA are the only possible sources of hydrogen atoms in the reaction medium, then the reaction of **8b** with LDA-d_2 in THF-d_8 should have resulted in a 100% (or close to 100%) d_1 incorporation in **1c**; however, analysis revealed only 38% d_1 in **1c**. The reason underlying such a low value is that the LDA-d_2 that was prepared was found to have a deuterium content of 84%. Therefore, the 16% protio LDA that was present could have served as a source of the 62% hydrogen that was incorporated in **1c** because of the protium–deuterium kinetic isotope effect. Also, this 16% protio LDA must have functioned as a hydrogen atom donor, along with THF, when the reaction of **8b** was carried out with LDA-d_2 in THF (where **1c** was found to contain 15% d_1).

Due to the relatively low yields of the cyclized monoiodo compounds **11** and **12** (3% each) obtained in the reaction of **8b** with LDA-d_2, a reliable value for the deuterium content in these two compounds could not be determined. Also, the molecular ion peaks of **11** and **12** cannot be easily observed in their respective MS spectra when the compounds are formed in such low yields.

It should be mentioned that during the analyses of the products formed in the reaction of **8b** with LDA, a red-brown solid product was isolated only at 1:5 stoichiometry. This compound, on the basis of the MS fragmentation data (EI as well as CI employing NH_3) and ^1H NMR data, is thought to be *N*-iododiisopropylamine, **Z**. Although *N*-iodoamines are rare, the few that have been reported are found to exist as colored solids. If indeed the isolated solid is *N*-iododiisopropylamine, it could be formed in the reaction of **8b** with LDA as outlined in Scheme 13.

---

[25] Newcomb, M.; Varick, T. R.; Goh, Swee-Hock. *J. Am. Chem. Soc.* **1990**, *112*, 5186.

[26] Bunnett, J. F.; Winiarski, J. *J. Am. Chem. Soc.* **1985**, *107*, 5271.

Experimental Section

Materials. Diisopropylamine was purchased from Aldrich and distilled over calcium hydride prior to use. Methyllithium, as a 1.6 M solution in diethyl ether, was purchased from Aldrich and titrated before use. Tetrahydrofuran was purchased from Fisher Scientific and distilled from sodium benzophenone ketyl. THF-d_8 was purchased from Aldrich and used as received. All other materials required for the synthesis and purification of the starting materials are described in one of our earlier works.[21]

General Procedures. All reactions were carried out in a nitrogen or argon inert atmosphere in glassware that was dried in an oven for at least 2 h at 150 °C. Solutions and solvents were transferred by means of syringes or, at times, cannulas under a stream of inert gas. GLC analyses were performed using a Varian 3700 gas chromatograph equipped with a flame ionization detector and a 30 m fused silica DB-5 column (0.32 mm i.d.). All analyses were conducted using n-decane as an internal reference. A typical procedure employed a He flow rate of 1 mL/min, and temperature programming from 50 °C (held for 5 min) to 250 °C or 270 °C (held for 15 min), at 15 °C/min. The injection port was maintained at 250 °C with the detector at 280 °C. All product yields reported were obtained by GLC. NMR spectra were recorded in $CDCl_3$ solution, with tetramethylsilane as the reference (δ 0.0), using a 300 MHz Varian Gemini spectrometer. Mass spectra were recorded using a VG 70-SE instrument equipped with a double sector magnetic analyzer. The percent deuterium incorporation in products, where applicable, was calculated on the basis of MS data. Preparative GLC was performed using a Varian 1400 Series dual column gas chromatograph equipped with a thermal conductivity detector. For purposes of isolation of compounds, the columns that were used were (A) 10% OV-101, 10 ft × 1/4 in., (B) 10% Carbowax, 10 ft × 1/4 in., and (C) 10% SE-30, 6 ft × 1/4 in.

Preparations. 6,6-Dichloro-5,5-dimethyl-1-hexene (8a): prepared as described earlier.[21]

6,6-Diiodo-5,5-dimethyl-1-hexene (8b): prepared as described earlier.[21]

Procedure for Reaction of the Geminal Dihalides with LDA and Subsequent Isolation/Characterization of Products. A typical procedure that was adopted when carrying out a reaction between the dihalide and LDA with a molar ratio of 1:5 involved an initial addition of 0.50 ml (3.46 mmol) of diisopropylamine to 2.70 mL of dry THF at −78 °C, with vigorous stirring, under a stream of N_2. To this solution was added 1.80 mL (2.50 mmol) of methyllithium (1.4 M solution in diethyl ether). The mixture was stirred at −78 °C for 30 min, after which time it was gradually warmed to 25 °C and the solvent removed under vacuum. There remained a white solid (LDA) in the flask. The flask was immediately cooled to 0 °C under nitrogen and 2.50 mL of fresh dry THF was added to prepare a solution of LDA. Subsequently, a solution of the dihalide (0.50 mmol) in 2.50 mL of dry THF was added dropwise while stirring was maintained. The status of the reaction was monitored periodically by drawing out small volumes of the reaction mixture, quenching these with water (or D_2O) and analyzing the products in the organic layer by GLC. The termination of the reaction was accomplished by quenching the mixture with water and extracting the contents with anhydrous diethyl ether.

The reaction of 6,6-dichloro-5,5-dimethyl-1-hexene (**8a**) with LDA afforded one product which was isolated by preparative GLC using a 10% OV-101 (10 ft × 0.25 in.) column under temperature programming conditions of 60 °C to 180 °C at 10 °C/min, with a He flow rate of 40 mL/min This product was identified as **1-chloro-2,2-dimethylbicyclo[3.1.0]hexane (9)**. MS, *m/e* (relative intensity): 144 (5), 129 (40), 109 (100), 103 (42), 93 (71), 67 (64). High resolution mass spectrum: $C_8H_{13}Cl$; calculated: 144.070690, observed: 144.065430. NMR: δ 1.05 (s, 3H), 1.10 (s, 3H), 0.87 (s, 1H), 0.90 (s, 1H), 1.40 (m, 1H), 1.50 (m, 1H), 1.65 (m, 1H), 1.95 (m, 1H), 1.1–1.2 (overlapped by methyl proton signal, m, 1H).

The products that were obtained, and the modes of their characterization, in the reaction of 6,6-diiodo-5,5-dimethyl-1-hexene (**8b**) with LDA are listed below:

1,1,3-Trimethylcyclopentane (2). The MS data of this product matched the MS data obtained for an authentic sample obtained from Wiley Organics. Also, the GLC retention time of **2** was the same as that of the commercial sample.

1,3,3-Trimethylcyclopentene (10). The structure was assigned on the basis of matching MS data with that reported in the literature.[27]

2,2-Dimethylbicyclo[3.1.0]hexane (5). The structure was assigned on the basis of matching MS data with that reported in the literature.[9,28]

***trans*-2-Iodo-1,1,3-trimethylcyclopentane (11).** This compound was synthesized in much larger yields in a reaction involving **8b** and $LiAlH_4$ and was isolated by preparative GLC using a 10 ft × 1/4 in. 10% OV-101 column, with a He flow rate of 40 mL/min. NMR: δ 0.97 (s, 3H), 1.03 (s, 3H), 1.07 (d, 3H), 1.40–2.00 (m, 4H), 2.27 (m, 1H), 3.49 (d, J = 11.1 Hz, 1H, CHI). MS, *m/e* (relative intensity): 238 (<2), 127 (5), 111 (80), 69 (100), 55 (50), 41 (35).

***cis*-2-Iodo-1,1,3-trimethylcyclopentane (12).** This compound showed the following spectroscopic characteristics. NMR: all values of the chemical shifts for all protons in the molecule were the same as those listed for **11** except for the value pertaining to the CHI proton at δ 4.27 (d, J = 6.0 Hz, 1H). MS, *m/e* (relative intensity): 238 (<2), 127 (5), 111 (100), 69 (95), 55 (60), 41 (35).

***cis*-2-Iodo-3-(iodomethyl)-1,1-dimethylcyclopentane (13).** This compound was also synthesized in much higher yields in a reaction between **8b** and $LiAlH_4$ followed by seperation from the *trans* isomer **14** by flash column chromatography, using silica gel with hexane as eluent. NMR: δ 1.15 (s, 3H), 1.25 (s, 3H), 1.55–2.00 (m, 4H), 2.15 (m, 1H), 3.23 (m, 2H), 4.32 (d, J = 4.80 Hz, 1H, CHI). MS, *m/e* (relative intensity): 364 (85), 254 (40), 237 (40), 109 (95), 67 (90), 55 (70). High resolution mass spectrum: $C_8H_{14}I_2$; calculated 363.9185, observed 363.9168.

***trans*-2-Iodo-3-(iodomethyl)-1,1-dimethylcyclopentane (14).** This compound was synthesized by reacting **8b** with $LiAlH_4$ and was separated from the *cis* isomer **13** by flash column chromatography, using silica gel with hexane as the eluent. NMR: all the chemical shift values for the protons in this molecule were the same as those in **13** except for the CHI unit at δ 3.62 (d, 1H, J = 10.5 Hz). MS, *m/e* (relative intensity): 364 (85), 254 (25), 237 (100), 109 (95), 127 (10), 69 (75), 55 (50). High resolution mass spectrum: $C_8H_{14}I_2$; calculated 363.9185, observed 363.9112.

1-Iodo-2,2-dimethylbicyclo[3.1.0]hexane (15). This product was isolated by preparative GLC using a 10% SE-30 (6 ft × 1/4 in.) column under isothermal conditions at 80 °C (retention time of 28 min), with a He flow rate of 40 mL/min. NMR: δ 1.05 (s, 3H), 1.10 (s, 3H), 0.90 (s, 1H), 0.95 (s, 1H), 1.0–1.2 (m, 1H, overlapped by methyl proton signal), 1.40–1.95 (m, 4H). MS, *m/e* (relative intensity): 236 (22), 221 (5), 127 (4), 109 (100), 94 (12), 79 (19), 67 (51). High resolution mass spectrum: $C_8H_{13}I$; calculated 236.00620, observed 236.00618.

1-[(Diisopropylamino)methyl]-3,3-dimethylcyclopentene (16). This compound was isolated in pure form by preparative GLC using a 10% OV-101 column (10 ft × 0.25 in.), under temperature programming conditions of 70 °C to 250 °C at a rate of 10 °C/min (He flow rate of 40 mL/min). NMR: δ 0.90 (s, 3H), 1.0 (s, 3H), 1.10 (d, 12H), 1.40–2.10 (m, 4H), 2.90 (m, 2H), 3.05 (broad s, 2H), 5.30 (broad s, 1H). MS, *m/e* (relative intensity): 209 (12), 194 (100), 109 (70), 86 (52), 67 (17). High resolution mass spectrum: $C_{14}H_{27}N$; calculated 209.214350, observed 209.212265.

6-Iodo-5,5-dimethyl-1-hexene (1c). This product was identified on the basis of matching MS data with that reported in the literature.[10d]

---

(27) Wolinsky, J.; Clark, G. W.; Thorstenson, P. C. *J. Org. Chem.* **1976**, *41*, 745.

(28) Ph.D. Dissertation of B. Park, Georgia Institute of Technology, Atlanta, GA, 1988.

1-(3,3-Dimethyl-1-methylcyclopentenyl)-3,3-dimethylcyclopentene (17). This product was isolated in 80% purity (the contamination being the other dimer, **18**), by flash column chromatography, using silica gel, with hexane as the eluent. The structure was established by ^{13}C and ^{1}H NMR data. ^{1}H NMR: δ 1.05 (s, 12H), 1.65 (t, 4H), 2.15 (s, 4H), 2.30 (t, 4H), 5.13 (s, 2H). ^{13}C NMR (main characteristic shifts): δ 135 (ring =CH—), 142 (ring >C=). MS, *m/e* (relative intensity): 218 (38), 203 (82), 147 (20), 109 (100), 93 (38) 81 (28), 67 (33), 55 (20). High resolution mass spectrum: $C_{16}H_{26}$; calculated 218.1994, observed 218.1978.

2-(3,3-Dimethyl-1-methylcyclopentenyl)-3,3-dimethylmethylenecyclopentane (18). The product was separated from isomer **17** by flash column chromatography, using silica gel with hexane as the eluent, and was characterized by NMR (^{13}C and ^{1}H). ^{1}H NMR (only key values): δ 4.81 (s, 1H), 4.85 (s, 1H), 5.18 (s, 1H). ^{13}C NMR (main characteristic shifts): δ 106 (=CH_2), 148 (>C=). MS, *m/e* (relative intensity): 218 (10), 203 (60), 147 (14), 109 (100), 81 (95), 69 (49), 55 (40). High resolution mass spectrum: $C_{16}H_{26}$; calculated 218.2034, observed 218.2003.

Acknowledgment. The authors gratefully acknowledge the National Science Foundation (grant no. CHE 8403024) for support of this work.

JO9414816