Mechanism of Reaction of Geminal Dihalides with Lithium Aluminum Hydride. Evidence for Single Electron Transfer as the Major Reaction Pathway

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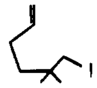
The reactions of a sterically hindered geminal dichloride **4a** and the corresponding diiodide **4b** with $LiAlH_4$ (LAH) were found to involve an electron-transfer mechanism. Whereas the monochloro analog of **4a** (**8**) is inert toward LAH, **4a** was more reactive. Observation of radical-derived products in the reaction of **4a** with LAH indicates that the presence of two chlorine atoms on the same carbon atom results in a favorable reduction potential for **4a**, as compared to **8**. These results show that LAH can function as a one-electron donor toward geminal dichlorides. It was found that the diiodo analog **4b** is more reactive toward LAH than **4a** due to the inherent favorable reduction potentials of alkyl iodides compared to chlorides. The reactivity of **4b** toward LAH was also found to be greater than that of the monoiodo analog (**1b**) in keeping with the more favorable reduction potential of the diiodide (**4b**) compared to the monoiodide (**1b**). The rates of cyclization of the corresponding haloalkyl radicals generated from **4a** and **4b** were also determined and were found to be 7.4×10^5/s for the chloroalkyl and 5.5×10^5/s for the iodoalkyl radical at 25 °C. The formation of small amounts of the carbene-derived product, **5**, in the reactions of both **4a** and **4b** with LAH appeared to be preceded by a radical intermediate.

Introduction

Lithium aluminum hydride (LAH) has been proven to be a very powerful and versatile reducing agent in organic syntheses.[1] One of the many organic functionalities that can be reduced by LAH is the carbon–halogen bond (eq 1).

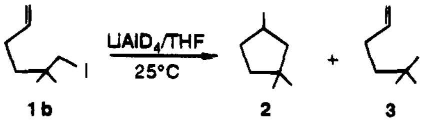
$$RX + LiAlH_4 \rightarrow RH + AlH_3 + LiX \qquad (1)$$

The mechanism of the reaction of an alkyl halide with LAH has received considerable attention during the last decade with most of the effort directed toward resolving the controversy as to whether the reaction proceeds by a S_N2 or a single electron-transfer (SET) mechanism.[2,3] A considerable amount of work has been carried out by this group concerning the mechanism of the reaction of LAH with alkyl halides,[4] and in 1984 we reported that the reaction of a hindered alkyl iodide with LAH involves a radical intermediate that accounts for the observed hydrocarbon products.[4d] Although the involvement of electron transfer in such a reaction has been argued against by Newcomb et al. on the basis of kinetic[5] and probe studies,[6] in favor of a polar mechanism,[2] the validity of an electron-transfer pathway has been clearly established by extensive studies carried out by this group[3,4h] involving the use of the sterically hindered neopentyl iodide **1b** as the radical probe.



1b

The two hydrocarbon products that were obtained when **1b** was allowed to react with $LiAlD_4$ (LAD) in a 1:5 ratio, at 25 °C, for 48 h were the hydrocarbons **2** and **3** (eq 2).[4h] The yield of **2** was 89% (59% d_1) and **3** was



(2)

5.5% (69% d_1). The high yield of the cyclized hydrocarbon, **2**, was attributed to radical cyclization followed by abstraction of a hydrogen atom from solvent. On the basis of the results of deuterium-labeling studies using LAD and protio THF, especially in the formation of **2**, it is clear that the reaction of the iodide, **1b**, with LAH involves an electron-transfer pathway (Scheme 1). In this scheme, radicals are formed that are trapped by the solvent.[4h] The suggestion[5,6] that **1b** reacts with an unknown impurity to form a radical which undergoes a rapid halogen atom radical chain process to form the cyclized iodide which is then reduced by LAH (pathway

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[1] (a) House, H. O. *Modern Synthetic Reactions*, 2nd ed.; W. A. Benjamin: Menlo Park, CA, 1972. (b) Brown, H. C.; Krishnamurthy, S. *J. Org. Chem.* **1980**, *45*, 849. (c) Krishnamurthy, S. *J. Org. Chem.* **1980**, *45*, 2550. (d) Chung, S.; Chung, F. *Tetrahedron Lett.* **1979**, 2473. (e) Chung, S. *J. Org. Chem.* **1980**, *45*, 3513. (f) Singh, P. R.; Khurana, J. M.; Nigam, A. *Tetrahedron Lett.* **1980**, *21*, 4753. (g) Singh, P. R.; Khurana, J. M.; Nigam, A. *Tetrahedron Lett.* **1981**, *22*, 2901. (h) Hatem, J.; Waegell, B. *Tetrahedron Lett.* **1973**, *14*, 2023.

[2] Newcomb, M.; Curran, D. P. *Acc. Chem. Res.* **1988**, *21*, 206.

[3] Ashby, E. C. *Acc. Chem. Res.* **1988**, *21*, 414.

[4] (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. (h) Ashby, E. C.; Pham, T. N.; Madjdabadi, A. A. *J. Org. Chem.* **1991**, *56*, 1596. (i) Ashby, E. C.; Welder, C. O.; Doctorovich, F. *Tetrahedron Lett.* **1993**, *34*, 7235.

[5] (a) Newcomb, M.; Sanchez, R. M.; Kaplan, J. *J. Am. Chem. Soc.* **1987**, *109*, 1195. (b) Newcomb, M.; Kaplan, J. *Tetrahedron Lett.* **1988**, *29*, 3449.

[6] (a) Newcomb, M.; Kaplan, J.; Curran, D. P. *Tetrahedron Lett.* **1988**, *29*, 3451. (b) Newcomb, M.; Park, S. U.; Chung, S. K. *J. Org. Chem.* **1987**, *52*, 3275. (c) Newcomb, M.; Park, S. U.; Chung, S. K. *J. Am. Chem. Soc.* **1986**, *108*, 240.

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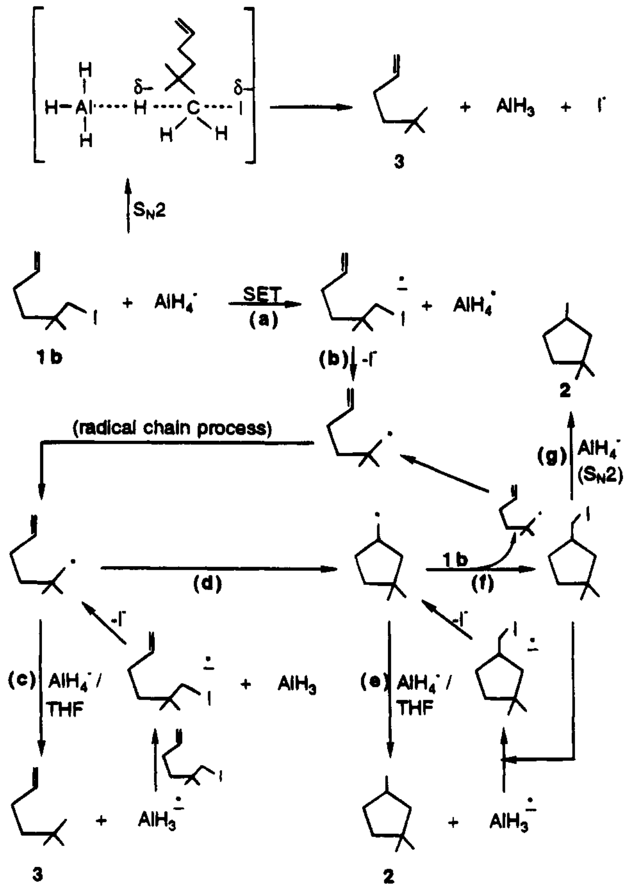
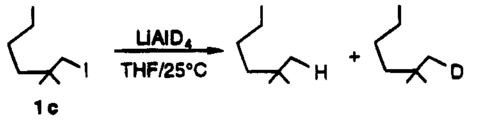
Scheme 1



g, via S$_N$2) is unreasonable. We have found that the reduction of the cyclized iodide (synthesized independently) in Scheme 1 by LAD affords **2** which has 98% deuterium incorporation whereas in the reaction of **1b** with LAD the product **2** contains only 59% deuterium incorporation. This result necessitates that **2** be formed to a large extent via pathway e. All of our studies indicate that LAH initiates the reaction by SET followed by various radical chain processes producing radicals that abstract hydrogen atoms from the tetrahydroaluminate anion. More recently,[4i] we have shown that the reaction of the saturated counterpart of **1b**, namely **1c** (eq 3), with

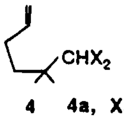


1c (3)

LAD produces octane with only 20–40% deuterium incorporation, a result not explainable by a polar S$_N$2 process but easily explainable by a SET process involving an alkyl radical intermediate that abstracts a hydrogen atom from the solvent (THF). This reaction is devoid of the possibility of a halogen atom radical chain process and once again necessitates the formation of a radical intermediate which abstracts a hydrogen atom from AlH$_4^-$ and THF.

Although all the data reported by this group are consistent with a SET mechanism to describe the reaction of sterically hindered primary alkyl iodides and secondary alkyl iodides with LAH,[3,4] no evidence for SET has, so far, been reported in the reactions of sterically hindered alkyl chlorides and bromides with LiAlH$_4$. It is reasonable to expect a SET pathway in the case of the alkyl iodides due to their highly favorable reduction potentials compared to those of the corresponding chlorides and bromides.

The lack of reactivity of alkyl chlorides with LAH prompted us to study the reaction of an aliphatic geminal dichloride (**4a**) with LAH. This decision was made on

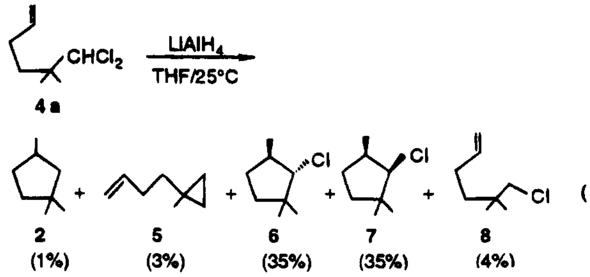


4 **4a**, X=Cl
4b, X=I

the basis that no such studies have been carried out so far and that the presence of two chlorine atoms on the same carbon atom should favorably influence the reduction potential of the molecule and hence its reactivity via a SET pathway. It was also decided to study the reaction of the coresponding geminal diiodide (**4b**) with LAH and thereby be able to compare the reactivity of the monoiodide (**1b**) with that of the structurally similar geminal diiodide (**4b**) in their reactions with LAH. Such a study is important in light of the report by Shaik[7] that geminal dihalides react with strong nucleophiles by a S$_N$2 process at a slower rate than the corresponding monohalides. On the contrary, the monohalo anolog of **4a** did not react with LAH yet the geminal dichloride, **4a**, does react; therefore, it does not appear that a S$_N$2 pathway would be involved in the case of **4a**. For this reason it was expected that the results of these reactions would shed some light on how the reaction is influenced mechanistically by the number and type of halogen atoms on the same carbon atom.

Results and Discussion

Reaction of 6,6-Dichloro-5,5-dimethyl-1-hexene (4a) with LAH. The reaction of 6,6-dichloro-5,5-dimethyl-1-hexene (**4a**) with LAH in THF was studied at 25 °C at a molar ratio of 1:7 (**4a**:LAH). Product formation was detected only after about 3 h, and the reaction took about 30 h for complete conversion of **4a** to products (eq 4).



(4)

The formation of products **2**, **6**, **7**, and **8** suggests the possibility of a radical pathway in the reaction of **4a** with LAH. It is known that if a methyl-substituted 5-hexenyl radical cyclizes the *cis*:*trans* ratio of the isomeric cyclopentane products is typically 2.8 at 25 °C and that this ratio increases as the temperature is lowered. In the case of the chloro-substituted methylcyclopentanes that were obtained (eq 4), the *cis* and *trans* isomers were found to have a ratio of 1.0. In order to determine if this ratio (1.0) truly represents the ratio resulting from cyclization of chloro radicals, **4a** was allowed to react with n-Bu$_3$SnH, in the presence of AIBN, in THF at 25 °C (eq 5). The *cis*:*trans* ratio (**7**:**6**) of 1.1 is consistent with the *cis*:

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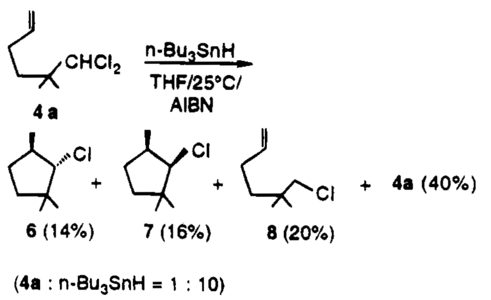
(7) Shaik, Sason S. *J. Am. Chem. Soc.* **1983**, *105*, 4359.



(5)

trans ratio (1.0) found in the reaction of **4a** with LAH. Since the reaction represented by eq 5 is known to proceed via a radical intermediate, it is reasonable to assume that the reaction represented by eq 4 to produce **6**–**8** also proceeds via a radical intermediate.

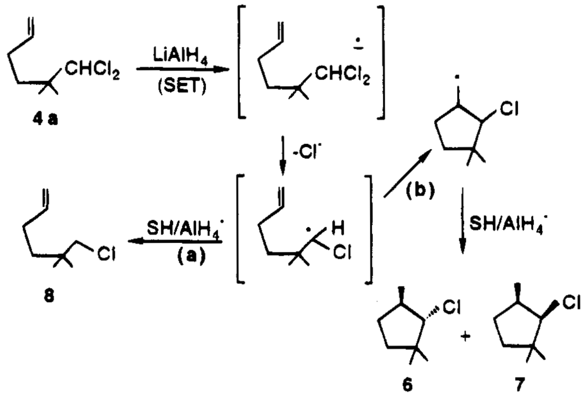
Although **8** was formed in 20% yield in the reaction of **4a** with n-Bu$_3$SnH, it was formed only as a minor product when **4a** was allowed to react with LAH. These differences can be explained by considering that the rate at which the initially formed chloro radical abstracts hydrogen atoms from n-Bu$_3$SnH (**4a**:n-Bu$_3$SnH = 1:10) could be much faster than the rate at which it abstracts hydrogen atoms from AlH_4^-.

If radical intermediates were indeed involved in the reaction of **4a** with LAH, then the formation of products **6**–**8** can be explained on the basis of a SET pathway (Scheme 2). An electron transfer from LAH to **4a** would generate the radical anion of **4a**. On losing Cl^-, this radical anion would produce the open chain chloro radical. Once formed, the chloro radical can abstract a hydrogen atom (from solvent and/or LAH) to form **8** (pathway a) and/or cyclize (pathway b) followed by hydrogen atom abstraction (from solvent and/or LAH) which would lead to the cyclized isomers **6** and **7**. Products **6** and **7** could not have been formed via a halogen atom radical chain process because (i) a halogen atom radical chain process involving chlorine is much too slow and (ii) the intermediate cyclized dichloro compounds were not observed.

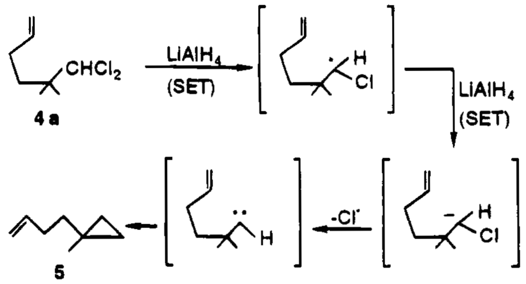
In addition to the three monochloro compounds, the reaction of **4a** with LAH also afforded hydrocarbon **5** in 3% yield and the trimethylsubstituted cylopentane **2** in 1% yield. The fact that **5** was formed, although in low yield, suggests a carbene precursor. Work carried out by this group concerning mechanistic studies of the reactions of the sterically hindered alkyl halides, 6-chloro-5,5-dimethyl-1-hexene, 6-bromo-5,5-dimethyl-1-hexene, and 6-iodo-5,5-dimethyl-1-hexene, with LDA has revealed that among the products formed in these reactions, **5** is a major carbene-derived (C—H insertion) product.[8] On the basis of this confirmed result, it is reasonable to assume that in the reaction of **4a** with LAH, **5** is also formed via a carbene intermediate.

The most plausible pathway for the formation of the carbene involves SET to the initial open chain chloro radical (from **4a**) leading to the chloro carbanion, which can lose Cl^- resulting in the formation of the carbene. An intramolecular C—H insertion by this carbene then produces **5** (Scheme 3).

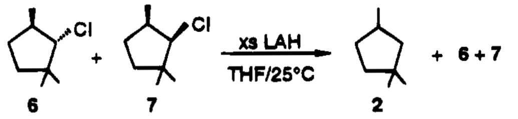
Scheme 2



Scheme 3



The observation that **2** was formed in 1% yield indicates that one of the monochloro products (**6**, **7**) formed in the reaction of **4a** with LAH reacted further with LAH and was reduced to **2**. It was shown earlier[4h] that **8** was inert to LAH. This would mean that **2** could not be formed from **8** in the reaction of **4a** with LAH. To confirm if **6** and/or **7** reacted with LAH to produce **2**, a mixture of **6** and **7** (1:1 ratio) was allowed to react with excess LAH in THF at 25 °C (eq 6). The reaction was carried out for 24 h, and at the end of this period, **2** was formed in 2% yield. A considerable amount of unreacted **6** and **7** remained. However, it was noticed that the ratio of the remaining **6** to **7** was 1:0.85; therefore, more of the *cis* isomer (**7**) had reacted to produce **2**. There is no evidence that the formation of **2** from **6** or **7** involves a SET pathway; indeed, work carried out by this group[4a,d] concerning reactions of sterically hindered primary alkyl chlorides and nonhindered secondary alkyl chlorides with LAH indicates that such reactions probably follow a S$_N$2 pathway.



(6)

Studies to Support Radical Involvement. In order to substantiate the involvement of radicals in the reaction of **4a** with LAH and obtain evidence to support the proposed mechanism (Scheme 2), two experiments were conducted (Table 1, experiments 1 and 2). First, the reaction was carried out using LAD in THF (experiment 1) and then the reaction was carried out using LAD and THF-d_8 (experiment 2). The deuterium content of products **6**–**8** (suspected of being derived from radical intermediates) was established in both experiments. The percent deuterium incorporation in **6** increased from 41% in experiment 1 to 98% in experiment 2 with an equally significant increase in the case of **7** from 36% in experiment 1 to 96% in experiment 2. These differences in deuterium contents in both the cyclized monochloro isomers serve as positive evidence for a radical precursor for **6** and **7** in the reaction of **4a** with LAH. The results indicate that the formation of **6** and **7** was preceded by

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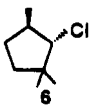
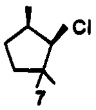
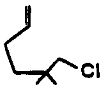
(8) (a) Ashby, E. C.; Park, B. *Acta. Chem. Scand.* **1990**, *44*, 291. (b) Ashby, E. C.; Park, B.; Patil, G. S.; Gadru, K.; Gurumurthy, R. *J. Org.Chem.* **1993**, *58*, 424.

Table 1. Reaction of 6,6-Dichloro-5,5-dimethyl-1-hexene (4a) with LAD at 25 °C[a]

		% deuterium in products[b]		
expt no.	condns	 6	 7	 8
1	LAD/THF	41	36	82
2	LAD/THF-d_8	98	96	99

[a] The ratio of 4a to LAD was 1:7. [b] The %D incorporation was analyzed in products that were suspected to be derived from radical intermediates.

Table 2. Effect of Light on the Reaction of 4a with LAH in THF at 25 °C

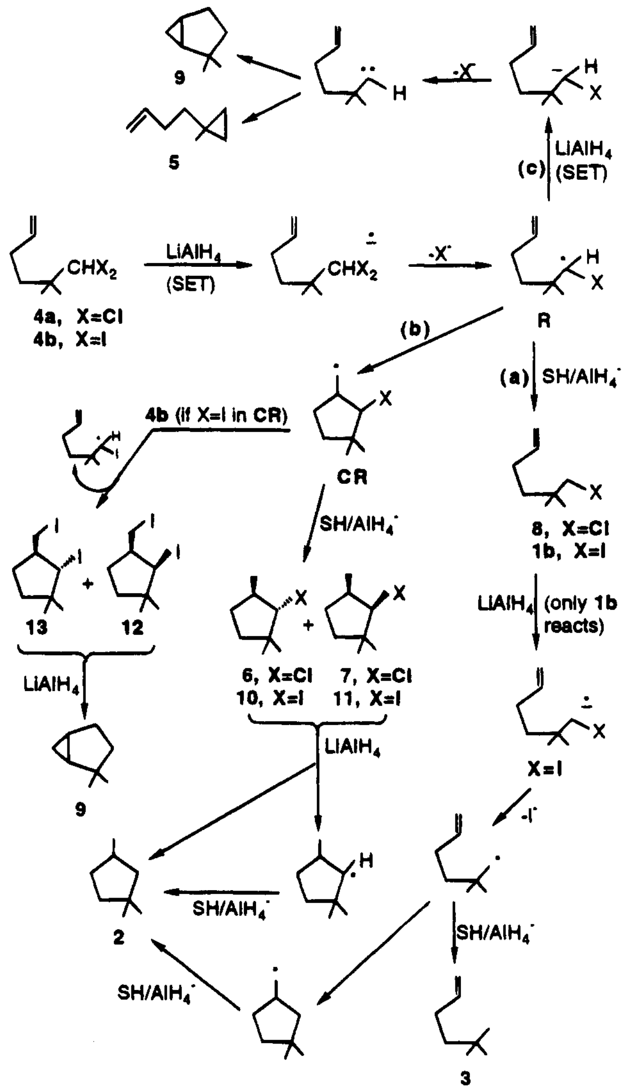
		% unreacted 4a				
expt no.	condns	6 h	16 h	24 h	38 h	48 h
3	dark[a]			25	15	10
4	lab light[b]	60	30	10	0	
5	irradiation[c,d]	20	0			

[a] Products 6–8 were formed, with neither 2 nor 5 being detected. [b] Main products formed were 6–8, with 2 (1%) and 5 (3%) also being detected. [c] Reaction was irradiated by sun lamp, and the complete consumption of 4a required less than 16 h. [d] The main products were 6 and 7, with 4% of 2 also being detected. Products 8 and 5 were not formed in experiment 5.

the corresponding cyclized radical that abstracted hydrogen atoms from both LAD and THF leading to a mixture of **6** and **7** in a 1:1 ratio. This cyclized radical was in turn a result of the cyclization of the initially formed open chain chloro radical from **4a** as a result of SET from LAD (Scheme 2). A small percentage of the open chain chloro radical was trapped by LAD and THF (mainly LAD) and converted to **8**. Also, an even smaller percentage of the open chain chloro radical underwent further reduction to the carbene via the chloro carbanion (Scheme 3) to produce **5**.

Three very elementary, but informative, experiments were conducted to further support the intermediacy of radicals in the reaction of the geminal dichloro compound **4a** with LAH (Table 2, experiments 3–5). It was observed that in the presence of laboratory light, the reaction of **4a** with LAH proceeded faster (experiment 4) than the same reaction carried out in the dark (experiment 3). Also, **2** and **5** were not detected in the reaction carried out in the dark.. The reaction was even more accelerated when it was irradiated by a sun lamp (experiment 5). The normal time that it took for the substrate to be completely converted to products under laboratory light was approximately 30 h, but on irradiation, the complete consumption of **4a** took less than 16 h. However, the product distribution of the reaction under irradiation conditions was slightly different from the reaction performed under normal laboratory light conditions. The difference was the complete absence of **5** and **8** in experiment 5, probably indicating that radical cyclization is accelerated to a considerable extent upon irradiation. In addition, **2** was formed in 4% yield in experiment 5 within 12 h following the complete consumption of **4a**. Considerable amounts of unreacted **6** and **7** remained even under irradiation conditions.

Scheme 4



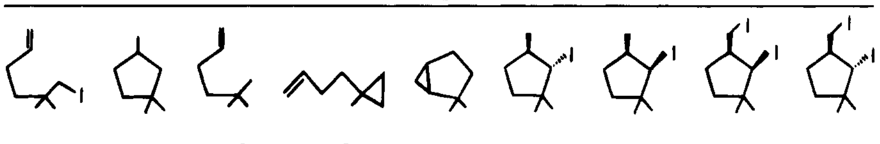
On the basis of the products, product yields, relative rates of reaction under various experimental conditions, and previous knowledge concerning the mechanism of reactions of alkyl monohalides with LAH, a mechanism describing the reaction of 6,6-dichloro-5,5-dimethyl-1-hexene with LAH is outlined in Scheme 4. As shown, the initially formed open chain chloro radical, R (X=Cl), produced by SET from LAH to **4a** accounts for all the products formed in the reaction.

When the reaction between a mixture of **6** and **7** and LAH at 25 °C was quenched with D$_2$O, no deuterium incorporation was detected in **2**. This result indicates that a stable organolithium product was not likely to be an intermediate during the formation of **2** from **6/7**.

During the course of our studies of the reaction of **4a** with LAH, two products were detected that appeared to possess very close boiling points (based on their respective GLC retention times). Apart from the fact that these two products were isomeric, a fact that was established on the basis of their MS patterns, we were unable to obtain any other information pertaining to the structures of these two compounds. Numerous attempts to isolate these isomeric products independently by preparative GLC and flash column chromatography were futile.

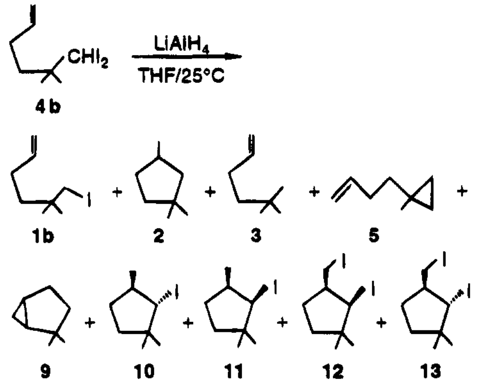
Reaction of 6,6-Diiodo-5,5-dimethyl-1-hexene (4b) with LiAlH$_4$. Effect of Stoichiometry. The reaction of 6,6-diiodo-5,5-dimethyl-1-hexene (**4b**) with LAH was studied at molar ratios of 1:0.5 and 1:1.5, in THF at 25 °C (eq 7). Product formation was detected instantaneously at both ratios. No change in the product composition was observed even after 24 h at the ratio of 1:0.5 (Table 3, experiment 6). The results of the reaction carried out at the 1:1.5 ratio are also shown in Table 3

Table 3. Reaction of 6,6-Diiodo-5,5-dimethyl-1-hexene (4b) with LAH in THF at 25 °C



			% yield of products[a]								
expt no.	ratio **4b**:LAH	% unreacted **4b**	**1b**	**2**	**3**	**5**	**9**	**10**	**11**	**12**	**13**
6	1:0.5	5	16	0	0	1	2	0	0	41	23
7	1:1.5	0	26	7	10	1	9	5	12	3	15

[a] The products shown were formed immediately after adding **4b** to a solution of LAH. The yields shown in expt 6 were found to remain unchanged even after 24 h. The yields shown in experiment 7 correspond to the observed yields after 21 h.



(7)

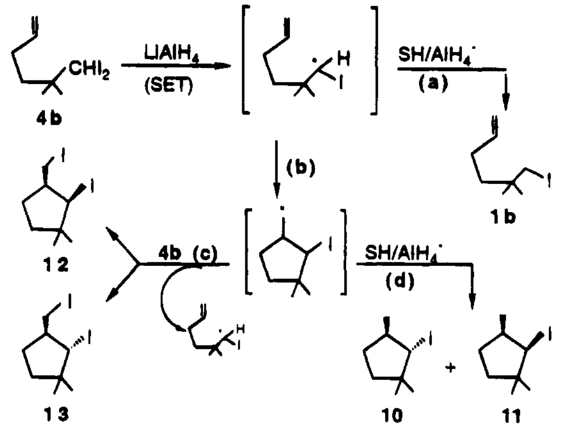
(experiment 7), and represent the final product composition after 21 h.

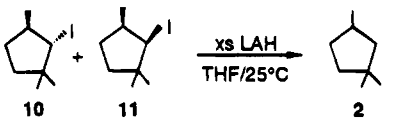
The reaction of **4b** with LAH at a 1:0.5 ratio produced 5% of unreacted **4b** after 24 h, with **1b**, **12**, and **13** being formed in yields of 16%, 41%, and 23%, respectively (experiment 6). The formation of the cyclized diiodo isomeric compounds **12** and **13** suggests a radical pathway in the reaction of **4b** with LAH. These two products could arise from a halogen atom radical chain mechanism (Scheme 5, pathway c) in which a cyclized radical abstracts an iodine atom from **4b** to afford the two isomers, **12** and **13**. The cyclized radical (pathway b) could, in turn, be derived from the open chain iodo radical generated by SET from LAH to **4b**. Also, it can be seen that **1b** can be a result of hydrogen atom abstraction by the initial open chain iodo radical (pathway a). The cyclized radical in Scheme 5, on abstracting a hydrogen atom, can produce **10** and **11** (pathway d). Although not detected in experiment 6 (at a 1:0.5 ratio), **10** and **11** were formed in 5% and 12% yield, respectively, at the higher ratio in experiment 7 (1:1.5). These results indicate that the formation of **10** and **11** is dependent on the amount of LAH present. It is important to note that at the higher ratio, the yields of the cyclized diiodo compounds **12** and **13** were reduced to 3% and 15%, respectively, while the amounts of **1b**, **2**, **3**, **10**, and **11** increased substantially. These results are expected since an increase in the amount of LAH should increase the rate of pathways a and d at the expense of pathway c.

Earlier work by this group had shown that when **1b** was allowed to react with LAH, in a 1:5 ratio, at 25 °C in THF, the products obtained, after 48 h, were **2** and **3** in 84% and 15% yield, respectively (eq 2).[4h] Therefore, it is reasonable to suggest that **2** and **3** are formed from **1b** in the reaction of **4b** with LAH.

When **10** and **11** were allowed to react with excess LAH at 25 °C in THF, **2** was formed in quantitative yield (eq 8). Complete consumption of **10** and **11** required approximately 18 h. This result makes it clear that the formation of **2** in the reaction of **4b** with LAH (in experiment 7 only) can be the result not only of the reaction of **1b** with LAH but also of the reaction of **10** and **11** with excess LAH. Formation of **2** from the reaction of **10** and **11** with LAH probably involves a radical mechanism, since we have shown earler that secondary iodides react with LAH predominatly by a SET pathway.[4d]

Scheme 5





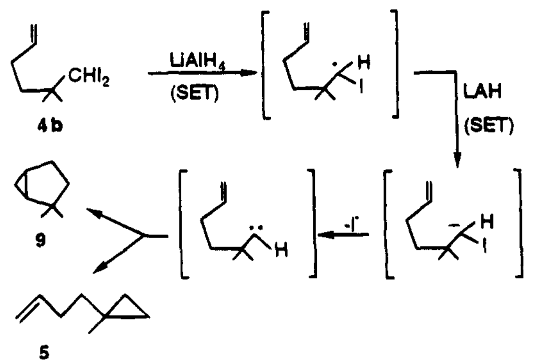
(8)

The observation that compounds **5** and **9** were detected among the products formed in the reaction of **4b** with LAH indicates that a carbene intermediate was generated which underwent a C—H insertion process to form **5** and an intramolecular addition across the C═C bond to produce **9**.[8] The formation of a carbene intermediate can be rationalized by assuming that once an open chain iodo radical is formed from **4b** (by SET from LAH), it could then accept an electron from LAH to produce the iodo carbanion. Loss of an iodide ion would then afford the carbene (Scheme 6).

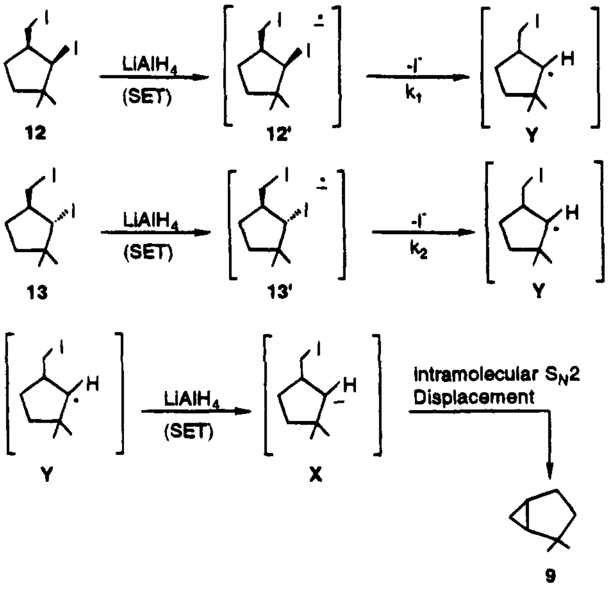
The carbene shown in Scheme 6 would be expected to undergo intramolecular insertion into a C—H bond preferentially over addition across a C═C bond; thus, the yield of **5** should be higher than the yield of **9**. As can be seen, the reverse is true. In fact, in experiment 7, the yield of **9** is too high to be accounted for by only a carbene pathway. Also, the yield of **5** suggests that the carbene pathway constitutes a minor contribution to the reaction of **4b** with LAH. It thus appears that, in the reaction of **4a** with LAH, **9** could also have been formed by a pathway that did not involve a carbene.

It is reasonable to suppose that **9** could be the result of a reaction between an iodo compound, formed in the

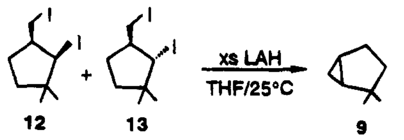
Scheme 6



Scheme 7



reaction of **4b** with LAH, and excess LAH. On the basis of the results of the reaction of **1b** with LAH,[4h] and the reaction of a mixture of **10** and **11** with excess LAH (eq 8), it is obvious that these three monoiodo compounds (**1b**, **10**, and **11**) are not the precursors to **9**. This means that either **12** or **13** (or both) could lead to **9** on reaction with LAH. In order to test this possibility, a mixture of **12** and **13** was treated with excess LAH (eq 9). The *cis*

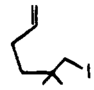
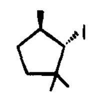
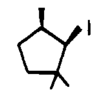


(9)

isomer, **12**, was completely consumed in less than 20 min, whereas all of the *trans* isomer, **13**, was consumed in about 60 min. Thus, it appears that the major sources of **9** in the reaction of **4b** with LAH are **12** and **13**. The lower reactivity of **13** toward LAH is reflected in the results of experiment 7 (at a ratio of 1:1.5) which shows that **13** was formed in 15% yield which is five times that of **12** (3% yield). Obviously, the excess LAH consumed most of **12** that was formed, whereas a large fraction of the amount of **13** formed remained unreacted.

The formation of **9** from **12**/**13** can be rationalized by the mechanism proposed in Scheme 7. As shown, the first step involves SET from LAH to the diiodo compounds **12** and **13** to form the corresponding radical anions **12′** and **13′**. The rates of formation of **12′** and **13′** would be expected to be comparable since steric hindrance plays such a small part in electron-transfer reactions. Once the radical anions are formed, they then lose I⁻ to produce the same radical (**Y**). The rate at which this radical is formed is determined by the rates of dissociation of **12′** and **13′**. Loss of I⁻ from **12′**, to produce the radical **Y**, probably occurs more rapidly (than the comparable reaction with **13′**) in order to relieve the strain caused by the two iodine atoms *cis* to each other ($k_1 > k_2$).

Table 4. Reaction of 4b with LAD in THF at 25 °C[a]

		% deuterium in products[b]		
				
expt no.	condns	**1b**	**10**	**11**
8	LAD/THF	37	45	61
9	LAD/THF-d_8	91	93	96

[a] The ratio of **4b** to LAD was 1:1.5. [b] The reaction was terminated after 16 h.

Studies to Support Radical Involvement. In an attempt to confirm the possibility of a radical pathway during the formation of the observed products in the reaction of **4b** with LAH and support the mechanism proposed in Scheme 5, two experiments were carried out (Table 4, experiments 8 and 9). One experiment employed the use of LAD in THF (experiment 8), the other experiment employed the use of LAD in THF-d_8 (experiment 9), and the deuterium content in products **1b**, **10**, and **11** was analyzed. It was observed that in experiment 8 (LAD/ THF), the deuterium incorporation was 37% in **1b**, 45% in **10**, and 61% in **11**. Analysis of the deuterium content of each product in experiment 9 (LAD/THF-d_8) revealed values of 91%, 93%, and 96%, respectively. The results obtained in experiments 8 and 9 clearly show that the reaction of **4b** with LAH to produce products **1b**, **10**, and **11** proceeds by a radical pathway. Once formed, the radicals abstract H atoms from the solvent THF as well as from LAD. These results show that both LAH and THF can function as hydrogen atom donors toward haloalkyl radicals.[4h]

In order to test for possible halogen–metal exchange (HME) involvement in the reaction of **4b** with LAH, the reaction was quenched with D_2O. Lack of deuterium incorporation in any of the products helped eliminate the possibility a HME process. Also, on quenching the reactions represented by experiments 8 and 9 with D_2O, the values of deuterium incorporation were found to remain the same as those when the reactions in experiments 8 and 9 were quenched with H_2O.

On the basis of all the evidence gathered from the reactions that were carried out under various conditions, it appears that the reaction of 6,6-diiodo-5,5-dimethyl-1-hexene (**4b**) with LAH proceeds predominantly by a SET pathway involving radical intermediates. An overall mechanism for this reaction is shown in Scheme 4.

As shown in Scheme 4, transfer of an electron from LAH to **4b** leads to the formation of the radical anion of **4b** (X = I). This is then followed by loss of an I⁻ ion to afford the open chain iodo radical, R (X = I). Once this radical is formed, it can then undergo a variety of reactions that lead to the observed products in the reaction of **4b** with LAH.

Determination of Rates of Cyclization of Haloalkyl Radicals Generated from 4a and 4b. In order to determine the values of the rates of cyclization of the haloalkyl radicals (R in Scheme 4) that are produced from

4a and **4b**, we examined the product composition of the reaction of **4a** with n-Bu_3SnH and of **4b** with n-Bu_3SnH.

On the basis of the yields of open chain and cyclized products derived from **4a**, we determined the ratio of the rate of cyclization of R (X = Cl), k_c1, to the rate of hydrogen atom abstraction by R, k_h1 to be 0.31. Since it is known that the bond dissociation energy of the C—H bond in CH_3Cl is only 4 kcal/mol less than that in CH_4,[9] and that the rate of hydrogen atom abstraction by the 5-hexenyl radical is 2.4×10^6/s at 25 °C,[10] it is reasonable to assume that for the chloroalkyl radical generated from **4a**, k_h1 would not be much different from 2.4×10^6/s. Using this value, *the rate of cyclization of the chloroalkyl radical, k_c1, was determined to be* 7.4×10^5/s *at 25 °C*.

Similarly, with the help of the yields of all open chain and cyclized products obtained in the reaction of **4b** with n-Bu_3SnH, we were able to determine the value of the corresponding ratio, k_c2/k_h2, as being 0.23. It has been reported that the hydrogen atom abstraction rates of primary, secondary, and tertiary radicals are almost equal at 25 °C (approximately 2.0×10^6/s)[11] and that these rates are not influenced by the overall structure of the alkyl radical. Therefore, if the iodoalkyl radical generated from **4b** (R, X = I in Scheme 4) is considered to be a secondary radical, and if it is assumed to have a rate of hydrogen atom abstraction value, k_h2, of 2.4×10^6/s, then *the rate at which the iodoalkyl radical derived from **4b** cyclizes, k_c2, will have a value of 5.5×10^5/s at 25 °C.*

Experimental Section

Materials. Ethyl isobutyrate and diisopropylamine were purchased from Aldrich and distilled over calcium hydride prior to use. Pyridinium chlorochromate, phosphorus pentachloride, triethylamine, hydrazine hydrate, and THF-d_8 were purchased from Aldrich and used as received. Methyllithium, as a 1.6 M solution in diethyl ether, was purchased from Aldrich and titrated before use. 4-Bromo-1-butene was purchased from Wiley Organics and distilled over calcium hydride prior to use. Tetrahydrofuran and diethyl ether were purchased from Fisher Scientific and distilled from sodium benzophenone ketyl. Methylene chloride was also purchased from Fisher and distilled over calcium hydride just prior to use. HPLC-grade hexane, from Fisher, was used as received. Neutral Alumina (Brockman activity I, 60–325 mesh) was purchased from Fisher Scientific, and silica gel (200–400 mesh, 60 Å) was purchased from Aldrich.

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 with *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°/min. The injection port was maintained at 250 °C with the detector at 280 °C. All product yields 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. Ethyl 2,2-Dimethylhex-5-enoate (14). This compound was prepared according to the method described by Beckwith and Lawrence.[12] The spectral data of the product matched with that reported in the literature.[12]

2,2-Dimethylhex-5-en-1-ol (15). Fifteen g (0.09 mol) of ester **14** was added dropwise to a suspension of 7.40 g (0.19 mol) of $LiAlH_4$ in 350 mL of anhydrous diethyl ether at 0 °C, with vigorous stirring. The mixture was then allowed to warm to 25 °C and stirred for a period of 18 h. The excess $LiAlH_4$ was then destroyed by sequential addition of 7.40 mL of water, 7.50 mL of 15% NaOH solution, and finally, 22.5 mL of water. Next, the supernatant was decanted, and the ether was removed using a rotary evaporator. The residual liquid was then distilled under reduced pressure to afford 9.60 g of the alcohol (bp 85 °C at 10 mmHg); the yield was 83% based on the ester. The spectroscopic data of this alcohol was the same as that reported in the literature.[12]

2,2-Dimethylhex-5-en-1-al (16). This aldehyde was prepared from alcohol **15** using the general procedure described for the synthesis of aldehydes by Corey and Suggs.[13] Accordingly, 8.00 g (0.06 mol) of alcohol **15** dissolved in 12.0 mL of dry methylene chloride was added, in one portion, to a suspension of 20.0 g (0.09 mol) of pyridinium chlorochromate in 120 mL of dry methylene chloride, with vigorous stirring, at 25 °C. The reaction mixture was then stirred at 25 °C for about 2 h, after which it was diluted with 120 mL of diethyl ether. The supernatant was decanted, and the residue was washed with three 30.0-mL portions of diethyl ether. The combined organic layer was passed through a pad of Florisil, repeatedly, in order to obtain a clear solution. The solvent was then removed on a rotary evaporator. On analyzing the residual liquid by GLC, it was found that the product was 97% pure. The NMR data obtained for the product matched those reported for compound **16** in the literature.[14] This aldehyde was used in subsequent syntheses without any further purification.

6,6-Dichloro-5,5-dimethyl-1-hexene (4a). To a suspension of 6.70 g (0.032 mole) of PCl_5 in 25.0 mL of HPLC-grade hexane was added, dropwise, 4.0 g of aldehyde **16** in 25.0 mL of hexane, with vigorous stirring at 25 °C. Following the addition of the aldehyde, the contents were then stirred at 25 °C for 24 h. The reaction flask was then cooled to 0 °C, and the reaction was quenched with a saturated solution of Na_2CO_3. The lower layer was discarded, and the hexane layer was washed with 10% HCl, after which it was dried over anhydrous K_2CO_3. The hexane was then removed on a rotary evaporator, and the dark residual liquid that was obtained was passed through a short column of neutral alumina, using hexane as the eluent, to obtain a clear liquid. The pure geminal dichloride was finally obtained by preparative GLC using a 10% Carbowax column (10 ft × 1/4 in.). By employing isothermal conditions (110 °C) and a He flow rate of 40.0 mL/min, the pure product was collected after 16.0 min. The geminal dichloride **4a** exhibited the following characteristics: NMR, the following peak assignments were made by comparing the NMR data reported for the corresponding protons of **14**[12] δ 1.10 (6H, s, 2 × CH_3), 1.50–2.20 (4H, m, $-CH_2CH_2-$), 4.90–5.20 (2H, m, $=CH_2$), 5.70–6.10 (1H, m, $=CH-$), and the following assignment was made on the basis of calculated values reported[15] 5.65 (1H, s, $-CHCl_2$); MS *m/e* (relative intensity) 180 (2), 145 (2), 109 (10), 97 (68), 81 (29), 69 (45), 55 (100), 41 (32); high-resolution mass spectum $C_8H_{14}Cl_2$ calcd 180.047 256, obsd 180.046 722.

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6,6-Diiodo-5,5-dimethyl-1-hexene (4b). This compound was synthesized from aldehyde **16**, via the corresponding hydrazone **17**. The hydrazone was prepared according to the general procedure described by Pross and Sternhell.[16] The aldehyde (2.0g) in 15.0 mL of absolute ethanol was added slowly to 4.0 g of hydrazine hydrate, with vigorous stirring. The resulting mixture was then allowed to reflux on a steam bath for 1 h. The contents were then cooled and extracted with chloroform. The chloroform layer was washed with water and dried over anhydrous K_2CO_3. Removal of the solvent using a rotary evaporator afforded hydrazone **17** as a colorless viscous liquid. Its formation was confirmed by MS and NMR data. The hydrazone was then used in the subsequent synthesis of the geminal diiodide without any further purification.

The crude hydrazone (2.0 g) was added dropwise with stirring to a solution of 7.0 g of iodine in 25.0 mL of diethyl ether. Following the addition of the hydrazone, triethylamine was added very slowly until the evolution of nitrogen ceased. The contents were then diluted with 25.0 mL of diethyl ether and the resulting organic layer washed with 5% $Na_2S_2O_3$, followed by 3 N HCl and, finally, a 5% solution of Na_2CO_3 in water. The organic layer was then dried over anhydrous K_2CO_3 and the solvent (and any excess triethylamine) removed under vacuum. The residual oil that was obtained was passed through a short silica gel column, with hexane as the eluent. The product that was obtained showed a single peak on GLC analysis. The MS and NMR data of this product confirmed that it was the desired geminal diiodide **4b**. Its approximate yield based on aldehyde **16** was found to be 28%: NMR, the following peak assignments were made by comparing the NMR data reported for the corresponding protons of **14**[12] δ 1.15 (6H, s, 2 × CH_3), 1.50–2.10 (4H, m, $-CH_2CH_2-$), 4.90–5.10 (2H, m, $=CH_2$), 5.70–6.00 (1H, m, $=CH-$), and the following assignment was by comparing with a reported value for a geminal diiodide[17] 5.25 (1H, s, $-CHI_2$); MS *m/e* (relative intensity) 364 (3), 239 (20), 183 (15), 127 (10), 109 (100), 69 (97), 55 (90), 41 (71); high-resolution mass spectrum $C_8H_{14}I_2$ calcd 363.918 504, obsd 363.918 640.

Procedure for the Reaction of the Geminal Dihalides with LAH and the Subsequent Isolation/Characterization of Products. A standard solution of LAH was prepared in THF and stored at 25 °C. To a calculated volume of this standard solution was added a solution of the dihalide (with *n*-decane as the internal reference) in THF, dropwise, at 25 °C at a desired stoichiometry (typically 1:7 for the dichloride **4a** and 1:2 or less for the diiodide **4b**). The reaction mixture was then stirred at 25 °C for 8 h or less in the case of **4b** and for about 30 h in the case of **4a**. The reactions were monitored at specific intervals by drawing out small volumes of the reaction mixtures, quenching them with water (or D_2O), extracting the products with Et_2O and analyzing the product composition by GLC. Reactions that were not monitored were terminated by quenching with water and extracting the products in diethyl ether. Typically, the initial concentration of the dihalide was approximately 0.05 M.

The reaction of 6,6-dichloro-5,5-dimethyl-1-hexene (**4a**) with LAH, in THF, at 25 °C, gave the products that are listed below with their respective modes of isolation/characterization.

***trans*-2-Chloro-1,1,3-trimethylcyclopentane (6).** This product was isolated by preparative GLC using a 10% Carbowax column (10 ft × 1/4 in.) under temperature programming conditions of 70 °C to 180 °C at 4 °C/min and a helium flow rate of 40 mL/min. **6** was collected after 10 min: NMR, the following peak assignments were made by comparing the NMR data reported for the corresponding protons of **2**[12] δ 0.95 (s, 3H, $-CH_3$), 1.05 (s, 3H, $-CH_3$), 1.10 (d, 3H, $-CH_3$), 1.20–2.00 (m, 5H, ring $-CH$ and $-CH_2CH_2$), and the following assignment was made on the basis of calculated values reported[15] 3.40 (d, $J = 10.2$ Hz, 1H, $-CHCl$); MS *m/e* (relative intensity) 146 (30), 110 (22), 95 (42), 69 (100), 56 (40), 55 (50); high-resolution MS $C_8H_{15}Cl$ calcd 146.086 228, obsd 146.085 892.

***cis*-2-Chloro-1,1,3-trimethylcyclopentane (7).** This compound was also isolated by preparative GLC under the same conditions that were employed for the isolation of **6**, and it had a retention of 14 min: NMR all H shift values were essentially the same as those for the *trans* isomer **6**, except for the $-CHCl$ unit at δ 4.00 (d, $J = 5.10$ Hz, 1H); MS *m/e* (relative intensity) 146 (26), 110 (22), 95 (45), 69 (100), 56 (61), 55 (59); high-resolution MS $C_8H_{15}Cl$ calcd 146.086 228, obsd 146.085 953.

6-Chloro-5,5-dimethyl-1-hexene (8). This product was identified by matching its MS data with that reported in the literature.[4d]

1-(3-Butenyl)-1-methylcyclopropane (5). The structure was established by matching the MS data obtained with that reported for an authentic sample.[18]

When 6,6-diiodo-5,5-dimethyl-1-hexene (**4b**) was allowed to react with LAH, the following products were obtained.

1-(3-Butenyl)-1-methylcyclopropane (5) which was identified as described earlier.

6-Iodo-5,5-dimethyl-1-hexene (1b). This product was identified by matching its MS data with that reported in the literature.[4d]

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

5,5-Dimethyl-1-hexene (3). The structure was assigned on the basis of the MS data that matched with that reported in the literature for 5,5-dimethyl-1-hexene.[19]

2,2-Dimethylbicyclo[3.1.0]hexane (9). The structure was assigned on the basis of matching MS data with that reported for an authentic sample of 2,2-dimethylbicyclo[3.1.0]hexane prepared in earlier work carried out by this group.[8]

***trans*-2-Iodo-1,1,3-trimethylcyclopentane (10).** This compound 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, the following peak assignments were made by comparing the NMR data reported for the corresponding protons of **2**[12] δ 0.97 (s, 3H, $-CH_3$), 1.03 (s, 3H, $-CH_3$), 1.07 (d, 3H, $-CH_3$), 1.40–2.00 (m, 4H, 2 × ring $-CH_2-$), 2.27 (m, 1H, $-CH-$), and the following assignment was made on the basis of calculated values reported[15] 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 (11).** This compound showed the following spectroscopic characteristics: NMR, all values of the chemical shifts for all protons in the molecule were the same as that listed for **10** above 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 (12).** This compound was isolated by flash column chromatography, using silica gel with hexane as eluent: NMR, the following peak assignments were made by comparing the NMR data reported for the corresponding protons of **2**[12] δ 1.15 (s, 3H, $-CH_3$), 1.25 (s, 3H, $-CH_3$), 1.55–2.00 (m, 4H, 2 × ring $-CH_2-$), 2.15 (m, 1H, $-CH-$), and the following assignments were made on the basis of calculated values reported[15] 3.23 (m, 2H, $-CH_2I$), 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).

***trans*-2-Iodo-3-(iodomethyl)-1,1-dimethylcyclopentane (13).** This compound was also isolated 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 **12**, 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).

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