Competing Radical, Carbanion, and Carbene Pathways in the Reactions of Hindered Primary Alkyl Halides with Lithium Dialkylamides

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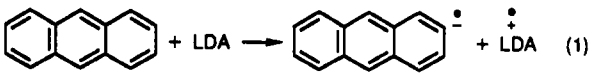
A variety of methods were utilized to study the mechanism of reaction of 6-iodo-5,5-dimethyl-1-hexene and its bromo, chloro, and tosylate derivatives with LDA and several other lithium dialkylamides. In the reaction of 6-iodo-5,5-dimethyl-1-hexene with LDA in THF, radical, carbanion, and carbene pathways occurred simultaneously. However, when the corresponding bromide was allowed to react with LDA, the radical pathway was minor and when the corresponding chloride or tosylate was allowed to react with LDA, no evidence for radical products was observed. This is the first time that competing radical, carbanion, and carbene pathways have been detected in the reaction of a primary alkyl halide with any nucleophile.

Introduction

Single-electron transfer (SET) is an important mechanistic pathway in organic reactions. Radical intermediates suggestive of a SET pathway have been detected by ESR and CIDNP, the use of cyclizable radical probes, and the use of radical trapping agents. Using these methods, reactions of nucleophiles such as metal alkyls,[1] metal hydrides,[2] alkoxides,[3] enolates,[4] and trimethyltin anion[5] with alkyl halides have been shown to be consistent with a SET pathway.

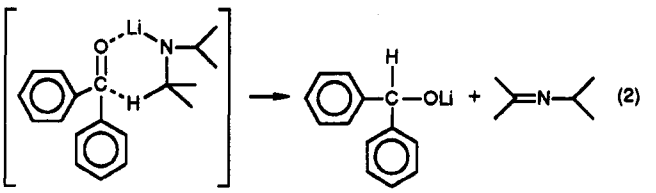
In earlier reports from this laboratory, evidence of radical involvement in the reaction of lithium diisopropylamide (LDA) with polynuclear hydrocarbons (such as anthracene and perylene) (eq 1) and the cyclizable probe 6-iodo-5,5-



(1)

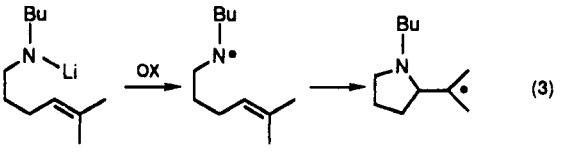
dimethyl-1-hexene was presented.[6,7] In addition to these results other workers have found lithium dialkylamides to behave as single-electron donors toward π-deficient aromatic heterocyclic compounds,[8] α-bromo imines,[9] a conjugated yneone,[10] alkyl sulfonates[11] and benzophenone.[12] These results are intriguing because previously LDA had been used in organic synthesis primarily as a hindered, weakly nucleophilic, strong base.[13]

On the other hand, previous studies suggest that LDA reacts with benzophenone by a polar mechanism in which a hydride ion is transferred to the ketone. Kowalski[14] proposed the mechanism of reaction of benzophenone with LDA to produce benzhydrol, to proceed via a six-centered transition state as shown in eq 2. Newcomb[15] also reported



(2)

similar results in which a β-hydride ion was transferred from LDA to benzophenone to produce benzhydrol. In addition, Newcomb used a radical probe[16] which could cyclize, if a radical was formed at the nitrogen atom (eq 3) of a lithium amide. However, when *N*-lithio-*N*-butyl-



(3)

5-methyl-1-hex-4-enamine was used as a mechanistic probe in a study of the reaction with benzophenone[17] and various other compounds,[18] no cyclized compounds containing a nitrogen atom in the ring were produced. Based on these results, they concluded that SET does not occur when a

(1) Ashby, E. C.; Bowers, J. S. *J. Am. Chem. Soc.* **1981**, *103*, 2242.
(2) (a) Ashby, E. C.; Goel, A. B.; DePriest, R. N. *J. Am. Chem. Soc.* **1980**, *102*, 7779. (b) Ashby, E. C.; Goel, A. B.; DePriest, R. N.; Prasad, H. *J. Am. Chem. Soc.* **1981**, *103*, 973. (c) Ashby, E. C.; DePriest, R. N.; Goel, A. B. *Tetrhedron Lett.* **1981**, *22*, 1763. (d) Ashby, E. C.; Goel, A. B. *Tetrahedron Lett.* **1981**, *22*, 1981. (e) Ashby, E. C.; DePriest, R. N.; Pham, T. N. *Tetrahedron Lett.* **1983**, *24*, 2825.
(3) (a) Ashby, E. C.; Goel, A. B.; Argyropoulos, J. N. *Tetrahedron Lett.* **1982**, *23*, 2273. (b) Ashby, E. C.; Argyropoulos, J. N. *Tetrahedron Lett.* **1986**, *27*, 465.
(4) (a) Ashby, E. C.; Argyropoulos, J. N.; Meyer, R.; Goel, A. B. *J. Am. Chem. Soc.* **1982**, *104*, 6788. (b) Ashby, E. C.; Park, W. S. *Tetrahedron Lett.* **1983**, *104*, 6788. (c) Ashby, E. C.; Argyropoulos, J. N. *J. Org. chem.* **1985**, *50*, 3274.
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(11) Creary, X. *J. Org. Chem.* **1980**, *45*, 2419.
(12) Scott, L. T.; Carlin, K. J.; Schultz, T. H. *Tetrahedron Lett.* **1978**, 4637.
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(15) Newcomb, M.; Burchill, M. T. *J. Am. Chem. Soc.* **1984**, *106*, 8276.
(16) Newcomb, M.; Burchill, M. T. *J. Am. Chem. Soc.* **1984**, *106*, 2450.
(17) Newcomb, M.; Burchill, M. T. *J. Am. Chem. Soc.* **1983**, *105*, 7759.
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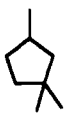
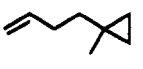
0022-3263/93/1958-0424$04.00/0

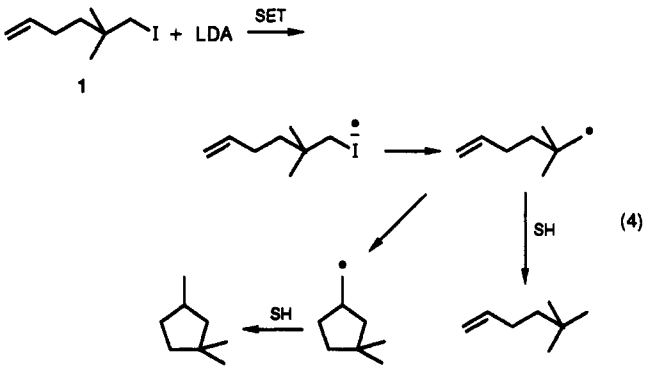
Table I. Reaction of 6-Halo/OTs-5,5-dimethyl-1-hexene (RX) with LDA in THF at 0 °C[a]

				% yield[b]				
								
exp	X	reaction time (h)	RX recovered	A	B	C	D	E
1	I (1)	<48	0.0	8.2	48.0	11.3	22.4	10.1
2	Br (2)	72	27.4	19.8	2.1	12.2	31.0	7.5
3	Cl (3)	120	52.6	9.4	0.0	5.6	22.0	10.4
4	OTs (4)	72	>99	0.0	0.0	0.0	0.0	0.0

[a] The ratio of RX to LDA was 1:5, the concentration of RX was 0.1 M. [b] Percent product yields were determined by GLC (FID detector) using a 30M DB-1 capillary column with an internal standard. Yields were normalized to 100% (absolute yield range was 92–95%).

lithium dialkylamide is allowed to react with substrates that have a reduction potential less than 0.0 V vs NHE.

It is known that primary alkyl halides can react with strong bases such as CH_3Li, *n*-BuLi, PhLi, and PhNa, etc., to deprotonate the α-carbon atom to form a carbene intermediate,[19] and it has been reported that LDA reacts with benzylic halides to form carbenes.[20] Since both polar and SET mechanistic pathways are possible in reactions of alkyl halides with lithium dialkylamides, we were prompted to study these reactions in detail in an attempt to determine if indeed both pathways are operable. Of the possible alkyl groups, we found the 5,5-dimethyl-1-hexenyl system to be of particular interest (eq 4) since



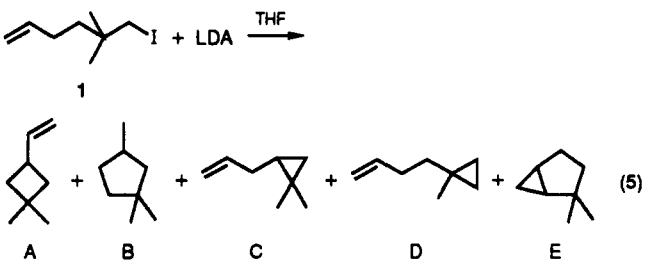
(4)

1,2-dehydrohalogenation by LDA is not possible and also because the 5,5-dimethyl-1-hexenyl radical cyclizes at an appreciable rate (3.6×10^6 s^{-1}). In addition, competing S_N1 and S_N2 pathways are discouraged because of the neopentyl nature of the alkyl halide.

Results and Discussion

In order to study the mechanism of reaction of cyclizable alkyl halides with LDA, those factors that might affect the mechanism of reaction and hence the product distribution were studied, namely, the effect of the halide, the steric requirement of the amide, the one electron donor capabilities of the amide, the effect of a radical trapping agent, solvent, stoichiometry, and temperature.

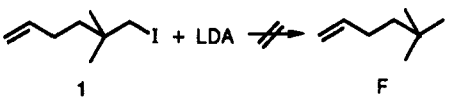
1. Effect of Halide. The products formed in the reaction of LDA with 6-iodo-5,5-dimethyl-1-hexene (1) are all cyclic hydrocarbons (eq 5): 1-ethenyl-3,3-dimethylcyclobutane (A); 1,1,3-trimethylcyclopentane (B); 1,1-dimethyl-2-(2-propenyl)cyclopropane (C); 4-(1-methylcyclopropyl)-1-butene (D); and 2,2-dimethylbicyclo[3.1.0]hexane (E). The results of the reaction of LDA



(5)

with 1 and its bromo (2), chloro (3), and tosylate (4) derivatives are shown in Table I. The results show pronounced effects on both product distribution and the rate of reaction as the halide–tosylate is varied. We will attempt to show that these reactions proceed by a mixture of three possible pathways: a polar reaction involving a carbanion intermediate, a carbene forming reaction, and an electron-transfer reaction involving a radical intermediate.

The order of leaving group ability in a polar reaction[21] is iodide ≃ tosylate > bromide ≫ chloride. If the reaction had proceeded by a polar process, tosylate (4) would have given a result similar to that of iodide (1). However, even after a long period of time, tosylate (4) did not react. On the other hand, it is known that LDA transfers hydride to benzophenone;[14,15] therefore, there is some reason to believe that a similar reaction pathway is involved in the reaction of 1 with LDA. However, if hydride transfer is involved in the reaction of LDA with 1, straight chain hydrocarbon F sould have been produced (eq 6), and it



(6)

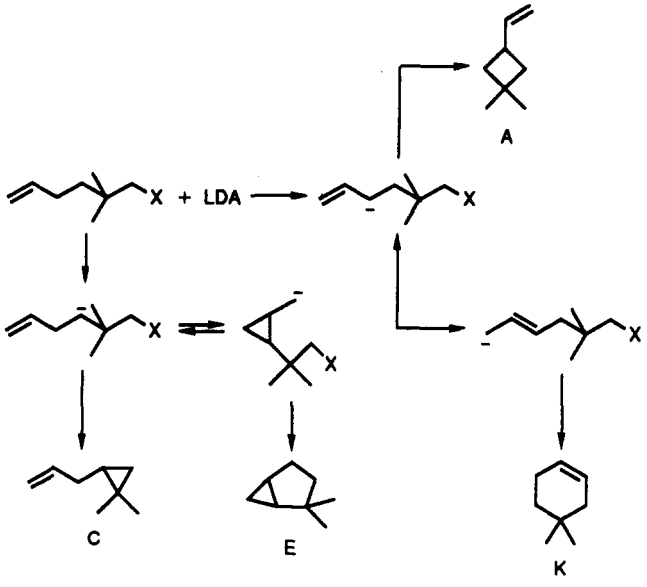
was not; therefore, a hydride transfer from LDA to 1 by a polar process is not likely. However, there is another possibility that a polar process could occur by abstracting a proton from the allylic or homoallylic positions of the alkyl halide by LDA[13a] to give products A, C, and E (Scheme I). If this is true, iodide 1 and tosylate 4 should give similar results with respect to the formation of A since both leaving groups would have the same chance to be attacked by an allylic anion from the backside in a S_N2 process. However, once again, the tosylate did not react. It is unlikely that LDA (pK_a 35–36) would abstract a proton

(19) (a) Friedman, L.; Berger, J. G. *J. Am. Chem. Soc.* **1960**, *82*, 5758. (b) Kirmse, W.; Doering, W. *Tetrahedron Lett.* **1960**, 266. (c) Closs, G. L.; Closs, L. E. *J. Am. Chem. Soc.* **1960**, *82*, 5723.

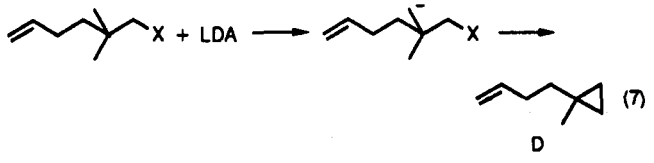
(20) Dougherty, C. M.; Olofson, R. A. *Org. Synth.* **1978**, *58*, 38. Creary, X. *J. Am. Chem. Soc.* **1977**, *99*, 7632.

(21) Pine, S. H.; Hendrickson, J. B.; Cram, D. J.; Hammond, G. S. *Organic Chemistry*, 4th ed.; McGraw-Hill: New York, 1980; Table 9-1, p 379.

Scheme I. Reaction of RX with LDA as a Strong Base by a Polar Process



from the homoallylic position to form C and E or the methyl group ($pK_a > 41$) to yield product D (eq 7). Although

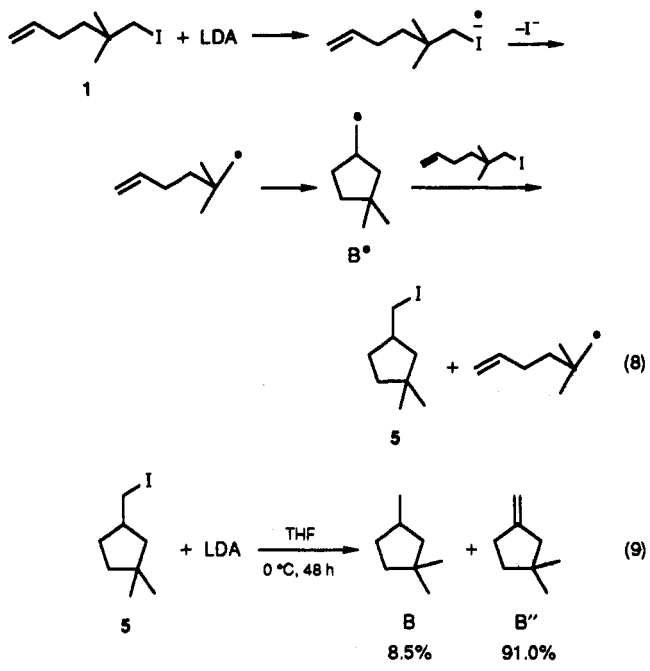


product K is predicted to form with product A, K was not observed. Deuterium tracer studies to be discussed later in this report show that C, D, and E could not have been produced via a carbanion intermediate; however, some of product A did occur through the formation of an allylic carbanion.

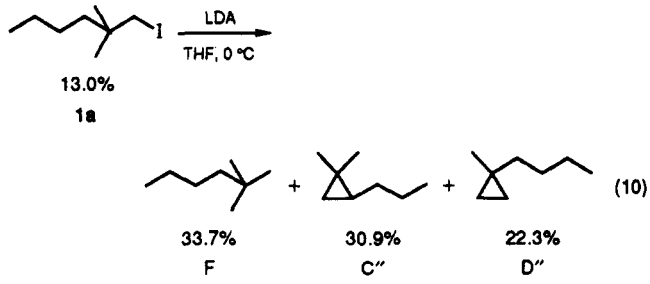
Finally, in order to detect the presence of carbanions that could be produced by reaction of 1 with LDA, *tert*-butylamine (TBA), which is known to trap carbanions efficiently,[22] was employed as a trapping agent. However, lithium *tert*-butylamide (*t*-BuNHLi) reacts with iodide 1 to give the same products as does a mixture of LDA and *t*-$BuNH_2$ with 1 indicating that LDA reacts with *tert*-butylamine to form *t*-BuNHLi. Therefore, TBA was not a valid trapping agent for this purpose.

It is possible to explain the formation of the cyclic hydrocarbon B by a hydride transfer from LDA to the cyclized iodide, 1-(iodomethyl)-3,3-dimethylcyclopentane (**5**)[14-16,23] formed by a halogen atom radical chain process, eq 8. In order to confirm this, 1-(iodomethyl)-3,3-dimethylcyclopentane (**5**) was prepared[24] and allowed to react with LDA in THF at 0 °C for 48 h (eq 9). The results show that 3,3-dimethyl-1-methylenecyclopentane (B″), which could be formed via an elimination reaction, was the major product (91.0%). Since there was no B″ formed in experiment 1, Table I, then B cannot originate from cyclized iodide (**5**).

Additionally, the reaction of the saturated counterpart of **1**, i.e. **1a**, was allowed to react with LDA in THF at 0



°C for 48 h since hydrocarbon product cannot be formed as a consequence of the halogen atom exchange process described by eq 8. The reaction produced three products: F, C″, and D″ (eq 10). The hydrocarbon product F, formed



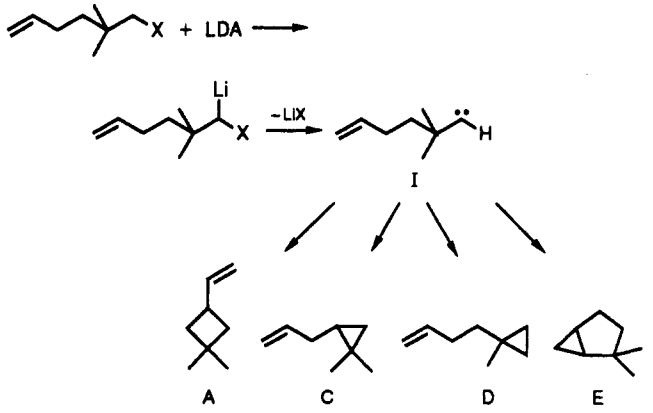
in 33.7% yield, (the equivalent of B when 1 was the reactant) is the result of a radical precursor whereas C″ and D″ (as we shall see later) are probably the result of a carbene precursor. The important point is that, if B is predominantly a result of halogen atom exchange (eq 8), then when the halogen atom exchange is eliminated, one should observe very little of the hydrocarbon product (eq 10), whereas 33.7% was observed.

In summary then, the data reported in Table I, with respect to the formation of B, show that alkyl iodides are more easily reduced by a one electron transfer process than the corresponding bromide, which is more easily reduced than the corresponding chloride and tosylate.[25] This order of reduction potential is the same as the rate of the reaction of the alkyl halides with LDA (Table I). Furthermore, the substantial formation of B from 1 decreases rapidly in the order I > Br > Cl > OTs, exactly what is expected if B is formed by an electron-transfer process.

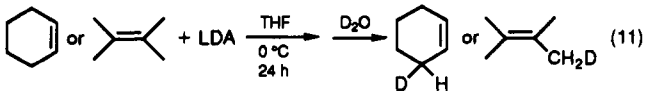
It is also possible that the four products A, C, D, and E obtained from the reaction of the alkyl halides (X = I, Br, Cl) with LDA could be formed from a carbene intermediate I. Since LDA is a strong base, intermediate

(22) Smith, G. F.; Kuivila, H. G.; Simon, R.; Sultan, L. *J. Am. Chem. Soc.* **1981**, *103*, 833.
(23) Beletskaya, I. P.; Artamkina, G. A.; Rentov, O. A. *Russ. Chem. Rev.* **1976**, *45* (4), 330. Brace, N. O. *J. Am. Chem. Soc.* **1964**, 86.
(24) Curran, D. P.; Kim, D. *Tetrahedron Lett.* **1986**, *27*, 5821.
(25) (a) Lipshutz, B. H.; Wilhelm, R. S.; Nugent, S. T.; Little, R. D.; Baizen, M. M. *J. Org. Chem.* **1983**, *48*, 3306. (b) Mbarok, M.; Peters, D. G. *J. Org. Chem.* **1982**, *47*, 3387.

Scheme II. Reaction of RX with LDA via a Carbene Intermediate



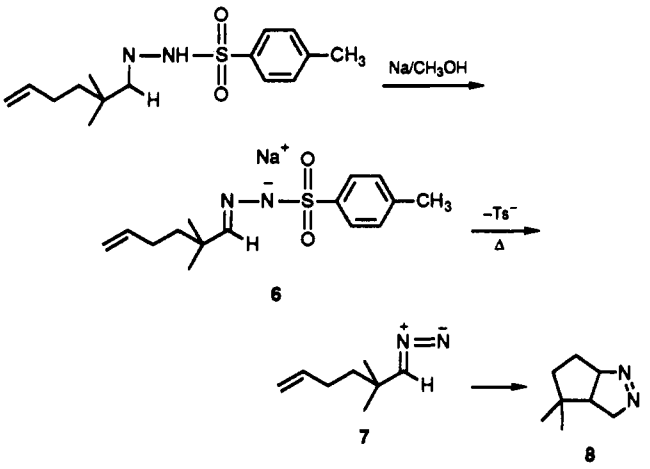
I could be produced[26] according to Scheme II. This intermediate would then undergo C–H insertion at C3 to give A, C–H insertion at C4 to give C, C–H insertion at the 5,5-dimethyl groups to give D, and addition to the double bond to give E. For this reason two carbene trapping agents, cyclohexene and 2,3-dimethyl-2-butene, were used in an attempt to trap the carbene intermediate.[27,28] Control experiments of the trapping agents with LDA (carried out in order to determine the stability of these reagents to LDA) showed less than 6% deuterium incorporation in the recovered starting material on hydrolysis with D_2O (eq 11). Although the presence of 6%



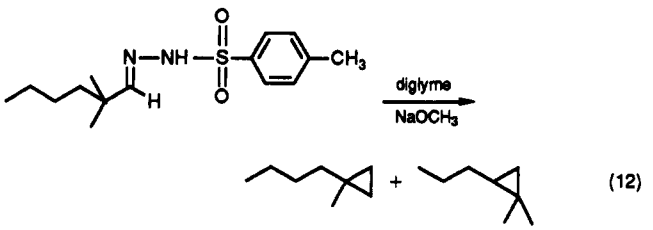
(11)

of the corresponding lithio compound was indicated, sufficient reagent was still present in order to trap intermediate I. However, there was no trace of the corresponding cyclopropane compound that could prove the presence of the carbene although the reaction was slowed down somewhat. Such a result does not exclude a carbene intermediate since intramolecular C–H insertion by the carbene would be undoubtedly faster than the intermolecular reaction involving I and the trapping agent.[27,29] Since the carbene trapping experiments failed, further efforts to establish the intermediacy of a carbene were pursued. One approach was to prepare carbene I by a known method and see if the same products (A, C, D, and E) are formed. Pyrolysis of the sodium salt of the corresponding tosylhydrazone, prepared by the reaction of tosylhydrazine and the corresponding aldehyde, is the standard method for the preparation of a carbene.[30] The sodium salt of the tosylhydrazone (compound 6, Scheme III) was thermally decomposed at 150 °C; however, products A, C, D, and E were not formed. Instead a compound with a molecular weight of 138 was isolated whose spectral characterization revealed the compound to be 8. It appears that the presence of a double bond in

Scheme III. Thermal Decomposition of the Sodium Salt of Tosylhydrazone 6



the molecule induces the diazo compound 7, which is formed as an intermediate in the decomposition of 6, to cyclize rather than expel nitrogen, thus leading to the formation of 8. However, Kirmse and Wachtershauser[31] have found that in the thermal decomposition of 6 without a terminal double bond, 1-butyl-1-methylcyclopropane and 1,1-dimethyl-2-propylcyclopropane were formed (eq 12),



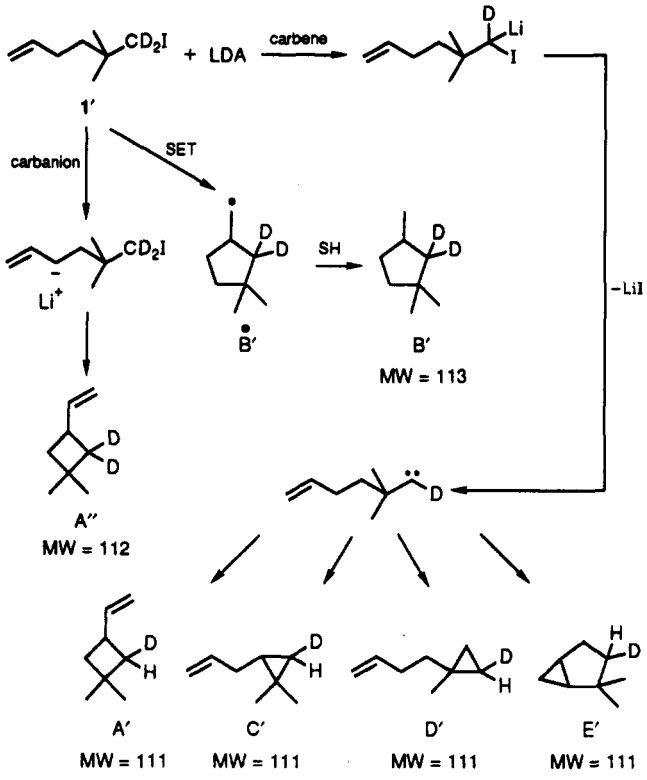
(12)

which correspond to products D and C, respectively, in Table I. Compound E is not possible in this system because of the absence of the double bond. It appears to us that the difficulty in generating carbenes by thermal decomposition of tosylhydrazones may be a regular feature in compounds where the double bond is placed such that cyclization of the intermediate diazo compound to form a five-membered ring is possible. We are pursuing this line of investigation, and the details will be reported elsewhere.

With a view to further establish the intermediacy of carbenes, 1 was prepared with two deuterium atoms at the C6 position. If this compound is allowed to react with LDA and a carbene intermediate is formed, incorporation of one deuterium atom in each product should take place (Scheme IV). When 6,6-dideuterio-6-iodo-5,5-dimethyl-1-hexene (1′) was allowed to react with LDA at 0 °C for 24 h, the reaction gave the same number of products as observed earlier in the reaction of 1 with LDA. Three hydrocarbons C′, D′, and E′ gave 100% d_1 product; however, compound A′ showed 10% d_1 and 90% d_2 product whereas compound B′ showed 100% d_2 content. The 90% d_2 content of A′ can be explained by an isotope effect. Since the C–H bond is weaker than the C–D bond, it should be easier for LDA to abstract an allylic proton from C3 of 1′ rather than the C6 deuterium of 1′. The resulting lithio compound would then produce A″, containing two deuterium atoms, by a polar process (Scheme IV). The fact that B′ contains 100% d_2 product is consistent with its

(26) Olofson, R. A.; Dougherty, C. M. *J. Am. Chem. Soc.* **1973**, *95*, 581, 582.
(27) Goldstein, M. J.; Dolbier, W. R., Jr. *J. Am. Chem. Soc.* **1965**, *87*, 2293.
(28) Kirmse, W. *Carbene Chemistry*, 2nd ed.; Academic Press: New York, 1971; Table X, p 294.
(29) Kirmse, W. *Carbene Chemistry*; Academic Press: New York, 1964; Chapter 3.
(30) Kirmse, W. *Carbene Chemistry*, 2nd ed.; Academic Press: New York 1971; Chapter 2, p 29.
(31) Kirmse, W.; Washtershauser, G. *Tetrahedron* **1966**, *22*, 63.

Scheme IV. Carbene/Carbenoid Intermediacy Indicated by Deuterium Incorporation

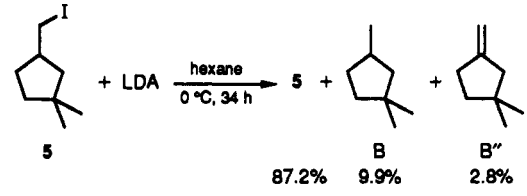


formation via a SET process (Scheme IV). The ratio of [A + C + D + E/B] (where A, C, D, and E originate from a carbene process and B originates from a SET process) is 1.1 for the iodide 1 and 33.6 for the bromide 2. This indicates that with iodide 1 the carbene process and the SET process occurred competitively; however, with the bromide 2, which has a less favorable reduction potential than 1, the carbene process is predominant. On the other hand, when the chloride 3 was allowed to react with LDA, only the carbene products were observed since the even less favorable reduction potential of the chloride compared to the bromide would make a SET process even less likely. It is interesting that in the reaction of 1' with LDA, the amount of A' and A'', relative to the other products formed, increased substantially over A (34.0% vs 8.2%) produced in the reaction of LDA with 1, indicating the allylic proton abstraction of 1 becomes a much more prominent reaction when the proton that is normally abstracted from C1 is replaced by deuterium.

2. Rate Profile Study. In order to determine the constancy of the ratio of products formed throughout the reaction, iodide 1 and bromide 2 were allowed to react with LDA in THF at 0 °C with samples taken over a period of time (Table II). Experiments 1 and 9 show that there is no change in product distribution after the products are formed. The fact that the SET to carbene product ratio remains constant throughout the reaction indicates that both kinds of products could originate from the same intermediate. We are presently exploring this possibility. On the other hand, bromide 2 produced a higher ratio of carbene to SET products compared to iodide 1. This higher ratio is due to a less favorable reduction potential of RBr compared to RI which causes the reaction of RBr with LDA to proceed predominantly by a carbene process.

3. Effect of Solvent. In order to determine the effect of solvents less basic than THF, 1 was allowed to react with LDA in ether and hexane (Table III). In ether (experiment 13), the reaction was slower than in THF, and the major product was the SET product (B) which formed in 78% yield. Since ether is less basic than THF, the coordination between ether molecules and lithium in LDA is not as strong as in THF. Therefore, LDA in ether would be expected to be less anionic and more sterically hindered than in THF. This would cause LDA to be a less effective base in removing the proton at C6, thus decreasing the amount of carbene product relative to SET product. In other systems, ether has always produced more radical cyclized product than in THF.[32] In hexane (experiment 14), only SET product B and cyclized iodide 5 were formed, and the starting material was recovered in 46.1% yield. Since hexane is a nonbasic, noncoordinating solvent, LDA is oligomeric.[33] Thus, in hexane, LDA should have a greater steric requirement than in THF causing it to behave as a weaker base. Product B is formed in 39.1% yield by a SET process and product 5 formed in 14.7% yield by a halogen atom exchange process described earlier.[23,32,34] In ether, cyclized radical (B•) abstracts a hydrogen atom more readily than in hexane;[35] thus more B is formed and only a small amount of 5 is produced in ether compared to hexane solvent.

Next, the cyclized iodide 5 was allowed to react with LDA in hexane in an attempt to determine if B can be formed by hydride transfer from LDA to 5. Equation 13



(13)

supports the position that B did not originate from the cyclized iodide 5 by hydride transfer because not even a trace of B'' was formed in experiment 14. Furthermore it is clear that B is formed very slowly via the reaction of 5 with LDA and therefore could not account for the formation of B in experiment 14. In an attempt to use a solvent more highly coordinating than THF, 1 was allowed to react with LDA in DME. Indeed, DME (experiment 15) coordinates more strongly with the lithium of LDA than does THF, thus making LDA more basic and less sterically hindered than in ether or THF. Thus LDA in DME should more easily attack one of the allylic hydrogens in 1 to produce more of A by a polar process (Scheme IV), and it does.

4. Effect of Stoichiometry. The results of a change in stoichiometry in the reaction of iodide 1 with LDA are shown in Table IV. Seebach[36a] and Fox[36b] studied the structure of several lithium dialkylamide bases by cryoscopic and cyclic voltametric methods respectively and have concluded that LDA exists in solution in a monomer–dimer equilibrium. However, recent studies by Collum[36c]

(32) Ashby, E. C.; DePriest, R. N.; Goel, A. B.; Wenderoth, B.; Pham, T. N. *J. Org. Chem.* **1984**, *49*, 3545.

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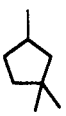
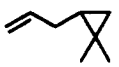
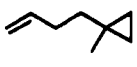
(34) (a) Evans, F. W.; Fox, R. J.; Szwarc, M. *J. Am. Chem. Soc.* **1960**, *82*, 6414. (b) Cooper, R. A.; Lawler, R. G.; Ward, H. R. *J. Am. Chem. Soc.* **1972**, *94*, 545, 552.

(35) Kochi, J. K. *Free Radicals*; Wiley and Sons: New York, 1973; Vol. 1, Chapters 2, 4, 7.

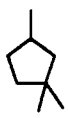
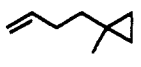
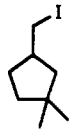
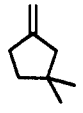
(36) (a) Seebach, D.; Bauer, W. *Helv. Chem. Acta* **1984**, *67*, 1972. (b) Renaud, P.; Fox, M. A. *J. Am. Chem. Soc.* **1988**, *110*, 5702. (c) Galiano-Rogh, A. S.; Collum, D. B. *J. Am. Chem. Soc.* **1989**, *111*, 6772.

Table II. Reaction Rate Profile Study of the Reaction of 6-Iodo- and 6-Bromo-5,5-dimethyl-1-hexene (1 and 2) with LDA in THF at 0 °C[a]

				% yield[b]				
								
exp	X	reaction time (h)	RX recovered	A	B	C	D	E
5	I (1)	2	83.2	1.9	9.0	2.0	2.7	1.1
6		7	69.5	3.3	13.2	4.5	6.8	2.7
7		15	31.6	7.0	30.5	8.0	16.1	6.7
8		24	7.6	7.9	42.5	11.8	21.1	9.1
1		48	0.0	8.2	48.0	11.3	22.4	10.1
9		72	0.0	8.2	48.3	10.9	21.7	10.6
10	Br (2)	20	59.4	11.6	1.3	7.6	17.7	2.4
11		50	42.2	16.9	1.9	9.5	25.5	4.1
12		72	27.4	19.8	2.9	12.2	31.0	7.5

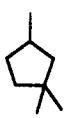
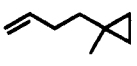
[a] The ratio of RX to LDA was 1:5. The concentration of RX was 0.1 M. [b] Product yields were determined by GLC (FID detector) using a 30M DB-1 capillary column with an internal standard. Yields were normalized to 100% (absolute yield range was 92–95%).

Table III. Effect of Solvent on the Reaction of 6-Iodo-5,5-dimethyl-1-hexene (1) with LDA at 0 °C[a]

			% yield[b]						
									
exp	solvent	RI recovered	A	B	C	D	E	5	B″
1	THF	0.0	8.2	48.0	11.3	22.4	10.1	0.0	0.0
13	ether	14.1	tr[c]	77.6	tr[c]	1.6	tr[c]	3.6	3.0
14	hexane	46.1	0.0	39.1	0.0	0.0	0.0	14.7	0.0
15	DME	44.4	14.7	15.7	13.4	13.4	2.8	0.0	0.0

[a] The ratio of 1 to LDA was 1:5. The concentration of 1 was 0.1 M; all reaction were carried out for 48 h except experiment 15 which was for 24 h. [b] Percent yield was calculated by GLC (FID detector) using a 30M DB-1 capillary column with an internal standard. Yields were normalized to 100%. [c] Trace 1%.

Table IV. Effect of Stoichiometry in the Reaction of 6-Iodo-5,5-dimethyl-1-hexene (1) with LDA in THF at 0 °C[a]

			% yield[b]				
							
exp	ratio of RI:LDA	RI recovered	A	B	C	D	E
16	1:1	84.8	0.6	10.0	1.3	2.1	1.0
17	1:2	17.0	6.9	30.4	11.4	25.5	8.8
18	1:3	3.8	7.9	44.8	11.8	21.3	10.4
1	1:5	0.0	8.2	48.0	11.3	22.4	10.1
19[c]	1:10	0.0	7.1	62.1	8.4	14.1	8.3

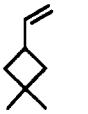
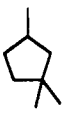
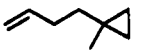
[a] The concentration of 1 was 0.1 M, and all reactions were carried out for 48 h. [b] Percent was calculated by GLC (FID detector) using a 30M DB-1 capillary column with an internal standard. [c] Experiment 19 was quenched after 20 h.

using ^{6}Li and ^{15}N NMR revealed resonances and couplings characteristic of only the dimeric form. We were interested in finding out if complexation occurs prior to reaction between 1 and LDA, as has been detected in the case of some organolithium compounds,[37] and toward that end carried out some IR studies mainly in the far infrared region. However, the weak absorbance at 605 cm^{-1} due to C–I stretching in 1 was not any different in the presence or absence of LDA nor could we discover any new peaks that could be attributed to complex formation. Moreover, the fact that 15% of the starting material is consumed when iodide 1 and LDA are allowed to react in a 1:1 molar ratio argues against the formation of a stable 1:1 complex comprised of 1 and LDA dimer, but is not inconsistent with the reaction of 1 with a partially dissociated complex or reaction of 1 with LDA as a monomer ⇌ dimer equilibrium. The results of Table IV also show that the SET pathway increases at the expense of the carbene pathway as the ratio of LDA to 1 increases.

5. Effect of Temperature. Table V (experiment 20) shows that at −78 °C, no reaction occurs between 1 and LDA after 120 h. When the temperature was raised to −50 °C for 48 h (experiment 21), B was formed as the only product (5.8%), indicating independently that abstraction of a proton to effect carbene formation does not take place at −50 °C. When the reaction was carried out at room temperature and reflux temperature[38] (experiments 23 and

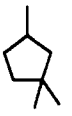
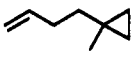
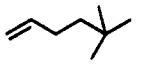
(37) (a) Aseur, M.; Beak, P.; Hay, D.; Kempf, D. J.; Mills, S.; Smith, S. G. *J. Am. Chem. Soc.* **1983**, *105*, 2080. (b) Meyers, A. I.; Rieker, W. F.; Fuenters, L. M. *J. Am. Chem. Soc.* **1983**, *105*, 2082.

Table V. Effect of Temperature on the Reaction of 6-Iodo-5,5-dimethyl-1-hexene (1) with LDA in THF[a]

				% yield[b]				
								
exp	temp (°C)	reaction time (h)	RI recovered	A	B	C	D	E
20	−78	120	>98	0.0	0.0	0.0	0.0	0.0
21	−50	48	94.1	0.0	5.8	0.0	0.0	0.0
22	−21	48	69.0	6.2	9.2	4.2	7.3	3.8
1	0	48	0.0	8.2	48.0	11.3	22.4	10.1
23	rt	24	0.0	5.8	56.7	8.7	19.5	9.2
24	reflux	1	0.0	5.4	57.3	11.2	19.9	6.1

[a] The ratio of 1 to LDA was 1:5. The concentration of 1 was 0.1 M. [b] Percent yield was calculated by GLC (FID detector) using a 30M DB-1 capillary column with an internal standard. Yields were normalized to 100%.

Table VI. Effect of Radical Traps on the Reaction of 6-Iodo-5,5-dimethyl-1-hexene (1) with LDA in THF at 0 °C[a]

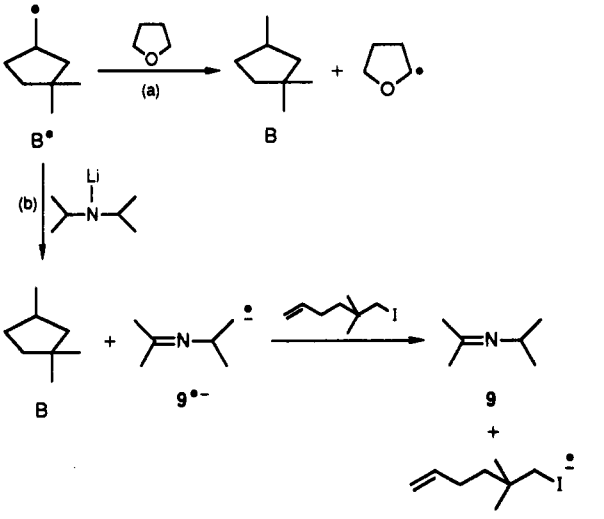
			% yield[b]					
								
exp	additive	RX recovered	A	B	C	D	E	F
1	none	0.0	8.2	48.0	11.3	22.4	10.1	0.0
25	dark[c]	13.7	10.5	33.7	11.2	21.6	9.2	0.0
26	10% *p*-DNB[d]	0.0	5.9	20.9	14.6	32.2	14.5	3.1
27	10% DBNO[e]	0.0	8.1	40.3	9.4	20.7	9.8	2.7

[a] The ratio of 1 to LDA was 1:5. The concentration of 1 was 0.1 M; reaction time was 48 h. [b] Percent yield was calculated by GLC (FID detector) using a 30M DB-1 capillary column with an internal standard. [c] Reaction flask was wrapped with aluminum foil. [d] *p*-Dinitrobenzene. [e] Di-*tert*-butylnitroxyl radical.

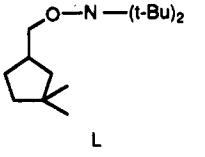
24), the rate of reaction increased and the relative amount of B with respect to A, C, D, and E increased.

6. Effect of Radical Traps. In order to determine if radical anions or free radicals are involved in the formation of B, some radical anion and free-radical trapping experiments were carried out (Table VI). Russell has shown that light can catalyze electron-transfer reactions.[39] Experiment 25 shows that A, C, D, and E were formed at approximately the same rate in the dark or in the light; however, the amount of B formed in the dark decreased significantly, thus providing evidence of a radical precursor in the formation of B. The reaction of 1 with LDA in the presence of 10 mol % of *p*-dinitrobenzene (a good radical-anion scavenger[40]) resulted in a decrease in the yield of B from 48.0% to 20.9% whereas there was a significant increase in the yield of D from 22.4% to 32.2%. These data are consistent with the formation of a radical anion as the precursor to B. Also it was found that in the presence of 10 mol % of di-*tert*-butylnitroxyl radical,[41] the amount of B decreased from 48.0% in experiment 1 to 40.3% in experiment 27, and a new product formed. The compound was not formed in sufficient amounts to be isolated and characterized by NMR spectroscopy; however, molecular weight and mass spectral fragmentation data suggest the formation of coupling product L. The trapping results indicate that the formation of B is via a radical anion-free radical pathway as shown in Scheme V. Since a hydrogen

Scheme V. Hydrogen Atom Abstractions To Form B



atom source is necessary to convert the cyclized radical B• to B, we decided to investigate the nature of the hydrogen



atom donor in the system. The two most obvious hydrogen atom donors are the solvent THF (pathway a), and the α-hydrogens of the base, LDA (pathway b). In the latter case a chain reaction could be initiated with the subsequent electron donor being the radical anion of isopropylidene isopropylamine (9•−).

(38) After 1 h reflux, IR and GLC showed >95% stability, compared with LDA at 0 °C.

(39) (a) Russel, G. A.; Geels, E. J. *Tetrahedron Lett.* **1963**, 1333. (b) Russel, G. A.; Daneu, W. C. *J. Am. Chem. Soc.* **1966**, *88*, 5663. (c) Russel, G. A.; Daneu, W. C. *J. Am. Chem. Soc.* **1968**, *90*, 347.

(40) (a) Bunnett, J. F. *Acc. Chem. Res.* **1968**, 299. (b) Rossi, A. *Acc. Chem. Res.* **1982**, 164.

(41) Hoffmann, A. K.; Feldman, A. M.; Gelblum, E.; Hodgson, G. *J. Am. Chem. Soc.* **1964**, *86*, 639.

Table VII. Reaction of 6-Iodo-5,5-dimethyl-1-hexene (1) and 6-Iodo-6,6-dideuterio-5,5-dimethyl-1-hexene (1') with LDA and LDA-d_2 at 0 °C for 48 h[a]

exp	substrate	solvent	amide	% B (% d)
28	1	THF	LDA-d_2	46.5 (11)
29	1	THF-d_8	LDA	80.2 (2.6)
30	1	THF-d_8	LDA-d_2	38.8 (73)
31	1'	THF-d_8	LDA-d_2	30.0 (93)

[a] The ratio of iodide 1 to LDA was 1:5. The concentration of RX was 0.1 M.

Table VIII. Reaction of 6-Iodo-5,5-dimethyl-1-hexene and Its α,α-Dideuterio Analog with Lithium Tetramethylpiperidide (LiTMP) at 0 °C for 48 h[a]

exp	substrate	solvent	% B (% d)[b]
32	1	THF	22.0
33	1	THF-d_8	2.2 (34)
34	1'	THF-d_8	4.0 (39)

[a] The ratio of iodide 1 to LDA was 1:5. The concentration of RX was 0.1 M. [b] Percent yield was calculated from GLC data (FID detector) using a 30M DB-5 capillary column with an internal standard.

If pathway b is operative, then imine **9** should be present in the product mixture. Despite a careful search, we could not observe the presence of **9** as one of the products by GC/MS analysis. However, trace amounts of acetone and isopropylamine were detected as part of the product mixture. An authentic sample of isopropylideneisopropylamine (**9**) was prepared by a reported procedure[42] and subjected to our workup conditions. An immediate hydrolysis to acetone and isopropylamine took place. However, it was observed that if the reaction mixture was hydrolyzed with dry methanol and the resulting solution distilled into an ice-cooled receiver, imine **9**, if present, was stable and could be detected. However, subjecting the reaction of 1 with LDA to the same workup conditions did not yield any of imine **9**, only trace amounts of acetone and isopropylamine. This seems to indicate that the main source of hydrogen atoms in the conversion of B• to B is the solvent THF with minor amounts being contributed by pathway b. To confirm this suggestion α,α-dideuteriodiisopropylamine was prepared[43] and its lithium salt allowed to react with iodide 1 (experiment 28, Table VII); however, product B contained only 11% deuterium. Experiment 29 shows the results when the deuterium label is placed in the THF rather than the LDA. The amount of B increased from 46.5 to 80.2%, but with only a 2.6% deuterium incorporation. Even though this result suggests that there might be a hydrogen atom donor other than the two sources listed above (Scheme V), it can also mean that there is a very small difference between THF and LDA as hydrogen donors with the balance in favor of THF under normal experimental conditions (such as experiment 1). However, when the C–H bonds of THF are made stronger by replacing hydrogen with deuterium, the balance tilts in favor of LDA to offset the primary deuterium kinetic isotope effect. In this case pathway b would now be operative, and a chain mechanism is initiated leading to enhanced yields of B. It might be appropriate to add here that in this experiment (experiment 29), 63.4% of isopropylideneisopropylamine (**9**), based on the amount of B formed, was also isolated.

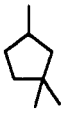
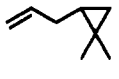
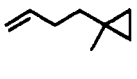
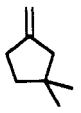
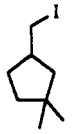
In order to confirm the above rationale, 1 was allowed to react with the lithium salt of α,α-dideuteroisopropylamine in THF-d_8 at 0 °C for 48 h. The results of experiment 30 show that the yield of B decreased to 39% which is not surprising since hydrogen abstraction by B• is made more difficult by strengthening the C–H bonds of THF as well as the α-positions of LDA by replacing hydrogen with deuterium. However, what is more important is that the deuterium content of B rose to 73%. The 27% protium content of product B (experiment 30) could be a result of hydrogen atom abstraction from the N–H bond of the neutral α,α-dideuterioisopropylamine[44] which is generated when a proton is abstracted by the amide from the α-position of the iodide to form the carbene. In order to confirm this, the α,α-dideutero iodide 1' was allowed to react with LDA-d_2 in THF-d_8. The yield of B decreased from 39 to 30% as expected; however, the deuterium content of B rose from 73 to 93%, thus establishing the origin of hydrogen in the formation of B.

When the amide, lithium 2,2,6,6-tetramethylpiperidide (LiTMP), which has no α-hydrogens, was allowed to react with iodide 1, several products formed, including B, which was formed in 22% yield (experiment 32, Table VIII). The lack of α-hydrogens in the amide suggests that all the hydrogen in the conversion of B• to B must be supplied by THF. This was confirmed by the result of reactions carried out in THF-d_8 (experiment 33) whereby the yield of B decreased from 22 to 2.2%; however, the deuterium content of the product was only 34%. Since 2,2,6,6-tetramethylpiperidine is formed in the reaction as a result of a parallel carbene reaction, abstraction of hydrogen from the N–H bond[44] might be contributing to the 66% protium content of B. To confirm this, the amide was allowed to react with the α,α-dideutero iodide 1' so that a deuterium atom rather than a hydrogen atom would be abstracted by the amide resulting in the formation of an N–D bond and subsequent abstraction by the radical B• would increase the deuterium content of B. Experiment 34 shows that in this reaction, B was formed in 4.0% yield with a deuterium content of 39%. We believe that because B was formed in such low yield in three experiments (2–4%), it was not possible to determine the deutrium content of B accurately. Regardless of the deuterium content of B, the large decrease in the yield of B, when LiTMP is the amide and THF-d_8 is the solvent, is further evidence that B is mainly a result of hydrogen atom abstraction from the solvent and the α-position of LDA.

If our contention that the hydrogen donating ability of THF and LDA are similar (Scheme V) and one pathway predominates over the other by changing the strength of the C–H bond to the C–D bond in the solvent or LDA, then carrying out the reaction of 1 with LDA in a solvent that is known to be a weaker hydrogen atom donor[45] than THF, should push the reaction toward pathway b (Scheme V) and increase the yields of B and the imine byproduct. We therefore decided to study the reaction of 1 with LDA in diethyl ether more closely. In addition to the products listed in Table III, experiment 13, the imine **9** was formed in 42.6% yield, based on the amount of B formed. Since a small amount of the cyclic iodide **5** was formed, we wished to determine if a halogen atom radical chain cyclization

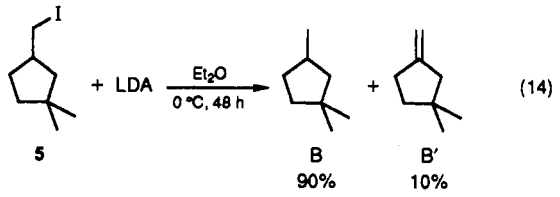
(42) Norton, D. G.; Haury, V. E.; Davis, F. C.; Michell, L. J.; Ballard, S. A. *J. Org. chem.* **1954**, *19*, 1054.
(43) Newcomb, M.; Varick, T. R.; Goh, S. H. *J. Am. Chem. Soc.* **1990**, *112*, 5186.
(44) Inbar, S.; Linschitz, H.; Cohen, S. C. *J. Am. Chem. Soc.* **1980**, *102*, 1419.
(45) Griller, D.; Howard, J. A.; Mariott, P. R.; Scaian, J. C. *J. Am. Chem. Soc.* **1981**, *103*, 619.

Table IX. Reaction of 6-Iodo-5,5-dimethyl-1-hexene (1) with Lithium Dicyclohexylamide (LiDCHA) at 0 °C for 48 h[a]

			% yield						
									
exp	solvent	RX recovered	A	B	C	D	E	B″	5
35	THF	9.7	9.8	15.6	14.9	29.0	14.3	0.0	0.0
36	Et_2O	38.7	1.1	15.2	0.8	1.6	1.1	3.1	35.7

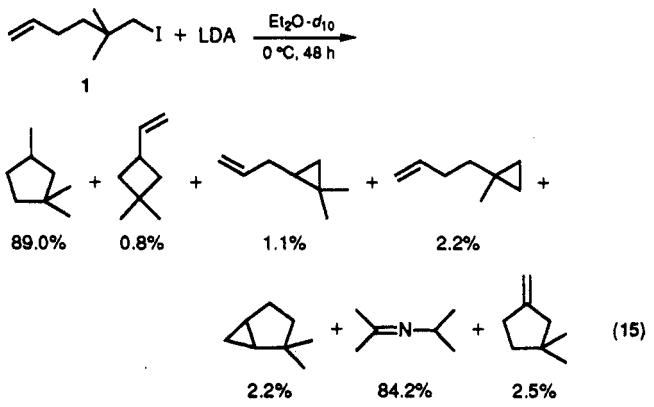
[a] The ratio of RX to LiDCHA was 1:5. The concentration of RX was 0.1 M.

was important in this reaction. In this connection, we allowed cyclic iodide 5 to react with LDA in Et_2O. As can be seen in eq 14, this reaction produced B in 90% yield



5 B 90% B′ 10% (14)

and the dehydrohalogenation product B″ in only 10% yield. This result indicates that although halogen atom radical chain cyclization can contribute to the formation of B, not more than 27% (based on the amount of B″ formed in reaction 13) can come from that pathway, and the rest has to be formed by SET reduction of iodide 1. This view is further reinforced by the results of the reaction of 1 with LDA in Et_2O-d_{10} (eq 15). In this case, the yield

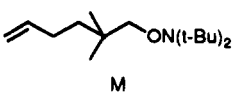


1 89.0% 0.8% 1.1% 2.2% 2.2% 84.2% 2.5% (15)

of B increased to 89% (0% d_1), no starting material remained and 84.2% of the imine 9 was isolated, based on the amount of B formed. Had the reaction proceeded exclusively via the intermediacy of cyclic iodide 5, then changing the solvent from Et_2O to Et_2O-d_{10} would not have changed the reaction products so significantly. However, if it is considered that the abstraction of hydrogen from Et_2O is made more difficult by replacing hydrogen with deuterium, then more hydrogen is abstracted from LDA as discussed earlier, and the initiation of a chain reaction leads to an increased amount of B via pathway b, Scheme V.

Since we were unable to detect 100% imine 9 in the reaction of 1 with LDA (at best only 84.2% could be detected) and, suspecting that the low yield might be due to hydrolysis during work up, an amide system was sought in which the imine, if generated, would be more stable to hydrolysis and therefore could be detected in higher yield. In this connection, 1 was allowed to react with lithium dicyclohexylamide (LiDCHA) in THF. The products formed were similar to the products formed with LDA although they were formed in different proportions (Table IX, experiment 35). Hydrocarbon B was formed in only 15.6% yield, indicating that LiDCHA is a less efficient electron donor compared to LDA and/or is a stronger base than LDA resulting in a higher yield of deprotonation (carbene) products. However, in this reaction, *N*-cyclohexylidenecyclohexylamine, corresponding to imine 9 with LDA, was not detected. This means that THF acts predominantly as the hydrogen atom donor in this system. The use of diethyl ether instead of THF (experiment 36) slows down the overall reaction considerably; however, B was formed in approximately the same amount. A large amount of cyclized iodide 5 was formed at the expense of carbene products, indicating once again that an amide in diethyl ether is a weaker base than in THF. In diethyl ether, which is less viscous than THF, escape of radicals from the solvent cage to initiate a halogen atom radical chain process competes effectively to become the main pathway for the reaction of 1 with LiDCHA.

In a further attempt to isolate an imine in 100% yield corresponding to imine 9 in the reaction of an amide with 1, a literature search was made to identify a dialkylamide that is known to be a better hydrogen atom donor than THF. The rate constant for hydrogen atom abstraction by the *tert*-butoxy radical from pyrrolidine ($k = 7.9 \times 10^7$ M^{-1} s^{-1})[45] is reported to be 1 order of magnitude larger than that from THF ($R = 8.25 \times 10^6$ M^{-1} s^{-1}).][46] The reaction of 1 with lithium pyrrolide in the THF at 0 °C proved very interesting. The reaction was over in 1 h, and the products are listed in Table X, experiment 37. Lithium pyrrolide is a better electron donor than LDA since B was formed in such high yield (78%). D_2O quenching of the reaction mixture gave no deuterium incorporation in the products. Radical trapping experiments (experiment 38) showed a slight decrease in the amount of products formed; however, two additional products (L and M) formed whose

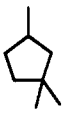
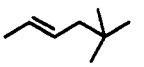
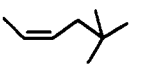


M

molecule weights and mass fragmentation patterns were consistent with the structures shown. Incidentally, the mass spectral characteristics of the former compound matched with that formed in the reaction of 1 with LDA (experiment 27). The rate of reaction in the presence of 10 mol % *p*-dinitrobenzene (experiment 39) decreased substantially, and 24% of the starting material was recovered. The reaction in the absence of light (experiment

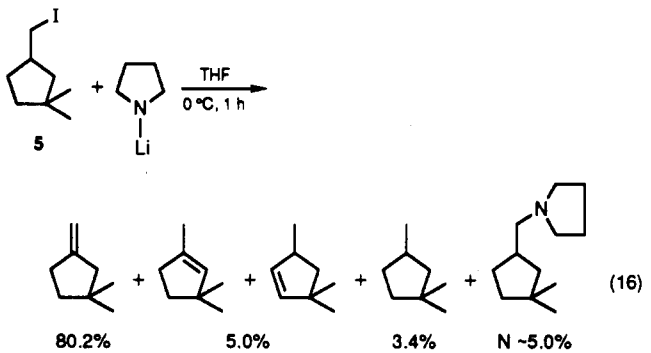
(46) Malatesta, V.; Scaiano, J. C. *J. Org. Chem.* **1982**, *47*, 1455.

Table X. Reaction of 6-Iodo-5,5-dimethyl-1-hexene (1) with Lithium Pyrrolidide at 0 °C in THF and in the Presence of Radical Traps[a]

			% yield			
						
exp	additive	recovered RX	B	G	H	others[b]
37	none	0.0	78.0	11.0	5.6	
38	10% DBNO	0.0	75.5	8.3	4.0	L and M[b]
39	10% PDNB	24.0	48.0	13.0	6.2	
40	dark	11.4	67.0	13.4	6.2	

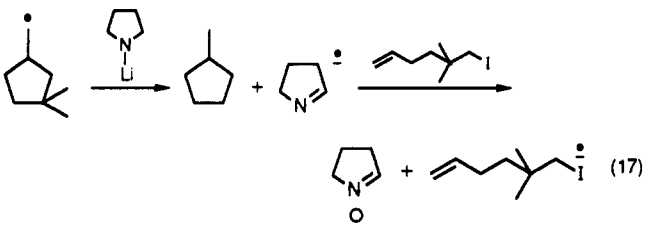
[a] The ratio of RX to lithium pyrrolidide was 1:5. The concentration of RX was 0.1 M. All reactions were carried out for 1 h. [b] The formation of these compounds was indicated by GC/MS (molecular weight 255), but they could not be isolated.

40) was also slower and 11.4% of the starting material was recovered unreacted. In order to determine if the cyclic iodide **5** was an intermediate in this reaction, an authentic sample of **5** was allowed to react with lithium pyrrolidide. Equation 16 shows that in this reaction 1-methylene-3,3-dimethylcyclopentane as well as its isomers are the major products formed and that hydrocarbon B is formed to the extent of only 3.4%. These results indicate that B is formed in experiment 37 via a radical process and that the formation of B from cyclic iodide **5** is not important. The formation of compound N was suggested from GC/MS analysis; however, it was not possible to isolate or characterize it further.



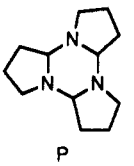
(16)

Our main intention in using lithium pyrrolidide was to employ an amide that is a better hydrogen atom donor than THF and to identify the presence of imine O in experiment 37 (eq 17); however, we were not able to detect



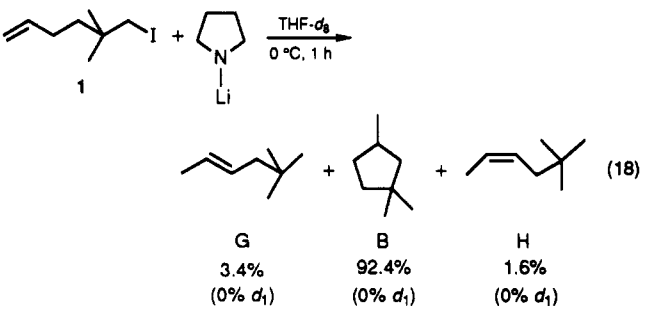
(17)

the presence of O by GC or GC/MS analysis. An authentic sample of 1-pyrroline (O) was prepared by a known method;[47] however, it was found to be stable only in dilute solution. Upon concentrating the solution, trimerization takes place yielding P as the main product.[48] NMR analysis of an ether solution of O showed that the compound is monomeric (the absorption of the olefinic proton at 7.56 ppm could be clearly seen) and the concentration of the compound in ether could be determined. Upon addition of compound O to the reaction



P

mixture of experiment 37, it was observed that in the presence of a large excess of pyrrolidine, it is not possible to detect the presence of O because of the close proximity of the retention times of the two compounds. Thus, we conclude that even though we were not able to detect the presence of O by GC in the reaction of 1 with lithium pyrrolidide, it does not necessarily mean that it was not formed in the reaction. Also when the reaction of 1 with lithium pyrrolide was carried out in THF-d_8 (eq 18), the



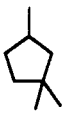
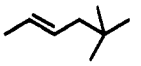
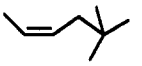
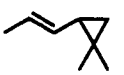
(18)

yield of B increased to 92.4%, the yield of the straight-chain hydrocarbons decreased and no deuterium incorporation was found in any of the products. The increase in the yield of B was expected since THF-d_8 is not as good a hydrogen atom donor as THF; therefore, the reaction proceeds mainly through the radical chain process described earlier (Scheme V, path b). Products G and H were presumably formed by the isomerization of 1 by lithium pyrrolidide followed by SET to form the corresponding radical which then abstracts hydrogen from the amide.

Since the reduction of iodide 1 with lithium pyrrolidide was rapid, we were prompted to study the effect of this reagent on 6-bromo-5,5-dimethyl-1-hexene (**2**). The reaction was considerably slower than the reaction with 1; however, a considerable amount of B was formed, indicating a significant amount of SET involved in the case of the alkyl bromide **2**. In addition to products B, G, and H, a new compound was formed in 10% yield which was found to be 1,1-dimethyl-2-(1-propenyl)cyclopropane (J) (Table XI, experiment 41). Since halogen atom radical

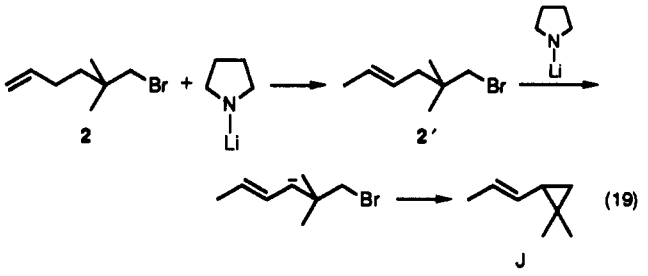
(47) Scully, F. E., Jr. *J. Org. Chem.* **1980**, *45*, 1515.
(48) Ogawa, K.; Nomwia, Y.; Takeuchi, Y.; Tomoda, S. *J. Chem. Soc., Perkin Trans. 1* **1982**, 3031.

Table XI. Reaction of 6-Bromo-5,5-dimethyl-1-hexene (2) with Lithium Pyrrolidide in THF at 0 °C for 12 h and in the Presence of Radical Trapping agents[a]

			% yield			
						
exp	additive	recovered RX	B	G	H	J
41	none	0.0	34.2	40.4	16.2	10.0
42[b]	10% DBNO	34.6	29.5	29.5	14.0	10.1
43	10% PDNB	0.0	13.3	12.6	4.2	35.0

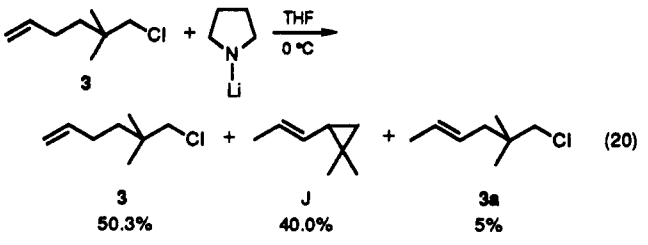
[a] The ratio of RX to lithium pyrrolidide was 1:5. The concentration of RX was 0.1 M. [b] In this reaction two additional compounds were with a mol wt = 255 detected by GC/MS analysis. The fragmentation pattern matched those formed in the corresponding experiment with iodide 1.

chain cyclization is very slow with bromides compared to iodides, formation of product B must be via a free-radical pathway. In order to confirm this, radical trapping experiments were carried out. In the presence of 10 mol % of di-*tert*-butyl nitroxide radical (Table XI, experiment 42), the yield of products B, G, and H decreased, the yield of product J remained the same, and two additional compounds with a molecular weight of 255 were detected. The mass spectral fragmentation pattern of these compounds matched those formed in the previous experiment (L and M) with the corresponding iodide (Table X, experiment 38). *p*-Dinitrobenzene (10 mol %) (Table XI, experiment 43) slows down the reaction of lithium pyrrolidide with 2 considerably and there is a significant increase in the yield of product J. The trapping data clearly show that B, G, and H have radical precursors; however, product J can be rationalized in terms of an allylic proton abstraction (eq 19) from the isomerized bromide 2′ followed



(19)

by cyclization with expulsion of bromide ion to yield J. That compound J was indeed formed by an anionic pathway was confirmed by the reaction of 6-chloro-5,5-dimethyl-1-hexene (3) with lithium pyrrolidide at 0 °C in THF. At the end of 48 h, compound J was formed in 40% yield (eq 20) compared to 10% yield for the corresponding



(20)

bromide 2 (experiment 41). Since chloride 3 has a less favorable reduction potential than the corresponding bromide and iodide, electron transfer is not anticipated and consequently no electron-transfer products such as B, G, or H were produced. In the absence of SET, a more polar pathway would be anticipated, and indeed more of compound J was found in the reaction of chloride 3 compared to the corresponding bromide 2.

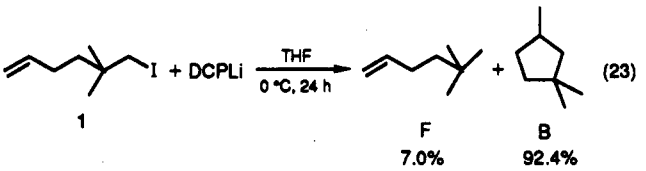
7. Effect of DCPH. Kuivila[49] has used dicyclohexylphosphine (DCPH) as a trapping agent for radicals (eq 21), and we also have found it to be very effective in several

$$R^{\bullet} + DCPH \rightarrow RH + DCP^{\bullet} \qquad (21)$$

systems. It would be important in this study to trap the radicals formed in the reaction of 1 with LDA in the presence of DCPH. However, before this is done, one needs to show that DCPH is a valid radical trap in the presence of LDA. Toward this end, DCPH was allowed to react with LDA in 1:1 ratio in THF (eq 22). When the product

$$LDA + DCPH \xrightarrow[0\,^{\circ}C,\ 24\ h]{THF} \xrightarrow{D_2O} DCPH\ (30\%\ d_1) \qquad (22)$$

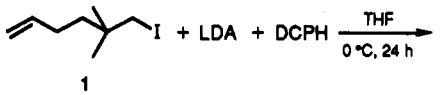
was hydrolyzed with D_2O, the DCPH recovered contained 30% d_1, indicating that DCPLi was formed as an intermediate. The formation of DCPLi in the presence of LDA introduces a complication in that now DCP^- can act as a one-electron donor. Further experimentation to determine the validity of DCPH as a radical trap in the reaction of 1 with LDA shows that DCPLi does indeed react with 1 in 1:5 ratio and F and B were formed in 7.6% and 92.3% yield, respectively (eq 23). Furthermore, when 1 was



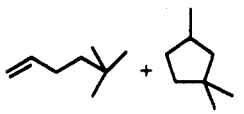
(23)

allowed to react with LDA and DCPH in 1:5:5 ratio, very similar results were obtained (eq 24) as in the previous experiment. All of these data indicate that DCPLi, which itself is a one-electron donor, is formed in these reactions; therefore, one must conclude that DCPH is not a valid radical trap for this system. Since DCPH is a weak acid (pK_a = 35), other hydrogen atom radical traps could not be used since they would be even more acidic than DCPH. On the other hand these data do show that DCP^- reacts with a sterically hindered primary alkyl iodide such as 1 by a one electron transfer process. We shall report in detail on this reaction at a later time.

(49) (a) Kuivila, H. G.; Smith, G. H. *J. Org. Chem.* **1980**, *45*, 2918. (b) Kuivila, H. G.; Alnajjar, M. S. *J. Org. Chem.* **1981**, *46*, 1053.



1



F 7.6% B 92.3% (24)

In summary then, the mechanism of reaction of 1 with LDA and similar amides can be represented by the mechanism in Scheme VI.

Conclusion

An attempt has been made to determine the mechanism of reaction of alkyl halides with LDA using a model system that would indicate the intermediacy of radicals. The effects of leaving group, solvent, temperature, trapping agents, stoichiometry and the nature of the products were carefully investigated and these effects on the mechanistic pathway determined. In the reaction of 6-iodo-5,5-dimethyl-1-hexene (1) with LDA in THF, both SET (product B) and carbene/carbenoid pathways (products A, C, D, and E) occurred simultaneously. In addition it was shown that product A can also be produced via a carbanion pathway. However, when the corresponding bromide 2, which has a less favorable reduction potential than that of iodide 1, was allowed to react with LDA, the carbene/carbenoid process was predominant. When chloride 3 was allowed to react with LDA, no SET product (B) was observed, but carbene or carbenoid products A, C, D, and E were formed. The reaction was carried out with several dialkylamides, and the resultant imine byproduct was isolated in high yield. Other products formed in the reactions were shown to be consistent with the pathways proposed for reactions with LDA. This is the first report of simultaneous carbene, carbanion, and SET pathways involved in the reaction of a primary alkyl halide with any nucleophile.

Experimental Section

Materials. Solvent grade *n*-pentane, *n*-hexane, and benzene were distilled from $NaAlH_4$ under N_2 after conventional washing and drying. Reagent-grade dimethoxyethane (DME), anhydrous tetrahydrofuran (THF), anhydrous diethyl ether, and *n*-hexane (HPLC grade) were purchased from Fisher and distilled from a deep purple solution of solution benzophenone ketyl under N_2 prior to use. Hexamethylphosphoramide (HMPA) from Fisher and dicyclohexylphosphine (DCPH) from Aldrich were distilled under vacuum over sodium and CaH_2, respectively. *n*-Decane 99%, diisopropylamine, 2,2,6,6-tetramethylpiperidine, pyrrolidine, dicyclohexylamine, *tert*-butylamine, 4-bromo-1-butene, and cyclohexene were purchased from Aldrich and distilled from CaH_2 under N_2. *n*-Butyllithium and methyllithium were purchased from Aldrich and used after titration by the Watson–Eastham method.[50] A 98% pure sample of 1,1,3-trimethylcyclopentane (B) from Chemical Samples, hexaphenylditin and di-*tert*-butylnitroxyl from Alfa, *p*-dinitrobenzene from Eastman, tetramethylethylene, and sodium cyanoborodeuteride (98% pure) and THF-d_8 from Aldrich, and diethyl ether-d_{10} (Cambridge Isotope Laboratories Inc.) were used as received.

General Procedures and Apparatus. All glassware and syringes with stainless steel needles were oven-dried at 150 °C and cooled under N_2 just before use. The transfer of chemicals was accomplished under N_2 using bench top techniques. Stirring of the reaction mixtures was carried out using a Teflon-coated magnetic stirring bar. Experiments at low temperature were carried out using an Ultra Kryomat TK 30D. Proton NMR spectra were recorded using either a Varian 60A or a Bruker WM-300 FT instrument using tetramethylsilane (TMS) as a reference. Mass spectral analyses were performed using a Varian MAT-112S mass spectrometer. IR spectra were recorded on a Perkin-Elmer 299 infrared spectrophotometer. 5,5-Dimethyl-1-hexene (F),[32] 5,5-dimethyl-2-hexene (G and H) (cis and trans),[51] 1,1,3-trimethylcyclopentane (B),[51a] 3,3-dimethyl-1-methylenecyclopentane (B″),[51b] 1,3,3-trimethylcyclopentene,[52a] and 1,4,4-trimethylcyclopentene[52b] were identified from published spectra. A, C, D, and J were identified by NMR and mass spectral analysis.

1-Ethenyl-3,3-dimethylcyclobutane (A): ^1H NMR (300 MHz, $CDCl_3$) 1.02 (3 H, s), 1.13 (3 H, s), 1.59–1.65 (2 H, td, J = 8.8 Hz, J = 2.4 Hz), 1.84–1.92 (2 H, td, J = 8.8 Hz, J = 2.3 Hz), 2.82–2.85 (1 H, m), 4.83–4.93 (2 H, m), 5.84–5.995 (1 H, m); mass spectrum, *m/e* (relative intensity) 110 (1.96), 95 (25.05), 56 (94.12), 54 (100.00), 41 (45.01), 39 (28.67); high resolution (mass spectrum) of C_8H_{14} found 110.1100, calcd 110.1096.

1,1-Dimethyl-2-(2-propenyl)cyclopropane (C): ^1H NMR (300 MHz, $CDCl_3$) 0.05–0.03 (1 H, m), 0.38–0.42 (2 H, m), 1.02 (3 H, s), 1.04 (3 H, s), 2.01–2.05 (2 H, m), 4.93–5.08 (2 H, m), 5.85–5.91 (1 H, m); mass spectrum, *m/e* (relative intensity) 110 (3.32), 95 (24.09), 69 (84.43), 67 (33.21), 41 (100.00), 39 (30.79); high resolution (mass spectrum) of C_8H_{14} found 110.1107, calcd 110.1096.

4-(Methylcyclopropyl)-1-butene (D): ^1H NMR (300 MHz, $CDCl_3$) 0.21–0.26 (4 H, m), 1.03 (3 H, s), 1.2–1.3 (2 H, t, J = 5.3 Hz), 2.12 (2 H, q, J = 5.9 Hz), 4.88–5.01 (2 H, m), 5.77–5.87 (1 H, m); mass spectrum, *m/e* (relative intensity 110 (0.35), 95 (20.12), 81 (22.09), 69 (39.23), 68 (49.45), 67 (31.56), 55 (28.89), 41 (100.00), 39 (29.56); high resolution (mass spectrum) of C_8H_{14} found 110.1072, calcd 110.1096.

2,2-Dimethylbicyclo[3.1.0]hexane (E): ^1H NMR (300 MHz, $CDCl_3$) 0.07–0.22 (2 H, m), 0.86–0.93 (2 H, m), 0.98 (3 H, s), 0.99 (3 H, s), 1.0301.21 (2 H, m), 1.53–1.80 (2 H, m); mass spectrum, *m/e* (relative intensity) 110 (11.56), 95(60.78), 81 (38.89), 69 (87.56), 67 (59.23), 55 (28.00), 41 (100.00), 39(36); high resolution (mass spectrum) of C_8H_{14} found 110.1075, calcd 110.1096.

(*E*/*Z*)-1,1-Dimethyl-2-(1-propenyl)cyclopropane (J): ^1H NMR (300 MHz, CD_3COCD_3) 0.2–0.7 (2 H, m) 1.03 (3 H, s), 1.09 (3 H, s), 1.3 (1 H, m), 1.69 (3 H, dd, J = 6.9, J = 1.5), 5.0–5.5 (2 H, m); mass spectrum, *m/e* (relative intensity) 110 (41.0), 95 (100), 67 (61.3), 55 (42.0), 41 (40.0), 39 (29.0).

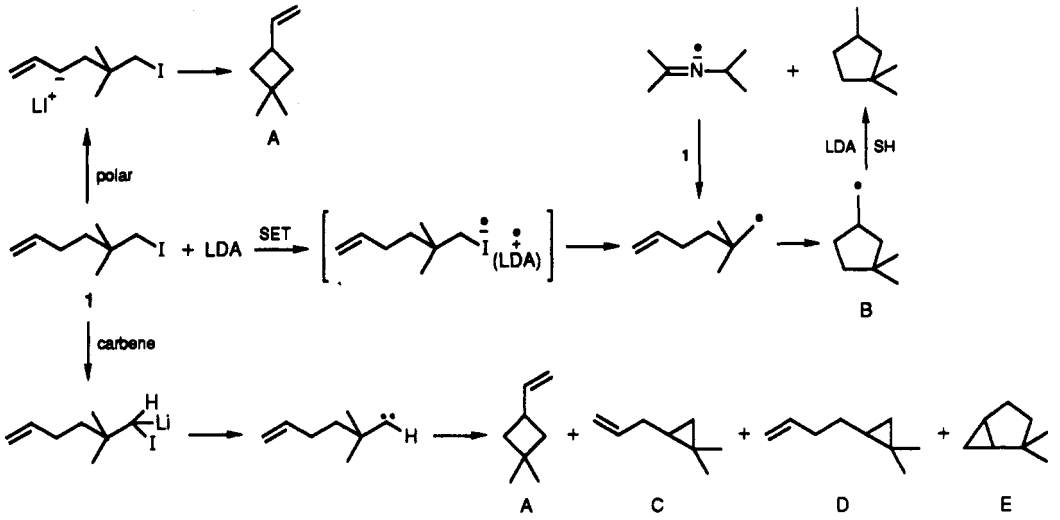
Compounds A–E were prepared by the reaction of 1 with LDA on a large scale and separated using the columns mentioned below. Column A: 25 ft, 1/4 in., 10% Apiezon L on Chromosorb P. Column B: 6 ft, 1/4 in., 10% carbowax 20M. Column C: 20 ft, 1/4 in., 10% diisodecylphthalate (DIP) on Chromosorb W. Column A was used to separate compounds A, B, C, D, and E at 70 °C, 18 psi (He); column C at 130 °C, 60 psi (He) was used to separate A from B, and 130 °C, 50 psi (He) was used to separate D from E. Compound J was isolated from the reaction of 3 with lithium pyrrolidide using a 10-ft SE-30 on Chromosorb W at 40 psi (He), injector temperature 140 °C, detector temperature 145 °C, column temperature 80 °C. Quantitative gas–liquid chromatographic (GLC) analyses were conducted on a Varian Model 37100 equipped with a CDS 111 electronic integrator and a flame ionization detector. GLC yields were determined by using an internal standard and comparing peak areas which were corrected using response factors. Preparative GLC separations were performed on a F&M Model 720 instrument equipped with a thermal conductivity detector using the proper column mentioned above. For quantitative GLC analyses, the following conditions were used (retention times are given relative to the internal standard used): 35 °C for 7 min, followed by 15 °C/min to 250 °C for 5 min, 5,5-Dimethyl-1-hexene (0.49), 5,5-dimethyl-2-hexene

(50) Watson, S. C.; Eastham, J. F. *J. Organomet. Chem.* **1967**, *9*, 165.

(51) (a) Glaze, W. H.; Hanicak, J. E.; Berry, D. J.; Duncan, D. P. *J. Organomet. Chem.* **1972**, *44*, 49. (b) Compared with an authentic sample from Chemical Samples Co. (c) Adlercreutz, P.; Masnusson, G. *Acta Chem. Scand. Ser. B* **1980**, *B34*, 647.

(52) (a) Wolinsky, J.; Clark, G. W.; Thorstenson, P. C. *J. Org. Chem.* **1976**, *41*, 745. Rei, N.-H. *J. Org. Chem.* **1978**, *43*, 2173. (b) Magnusson, G.; Thoren, S. *Tetrahedron* **1974**, *30*, 1431.

Scheme VI. Mechanism of Reaction of 1 with LDA in THF Solvent



(trans) (0.50), 5,5-dimethyl-2-hexene (cis) (0.55), 1,1,3-trimethylcyclopentane (0.52), 6-iodo-5,5-dimethyl-1-hexene (1.10), 6-bromo-5,5-dimethyl-1-hexene (1.02), 6-chloro-5,5-dimethyl-1-hexene (0.97), 2,2-dimethyl-5-hexenyl tosylate (1.83), 1-(iodomethyl)-3,3-dimethylcyclopentane (1.16), 3,3-dimethyl-1-methylenecyclopentane (0.58), hydrocarbon A (0.47), C (0.54), D (0.61), E (0.64), J (0.65), and *n*-decane (1.00).

Preparations. 2,2-Dimethyl-5-hexen-1-ol. This alcohol was prepared by a modified published method.[53] Lithium diisopropylamide (0.10 mol) was prepared by the reaction of MeLi (0.10 mol) with diisopropylamine (0.12 mol) in ether. In order to ensure that no MeLi remained in the LDA, disopropylamine was used in 20% excess. After complete reaction, the excess diisopropylamine was removed under vacuum and the LDA quenched with D_2O. Deuterium analysis of the resulting diisopropylamide was >98%. THF (100 mL) was then added to the LDA solution and the resulting solution stirred at −78 °C while ethyl isobutyrate (11.5 g, 0.10 mol), distilled under N_2 over CaH_2, was added dropwise with stirring for 30 min. After a slow addition of 4-bromo-1-butene (13.5 g, 0.10 mol) in hexamethylphosphoramide (HMPA, 20 mL), the mixture was allowed to warm over a 12-h period to room temperature. The reaction mixture was diluted with H_2O and extracted with petroleum ether and washed with dilute aqueous HCl and then with sodium bicarbonate solution. After the solvent was removed, the organic layer was distilled to give the ester (13 g, 82%) which gave the same spectral data reported earlier.[32] This ester (4.2 g, 0.016 mol) was stirred with lithium aluminum hydride (1.0 g, 0.026 mol) in ether (50 mL) overnight. After dropwise addition of H_2O to the mixture at 0 °C, the supernatant liquid was decanted and distilled to give 2.4 g (80.5%) of 2,2-dimethyl-5-hexen-1-ol which exhibited the following properties: bp 81–83 °C at 25 mmHg; ^{1}H NMR (60 MHz, $CDCl_3$) 0.85 (6 H, s), 1.1–1.4 (2 H, m), 1.7–2.4 (2 H, m), 3.2 (1 H, s), 3.3 (2 H, s), 4.7–6.2 (3 H, m).

Tosylate of 2,2-Dimethyl-5-hexen-1-ol (4). To 50 mL of benzene at 0 °C was added 1.91 g (0.010 mol) of *p*-toluenesulfonyl chloride, 5.0 mL of pyridine, and 1.28 g (0.010 mol) of 2,2-dimethyl-5-hexen-1-ol. The mixture was warmed to room temperature and allowed to stir for 12 h. After filtration the mixture was distilled to give 1.82 g (61%) of the pure product which exhibited the following properties: bp 144–146 °C at 30 mm Hg; ^{1}H NMR (60 MHz, $CDCl_3$) 0.92 (6 H, s), 1.05–2.15 (4 H, m), 2.47 (3 H, s), 3.60 (2 H, s), 4.77–6.05 (3 H, m); mass spectrum (CI), *m/e* (relative intensity) 283 (0.74), 112 (8.61), 111 (100.00), 110 (6.25).

6-Iodo-5,5-dimethyl-1-hexene (1).[32] To a 250-mL flask were added 21.0 g (0.040 mol) of triphenylphosphine (dried in vacuo over P_2O_5 for 5 h), 80 mL of benzene, 10 g (0.36 mol) of I_2, 20 mL of pyridine, and 4.90 g (0.036 mol) of 2,2-dimethyl-5-hexen-1-ol. After reflux for 24 h, the mixture was diluted with hexane (150 mL), cooled, and filtered. After the solvent was removed, distillation of the organic layer gave 8.71 g (93%) of pure 1 (99% by GLC DB-1 30 M column). The following data were obtained: bp 82–83 °C at 22 mmHg; ^{1}H NMR (60 MHz, $CDCl_3$) 1.05 (6 H, s), 1.27–2.27 (4 H, m), 3.13 (2 H, s), 4.80–6.17 (3 H, m); mass spectrum, *m/e* (relative intensity) 238 (1.55), 183 (2.54), 127 (2.64), 112 (2.10), 111 (22.4), 95 (4.41), 69 (100.00), 55 (59.5). Its bromo (from Br_2(l), Ph_3P, pyridine, and benzene) and chloro compound (from CCl_4 and Ph_3P) were prepared by a similar procedure and the products exhibited the following.

6-Bromo-5,5-dimethyl-1-hexene (2): bp 79–80 °C at 25 mmHg; ^{1}H NMR (60 MHz, $CDCl_3$) 1.03 (6 H, s), 1.05–2.25 (4 H, m), 3.22 (2 H, s), 4.80–6.22 (3 H, m); mass spectrum, *m/e* (relative intensity) 192 (0.42), 190 (0.40), 137 (15.06), 135 (15.37), 111 (33.30), 97 (28.12), 81 (10.15, 69 (58.38, 55 (100.00).

6-Chloro-5,5-dimethyl-1-hexene (3): bp 72–73 °C at 25 mmHg; ^{1}H NMR (60 MHz, $CDCl_3$) 0.98 (6 H, s), 1.21–2.25 (4 H, m), 3.35 (2 H, s), 4.80–6.18 (3 H, m); mass spectrum, *m/e* (relative intensity) 146 (.756), 97 (20.34), 91 (21.11), 90 (20.45), 69, (8.05), 56, (81.16), 55 (100.00), 41 (23.10).

6,6-Dideuterio-6-iodo-5,5-dimethyl-1-hexene (1′). This compound was prepared by the same method as 1 except LAD was used instead of LAH: bp 82–83 °C at 16 mmHg; ^{1}H NMR (60 MHz, CDCl3), 1.05 (6 H, s), 1.25–2.27 (4 H, m), 4.80–6.15 (3 H, m); mass spectrum, *m/e* (relative intensity) 240 (5.10), 185.0 (11.00), 127.0 (8.00), 113.0 (87.13), 97.1 (10.50), 70.0 (100.0), 55.0 (83.0), 41.0 (74.05).

1-(Iodomethyl)-3,3-dimethylcyclopentane (5). This compound was prepared by a modified published procedure:[24] 1.0 g (4.2 mmol) of 6-iodo-5,5-dimethyl-1-hexene (99% pure) was added to 10 mL of benzene distilled in a 50-mL two-necked flask equipped with a condenser and the reaction carried out under N_2. A catalytic amount of hexaphenylditin was added to the benzene solution, then by using a 275-W General Electric sun lamp, the resulting solution was refluxed for 15 h. The reaction mixture was cooled to room temperature, and the resulting solution was filtered and concentrated. Then a 10 ft, 1/4 in., SE-30 on Chromosomb W was used to separate the desired product (60%) from the starting iodide (ratio 1.5:1 = cyclized: straight chain) at 135 °C 40 psi (He): mass spectrum, *m/e* (relative intensity) 238 (0.10) 111 (55.4), 69 (100), 55 (50.3), 41 (32.1); ^{1}H NMR ($CDCl_3$) δ 0.95 (3 H, s), 1.03 (3 H, s), 1.3–2.0 (6 H, m), 2.33 (1 H, m), 3.2 (2 H, d).

Isopropylideneisopropylamine (9) was prepared by a reported procedure:[41] bp 93 °C; mass spectrum, *m/e* (relative intensity) 99 (31.9), 98 (13.4), 84 (100) 43 (18.4), 42 (4.3), 41 (19.8); ^{1}H NMR ($COCl_3$) δ 1.1 (6 H, d), 1.8 (3 H, s), 2.0 (3 H, s), 3.6 (1 H, m).

Diisopropylamine (2-d_2). This compound was prepared from acetone, sodium cyanoborodeuteride, and ammonium acetate

(53) Beckwith, A. L.; Lawrence, T. *J. Chem. Soc., Perkin Trans.* **1979**, 2, 1535.

by a recently published procedure:[54] bp 85 °C; mass spectrum, *m/e* (relative intensity) 104 (12.0), 89 (100), 46 (94); ^{1}H NMR ($CDCl_3$) δ 0.95 (s).

1-Pyrroline (P). This compound was prepared by modification of a reported procedure.[47] In a 250-mL three-necked flask equipped with a mechanical stirrer and an addition funnel was placed 9.4 g (70.7 mmol) of *N*-chlorosuccinimide (Aldrich) in 75 mL of ether. The mixture which was cooled in an ice salt bath was vigorously stirred while adding 5.9 mL (70.8 mmol) of pyrrolidine dropwise via an addition funnel. Upon completion of the addition, the reaction mixture was stirred at room temperature for 2 h. After completion of the reaction, the mixture was filtered and the precipitate washed with ether. The filtrate and the ether washes were combined, washed with water, and dried over sodium sulfate. To this ether solution containing *N*-chloropyrrolidine was added 10 g (140 mmol) of potassium superoxide (Aldrich) and 100 mg of 18-crown-6, and the resulting mixture was stirred for 9 h. Upon completion, the reaction mixture was filtered and the resulting products isolated by removal of the ether. The product was analyzed by NMR. The compound was stored in a refrigerator and was found to be stable indefinitely: mass spectrum, *m/e* (relative intensity), 69 (68.2), 68 (27.4), 42 (45.0), 41.0 (100); ^{1}H NMR ($CDCl_3$) 1.75 (2 H, m), 2.5 (2 H, 6 t), 3.8 (2 H, m), 7.55 (1 H, bs).

2,2-Dimethyl-5-hexen-1-al. Pyridinium chlorochromate (16.15 g, 75 mmol) was suspended in 100 mL of dry CH_2Cl_2, 6.4 g (50 mmol) of 2,2-dimethyl-5-hexen-1-ol in 10 mL of dry CH_2Cl_2 was added in one portion, and the reaction mixture was stirred magnetically at room temperature for 2 h. Dry ether (100 mL) was added, and the supernatant liquid was decanted from the black gum. The residue was washed three times with 25-mL portions of dry ether and the combined organic layer filtered through a short pad of Fluorosil. Evaporation of the solution produced crude aldehyde which was purified by distillation under vacuum, bp 52 °C at 15 mmHg (4.9 g, 78% yield): ^{1}H NMR ($CDCl_3$) δ 1.1 (6 H, s), 1.6 (2 H, m), 2.0 (2 H, m), 5.0–5.8 (3 H, m), 9.5 (1 H, s).

Tosylhydrazone of 2,2-dimethyl-5-hexen-1-al. A solution of 1.49 g (8 mmol) of (*p*-toluenesulfonyl)hydrazine in 25 mL of ethanol and 1.2 mL of acetic acid was treated with 1 g (8 mmol) of the aldehyde dissolved in 1.6 mL of ethanol. The reaction mixture was kept at room temperature for 2 h and later cooled to 0 °C, and ice-cold water was added, after which time the tosylhydrazone precipitated. The solid was filtered and recrystallized from ethanol–water: mp 65 °C (1.74 g, 74% yield); ^{1}H NMR ($CDCl_3$) δ 1.0 (6 H, s), 1.4 (2 H, m), 1.7 (2 H, m) 2.4 (3 H, s), 4.9 (2 H, m), 5.7 (1 H, m), 7.0 (1 H, s), 7.3–7.8 (4 H, m), 7.5 (1 H, bs).

Sodium Salt of the Tosylhydrazone of 2,2-Dimethyl-5-hexen-1-al (6). The tosylhydrazone (0.5 g, 1.9 mmol) prepared as described above was dissolved in 15 mL of freshly distilled methanol, and freshly cut Na (0.17 g, 7.5 mmol) was added to this solution. The mixture was allowed to stir for 30 min after which the excess methanol was removed under vacuum. The resulting solid dissolved in D_2O was subject to NMR analysis. The NMR spectrum was identical to the above hydrogens except that it did not show any N–H absorption (δ 7.5).

Decomposition of the Sodium Salt of the Tosylhydrazone (6). The sodium salt of the tosylhydrazone 6 (0.32 g, 3.7 mmol) was placed in a 25-mL round-bottomed flask, which was connected through a short-path distillation head to a vacuum system. The flask was gradually heated in an oil bath. At the temperature of a 150 °C, decomposition of the tosylhydrazone was observed to begin. About 380 mg of a colorless liquid was collected at a temperature between 160 and 190 °C (1 mmHg). This liquid turned yellow on exposure to air. GLC analysis showed a 1:4.8 mixture of two products. After 2 h, the higher retention time product was converted to the lower retention time product. The product was chromatographed over silica gel (230–400 mesh, Aldrich) and eluted with hexane–ether (70:30). The solution was then subjected to vacuum to produce a yellow liquid (120 mg) (TLC, R_f = 0.7, ether–hexane (30:70)): mass spectrum, *m/e* (relative intensity) 138 (24.3), 95 (100), 82 (37.7), 87 (79.9), 69 (32.3), 68 (26.7), 67 (34.5), 55 (54.6), 41 (41.0); high-resolution mass spectrum of $C_8H_{14}N_2$ found 138.118, calcd 138.115. The ^{13}C NMR was in agreement with the structure proposed for this compound. The details will be published in a subsequent paper.

Lithium Dicyclohexylphosphide. To 2.6 g (0.11 mol) (30% Li in paraffin oil) of lithium, washed in distilled and dried *n*-pentane, was added 15 mL of distilled and dried THF at 0 °C under N_2. Then 5.00 mL of distilled DCPH was added slowly at 0 °C under N_2 with stirring. After 12 h, the reaction mixture was filtered using a sintered-glass filter containing Celite in order to separate unreacted lithium metal. About 10 mL of a slightly yellow product was collected. Acid–base titration showed a 50% yield.

General Procedure for Reaction of an Alkyl Halide with LDA. LDA (2.50 mmol) was prepared by reaction of i-Pr_2NH (4.20 mL, 3.00 mmol) with MeLi (1.85 mL, 2.50 mmol) in 1.2:1 ratio in THF at −78 °C for 30 min. After the LDA was prepared, it was subjected to a Gilman test[55] and gas evolution analysis[56] in order to detect unreacted CH_3Li. In order to ensure that no MeLi remained in the LDA, diisopropylamine was used in 20% excess. After complete reaction the excess diisopropylamine was removed under vacuum and the LDA quenched with D_2O. Deuterium analysis of the resulting diisopropylamine showed 97% deuterated diisopropylamine. The temperature of the solution was then allowed to increase slowly to room temperature while the solvent was removed under vacuum. Finally, to the resulting white powdered LDA was added solvent at 0 °C under N_2. Then alkyl halide, 0.50 mmol, was added slowly to give a 0.1 M solution based on RX.

Whenever an additive was required (such as DCPH, *p*-DNB, or di-*tert*-butylnitroxyl radical), the alkyl halide solution was prepared with the additive first, then the dialkylamide solution was added. For convenience, the total volume of the solution was kept at 5.00 mL.

After a certain period of time, the reaction was quenched slowly with either distilled H_2O or D_2O (99.5%) at 0 °C in an ice water bath. An internal standard was then added to the mixture. The organic layer was extracted with *n*-pentane. GLC analyses were conducted using a DB-5 column, and all products were identified by comparison of their GLC retention times and mass spectral cracking patterns with authentic samples.

Acknowledgment. We are indebted to the National Science Foundations (Grant No. CHE 8403024) for support of this work.

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(55) Gilman, H. *J. Am. Chem. Soc.* **1925**, *47*, 2002.

(56) Ashby, E. C.; Dobbs, R. F.; Hopkins, H. P. *J. Am. Chem. Soc.* **1973**, *95*, 2823.