Experimental Section

NMR spectra were recorded on a Varian XL-300 spectrometer. The high-resolution mass spectral data were obtained on a Finnigan 4021 spectrometer. The GLC analyses were carried out on a Varian 3700 gas chromatograph.

Nitration of Dithieno[3,4-b:3′,4′-d]pyridine (1). Compound 1[7] (0.6 g, 3.2 mmol) was dissolved in 10 mL of TFA. Concentrated HNO₃ (0.54 mL, 12.8 mmol) was added to the solvent stirred for 7 h on the room temperature. The solvent was evaporated, and the residue was neutralized with NaHCO₃ solution. The raw material was chromatographed on a silica gel column using ethylacetate/ether, 1:1, as eluent. Isolated yields: 1-nitro derivative (2), 0.22 g (28.6%); 8-nitro derivative (4), 0.25 g (32.5%). The minor product the 3-nitro derivative (3), was isolated by column chromatography of the reaction mixture, using cyclohexane/ethyl acetate, 2:1, as eluent. Melting points: 212-4 °C (2), 258-60 °C (3), and 229-30 °C (4). Mass spectra: m/e 236 (2, 3, 4). Anal. Found for 2: C, 45.7; H, 1.6. For 3: C, 45.5; H, 1.9; N, 11.6. For 4: C, 45.5; H, 1.7; N, 11.7. Calculated: C, 45.8; H, 1.7; N, 11.9.

Determination of Isomer Distribution. To 50 mg (0.26 mmol) of 1 dissolved in 3 mL of TFA was added 0.083 mL (1.25 mmol) of 65% HNO₃ and urea (19 mg, 0.32 mmol). The reaction was interrupted after stirring for 1 h and 25 °C. The neutralized reaction mixture was separated on a DG1701 30-m capillary column. Temperature program: heating period, 150-250 °C, 5 °C/min, followed by 20 min hold time at 250 °C. Retention times: 24.4 min for 2, 26.2 min for 4, and 27.2 min for 3.

tert-Butyl N-(4-Bromo-5-nitro-3-thienyl)carbamate (5). 4-Bromo-5-nitro-3-thiophenecarboxylic acid[8] (2.5 g, 10 mmol) was converted to its carbamate.[7] After column chromatography in cyclohexane/ethyl acetate, 7:1, as eluent, 1.8 g (55%) of product was obtained. ¹H NMR (CDCl₃): δ (ppm) 7.85 (s, 1 H), 6.96 (s, 1 H), 1.53 (s, 9 H). Mass spectra: m/e 322, 324. Anal. Found: C, 33.2; H, 3.2; N, 8.6. Calculated: C, 33.5; H, 3.4; N, 8.7.

1-Nitrodithieno[3,4-b:3′,4′-d]pyridine (2). Starting from 0.4 g (1.2 mmol) of carbamate 5 and 0.4 g (1.2 mmol) of carbamate 5 and 0.4 g (2.6 mmol) of 4-bromo-3-thiopheneborornic acid, 0.16 g (55%) of nitro derivative 2 was synthesized via a Pd(0)-catalyzed coupling reaction.[7]

Supplementary Material Available: Internal coordinate systems (in Z-matrix form), optimized geometrical parameters, and vibrational frequencies of transition states (13 pages). Ordering information is given on any current masthead page.

Concerning the Mechanism of the Reaction of LiAlH₄ with Alkyl Halides

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A detailed study of the mechanism of reaction of LiAlH₄ with alkyl halides has been carried out with special emphasis on the use of radical probes. The data presented strongly support the validity of using radical probes in this reaction as an indication of an electron-transfer process. These studies also suggest a radical chain process (hydrogen atom transfer) in addition to the halogen atom transfer process on which we reported earlier. Studies to determine the influence of impurities as well as a potential metal–halogen exchange process are also reported.

Introduction

The reduction of alkyl halides to the corresponding hydrocarbons by LiAlH₄ is a well-known reaction (eq 1) that has been studied in some detail.[1] In 1984 we reported

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

that the results of a mechanistic study of this reaction indicated evidence for electron transfer in the cases of reaction of primary (neopentyl type) and secondary alkyl iodides with LiAlH₄ in THF.[2] Although we have reported evidence for electron transfer in reactions of alkyl halides with other reagents,[3] it is only in the case of reduction of alkyl halides with LiAlH₄ that the presence of electron transfer has been questioned. Newcomb has argued from

both kinetic[4] and probe studies[5] that such reductions proceed by a polar S_N2 mechanism, and more recently Newcomb and Curran have summarized a joint position supporting a polar mechanism, for the reaction of LiAlH₄ with alkyl iodides, arguing against the involvement of an electron-transfer process.[6] We have responded to the above arguments and have concluded that the evidence is overwhelming that electron transfer is indeed involved in this reaction and that the opposing arguments are invalid.[7] The following presentation represents our completed studies in this area; thus, at this time, we wish to summarize recent communications from our laboratory and add new data and discussion that strongly support the position that electron transfer is involved in the reaction of primary and secondary alkyl iodides with LiAlH₄ in THF solvent.

Results and Discussion

The most impelling argument that we presented in 1984 in favor of an electron-transfer pathway for the reaction

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

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

(3) (a) Ashby, E. C.; Argyropoulos, J. N. *J. Org. Chem.* **1985**, *50*, 3274. (b) Ashby, E. C.; DePriest, R. N.; Su, Wei-Yang *Organometallics* **1984**, *3*, 1718. (c) Ashby, E. C.; Pham, T. N. *J. Org. Chem.* **1987**, *52*, 1291. (d) Ashby, E. C.; Park, W. S.; Goel, A. B.; Su, W.-Y. *J. Org. Chem.* **1985**, *50*, 5184. (e) Ashby, E. C.; Coleman, D. *J. Org. Chem.* **1987**, *52*, 4554. (f) Ashby, E. C.; Pham, T. N. *Tetrahedron Lett.* **1987**, *28*, 3183.

(4) Newcomb, M.; Sanchez, R. M.; Kaplan, J. *J. Am. Chem. Soc.* **1987**, *109*, 1195. Newcomb, M.; Kaplan, J. *Tetrahedron Lett.* **1988**, *29*, 3449.

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

(6) Newcomb, M.; Curran, D. P. *Acc. Chem. Res.* **1988**, *21*, 206.

(7) Ashby, E. C. *Acc. Chem. Res.* **1988**, *21*, 414.
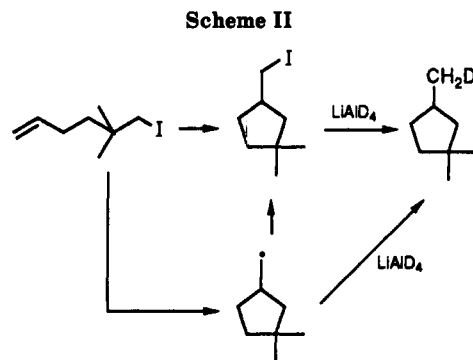
Scheme I

Scheme II
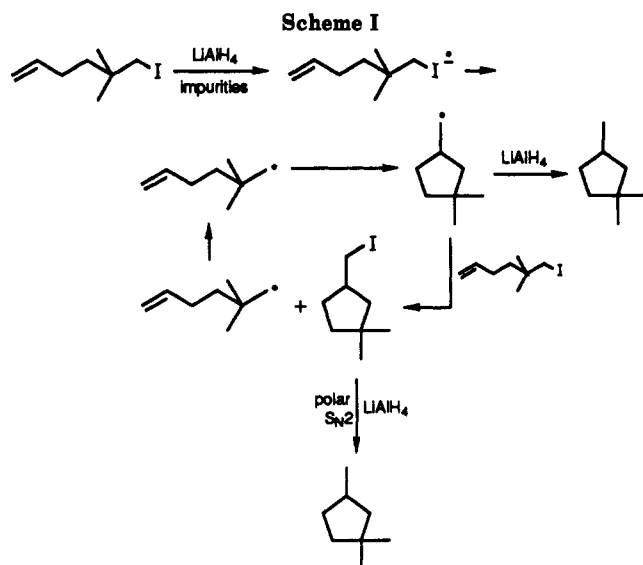
of primary and secondary alkyl iodides with LiAlH₄ was based on the formation of cyclized product in the reaction of a cyclizable alkyl iodide with LiAlD₄ with concurrent incorporation of protium in the products (eqs 2 and 3).

5.5% (69% d_1)   89% (59% d_1)   (2)
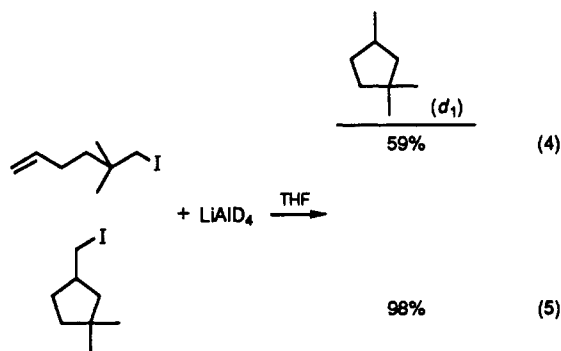

32% (100% d_1)   65% (88% d_1)   (3)
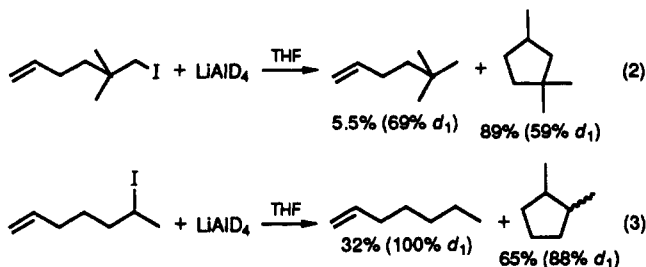
The 31% protium incorporation in the straight-chain hydrocarbon of eq 2 indicates the presence of a radical precursor that abstracts hydrogen from the solvent. Kinetic analysis of this reaction by Newcomb[5a] in support of a polar process resulted in a calculated deuterium incorporation value of 98% in the straight-chain hydrocarbon whereas 69% was actually observed. Protium incorporation in the cyclized products of eqs 2 and 3 also indicate the presence of a radical precursor. When reaction 3 was carried out in the presence of dicyclohexylphosphine (DCPH),[8] which is an excellent hydrogen atom donor, the straight-chain hydrocarbon was isolated in 28% yield and the cyclized hydrocarbon in 63% yield; however, these hydrocarbons contained only 12% and 8% deuterium, respectively. Clearly DCPH is more effective than THF as a hydrogen atom donor and has effectively trapped both of the precursor radicals in high yield (88 and 92%, respectively). Additionally we have reported that although 2-octyl tosylate, chloride, and bromide react with LiAlD₄ by inversion of configuration, the corresponding iodide reacts to form racemized product.[9] All of the above data are inconsistent with the position that alkyl iodides react with LiAlH₄ by a polar S$_N$2 process.[4-6]

In 1988 Newcomb and Curran suggested that the cyclized products of eqs 2 and 3 are a result of isomerization of the alkyl iodide (due to impurities) followed by a polar S$_N$2 reduction of the cyclized iodide (Scheme I).[5a,6] We

reported in 1984 the sequence of reactions shown in Scheme I, but without suggesting impurities as a source of radical initiation or cyclized hydrocarbon being formed from cyclized iodide as a result of a polar S$_N$2 process. We established the presence of a halogen atom radical chain process[10] and even monitored the cyclized iodide formed during the reaction; however, we concluded that although part of the cyclized product was undoubtedly formed by reduction of the cyclized iodide, the low deuterium content of the products (eqs 2 and 3) demanded that some of the product be formed via a radical precursor.[2] Particularly the low deuterium content of the cyclized hydrocarbons (eqs 2 and 3) suggests a significant radical involvent in the conversion of the cyclized iodides to the corresponding hydrocarbons. We have scrupulously purified the alkyl iodide, LiAlH₄, and THF used in these reactions and find no evidence of radical initiation due to impurities. Thus, we have concluded that since reactions 4 and 5 produced cyclized hydrocarbons containing 59 and 98% deuterium, respectively, the cyclized iodide could not be the precursor of all of the cyclized hydrocarbon, produced in eq 4. In-


deed, if all of the cyclized hydrocarbon was produced by a S$_N$2 reaction of LiAlH₄ with the alkyl iodide as Newcomb suggests, then the deuterium content of the cyclized hydrocarbons (eqs 4 and 5) would be the same. Thus it is clear that the cyclized hydrocarbon is produced to a significant extent via the cyclized radical (Scheme II).

The radical chain process (Scheme I) that causes the cyclization of an alkyl iodide radical probe does not appear to take place for the corresponding bromide or chloride. Therefore, the use of radical probes in investigating the involvement of radicals in reactions of alkyl bromides or chlorides is not in question. In this regard we have previously shown that secondary alkyl iodides, bromides, and chlorides react with Me₃Sn⁻ to form cyclized product which could not be a result (in the case of the bromide and chloride) of halogen atom exchange via a radical chain

(8) Kuivila, H. G.; Smith, G. F. *J. Org. Chem.* **1980**, *45*, 2918. Smith, G. F.; Kuivila, H. G.; Simon, R.; Sultan, L. *J. Am. Chem. Soc.* **1981**, *103*, 833. Ashby, E. C.; DePriest, R. N.; Su, W. Y. *Organometall.* **1984**, *3*, 1718.

(9) Ashby, E. C.; DePriest, R. N.; Pham, T. N. *Tetrahedron Lett.* **1983**, *24*, 2825.

(10) An iodine atom radical chain process was first reported by Brace involving the reaction of iodoperfluoroalkanes with 1,6-heptadiene. Brace, N. O. *J. Am. Chem. Soc.* **1964**, *86*, 523.

Scheme III
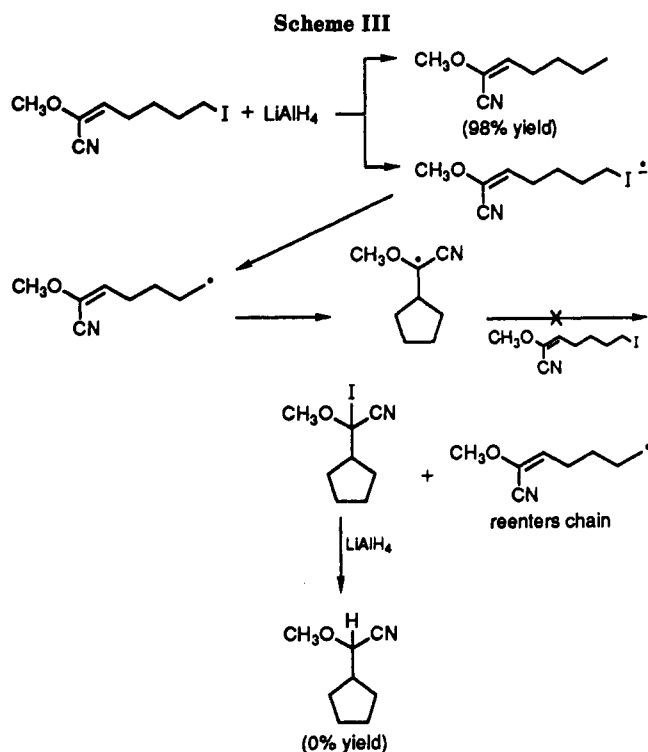
process (eq 6)[3b] since halogen atom exchange involving bromide or chloride is too slow.
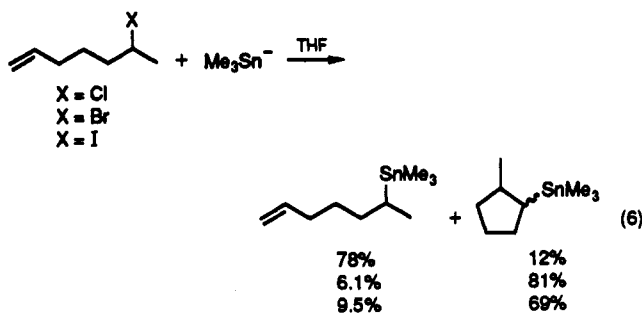

The previous discussion was necessary in order to understand one of the arguments of Newcomb which will now be presented. Newcomb suggests[4-6] that the cyclized product that we observed in the reaction of primary alkyl iodides with LiAlH$_4$ is due entirely to the polar reduction of the cyclized iodide which he suggests is formed by the impurity induced halogen atom radical chain process on which we reported earlier and is represented in Scheme I. Therefore, if a reaction can be found that does not undergo the halogen atom radical chain process, Newcomb maintains that cyclized product should not be formed. It was suggested[5b] that the alkyl iodide represented in Scheme III should not produce cyclized hydrocarbon because the halogen atom radical chain process would involve the conversion of a tertiary radical to a primary radical which is not energetically likely. When he carried out the reaction, he did not obtain any cyclized hydrocarbon; thus he concluded that cyclized product is produced only through the halogen atom radical chain process. We considered this report carefully since the conclusion is not consistent with the deuterium incorporation studies reported earlier.

We have repeated the above work;[11] however, we do not agree with the conclusions of Newcomb. We did indeed

observe, under the conditions that the reaction had been previously carried out, a 98% yield of the straight-chain hydrocarbon and 0% of the cyclized hydrocarbon (eq 7)
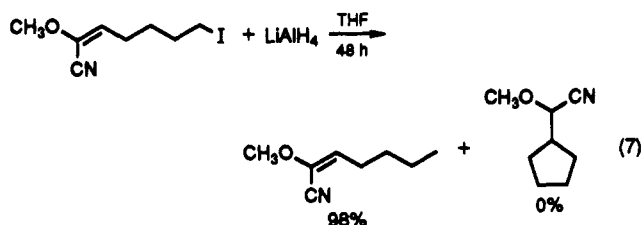
just as Newcomb reported earlier.[5b] However, when we carried out the reaction with LiAlD$_4$ in the presence of the radical trap 1,4-cyclohexadiene, the product contained 6% protium indicative of a radical intermediate (eq 8).
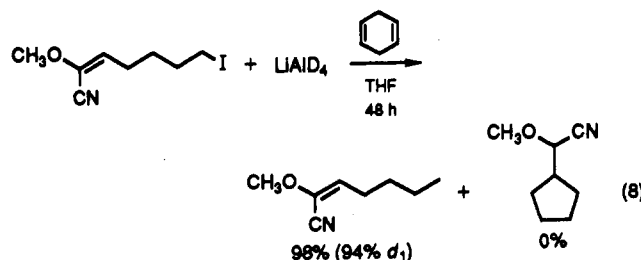
Perhaps even more important is the fact that the starting alkyl iodide had an E/Z ratio of 62/38, but the straight-chain hydrocarbon product had a ratio of 84/16 indicating that the double bond had isomerized during the reaction (eq 9). Since the radical probe used in these studies is
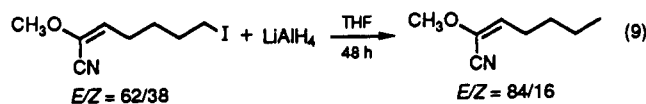

an α,β-unsaturated nitrile, it is possible that electron transfer took place at the α,β-unsaturated nitrile group rather than at the carbon–iodine bond. This observation would allow for isomerization of the double bond and explain the lack of cyclization during the reaction. The fact that LiAlH$_4$ reduces the nitrile function as well as the carbon–iodine function is also a complication in this reaction. Newcomb's idea of studying a model system that forms a stable tertiary radical that should not undergo halogen atom exchange converting a tertiary to a primary radical, as a method of showing that halogen atom exchange is the only pathway to cyclized product, is an excellent one. Unfortunately in this case we do not believe that this model system is valid because the isomerization of the double bond in the model system indicates that electron transfer took place at the α,β-unsaturated nitrile group. In addition, the trapping study with 1,4-cyclohexadiene indicates that a radical intermediate was formed in the reaction.

In the use of radical probes as a method for determining the presence of electron transfer in a reaction, we are always careful not to interpret the lack of cyclization of the probe to indicate the absence of a radical intermediate. If one does not observe a cyclized product, it could simply be due to the fact that geminate coupling, which always competes with cyclization, is the predominant reaction. This conclusion is clearly exemplified in a study involving the reaction of 6-bromo-1-hexene with NaSnMe$_3$ in THF which showed no cyclized product and thus the reaction was concluded[12] not to give evidence of a radical inter-

(11) Ashby, E. C.; Pham, T.; Madjdabadi, A. A. *J. Org. Chem.* 1988, 53, 6156.

(12) Park, S.-U.; Chung, S.-K.; Newcomb, M. *J. Org. Chem.* 1987, 52, 3275.

mediate (eq 10). Yet when we carried out the same re-

(10)

THF	99%	0%
THF–ether	92%	8%
THF–pentane	91%	9%
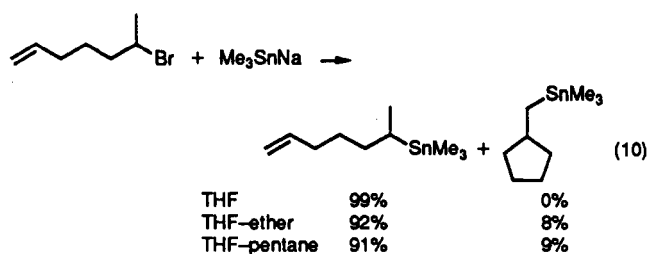
action using THF–Et$_2$O (1:1) and THF–pentane (1:1), a significant amount of cyclized product was formed.[13] Thus the observation of cyclized product indicates a radical precursor whereas the absence of cyclized product does not necessarily give evidence of the opposite conclusion.

In an attempt to follow up on Newcomb's excellent idea for which he used the model system in eq 7,[5b] we decided to study a model system which would test the concept (Scheme III) but not have the problems presented by an α,β-unsaturated nitrile.[11] When the reaction represented by eq 11 was carried out, a significant amount (10%) of


E/Z = 62/38

(11)

E/Z = 62/38
88%   10%
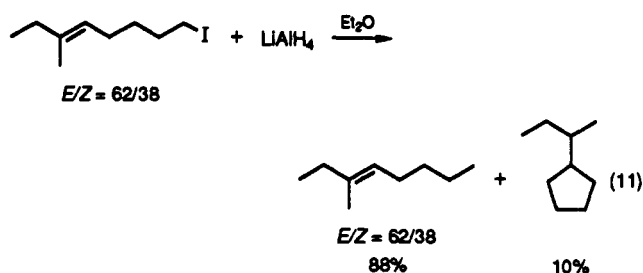
cyclized product was formed in spite of the fact that a halogen atom radical chain process (3° radical to 1° radical) is discouraged. The suggestion, of course, is that the cyclized product was not formed through the cyclized iodide via a halogen atom radical chain process, but rather by direct hydrogen atom abstraction of LiAlH$_4$ by the cyclized radical. This conclusion is further verified by the results of eq 12 which shows that a minimum of 11% of

E/Z = 62/38

(12)

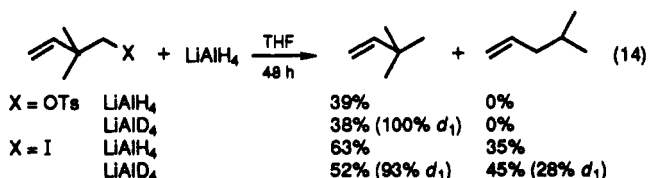E/Z = 62/38
79% (95% d$_1$)   18% (89% d$_1$)
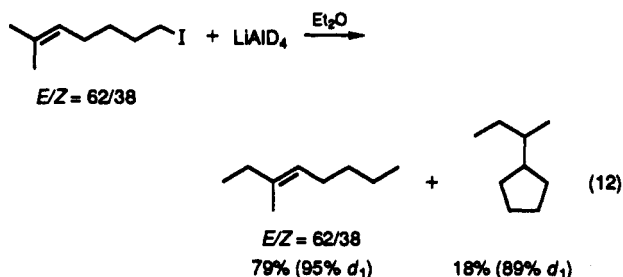
the cyclized product must have had a radical precursor in order to abstract hydrogen from the solvent. The larger amount (18% vs 10%) of cyclized hydrocarbon product found in the reaction of LiAlD$_4$ compared to LiAlH$_4$ is due to the primary deuterium kinetic isotope effect. As a result of the slower rate of deuterium abstraction by the straight-chain radical, the straight-chain radical should cyclize to a greater extent than when the competing reaction is that of protium atom abstraction. In addition, it is important to note that the E/Z ratio of the reactant and product is the same, unlike the results of eq 9, indicating that the present probe (eq 12) is a valid probe for detecting a radical intermediate. Further support of these conclusion is based on the results of eq 13, which show that

(13) Ashby, E. C.; Su, W.-Y.; Pham, T. *Organometallics* **1985**, *4*, 1493.

Scheme IV
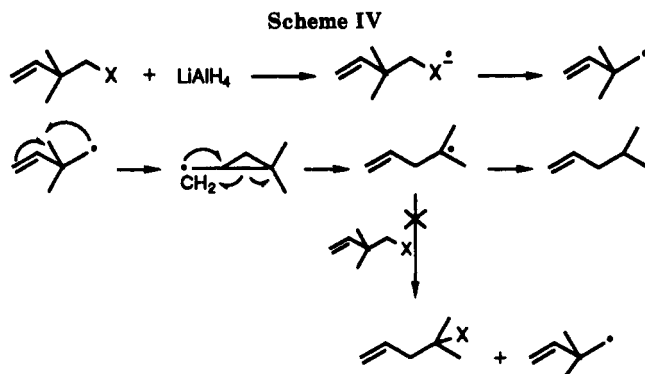
the cyclized iodide was not formed by a halogen atom radical chain process when the straight chain radical was formed in the reaction of the alkyl iodide with hexaphenylditin.

(13)

0%
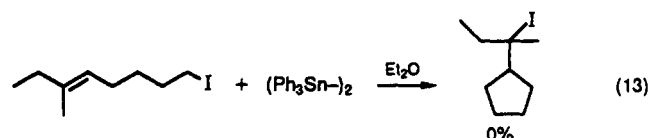
Because of the importance of these conclusions, another model system of a different type than the one above was chosen in order to test the concept that, if a halogen atom radical chain process is shut down (tertiary → primary radical), then cyclized hydrocarbon can still be formed in the reaction of LiAlH$_4$ with a cyclizable straight chain alkyl iodide if a radical intermediate is involved. The model system we chose was one reported earlier by Newcomb.[14] Scheme IV shows that if the primary radical (2,2-dimethyl-3-buten-1-yl) is formed, it should readily arrange to the more stable tertiary radical (2-methyl-4-buten-2-yl), which should not undergo a halogen atom radical chain process to form the less stable primary radical (2,2-dimethyl-3-buten-1-yl). The data presented in (eq 14) show

(14)

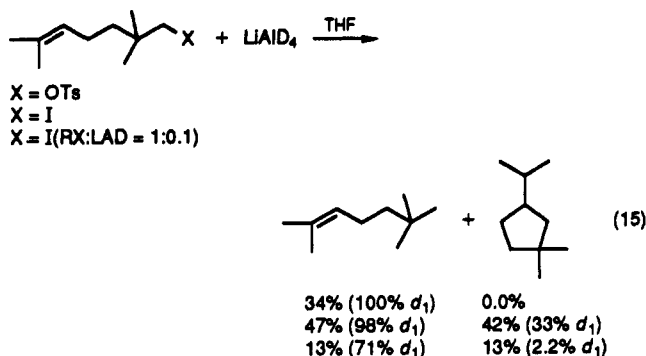| X = OTs	LiAlH$_4$	39%	0%
	LiAlD$_4$	38% (100% d$_1$)	0%
X = I	LiAlH$_4$	63%	35%
	LiAlD$_4$	52% (93% d$_1$)	45% (28% d$_1$)

that the tosylate of the 2,2-dimethyl-3-buten-1-yl system shows no evidence whatsoever of a radical intermediate and is not expected to do so because of the unfavorable reduction potential of the tosylate. On the other hand, the corresponding iodide showed a large amount of cyclized product accompanied by low deuterium incorporation clearly showing that the majority of the rearranged product could not have been produced by a polar S$_N$2 reduction of the cyclized iodide by LiAlD$_4$.

A final model system (eq 15) was chosen in order to be able to compare the neopentyl system shown in eqs 2, 3 with the model system shown in eqs 2 and 11. With this system we were able to test a neopentyl radical probe that will cyclize to a tertiary radical which should not undergo halogen atom exchange to form a primary radical. The results show that significant cyclization of the radical probe takes place when X = I and, when the probe is allowed to react with LiAlD$_4$ in 1:0.1 ratio, that significant protium incorporation of the straight chain hydrocarbon takes place indicating a radical precursor. In this reaction 71% of the

(14) Newcomb, M.; Glenn, A. G.; Williams, W. G. *J. Org. Chem.* **1989**, *54*, 2675.

X = OTs
X = I
X = I(RX:LAD = 1:0.1)

(15)

34% (100% d_1)   0.0%
47% (98% d_1)   42% (33% d_1)
13% (71% d_1)   13% (2.2% d_1)

alkyl iodide was recovered. Thus formation of cyclized product with 67% protium incorporation is not consistent with the formation of the corresponding cyclized iodide followed by S_N2 reaction with $LiAlD_4$.
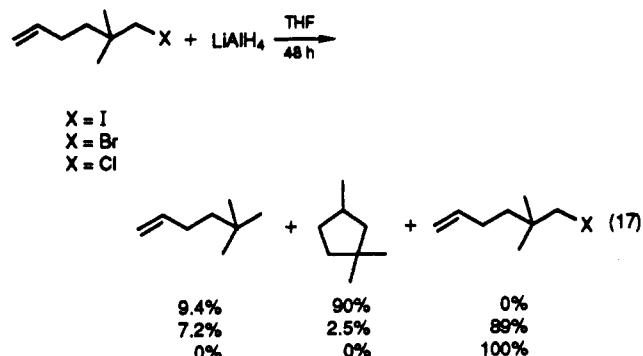
In addition to the *halogen* atom radical chain process that we described in 1984 (Scheme I and Scheme Va), we have recently obtained evidence to support a *hydrogen* atom radical chain process (Scheme Vc).[15] We had suggested earlier that the straight chain and cyclized radical, formed on reaction of the probe iodide with $LiAlH_4$, abstracted a hydrogen atom form $LiAlH_4$·$^+$ (Scheme Vb). However, we now have evidence that supports the suggestion that the cyclized radical abstracts a hydrogen atom from $LiAlH_4$, which produces not only the cyclized hydrocarbon but also AlH_3·$^-$ (Scheme Vc), which now becomes the one-electron donor in the process that reduces the probe iodide to the resulting radical anion. It would be expected that AlH_3·$^-$ would be a much better one electron donor than $LiAlH_4$ to reduce the probe iodide.

In order to obtain evidence for the hydrogen atom radical chain process we have carried out two studies, the results of which are consistent with this hypothesis. First, we have carried out the reaction shown in eq 16 varying

(16)

1 : 0.1   3.3%   97%
1 : 1   9.4%   90%
1 : 5   15%   84%
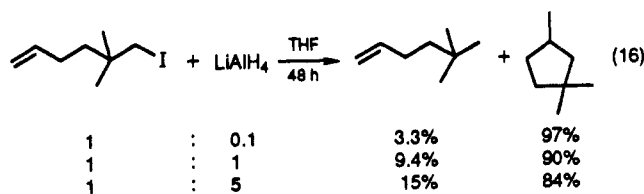
the stoichiometry of the reaction over a 50-fold range. As the ratio of $LiAlH_4$ to the probe iodide increased from 0.1 to 5, the amount of straight-chain hydrocarbon increased from 3.3 to 15.2%. If hydrogen atom abstraction was from $LiAlH_4$·$^+$, then increasing the amount of $LiAlH_4$ in the reaction would result in a decrease in the amount of straight-chain hydrocarbon formed. On the other hand, if the hydrogen atom abstraction was from $LiAlH_4$ then increasing the amount of $LiAlH_4$ should result to a greater degree in the trapping of the straight-chain radical and hence produce more straight chain hydrocarbon.

The second study carried out that supports a hydrogen atom radical chain process involves an entrainment reaction. Scheme VI shows the hydrogen atom radical chain process involving the probe iodide to which has been added the probe chloride. Equation 17 shows that although the probe iodide produces the cyclized hydrocarbon in 90% yield, the corresponding bromide produces the cyclized hydrocarbon in only 2.5% yield and no reaction whatsoever takes place using the probe chloride. The reason presumably is that the reduction potential of the probe

(15) A hydrogen atom radical chain process was first reported by Groves and Ma involving the reaction of $NaBH_4$ with 7,7-dibromonorcarane. Groves, J. T.; Ma, K. W. *J. Am. Chem. Soc.* 1974, *96*, 6527.

X = I
X = Br
X = Cl

(17)

9.4%   90%   0%
7.2%   2.5%   89%
0%   0%   100%

chloride is too unfavorable for the reaction to take place. On the other hand, when a 50/50 mixture of the probe iodide and probe chloride was allowed to react with Li-AlH_4, 28% of the probe chloride reacted (eq 18). In a

(18)

6.0%   56%

72%
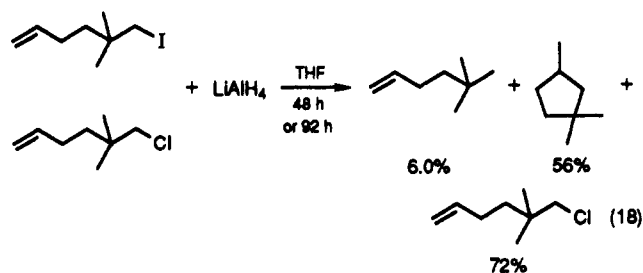
similar experiment involving a 50/50 mixture of the probe bromide, 56% of the probe bromide reacted when only 10% reacted in the absence of the probe iodide (eq 19). These results are consistent with a hydrogen atom radical chain process in which AlH_3·$^-$, produced in the reaction of the probe iodide with $LiAlH_4$, reduces the probe chloride to the corresponding radical anion.

(19)

9.1%   67%

44%
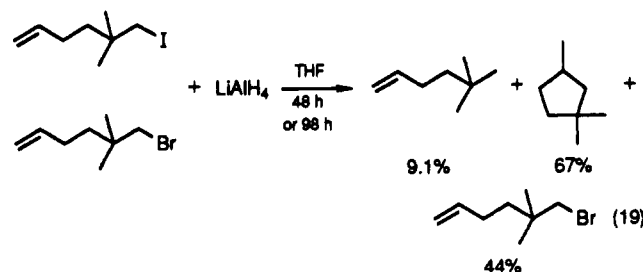
A very basic experiment designed to test the radical chain nature of the reaction of an alkyl iodide with $LiAlH_4$ was carried out using anthracene as a radical anion scavenger. If AlH_3·$^-$ is the reducing agent, then carrying out the reaction in the presence of anthracene should result in the transfer of the electron from AlH_3·$^-$ to anthracene in competition with that of the probe iodide (eq 20). The

+ AlH_3·$^-$ ⟶ AlH_3 +   (20)
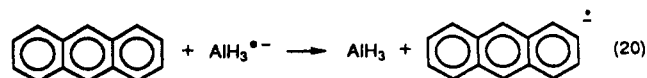
results of the study are shown in eq 21. When 1 equiv of anthracene was added to the reaction (eq 21), the reaction was slowed down considerably. When 1 equiv of benzene was added instead of 1 equiv of anthracene, the results were the same as in pure THF solvent. The latter experiment was carried out in order to determine if the result produced by anthracene was a solvent effect of the added hydrocarbon rather than an effect due to the radical anion trapping nature of the anthracene. These results are not consistent with a polar S_N2 process but are consistent with a reaction involving a radical anion intermediate.

no additive
1 equiv of anthracene
1 equiv of benzene

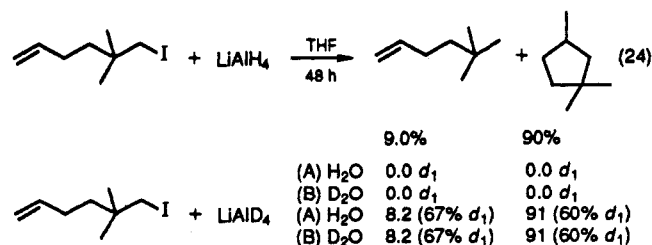| 12% | 87% | 0% | 0% |
| 6.0% | 1.2% | 0% | 91% |
| 11% | 87% | 0% | 0% |
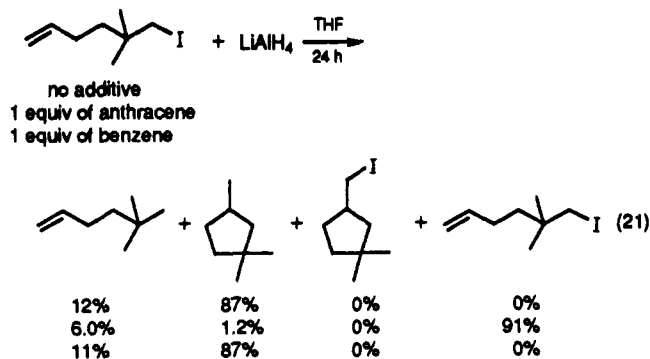
There has been a suggestion[16] that the formation of cyclized hydrocarbon product is a result of halogen–metal exchange followed by cyclization of the resulting organolithium compound (eq 22). In order to test this possibility,
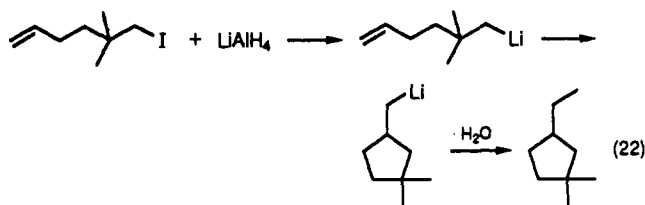
we carried out a study using the secondary probe iodide shown in eq 23. The reason for using a secondary iodide is because if the product is due to carbanion cyclization, the ratio of cis/trans product would be less than one; however, if, on the other hand, a radical cyclization takes place, the product should have a value of ~3.6 when the reaction is carried out at 0 °C.[2,7] The results reported here are perfectly consistent with a radical cyclization.

	:	1
1	:	1
1	:	5
1	:	1 (LiAlD4)

		cis	trans	(23)
21%	72%	3.7
69%	30%	3.8
42%	58%	3.6
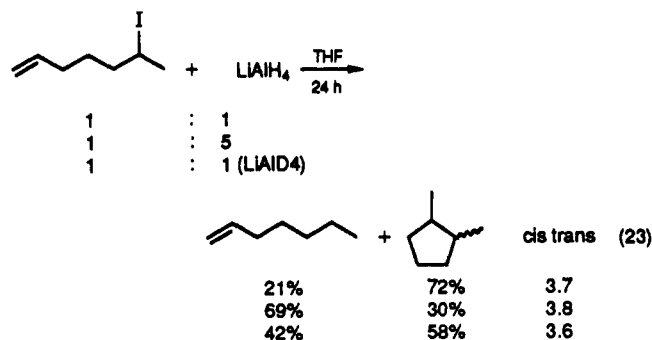
In order to test further the possibility of metal–halogen exchange (eq 24), we decided to carry out the reactions of the secondary probe iodide with LiAlH₄ and then quench the reaction product with D₂O and also carry out the reactions with LiAlD₄ and quench the reaction product with H₂O. The data (eq 24) show no deuterium incorporation

	9.0%	90%
(A) H₂O	0.0 d_1	0.0 d_1
(B) D₂O	0.0 d_1	0.0 d_1
(A) H₂O	8.2 (67% d_1)	91 (60% d_1)
(B) D₂O	8.2 (67% d_1)	91 (60% d_1)

in the product when the reaction involving LiAlH₄ was quenched with D₂O (hydrolysis with H₂O used as a standard). Furthermore when the reaction involved Li-
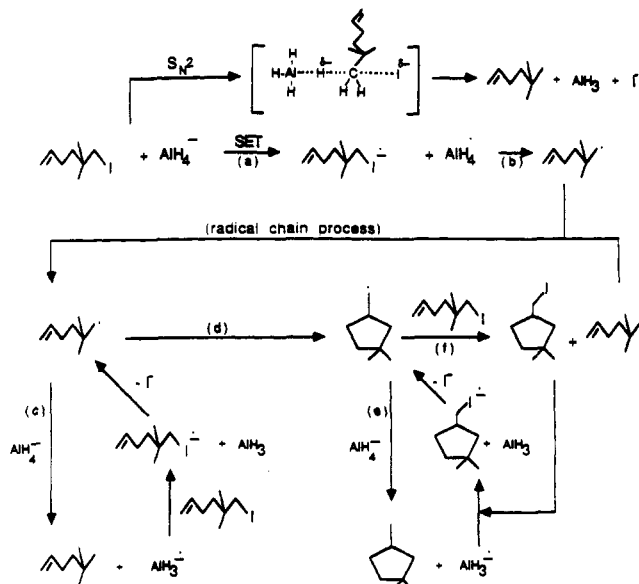
(16) Beckwith, A. J. J.; Goh, S. H. *J. Chem. Soc., Chem. Comm.* **1983**, 905.

Figure 1. Proposed mechanism of the reaction of 6-iodo-5,5-dimethyl-1-hexene with LiAlH₄.

AlD₄, the deuterium incorporation of the product was the same whether the reaction product was quenched with H₂O or D₂O. In addition material balances were excellent and we could find no evidence of RLi ether cleavage products. Thus we could find no indication whatsoever of an intermediate organolithium compound that could have cyclized. Neither the quenching experiments nor the stereochemistry experiment (cis/trans ratios of the cyclized product) are consistent with the intermediate formation of an organolithium compound, but the results of these experiments are consistent with the involvement of a radical intermediate in the formation of both straight chain and cyclized hydrocarbons.

When considering all of the data that we have obtained in this study and in previous studies, we conclude the following: (1) secondary alkyl iodides and hindered primary alkyl iodides react with LiAlH₄ to a significant extent by SET. (2) Although alkyl chlorides and bromides can react by SET with certain nucleophiles (e.g. Me₃Sn⁻), we have found no evidence that SET is involved in reactions of alkyl chlorides and bromides with LiAlH₄ in THF at 0–25 °C to a significant extent in the absence of a catalyst. The entrainment studies do show that it is possible for even the bromides and chlorides to react by SET if a catalyst is used to initiate the reaction to produce AlH₃·⁻, at which time the reaction becomes self sustaining. (3) There is evidence that even unhindered primary alkyl iodides react with LiAlH₄, at least to some extent, by a SET pathway.

A proposed detailed mechanism of the SET nature of the reaction of LiAlH₄ with the primary model system, with which we have worked, in THF is shown in Figure 1. In step a the reaction is initiated by electron transfer from LiAlH₄ to the alkyl iodide to form the corresponding radical anion followed by step b, the rapid dissociation of the radical anion to form the free radical. At this stage the free radical can diffuse from the solvent cage and react by step c with AlH₄⁻ in a *hydrogen* atom radical chain process to form the straight-chain hydrocarbon and generate AlH₃·⁻ which now behaves as the predominant one electron donor in the reaction to reduce the alkyl iodide. The free radical can also cyclize by step d to form the cyclized radical which then can be involved in the same *hydrogen* atom radical chain process by step e as shown in step c, for the straight-chain radial. The cyclized radical

Scheme V
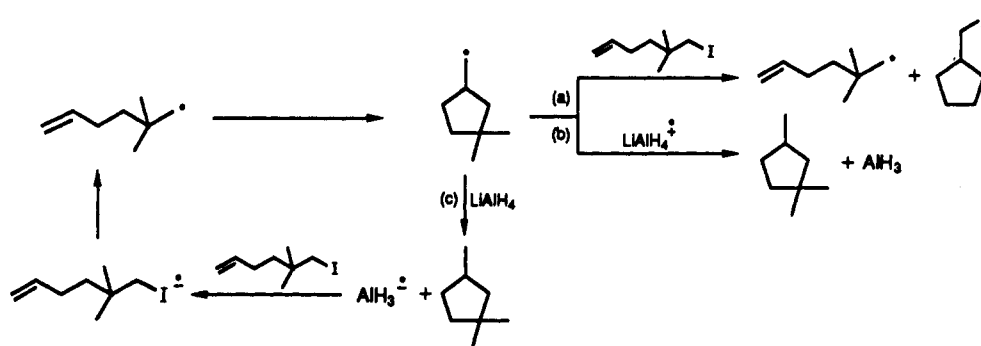
Scheme VI
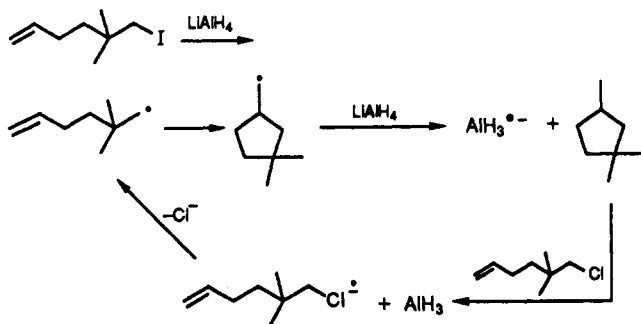
can also undergo a *halogen* atom radical chain process as shown in step f. Thus two radical chain processes are involved and AlH_3^{-} is the major one-electron donor. To exactly what extent a polar S_N2 process is involved in the reaction of this particular alkyl iodide with $LiAlH_4$ is unknown; however, the S_N2 pathway is believed to be the minor pathway.

Experimental Section

Materials. Solvent-grade pentane, hexane, and benzene were stirred over concentrated H_2SO_4, washed with water, dried with $MgSO_4$, and distilled under nitrogen. Reagent-grade diethyl ether (Fisher) and reagent-grade tetrahydrofuran (THF) were distilled under nitrogen from deep purple solutions of sodium benzophenone ketyl. Solutions of $LiAlH_4$[17] and $LiAlD_4$[18] were prepared according to known procedures. A sample of anthracene was recrystallized from hexane and was obtained in 99.8% purity. 3,3-Dimethyl-1-butene and 4-methyl 1-pentene were obtained from Aldrich and used as received. Ethyl 2-bromopropionate (bp 158–160 °C) was purchased from Lancaster Synthesis and purified by distillation from CaH_2. Acetaldehyde was distilled through a 2-in. Vigreux column and stored at 0 °C under nitrogen. 5-Bromo-2-methyl-2-pentene was purchased from Aldrich and used as received. Hexamethylphosphoramide (HMPA) was distilled from sodium under reduced pressure.

General Procedures. Reactions were performed under nitrogen at the bench with the use of Schlenk tube techniques or in a glovebox equipped with a recirculating system using manganese oxide columns to remove oxygen and a dry ice–acetone trap to remove solvent vapors. Calibrated syringes equipped with stainless steel needles were used for transfer of reagents. Glassware and syringes were flamed and cooled under a flow of nitrogen. Stock solutions of reagents and reaction vessels were protected from light with aluminum foil. Reactions were carried out in round-bottomed flasks equipped with T-bore stopcocks attached to male 24/40 standard tape joints (allows nitrogen flush while reagents are being added or removed through the stopcock by syringe) and a Teflon-coated magnetic stirring bar. The appropriate amounts of solvents and reagents were syringed into the flask under a nitrogen flush. After complete reaction, the mixture

was hydrolyzed with cold water. In some case the organic layer was separated, dried over anhydrous $MgSO_4$, and filtered, and the solvent was removed under vacuum. In other cases the organic layer was analyzed directly by an appropriate method. Quantitative GLC analyses were obtained by using a FID detector and response-factor corrected peaks areas using an internal standard. Proton NMR chemical shifts are reported relative to $(CH_3)_4Si$. IR spectra were recorded on a Perkin-Elmer Model 621 spectrophotometer. Mass spectra were obtained on a Varian MAT 1125, and carbon–hydrogen microanalyses were conducted by Atlantic Microlabs, Inc., of Atlanta, GA.

General Procedure for Reduction of Alkyl Halides. Equimolar amounts of the desired alkyl halide and $LiAlH_4$ were rapidly combined in a reaction vessel (0.17 M in each reagent) under nitrogen in the desired solvent by the use of syringes. In cases where additives were employed (1,4-cyclohexadiene, anthracene, or sodium), the additive was added to the mixture immediately after the major components were combined. At the chosen time, reaction mixtures were quenched carefully with cold water, internal standards were added, and GLC analyses were performed. Deuterium incorporation was evaluated by GLC–mass spectral analysis.

Preparations. 2,2-Dimethyl-3-buten-1-ol. The title compound was prepared in 75% yield by a previously described method[19] and exhibited the following: ^1H NMR $(CDCl_3)$ 1.05 ppm (s, 6 H), 2.40 (s, 1 H), 3.18 (s, 2 H), 4.80–6.18 (m, 3 H); bp 128–129 °C (lit.[20] bp 128.5–131 °C).

Tosylate of 2,2-Dimethyl-3-buten-1-ol. To 50 mL of pyridine at 0 °C was added 5.0 g (0.026 mol) of tosyl chloride and 1.5 g (0.015 mol) of 2,2-dimethyl-3-buten-1-ol. The mixture was allowed to stand at 8 °C for 48 h. After filtration, the mixture was diluted with 200 mL of pentane, washed with dilute HCl, washed with water, and dried with $MgSO_4$, and the solvent was removed under vacuum to yield 1.8 g of a crude yellow oil. Purification by chromatography on silica with hexane as eluent yielded the analytically pure tosylate, which exhibited the following: ^1H NMR $(CDCl_3)$ 1.08 ppm (s, 6 H), 2.42 (s, 3 H), 3.68 (s, 2 H), 4.80–6.10 (m, 3 H), 7.20–7.80 (m, 4 H).

3,3-Dimethyl-4-iodo-1-butene. In a 250-mL flask were combined 10.5 g of PPh_3 (0.04 mol, dried under vacuum over P_2O_5), 100 mL of benzene, 8 g of I_2 (0.031 mol), 20 mL of pyridine, and 3.1 g (0.031 mol) of 2,2-dimethyl-3-buten-1-ol. After reflux for 24 h, the mixture was diluted with pentane (150 mL), chilled, and filtered. Distillation of the solid residue (bp 61–62 °C at 25 mmHg) yielded 2.0 g (32%) of pure 3,3-dimethyl-4-iodo-1-butene, which exhibited the following: ^1H NMR $(CDCl_3)$ 1.05 ppm (s, 6 H), 3.18 (s, 2 H), 4.81–6.05 (m, 3 H); mass spectrum (M^+) 210. Anal. Calcd for $C_6H_{11}I$: C, 34.30; H, 5.29. Found: C, 34.25; H, 5.30.

2,2,6-Trimethyl-5-hepten-1-ol. To 8.1 g (0.07 mol) of ethyl isobutyrate in 200 mL of freshly distilled THF was added 57.1 mL of a 1.4 M solution (0.08 mol) of lithium diisopropylamide in ether at −78 °C. The solution was then allowed to react with 10 g (0.06 mol) of 5-bromo-2-methyl-2-pentene dissolved in 20 mL of HMPA. The reaction mixture was allowed to warm to room temperature and then allowed to stir overnight. The mixture was hydrolyzed with water, extracted with ether (3 × 150 mL), and

(17) Krishnamurthy, S.; Brown, H. C. *J. Org. Chem.* **1980**, *45*, 849.
(18) Ashby, E. C.; Boone, J. R. *J. Am. Chem. Soc.* **1976**, *98*, 5524–7.
(19) Courtot, M. A. *Bull. Soc. Chim. Fr.* **1906**, *35*, 111.
(20) Kulkarni, S. U.; Patil, V. D. *Heterocycles* **1982**, *18*, 163.

dried over anhydrous $MgSO_4$, and the ether was removed under vacuum. The resulting liquid, ethyl 2,2,6-trimethyl-5-heptenoate, was distilled and gave a colorless liquid which exhibited the following: bp 99–100 °C at 20 mmHg; ¹H NMR ($CDCl_3$) 1.25 ppm (s, 6 H), 1.18–2.2 (m, 13 H, contains triplet), 3.98–4.38 (q, 2 H), 4.91–5.30 (m, 1 H). This ester was dissolved in 150 mL of dry ether and excess $LiAlH_4$ in ether was added at 0 °C. Standard workup gave a colorless liquid: bp 109–110 °C at 25 mmHg; ¹H NMR ($CDCl_3$) 1.05 ppm (s, 6 H), 1.20–2.20 (m, 10 H), 3.39–3.41 (br s, 2 H), 4.90–5.31 (m, 1 H); mass spectrum (M⁺) 156.

Tosylate of 2,2,6-Trimethyl-5-hepten-1-ol. To 50 mL of pyridine at 0 °C was added 4.0 g (0.021 mol) of tosyl chloride and 1.0 g (0.0064 mol) of 2,2,6-trimethyl-5-hepten-1-ol. The mixture was allowed to stand at 8 °C for 48 h. Standard workup and purification by column chromatography on silica gel with hexane as eluent yielded the analytically pure tosylate, which exhibits the following: ¹H NMR ($CDCl_3$) 1.08 ppm (s, 6 H), 1.18–2.20 (m, 10 H), 2.40 (s, 3 H), 3.70–3.74 (s, 2 H), 4.91–5.30 (m, 1 H), 7.20–7.75 (m, 4 H).

2,6,6-Trimethyl-7-iodo-2-heptene. In a 250-mL flask were combined 10.5 g (0.04 mol) of PPh_3 (dried in vacuo over P_2O_5), 100 mL of benzene, 8 g (0.031 mol) of I_2, 20 mL of pyridine, and 4.68 g (0.30 mol) of 2,2,6-trimethyl-5-hepten-1-ol. After reflux for 24 h, the mixture was diluted with pentane (150 mL) chilled, filtered. Distillation of the residue yielded 3.8 g (40% yield) of pure 2,6,6-trimethyl-7-iodo-2-heptene, which exhibited the following: bp 94–95 °C at 5 mmHg; ¹H NMR ($CDCl_3$) 1.10 ppm (s, 6 H), 1.20–2.22 (m, 10 H), 3.05 (s, 2 H), 4.90–5.32 (m, 1 H). Anal. Calcd for $C_{10}H_{19}I$: C, 45.12; H, 7.21. Found: C, 45.10; H, 7.18.

8-Iodo-3-methyl-3-octene. *sec*-Butyltriphenylphosphonium iodide was prepared by combining 22 g (0.084 mol) of Ph_3P and 12.8 g (0.07 mol) of 2-iodobutane under nitrogen in a three-neck flask fitted with a reflux condenser and a means of heating with a steam bath for 20 h. After cooling, the solid product was washed with benzene (3 × 100 mL). Recrystallization from $EtOH/Et_2O$ yielded 15 g (0.034 mol) of *sec*-butyltriphenylphosphonium iodide in 48% yield, mp 205.2–206.5 °C. *sec*-Butyltriphenylphosphonium (15.0 g, 0.034 mol) was slurried in 150 mL of ether under nitrogen, 24.0 mL of 1.40 M (0.034 mol) methyllithium was added slowly, and the orange solution was stirred for 6 h. 5-Bromopentanal[20] (5.07 g, 0.034 mol) in 10 mL of ether was added slowly, whereupon a white precipitate formed. After 6 h the mixture was poured into 150 mL of H_2O and filtered, and the remaining solids were washed with ether (3 × 50 mL). The aqueous portion was then washed with ether (2 × 50 mL), and the combined ether extracts were dried over $MgSO_4$. Concentration of the solution produced a yield of 4.0 g of a mixture of crude 8-bromo-3-methyl-3-octene and its corresponding iodide (GC ratio: 80/20). This crude product was used directly in the preparation of 8-iodo-3-methyl-3-octene. To 250 mL of actone were added 4.0 (0.019 mol) of the above bromide and 4.50 g (0.03 mol) of NaI. The reaction mixture was allowed to reflux for 24 h. Standard workup and

distillation yielded analytically pure 8-iodo-3-methyl-3-octene which exhibited the following: bp 90–91 °C at 5 mmHg; ¹H NMR ($CDCl_3$) 1.20–2.41 ppm (m, 14 H), 3.25–3.55 (m, 2 H), 4.85–5.20 (m, 1 H). Anal. Calcd for $C_9H_{17}I$: C, 58.54; H, 8.37. Found: C, 58.50; H, 8.40.

Reaction of 2,6,6-Trimethyl-7-iodo-2-heptene with LiAlH₄. In a 100-mL flask was added 2.66 g (0.010 mol) of 2,6,6-trimethyl-7-iodo-2-heptene in 50 mL of THF and 0.46 g (0.012 mol) of $LiAlH_4$. After 48 h, the mixture was hydrolyzed, extracted with Et_2O, and dried over $MgSO_4$. The solution was concentrated on a rotary evaporator. The mixture was separated by preparative GLC using a 9-ft. 10% apiezon column, oven temperature 150 °C, injection port 170 °C, and detector temperature 190 °C. The following products were obtained. (a) 2,6,6-Trimethyl-2-heptene: ¹H NMR ($CDCl_3$) 0.92 ppm (s, 9 H), 1.10–2.20 ppm (m, 10 H), 4.90–5.31 (m, 1 H); mas spectrum (M⁺) 140.

Anal. Calcd for $C_{10}H_{20}$: C, 85.72; H, 14.28. Found: C, 85.76; H, 14.26.

(b) 1-Isopropyl-3-methylcyclopentane: ¹H NMR ($CDCl_3$) 0.80–2.15 ppm (m, 20 H); mass spectrum (M⁺) 140.

Anal. Calcd for $C_{10}H_{20}$: C, 85.72; H, 14.28. Found: C, 85.74; H, 14.27.

(c) 3,3 Dimethyl-1-isopropylidenecyclopentane: ¹H NMR ($CDCl_3$) 1.2 ppm (s, 6 H), 1.6–2.0 (broad s + m, 8 H), 2.20–2.81 (m, 4 H); mass spectrum (M⁺) 140.

Anal. Calcd for $C_{10}H_{20}$: C, 85.72; H, 14.28. Found: C, 85.69; H, 14.23.

Reaction of 8-Iodo-3-methyl-3-octene with LiAlH₄. In a 100-mL flask was added 2.52 g (0.010 mol) of 8-iodo-3-methyl-3-octene, 50 mL of Et_2O, and 0.46 g (0.012 mol) of $LiAlH_4$. After 48 h the mixture was hydrolyzed, extracted with Et_2O, and dried over $MgSO_4$. The solution was concentrated on a rotary evaporator. The mixture was separated by preparative GLC using a 9-ft 10% apiezon column, and the following products were obtained. (a) 3-Methyl-3-octene: ¹H NMR ($CDCl_3$) 1.19–2.38 ppm (m, 17 H), 4.85–5.20 (m, 1 H); mass spectrum (M⁺) 126.

Anal. Calcd for C_9H_{18}: C, 85.73; H, 14.27. Found: C, 85.69; H, 14.29.

(b) *sec*-Butylcyclopentane: ¹H NMR ($CDCl_3$) 0.82–2.15 ppm (m, 18 H); mass spectrum (M⁺) 126.

Anal. Calcd for C_9H_{18}: C, 85.73; H, 14.27. Found: C, 85.71; H, 14.25.

Reaction of Hexaphenylditin with Alkyl Halides. The desired amount of alkyl halide (0.1 mol) and hexaphenylditin (0.1 mol) were combined under nitrogen in the desired solvent in a reaction vessel equipped with a condensor and magnetic stirring bar. The mixture was irradiated with a sunlamp (250 W). At the chosen time, reaction mixtures were analyzed by GLC.