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Reactions of Saturated and Unsaturated Tertiary Alkyl Halides and Saturated Secondary Alkyl Iodides with Lithium Aluminum Deuteride. Convincing Evidence for a Single-Electron-Transfer Pathway

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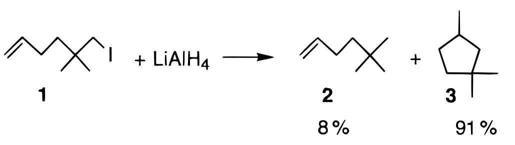
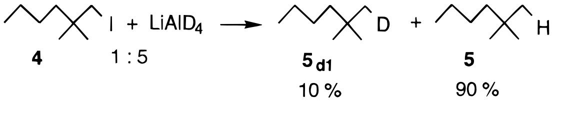
Reactions of saturated secondary and tertiary alkyl halides with $LiAlH_4$ (LAH) and $LiAlD_4$ (LAD) have been carried out, and convincing evidence for a single-electron-transfer (SET) pathway has been obtained. Reactions involving saturated alkyl halides with LAD provide a model system in which a halogen-atom radical chain process is not possible, and therefore, the observation of large quantities (in some cases >90%) of protium in the reduction product provides strong evidence for a radical intermediate and a SET pathway. Specifically, the reaction of 2-iodooctane (**10**) with LAD produced octane with a deuterium content as low as 21%. Also, the reaction of the tertiary halide 2-iodo-2-methylheptane (**15**) with LAD produced 2-methylheptane (**16**) with a deuterium content as low as 8%. The effect of stoichiometry, halogen type, and reaction vessel surface on these reactions was studied. Reaction of the unsaturated tertiary halide 6-iodo-6-methyl-1-heptene (**25**) with LAD was also studied and was found to proceed predominantly by a SET process involving a halogen-atom radical chain process. The possibility of a carbocation intermediate in all of these reactions is discussed.

Introduction

As early as 1984, we reported evidence for extensive cyclization in the reaction of the hindered alkyl iodide radical probe 6-iodo-5,5-dimethyl-1-hexene (**1**) with $LiAlH_4$ (LAH; eq 1) and proposed that this reaction proceeds by a single-electron-transfer (SET) process involving a radical intermediate.[1] More recently we have reported that the saturated alkyl iodide probes, namely, the hindered primary probe 1-iodo-2,2-dimethylhexane (**4**)[2] and the unhindered primary probe 1-iodooctane (**6**),[3] react with $LiAlD_4$ (LAD) to form substantial amounts of the nondeuterated reduction products 2,2-dimethylhexane (**5**) and *n*-octane (**7**), respectively (eqs 2 and 3). We chose saturated probes in order to eliminate the possibility of a halogen-atom radical chain process that is available to the unsaturated, cyclizable probes (Scheme 1). It has been argued that the halogen atom radical chain process shown in Scheme 1 can be initiated by unknown impurities,[4] and therefore, the amount of cyclized product, indicative of a radical precursor, cannot be used to quantitate the amount of initial electron transfer from the nucleophile.[4,5] Removal of the double bond in the alkyl halide probes results in removal of the possibility of a halogen-atom radical chain process, making halogen-atom exchange between radical intermediates and starting materials a nonproductive process.



(1)



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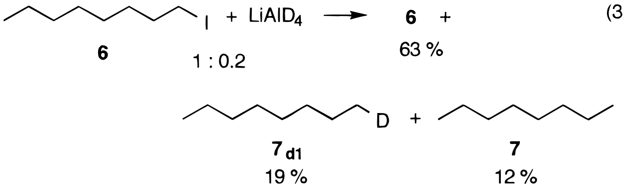

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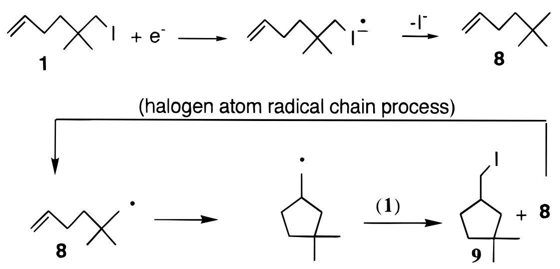
Scheme 1



As explained previously,[2] the product of a SET reaction of **4** with LAH would be indistinguishable from the S_N2 product; therefore, LAD was necessarily chosen as the nucleophile in the study of saturated probes so that in

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[1] (a) Ashby, E. C.; Pham, T. N.; Amrollah-Madjdabadi, A. *J. Org. Chem.* **1991**, *56*, 1596. (b) Ashby, E. C. *Acc. Chem. Res.* **1988**, *21*, 414. (c) Ashby, E. C.; DePriest, R. N.; Goel, A. B.; Wenderoth, B.; Pham, T. N. *J. Org. Chem.* **1984**, *49*, 3545. (d) Tolbert, L. M.; Sun, X. J.; Ashby, E. C. *J. Am. Chem. Soc.* **1995**, *117*, 2681.

[2] Ashby, E. C.; Welder, C. O. *J. Org. Chem.* **1997**, *62*, 3542.

[3] Welder, C. O.; Ashby, E. C. *J. Org. Chem.* **1997**, *62*, 4829.

[4] (a) Newcomb, M.; Curran, D. P. *Acc. Chem. Res.* **1988**, *21*, 206. (b) Newcomb, M.; Kaplan, J. *Tetrahedron Lett.* **1988**, *29*, 3449. (c) Newcomb, M.; Kaplan, J.; Curran, D. P. *Tetrahedron Lett.* **1988**, *29*, 3451. (d) Newcomb, M.; Sanchez, R. M.; Kaplan, J. *J. Am. Chem. Soc.* **1987**, *109*, 1195. (e) Park, S. U.; Chung, S. K.; Newcomb, M. *J. Org. Chem.* **1987**, *52*, 3275.

[5] Curran, D. P.; Kim, D. *Tetrahedron Lett.* **1986**, *27*, 5821.

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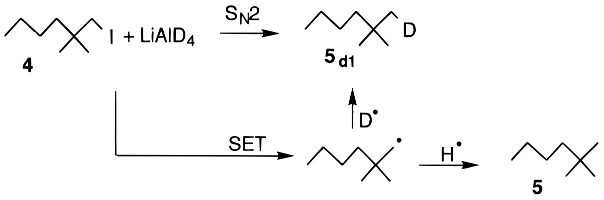
the S_N2 reaction of LAD with an alkyl halide only deuterated alkane is expected. However, for a reaction involving radical intermediates, hydrogen atoms (from solvent) as well as deuterium atoms (from LAD and its byproducts) may be abstracted so that both the nondeuterated and the deuterated alkane could be formed (eq 4).



(4)

To further extend the scope of the reaction of LAH with alkyl halides, we have studied the reaction of typical tertiary alkyl halides with LAD. The only reactions of tertiary alkyl halides with LAD that we reported previously involve the 1-halonorbornanes.[6] In the 1-halonorbornane/LAD system, we found significant evidence for SET, as evidenced by low deuterium incorporation in the product (norbornane). We present herein the results of the reactions of the saturated, noncyclizable tertiary halides (2-halo-2-methylheptanes), the unsaturated, cyclizable tertiary halides (6-halo-6-methyl-1-heptenes), and the saturated secondary alkyl halide (2-iodooctane, **10**) with LAD.

Results and Discussion

I. Reactions of Saturated Secondary Alkyl Halides with LAD. Effect of Stoichiometry on the Reaction of 2-Iodooctane (10) with LAD. The trends of the reactions of secondary alkyl halides with LAD were expected to follow the same patterns as those observed for the primary systems discussed earlier.[2,3] Therefore, it was predicted that a decrease in the number of equivalents of LAD present in the reduction of **10** should lead to a decrease in the deuterium content of the resulting alkane, if a radical mechanism was involved.

As reported in Table 1, when a 5-fold excess of LAD was allowed to react with **10**, no clear evidence of electron transfer was obtained (experiment 1). A trace amount of dimer formation was noted, and the 95% D found in the octane was only a little low for the results expected for a pure S_N2 reaction. However, when the stoichiometry of the reaction was reduced from a RI/LAD ratio of 1:5 to 1:1, after 6 h a significant amount of nondeuterated alkane **11** (19% of the octane) was obtained (experiment 2). At a stoichiometry of 1:0.2, after 96 h, 79% of the octane formed was nondeuterated. This trend is consistent with radical formation via SET for the reaction of **10** with LAD as well as the stoichiometry studies presented earlier for 1-iodooctane (**6**)[3] and 1-iodo-2,2-dimethylhexane (**4**).[2]

Table 1. Effect of Stoichiometry on the Reaction of 2-Iodooctane (10) with LAD in THF[a]

exp	RI/Nuc	time, h	% **10**	% **11** (% D)	% dimers	material balance
1	1:5	1	20	79	trace	99
		2	trace	89	trace	89
		5	0	94 (95)	trace	94
2	1:1	0.5	62	37 (87)		99
		1	45	53 (86)	trace	98
		2	25	74 (84)	trace	99
		4	9	91 (82)	trace	100
		6	0	97 (81)	trace	97
3	1:0.2	1	81	13 (52)	1	95
		2	74	18 (46)	2	94
		5	69	23 (33)	2	94
		8	67	26 (29)	2	95
		24	65	27 (27)	2	94
		48	63	31 (23)	2	96
		96	60	35 (21)	2	97

[a] All reactions were carried out at a RI concentration of 0.070 M in an Ar atmosphere glovebox in the absence of light at room temperature in used Pyrex flasks and with the use of Teflon-coated stir bars.

Table 2. Effect of Reactor Surface on the Reaction of 2-Iodooctane (10) with LAD in THF[a]

exp	reaction vessel	RI/LAD	time, h	% **10**	% **11** (% D)	% dimers	material balance
1	used Pyrex	1:1	0.5	62	37 (87)	trace	99
			1	45	53 (86)	trace	98
			2	25	74 (84)	trace	99
			4	9	91 (82)	trace	100
			6	0	97 (81)	trace	97
2	quartz	1:1	0.5	82	18 (92)		100
			1	68	29 (89)	trace	97
			2	45	47 (84)	1	93
			4	16	63 (78)	3	82
			6	5	71 (70)	5	81
			24	0	75 (67)	6	81

[a] All reactions were carried out at a RI concentration of 0.070 M in an Ar atmosphere glovebox in the absence of light at room temperature and with the use of Teflon-coated stir bars.

Effect of Reactor Surface on the Reaction of 2-Iodooctane (10) with LAD. Because the nature of the vessel surface was found to have an effect on the reaction of the primary alkyl iodides with LAD,[7] vessels other than used Pyrex were employed in a study of the reaction of **10** with LAD. The type of reactor surface was shown to have an effect on the reduction of the secondary iodide **10** by LAD (Table 2). The reaction in a used Pyrex vessel (experiment 1) proceeded somewhat more rapidly than the reaction in quartz (experiment 2) carried out under otherwise identical conditions. Also, it is evident that the deuterium content in the octane was lower and the dimer formation higher in quartz than in the used Pyrex vessel, indicating a higher free radical content in the quartz vessel. Because more radical formation was observed in the reactions carried out in quartz, the reactions carried out in Pyrex should represent a minimum amount of products, indicative of a radical pathway.

Reaction of 2-Bromooctane with LAD. Less SET was expected for the reaction of 2-bromooctane (**12**) with LAD than the corresponding iodide **10** because of the less favorable reduction potential of alkyl bromides compared to alkyl iodides. When alkyl bromide **12** was allowed to react with LAD at 1:5, 1:1, and 1:0.2 ratios, no evidence for SET was obtained.

Proposed Mechanism of the Reduction of 2-Iodooctane (10) by LAD. As shown in Scheme 2, it is suggested that alkyl iodide **10** can react with LAD by either an S_N2 or SET pathway. As shown in step a, LAD can react in an S_N2 fashion to yield $\mathbf{11_{d1}}$, AlD_3, and LiI. On the other hand, LAD can transfer an electron to **10** to form the corresponding radical anion **13** (step b) which rapidly dissociates to form radical **14** (step c). Radical

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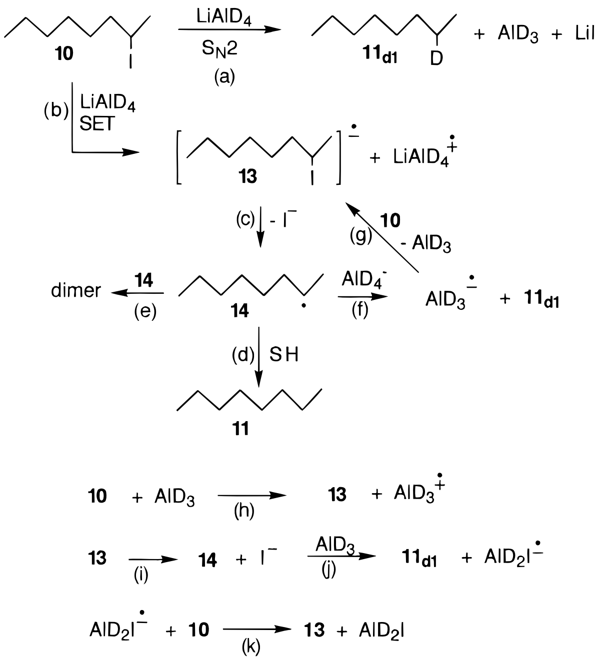
[6] Ashby, E. C.; Sun, X.; Duff, J. L. *J. Org. Chem.* **1994**, *59*, 1270.

[7] For a study of the effect of reactor surfaces on SET reactions, see: Ashby, E. C.; Welder, C. O. *Tetrahedron Lett.* **1995**, *36*, 7171.

Scheme 2



14 can then react with a suitable hydrogen-atom donor, such as the solvent, to form octane (**11**) (step d), it can combine with another alkyl radical **14** in solution to form a dimer (step e), or it can abstract a deuterium atom from AlD_4^- to form 2-deuteriooctane (**11$_{d1}$**) (step f) and the AlD_3 radical anion. The AlD_3 radical anion can then act as the major single-electron donor to the starting iodide **10** (step g) yielding radical anion **13** and AlD_3, thus producing a hydrogen atom radical chain process. The AlD_3 byproduct can then react with **10** (steps h−k) to form **13** as shown.

II. Reactions of Saturated Tertiary Alkyl Halides with LAD. Tertiary alkyl halides are not expected to undergo S_N2 reactions; therefore, the S_N2 pathway should not compete with the SET pathway for tertiary systems. However, other pathways (S_N1, E1, and E2) can compete with SET in the tertiary system. To study the competition between these pathways, several tertiary halides were allowed to react with LAD.

Effect of Stoichiometry on the Reaction of 2-Iodo-2-methylheptane (15) with LAD. Five products were identified in the reaction of tertiary iodide **15** with LAD (eq 5). The observation that the percentage of alcohol **19** decreases as the starting alkyl iodide **15** is consumed supports the hypothesis that alcohol **19** is formed in the aqueous workup procedure (Table 3). The observation that the percentage of alkenes **17** and **18** increases as the percentage of **15** and **19** decreases implies that the alkenes are produced during the reaction of **15** with LAD and not solely in the aqueous workup. Therefore, only four true products were obtained in the reaction of **15** with LAD: **16**, **16$_{d1}$**, **17**, and **18**.

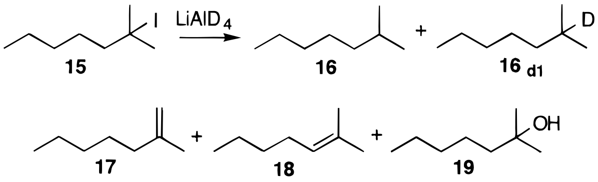


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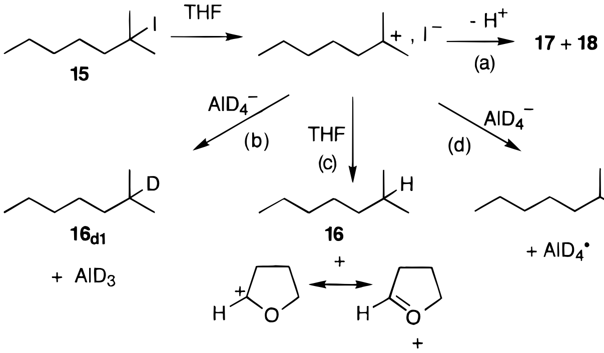
Table 3. Effect of Stoichiometry on the Reaction of 2-Iodo-2-methylheptane (15) with LAD[a]

exp	RI/LAD	time, h	% **15**	% **16** (% D)	% **17**	% **18**	% **19**	% dimers	material balance
1	1:5	0.5	47	2	5	16	30		100
		1	57	3 (62)	5	20	13		98
		2	33	7 (59)	7	35	15		97
		5	8	17 (51)	10	51	9		95
		24	trace	26 (47)	12	61	trace	trace	99
2	1:0.2	1	81	2 (14)	2	4	8	trace	95
		5	60	11 (10)	6	5	5	trace	87
		8	49	15 (8)	7	8	6	2	87
		24	40	15 (8)	8	20	5	3	91
		48	35	16 (8)	9	27	3	4	94

[a] All reactions were carried out at a RI concentration of 0.070 M in an Ar atmosphere glovebox in the absence of light at room temperature in used Pyrex flasks and with the use of Teflon-coated stir bars.

Table 3 reports the results of the reaction of **15** with LAD carried out at two different stoichiometries (1:5 and 1:0.2). In both cases, significant evidence of SET was observed, as noted by the low deuterium content in alkane **16**. Conversion of the absolute yields to relative yields, based on the amount of starting material consumed, shows that the percent of octane formed (26%) was identical for experiments 1 and 2. However, only 8% D was found in the octane when 0.2 equiv of LAD was present in the reaction as compared to 47% D when equiv of LAD was present in the reaction. Therefore, much more hydrogen-atom abstraction from the THF took place in experiment 2 than in experiment 1, as expected.

There is a possibility of carbocation formation which can lead to **16**, **16$_{d1}$**, **17**, and **18** (eq 6). If carbocation formation were the precursor to the formation of **16$_{d1}$** (step b, eq 6), then one would expect the amount of **16$_{d1}$** to increase (as compared to **16**) as the ratio of LAD to **15** increases. Just the opposite was observed. Another pathway to **16** from a carbocation involves hydride ion abstraction from THF (step c) which is not nearly as energetically favorable as hydrogen atom abstraction from THF by a radical intermediate. In a previous study,[6] we were able to show that the tertiary iodide 1-iodonorbornane, which is not easily capable of forming a bridgehead carbocation,[8] still reacts with LAD to form predominantly the protio product (eq 7). Such a result



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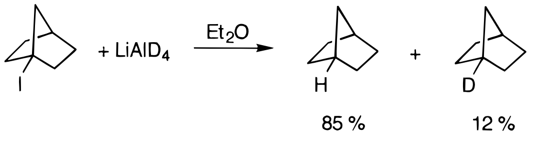


(7)

can only be explained by a reaction involving a free radical intermediate.

Effect of Reactor Surface on the Reaction of 2-Iodo-2-methylheptane (15) with LAD. In the previously reported reactions,[7] quartz was found to be the reaction vessel of choice for the unequivocal observation of SET products. The reaction of **15** with LAD was carried out in used Pyrex and compared to the same experiment carried out in quartz (Table 4, expts 1 and 2). The reaction proceeds faster in quartz than in used Pyrex. (Recall that alcohol **19** is a product of the workup so that the true amount of remaining starting material **15** must be calculated by adding the amount **19** to the amount **15**.) Also, the ratio of 2-methylheptane (**16**) to elimination products **17** and **18** was higher in the quartz vessel, indicating that the used Pyrex flask affects the formation of dehydrohalogenation products **17** and **18**. Note that the deuterium content of **16** is much lower for the experiment carried out in the quartz vessel (21% D, experiment 2) than that of **16** in the corresponding experiment in used Pyrex (47% D, experiment 1). Finally, a much higher formation of dimers was noted in quartz (6% dimers, experiment 2) than in used Pyrex (trace dimers, experiment 1). Thus, once again, the data show that a used Pyrex surface has some effect on the reaction of alkyl iodides with LAD, although the major pathways of the reaction appear to be the same in either vessel. In comparison, very little difference between the reactions carried out in used Pyrex (experiment 3) and Teflon (experiment 4) at the lower stoichiometry of 1:0.2 was noted.

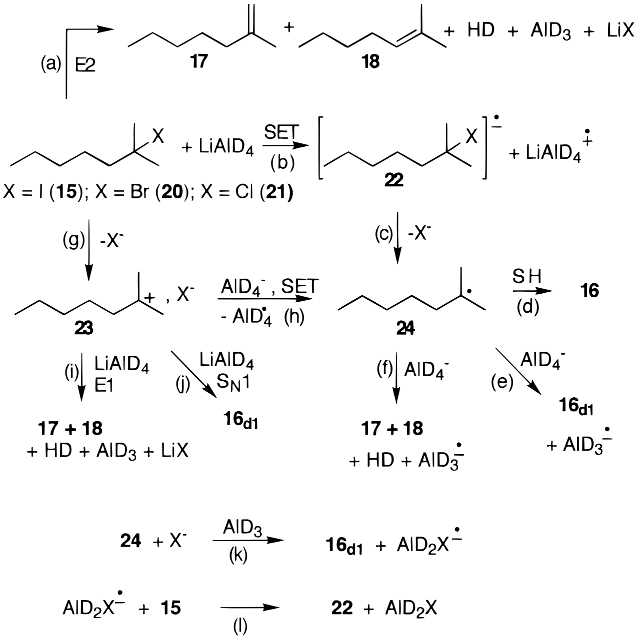
Effect of the Leaving Group on the Reaction of 2-Halo-2-methylheptanes with LAD. The effect of the halide leaving group was studied by varying the halide from iodide to bromide to chloride. Since the reduction potential becomes less favorable in the order alkyl iodides > bromides > chlorides, the SET reaction rates of alkyl halides would be expected to be in the same order.

The expected trend of reaction rates was indeed observed. Alkyl iodide **15** (Table 5, experiment 1) reacted with LAD faster than did alkyl bromide **20** (experiment 2), which reacted faster than did alkyl chloride **21** (experiment 3). Even though the reaction rates varied dramatically, the distribution of products remained remarkably similar, indicating that electron transfer to form the alkyl halide radical anion **22** (Scheme 3, step b) is the rate-determining step of the reaction. The product ratios of **16**/**17**/**18** were almost identical for the alkyl iodide **15** and bromide **20**. All three reactions indicated significant amounts of hydrogen atom abstraction to form the nondeuterated alkane **16**.

It is important to note that previous mechanistic studies involving LAH or LAD support SET as a viable reaction pathway for alkyl iodides and, to a lesser extent, alkyl bromides. However, this is the first known report of SET from LAD to an alkyl chloride. The reason for observing SET with the tertiary chloride **21** while not observing SET for primary and secondary alkyl chlorides probably is due to the difference in the alkyl radical stabilities.

Proposed Mechanism of Reduction of 2-Halo-2-methylheptanes by LAD. As shown in Scheme 3, it is proposed that LAD can react with tertiary halides in an E2 fashion to give alkenes **17** and **18** (step a). LAD can also act as a single-electron donor toward the alkyl halides **15**, **20**, or **21** to form the corresponding radical anion **22** (step b) from which products **16**−**18** are formed (steps d−f).

Scheme 3



If carbocation **23** is formed (step g), then it would be expected to react much more rapidly with $LiAlD_4$ (step j) to form $\mathbf{16_{d1}}$ than with THF to form **16** (eq 6). Just the opposite is observed; **16** is formed in higher yield than $\mathbf{16_{d1}}$. Because deuterium incorporation is as low as 8% (Table 3, experiment 2), step j would have to play, at best, a minor role. Also, the formation of carbocation **23** (step g) would be expected to be a slow reaction compared to the electron-transfer process (step b), especially between **15** and LAD. A further argument against carbocation **23** acting as a major intermediate in the reaction of **15** with LAD lies in the results of the reaction of **25** (the unsaturated counterpart of **15**) with LAD to form radical cyclized products (as discussed in the next section). The comparable carbocation cyclizations would be expected to be much slower than the corresponding radical cyclizations.[9]

III. Reactions of Unsaturated Tertiary Alkyl Halides with LAD. To further test the conclusions formed in the reactions of the saturated halides **15**, **20**, and **21**, we decided to study the reactions of the comparable terminally unsaturated halides.

Effect of Stoichiometry on the Reaction of 6-Iodo-6-methyl-1-heptene (25) with LAD. The tertiary iodide **25** was allowed to react with a 5-fold excess of LAD (eq 8 and Table 6, experiment 1). The reaction of **25** with LAD produced almost exclusively the reduced cyclized alkane **27** with no evidence of the reduced uncyclized counterpart of **25**. This observation argues against the

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(8) Bingham, R. C.; Schleyer, P. v. R. *J. Am. Chem. Soc.* **1971**, *93*, 3189.

(9) (a) Hill, E. A.; Davidson, J. A. *J. Am. Chem. Soc.* **1964**, *86*, 4663. (b) Hill, E. A.; Theissen, R. J.; Taucher, K. *J. Org. Chem.* **1969**, *34*, 3061. (c) Hill, E. A.; Theissen, R. J.; Doughty, A.; Miller, R. *J. Org. Chem.* **1969**, *34*, 3681. (d) Kossa, W. C., Jr.; Rees, T. C.; Richey, H. G., Jr. *Tetrahedron Lett.* **1971**, *37*, 3455.

Table 4. Effect of Reactor Surface on the Reaction of 2-Iodo-2-methylheptane (15) with LAD in THF[a]

exp	rxn vessel	RI/LAD	time, h	% **15**	% **16** (% D)	% **17**	% **18**	% **19**	% dimers	material balance
1	used Pyrex	1:5	0.5	47	2	5	16	30		100
			1	57	3 (62)	5	20	13		98
			2	33	7 (59)	7	35	15		97
			5	8	17 (51)	10	51	9		95
			24	trace	26 (47)	12	61	trace	trace	99
2	quartz	1:5	0.5	61	11 (16)	9	10	7	1	99
			1	43	17 (19)	12	13	8	2	95
			2	27	25 (19)	16	17	5	3	93
			5	5	40 (21)	20	22	4	5	96
			8	trace	45 (21)	21	23	2	5	96
			24	0	44 (21)	25	23	1	6	99
3	used Pyrex	1:0.2	1	81	2 (14)	2	4	8	trace	95
			5	60	11 (10)	6	5	5	trace	87
			8	49	15 (8)	7	8	6	2	87
			24	40	15 (8)	8	20	5	3	91
			48	35	16 (8)	9	27	3	4	94
4	Teflon[b]	1:0.2	1	68	3 (13)	3	6	15	trace	95
			5	61	10 (10)	6	6	5	2	90
			8	48	13 (9)	7	9	11	2	90
			24	37	15 (9)	9	15	8	2	86

[a] All reactions were carried out at a RI concentration of 0.070 M in an Ar atmosphere glovebox in the absence of light at room temperature. Experiments 1, 3, and 4 employed Teflon-coated stir bars while experiment 2 was carried out in the absence of Teflon. [b] Teflon was found to be reactive toward $LiAlH_4$, and thus, it is inappropriate for mechanistic studies involving LAH or LAD.[7]

Table 5. Effect of Leaving Group on the Reactions of 2-Halo-2-methylheptanes with LAD in THF[a]

exp	X	time	% RX	% **16** (% D)	% **17**	% **18**	% **19**	material balance
1	I (**15**)	0.5 h	47	2	5	16	30	100
		1 h	57	3 (62)	5	20	13	98
		2 h	33	7 (59)	7	35	15	97
		5 h	8	17 (51)	10	51	9	95
		24 h	trace	26 (47)	12	61	trace	99
2	Br (**20**)	5 h	89	trace	trace	9	2	100
		24 h	66	6 (82)	4	23	1	100
		3 days	26	16 (73)	8	43	2	95
		7 days	4	23 (73)	10	56	0	93
		13 days	0	26 (69)	11	59	0	96
3	Cl (**21**)	24 h	92	trace	trace	trace	0	92
		7 days	92	4 (61)	trace	4	0	100
		13 days	77	8 (56)	2	9	0	96

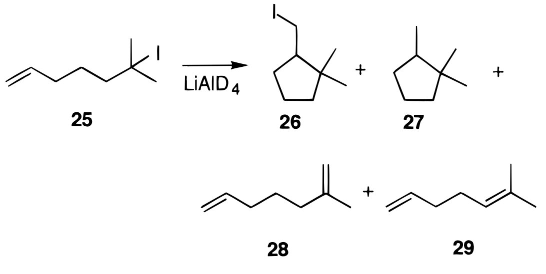
[a] Reactions were carried out at a RX concentration of 0.070 M at a RI/Nuc ratio of 1:5 in an Ar atmosphere glovebox in the absence of light at room temperature in used Pyrex flasks and with the use of Teflon-coated stir bars.

Table 6. Effect of Stoichiometry on the Reaction of 6-Iodo-6-methyl-1-heptene (25) with LAD[a]

exp	RI/LAD	time, h	% **26**	% **27** (% D)	% **28**	% **29**	% dimers	material balance
1	1:5	1	20	74 (79)	trace	trace	trace	94
		2	3	90 (78)	trace	trace	1	93
		5	0	96 (78)	trace	trace	2	98
2	1:1	2	38	55 (27)	trace	trace	4	97
		5	6	85 (22)	trace	trace	5	96
		11	0	91 (21)	trace	trace	6	97

[a] Reactions were carried out at a RI concentration of 0.070 M in an Ar atmosphere glovebox in the absence of light at room temperature in used Pyrex flasks and with the use of Teflon-coated stir bars.

formation of a carbocation because AlD_4^- would be expected to trap the carbocation rapidly.



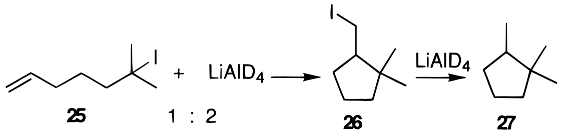
(8)

When the stoichiometry of **25**/LAD was reduced from 1:5 to 1:1, similar results were obtained (Table 6, experiment 2) except that compound **27** contained a much lower percent deuterium. This result was expected because much less LAD was available to trap the intermediate radical (as compared to experiment 1), and hence, more radical was trapped by THF.

The reaction of the unsaturated tertiary iodide **25** with LAD (Table 6, experiment 1) was found to be different from the reaction of the corresponding saturated tertiary iodide **15** (Table 5, experiment 1) in several ways. In the saturated system, the products observed were the saturated hydrocarbon **16** (and $\mathbf{16_{d1}}$), the alkenes **17** and **18**, and the alcohol **19** which was formed from iodide **15** during the workup procedure (eq 5). For the unsaturated tertiary system, none of the uncyclized hydrocarbon 6-methyl-1-heptene (corresponding to alkane **16** in the saturated tertiary system) was formed, and the dienes **28** and **29** (corresponding to alkenes **17** and **18**) were formed only in trace quantities. The low yield of dienes in the reaction of alkyl iodide **25** with LAD was surprising because the elimination products **17** and **18** represented the major products in the saturated tertiary system.

The results of the reaction of the cyclizable tertiary radical probe **25** were also surprising in light of the results of the radical probe studies of cyclizable primary and secondary systems. For example, when the hindered primary alkyl iodide **1** was allowed to react with LAD, the uncyclized alkene **2** was formed in 8% yield (as shown in eq 1 for LAH). We reported in 1983[10] that the secondary iodide, 6-iodo-1-heptene, was found to yield 1-heptene in 42% yield upon reaction with LAD. However, in the tertiary system, as reported in Table 6, the uncyclized alkene, 6-methyl-1-heptene, was not observed. Because the product distribution in the reaction of the unsaturated tertiary alkyl iodide **25** with LAD was not as expected, the reaction was carefully monitored.

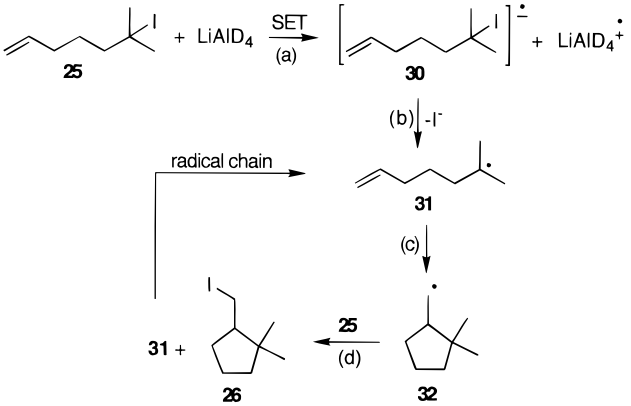
Careful monitoring of the reaction of alkyl iodide **25** with a 2-fold excess of LAD revealed the rapid formation of cyclized iodide **26** as a major intermediate in the reaction (eq 9).[11] (Cyclized iodide **26** was isolated from the reaction and analyzed by ^{1}H NMR and GC/MS to confirm its structure.) It is apparent from the data that the tertiary iodide **25** rapidly undergoes a halogen-atom radical chain process to form the primary iodide **26**, which is then reduced by LAD to alkane **27**. Therefore, this reaction does not accurately represent the reduction of a tertiary alkyl iodide but instead represents the reduction of a hindered primary alkyl iodide (**26**).



(9)

time, min	%25	%26	%27
0	100	0	0
5	4	91	5
15	3	89	8
30	3	83	14
54	1	75	24
100	trace	51	49

Scheme 4

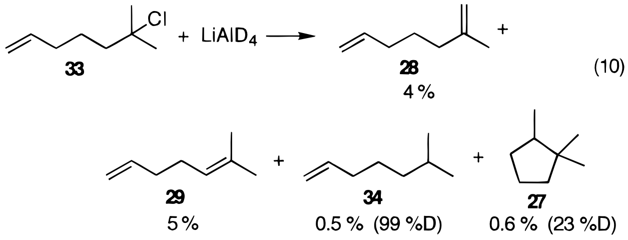


As shown in Scheme 4, the formation of the cyclized iodide **26** is similar to the mechanism reported earlier by us[1a,c] and others.[12] Because no uncyclized 6-methyl-1-hexene was observed, it is proposed that cyclization of **31** to **32** is faster than hydrogen- or deuterium-atom abstraction to form the uncyclized alkene.

It is interesting to note the difference in the reactivity of 1-(iodomethyl)-3,3-dimethylcyclopentane (**9**) and alkyl iodide **26**. As discussed previously,[2] when cyclized iodide **9** was allowed to react with LAD, 1,1,3-trimethylcyclopentane (**3**) was formed in 99% yield containing 98% D. On the other hand, significant hydrogen atom abstraction was observed in the reaction of alkyl iodide **26** with LAD as noted by the low deuterium incorporation in 1,1,2-trimethylcyclopentane (**27**). Therefore, it is suggested that cyclized iodide **26** is sufficiently hindered as to give significant evidence of SET upon reaction with LAD whereas alkyl iodide **9** is not sufficiently hindered.

The reaction of alkyl iodide **25** with LAD showed similar results whether the reaction was carried out in a used Pyrex or a quartz vessel.

Effect of the Leaving Group on the Reactions of the 6-Halo-6-methyl-1-heptenes with LAD. As shown in eq 9, the unsaturated tertiary iodide **25** first cyclized to **26**, which was then reduced to the cyclized alkane **27**. By comparison, very little of the corresponding alkyl chloride **33** reacted over a 14 day period (eq 10).



Even though only trace quantities of reduction products **34** and **27** were observed, the deuterium content of these products was determined. The deuterium incorporation in the uncyclized alkane **34** was quantitative (99% D) whereas the deuterium incorporation in the cyclized alkane **27** was quite low (23% D), indicating significant protium incorporation in the cyclized product which suggests a radical precursor.

Proposed Mechanism of Reduction of 6-Iodo-6-methyl-1-hexene (25) with LAD. The proposed mechanism of reaction of iodide **25** with LAD is shown in Scheme 5. It is suggested that iodide **25** can react by an E2 mechanism (step a) to yield dienes **28** and **29**. The SET process (step b) is initiated by an electron transfer from LAD to the alkyl iodide **25**, resulting in the radical anion **30** which rapidly dissociates (step c) to radical **31** and further cyclizes to radical **32** (step d) from which both dimers and compounds **26**, **27**, and **27$_{d1}$** are formed. It is suggested that cyclized iodide **26**, a hindered primary alkyl iodide, reacts with LAD in an S$_N$2 or a SET fashion. An S$_N$2 reaction (step k) would result in the deuterated alkane **27$_{d1}$** whereas a SET reaction would lead to radical anion **35** (step l) which can lose an iodide ion to form radical **32** (step m). It is clear from the data that the major reaction for the formation of **27** is by the SET process (Table 6, experiment 2). Radical **32** then follows one of the available pathways (e, f, h, or i) until a stable product is formed. Another available pathway for alkyl iodide **25** is the E1 pathway that leads to the carbocation **36** (step n). Carbocation **36** either can react with LAD or its byproducts in a SET fashion (step o) to form radical **31** (which then reacts as discussed above) or can yield elimination products **28** and **29** (step p). Because no uncyclized alkene was observed from alkyl iodide **25**, the

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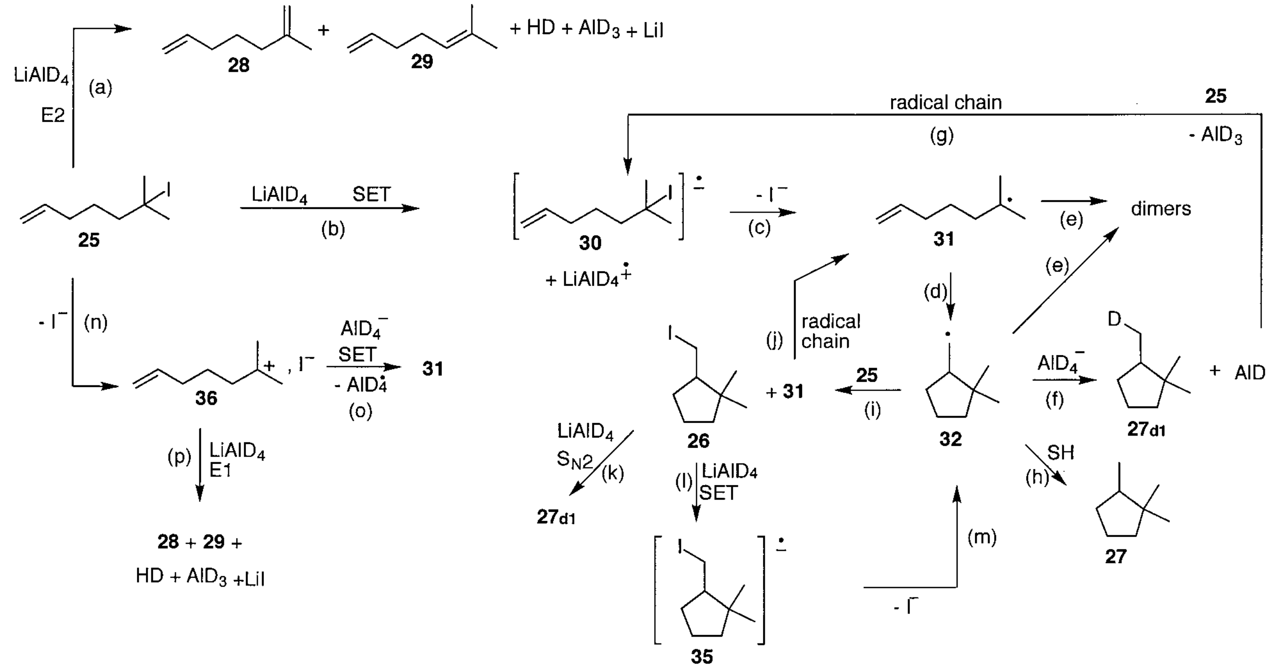
[10] Ashby, E. C.; DePriest, R. N.; Pham, T. N. *Tetrahedron Lett.* **1983**, *24*, 2825.

[11] No internal standard for GC analysis was added so that isolation of the cyclized iodide **26** would be more convenient. Therefore, the relative areas approximate the molar ratios of the components shown. This is the ONLY mechanistic experiment reported in which a GC internal standard was not used.

[12] Brace, N. O. *J. Org. Chem.* **1967**, *32*, 2711.

Scheme 5



S_N1 pathway is not a likely pathway for the reduction of iodide **25** by LAD.

Summary and Conclusions

Because it has been convincingly shown that both hindered[2] and unhindered[3] primary alkyl iodides and secondary[1a,c,10] alkyl iodides react with $LiAlH_4$ via a predominantly SET pathway, it is not surprising that tertiary alkyl iodides would do likewise because tertiary alkyl iodides should be more easily reduced to the corresponding radical than primary or secondary alkyl iodides. By choosing saturated alkyl halides for this study, we eliminate the possibility of the results being explainable by means of a halogen-atom radical chain process as has been suggested to explain previous results concerning the use of unsaturated alkyl halides as cyclizable radical probes. The difference between tertiary alkyl halides and primary and secondary alkyl halides is that the tertiary alkyl halides have a better possibility of reacting via a carbocation as well as a radical. In addition to not expecting tertiary alkyl halides to ionize readily in THF, convincing evidence has been presented that supports the contention that the results reported herein are not consistent with the major reaction pathway proceeding via a carbocation.

Experimental Section

Materials. Carbon disulfide was purchased from Fisher Scientific and distilled from calcium chloride prior to use. Diphosphorus tetraiodide (Aldrich) and concentrated hydrobromic acid (Baker) were used as received. 2-Iodooctane (Lancaster) was distilled prior to use. Authentic samples of 2-methylheptane (Aldrich) and 1,1,3-trimethylcyclopentane (Wiley Organics) were obtained in order to verify their formation in mechanistic studies. Additional information on materials, instrumentation, deuterium content calculations, and titrations of LAH/LAD solutions was reported previously.[2]

Reduction of Alkyl Halides. The procedure for the reduction of alkyl halides by LAH or LAD has been previously reported.[2]

2-Bromooctane (12). Alkyl bromide **12** was synthesized from 2-octanol in a manner analogous to that reported for 3-bromo-1-phenylprop-1-ene.[13] The product was purified by silica chromatography using hexane as the eluent. ^{1}H NMR ($CDCl_3$): δ 4.20−4.07 (m, 1H), 1.94−1.73 (m, 2H), 1.71 (d, 3H, J = 6.7 Hz), 1.55−1.22 (m, 8H), 0.89 (m, 3H).

2-Methyl-2-heptanol (19). Alcohol **19** was synthesized via a Grignard reaction from 1-bromopentane and acetone in a manner analogous to that reported for 2-methylhexan-2-ol.[14] Distillation of the crude product (64.0−66.0 °C/12 mmHg) followed by silica column chromatography (petroleum ether to petroleum ether/diethyl ether mixtures as eluent) afforded the purified alcohol in 63% yield. ^{1}H NMR ($CDCl_3$): δ 1.51−1.41 (m, 2H), 1.41−1.23 (m, 7H), 1.21 (s, 6H), 0.90 (t, 3H, J = 6.9 Hz). MS *m/e* (relative intensity, $C_8H_{18}O$): 115 (80), 97 (23), 59 (100), 55 (44), 43 (51).

2-Chloro-2-methylheptane (21). Alkyl chloride **21** was synthesized from 2-methyl-2-heptanol and HCl in a manner analogous to that reported for *tert*-butyl chloride.[15] The crude product was purified by silica chromatography with hexane as eluent. ^{1}H NMR ($CDCl_3$): δ 1.79−1.70 (m, 2H), 1.57 (s, 6H), 1.55−1.22 (m, 6H), 0.91 (t, 3H, J = 6.9 Hz). MS *m/e* (relative intensity, $C_8H_{17}Cl$): 135 (0.2), 133 (0.7), 121 (0.2), 69 (54), 57 (75), 56 (100), 55 (57), 43 (53), 41 (71).

2-Bromo-2-methylheptane (20). 2-Methyl-2-heptanol (2.52 g, 19.4 mmol) was added to a flask followed by concentrated hydrobromic acid (2.5 mL). The reaction mixture was stirred for 18 h at room temperature. The resulting organic layer was washed with water until neutral to litmus and then dried over calcium chloride. The solvent was removed by rotary evaporation, and distillation of the residue (70.8−72.0 °C/18 mmHg) afforded the desired product (1.86 g, 49.7%). Note that tertiary bromide is not stable on silica or neutral alumina or under the thermal conditions required for preparative GC. ^{1}H NMR ($CDCl_3$): δ 1.81−1.73 (m, 2H), 1.75 (s, 6H), 1.60−1.42 (m, 2H), 1.41−1.23 (m, 4H), 0.91 (t, 3H, J = 6.9 Hz). MS *m/e* (relative intensity, $C_8H_{18}Br$): 137 (0.8), 135 (0.8), 113 (90), 71 (95), 57 (100), 43 (86), 41 (67).

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(13) Vogel, A. I. *Vogel's Textbook of Practical Organic Chemistry*, 5th ed.; John Wiley & Sons: New York, 1989; p 565.

(14) Vogel, A. I. *Vogel's Textbook of Practical Organic Chemistry*, 5th ed.; John Wiley & Sons: New York, 1989; p 538.

(15) Vogel, A. I. *Vogel's Textbook of Practical Organic Chemistry*, 5th ed.; John Wiley & Sons: New York, 1989; p 556.

2-Iodo-2-methylheptane (15). The title compound was prepared by a known method;[16] however, a more detailed procedure is reported in the Supporting Information. ^{1}H NMR ($CDCl_3$): δ 1.92 (s, 6H), 1.65−1.20 (m, 8H), 0.91 (t, 3H, J = 6.6 Hz).

2-Methyl-6-hepten-2-ol. The title compound was synthesized in a manner analogous to that reported above for **19** (substituting 5-bromo-1-pentene for the 1-bromopentane) in 55% yield. ^{1}H NMR ($CDCl_3$): δ 5.89−5.76 (m, 1H), 5.10−4.97 (m, 2H), 2.12−2.03 (m, 2H), 1.50−1.42 (m, 4H), 1.30−1.20 (m, 7H). MS *m*/*e* (relative intensity, $C_8H_{16}O$): 113 (11), 95 (14), 59 (100), 43 (35).

6-Chloro-6-methyl-1-heptene (33). Alkyl chloride **33** was synthesized from 2-methyl-6-hepten-2-ol and HCl in a manner analogous to that reported for *tert*-butyl chloride.[15] ^{1}H NMR ($CDCl_3$): δ 5.90−5.73 (m, 1H), 5.07−4.96 (m, 2H), 2.13−2.04 (m, 2H), 1.80−1.72 (m, 2H), 1.67−1.53 (m, 2H), 1.58 (s, 6H). MS *m*/*e* (relative intensity, $C_8H_{15}Cl$): 148 (3), 146 (10), 111 (19), 95 (80), 69 (100), 56 (66), 55 (53), 41 (86).

6-Iodo-6-methyl-1-heptene (25). The title compound was synthesized in a manner analogous to that reported for **15** (substituting 2-methyl-6-hepten-2-ol for **19**). ^{1}H NMR ($CDCl_3$): δ 5.90−5.75 (m, 1H), 5.10−4.96 (m, 2H), 2.16−2.08 (m, 2H), 1.93 (s, 6H), 1.65−1.60 (m, 4H). ^{13}C NMR ($CDCl_3$): δ 138.8, 115.3, 52.5, 50.0, 38.2, 33.5, 27.8. MS *m*/*e* (relative intensity, $C_8H_{15}I$): 169 (0.7), 128 (4), 127 (7), 112 (12), 111 (97), 69 (100), 57 (11), 56 (11), 55 (61), 53 (10), 43 (16), 41 (53), 39 (26).

Rearrangement of 6-Iodo-6-methyl-1-heptene (25) to 1-(Iodomethyl)-2,2-dimethylcyclopentane (26). To 6-iodo-6-methyl-1-heptene (0.038 g, 0.16 mmol) was added THF (1.93 mL) followed by a homogeneous solution of LAD in THF (0.35 mL, 0.90 M, 0.32 mmol). After 30 min, the solution was quenched by addition to cold water (1 mL), and the resulting mixture was then extracted with diethyl ether (2 × 1 mL). The combined organic layers were dried over anhydrous $MgSO_4$, filtered, and concentrated. GC indicated that the desired compound was formed in 89% relative yield. (For this experiment only, the absolute yield was not determined.) ^{1}H NMR ($CDCl_3$): δ 3.23 (dd, 1H, J = 9.3, 3.9 Hz), 2.94 (dd, 1H, J = 9.3, 11.4 Hz), 2.20−2.03 (m, 1H), 1.70−1.20 (m, 6H), 1.03 (s, 3H), 0.77 (s, 3H). MS *m*/*e* (relative intensity, $C_8H_{15}I$): 238 (0.9), 223 (1.5), 111 (100), 69 (65).

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Supporting Information Available: Methods and experimental data for **15** (1 page). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of this journal, and can be ordered from the ACS; see any current masthead page for ordering information.

JO9807058

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[16] Lauwers, M.; Regnier, B.; Van Eenoo, M.; Denis, J. N.; Krief, A. *Tetrahedron Lett.* **1979**, *20*, 1801.