Convincing Evidence, Not Involving Cyclizable Radical Probes, That the Reaction of $LiAlH_4$ with Hindered Alkyl Iodides Proceeds Predominantly by a Single Electron Transfer Pathway[†,‡]

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Previous workers have maintained that evidence for the radical nature of the reaction of $LiAlH_4$ with sterically hindered alkyl iodides is due to radical initiation by impurities followed by a halogen atom radical chain process involving the cyclizable alkyl iodide probe and that the reduction of the C−I bond actually proceeds by an S_N2 pathway. In order to resolve the validity of this explanation, 1-iodo-2,2-dimethylhexane (the saturated counterpart of the cyclizable probe), which is not capable of this halogen atom radical chain process, was allowed to react with $LiAlD_4$. The reduction product, 2,2-dimethylhexane, contained only 4−76% deuterium depending on the conditions of the reaction. This result is consistent with the reaction proceeding by a SET process via a radical intermediate and is inconsistent with an S_N2 pathway. We have determined the influence of the nature of the reaction on the type of reactor surface (Pyrex, Teflon, stainless steel, and quartz) used in the reaction. We have also studied the influence of AlD_3 (a byproduct in the reduction) in the mechanistic evaluation of this reaction.

Introduction

Of all the nucleophiles[1−18] that have been reported as one-electron donors, only lithium aluminum hydride (LAH) has been questioned as to its electron donor ability. In 1984 we published an article that supports the SET nature of LAH in the reduction of sterically hindered alkyl halides.[5e] The methodology used to establish the mechanism of the reduction included the following: (1) direct spectroscopic evidence of radical intermediates by electron paramagnetic resonance (EPR) spectroscopy, (2) cyclization of cyclizable alkyl halides that contain the 5-hexenyl group, (3) use of radical traps, and (4) stereochemical studies. The extent of electron transfer was studied as a function of solvent, substrate, leaving group, and the hydride reagent.

Upon study of the reaction of unhindered primary cyclizable probes, 6-halo-1-hexenes (X = I, Br, Cl), with $LiAlH_4$, we reported that no cyclized products were observed. Also, deuterium incorporation in the uncyclized product (1-hexene) was quantitative when $LiAlD_4$ (LAD) was used as the nucleophile. It was concluded that either an S_N2 mechanism best describes the reaction or the radical species involved collapse to product substantially faster than cyclization to the cyclopentylmethyl radical ($k_{\text{cyclization}} = 2.5 \times 10^5\ s^{-1}$ at 25 °C).[19]

[†] The initial studies were communicated earlier. Ashby, E. C.; Welder, C. O. *Tetrahedron Lett.* **1995**, *36*, 7171. Ashby, E. C.; Welder, C. O.; Doctorovich, F. *Tetrahedron Lett.* **1993**, *34*, 7235.

[‡] This paper is dedicated to Professor Ernest Eliel who introduced E.C.A. to $LiAlH_4$ 42 years ago as a student at the University of Notre Dame. Professor Eliel has been a role model for many, a man of excellence in scientific investigation and teaching, and a man of character and integrity.

[⊗] Abstract published in *Advance ACS Abstracts,* May 1, 1997.

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(18) For reactions involving 1-halonorbornanes with Me_3Sn^-, Ph_2P^-, $N(iPr)_2^-$, PhS^-, and the 2-nitropropyl anion, see: Ashby, E. C.; Sun, X.; Duff, J. L. *J. Org. Chem.* **1994**, *59*, 1270. For reactions involving cyclizable norbornene probes with Na, Mg, sodium naphthalenide, and Bu_2SnH, see: Ashby, E. C.; Pham, T. N. *Tetrahedron Lett.* **1984**, *25*, 4333.

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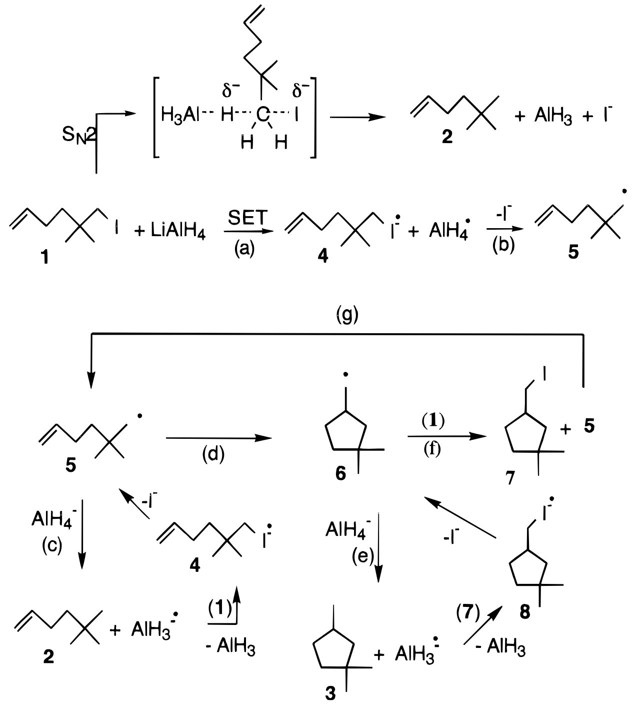
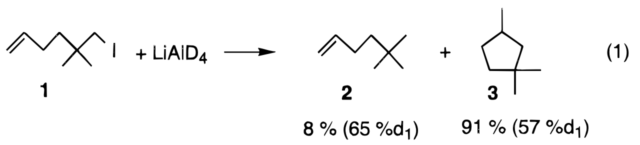
Scheme 1

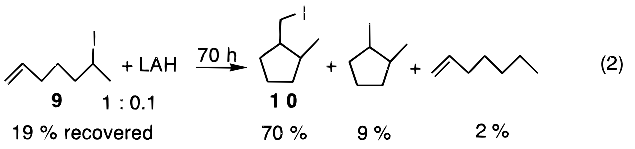


It was necessary to add two methyl groups to the 5-position of the 6-halo-1-hexene system in order to slow the competing S_N2 reaction and/or the competing hydrogen atom abstraction reaction in order to obtain evidence for SET. Indeed, significant evidence for electron transfer was observed for the reaction of 6-iodo-5,5-dimethyl-1-hexene (**1**) with LAH as evidenced by formation of the cyclized product 1,1,3-trimethylcyclopentane (**3**) in high yield (eq 1). (Less cyclized product was observed with the corresponding bromide and no cyclized product was observed for the corresponding chloride or tosylate.) Studies employing LAD as the nucleophile reacting with iodide **1** show significant protium incorporation in both the uncyclized product **2** and the cyclized product **3**. When dicyclohexylphosphine (DCPH), a radical trapping agent, was added to the reaction, significantly more radical intermediate was trapped by the DCPH as evidenced by lower deuterium incorporation in products **2** and **3**.

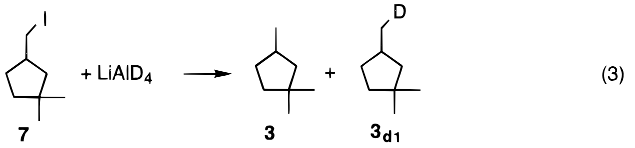


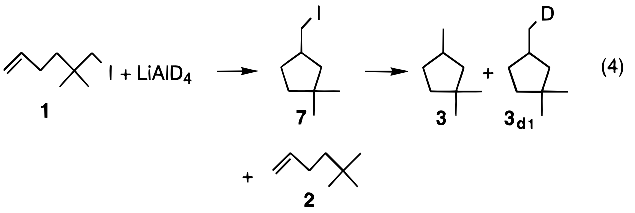
In 1991 the mechanism shown in Scheme 1 was published[5b] for the reduction of 6-iodo-5,5-dimethyl-1-hexene (**1**), specifying the hydrogen atom radical chain nature of the reaction. It was proposed that, in step a, LAH transfers one electron to alkyl iodide **1** to form the corresponding radical anion **4**, which rapidly dissociates in step b to form the radical **5**. Radical **5** can enter a halogen atom radical chain process as shown in steps d, f, and g; it can react with AlH_4^- (step c) in a hydrogen atom radical chain process yielding alkene **2**; or it can cyclize (step d) to form radical **6**. Cyclized radical **6** can then undergo a hydrogen atom radical chain process (step e) to form alkane **3**. We have also reported[5b] that the AlH_3 radical anion is the major one-electron donor in the system and that the S_N2 pathway is believed to be a minor pathway.

It is important to note that the radical chain process shown in Scheme 1, steps d, f, and g, was discussed by us in detail in 1984.[5e] We reported the reaction of 6-iodo-1-heptene (**9**) with LAH in 1:0.1 ratio (eq 2). This experiment was specifically designed to uncover the extent of the halogen atom radical chain process, and indeed, the formation of the cyclized iodide **10** in 70% yield provided this evidence.



In the past 10 years several reports[20] have appeared that suggest that a trace amount of radical initiator can result in a significant yield of cyclized alkyl halide formed via a halogen atom radical chain process and that the cyclized alkyl halide could then react with LAH by a conventional polar (S_N2) process.[20b] In order to address this possibility, we independently synthesized 1-(iodomethyl)-3,3-dimethylcyclopentane (**7**).[5d] If all of the cyclized hydrocarbon is a result of the reduction of alkyl iodide **7** in an S_N2 fashion, then when LAD is substituted for LAH as nucleophile, the following two reactions (eqs 3 and 4) should give identical results as to the ratio of **3** to $\mathbf{3_{d1}}$:





We found that the reduction of **7** gave 99% 1,1,3-trimethylcyclopentane containing 98% D (eq 3). Therefore, no evidence of SET was observed in the reduction of **7** by LAD. However, when iodide **1** was allowed to react with LAD, 91% 1,1,3-trimethylcyclopentane was observed, but it contained only 57% D (eqs 1 and 4). These results show that products **3** and $\mathbf{3_{d1}}$ do not result solely from **7** or else the same ratio of **3** to $\mathbf{3_{d1}}$ would have been observed in eqs 3 and 4. Clearly a radical intermediate is formed in eq 4 which abstracts hydrogen atoms from a source other than LAD. These data are contrary to the suggestion that the reduction of **1** by LAH proceeds by an S_N2 process. Also, if the radical anion **4** is initiated by an impurity in eq 4, then the same impurity would be expected to initiate the formation of radical anion **8** in eq 3 while it clearly does not. These

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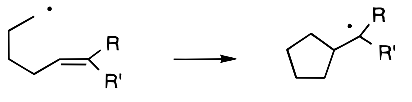
[20] (a) Newcomb, M.; Curran, D. P. *Acc. Chem. Res.* **1988**, *21*, 206. (b) Newcomb, M.; Kaplan, J.; Curran, D. P. *Tetrahedron Lett.* **1988**, *29*, 3451. (c) Park, S. U.; Chung, S. K.; Newcomb, M. *J. Org. Chem.* **1987**, *52*, 3275. (d) Newcomb, M.; Sanchez, R. M.; Kaplan, J. *J. Am. Chem. Soc.*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

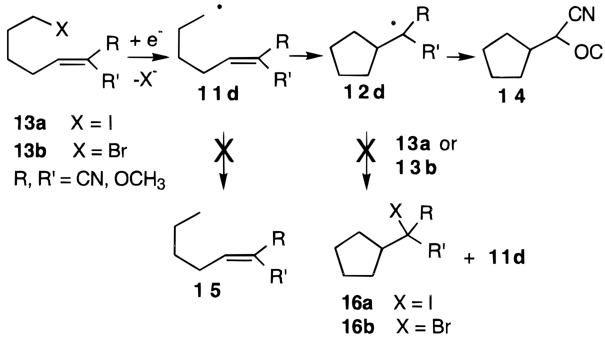
results are inconsistent with the notion that the reaction of **1** or **7** is initiated by impurities.

In 1986 Newcomb and co-workers studied the rates of cyclization of 6-substituted hex-5-en-1-yl radicals (eq 5).[21] They reported that radicals are stabilized by electron acceptors (such as CN) and donors (such as OCH_3) and that radical **12d**, which incorporates both an acceptor and a donor in the same molecule, has greater stability than the sum of the individual components. Therefore, by definition, captodative stabilization exists for **12d**. In 1987 the same group used the new cyclizable radical **11d** to study the reactions of unhindered primary alkyl iodides and bromides with boron and aluminum hydride reducing agents to determine whether the reductions proceeded by an S_N2 or an SET pathway.[20c] According to Newcomb, due to the faster cyclization of radical **11d** to radical **12d** over most other probe rearrangements, "problems with trapping of free radical intermediates before rearrangement should not arise with [**11d**]".[22] More importantly, Newcomb and co-workers "believed that cyclic radical [**12d**] would be so stable that it would be incapable of abstracting halogen from [**13**] in a radical chain isomerization propagation step"[22] (eq 6). Since the halogen atom radical chain process should then be inoperative, it was hoped that quantitation of the extent of SET would be possible.



(5)

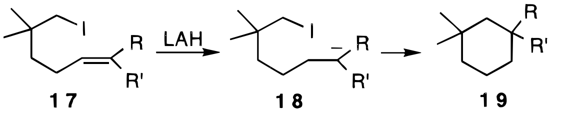
11a R = R'= H	**12a**
11b R, R' = H	**12b**
11c R, R'= H, OCH_3	**12c**
11d R, R'= CN, OCH_3	**12d**



(6)

Newcomb's stated premises are that (1) *all* of the alkyl halide that is converted to radical **11d** will lead to rearranged radical **12d**, (2) radical **12d** cannot abstract halogen atom from **13**, and (3) the uncyclized reduction product 2-methoxy-2-heptenenitrile (**15**) could not arise from trapping of radical **11d** before cyclization because substantially slower radical probes have rearranged in the presence of various boron and aluminum hydrides. No radical-derived cyclized products were observed; therefore, it was concluded that SET from the reducing agent to the halide to give a free radical was not an important process. Newcomb further states that in previous mechanistic studies it is reasonable to suspect that only limited amounts of SET occurred even when substantial amounts of rearranged products were detected. He warns that adventitious impurities or side reactions can be responsible for initiation of a radical chain isomerization process in reactions of *any* alkyl halide probe (even though he only studied *unhindered* primary probes) with boron or aluminum hydride reducing agents.[20c]

Recall that as early as 1984 we reported no evidence of SET when the primary *unhindered* 6-halo-1-hexenes (X = I, Br, Cl) were reduced by various metal hydrides, including LAH.[5e] Therefore, it was not surprising to us when the report appeared stating that there is no evidence of SET with primary unhindered probes **13a** and **13b**. Additionally, we were surprised that an *unhindered* primary probe, such as **13a**, would be used to refute the mechanism suggested for a *hindered* primary probe. After all, our reported mechanism of SET was reported for hindered primary alkyl halides. Because of this improper comparison we modified the captodative probe **13a**. Insertion of the geminal dimethyl group into probe **13a** yielded the neopentyl type probe 7-iodo-6,6-dimethyl-2-methoxy-2-heptenenitrile (**17**), which still incorporates the captodative system proposed by Newcomb, but also adds the steric hindrance that is usually necessary to observe SET in primary alkyl iodides. This is the probe that should have been studied in order to challenge our initial report since we did not work with a unhindered primary system but with a hindered neopentyl type system. When probe **17** was allowed to react with LAH, the mechanism of the reaction was altered significantly as compared either to probe **13a** or the original neopentyl type probe **1**. As shown in eq 7, a Michael addition of hydride to probe **17** resulted in anion **18** which then cyclized to the six-membered ring product **19**. Therefore, probe **17** cannot be used in a manner analogous to probe **1** because in probe **17**, reaction occurred at the α,*β*-unsaturated nitrile, whereas in probe **1**, reaction occurred at the carbon−iodine bond.[23] (Undesirable reaction at the α,*β*-unsaturated nitrile also occurred in reactions involving the uncyclized probe **13**.)



(7)

17 **18** **19**

R,R' = CN, OCH_3

Data from the present report will conclusively support our position that the reaction of $LiAlH_4$ with **1** is an SET process and not an S_N2 process. This is accomplished by removing the possibility of a halogen atom radical chain process by allowing the saturated analog of **1** to react with $LiAlD_4$. Thus protio product formed in the reaction can only be the result of a radical reaction with the solvent.

To this end, 1-iodo-2,2-dimethylhexane (**20**), the saturated counterpart of **1**, was chosen for study. Since the product of a SET reaction with LAH would be indistinguishable from the S_N2 product [2,2-dimethylhexane (**22**)], LAD was necessarily chosen as the nucleophile in the study of the saturated probe. Distinction between SET and S_N2 is thus possible. For a reaction involving radical intermediates, hydrogen atoms (from solvent)

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[21] Park, S. U.; Chung, S. K.; Newcomb, M. *J. Am. Chem. Soc.* **1986**, *108*, 240.

[22] Park, S. U.; Chung, S. K.; Newcomb, M. *J. Org. Chem.* **1987**, *52*, 3276.

[23] Sun, Xiao-Jing. The Extent and Importance of Single Electron Transfer in Organic Reactions. Ph.D. Dissertation, Georgia Institute of Technology, 1994.

Table 1. Variation of Stoichiometry in the Reaction of 1-Iodo-2,2-dimethylhexane (20) with LAD in THF[a]

			products			
exp	**20**:LAD	time, h	% **20**	% **22** (% D)	% dimers	MB[b]
1	1:20	1	74	26	trace	100
		5	21	68	trace	89
		7	11	82 (72)	trace	93
2	1:5	1	88	4 (48)		92
		5	60	33 (42)	trace	93
		8	33	58 (39)	trace	91
		24	5	84 (34)	3	92
3	1:1	20	28	67 (6)		95
4	1:0.2	1	90	7 (5)	trace	97
		5	74	19 (8)	trace	93
		8	71	22 (5)	trace	93
		24	61	30 (3)	trace	91
		48	61	31 (4)	trace	92

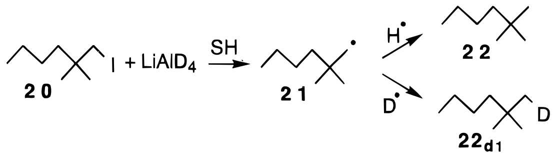
[a] All reactions were carried out in an Ar atmosphere glovebox in the absence of light at room temperature and at a concentration of 0.070 M with respect to **20**. Reactions were carried out in used Pyrex flasks using Teflon-coated stir bars. [b] MB is material balance.

Table 2. Variation of Concentration in the Reaction of 1-Iodo-2,2-dimethylhexane (20) with LAD in THF[a]

			products		
exp	[**20**], M	time, h	%**20**	%**22** (% D)	MB[b]
1	0.27	22	0	100 (67)	100
2	0.070	8	0	100 (28)	100
3	0.035	20	2	86 (21)	88

[a] All reactions were carried out in an Ar atmosphere glovebox in the absence of light at room temperature and at a **20**:LAD ratio of 1:5. Reactions were carried out in used Pyrex flasks using Teflon-coated stir bars. [b] MB is material balance.

and/or deuterium atoms (from LAD and its by-products) may be abstracted. Therefore, both the nondeuterated and the deuterated alkane could be formed (eq 8). On



(8)

the other hand, for an S_N2 reaction, only product $\mathbf{22_{d1}}$ is expected. Product **22** can be formed only through a radical intermediate and thus provides evidence for a SET process. Therefore, nondeuterated alkane **22** represents the minimum amount of product formed through a radical pathway.

As will be discussed, conclusive evidence for a SET pathway was obtained for iodide **20**, even in the absence of the halogen atom radical chain process depicted in Scheme 1 (steps d, f, and g). The formation of nondeuterated **22** in yields over 90% in the reaction of **20** with $LiAlD_4$ provides incontrovertible evidence that the predominant reaction involves the formation of a radical intermediate, and therefore, the product is not formed by an S_N2 process.

Results and Discussion

Effect of Stoichiometry on the Reaction of LAD with 1-Iodo-2,2-dimethylhexane (**20**). If an SET mechanism were in effect in the reaction of alkyl iodide **20** with LAD, then a variation in the stoichiometry of **20**:LAD should have an effect on the ratio of nondeuterated alkane **22** to deuterated alkane $\mathbf{22_{d1}}$ (eq 8). Radical **21** in solution can abstract a deuterium atom from LAD or its byproducts (e.g. AlD_3), or it can abstract a hydrogen atom from the solvent. Higher stoichiometries of LAD increase the probability that **21** will encounter a deuterium atom over a hydrogen atom. Likewise, at lower LAD stoichiometries, radical **21** has a higher probability of encountering a THF molecule, and thus more protio hydrocarbon should be formed.

The expected trend described above was indeed observed for the reaction of **20** with LAD (Table 1). The results of experiment 1 for a 20-fold excess of LAD show that, after 7 h, 82% 2,2-dimethylhexane (**22**) containing 72% D was formed. Therefore, at least 28% of the hydrocarbon formed was derived from radical **21** that abstracted a hydrogen atom from the solvent. Obviously, more than a trace amount of radicals were formed even in the absence of the halogen atom radical chain process described in Scheme 1 (steps d, f, and g). When the stoichiometry was reduced from a 20-fold excess of LAD to a 5-fold excess (Table 1, experiment 2), an even lower deuterium content was observed in the resulting hydrocarbon (34%). The trend of an increasing ratio of nondeuterated alkane **22** to deuterated alkane $\mathbf{22_{d1}}$ continued as the stoichiometry of LAD dropped further to 1:1 (experiment 3) and 1:0.2 (experiment 4) as expected. Indeed, at the stoichiometries of 1:1 and 1:0.2, the deuterium content of the product dropped to 3−8%, indicating that the majority of the product (>90%) is formed via a radical intermediate. These results are inconsistent with an S_N2 process.

Effect of Concentration on the Reaction of 1-Iodo-2,2-dimethylhexane (20) with LAD. The concentration of LAD in a reaction should affect the ratio of nondeuterated to deuterated product. A variation in concentration of LAD in solution automatically leads to a variation in the ratio of deuterium atom donors (LAD and its byproducts) to hydrogen atom donors (e.g. the solvent). Therefore, as the concentration of LAD in solution decreases, radical intermediates formed in the reaction are less likely to encounter a deuterium atom donor, and thus, the ratio of deuterated product to nondeuterated product should decrease. Table 2 shows the results of variation of concentration of alkyl iodide **20** on the deuterium content in the resulting hydrocarbon. When the initial concentration of **20** was 0.27 M, the resulting 2,2-dimethylhexane (**22**) was found to contain 67% D (experiment 1). Therefore, 33% of the alkane **22** resulted from the trapping of radical **21** by hydrogen atoms from THF. At the lower concentration of 0.070 M, more efficient hydrogen atom abstraction from the solvent was observed in that the resulting alkane **22** contained only 28% D. Further dilution of the reaction to 0.035 M resulted in even more hydrogen atom abstraction from the solvent (as expected), yielding only 21% D in **22**. Therefore, the predicted trend of lower deuterium incorporation in the product at lower concentrations of alkyl iodide **20** was observed. These results, of course, are consistent with the proposal that this reaction is proceeding via the formation of a radical intermediate.

Effect of Variation of Solvent and Nucleophile on the Reaction of 1-Iodo-2,2-dimethylhexane (20). The experiments in Table 3 were carried out in order to show that SET was not exclusive to THF as the solvent and to provide evidence that the solvent was indeed the source of hydrogen atoms which were abstracted by radicals in solution. Experiments 1 and 2 were reported in earlier

Table 3. Variation of Solvent in the Reactions of 1-Iodo-2,2-dimethylhexane (20) with LAD and LAH[a]

					products			
exp	solvent	time	nuc	**20**:nuc	% **20**	% **22** (% D)	% dimers	material balance
1	THF	8 h	LAD	1:5	0	100 (28)	trace	100
2	THF	20 h	LAD	1:1	28	67 (6)		95
3	Et_2O	2 d	LAD	1:5	8	84 (33)	trace	92[b]
4	Et_2O	4 d	LAD	1:1	26	63 (8)	trace	89[b]
5	THF-d_8	2 h	LAH	1:5	0	96 (1)	trace	96
6	THF-d_8	2 d	LAH	1:1	0	88 (15)	9	100[c]
7	THF-d_8	3 d	LAD	1:5	0	91 (89)	trace	91

[a] All reactions were carried out in an Ar atmosphere glovebox in the absence of light at room temperature and at a concentration of 0.070 M with respect to **20**. Reactions were carried out in used Pyrex flasks and Teflon-coated stir bars were employed. [b] A trace quantity of 5,5-dimethyl-1-hexene was observed. [c] 5,5-Dimethyl-1-hexene (3%) was also obtained.

tables and are repeated in this table for convenience of comparison.

Experiment 1, carried out in THF, may be directly compared to experiment 3, which was carried out in diethyl ether at the same concentration and stoichiometry. Even though the LAD reaction was carried out in two different solvents, the extent of hydrogen atom abstraction, as noted by the deuterium incorporation in alkane **22**, was comparable with 28% D (72% hydrogen atom abstraction) at completion in the THF reaction (experiment 1) and 33% D (67% hydrogen atom abstraction) near completion in the diethyl ether reaction (experiment 3). A comparison of the data in THF and diethyl ether (experiments 2 and 4, respectively) at the lower stoichiometry of 1:1 also shows the similarity of the two solvents.

In order to support the solvent as the source of hydrogen atoms, experiments were carried out in deuterated THF (experiments 5–7). When a 5-fold excess of LAH was employed in a reaction with THF-d_8 as solvent, only 1% D was found in the product hydrocarbon (experiment 5). This result is not surprising due to the kinetic isotope effect. Not only was the strength of the aluminum–deuterium bond of LAD weakened to an aluminum–hydrogen bond, but also, the carbon–hydrogen bond of THF was strengthened to a carbon-deuterium bond in THF-d_8, making deuterium atom abstraction from the solvent a higher energy process. However, when the 5-fold excess of LAH employed in experiment 5 was reduced to 1 equiv of LAH (experiment 6), the product was found to contain 15% D. The relatively high deuterium incorporation (15% D) in the alkane **22** supports deuterium atom abstraction from the solvent by a radical intermediate which in turn indicates that THF acts as a hydrogen atom donor in the experiments that use LAD as the nucleophile. The high yield of dimers in experiment 6 supports the formation of radical intermediates which combined to form dimers rather than abstracting a deuterium atom from the THF-d_8 or a hydrogen atom from LAH or its byproducts. Experiment 7 was included to determine the deuterium content in **22** when both solvent and nucleophile are labeled with deuterium. Alkane **22** was found to contain 89% D. When one takes into account isotopic purities (THF-d_8 contains 99.5% D and $LiAlD_4$ contains 98.5% D) and the kinetic isotope effect ($k_H/k_D \approx 7$), the observed deuterium content of 89% can be rationalized.

It can be concluded from the solvent and isotope studies that SET from LAD to 1-iodo-2,2-dimethylhexane (**20**) was not exclusive to reactions carried out in THF and that the solvent acts as a hydrogen atom source (or a deuterium atom source for reactions in THF-d_8) toward radical species formed during the course of the reaction.

Table 4. Effect of Light on the Reaction of 1-Iodo-2,2-dimethylhexane (20) with LAD[a]

			products				
exp	lighting	time, h	% **20**	% **22** (% D)	% dimers	other[b]	material balance
1	dark	1	88	4 (48)			92
		5	60	33 (42)	trace		93
		8	33	58 (39)	trace		91
		24	5	84 (34)	3		92
2	mercury lamp	0.5	46	37 (13)	10	2	95
		1	13	67	16	3	99
		1.5	1	69	18	4	92
		2	0	71 (12)	19	4	94

[a] Reactions were carried out at a concentration of 0.070 M with respect to **20** and a RI:LAD ratio of 1:5 in an Ar atmosphere glovebox. Experiment 1 was carried out in a used Pyrex flask at room temperature. Experiment 2 was carried out in a Pyrex test tube. [b] A total of six "other" compounds of unknown structure were observed in the photochemical experiment, each in <1% yield all having a *m/e* of 111.

Alkyl iodides **1** and **20** vary only in the fact that **1** possesses a remote double bond while **20** does not. Since significant evidence of SET has been reported above for the reaction of the saturated alkyl iodide **20** with LAD, it is again suggested that the unsaturated alkyl iodide **1** also reacts by SET since the presence of a remote double bond in **1** is hardly cause to suggest that the reaction mechanism changes from SET to S_N2.

Effect of Light on the Reaction of 1-Iodo-2,2-dimethylhexane (20) with LAD. Photochemical excitation is known to enhance the formation of radical species in solution. In order to observe the effect of photochemical excitation on the reaction of **20** with LAD, an experiment was carried out in the presence of a mercury lamp. It is important to note that, in the absence of LAD, no reaction occurred when iodide **20** was exposed to the lamp.

As can be seen in Table 4, the rate of the reaction of 1-iodo-2,2-dimethylhexane (**20**) with LAD was significantly enhanced in the presence of the mercury lamp. The reaction carried out in the dark (experiment 1) was not yet complete after 24 h, while the reaction carried out in the presence of the mercury lamp (experiment 2) was complete within 2 h.

The deuterium incorporation in alkane **22** was much lower for the photochemical experiment (experiment 2), indicating more hydrogen atom abstraction in the presence of the photochemical lamp than in the corresponding experiment carried out in the dark. Not only was the deuterium content of the product low, but it was also consistent throughout the reaction. Unlike any reaction presented thus far, the deuterium content in the initial aliquot (37% alkane containing 13% D) was within experimental error of the deuterium content at comple-

Table 5. Effect of the Byproducts Aluminum Deuteride and Lithium Iodide in the Reaction of 1-Iodo-2,2-dimethylhexane (20)[a]

			products			
exp	nuc	time, h	% **20**	% **22** (% D)	% dimers	MB[b]
1	LAD	1	88	4 (48)		92
		5	60	33 (42)	trace	93
		8	33	58 (39)	trace	91
		24	5	84 (34)	3	92
2	AlD_3	48	38	60 (5)	trace	98
		70	33	65	trace	98
3	AlH_3	24	18	80	trace	98[c]
		66	trace	95	trace	98[c]
4[d]	LAD	1	88	10 (49)		98
		5	31	58 (38)	3	92
		24	0	76 (33)	7	83

[a] All reactions were carried out at a concentration of 0.070 M with respect to **20** 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 using Teflon-coated stir bars. [b] MB is material balance. [c] A trace quantity of 5,5-dimethyl-1-hexene was observed. [d] One equivalent of lithium iodide was initially added to the reaction.

Table 6. Reaction of 1-Iodo-2,2-dimethylhexane (20) with LAD in Used Pyrex Flasks[a]

		products			
exp	time, h	%**20**	%**22** (%D)	% dimers	MB[b]
1	1.25	68	26		94
	5	12	72		84
	7	0	94 (29)		94
2	1.25	80	6		86
	5	64	21		85
	48	0	100 (57)		100
3	1.25	75	9		84
	5	44	35		79
	48	0	100 (35)		100
4	1	97	4		101
	5	55	35 (29)		90
5	1	89	4		93
	5	65	29 (56)		94
	24	trace	86 (44)	4	90
6	1	90	5 (50)		95
	5	55	36 (41)	trace	91
	24	9	77 (39)	2	88
7	1	88	4 (48)		92
	5	60	33 (42)	trace	93
	24	5	84 (34)	3	92
8	48	0	100 (66)		100
9	48	0	90 (76)		90

[a] All reactions were carried out at a concentration of 0.070 M with respect to **20** at a RI:LAD ratio of 1:5 in an Ar atmosphere glovebox in the absence of light at room temperature using Teflon-coated stir bars. [b] MB is material balance.

tion of the reaction (71% alkane containing 12% D). Dimer formation was also enhanced in the photochemical experiment. In reactions carried out in the dark, dimers were typically observed in trace quantities. However, as the data from experiment 2 show, a significant amount of alkyl iodide **20** was converted to dimeric compounds under photochemical excitation with 19% dimer formation by the completion of the reaction. New products were formed in the photochemical experiment that were not observed in any other reactions studied. Six compounds, each formed in trace quantity, were observed by GC/MS, and all were found to have a *m/e* of 111. Each of the compounds was formed in low yield, and the compounds had very similar GC retention times. Since clean separation was not possible, probably due to the similarity of the structures, no attempt was made at further characterization.

Decreased reaction time, decreased deuterium incorporation in the 2,2-dimethylhexane, and increased dimer formation can all be explained by the enhancement of a radical process induced by photochemical excitement.[24]

Effect of Aluminum Deuteride on the Reaction of 1-Iodo-2,2-dimethylhexane (20) with LAD. As early as 1983 we reported evidence that the AlH_3 produced in situ during the LAH reduction of alkyl halides can also be a one-electron transfer agent.[5e,g] Since aluminum deuteride, AlD_3, is an expected byproduct of the reaction of **20** with LAD, we considered it to be of value to independently study the effect AlD_3 has on **20**.

As shown in Table 5, AlD_3 reacts with **20** at a much slower rate than does LAD under the same conditions (experiments 1 and 2). Both the reaction of **20** with LAD and with AlD_3 gave high yields of 2,2-dimethylhexane (**22**). However, the deuterium incorporation in alkane **22** was significantly lower when AlD_3 was used as the nucleophile. Once again, lower deuterium incorporation in the product indicates more hydrogen atom abstraction of a radical intermediate from the solvent. The results of experiment 3 show that the reaction of **20** with AlD_3 is much slower than the corresponding reaction with AlH_3.

Effect of Lithium Iodide on the Reaction of 1-Iodo-2,2-dimethylhexane (20) with LAD. Lithium iodide is also an expected byproduct of the reaction of LAD with alkyl iodides. In order to determine whether or not the lithium iodide produced in situ had an effect on the reduction of iodide **20** by LAD, a reaction was carried out in which 1 equiv of LiI was initially added to the reaction mixture (Table 5, experiment 4).

As can be seen in Table 5, the reaction carried out in the absence of added LiI (experiment 1) and the reaction carried out in presence of added LiI (experiment 4) were very similar except that the rate was somewhat faster in the presence of added LiI. The deuterium content of alkane **22** over the course of the experiments had a high correlation, with the initial deuterium content of 48−49% D and the final deuterium content of 33−34% D. Therefore, it appears that the LiI byproduct has little, if any, effect on the mechanistic course of the reaction.

Effect of Reactor Surfaces on the Reaction of 1-Iodo-2,2-dimethylhexane (20) with LAD. As can be seen in Table 6, nine experiments carried out in different used Pyrex flasks varied in reaction rate and/or deuterium content of the product. After 5 h, the remaining starting material **20** varied from 12% (experiment 1) to 65% (experiment 5). More importantly, the deuterium content in 2,2-dimethylhexane (**22**) varied from 29% D at completion (experiment 1) to 76% D at completion (experiment 9). We have been troubled by our inability, in the present work, to obtain the kind of consistency of data in duplicate experiments that we have observed in the past. The only variable in this reaction that we had not studied previously is the nature of the reactor surface. Therefore, a study was initiated to determine the effect of different reactor surfaces on the reaction of **20** with LAD in order to find a vessel in which consistent data would be available. The results of this study are shown in Table 7.

Teflon has been used as a reactor surface in reactions in which glass has been suspected of catalyzing the

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(24) Radical species formed by photochemical excitation are not expected to be identical to the radical species formed during thermal reactions. See: Kropp, P. J. *Acc. Chem. Res.* **1984**, *17*, 131.

Table 7. Reaction of 1-Iodo-2,2-dimethylhexane (20) with LAD in Various Reaction Vessels[a]

			products			
exp	reaction vessel	time, h	% **20**	% **22** (% D)	% dimers	MB[b]
1	used Pyrex	1	88	4 (48)		92
		5	60	33 (42)	trace	93
		8	33	58 (39)	trace	91
		24	5	84 (34)	3	92
2	Teflon	1	90	3 (61)		93
		5	74	18 (54)		92
		8	61	33 (52)	trace	94
		24	9	77 (42)	1	87
3	stainless steel	1	61	17 (26)	21	99
		2	37	24 (26)	31	92
		5	16	34 (27)	45	95
		8	8	41 (27)	48	97
		24	0	47 (27)	50	97
4	treated Pyrex	1	93	4 (37)		97
		5	51	32 (34)	2	85
		8	29	44 (32)	4	77
		24	1	83 (29)	7	91
5	new Pyrex	1	94	5 (40)		99
		5	64	26 (39)	trace	90
		8	45	39 (39)	1	85
		24	7	71 (32)	2	80
		48	0	78 (35)	5	83
6	quartz	1	96	4 (40)		100
		5	62	31 (35)	trace	93
		8	33	53 (34)	trace	86
		24	0	88 (30)	2	90

[a] All reactions were carried out at a concentration of 0.070 M with respect to **20** at a RI:LAD ratio of 1:5 in an Ar atmosphere glovebox in the absence of light at room temperature in the absence of Teflon-coated stir bars. [b] MB is material balance.

Table 8. Reactions of 1-Halo- and 1-Tosyl-2,2-dimethylhexanes with LAD[a]

			products			
exp	X	time	% RX	% **22** (% D)	% dimers	MB[b]
1	I	24 h	5	84 (34)	3	92
2	Br	12 d	53	47 (84)		100
3	OTs	4 d	59	27 (95)		95[c]

[a] All reactions were carried out at a concentration of 0.070 M with respect to RX and at a RX:LAD ratio of 1:5 in an Ar atmosphere glovebox in the absence of light at room temperature in used Pyrex flasks. Teflon-coated stir bars were employed. [b] MB is material balance. [c] 2,2-Dimethyl-1-hexanol (9%) was also observed.

reaction. To test the integrity of Teflon as a reaction vessel in the presence of LAH, a homogeneous solution of LAH in THF (0.32 M) was allowed to stir in a Teflon flask for 2 days. Ion chromatographic analysis of the quenched basic solution revealed the presence of fluoride ions. Therefore, LAH reacted with Teflon, and even though data were included using a Teflon reaction vessel (experiment 2), it was concluded that Teflon is not a suitable vessel for reactions involving LAH. Likewise, the use of Teflon-coated stirring bars should be avoided when studying the mechanism of reactions involving LAH.

A stainless steel vessel was employed so that the effect of a metal surface could be observed (experiment 3). In this experiment, the formation of several dimers was observed very early in the reaction and, at the completion of the reaction, dimer formation was found to be much more extensive than had been previously observed. The stainless steel surface appears to catalyze the reduction of alkyl iodide **20**, and thus, it is inappropriate as a reaction vessel.

Reactions in used Pyrex flasks that had been treated with dichlorodimethylsilane to deactivate the surface were monitored as well (experiment 4). Encouragingly, consistent results were obtained with the deuterium content of **22** found to be 37% D in the initial aliquot (4% reaction) and 29% D near completion. (Decreasing deuterium content over the course of the reaction was also observed in used Pyrex and Teflon flasks; however, the amount of deuterium in product **22** was not consistent between duplicate experiments.)

Consistent results were also obtained for reactions that were carried out in previously unused (new) Pyrex flasks (experiment 5). The deuterium content of alkane **22** after 5% reaction was found to be 40% D which decreased to 35% D by completion. A comparison of experiments 4 and 5 reveals little difference between the reactions carried out in treated Pyrex with those carried out in new Pyrex. The similarity of the reactions carried out in these two vessels adds credibility to the conclusion that the treated Pyrex and new Pyrex vessels did not interfere with the product distribution and are appropriate for use in mechanistic studies involving LAH/LAD.

Reactions were also carried out in quartz (experiment 6). Encouragingly, the data was not only consistent between duplicate experiments, but it also closely resembled the data obtained in treated Pyrex and new Pyrex vessels. Importantly, the integrity of the quartz vessel did not appear to change with repeated use.

The surface of the reaction vessel was not the only surface that played a significant role in this reaction. When unfiltered, heterogeneous solutions of LAH or LAD were employed, inconsistent results were noted. Formation of dimers originating from the alkyl radical **21** ranged from <0.5−25% when undissolved solids were present in the flask. On the other hand, when filtered, homogeneous solutions were employed in the reaction, dimers were consistently formed in low yield (Table 7). Only filtered, homogeneous solutions of LAH and LAD were used throughout the present studies.

The following generalizations, derived by combining the above information on the involvement of reactor surfaces, should be applied to future mechanistic studies: (1) Teflon-coated stir bars should be avoided because Teflon was found to react with LAH, (2) reactions may be carried out in dichlorodimethylsilane-treated Pyrex, new Pyrex, or quartz vessels, and (3) homogeneous solutions of LAH or LAD should be employed since the surface of undissolved nucleophile was found to affect product distribution.

Since the effect of the reactor surface was determined late in this study, many of the reactions presented herein were carried out in used Pyrex flasks. However, since the data obtained in treated Pyrex, new Pyrex, or quartz vessels (with no Teflon stir bar present) always gave more evidence of radical formation than did the corresponding reaction in used Pyrex vessels, it was concluded that the hydrogen atom abstraction observed in used Pyrex vessels represents the minimum trapping of radicals that can occur in the reactions of LAD with the alkyl halides studied.

Effect of the Leaving Group on the Reaction of 1-Halo-2,2-dimethylhexanes with LAD. In order to broaden the scope of this reaction, a study was carried out on the effect of changing the leaving group from iodide to bromide to tosylate (Table 8). Since the alkyl bromide has a less favorable reduction potential than the alkyl iodide, electron transfer from LAD to the alkyl bromide would be less favored than for the corresponding alkyl iodide. The tosylate of 2,2-dimethyl-1-hexanol (**23**) has such an unfavorable reduction potential that it is not expected to act as an electron acceptor, thus lessening the possibility of the SET pathway. The tosylate should, however, behave similarly to the iodide if an S_N2 reaction were involved since the two groups display similar nucleofugacity. Therefore, the reaction of tosylate **23** should represent the maximum extent of deuterium incorporation for reactions of the alkyl halide, if an S_N2 pathway is in effect.

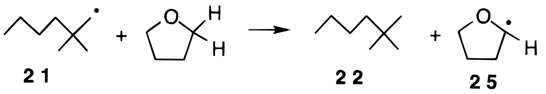
1-Bromo-2,2-dimethylhexane (**24**) was allowed to react with LAD (experiment 2). Even though the reaction with LAD was much slower than the reaction of the corresponding iodide **20**, once again, significant evidence for an SET pathway was observed in that 16% of the hydrocarbon formed in the reduction did not contain deuterium and hence indicates the presence of a radical precursor that abstracted a hydrogen atom from the solvent.

As shown in experiment 3, after 4 days 59% of tosylate **23** still remained unreacted while iodide **20** was almost completely consumed in 1 day (experiment 1). Some of the tosylate **23** (9%) was converted to the alcohol, 2,2-dimethyl-1-hexanol, due to the cleavage of the tosylate by LAD. Obviously, the S_N2 displacement of the tosyl group was severely impeded by the neighboring geminal dimethyl groups. Also, note that the 2,2-dimethylhexane (**22**) that was formed had a very high deuterium content (95% D), suggesting that little, if any, of the hydrocarbon was derived from an SET pathway. If **20** reacts with LiAlH$_4$ via an S_N2 pathway, then the results of the reaction of **20** and **23** should be similar. The results are very different.

Possibility of Other Radical Chain Processes. We mentioned in our 1993 communication[†] that a radical chain process involving THF is possible in the reaction of **20** with LAD (eqs 9 and 10). Although we cannot rigorously eliminate this possibility, we have not been able to acquire evidence for its existence. All attempts to isolate the α-iodo THF or its dehydrohalogenation product, 1,2-dihydrofuran, required of this process, were not successful. In addition, we found that the reduction of **7** with LAD produced **3** containing 98% D (eq 11). If the reaction represented by eq 11 proceeded according to the radical chain process (eq 12), then product **3** should have been formed with a much lower degree of deuterium incorporation as observed for all the other cases when a radical chain process was observed. Furthermore, radical **25** should be considerably more stable than radical **21**, due to the resonance stablization of **25** and, hence, less likely than **21** to participate in a halogen atom radical chain process.

Previously we had reported[5e] that the reaction of 6-iodo-1-heptene (**9**) with LiAlH$_4$ in a 1:0.1 ratio shows evidence of a halogen atom radical chain process but not a radical chain process involving THF (eq 2). After 70 h, the starting iodide **9** was recovered in 19% yield and the cyclized iodide **10** was formed in 70% yield, indicating a halogen atom radical chain process. However, the combined hydrocarbon yield was only 11%, indicating that a radical chain process involving the THF radical is not involved.

If the THF radical (**25**) were involved in a radical chain process (eqs 9 and 10) in the reaction of **20** with LAD in a 1:0.2 ratio, then the rate of product formation should not vary greatly beyond the 20% mark. What we observed is that the rate of formation of the product slows down dramatically at approximatley 20% reaction. Product does continue to be formed at a slower rate beyond the 20% mark due to the reaction of **20** with the byproduct, AlD$_3$. On the basis of all of the above observations, we conclude that a radical chain process involving THF is not significant.



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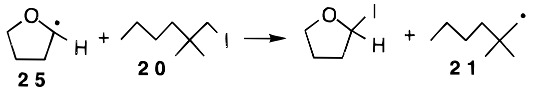

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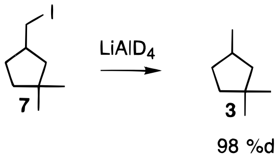

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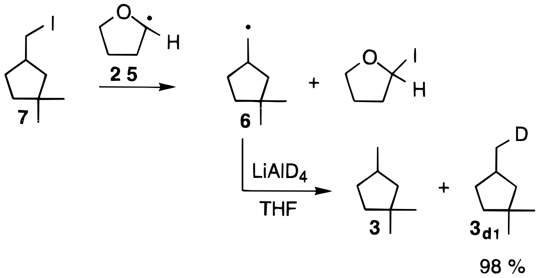
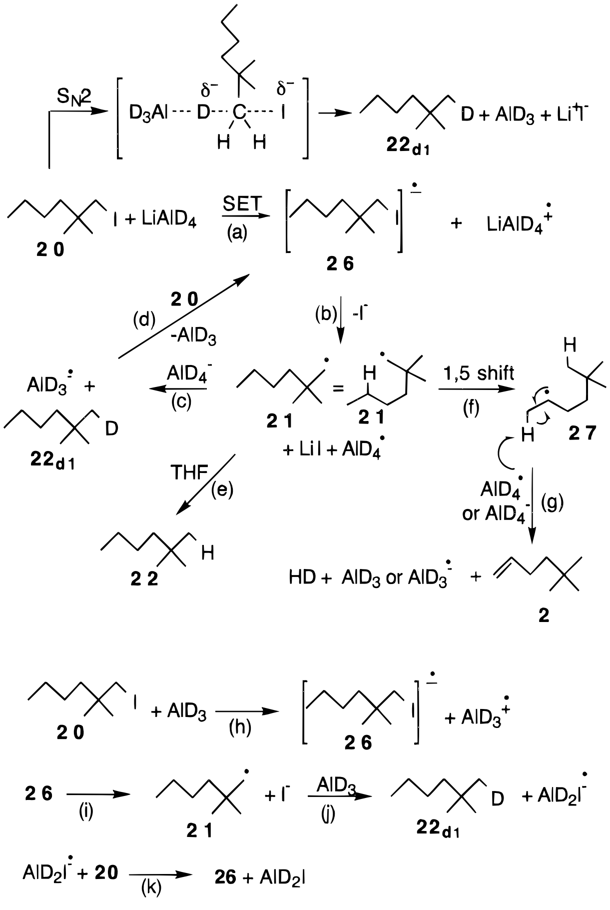


(12)

The question as to whether the reaction of **1** and/or **20** with LAH is initiated by SET, as we have held, or impurities, as Newcomb has held, rests on the results of a number of experiments. We have carried out reactions of **1** with doubly recrystallized LAH, doubly distilled **1** in THF doubly distilled over NaAlH$_4$, and found no difference in the rate or product ratios compared to the reactions carried out under normal conditions where the LAH used is from a filtered solution of LAH in THF, and both the alkyl halide and THF are singly distilled.[5e] Also, addition of trace transition metals as well as experiments involving rigorous exclusion of oxygen or addition of large amounts of oxygen had little effect on the reactions. In the absence of any evidence that the reaction is initiated by impurities rather than initiated by the electron rich AlH_4^- ion, we conclude that the reaction of sterically hindered alkyl iodides is initiated by electron transfer from the electron rich nucleophile AlH_4^- to the favorable electron acceptor alkyl iodide followed by a hydrogen atom radical chain process and, less likely, by a THF or halogen atom radical chain process, to produce the reduction product predominantly, if not entirely, via a radical intermediate which abstracts a hydrogen atom from the solvent. (Also see arguments presented in the introduction relating to eqs 3 and 4.)

Proposed Mechanism of the Reaction of 1-Iodo-2,2-dimethylhexane (20) with LAD. With all the combined information from the preceding experiments, the following mechanism is proposed for the reduction of **20** by LAD (Scheme 2). It is suggested that alkyl iodide **20** accepts an electron from LAD (step a) to form the corresponding radical anion **26** which rapidly dissociates (step b) to form radical **21**. Radical **21** abstracts a deuterium atom from AlD_4^- (step c) to form the deuter-

Scheme 2



ated alkane $\mathbf{22_{d1}}$. The aluminum deuteride radical anion reacts with the starting material **20** (step d) to form the corresponding radical anion **26** and AlD_3 in a hydrogen atom radical chain process. Radical **21** also reacts with a suitable hydrogen atom donor, such as THF (step e), to form the nondeuterated alkane **22**. A third fate of primary radical **21** is rearrangement to the secondary radical **27** by a 1,5 hydrogen atom shift.[25] It is proposed that LAD or one of its Al−D byproducts then abstracts a hydrogen atom from radical **27** as shown (step g) to form 5,5-dimethyl-1-hexene (**2**) in trace yield. Any AlD_3 radical anion formed in step g can then react as shown in step d. The AlD_3 formed during the reaction can also react by SET with alkyl iodide **20** as shown in step h. Radical anion **26** dissociates to radical **21** and iodide ion (step i). As shown in step j, AlD_3 can act as a deuterium atom source to radical **21** forming $\mathbf{22_{d1}}$ and the AlD_2I radical anion. Then AlD_2I radical anion can function as a single-electron donor to alkyl iodide **20** (step k) to form AlD_2I and radical anion **26**, which can dissociate as described above.

Conclusions

The reaction of 1-iodo-2,2-dimethylhexane (**20**), the saturated analog of 6-iodo-5,5-dimethyl-1-hexene (**1**), with $LiAlH_4$ and $LiAlD_4$ has been studied in detail. The results clearly show that the reaction of **20** with LAH or LAD cannot be described by an S_N2 process and indeed shows all the characteristics expected for an SET process. Since the difference between **20** and **1** is the presence of a remote double bond in the terminal position of the molecule and since the results of reactions of **20** and **1** with LAH or LAD are similar, we continue to maintain the position that **1** reacts with LAH or LAD by an SET process. The nature of the vessel surface was found to have some effect on the reaction; however the results involving the use of old Pyrex, used in these and previous studies, compared to quartz or new Pyrex, as demonstrated in the present studies, was not significantly different, and hence the SET nature of the reaction cannot be attributed to the reaction vessel surface.

Experimental Section

Materials. THF and diethyl ether were distilled from sodium benzophenone ketyl and then further distilled from $NaAlH_4$ prior to use in mechanistic studies. THF-d_8 (Aldrich) was distilled from $NaAlH_4$ prior to use. Diisopropylamine and ethyl isobutyrate were purchased from Aldrich and distilled from CaH_2. $LiAlH_4$ and $LiAlD_4$ were purchased from Aldrich, allowed to stir in the desired solvent overnight, and then filtered in an argon atmosphere glovebox to obtain homogeneous solutions which were titrated before use (see below). Bromobutane and methyllithium (1.4 M in diethyl ether) were purchased from Aldrich and used as received. EDTA (Baker) was dried at 80−120 °C prior to use. An authentic sample of 2,2-dimethylhexane (Wiley Organics) was used in order to verify its formation in reactions involved in the mechanistic studies. All synthetic reactions were carried out under a nitrogen atmosphere. All mechanistic reactions were carried out in an argon atmosphere glovebox. Glassware was allowed to dry for at least 2 h at 200 °C and cooled in a desiccator prior to use. Solutions of aluminum hydride were prepared according to literature procedure.[26]

Instrumentation. GLC analyses were performed on a Varian 3700 gas chromatograph with a J & W DB-5 fused silica column (30 m, 0.25 mm i.d., 25 μm film thickness) equipped with a FID. Mass spectra were obtained from a VG 70-SE mass spectrometer equipped with a double sector magnetic analyzer. NMR spectra were obtained from a Varian Gemini 300 MHz instrument with chemical shifts reported relative to tetramethylsilane (δ 0.00). Photochemical experiments were carried out in Pyrex glassware using a 450 W Hanovia immersion lamp.

General. Yields were determined by gas chromatography relative to an internal standard. The following equation was used to calculate the deuterium incorporation of a compound from mass spectral data collected in the selected ion resonance mode:

$$\%\,\mathrm{D} = 100\{1 - [(A + B + C)/A][a/(a + b + c)]\}$$

where $A = \mathrm{M}$, $B = \mathrm{M} + 1$, and $C = \mathrm{M} + 2$ for a sample of natural abundance isotopes and $a = \mathrm{M}$, $b = \mathrm{M} + 1$, and $c = \mathrm{M} + 2$ for a sample with suspected deuterium incorporation. (Only the molecular ion was used to calculate % D.) In order for this equation to be valid, the $\mathrm{M} - 1$ peak for a nondeuterated sample must be negligible (<10% of M). A, B, and C are ideally obtained from a sample of natural abundance isotopes, but Benyon's Table[27] may be used for the values of A, B, and C if necessary.

Titration of LAH/LAD Solutions. A 0.10 mL aliquot of a homogeneous solution of LAH was quenched in ~30 mL of deionized water. EDTA (10.00 mL, 0.02 M) was added to the aluminum sample so that at least a 10% excess of EDTA was employed. The solution was boiled for 2−3 min until the cloudiness disappeared and then cooled to room temperature or below. Once cool, a buffer solution (10 mL of stock solution made from 77 g of ammonium acetate and 230 mL of glacial

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(25) For a review on radical rearrangements, see: Freidlina, R. Kh.; Terent'ev, A. B. *Acc. Chem. Res.* **1977**, *10*, 9.

(26) (a) Brown, H. C.; Yoon, N. M. *J. Am. Chem. Soc.* **1966**, *88*, 1464. (b) Brown, H. C.; Krishnamurthy, S. *J. Org. Chem.* **1980**, *45*, 849.

(27) Silverstein, R. M.; Bassler, G. C.; Morrill, T. C. *Spectometric Identification of Organic Compounds*, 4th ed.; John Wiley & Sons: New York, 1981.

acetic acid diluted to 1.0 L and adjusted to pH = 4) was added. Ethanol was then added to equal the amount of solution already present. Diphenylthiocarbazone (dithizone) indicator, 1−2 mL (60 mg of dithizone in 250 mL of absolute ethanol stored in a dark bottle), was also added. The excess EDTA was then titrated with zinc sulfate (0.02 M). The endpoint was noted by a sharp color change from blue to pink. All calculations were based on a 1:1 metal:EDTA stoichiometry.

Reduction of Alkyl Halides. To a flask, in an argon atmosphere glovebox at room temperature, were added the desired alkyl halide (0.1 mmol), decane (10 μL, an internal standard for GC), and the desired solvent. To this solution was added a homogeneous solution of LAH or LAD in the same solvent. The concentration of the reaction was calculated on the basis of the alkyl halide (usually 0.070 M). The reaction vessel was then covered in aluminum foil to shield the reaction from light. At the desired time, an aliquot (0.1−0.2 mL) was removed and quenched in water (0.2 mL). The organic compounds were extracted with diethyl ether (0.2 mL), and the organic layer was analyzed by GC and/or GC/MS.

Photochemical Reduction of 1-Iodo-2,2-dimethylhexane (20). To a Pyrex test tube in an argon atmosphere glovebox were added 1-iodo-2,2-dimethylhexane (0.040 g, 0.17 mmol), decane (15 μL, 0.077 mmol), and THF (1.69 mL). The test tube was capped with a rubber septum, removed from the glovebox, and placed in the sample holder for the Hanovia mercury lamp. An oil bubbler was added to the test tube through the rubber septum. A homogeneous solution of LAD in THF (1.2 M, 0.69 mL, 0.83 mmole) was added to the test tube by syringe. The lamp was turned on. At the desired time the lamp was turned off and an aliquot (0.2 mL) was removed from the test tube by syringe and quenched in water (0.2 mL). The organic compounds were extracted with diethyl ether (0.2 mL), and the organic layer was analyzed by GC and GC/MS. Note: the mercury lamp required a 5 min cooling time before it would turn on again. Therefore, for each 30 min of reaction, the lamp was on for only 25 min.

2,2-Dimethyl-1-hexanol. A solution of lithium diisopropylamide (LDA) in THF was prepared as follows: to a solution of diisopropylamine (12.3 mL, 8.88 g, 87.8 mmol) in 70 mL of THF was added a solution of methyllithium (1.3 M in ether, 57 mL, 74 mmol) at −78 °C under N_2. After 1 h a solution of ethyl isobutyrate (9.9 mL, 8.5 g, 73 mmol) in 20 mL of THF was added over 25 min. The solution was stirred at −78 °C for an additional 75 min. 1-Bromobutane (7.8 mL, 10. g, 73 mmol) was then added to the flask dropwise over 20 min. The solution was allowed to warm to room temperature. After 3.5 h the reaction was quenched with water (35 mL) and extracted with ether (3 × 50 mL). Combined ether layers were dried over $MgSO_4$, filtered, concentrated, and then distilled (105−110 °C/66 mmHg) to obtain a colorless liquid (10.3 g, 82% yield). A solution of the resulting ethyl 2,2-dimethylhexanoate in 40 mL of ether was added over 40 min to a suspension of $LiAlH_4$ (4.54 g, 120 mmol) in 100 mL of diethyl ether at 0 °C. After 2 h, the reaction was quenched with water (50 mL), the gelatinous residue was washed with diethyl ether (4 × 50 mL), and the combined washes were dried over $MgSO_4$. The product was obtained by vacuum distillation (109−113 °C/87 mmHg) in 73% overall yield (6.94 g: ^{1}H NMR ($CDCl_3$) δ 3.32 (s, 2H), 1.38−1.18 (m, 6H), 0.90 (t, 3H, $J = 6.7$ Hz), 0.86 (s, 6H).

1-Bromo-2,2-dimethylhexane (24). The title compound was prepared from 2,2-dimethyl-1-hexanol by a method analogous to the previously described synthesis of 1-bromo-2,2-dimethyl-5-hexene[5e] in 36% yield upon vacuum distillation (69−70 °C/14 mmHg: ^{1}H NMR ($CDCl_3$) δ 3.29 (s, 2H), 1.38−1.14 (m, 6H), 0.99 (s, 6H), 0.91 (t, 3H, $J = 7.0$ Hz); MS *m/e* (relative intensity) ($C_8H_{17}Br$) 179 (0.2), 177 (0.2), 137 (13), 135 (13), 99 (91), 57 (100).

1-Iodo-2,2-dimethylhexane (20). The title compound was prepared from 2,2-dimethyl-1-hexanol by a method analogous to the previously described synthesis of 2,2-dimethyl-1-iodo-5-hexene[5e] in 65% yield upon vacuum distillation (87−90 °C/17 mmHg): ^{1}H NMR ($CDCl_3$) δ 3.16 (s, 2H), 1.38−1.12 (m, 6H), 1.02 (s, 6H), 0.91 (t, 3H, $J = 6.9$ Hz); MS *m/e* (relative intensity) ($C_8H_{17}I$) 240 (3), 183 (39), 113 (95), 71 (100), 57 (99), 55 (64), 43 (82), 41 (72).

Tosylate of 2,2-Dimethyl-1-hexanol (23). To a solution of tosyl chloride (4.01 g, 21.0 mmol) in 50 mL of pyridine cooled in an ice bath was added 2,2-dimethyl-1-hexanol (1.025 g, 7.87 mmol). The mixture was allowed to stir for 24 h at 4 °C. Water (50 mL), followed by 10% aqueous HCl (50 mL) and diethyl ether (60 mL), was added to the flask. The water layer was extracted with ether (2 × 50 mL). The combined organic layers were washed with 60 mL of 10% HCl then 50 mL of 10% $NaHCO_3$. The organic layer was dried over $MgSO_4$, filtered, and concentrated by rotary evaporation. The product was purified by neutral alumina chromatography using petroleum ether as the eluent in 76% yield (1.71 g): ^{1}H NMR ($CDCl_3$) δ 7.80 (d, 2H, $J = 8.1$ Hz), 7.35 (d, 2H, $J = 8.1$ Hz), 3.68 (s, 2H), 2.46 (s, 3H), 1.30−1.00 (m, 6H), 0.85 (s, 6H), 0.84 (t, 3H, $J = 7.1$ Hz). MS *m/e* (relative intensity) ($C_{15}H_{24}O_3S$) 187 (15), 157 (14), 155 (31), 112 (21), 99 (56), 98 (60), 91 (51), 57 (100).

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