mixture was further analyzed in order to assess the extent of deuterium incorporation. The ^1H NMR spectrum was virtually identical with the spectra of the authentic samples, thus indicating that the cyclopropane derivative contains at least 80% the C–H compound. In the ^{13}C NMR spectrum two signals for the CH_3 carbons of 1,1-diphenyl-2-methylpropene (δ 22.60, 22.85, lower intensity, split) were found. GC–MS analyses gave M = 209 for 1,1-diphenyl-2-methylpropene (at least 80% of deuterium) and mass 208 (100) and 209 (35) for 1-methyl-2,2-diphenylcyclopropane (up to 15% of C–D compound).

Attempted Preparation of 1-Methyl-2,2-diphenylcyclopropylsamarium(III). *tert*-Butyllithium (1 mmol; pentane) was added dropwise, with stirring, to a solution of (*S*)-(+)-1-bromo-1-methyl-2,2-diphenylcyclopropane (7) (140 mg, 0.5 mmol, ee = 81%) in THF at -90 °C. The reaction mixture was stirred for 0.5 h and injected to a suspension of samarium triiodide in THF (prepared in situ from stoichometric amounts of samarium and iodine at -50 °C). After the reaction mixture was allowed to reach 0 °C (2 h) it was treated with 0.5 mL of DME and, after 0.5 h, quenched with MeOD. The reaction mixture was diluted with pentane (50 mL) and washed with water. The organic layer was separated and dried over magnesium sulfate and the solvent removed under reduced pressure. The oily residue was purified by radial chromatography (elution with pentane) to give 88 mg (85%) of 1-methyl-2,2-diphenylcyclopropane (3). The ^1H NMR spectrum was identical with that of an authentic sample (no deuterium incorporation). $[\alpha]^{25}_{Hg}$ -85° (*c* 1, $CHCl_3$, ee = 57%),[16] 78% retention of configuration.

The experiment described above was repeated starting with the (*S*)-(+)-7 (ee = 91%). The reaction mixture was kept at 0 °C for 18 h and then quenched with MeOD. No significant amount of deuterium could be found by ^1H NMR. $[\alpha]^{25}_{Hg}$ 62° (*c* 0.18, $CHCl_3$, ee = 47%) 52% retention of configuration.

^{7}Li NMR Experiment (Chemical Shifts Related to Lithium Iodide Solution in Water). 1-Methyl-2,2-diphenylcyclopropyllithium in THF was prepared in an NMR tube, and 5% of benzene-d_6 was added (for locking purposes). ^7Li NMR was taken at 104 MHz (Bruker 270-MHz apparatus). δ 0.5 LiBr, 2.1 broad, cyclopropyllithium derivative. Samarium triiodide suspension in THF was then added, and the NMR spectrum was taken again after 0.5 h. The broad signal at 2.1 completely disappeared.

Acknowledgment. This work was supported by a grant from the National Science Foundation to whom we are grateful.

Reinvestigation of a Criticized Mechanistic Probe Study of Metal Hydride Reductions of Alkyl Halides

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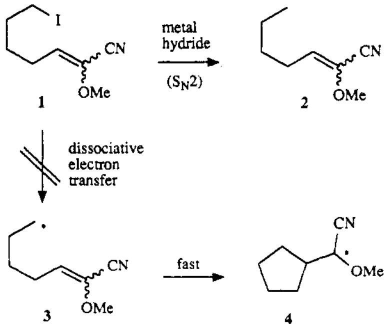
Published claims that $LiAlH_4$ promotes isomerizations of either 7-iodo-2-methoxy-2-heptenenitrile (1) or 2-methoxy-2-heptenenitrile (2) and the speculations resulting from these claims have led to new studies of reactions of 1 and 2. Highly isomerically enriched samples of 1 and 2 were prepared, and the equilibrium populations of isomers for both 1 and 2 were determined by iodine-mediated equilibrations. Reactions of isomerically enriched samples of 1 and 2 as well as mixtures of isomers with $LiAlH_4$ demonstrated that $LiAlH_4$-induced isomerizations did not occur. Absolute yields of product 2 from reactions of 1 with limited amounts of $LiAlH_4$ did not agree with previously reported results. Reactions of 2 with limited amounts of $LiAlH_4$ resulted in selective destruction of 2 with (*Z*)-2 reacting faster than (*E*)-2. On the basis of these facts and the fact that speculations regarding radical intermediates from reactions of 1 with $LiAlH_4$ are inconsistent with known kinetic values for radical reactions, the published criticisms of a study employing 1 as a probe for radical formation in reactions with metal hydrides are found to be without merit.

The use of mechanistic probes to implicate reactive intermediates and suggest the details of reaction pathways is of unquestioned utility. In studies of potential electron-transfer reactions of alkyl halides, a variety of radical probes have been applied, and the results of these studies have demonstrated unequivocally that radical intermediates are produced in many reactions; extensive pioneering studies by Ashby's group are perhaps best recognized in this regard.[2] However, one must remain aware of the shortcomings of probe studies that are product oriented; the implication of a specific reactive intermediate produced under a given set of conditions can provide inferences concerning the reaction mechanism, but establishing the mechanism is often considerably more difficult and usually requires detailed studies to verify that suggested pathways are kinetically competent. In the case of potential electron-transfer reactions of alkyl halides, probe studies can be seriously compromised by radical chain isomerizations of the alkyl halide that converts, for example, 5-hexenyl iodides to cyclopentylmethyl iodides in a process unrelated to the reaction of interest. The caveat is that small amounts of radical initiation from any of a

Scheme I



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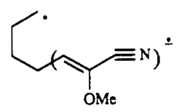
[2] Ashby, E. C. *Acc. Chem. Res.* 1988, *21*, 414.

variety of sources might result in large amounts of rearranged products, i.e. the isomerization sequence can amplify the extent of radical initiation.[3]

In 1987, Park, Chung, and Newcomb (PCN) reported a product-oriented probe study employing isomers of alkyl iodide **1** (and the corresponding bromide) in reactions with a number of metal hydrides. Probe **1** reacted with metal hydrides to give reduced products **2** and no dectectable amounts of cyclic products (Scheme I).[8] Compounds **1** can be considered as very sensitive radical probes because both isomers of radical **3** that would be formed from **1** in a dissociative electron-transfer reaction cyclize very fast.[9] With rate constants of $2.5 \times 10^8\ s^{-1}$ at 50 °C, these cyclizations are about 400 times faster than that of the parent 5-hexenyl radical and, indeed, much faster than other reported 5-*exo* cyclizations of alkyl, all-carbon systems. Therefore, it followed that if a given reaction milieu is compatible with cyclization of a simple 5-hexenyl system, then production of radicals **3** in the same medium will result in cyclizations to radical **4**. In reactions of probe **1** with a variety of metal hydrides, acycle **2** was formed, but no cyclic products from radical **4** were detected. The conclusion was that these reactions proceeded mainly by polar S_N2 pathways or their mechanistic equivalents in which no discrete radicals were formed; there was no evidence for radical-derived products that would have arisen by dissociative electron-transfer pathways.[8]

In recent publications, the Ashby group has reported that the reaction of probe **1** with $LiAlH_4$ has been reinvestigated.[2,10] It would appear that several $LiAlH_4$ reductions of mixtures of isomers of **1** resulted in mixtures of acyclic isomers **2** and no detectable amounts of cyclic products, similar results to those reported in the PCN study. However, reactions of **1** with $LiAlD_4$ admixed with 1,4-cyclohexadiene gave 92–96% deuterium incorporation in acyclic products **2**.[10a] In addition, the Ashby group reported that the isomer ratio of products **2** was not the same as the initial isomer ratio in probe **1**. They speculated that isomerization had occurred and that $LiAlH_4$ reacted with **1** "probably in the formation of the radical anion of the α,β-unsaturated nitrile...thus providing a possible reason for inhibition of cyclization".[2] The Ashby group presented no structure for an intermediate that would satisfy the above claim, but, apparently, the idea is that the purported radical anion moiety is long-lived and that subsequent formation of a radical from the alkyl halide moiety gives a species such as **5** that avoids cyclization and is trapped at the radical end by hydrogen atom transfer and then oxidized at the radical anion end by an unknown pathway to give a mixture of acyclic products **2** with a new isomer distribution. The 92–96% deuterium incorporation and the new isomer ratios of product **2** comprise the evidence that **1** reacted with $LiAlH_4$ to form radicals, i.e. that "single electron transfer" (SET) reactions occurred.



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Scheme II

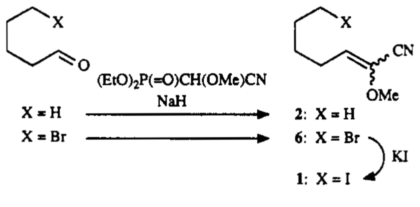

Table I. NMR Spectral Characteristics of 1, 2, and 6

compd	$^3J_{C-H}$ (Hz)[a]	$^1H\ \delta$ (OMe)	$^{13}C\ \delta$ (OMe)
(*E*)-2	11	3.59	56.7
(*Z*)-2	5	3.69	58.5
(*E*)-1	11	3.61	56.8
(*Z*)-1	4	3.71	58.5
(*E*)-6	11	3.62	56.8
(*Z*)-6	4	3.72	58.5

[a] Coupling constant of the vinyl proton to the cyano carbon determined by ^1H-coupled ^{13}C NMR spectroscopy; the uncertainty due to spectral resolution is 1 Hz.

The publications[2,10] of the above results with probe **1** have led us to investigate the chemistry in more detail. We will demonstrate in Discussion that the claim that the deuterium incorporation experiments implicate radical intermediates is untenable based on known kinetic values. The latter claim, that $LiAlH_4$-mediated isomerization of either **1** or **2** occurred, is the subject of new experimental results. We report that the purported isomerization of **1** and/or **2** by $LiAlH_4$ does not occur in competition with other reaction channels for both species and that the criticisms[2,10] of the PCN study and resulting conclusions are without merit.

Results

Compound Preparations and Identifications. As reported previously (Scheme II),[8] a mixture of isomers of iodide **1** was prepared by a Finkelstein reaction of a mixture of isomers of the corresponding bromide (**6**). Bromides **6** resulted from a Horner–Emmons reaction of 5-bromopentanal.[9] Similarly, a mixture of isomers of product **2** were available from pentanal as previously described.[9] Each pair of isomers of **1**, **2**, and **6** were cleanly resolved by GC.

Isomerically enriched samples of acycles **2** and iodides **1** were obtained by silica gel chromatography of the mixtures. One can also separate the isomers of bromides **6** by chromatography, and one sample of isomerically enriched iodide (*Z*)-**1** was prepared from isomerically enriched bromide (*Z*)-**6** to aid in compound authentication.

The isomers of each of the three compounds had distinct ^1H and ^{13}C NMR spectra (see the Experimental Section). Proton-coupled ^{13}C NMR spectra of each compound permitted structural identifications; the important values were the $^3J_{C-H}$ couplings of the vinyl protons to the nitrile

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(3) The alkyl halide radical chain isomerization sequence was described by Brace as a synthetic method as early as 1967[4] and has been observed more recently in several alkyl halide probe studies (for examples, see ref 2). The significance of the sequence as an interfering side reaction that complicates attempted mechanistic studies with alkenyl halide probes was enunciated some years ago[5] and has been described in the review literature.[6] Specific examples demonstrating the application of radical kinetics for calculations of product distributions in studies employing alkenyl halide probes have been published.[7]

(4) See, for example: Brace, N. O. *J. Org. Chem.* **1967**, *32*, 2711.

(5) (a) Newcomb, M.; Sanchez, R. M.; Kaplan, J. *J. Am. Chem. Soc.* **1987**, *109*, 1195. (b) Curran, D. P.; Kim, D. *Tetrahedron Lett.* **1986**, *27*, 5821.

(6) Newcomb, M.; Curran, D. P. *Acc. Chem. Res.* **1988**, *21*, 206. Newcomb, M. *Acta Chem. Scand.* **1990**, *44*, 299. Newcomb, M. In *Advances in Detailed Reaction Mechanisms*; Coxon, J. M., Ed., JAI Press: Greenwich, CT, in press.

(7) Newcomb, M.; Kaplan, J.; Curran, D. P. *Tetrahedron Lett.* **1988**, *29*, 3451.

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

(9) Park, S.-U.; Chung, S.-K.; Newcomb, M. *J. Am. Chem. Soc.* **1986**, *108*, 240.

(10) (a) Ashby, E. C.; Pham, T.; Madjdabadi, A. A. *J. Org. Chem.* **1988**, *53*, 6156. (b) Ashby, E. C.; Pham, T. N.; Amrollah-Madjdabadi, A. *J. Org. Chem.* **1991**, *56*, 1596.

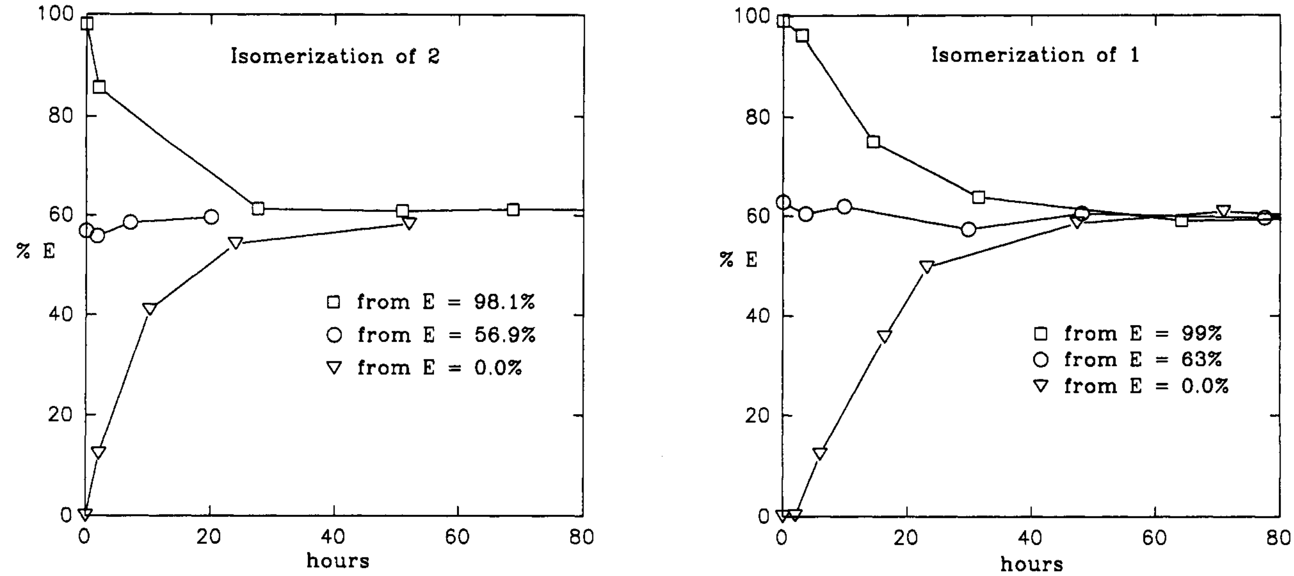

Figure 1. Results of iodine-catalyzed isomerizations of **2** and **1**.

carbons which were 4 or 5 Hz for the *Z* isomers (H and cyano syn) and 11 Hz for the *E* isomers (H and cyano anti). Table I contains a list of these observed $^3J_{C-H}$ couplings correlated with the characteristic chemical shifts of the methoxy signals from the ^{1}H and ^{1}H-decoupled ^{13}C NMR spectra.

The $^3J_{C-H}$ couplings to the cyano carbon atoms provide secure structural identifications, but the compound identities were further verified by chemical correlations. Thus, a sample of (*Z*)-**6** (>99% isomeric purity) was converted to a sample of (*Z*)-**1** (>99% isomeric purity) by reaction with KI in acetone. In addition, as discussed below, isomerically enriched samples of both isomers of **1** were reduced to the corresponding isomers of **2** upon treatment with $LiAlH_4$.

An error in NMR signal assignments by Ashby's group must be noted for clarification. They stated that their identifications were based on the chemical shifts of the methoxy singlets in the ^{1}H NMR spectra and that their *E*/*Z* ratios (presumably both for compounds **1** and **2**) were determined by methoxy signals at 3.70 (for the *E* isomers) and 3.60 (for the *Z* isomers) ppm.[11] As shown in Table I, these are the incorrect chemical shifts for the isomers of both **1** and **2**. However, the stereochemical labels assigned to the ratios of **1** and **2** reported by Ashby's group appear to be correct on the basis of our work. The two important observations are as follows: (1) the ca. 62:38 ratio (*E*/*Z*) for precursor **1** reported by Ashby's group[10a] is similar to that which we obtained in the preparation of bromides **6** and iodides **1** (from the mixture of bromides), (2) the direction of change in the isomer ratio of products **2** (increasing in the *E* isomer)[2,10] from $LiAlH_4$ reduction of **1** can be reproduced (although the yields cannot, see below). Thus, we conclude that the stereochemical results reported by Ashby's group are labeled correctly. In passing, we note that the attribution of the stereochemical assignments by Ashby[11] to previous work from our group is incorrect as no such assignments for **1**, **2**, or **6** were previously reported.[8,9]

Isomerization and Equilibration Reactions. Given the critical importance of the purported $LiAlH_4$-mediated isomerizations of **1** or **2**, a study of isomerizations and equilibrations of these compounds was in order. Reactions of each isomer of **1** and of **2** with $LiAlH_4$ did not result in facile isomerizations (see below). However, isomerizations could be achieved by treatment with a catalytic amount of molecular iodine.

Samples of **2** of isomeric ratios 98.1:1.9, 56.9:43.1, and 0.0:100.0 (*E*/*Z*) in THF containing 5–10 mol % of I_2 were allowed to stand at room temperature. Aliquots were removed periodically, and the isomer composition of **2** was determined by GC. The results, shown in Figure 1, clearly demonstrate an approach to equilibrium. The sample originally containing 98.1% (*E*)-**2** isomerized to a mixture containing (61.1 ± 0.2)% of the *E* isomer at 28 h which was invariant until the termination of the experiment at 120 h. The equilibrium *E*/*Z* ratio for **2** in THF at room temperature is 1.57 ± 0.01.

Probe **1** displayed similar behavior upon treatment with I_2. Thus, samples of **1** of isomeric ratios 99:1, 63:37, and 0.0:100.0 (*E*/*Z*) gave mixtures of isomers of **1** containing (61.2 ± 0.6)% of the *E* isomer after 127–142 h. Figure 1 shows the results for the first 80 h of the experiments; again, an approach to equilibrium is apparent. The equilibrium *E*/*Z* ratio for **1** in THF at room temperature is 1.58 ± 0.04. As one might have expected, the equilibrium ratios for **1** and **2** are virtually identical.

It is important to note that the equilibrium populations of isomers of both probe **1** and its $LiAlH_4$ reduction product **2** are nearly the same as the population of isomers obtained in the initial preparation of compound **1** both in this work and in the Ashby report.[10a] Because any isomerization process of these two compounds must result in an approach to the equilibrium values, the use of a starting mixture of nearly equilibrium composition would preclude the observation of the isomerization process.

$LiAlH_4$ Reactions. With purified samples and firm identifications of the isomers of **1** and of **2** in hand, reactions of each isomer of **1** with $LiAlH_4$ in THF were studied. The primary alkyl iodide moiety in **1** was readily reduced by $LiAlH_4$ to give product **2**, but compound **2** was not stable in the presence of $LiAlH_4$; we presume that the α,β-unsaturated nitrile moiety was subject to reaction, but the products from reaction of **2** were not determined.

Table II contains some of the results from the $LiAlH_4$ reduction experiments. Absolute yields were determined by quantitative GC employing an internal hydrocarbon standard. Reactions of the isomerically enriched samples of (*E*)- and (*Z*)-**1** gave the corresponding isomer of product

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(11) Footnote 8 in ref 10a.

Table II. Results of Reactions of 1 with $LiAlH_4$ in THF[a]

$[1]_0$[b]	% E_0[c]	% Z_0[c]	$[LiAlH_4]_0$[b]	time (h)	% yields[d] (E)-1	(Z)-1	(E)-2	(Z)-2
0.037	99	1	0.038	0.5	23	<1	59	1
0.06	98	2	0.038	0.5	26	<1	45	<1
0.067	99	1	0.016	0.5	68	1	17	<1
0.036[e]	99	1	0.036	4	30	1	20	<1
0.047	1	99	0.039	1	<1	<1	<1	22
0.041	62	38	0.039	3	23	4	32	7

[a] Reactions run at 24 °C unless noted. [b] Initial molar concentration. [c] Initial percentage of isomers. [d] Absolute percent yield at time *t*. [e] Run at 0 °C.

Table III. Results of Reactions of 2 with $LiAlH_4$ in THF at 24 °C

$[2]_0$[a]	% E_0[b]	% Z_0[b]	$(E/Z)_0$	$[LiAlH_4]_0$[a]	time (h)	% E_t[c]	% Z_t[c]	$(E/Z)_t$
0.024	0	100		0.011	1.7	0	66	
0.077	99	1		0.017	3.7	59	0	
0.041	8	92		0.013	1	5	41	
0.049	91	9		0.014	7	69	0	
0.13	64	36	1.78	0.028	1	56	30	1.87
0.14	67	33	2.0	0.054	8	54	15	3.6
0.030	52	48	1.08	0.0086	1	38	24	1.58

[a] Initial molar concentration. [b] Initial percentage of isomers. [c] Absolute percentage remaining at time *t*.

2. In no case did the absolute yield of the minor isomer of 2 exceed the amount of the minor isomer of 1 initially present in the sample. Similarly, no isomerization of 1 was apparent in reactions of isomerically enriched samples; the amount of the minor isomer of 1 in no case exceeded the amount initially present.

The final reaction shown in Table II was designed to match closely one of the reactions reported by Ashby's group wherein a 62:38 mixture (*E*/*Z*) of 1 was employed. The ratio of isomers of product 2 formed (4.6:1) was close to the ratio reported by the Ashby group (5.2:1), but the yield of 2 (53% based on converted 1) was substantially lower than the 94% yield reported.[10a] Importantly, the sum of the yields of (*E*)-1 and (*E*)-2 was less than the amount of (*E*)-1 initially employed.

In order to understand better the origin of the altered *E*/*Z* ratios in product 2, we investigated reactions of mixtures of isomers of 2 and isomerically enriched (*E*)-2 and (*Z*)-2 with limited amounts of $LiAlH_4$. Some of the results are given in Table III. The highly enriched samples of (*E*)-2 and (*Z*)-2 showed no evidence for formation of the alternative isomer in reactions with $LiAlH_4$, and it is clear that $LiAlH_4$-promoted isomerization was not competitive with destruction of the compounds. For the final three reactions listed in Table III, near equilibrium and near equimolar mixtures of the isomers of 2 were allowed to react with $LiAlH_4$. From these reactions, it is seen that (*Z*)-2 reacted with $LiAlH_4$ faster than did (*E*)-2. Thus, in these reactions, the *E*/*Z* ratio of the remaining 2 increased from that initially present. As was the case with the reaction of the mixture of isomers of 1, this behavior mimicked in a qualitative sense the change in isomer ratios of product 2 reported by Ashby's group from reactions of near equilibrium mixtures 1 with $LiAlH_4$.[2,10]

Discussion

In the published criticisms of the PCN study of reactions of probe 1 with metal hydride reagents, the Ashby group cited two pieces of experimental evidence. The more important result was stated to be the fact that the isomer ratios of reduction product 2 were not the same as those in the starting mixture of probe 1. The presumption was made that isomerization occurred by formation of a stable radical anion at the nitrile end of the molecule that somehow prevented cyclization when a radical was produced at the other end. This then led to further speculation that electron-transfer reactions from $LiAlH_4$ to 1 were important both in the purported isomerizations and in the reduction of the alkyl iodide moiety.[2,10] Accepting the rationalization of $LiAlH_4$-mediated isomerizations as a working hypothesis, one would conclude that an equilibrium population of isomers of product 2 should have been produced from any isomeric mixture of probe 1. In fact, however, the reported isomeric mixtures of product 2 ranged from 2.3:1 to 49:1 (*E*/*Z*) for reactions of a 62:38 (*E*/*Z*) mixture of 1 with $LiAlH_4$,[10a] far from the equilibrium ratio of 1.58.

Our results show that $LiAlH_4$-mediated isomerization of either 1 or 2 does not occur. As noted above, the equilibrium population of isomers both of probe 1 and of its reduction product 2 were nearly equal to the starting isomer ratio of 1 employed in the Ashby work,[10a] and, if isomerizations of either 1 or 2 had occurred, then the isomer populations of the mixtures would have remained virtually unchanged. The formation of nonequilibrated mixtures of 2 from a mixture of 1 that contained the proper isomer distribution for equilibrated 2 can only be explained by selective reaction of one of the isomers of either 1 or 2 or both. In the case of partial conversion of 1, one isomer of 1 might have been reduced to 2 faster than the other to produce a nonequilibrated mixture of 2. However, in the cases where consumption of 1 was complete or nearly complete, the changes in isomer ratios for 2 must have arisen by selective conversion of one isomer of 1 to a product other than 2, selective destruction of one isomer of 2, or a combination of both. In any event, the product ratios reported by Ashby's group require that the reactions occurred *under nonequilibrating conditions*.

The inferential conclusion based on the equilibrium ratios of products 2 was directly verified by the results obtained from reactions of the individual isomers of 1 with $LiAlH_4$. Each isomer of 1 was reduced to the corresponding isomer of 2 in a process that was stereospecific. This is neither remarkable nor unexpected given that the site of isomer differentiation is quite removed from the site of reduction; the important point is that no isomerization occurred.

As a corollary to the discussion thus far, many of the absolute product yields reported[10a] by Ashby's group appear to be error. For four reactions involving high conversion of a 62:38 (*E*/*Z*) mixture of 1, they report yields of (*E*)-2 ranging from 78 to 91%. However, the equilibrium value of 2 of 61:39 (E/Z) in THF at room temperature requires that the maximum possible yield of (E)-2 from the 62:38 mixture of 1 is 62% formed under nonequilibrating conditions. Experimentally, we were unable to reproduce a specific result[10a] (entry 6 in Table II). We also note that the high yield (98%) of a mixture of isomers of 2 from reaction of 1 with $LiAlH_4$ reported in the PCN study[8] could not be reproduced in this work; the greatest yield of 2 based on converted 1 found in this work was only 78%.

The origins of the differences in reported absolute yields of 2 are not completely clear, but they might involve incorrect GC response factors. GC analyses were employed in the PCN study,[8] but the method of product quantitation used by the Ashby group was not reported.[2,10] In this work, weight response factors for each isomer of 1 and 2 were determined independently. With flame ionization detection and splitless injection mode, relative to undecane, both isomers of 1 had response factors of 0.24, and both isomers of 2 had response factors of 0.51. In molar terms, this represents an 11–12% greater sensitivity for 2 under our conditions. The unknown byproducts of the $LiAlH_4$ reactions with 2 did not elute in the regions of compounds 1 or 2 under our GC conditions, and product analyses of reactions that did not contain internal standards would be highly inaccurate.

The *relative yields* of product 2 reported by Ashby's group are likely to be accurate on the basis of our determination that the GC response factors for the two isomers were essentially identical. They report increased E/Z ratios in product 2 relative to those in the initial mixture of isomers of 1. As noted above, in cases where most or all of 1 was consumed, these changes signal selective destruction of the Z isomer of 1, 2, or both. For compound 2, this is exactly the behavior we observed; (Z)-2 was consumed by $LiAlH_4$ more rapidly than (E)-2, and, at partial reaction of 2, mixtures of isomers of 2 were enriched in (E)-2 by kinetic discrimination. Thus, the qualitative aspects of the reports by Ashby's group are explained.

The second piece of evidence used to discredit the PCN study concerns the detection of 91.5–95.7% deuterium incorporation in acyclic product 2 when probe 1 was treated with $LiAlD_4$ in the presence of 1,4-cyclohexadiene; methods of isotopic analysis of the product or of $LiAlD_4$ admixed with 1,4-cyclohexadiene were not reported.[10a] These observations are stated to be "indicative of a radical intermediate".[10b] However, this supposition is clearly incorrect on the basis of known radical reaction rate constants. The rate constants[9] for cyclization of radicals 3 at 50 °C are about 2.5×10^8 s^{-1}, whereas the rate constant for reaction of 1,4-cyclohexadiene with primary radicals at 50 °C is in the range of $(1–5) \times 10^5$ M^{-1} s^{-1}.[12] Therefore, 1 M 1,4-cyclohexadiene will trap at most about 0.2% of radical 3 in competition with cyclization. As unfavorable a competition as this is, 1,4-cyclohexadiene actually reacts with primary radicals faster than does either $LiAlH_4$ or THF.[13] The apparent conclusion is that if radical 3 had been formed in the reaction of 1 with $LiAlD_4$ and 1,4-cyclohexadiene, then it would have predominantly cyclized.

Why does probe 1 produce no detectable amounts of cyclic products in the reaction with $LiAlH_4$ when simple alkenyl iodides, including primary iodides, yield measurable (often substantial) amounts of cyclic products in similar reactions? We have suggested that this results from the onset of the radical chain isomerization process in the cases of simple alkenyl iodide reactions and the failure of the isomerization process in the case of probe 1.[6] Although radicals 3 can readily cyclize to radical 4, the highly stabilized "capto-dative" radical 4 is unlikely to abstract an iodine atom from probe 1 at a rate that can compete with other radical reaction channels. Thus, the radical chain isomerization process is expected to collapse in the first cycle. The amount of cyclic products from probe 1, undetectable in the case of metal hydride reductions,[8] reflects the amount of radical initiation by SET or any other process.

Exact energetic calculations that support the above point are not possible due to insufficient experimental data, but reported bond dissociation energy (BDE) and radical stabilization energy (RSE) values permit a meaningful comparison. Substitution of a hydrogen atom in methane with a cyano or a methoxy group results in each case in about a 12 kcal/mol decrease in the C–H BDE, and, hence, a 12 kcal/mol RSE for each group for the isodesmic reaction in eq 1.[16] Recent experimental studies and theoretical calculations have been concerned with whether

$$GCH_2^{\bullet} + CH_4 \rightarrow GCH_3 + CH_3^{\bullet} \qquad (1)$$

radical substitution with both an acceptor (e.g. cyano) and a donor (e.g. methoxy) will result in additive or superadditive stabilizations (the crux of the capto-dative debate), but it is clear that such multiple substitution will yield a net RSE nearly equal to the sum of the individual contributions even if one adjusts for a saturation effect.[17] It would appear to be safe to assume that radical 4 is about 20 kcal/mol more stable than a simple primary radical. Nevertheless, in the absence of actual rate constants and measured C–I bond strengths, conjectures regarding diminishingly small rate constants for iodine atom transfer from 1 to 4 remain just that.

This point is important for a conclusion reached by the Ashby group that does not have experimental support.[2,10] They have presented probes such as 7 as superior to 1 because, it is claimed, tertiary radical 8 will not abstract an iodine atom from 7. Thus, reactions of species such as 7 that give rearranged products supposedly support SET reaction pathways because it is presumed that radical chain isomerization of 7 is not possible. However, whereas the BDE value for Et–H is 6 kcal/mol greater than that of t-Bu–H, the BDE value for Et–I is only 3 kcal/mol greater than that of t-Bu–I;[18] that is, iodine abstraction from Et–I by t-Bu$^{\bullet}$ is endothermic by only 3 kcal/mol. Further, it is known that iodine atom transfers from simple alkyl iodides to a primary alkyl radical are fast[5a] and that iodine atom transfer equilibria can be established between simple alkyl iodides and simple alkyl radicals.[19] Especially noteworthy in regard to the latter point is the fact that a simple secondary and tertiary system readily equilibrates via iodine atom transfer;[19] here the reaction of the tertiary

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[12] (a) Hawari, J. A.; Engel, P. S.; Griller, D. *Int. J. Chem. Kinet.* **1985**, *17*, 1215. (b) Newcomb, M.; Park, S.-U. *J. Am. Chem. Soc.* **1986**, *108*, 4132.

[13] A rate constant for reaction of a radical with $LiAlH_4$ (ca. 4×10^3 M^{-1} s^{-1} at 30 °C) can be derived[8] from extant data.[14] The pseudo-first-order rate constant for reaction of a primary radical with THF at room temperature is 6×10^3 s^{-1}.[12b,15] Comparisons of various radical reaction rate constants important in mechanistic probe studies have been published.[6]

[14] Beckwith, A. L. J.; Goh, S. H. *J. Chem. Soc., Chem. Commun.* **1983**, 907.

[15] Newcomb, M.; Kaplan, J. *Tetrahedron Lett.* **1988**, *29*, 3449.

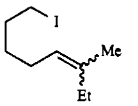
[16] McMillen, D. F.; Golden, D. M. *Annu. Rev. Phys. Chem.* **1982**, *33*, 493.

[17] See Bordwell, F. G.; Gallagher, T.; Zhang, X. *J. Am. Chem. Soc.* **1991**, *113*, 3495 and references therein. Pasto, D. J. *J. Am. Chem. Soc.* **1988**, *110*, 8164 and references therein.

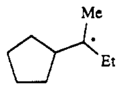
[18] Griller, D.; Kanabus-Kaminska, J. M.; Maccoll, A. *THEOCHEM* **1988**, *40*, 125.

[19] Castelhano, A. L.; Griller, D. *J. Am. Chem. Soc.* **1982**, *104*, 3655.

radical with the secondary alkyl iodide (endothermic by 2 kcal/mol)[18] must be fast. We suggest that extant evidence weighs in favor of the premise that a simple tertiary radical will abstraction an iodine atom from a primary alkyl iodide and that the claims to the contrary require kinetic verification.



7



8

In conclusion, the published[2,10] criticisms of the PCN study have been shown to be without merit as they rely on inaccurate product yields and untested assumptions regarding isomerizations. The reported[2,10] ratios of product 2 are far from the equilibrium values that should have resulted if isomerization of either 1 or 2 had occurred, and the purported[2,10] isomerizations of probe 1 or its reduction product 2 in reactions with $LiAlH_4$ have been shown in this work not to occur. The reported[2,10] changes in isomer ratios in mixtures of product 2 from those in the original reagent 1 most likely reflect the unequal rates of destruction of the isomers of 2 by $LiAlH_4$ as demonstrated in this work. The reported[2,10] detection of small amounts of protium incorporation into acyclic products 2 from reductions of 1 with $LiAlD_4$ admixed with 1,4-cyclohexadiene does not implicate a free-radical intermediate from probe 1 because known kinetic values require that such a radical must cyclize much faster than it can be trapped by any agent in the reaction medium. Our results suggest that the yields of 2 reported in the PCN study are too high, but they support the conclusions originally presented in that study;[8] metal hydride reductions of probes 1 are best explained as conventional polar S_N2 reactions or their mechanistic equivalents, and the studies provide no evidence for formation of radical 3 or for the SET reaction pathway.

Experimental Section

General. NMR spectra of $CDCl_3$ solutions containing Me_4Si as an internal standard were recorded on a Varian XL-200E at 200 MHz (^1H) and 50 MHz (^{13}C) employing standard pulse sequences. ^1H-coupled ^{13}C NMR spectra were recorded on the same instrument without proton irradiation; the tip angle was ca. 35°, and the delay was 1 s.

Radial chromatography was accomplished on a Chromatotron (Harrison Research, Model 7924T) using silica gel coated plates. GC was accomplished on Varian Model 3400 instruments equipped with flame ionization detectors; 15 m × 0.5 mm columns containing SE-30 (Alltech) and DB-5 (J&W Scientific) were employed. GC response factors were determined relative to decane or undecane standards. In both GC and LC on silica gel, the *Z* isomers of 1, 2, and 6 eluted before the *E* isomers.

Commercial $LiAlH_4$ (Aldrich) was used as received. THF was distilled immediately before use from a solution under nitrogen and containing potassium benzophenone.

2-Methoxy-2-heptenenitrile (2) was prepared as a mixture of isomers from pentanal as previously reported.[9] The isomer ratio in the mixture was 57:43 (*E*/*Z*) as determined by GC. A mixture of isomers was separated by radial chromatography (2-mm silica gel plate, hexanes elution) to give the individual isomers. The procedure gave one sample of (*Z*)-2 that contained <0.1% of the alternate isomer and one sample of (*E*)-2 that contained 0.3% of the alternate isomer as determined by GC which were used for NMR characterizations.

NMR spectra of (*E*)-2: (^1H) δ 0.90 (t, J = 6.7 Hz, 3 H), 1.34 (m, 4 H), 2.24 (apparent q, J = 7.7 Hz, 2 H), 3.59 (s, 3 H), 5.51 (t, J = 7.7 Hz, 1 H); (^{13}C) δ 13.68, 21.93, 27.50, 31.49, 56.74, 113.56, 120.21, 131.60.

NMR spectra of (*Z*)-2: (^1H) δ 0.88 (t, J = 6.7 Hz, 3 H), 1.34 (m, 4 H), 2.18 (apparent q, J = 7.6 Hz, 2 H), 3.69 (s, 3 H), 5.51 (t, J = 7.7 Hz, 1 H); (^{13}C) δ 13.69, 22.19, 24.90, 30.47, 58.48, 114.31, 128.12, 129.69.

7-Iodo-2-methoxy-2-heptenenitrile (1) was prepared as a mixture of isomers from the corresponding bromide (6) as previously reported.[8] ^1H NMR spectroscopy showed that the crude product contained no unreacted bromide and that the isomer ratio in the crude product was 62:38 (*E*/*Z*). Column chromatography of a portion of the crude product (silica gel, hexanes–ethyl acetate elution, 99.5:0.5) provided one sample of (*Z*)-1 that contained <0.1% contamination of the alternate isomer as determined by GC. The fraction from column chromatography containing (*E*)-1 was further purified by radial chromatography (2-mm silica gel plate, hexanes–ethyl acetate elution) to give a sample of (*E*)-1 that contained <0.1% contamination of the alternate isomer as determined by GC. These samples were used for NMR characterization.

Alternatively, isomerically enriched samples of 1 could be prepared from isomerically enriched samples of bromide 6 that had been separated by radial chromatography (2-mm silica gel plate, hexanes–ethyl acetate elution) by reaction with KI.[8] This approach was employed in a redundant synthesis of (*Z*)-1 (isomeric purity >99% as determined by NMR) from a sample of (*Z*)-6 (isomeric purity >99% as determined by NMR).

NMR spectra of (*E*)-1: (^1H) δ 1.4–2.0 (m, 4 H), 2.28 (apparent q, J = 7.6 Hz, 2 H), 3.19 (t, J = 6.8 Hz, 2 H), 3.61 (s, 3 H), 5.48 (t, J = 8 Hz, 1 H); (^{13}C) δ 6.14, 26.77, 30.14, 32.39, 56.75, 113.35, 118.77, 132.04.

NMR spectra of (*Z*)-1: (^1H) δ 1.4–2.0 (m, 4 H), 2.22 (apparent q, J = 7.5 Hz, 2 H), 3.16 (t, J = 6.9 Hz, 2 H), 3.71 (s, 3 H), 5.48 (t, J = 7.7 Hz, 1 H); (^{13}C) δ 6.05, 23.96, 29.07, 32.61, 58.48, 113.92, 126.40, 130.12.

NMR spectra of (*E*)-6: (^1H) δ 1.4–2.0 (m, 4 H), 2.28 (apparent q, J = 7.4 Hz, 2 H), 3.42 (t, J = 6.6 Hz, 2 H), 3.62 (s, 3 H), 5.50 (t, J = 8 Hz, 1 H); (^{13}C) δ 26.98, 27.83, 31.71, 33.14, 56.75, 113.37, 118.82, 132.07.

NMR spectra of (*Z*)-6: (^1H) δ 1.4–2.0 (m, 4 H), 2.22 (apparent q, J = 7.5 Hz, 2 H), 3.40 (t, J = 6.6 Hz, 2 H), 3.72 (s, 3 H), 5.50, (t, J = 7.7 Hz, 1 H); (^{13}C) δ 24.25, 26.86, 31.99, 33.09, 58.53, 117.89, 126.47, 132.56.

Equilibration Experiments. Samples of 1 and of 2 (0.03 to 0.06 M) containing iodine (ca, 5–10 mol %) and an internal standard of decane in THF were prepared and allowed to stand at 24 ± 2 °C. Periodically, an aliquot was removed and added to water. The resulting mixture was diluted with ether, and the organic phase was washed with an aqueous solution of sodium bisulfite and dried ($MgSO_4$). The samples were analzyed by GC. Results are given in the text.

Reduction Experiments. Samples containing 1 or 2 and an internal standard of decane or undecane in THF under nitrogen were prepared, and to these were added by syringe $LiAlH_4$ solutions in THF. For reactions of 2, the supernatent solution from the $LiAlH_4$ mixture was transferred. For reactions of 1, the $LiAlH_4$ solution was filtered and standardized before use.[20] After various reaction times, aliquots were withdrawn by syringe and rapidly added to water. The samples were diluted with ether, and the phases were separated. The organic phase was washed with saturated aqueous NaCl solution and dried ($MgSO_4$). The samples were analyzed by GC. Results are presented in Tables II and III.

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[20] Brown, H. C. *Organic Synthesis via Boranes*; Wiley: New York, 1975; p 243.