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ELECTRON TRANSFER IN THE REDUCTION OF PRIMARY HALIDES BY METAL HYDRIDES

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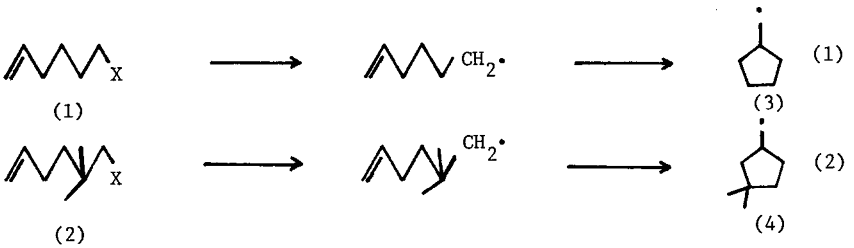
Abstract: The reactions of various main-group metal hydrides with 1-halo-5-hexenes and with 1-halo-2,2-dimethyl-5-hexenes produce both straight chain and cyclized reduction products. The formation of cyclic hydrocarbons clearly indicates the presence of radical intermediates during the course of these reactions.

For many years, main-group metal hydrides have been used as reducing agents for a wide variety of organic substrates. In general, hydrides such as $LiAlH_4$ have been thought to react as nucleophylic reagents in donating a hydride ion to substrate molecules, such as organic halides. However, various organic halides, e.g., aryl, vinyl, bridgehead, and cyclopropyl halides, that are generally considered to be inert toward an S_N2 or S_N1 process, are readily reduced to hydrocarbons by $LiAlH_4$.[2-3]

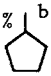
Previous mechanistic studies have described the kinetics of metal hydride reductions of organic halides.[3] Based on stereochemical studies, four-centered,[4] radical,[5] and S_N2[5] mechanisms have been proposed. More recent studies indicate that the reductions of aryl and vinyl halides occur with the intervention of radical intermediates.[6] The results presented herein show conclusively that the reduction of primary alkyl bromides and iodides by several metal hydrides (in addition to $LiAlH_4$) involve radical intermediates.

The alkyl radical, 5-hexene-1-yl, is known to cyclize rapidly ($k_{cyc} = 10^5 sec^{-1}$) yielding the cyclopentymethyl radical (eq. 1)[7], and the radical 2,2-dimethyl-5-hexene-1-yl cyclizes in a similar fashion to yield the 3,3-dimethylcyclopentylmethyl radical (eq. 2). Thus, the 1-halo-5-hexenes, (1) and the 1-halo-2,2-dimethyl-5-hexenes, (2), can serve as probes for the detection of free radical intermediates during metal hydride reduction of primary alkyl halides by the observation of cyclized hydrocarbon products.



In Table 1 is presented data for the reduction of (1) in the series X = Cl, Br, I, in THF. Note that when X = I, small amounts of cyclized hydrocarbon are formed in the reductions with hydrides of magnesium and boron (entries 7-9), however AlH_3 (entry 6) gives a significantly greater

TABLE 1: Reduction of (1), by Metal Hydrides in THF.[a]

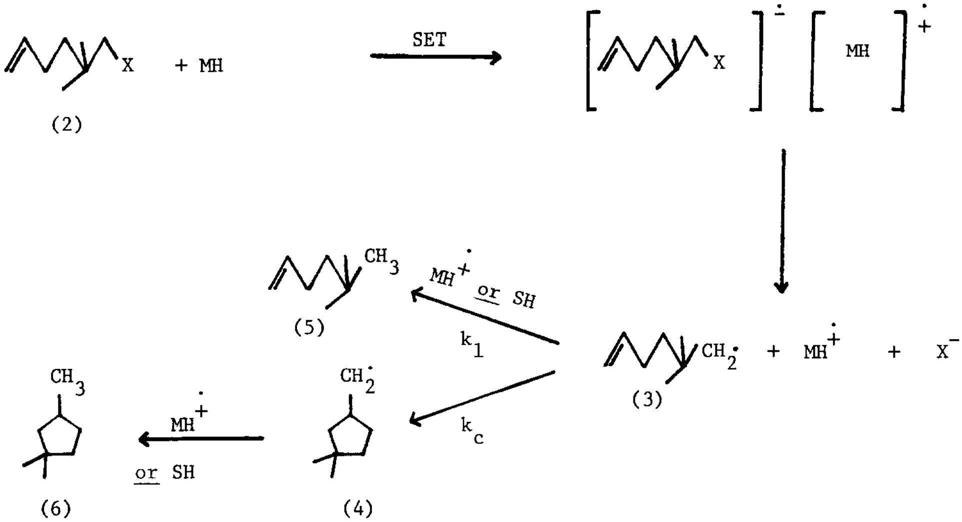
Entry No.	X in $CH_2=CH(CH_2)_4X$	Metal[c] Hydride	Reaction Time (hrs)	%  [b]	%  [b]
1	Cl	$LiAlH_4$	168	0.00	51
2	Br	$LiAlH_4$	24	0.00	97
3	Br	AlH_3	24	0.00	26
4	I	$LiAlH_4$	1	0.00	94
5	I	$LiAlD_4$	1	0.00	95[d] (100% d_1)
6	I	AlH_3	24	7.1	29
7	I	MgH_2	24	0.71	72
8	I	HMgCl	24	0.70	32
9	I	$LiBEt_3H$	1	0.50	52

[a] Reactions conducted in the dark at 24°C using 0.10 M initial concentrations of metal hydrides and organic halide. [b] Percent yields of hydrocarbons determined by gas chrom. using a 25 ft. column of 15% TCEP with 10% apiezon L at 65° and 50 ml/min with a flame ionization detector calibrated with cyclohexene as internal standard (limits of detection 0.50%). [c] Metal hydrides were analyzed by hydrogen gas evolution upon hydrolysis employing a standard vacuum line, and by EDTA titration of aluminum where applicable. [d] The 1-hexene was determed to be 100% d_1 incorporated by GC-MS.

amount of cyclic product. On the other hand, reduction of (1) when X = I, yields no detectable trace of methycyclopentane. Thus, although the relatively small percentages of cyclized product shown in Table 1 are indicative of radical intermediates, the evidence is not overwhelming. However, the rate of conversion of the 5-hexene-1-yl radical to hydrocarbon product might be faster than the rate of cyclization to the methylcyclopentyl radical. Consequently, the 1-halo-2,2-dimethyl-5-hexenes (2) where X = Cl, Br and I were prepared and allowed to react with several main-group metal hydride reagents. It was thought that if radical intermediates are involved in the reduction of primary halides, the steric hindrance of the neo-pentyl system should slow down the conversion of alkyl radical to hydrocarbon, allowing time for more cyclization to occur [(4) ⟶ (6)] as in Scheme 1 below.

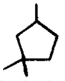
The data for the reduction of (2) in the series X = Cl, Br, and I by various hydride reagents are presented in Table 2. Note that when X = I, the major hydrocarbon product is the cyclized 1,1,3-trimethylcyclopentane, (6), regardless of the metal hydride used, except in the case of entry 11. Indeed, such evidence clearly indicates that (2) reacts with metal hydrides via a single electron transfer process, to produce an alkyl radical which then abstracts a hydrogen aton to yield reduction product (Scheme 1). Since the products in entry 7 Table 2 show 65% and 57% d_1 incorporation, the alkyl radical intermediate must abstract a hydrogen atom from both the solvent and the metal hydride radical cation to yield the final reduction product. The fact that (3) abstracts hydrogen from both the radical cation and solvent whereas its non-branched analog (Table 1, entry 5) shows only abstraction from the radical cation, indicates that indeed hydrogen abstraction by the radical produced from (2) is much slower than radicals produced from (1).

SCHEME I



The reaction in entry 11, Table 2 is clearly an exceptional case, since the major product is 5,5-dimethyl-1-hexene. Thus, when $LiEt_3BH$ is the reducing agent, k_1 must be significantly greater than k_c or the reduction is mainly via a polar process.

Table 2: Reduction of (2) by Metal Hydrides in THF.

Entry No.	X in  X	Metal[a] Hydride	Reaction Time (hrs.)	%  (b)	%  (b)
1	Cl	$LiAlH_4$	48	0.0	0.0
2	Br	$LiAlH_4$	90	3.1	2.1
3	Br	$LiAlH_4$	480	9.8	7.5
4	Br	AlH_3	480	0.0	0.0
5	I	$LiAlH_4$	24	3.4	81
6	I	$LiAlH_4$	98	2.5	96
7	I	$LiAlD_4$	48	5.5(65% d_1)	69(57% d_1)
8	I	AlH_3	54	0.0	25
9	I	HMgCl	54	0.0	0.40
10	I	MgH_2	54	7.1	34
11	I	$LiEt_3BH$	24	64	2.4

[a] Experimental conditions were the same as in Table 1, a. [b] Gas chrom. analysis conducted on 25 ft. 8% Apiezon L column at 65° with 20 ml/min and a FID calibrated with 1-heptone as internal standard (limits of detection 1.5%). [c] The deuterium incorporation (% d_1) was determined by GC-MS.

The present results clearly establish that reduction of (2) by several main group metal hydrides takes place via a SET pathway. These results indicate either (1) the reduction of primary alkyl halides by hydrides takes place by a SET pathway or (2) both polar and SET pathways are possible -- a polar pathway predominating for non-sterically hindered alkyl halides (faster reaction) and a SET pathway predominating for reactions involving sterically hindered halides (e.g. (2)) where the polar pathway (nucleophylic attack) would be expected to be hindered.

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