Reduction of 1-Bromo-2,4,6-trineopentylbenzene with Lithium Aluminium Hydride: Evidence for Radical Intermediates

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LiAlD$_4$ reduction of the title compound in ether solvent provides the hydrocarbon product, in which a substantial amount of deuterium was found in the neopentyl side chain, thus providing evidence for radical intermediates in the reduction.

An increasing number of reactions in which various organic functional groups are reduced by metal hydrides such as LiAlH$_4$ have recently been reported to proceed *via* radical intermediates or by an electron-transfer pathway, as opposed to the conventional, ionic hydride transfer in a single step.[1—4] The radical intermediates in these studies have either been directly observed by spectroscopic means[3,4] or been inferred by utilization of chemically based radical probes.[1,2] We have now examined the LiAlH$_4$ reduction of an aryl bromide by means of a chemically based radical probe that has not previously been utilized in the mechanistic studies, and report our observations which support the previous suggestion that the reduction involves the radical pathway to a significant degree.

Ingold and his co-workers reported that in kinetic e.s.r. experiments the reaction of the trimethyltin radical with 1-bromo-2,4,6-trineopentylbenzene in the temperature range -160 to 20 °C gave only a neopentyl type radical. On that basis, they concluded that the initially formed phenyl radical should undergo an extremely rapid, intramolecular hydrogen atom transfer *via* a six-membered cyclic transition state.[5] Therefore, we carried out the LiAlD$_4$ reduction of 1-bromo-2,4,6-trineopentylbenzene[6] under a variety of reaction conditions. The hydrocarbon product, 1,3,5-trineopentylbenzene, was analysed to provide the percentage incorporation and the sites of the deuterium label, and the results are summarized in Table 1.

The amount of deuterium incorporated into the reduction

Table 1

Run	[Substrate][a]/mM	LiAlD₄[a]	Solvent	%Reduction[b]	$^2H_1/^2H_0$[c]	²H₁ in side chain/ring	
						²H n.m.r.[d]	G.c.-m.s.[e]
1	75	4 × 75	Ether	89	74/26	16/83	21/79
2	33	4 × 33	Ether	29	29/71	19/81	21/79
3	33	2 × 33	Ether	13	24/76	25/75	26/74
4	75	4 × 75	THF	98	38/62	10/90	20/80
5	75	2 × 75	THF	62	22/78	12/88	0/100
6	75	4 × 75	THF, reflux	62	31/69	20/80	27/73
7	75	4 × 75[f]	THF	34	28/72	5/95	0/100
8	75	4 × 75[f]	THF, reflux	49	70/30	1/99	0/100

[a] Reactions were carried out at room temperature, under N₂ and in the dark unless indicated otherwise. Room light does not appear to have any significant effect on reaction rates. [b] Determined by g.c. analysis on 6 ft FFAP column on an Antek 300 instrument equipped with a Hewlett-Packard 3390A integrater. [c] Determined by mass spectral analysis of m/z 288 and 289 peaks on a Hewlett-Packard GC-MS Model 5982-A after correction for natural abundance. [d] Determined by ²H n.m.r. integration on either a Bruker WM-300 or a Varian XL-200 instrument. [e] Determined by mass spectral analysis (see text), and expressed as a percentage ratio. [f] The reaction was run with LiAlH₄ instead of LiAlD₄ (98% D, Aldrich), and quenched with D₂O-DCl (99% D, Ventron).
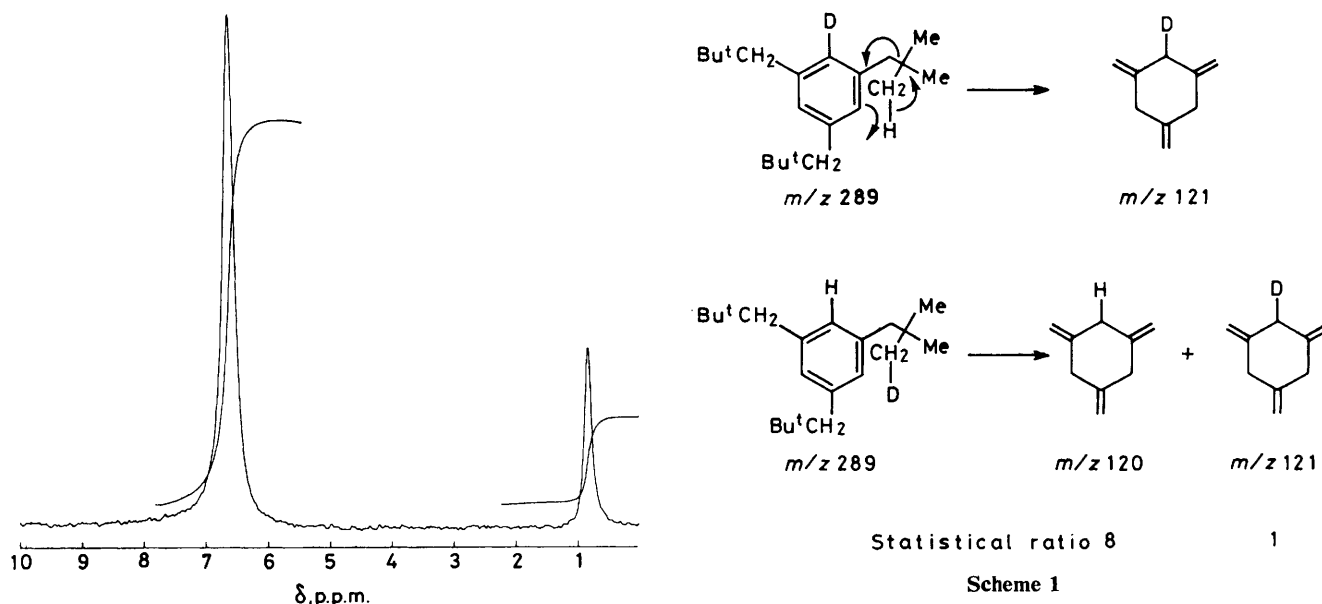

Figure 1. ²H N.m.r. spectrum of 1,3,5-trineopentylbenzene obtained from run 1 (Table 1), obtained on a Bruker WM-300 instrument.

product was determined by mass spectral analysis based on the ratios of the intensities of the m/z 289 ($M^+ + 1$) and 288 (M^+) ions after correction for the natural abundance contribution. The relative abundance of the deuterium label in the side chain and in the ring was determined by two methods. It could be measured most directly by the integration of the two deuterium peaks at δ 6.72 (aromatic) and 0.90 p.p.m. (aliphatic) in the ²H n.m.r. spectrum, since the two resonances are well separated and the integration of the deuterium resonances is quite reliable (Figure 1). The fact that the deuterium label is distributed between the two sites could also be confirmed by the ¹³C n.m.r. spectrum δ 138.1642 and 138.0793 (Δδ = 0.0849 p.p.m. for β-D shift), 130.2761 (unsubstituted aromatic carbon), 50.2495 and 50.1983 (Δδ = 0.0512 p.p.m. for γ-D shift of benzylic carbon), 31.9428 and 31.8718 (Δδ = 0.0720 p.p.m. for β-D shift of quarternary carbon), and 29.5530 p.p.m. (methyl carbon). The relative ratio of deuterium in the side chain and in the ring could also be determined on the basis of the major mass spectral fragmentation which gives rise to the formation of ions with m/z 121 and 120, assuming that there is no significant isotope effect during the fragmentation

Scheme 1

(Scheme 1). As shown in Table 1, the comparison of these two analyses is informative, but agreement between them is not very good. We believe that the ²H n.m.r. analyses should be inherently more reliable.

From the data shown in Table 1, several observations are immediately relevant to the mechanistic discussion. The total deuterium incorporation ($^2H_1/^2H_0$) into the product is dependent on the concentration of LiAlD₄ and the solvent employed, thus showing the competition between the metal hydride and the solvent for the hydrogen donation. It is apparent that the hydrogen donation occurs as hydrogen atoms, since tetrahydrofuran (THF) is known to be a better hydrogen atom donor than diethyl ether[7] (runs 1 and 4). The observation that a substantial amount of deuterium is incorporated into the neopentyl side chain of the product in all runs except the control experiments (runs 7 and 8) may also be taken as good evidence for the involvement of the phenyl radical and its rearrangement to the neopentyl type radical, as suggested by Ingold, et al. The increasing amount of side-chain deuteration with decreasing concentration of LiAlD₄ (runs 1—3) is likely to be due to the competition between the radical rearrangement (k_1) and the hydrogen atom transfer (k_2) (Scheme 2).

The control experiments (runs 7 and 8), which involve the LiAlH₄ reduction followed by D₂O-DCl quenching, show a
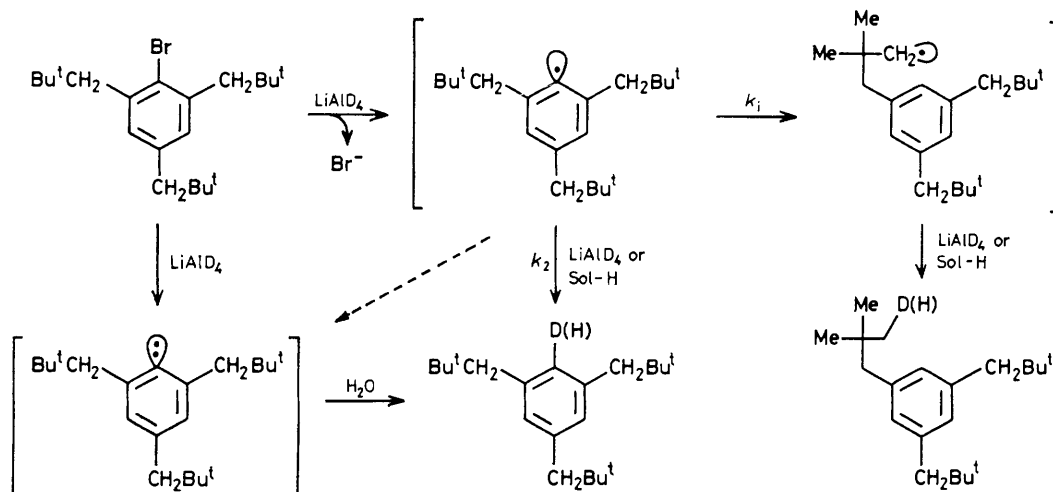
Scheme 2

significant incorporation of hydrogen as protium, thus indicating the possible intervention of a carbanionic intermediate. It is significant that in these cases the deuterium incorporation is found almost exclusively in the ring. We suggest that the amount of deuterium in the side chain for runs 1—6 is the minimum measure of the radical participation, and that the deuterium incorporation in runs 7 and 8 is also the minimum measure of the carbanion involvement. It appears possible that the carbanionic species is generated either directly or *via* the consecutive, stepwise electron transfer (Scheme 2).

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