Evidence for an Aryl Rearrangement Pathway in the Lithium Aluminium Hydride Reduction of Phenacyl Halides

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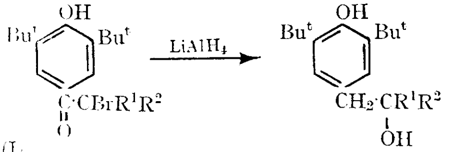
WE have studied the mechanism of the reduction of 2-bromo-4′-hydroxy-3′,5′-di-t-butylacetophenone (Ia) by lithium aluminium hydride. Our conclusions conflict with those of another recent study by A. A. Volod'kin, N. V. Portnykh, and V. V. Ershov.[1,2] These workers reported that the reduction of various 1-bromoalkyl 4-hydroxy-3,5-di-t-butylphenyl ketones (Ia—g) with lithium aluminium hydride led to the formation of 1-alkyl-2-(4-hydroxy-3,5-di-t-butylphenyl)ethanols (IIa—g). To account for these results, a mechanism involving an epoxide intermediate and its subsequent ring opening was proposed (see path A, below).

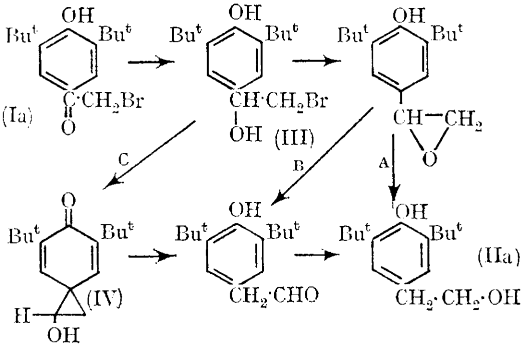


(I) (II)

a, $R^1=R^2=H$; b, $R^1=H$, $R^2=Me$
c, $R^1=H$, $R^2=Et$; d, $R^1=H$, $R^2=Pr^n$
e, $R^1=H$, $R^2=Pr^i$; f, $R^1=H$, $R^2=Ph$;
g, $R^1=R^2=Me$

We considered three possible pathways to account for the formation of the ethanol (IIa) from (Ia). Path A involves formation of an epoxide and subsequent hydride attack at the most substituted carbon atom. Path B involves formation of an epoxide, rearrangement to form an aldehyde, and finally reduction of the resulting carbonyl group. Both of these routes have previously been established in the $LiAlH_4$ reduction of bromohydrins and epoxides.[3] Path C involves formation of a dienone intermediate, (IV),† rearrangement of the resulting cyclopropanol moiety to an aldehyde, and reduction of the carbonyl group to the product. In order to distinguish between these pathways, (Ia) was reduced with $LiAlD_4$. Paths A, B, and C would lead to $ArCD_2·CH_2·OH$, $ArCHD·CHD·OH$, and $ArCH_2·CD_2·OH$, respectively.

2-Bromo-4′-hydroxy-3′,5′-di-t-butylacetophenone (Ia) (1·53 mmole), in ether, was added to $LiAlD_4$ (6·07 mmoles), in ether, and the mixture heated at reflux with vigorous stirring for 3 hr. N.m.r. spectroscopy of the crude product indicated the absence of hydrogen at C(1).‡ Crystallization from hexane yielded 1,1-dideuterio-2-(4-hydroxy-3,5-di-t-butylphenyl)ethanol (75% yield): m.p. 97—98°; n.m.r. ($CDCl_3$ with tetramethylsilane as standard), δ 1·43 (18H, s, t-butyl), 2·06 (1H, s, aliphatic OH), 2·76 (2H, br s, benzylic CH_2), 5·12 (1H, s, phenolic OH), 7·03 p.p.m. (2H, s, aromatic H).



The absence of hydrogen at C(1) is consistent with path C and eliminates paths A and B. The formation of (IIb—g) as previously reported,[1,2] is inconsistent with these results. For example, path C in the case of (Ib) would lead to 2-methyl-2-(4-hydroxy-3,5-di-t-butylphenyl)ethanol and not (IIb).

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† An alternate route which cannot be distinguished from path C by this work involves initial formation of a cyclopropanone, followed by reduction to (IV).

‡ The C(1) hydrogens of (IIa) give rise to a triplet at δ 3·82.

[1] V. V. Ershov, A. A. Volod'kin, and N. V. Portnykh, *Bull. Acad. Sci. U.S.S.R.*, 1966, 1632.
[2] A. A. Volod'kin, N. V. Portnykh, and V. V. Ershov, *Bull. Acad. Sci. U.S.S.R.*, 1967, 1352.
[3] M. N. Rerick and E. L. Eliel, *J. Amer. Chem. Soc.*, 1962, **84**, 2356.