

Remarkable Effects of Remotely Connected but Spatially Proximate Hydroxy-groups on the Birch Reduction of *o*-Xylene Moieties

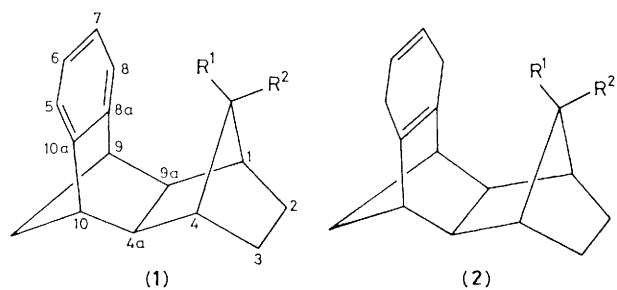
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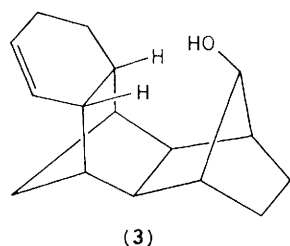
Birch reductions of the *syn*-alcohols (**1c**) and (**6**) (where the OH group is the substituent on the methano-bridge nearest to the aromatic ring) were atypical in that they were extremely rapid and gave products (**3**) and (**7**) respectively; these results are explained by the ability of the proximate hydroxy-group to act as an efficient proton source.

Three important generalisations may be made about the Birch reduction¹ of simple alkyl-substituted benzenes: i, they are reduced more slowly than benzene,² ii, protonation on alkylated positions does not readily occur,^{1,2} and iii, the major products of reduction are 1,4-cyclohexadienes.¹ For

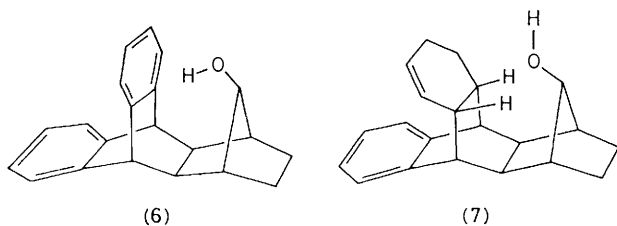
example *o*-xylene, which is representative of this class of substrates, is Birch-reduced about twenty times more slowly than benzene and gives mainly 1,2-dimethyl-1,4-cyclohexadiene and only a small amount of the isomer 2,3-dimethyl-1,4-cyclohexadiene.^{2,3} We report that all these



- a; $R^1, R^2 = H$
 b; $R^1 = OMe, R^2 = H$
 c; $R^1 = OH, R^2 = H$



(3)



(6)

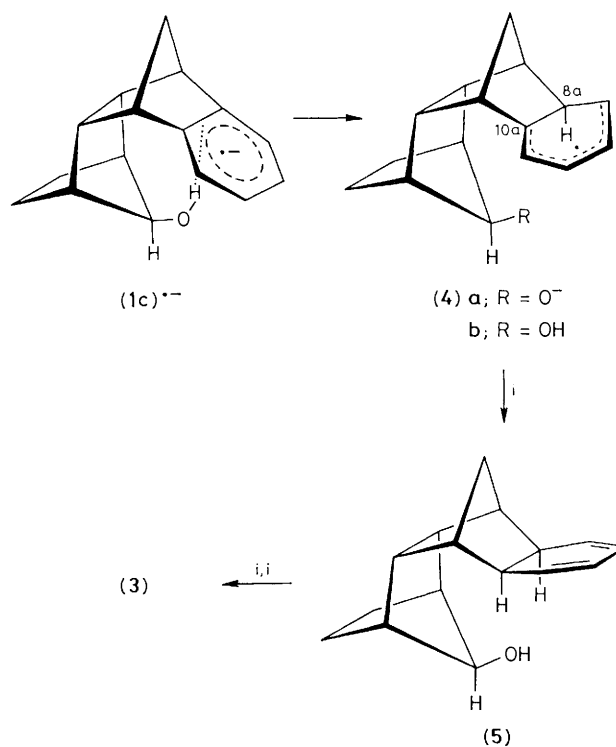
(7)

generalisations can be completely reversed in molecules containing a hydroxy-group in spatial proximity to an *o*-xylene moiety.

Birch reduction[†] of the dimethanoanthracene (**1a**) and the *syn*-methoxy derivative (**1b**) with an excess of lithium (1.3 mmol) slowly ($t_{0.5}$ ca. 10 h) gave the expected dienes (**2a**) and (**2b**) respectively. The structures were confirmed by 1H n.m.r. and mass spectral analysis and by their smooth oxidation to (**1a**) [from (**2a**)] and (**1b**) [from (**2b**)] with dichlorodicyanobenzoquinone.

In contrast Birch reduction of the *syn*-alcohol (**1c**) was so rapid that the lithium simply dissolved without turning the ammonia solution blue. The reduction came to an abrupt halt, as signalled by the development of the blue colour, only after 4 mol. equiv. of lithium had been consumed. A single product was isolated in quantitative yield and its structure was shown to be (**3**) on the grounds of its i.r., 1H n.m.r., and mass spectral data. In particular the location of the double bond follows from the presence of two distinct, yet coupled, olefinic proton resonances in the 1H n.m.r. spectrum: δ ($CDCl_3$) 5.53 (1H, d, J 11 Hz) and 5.87 (1H, br. d, J 11 Hz). The stereochemistry at C-8a and C-10a was confirmed by the observation that Birch reduction of the dienol (**5**), whose structure is known,⁴ also gave (**3**) in quantitative yield.

[†] All reductions were carried out by adding Li to a solution of the substrate (0.3 mmol) in refluxing liquid NH_3 (80 ml) containing tetrahydrofuran (15 ml) and *t*-butyl alcohol (100 mmol) as the proton source.



Scheme 1. Reagents: *i*, *c*, *t*-butyl alcohol.

The above result suggests the intermediacy of dienol (**5**) in the conversion of (**1c**) into (**3**). This possibility was supported by the fact that reduction of (**1c**) with less than 4 equiv. of lithium gave only (**3**) and unreacted (**1c**). Any intermediate diene must therefore be reduced much more rapidly than (**1c**). Indeed, competition experiments revealed this to be the case for (**5**).

The anomalous reactivity of (**1c**) towards Birch reduction is attributed to the ability of the hydroxy-group to act as a very efficient proton source by virtue of its proximity to the aromatic ring. This proposal is supported by the observation of normal behaviour of (**1b**) towards Birch reduction and by the stereochemistry of C-8a and C-10a in (**3**), *i.e.* protonation at these centres had occurred from the hydroxy-side of the aromatic ring.

The proposed mechanism for the reduction of (**1c**) is shown in Scheme 1. The anion radical (**1c**)^{•-} is expected to be strongly intramolecularly OH... π bonded, with the OH bond vector bisecting the C-8a-C-10a bond, because the neutral precursor (**1c**) is known to adopt this conformation.⁴ The proximity of the (OH)...C-8a atoms together with the near collinearity of the O-H and the (OH)...C-8a bond vectors in (**1c**)^{•-} should make intramolecular protonation of C-8a by the OH group, to give (**4a**), more favourable than the usually observed kinetic^{1,5} preference for C-8 protonation in substrates not containing a suitably located OH group, such as (**1a**) and (**1b**). Formation of (**5**) could occur either through protonation of (**4a**), by *t*-butyl alcohol, to give (**4b**) followed by electron addition and subsequent intramolecular protonation of C-10a; or by electron addition to (**4a**) to give a dianion followed by protonation of C-10a by *t*-butyl alcohol from beneath the cyclohexadienyl anion moiety which may be assisted by a lithium ion. The conversion of (**5**) into (**3**) is well precedented¹ and will not be discussed further.

Birch reduction of the *syn*-alcohol (**6**) rapidly gave (**7**) as

the exclusive product.‡ That the aromatic ring further removed from the hydroxy-group was not reduced further testifies to the potent effect that spatially proximate hydroxy-groups can have on Birch reductions of aromatic compounds.⁶

It is possible that this effect could be manifested in template directed reactions. In this context we note that cyclodextrins,⁷ flush with OH groups, and able to bind aromatic substrates into their cavities, could profoundly affect the regiochemistry and the rates of Birch reduction of aromatic systems.

We thank the Australian Research Grants Committee for financial support and H. K. Patney for discussions.

Received, 3rd August 1982; Com. 914

‡ The absence of an intramolecular OH . . . π bond in (7) firmly establishes that the aromatic ring closer to the OH group had been reduced.

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