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Investigation by Deuterium-labelling of the Isomerisation of Dihydroxyalkyl Radicals Formed upon Photolysis of Cobaloxime Complexes†

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Summary Anaerobic photolysis of 5-deuterio-4,5-dihydroxyhexyl(pyridine)cobaloxime at pH 3 gives 2-deuteriohexanal and probably 6-deuteriohexan-2-one.

Anaerobic photolysis of 4,5-dihydroxypentyl(pyridine)cobaloxime (**1a**) in 0·1 M acetic acid gives pentanal, pentane-1,2-diol, pent-1-ene-4,5-diol and decane-1,2,9,10-tetraol.[1–3] Under similar conditions, 5,6-dihydroxyhexyl(pyridine) cobaloxime (**1b**) gives as the carbonyl-containing products a mixture of hexanal and hexan-2-one, the latter predominating.[2,3] We proposed that dihydroxyalkyl radicals released from cobalt in these reactions produce pentanal or hexan-2-one *via* 1,5-hydrogen shifts, whilst hexanal is formed *via* a less favourable 1,6-hydrogen shift.‡ Pentan-2-one, a possible product from (**1a**) *via* a 1,4-hydrogen shift was not observed.[1,3] We now present the results of experiments with specifically deuteriated (**1a**) and (**1b**) which sustain our proposal that intramolecular hydrogen shifts occur in dihydroxyalkyl radicals produced during photodecomposition of these cobaloximes.

$RCo(dmg H)_2py$
(**1**)

a; $R = -[CH_2]_3CHOHCH_2OH$
b; $R = -[CH_2]_4CHOHCH_2OH$
c; $R = -[CH_2]_4C^2HOHCH_2OH$
d; $R = -C^2H_2[CH_2]_2CHOHC^2H_2OH$
dmg H = monoanion of dimethylglyoxime
py = pyridine

Cyclohex-2-en-1-one was reduced ($LiAl^2H_4$–ether) to 1-deuteriocyclohex-2-en-1-ol§ which was ozonised. The resulting ozonide was directly reduced ($NaBH_4$) to 2-deuteriohexane-1,2,6-triol§ which was converted into 4-deuterio-2,2-dimethyl-4-(4-hydroxybutyl)-1,3-dioxolan.§ G.l.c.–m.s. of the trimethylsilyl ether of this substance shows it to contain 94 ± 1% ^2H and 6 ± 1% ^1H (at C-4). From the toluene-*p*-sulphonate was obtained (**1c**),§ which therefore contains 94% ^2H at C-5 of the dihydroxyhexyl group. Irradiation (Pyrex filter) of a de-aerated 2·2 mM solution of (**1c**) in 0·1 M acetic acid at 291 K caused decomposition of the cobaloxime within 7 min. The resulting solution was extracted with pentane. G.l.c. of the pentane extract showed a ratio of hexan-2-one to hexanal of 1 : 5 [*cf.* hexan-2-one : hexanal = 3·7 : 1 from (**1b**)[2,3]]. Analysis of these products as their 2,4-dinitophenylhydrazones (DNP's) gave a combined yield of 4·1% [*cf.* 16% hexan-2-one + 4% hexanal from (**1b**)[2,3]]. A primary isotope effect strongly impedes the intramolecular 1,5-hydrogen shift but as expected, the rate of the competing 1,6-shift is largely unaffected and 2-deuteriohexanal (see below) is obtained from (**1c**) in similar yield to that of hexanal from (**1b**).

In another experiment, CCl_4 was used to extract (deuteriated) hexan-2-one and hexanal. After concentrating the combined extracts, ^1H n.m.r. spectroscopy of the concentrate showed the hexanal to be deuteriated at C-2 since H-1 appeared as a doublet (δ 9·75, J 1·76 Hz) (*cf.* triplet, δ 9·75, J 1·78 Hz in unlabelled hexanal). The signals from protons at C-5 and C-6 of hexan-2-one were not sufficiently resolved [even after addition of $Eu_2(fod)_6$] for the presence

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† No reprints available.

‡ On photolysis at pH 3, 3,4-dihydroxybutyl(pyridine)cobaloxime and 10,11-dihydroxyundecyl(pyridine)cobaloxime do not yield carbonyl product(s) derived from their dihydroxyalkyl group (see ref. 3).

§ Spectroscopic data for this compound are in accord with the assigned structure.

or absence of deuterium at C-6 to be discerned. Information on the deuterium content of the hexan-2-one was obtained by g.l.c.–m.s. of a pentane extract after photodecomposition of (**1c**). The mass spectrum of this hexan-2-one shows it to contain 60 ± 1% hexan-2-one and 40 ± 1% $[^2H_1]$hexan-2-one.¶ Since the molecular ion of the $[^2H_1]$-hexan-2-one gives an ion of *m/e* 58 $[CH_2\text{–}C(OH)CH_3]^{+\cdot}$ but not, significantly, *m/e* 59, its deuterium atom must be located at C-4, C-5, or C-6. As the selective transfer of deuterium from C-2 to C-4 or C-5 is improbable, it is highly likely that the deuterium is located at C-6.

Analogously, photolysis of 4,5-dihydroxy-1,1,5,5-tetradeuteriopentyl(pyridine)cobaloxime (**1d**) in 0·1 M acetic acid gave $C^2H_3(CH_2)_3C^2HO$ (identified by electron impact mass spectrometry of its DNP), 1,1,5,5-tetradeuteriopentane-1,2-diol, 4,5-dihydroxy-1,1,5,5-tetradeuteriopent-1-ene (characterised by their ^1H n.m.r. spectra) and decane-1,2,9,10-tetraol (probably octadeuterio).

Schrauzer[4] and Corey *et al.*[5] have recently criticised the so-called free-radical mechanism[6] for the adenosylcobalamin-dependent reactions catalysed by diol dehydrase [*e.g.* $MeCHOHCH_2OH \rightarrow MeCH_2CH(OH)_2 \rightarrow MeCH_2CHO$]. We will evaluate their alternative mechanistic proposals elsewhere. The presently described results and our previous findings show that primary alkyl radicals attack 1,2-diols regioselectively, in processes which reveal substantial primary kinetic isotope effects. The derived dihydroxyalkyl radicals decompose to aldehyde–ketone product. We have simulated therefore some of the apparent features[6] of the diol dehydrase reactions and whilst our results obviously do not constitute a proof of an enzymatic reaction pathway *via* organic radicals, they do show that such a pathway is possible in principle.

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¶ From these results the apparent primary kinetic isotope effect for intramolecular hydrogen transfer in the conversion of the 5,6-dihydroxyhexyl radical into the 1-(hydroxy-1-hydroxymethyl)pentyl radical can be computed as 23 [*n.b.* (**1c**) contains 94% $^2H_1$, *cf.* text]. This agrees with a value derived from the change in ratio of hexan-2-one to hexanal [*cf.* photolysis of (**1b**) and (**1c**)] and substantially exceeds the 'theoretical maximum value' (*cf.* F. H. Westheimer, *Chem. Rev.*, 1961, **61**, 265).

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