Further Evidence pertaining to the Mechanism of Alcoholysis of σ-2-Acetoxyalkyl(pyridine)cobaloximes

By B. T. GOLDING* and S. SAKRIKAR

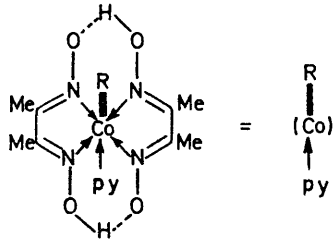
(*Department of Molecular Sciences, University of Warwick, Coventry* CV4 7AL)

Summary Results with chiral and specifically labelled substrates support the proposal that alcoholyses of σ-2-acetoxyalkyl(pyridine)cobaloximes proceed *via* an intermediate olefinic complex.

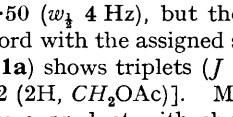
THE σ-2-acetoxyalkyl(pyridine)cobaloximes† (**1a**) and (**1b**) undergo remarkably ready alcoholysis under neutral conditions at 25° to afford high yields of ethers [e.g. (**1c**) and (**1d**), respectively, from methanolysis].[1] It was suggested[1] that (**1a**) and (**1b**) ionise to cationic intermediates [(**2a**) or (**2b**) from (**1a**), (**2c**) or (**2d**) from (**1b**); these and other possible structural representations are discussed in reference 1] which are principally captured by solvent to give ethers. There is likely to be appreciable restriction to rotation

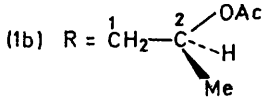
† Cobaloxime = bis(dimethylglyoximato)cobalt.

about the C(1)–C(2) bond in either (**2c**) or (**2d**) and it is therefore anticipated that chiral (**1b**) will solvolyse to an ether [e.g. (**1e**) from alcoholysis in benzyl alcohol] with complete retention of configuration at C(2). Furthermore, if (**2a**) is an intermediate or if (**2b**) is an intermediate which topomerises its methylene groups, perhaps *via* (**2a**) as transition state, then methanolysis of the specifically deuteriated compound (**1f**) may give rise to equal proportions of the ethers (**1g**) and (**1h**). We now report experiments which bear out these expectations.



(1a) R = CH_2CH_2OAc



(1b) R = 

(1c) R = CH_2CH_2OMe

(1d) R = $CH_2CH(OMe)Me$

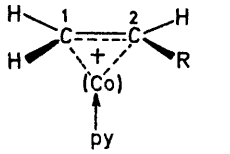
(1e) R =

(1f) R = CH_2CD_2OAc

(1g) R = CH_2CD_2OMe

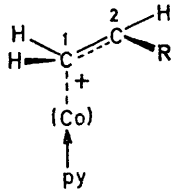
(1h) R = CD_2CH_2OMe

(1i) R = CD_2CH_2OAc



(2a) R = H

(2c) R = Me



(2b) R = H

(2d) R = Me

The (pyridine)cobaloxime(I) nucleophile prepared by reduction of bromo(pyridine)cobaloxime was alkylated with (*S*)-1-bromo-2-acetoxypropane (3 mol. equiv.) to yield (*S*)-(**1b**) [33%, $[\alpha]_D^{20}$ + 2·4° (*c* 2·9 in $CHCl_3$)]. Alcoholysis of (*S*)-(**1b**) gave the benzyl ether (**1e**) purified by t.l.c. and recrystallization.‡ The circular dichroism spectrum [$\Delta\epsilon$ + 0·50 (362 nm), −0·13 (403 nm)] of this specimen is identical within experimental error to that [$\Delta\epsilon$ + 0·47 (363 nm), −0·18 (403 nm)] of an authentic sample of (*S*)-(**1e**)‡ synthesised by alkylating (pyridine)cobaloxime(I) with (*S*)-2-benzyloxypropyl toluene-*p*-sulphonate.‡ Both the latter compound and (*S*)-1-bromo-2-acetoxypropane were synthesised from optically pure (*S*)-ethyl lactate. Samples of (*S*)-(**1e**) from solvolysis and independent synthesis were alternatively purified solely by chromatography. Their circular dichroism spectra show them to be of similar optical purity [> 10% (*R*)-(**1e**) in the sample derived by alcoholysis would have been detected]. We conclude that alcoholysis of (**1b**) in benzyl alcohol proceeds with overall retention of configuration (and probably stereospecifically) *via* (**2c**) or (**2d**).

Reduction of bromoacetyl bromide with $LiAlD_4$ gave 1,1-dideuterio-2-bromoethanol‡ (52%, b.p. 20°/3 mm.) which was acetylated to 1-acetoxy-1,1-dideuterio-2-bromoethane‡ (48%, b.p. 20°/1·8 mm). Alkylation of (pyridine)cobaloxime(I) with this compound gave (**1f**) (58%). The n.m.r. spectrum of (**1f**) in $CDCl_3$ shows a broad singlet at δ 1·50 ($w_{\frac{1}{2}}$ 4 Hz), but the absence of a signal at δ 3·72 in accord with the assigned structure [*n.b.* the n.m.r. spectrum of (**1a**) shows triplets (*J* 8 Hz) at δ 1·50 (2H, CO–CH_2) and 3·72 (2H, CH_2OAc)]. Methanolysis of (**1f**) (MeOH–$CDCl_3$) gave a product with chromatographic properties identical to those of (**1c**).[1] The n.m.r. spectrum of this material shows it to be a 1 : 1 mixture of (**1g**) and (**1h**), since broad singlets ($w_{\frac{1}{2}}$ 4 Hz) each equivalent in area to one proton appear at δ 1·57 and 3·05 [*n.b.* the n.m.r. spectrum of (**1c**) shows triplets (*J* 8 Hz) at δ 1·58 (2H, CO–CH_2) and 3·06 (2H, CH_2OMe)]. In agreement with these findings, methanolysis of 2-^{13}C-(**1a**) leads to ^{13}C-(**1c**) having the label equally distributed between C(1) and C(2).[3] It is conceivable that the observed scramblings of isotopic label could occur *via* some rapid reversible process [*e.g.* dissociation of (**1f**) to (pyridine)cobaloxime(I) and 2-methyl-1,3-dioxolan-2-ylium cation, followed by recombination to (**1f**) or (**1i**)], and then conversion into (**1g**) and (**1h**) takes place in a manner other than that suggested. However, although a signal indicative of (**1i**) appears and disappears at δ 3·72 during methanolysis [CD_3OD–$CDCl_3$] of (**1f**), its intensity is always less than that of the signal due to (**1h**) which appears at δ 3·06, and it could arise wholly by internal return [*i.e.* capture of dideuterio-(**2a**) or (**2b**) by acetate ion, leading to (**1f**) or (**1i**)].

π-Complexes of cobalamins [*i.e.* with oxidation state Co^{III} rather than Co^{I} [4]] are possibly important biochemical intermediates[3,5] and the above results with cobaloximes, as models[6] for cobalamins, are strongly suggestive of at least the existence of such species and are indicative of means by which they could be observed.

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‡ New compounds gave satisfactory combustion analyses and spectral data consistent with their assigned structure.

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[6] See *e.g.* G. N. Schrauzer, *Accounts Chem. Res.*, 1968, **1**, 97.