Model Experiments relevant to the Mechanism of Adenosylcobalamin-dependent Diol Dehydrase: Further Investigations of Isomerisations of Dihydroxyalkyl Radicals

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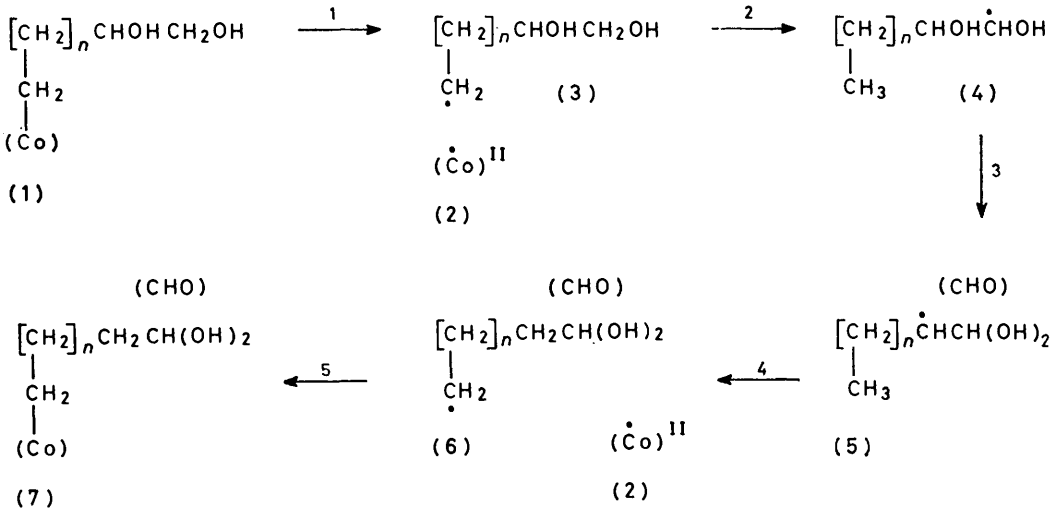
Anaerobic photolysis of 4,5-dihydroxypentyl(pyridine)cobaloxime in 0.1 M acetic acid (pH 3) gives *ca.* 10% of pentanal, whereas 1,1,5,5-tetradeuterio-4,5-dihydroxypentyl(pyridine)cobaloxime affords 0.6% of 1,5,5,5-tetradeuteriopentanal. Under similar conditions, 5-deuterio-5,6-dihydroxyhexyl(pyridine)cobaloxime gives *ca.* 1% of 6-deuteriohexan-2-one and 4% of 2-deuteriohexanal, in contrast to 5,6-dihydroxyhexyl(pyridine)cobaloxime which affords 16% of hexan-2-one and 4% of hexanal. These results support a mechanism for the photoconversion of dihydroxyalkylcobaloximes into aldehydes or ketones at pH 3, in which light-induced homolysis of the Co–C σ-bond to give a dihydroxyalkyl radical is followed by a 1,5-hydrogen shift. The resulting isomeric dihydroxyalkyl radical, possessing a hydroxy-group at the radical centre, undergoes an acid-catalysed transformation to aldehyde or ketone. With the deuteriated cobaloximes the 1,5-H shift is impeded by a primary isotope effect (k_H/k_D *ca.* 20). Anaerobic photolysis of 4,5-dihydroxycyclo-octyl(pyridine)cobaloxime at pH 3 yields *ca.* 40% of cyclo-octanone. This reaction owes its efficiency to a favourable transannular 1,5-H shift which converts the 4,5-dihydroxycyclo-octyl radical into the 1,2-dihydroxycyclo-octyl radical. The relevance of the above reactions to adenosylcobalamin-dependent reactions catalysed by diol dehydrase is discussed.

THE enzyme diol dehydrase, with adenosylcobalamin (AdoCbl) † and a monovalent cation (*e.g.* K^+), converts certain 1,2-diols into aldehydes and butane-2,3-diol into butanone.[1] Several reaction pathways and mechanisms have been proposed for these conversions, but available experimental evidence [2] favours the following sequence of events: AdoCbl, when bound to diol dehydrase, releases cob(II)alamin (Cbl^{II}) † and an adenosyl radical which attacks enzyme-bound diol to form 5′-deoxyadenosine and a 1,2-dihydroxyalkyl radical; ‡ this species rearranges [3,4] to a 1-(dihydroxymethyl)alkyl radical which abstracts a hydrogen atom from 5′-deoxyadenosine, regenerating adenosyl radical and producing a 1,1-diol which suffers enzymatic dehydration to an aldehyde.

Beside the need to prove this sequence, there are mechanistic questions to answer for each of its steps. To probe these details, we considered the model system shown in Scheme 1. The dihydroxyalkylcobalt complex (1) releases a cobalt(II) species (2) and a dihydroxyalkyl radical (3) which undergoes an intramolecular rearrangement, transferring a hydrogen atom from one end of its carbon chain to the other. The derived 1,2-dihydroxyalkyl radical (4) rearranges to either a 1-(dihydroxymethyl)alkyl radical (5) or a 1-formylalkyl radical. A second intramolecular hydrogen-shift transforms (5) to (6) which combines with (2) to give (7). Execution of this model system in the laboratory would corroborate the proposed enzymatic sequence, which it closely matches. So far, we have provided evidence for the occurrence of steps 1—3 (Scheme 1) in an experimental



SCHEME 1 Hypothetical model system for diol dehydrase

† For the nomenclature of cobalamins see *Biochemistry*, 1974, **13**, 1555.

‡ Alternatively, concerted fission of the Co–C bond of AdoCbl and transfer of a hydrogen atom from the substrate diol may occur (see ref. 3).

model system based on photoinduced transformations of dihydroxyalkylcobaloximes.[5-7]

Thus, pentanal, but not pentan-2-one, is obtained by anaerobic photolysis of 4,5-dihydroxypentyl(pyridine)-cobaloxime (8b) in 0.1M acetic acid.[7] Under comparable conditions, 5,6-dihydroxyhexyl(pyridine)cobaloxime (8c) gives a mixture of hexan-2-one and hexanal, with the former predominating, but 3,4-dihydroxybutyl-(pyridine)cobaloxime (8a) did not give butanal or butanone and 10,11-dihydroxyundecyl(pyridine)cobaloxime (8d) failed to produce undecanal or undecan-2-one. We suggested [7] that the cobalt atom of (8a—d) liberates its σ-alkyl group as a dihydroxyalkyl radical which produces pentanal from (8b) and hexan-2-one from (8c) *via* 1,5-hydrogen shifts, whereas hexanal from (8c) arises *via* a less favourable 1,6-hydrogen shift. The failure of (8a) and (8d) to produce aldehyde or ketone from their dihydroxyalkyl group, and of (8b) to give pentan-2-one, shows that 1,3-, 1,4-, 1,10-, and 1,11-hydrogen shifts do not occur with the dihydroxyalkyl radicals derived from these cobaloximes.

In this paper we describe the synthesis of the deuteriated analogues, (8a) and (8f), of (8b) and (8c) and a study of their photochemical decompositions. Our results support the mechanism for photodecomposition of cobaloximes (8b) and (8c) proposed in refs. 5–7. A preliminary report on this aspect of the paper has been published.[8] We also describe the synthesis and photodecomposition of a 4,5-dihydroxycyclo-octyl(pyridine)-cobaloxime (8g).

$RCo(dmgH)_2py$

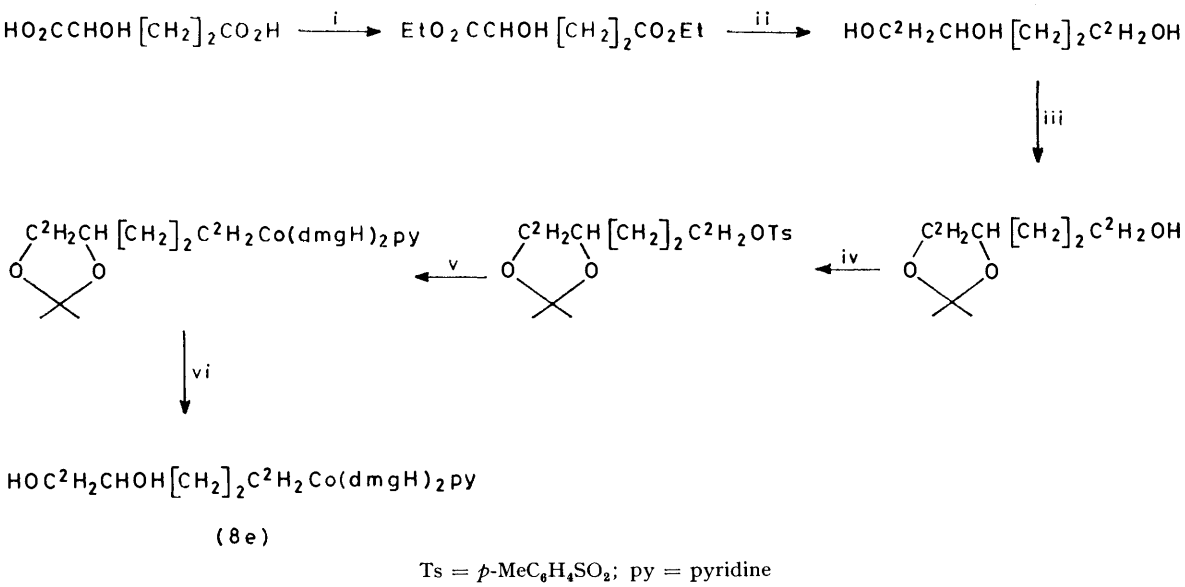
dmgH = dimethylglyoxime monoanion; py = pyridine

(8a) R = $[CH_2]_2CHOHCH_2OH$
(8b) R = $[CH_2]_3CHOHCH_2OH$
(8c) R = $[CH_2]_4CHOHCH_2OH$
(8d) R = $[CH_2]_9CHOHCH_2OH$
(8e) R = $C^2H_2CH_2CH_2CHOHC^2H_2OH$
(8f) R = $[CH_2]_4C^2HOHCH_2OH$
(8g) R = *trans*-4,5-dihydroxycyclo-octan-1-yl
(8h) R = 10,10-dimethyl-*trans*-9,11-dioxabicyclo[6.3.0]-undecan-5-yl

RESULTS

(A) *Synthesis and Photodecomposition of* (8e).—The route used to synthesise (8e) is shown in Scheme 2. (*S*)-2-Hydroxypentane-1,5-dioic acid [9,10] was converted into its diethyl ester which was reduced with $LiAl^2H_4$ (99 atom % ^2H) to 1,1,5,5-tetradeuteriopentane-1,2,5-triol. This compound was converted into (8e) by the route used [7] to prepare (8b) from pentane-1,2,5-triol. Three samples of (8e) were prepared in separate synthetic sequences. The exclusive location of deuterium at C-1 and C-5 of the σ-alkyl group of (8e) follows from comparing its ^1H n.m.r. spectrum with that of (8b) and is confirmed by comparing the ^1H n.m.r. spectra of deuteriated intermediates in its preparation with spectra for the corresponding unlabelled materials. One such comparison is shown in Figure 1. The isotopic purity of (8e) and its deuteriated precursors is near 100% $^2H_4$ as judged by their ^1H n.m.r. spectra (*cf.* Figure 1). This estimate was confirmed for sample 1 by electron-impact mass spectrometry of the trimethylsilyl ether of 4,4-dideuterio-5-(3,3-dideuterio-3-hydroxypropyl)-2,2-dimethyl-1,3-dioxolan which showed the presence of *ca.* 99% $^2H_4$-species.

We have reported [7] that anaerobic photolysis of a dilute solution of (8b) in 0.1M acetic acid gives pentanal (10%), pentane-1,2-diol (*ca.* 20%), 4,5-dihydroxypent-1-ene (*ca.*

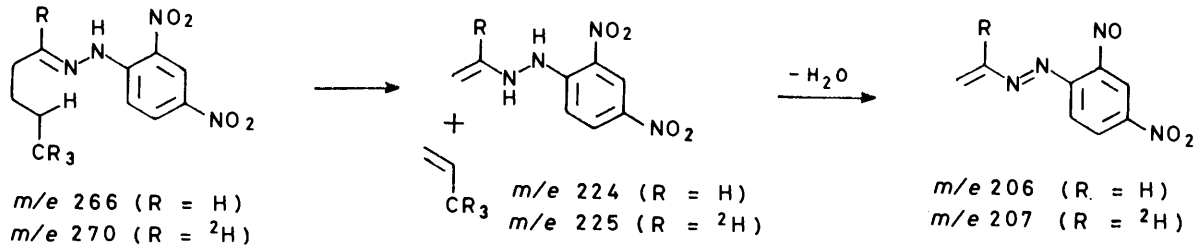


Ts = p-$MeC_6H_4SO_2$; py = pyridine

SCHEME 2 Synthesis of 1,1,5,5-tetradeuterio-4,5-dihydroxypentyl(pyridine)cobaloxime (8e). *Reagents:* i, $(EtO)_3CH$, H_2SO_4; ii, $LiAl^2H_4$–Et_2O; iii, Me_2CO, petrol, catalytic TsOH; iv, TsCl, py; v, $CoCl_2 \cdot 6H_2O$, $dmgH_2$, py, KBH_4, NaOH; vi, 0.1M aq. HCl, EtOH

30%) and decane-1,2,9,10-tetraol (*ca.* 20%). A similar photolysis of (8e) gave these products deuteriated, but the yield of deuteriated pentanal was only *ca.* 0.6% (determined from the u.v.–visible spectrum of its 2,4-dinitrophenylhydrazone), whereas the yields of the diols and tetraol were not appreciably affected. The reduction in yield of deuteriated pentanal from (8e) compared to pentanal from (8b) is consistent with the mechanism we proposed for the formation of pentanal (see Introduction and refs. 5—7), if there is a sizeable primary kinetic isotope effect (k_H/k_D *ca.* 20) in the step by which the 4,5-dihydroxypentyl radical is converted into the 1,2-dihydroxypentyl radical *via* a 1,5-hydrogen shift. Substantial isotope effects for 1,5-hydrogen shifts in pericyclic reactions,[11] thermal 1,5-shifts in oxy-radicals (*e.g.* Barton reaction [12]), and photochemically induced rearrangements (Norrish type II,[13] Hofmann–Loeffler–Freytag [14]) have been reported.

The very low yield of deuteriated pentanal made difficult the proof of its structure and, in particular, the location of its deuterium atoms. An attempt to examine the deuteriated pentanal by g.l.c.–mass spectrometry was unsuccessful and so it was isolated as its 2,4-dinitrophenylhydrazone (DNP). Although this substance was obtained chromatographically pure (column and t.l.c.) it showed peaks due to impurities in its ^{1}H n.m.r. spectrum and mass spectrum (principal impurity peaks at *m/e* 279 and 293). This made the n.m.r. spectrum unreliable for assessing the position and content of deuterium atoms, but the mass spectrum was usable. The electron impact mass spectrum of (unlabelled) pentanal DNP shows *inter alia* peaks at *m/e* 266, 224, and 206, which arise as shown in Scheme 3.[15] In the mass spectrum of the deuteriated pentanal DNP there are corresponding peaks as given in the Table. These data are consistent with the presence of $CH^2H_2[CH_2]_3C^2H$=NNHAr (Ar = 2,4-dinitrophenyl) and $C^2H_3[CH_2]_3C^2H$=NNHAr in the deuteriated pentanal DNP, the molecular ions



SCHEME 3 Fragmentation (McLafferty rearrangement + dehydration) of the molecular ion of pentanal-DNP and 1,5,5,5-tetradeuteriopentanal-DNP

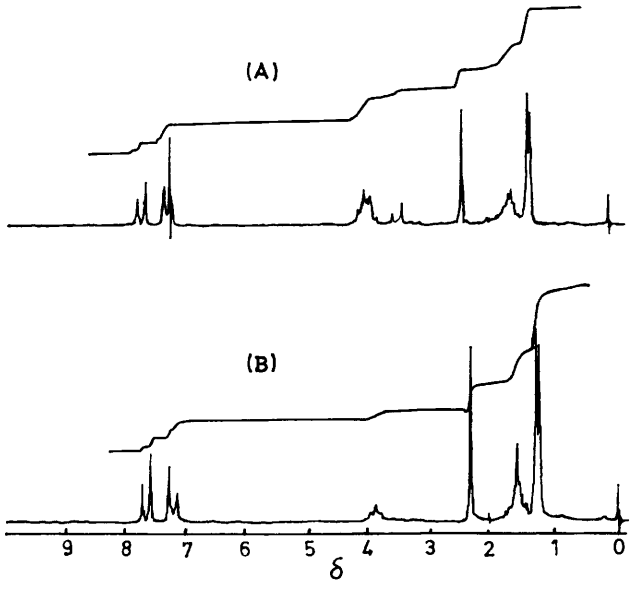


FIGURE 1 ^{1}H N.m.r. spectra (60 MHz) of 2,2-dimethyl-4-(3′-*p*-tolylsulphonyloxypropyl)-1,3-dioxolan (A) and its 3′,3′,5,5-tetradeuterio-analogue (B) in $CDCl_3$

of which fragment as shown in Scheme 3. The apparent ratio of these components varied in four runs on the three separately synthesised samples of (8e): *ca.* 2 : 3 in two runs on sample 1 of (8e), 3 : 2 on sample 2, and 1 : 2 on sample 3. Two possible explanations for the production of trideuteriopentanal DNP are as follows.

(i) Compound (8e) may be contaminated with a 4,5-dihydroxypentyl(pyridine)cobaloxime containing two deuterium atoms at C-1 and one deuterium atom at C-5. Because a primary kinetic isotope effect impedes 1,5-shift of deuterium, the radical $\cdot C^2H_2[CH_2]_2CHOHCH^2HOH$ will preferentially transfer hydrogen from C-5 to C-1 and this process will be appreciably faster than 1,5-deuterium transfer in the radical $\cdot C^2H_2[CH_2]_2CHOHC^2H_2OH$. Therefore, the proportion of trideuteriopentanal in tetradeuteriopentanal will considerably exceed the proportion of trideuterio-contaminant in (8e). Analysis of a precursor of (8e) (sample 1) showed the presence of *ca.* 99% [$^2H_4$]-species (see above). Assuming 0.5% of a trideuterio-species with one deuterium atom at C-5 of the dihydroxypentyl group and a primary kinetic isotope effect of *ca.* 20 leads to an estimated ratio of trideuterio- to tetradeuterio-pentanal of 1 : 10. These considerations can account for at least part of the trideuteriopentanal formed.

Accurate mass measurements in mass spectra of deuteriated pentanal DNPs

Ion	Measured *m/e* [a]	Calculated *m/e*
$C_{11}H_{10}{}^2H_4N_4O_4$ [b]	270.1265, 270.1271	270.1266
$C_{11}H_{10}{}^2H_3N_4O_4$	269.1203, 269.1208	269.1200
$C_8H_7{}^2HN_4O_4$ [c]	Not measured, 225.0608	225.0608
$C_8H_5{}^2HN_4O_3$	Not measured, 207.0506	207.0508

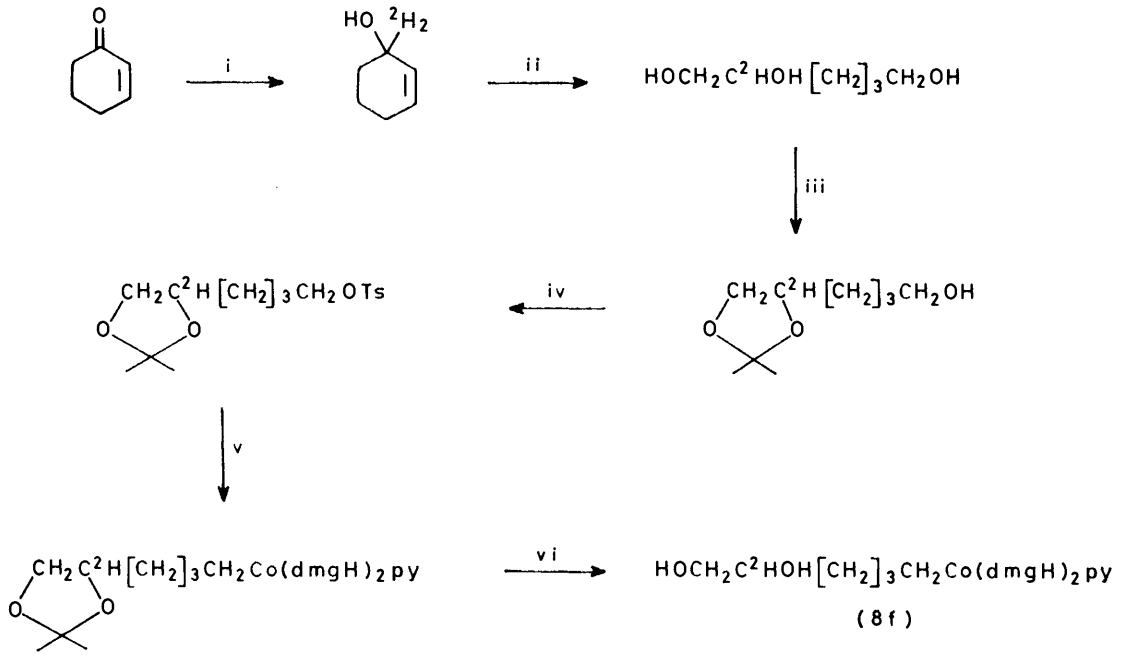
[a] Masses were measured with a precision of ±0.0005 on the most intense peak; data in the first column were obtained from sample 2, and in the second column from sample 3. [b] For undeuteriated pentanal DNP, M^+, found 266.1021, calc. for $C_{11}H_{14}N_4O_4$, 266.1015. [c] For undeuteriated pentanal DNP, M^+, found 224.0549, calc. for $C_8H_8N_4O_4$, 224.0545.

(ii) The 4,5-dihydroxypentyl radical from (8e) abstracts a hydrogen atom from dimethylglyoxime (O*H*) producing 1,1,5,5-tetradeuteriopentane-1,2-diol which might be con-

verted into 1,5,5-trideuteriopentanal under the reaction conditions by a process which releases one deuterium atom from C-1. Control experiments demonstrated [7] that no detectable pentanal arises in this manner from (8b).

That deuterium is located exclusively at C-1 and C-5 of deuteriated pentanal from (8c) was supported by ^2H n.m.r. spectroscopy. We reasoned that the problem of the low yield of deuteriated pentanal with the attendant difficulty of obtaining pure pentanal DNP could be overcome by C^2HN and C^2H_3, respectively, because CHN and CH_3 appear at δ 7.72 and 1.10, respectively, in the ^1H n.m.r. spectrum of pentanal-DNP (in C_6F_6).

(B) *Synthesis and Photodecomposition of* (8f).—The route used to synthesise a single sample of (8f) is shown in Scheme 4. Cyclohex-2-en-1-one was reduced with $LiAl^2H_4$ (99 atom % ^2H) to racemic 1-deuteriocyclohex-2-en-1-ol which was ozonised. The resulting ozonide was directly reduced with $NaBH_4$ to 2-deuteriohexane-1,2,6-triol which



SCHEME 4 Synthesis of 5-deuterio-5,6-dihydroxyhexyl(pyridine)cobaloxime. *Reagents:* i, $LiAl^2H_4$, Et_2O; ii, a, O_3, EtOH, b, $NaBH_4$; iii, Me_2CO, petrol, catalytic TsOH; iv, TsCl, py; v, $CoCl_2 \cdot 6H_2O$, $dmgH_2$, py, KBH_4, NaOH; vi, 0.1M aq. HCl, EtOH

diluting the deuteriated sample with unlabelled pentanal, which would act as a carrier and facilitate isolation of pure material. Because deuterium substitution at the C-1 and C-5 positions of the pentanal should approach 100%, a

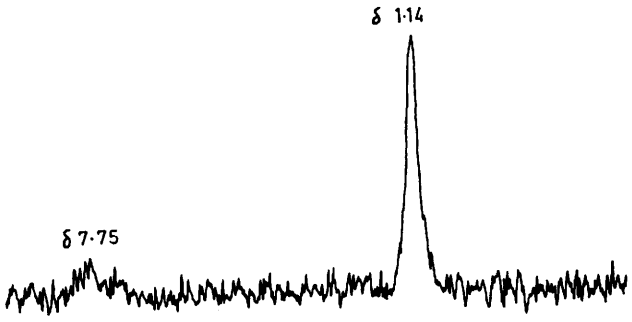


FIGURE 2 ^2H N.m.r. spectrum (external $CDCl_3$ reference) of 1,5,5,5-tetradeuteriopentanal DNP in C_6F_6

60-fold dilution would still leave an overall level of deuterium at C-1 and C-5 positions 100-fold above natural abundance (0.016%). The ^2H n.m.r. spectrum of deuteriated pentanal DNP (diluted with pentanal DNP) from (8e) is shown in Figure 2. Deuterium chemical shifts (p.p.m.) are very similar to proton chemical shifts,[16] so the two resonances (δ 7.75 and 1.14) in Figure 2 can be assigned to was converted into (8f) by the route used [7] to prepare (8c) from hexane-1,2,6-triol. The exclusive location of deuterium at C-5 of the σ-alkyl group of (8f) follows from comparing its ^1H n.m.r. spectrum and the spectra of its precursors with the ^1H n.m.r. spectra of the corresponding unlabelled compounds. The isotopic purity of (8f) at C-5 is 94% ^2H as judged by g.l.c.–mass spectrometry of the trimethylsilyl ether of its precursor 5-deuterio-5-(4-hydroxybutyl)-2,2-dimethyl-1,3-dioxolan which showed the presence of 94% $^2H_1$-species. Exchange processes causing loss of deuterium in the steps producing this compound from 2-deuteriohexane-1,2,6-triol or in the steps leading up to (8f) can be ruled out because none of the reaction conditions should affect a deuterium (hydrogen) atom attached to a carbon substituted with an oxygen atom and two saturated carbon atoms. It is possible that a small amount of exchange occurs during the reduction of the ozonide from 1-deuteriocyclohex-2-en-1-ol.

Anaerobic photolysis of (8f) in 0.1M acetic acid gave a mixture of hexanal and hexan-2-one which were both partially deuteriated. The ratio of total hexanal to hexan-2-one was 5 : 1 which contrasts with 1 : 3.7 from photodecomposition of (8c).[7] This dramatic reversal is again indicative of a large primary isotope effect (k_H/k_D 23) impeding a 1,5-hydrogen (deuterium) shift, which is a prerequisite for production of deuteriated hexan-2-one. The combined yield of partially deuteriated hexanal and hexan-

2-one from (8f) was 4.1% (as DNPs) which compares with 20% (16% hexan-2-one + 4% hexanal) from (8c).[7] Whereas the yield of hexanal (partially deuteriated) from (8f) is unaltered, that of hexan-2-one (partially deuteriated) is suppressed owing to the isotope effect.

G.l.c.–mass spectrometry of the partially deuteriated hexanal and hexan-2-one from (8f) gave a deuterium content for the hexanal of *ca.* 80% $^2H_1$ (an accurate figure was not obtained because of the low abundance of its molecular ion and the existence of an $M - 1$ fragment), and for hexan-2-one of 40% $^2H_1$. The latter value provides an independent check on the primary isotope effect in the 1,5-hydrogen (deuterium) shift leading to hexan-2-one: thus $k_H/k_D = 24$.

The location of deuterium in the deuteriated hexanal followed from the ^1H n.m.r. spectrum of a carbon tetrachloride extract of the aqueous solution from photolysis of (8f). In this spectrum there was a doublet (J 1.76 Hz) for H-1 of the hexanal (*cf.* triplet, J 1.78 Hz, in unlabelled hexanal) and so deuterium is at C-2. This is the expected result if deuteriated hexanal arises from the 5-deuterio-5,6-dihydroxyhexyl radical by a 1,6-hydrogen shift. The ^1H n.m.r. spectrum of the carbon tetrachloride extract also shows signals for deuteriated hexan-2-one, but even after addition of $Eu_2(fod)_6$ these were not sufficiently well defined to specify the position of deuterium. The mass spectrum (Figure 3) of the deuteriated hexan-2-one (from

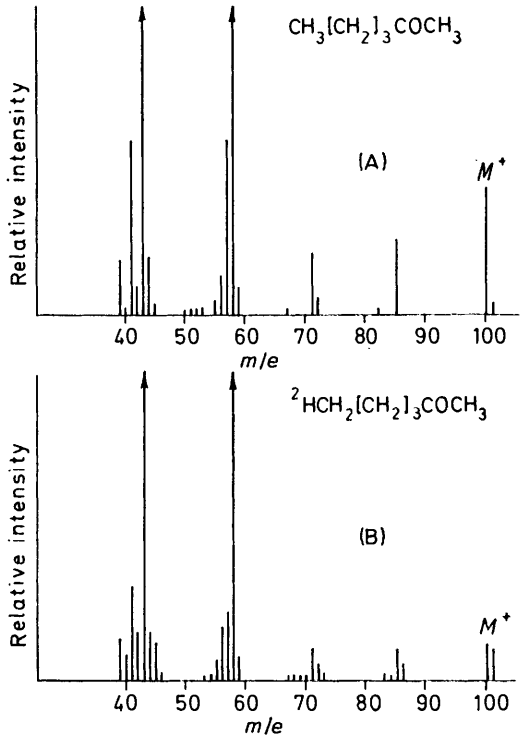


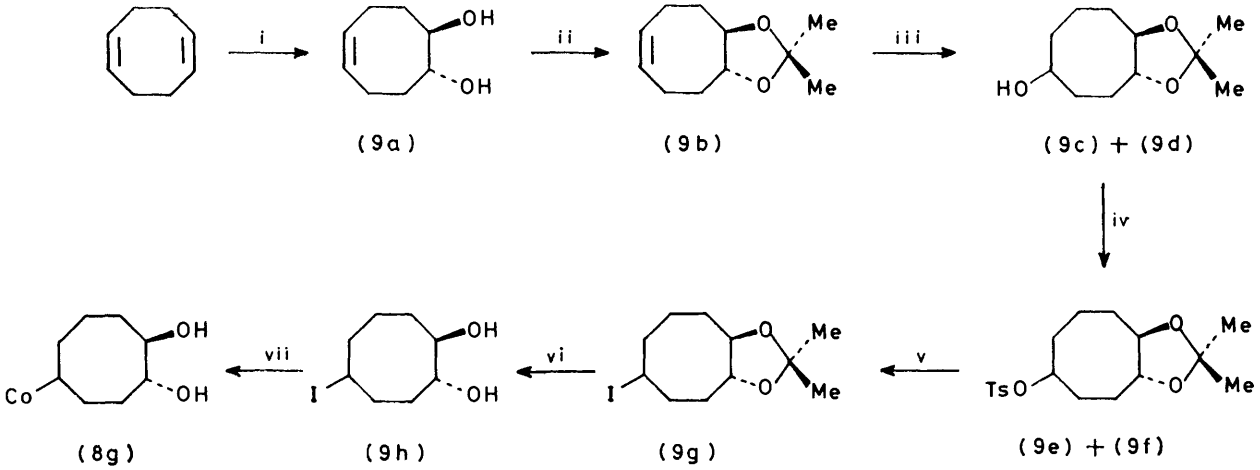
FIGURE 3 Mass spectrum of hexan-1-one (A) and 6-deuteriohexan-2-one (B) from (8f)

g.l.c.–m.s.; see above) shows an ion at *m/e* 58, CH_2=C(OH)-$Me^{+\bullet}$, which arises by McLafferty rearrangement from the molecular ion of hexan-2-one. The intensity of the *m/e* 59 ion relative to other peaks is not significantly greater than the intensity of the *m/e* 59 ion in the spectrum of unlabelled hexan-2-one (*cf.* Figure 3). Therefore deuterium is at C-4, C-5, or C-6 in the deuteriated hexan-2-one and is lost in propene during McLafferty rearrangement. Transfer of deuterium from C-5 of (8f) to C-4 or C-5 of the deuteriated hexan-2-one is unlikely. That deuterium is very probably at C-6 in the deuteriated hexan-2-one was supported by ^2H n.m.r. spectra. Two *ca.* 0.5-mmol lots of (8f) were photolysed in 0.1M acetic acid. Each reaction mixture was poured into acidic 2,4-dinitrophenylhydrazine. To one mixture was added 10 μl of hexan-2-one. To the other was added 10 μl hexanal. In both cases a DNP precipitate formed and was collected. It was hoped that the carriers would co-precipitate the corresponding deuteriated compound (*e.g.* hexanal), but reject the accompanying deuteriated compound (*e.g.* hexan-2-one). In practice, ^2H n.m.r. spectra of the DNPs from these experiments show that in each case deuteriated hexanal DNP and deuteriated hexan-2-one DNP co-precipitated (*n.b.* the m.p.s of hexanal and hexan-2-one DNP are identical). The ^2H n.m.r. spectrum of the DNP obtained using carrier hexanal shows signals at δ 2.67 and 1.15 (intensity ratio 5 : 1) corresponding to signals at δ 2.65 (2 × H-2) in the ^1H n.m.r. spectrum of hexanal DNP and 1.07 (3 × H-6) in the spectrum of hexan-2-one DNP. The ^2H n.m.r. spectrum of the DNP obtained using carrier hexan-2-one shows the same signals in a similar ratio. In the region of this spectrum corresponding to H-4 and H-5 in the ^2H n.m.r. spectrum of hexan-2-one DNP there is no intensity discernible above noise. It can be concluded that deuterium is absent from C-4 and C-5 of deuteriated hexan-2-one from (8f) and must therefore be at C-6.

(C) *Synthesis and Photodecomposition of* (8g).—The route used for the synthesis of (8g) from cyclo-oct-5-ene-*trans*-1,2-diol (9a) is shown in Scheme 5. The alcohols (9c) and (9d) were obtained either by hydroboration or, in better yield, by oxymercuration of (9b). A Dreiding model of (9b) shows that only one face of its double bond can be approached by a reagent, but the carbon atoms of this face are of comparable accessibility and so a mixture of diastereoisomers [(4*R*,7*R*,11*R*) (9c) and its enantiomer, (4*R*,7*S*,11*R*) (9d)] are obtained as indicated by the ^{13}C n.m.r. spectrum of the product. These were separated by fractional recrystallisation of their toluene-*p*-sulphonates [(9e) and (9f)] which were distinguishable by their m.p.s and ^{13}C n.m.r. spectra. We are unable from the spectral evidence to determine whether the isomer of lower m.p. is (9e) or (9f). It was hoped that separate cyclo-octylcobaloximes could be obtained from each toluene-*p*-sulphonate. The steric course of substitution at a secondary toluene-*p*-sulphonate by cobaloxime(I) has been determined [17] as inversion (S_N2). Therefore, a crystal structure analysis of either of the toluene-*p*-sulphonates or derived cyclo-octylcobaloximes would have unravelled the stereochemistry of all compounds in this series. However, both toluene-*p*-sulphonates failed to react with cobaloxime(I). Careful treatment of the mixture of toluene-*p*-sulphonates with iodide ion in acetone gave the unstable iodide (9g), as a mixture of diastereoisomers. These compounds reacted readily with cobaloxime(I) to yield the cyclo-octylcobaloxime (8h) which was not converted into (8g) by acidic hydrolysis [*cf.* the ready conversions of precursor acetals into (8a)—(8d)]. This failure stems from the unusual stability of the acetal in (8h) necessitating the use of stronger acid which causes degradation of the cobaloxime. However, the iodide (9g) could be hydrolysed satisfactorily to 1,2-dihydroxy-5-iodocyclo-

octanone (9h), although 1M aqueous hydrochloric acid was required with a long reaction time. The iodide (9h) was then treated with cobaloxime(I) to yield (8g). Although the n.m.r. spectroscopic data for (8g) are consistent with it being a single diastereoisomer, we are unable to specify its relative configuration at C-1. Crystals suitable for structure analysis could not be obtained. Note that the chiral centre at C-1 is destroyed after homolytic cleavage of the Co–C bond of (8g) to give a 4,5-dihydroxycyclo-octyl radical.

Anaerobic photolysis of (8g) in 0.1M acetic acid gave

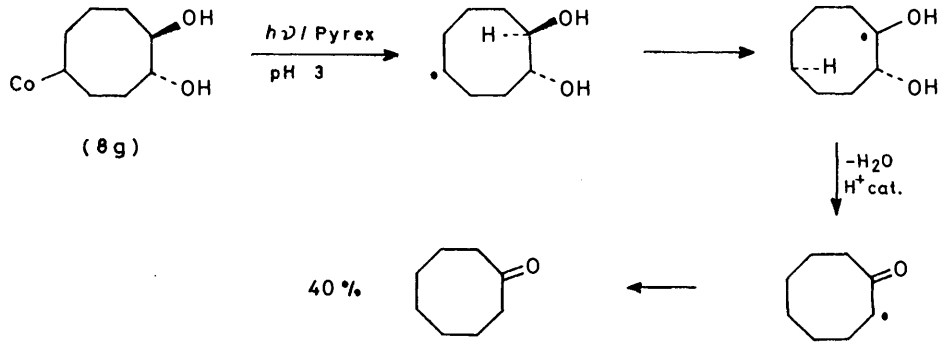


SCHEME 5 Synthesis of 4,5-dihydroxycyclo-octyl(pyridine)cobaloxime (8g). *Reagents:* i, HCO_2H, H_2O_2, aq. NaOH; ii, Me_2CO, petrol, catalytic TsOH; iii, $Hg(OAc)_2$, $NaBH_4$; iv, TsCl, py; v, NaI, Me_2CO; vi, aq. HCl, MeOH; vii, $CoCl_2 \cdot 6H_2O$, $dmgH_2$, py, KBH_4, NaOH

cyclo-octanone, isolated as its DNP in 30% yield. Because only *ca.* 80% of the cyclo-octanone formed will be recovered in this way [7] the actual yield of the ketone is *ca.* 40%. A suggested pathway for the formation of cyclo-octanone from (8g) is shown in Scheme 6. This parallels the pathway elucidated for the formation of pentanal from (8b) (see above and ref. 7).

DISCUSSION

As discussed in detail elsewhere,[7] the production of pentanal from anaerobic photolysis of (8b), predominantly hexan-2-one from (8c) and the failure of (8a) or (8d) to yield any aldehyde or ketone, are consistent with the reaction pathway of Scheme 1. Step 2 [(3) ⟶ (4)] only occurs when $n = 2$ or 3; when $n = 3$ the preference for a 1,5-hydrogen shift over a 1,6-hydrogen shift causes (3) ($n = 3$) to isomerise predominantly to the radical $Me[CH_2]_3\dot{C}(OH)CH_2OH$. The observation that the major product from anaerobic photolysis of (8f) in 0.1M acetic acid is hexanal (deuteriated at C-2), whereas the major product from (8c) is hexan-2-one, is convincing evidence that these products arise *via* 1,*n*-hydrogen shifts ($n = 5$ in the case of hexan-2-one, $n = 6$ for hexanal). With (8f), substitution of deuterium for hydrogen at C-5 makes the 1,5-atom transfer leading to 6-deuteriohexan-2-one more difficult than the corresponding reaction leading to hexan-2-one from (8c). The less favourable reaction with (8c), 1,6-hydrogen transfer leading to hexanal, is the more favourable reaction with (8f). For another example of such product switching on substituting deuterium for hydrogen see ref. 18. The primary kinetic isotope effects observed in the photodecompositions of (8e) and (8f) are both *ca.* 20 and are much larger than the ' theoretical maximum value ' of *ca.* 7.[19] Values appreciably larger than 7 have been reported for abstraction of hydrogen from C–H bonds by carbon radicals (*e.g.* $CF_3^{\bullet} + CH_4$).[20] Although unusually high values for primary kinetic isotope effects are frequently ascribed to



SCHEME 6 Pathway for the formation of cyclo-octanone from photolysis of (8g) at pH 3

tunnelling,[21] we are unable, without further work, to specify reasons for the high values reported here. It remains to establish how the 1,2-dihydroxypentyl radical is converted into pentanal and how the 1-hydroxy-1-(hydroxymethyl)pentyl radical goes to hexan-2-one. Recently, it has been suggested that dihydroxyalkylcobalt species are intermediates in analogous conversions (but *cf.* ref. 3).[22] Whatever the exact mechanism of these steps, the last step in our current model systems deviates from steps 4 and 5 of Scheme 1. This is because bis(aqua)cobaloxime(II), considered to be initially produced on photolysis of (8), is kinetically unstable at pH 3 and rapidly degrades to aquated cobalt(II) ion.[23] Therefore, an alkylcobaloxime is unlikely to re-form from either a 1-(dihydroxymethyl)-butyl radical (or 1-formylbutyl radical) or a 5,5-dihydroxypentyl radical.

Photolysis of 4,5-dihydroxycyclo-octyl(pyridine)-cobaloxime (8g) in 0.1M acetic acid gives *ca.* 40% of cyclo-octanone. The relative high efficiency of this conversion probably derives from the favourable 1,5-hydrogen shift which can occur in the intermediate 4,5-dihydroxycyclo-octyl radical (*cf.* Scheme 6). Efficient carbon-to-carbon 1,5-hydrogen shifts in cyclo-octyl radicals have been reported.[24] The present example provides a model for the conversion of butane-2,3-diol into butanone catalysed by diol dehydrase.[1]

EXPERIMENTAL

Solvents were either analytical grade or redistilled before use. Reagents were analytical grade if available or the best laboratory reagent grade, used without further purification. Ether for reductions with lithium aluminium hydride was first dried over sodium wire and then redistilled from lithium aluminium hydride under a dry nitrogen atmosphere. Lithium aluminium deuteride, obtained from Merck Sharpe & Doehm, was of 99% minimum isotopic purity. Silica gel for column chromatography (Merck No. 7754) was purified before use by heating with concentrated hydrochloric acid, washing with water, methanol, and chloroform, and finally heating at 120 °C for 24 h. ^{1}H n.m.r. spectra were recorded either using a Perkin-Elmer R12 instrument (60 MHz) at 310 K or with the aid of a Bruker WH-90 (90 MHz) spectrometer. ^{2}H N.m.r. spectra were recorded with a Bruker HFX-13 spectrometer at 15 MHz. Yields of DNPs were estimated by measuring the absorbance maximum of methanolic solutions at $\lambda_{max.}$ 358 nm (ε 2.2 × 10^4 l mol^{-1} cm^{-1}) using a calibrated Unicam S.P. 500 spectrophotometer. Mass spectra were recorded by P.C.M.U. (Harwell) on an MS9 instrument by the electron-impact technique using a 70 eV source.

1,1,5,5-*Tetradeuteriopentane*-1,2,5-*triol*.—Diethyl (*S*)-2-hydroxyglutarate [9,10] (2.97 g, 14.6 mmol) in ether (50 cm^3) was added during 15 min to a stirred suspension of lithium aluminium deuteride (1.67 g, 39.8 mmol) in ether (100 cm^3) at room temperature. The suspension was stirred for 16 h and then D_2O (5 cm^3) was added dropwise. The mixture was stirred for 15 min and filtered, and the solid was extracted (Soxhlet) with ethanol for 4 h. The extract was combined with the ethereal filtrate and the solvents were evaporated off giving a mixture of a yellow viscid oil and a white solid. This mixture was dissolved in water (10 cm^3) and 1M sulphuric acid was added to raise the pH to 7. The water was evaporated off and the residue was distilled *in vacuo*: yield 864 mg (7 mmol, 48%), b.p. 100—110 °C at 0.005—0.001 mmHg (Kügelrohr); n.m.r. (D_2O) δ 1.1—1.8 (m, 4 H) and 3.71 (t, 1 H).

1-*Deuteriocyclohex*-2-*en*-1-*ol*.—Cyclohex-2-en-1-one (4.66 g, 48.5 mmol) was dissolved in ether (50 cm^3) and the solution was stirred under dry nitrogen at room temperature for 20 min. The solution was cooled to 10 °C and a suspension of lithium aluminium deuteride (0.51 g, 12.1 mmol) in ether (50 cm^3) (prepared by boiling the solid with the ether for 10 min, cooling, and transferring to a dropping funnel under a nitrogen atmosphere) was added over 30 min. The suspension was finally stirred under nitrogen at room temperature for 15½ h. Acetone (3 cm^3) was added to decompose residual $LiAlD_4$ and after stirring for 5 min, saturated aqueous ammonium chloride (225 cm^3) was added (aqueous layer pH 8). The suspension was filtered and the ether layer was separated from the filtrate. The aqueous phase was extracted with ether (4 × 25 cm^3) and the combined ethereal extracts were washed with brine (25 cm^3) and dried ($MgSO_4$). The solvent was evaporated off to yield a yellow oil (3.88 g), contaminated with cyclohex-2-en-1-one according to t.l.c. (silica gel, CH_2Cl_2). The crude material was dissolved in CH_2Cl_2 (10 cm^3) and chromatographed on neutral alumina (type III, 60 g, 15 × 300 mm column) with dichloromethane as eluant (flow rate 1.5 cm^3 min^{-1}). The first 90 cm^3 were collected and the solvent was evaporated off. T.l.c. (silica gel, CH_2Cl_2) of the residual oil indicated the presence of a fast running impurity. The oil was dissolved in dichloromethane (5 cm^3) and filtered through silica gel (Merck 70—230 mesh, 20 g), rejecting the first 10 cm^3 of eluant dichloromethane. The eluate was dried ($MgSO_4$), solvent was evaporated off, and the residue was distilled to give an oil (2.7 g, 27.3 mmol, 56%), b.p. 160—162 °C at atmospheric pressure. This product was pure by t.l.c. (silica gel, CH_2Cl_2) but n.m.r. spectroscopy indicated the presence of an impurity (probably cyclohex-3-en-1-ol); n.m.r. (CCl_4) δ 1.0—2.9 (m, 7 H), 5.6—6.1 (m), and 5.70 (s) (total 2 H).

4-*Deuterio*-4-(4′-*hydroxybutyl*)-2,2-*dimethyl*-1,3-*dioxolan*.—1-Deuteriocyclohex-2-en-1-ol (2.32 g, 22.4 mmol) was dissolved in absolute ethanol (75 cm^3) and cooled to −15 °C. A stream of ozonised oxygen (*ca.* 5% v/v O_3; 1 dm^3 min^{-1}) was passed through the solution for 25 min. The resulting solution was added dropwise to a stirred, ice-cold suspension of sodium hydroborate (2.0 g, 52.6 mmol) in ethanol (75 cm^3). Stirring was continued for 2 h at 0 °C and then at room temperature for 21 h. The suspension was treated with 2M aqueous HCl (17 cm^3) until acidic (pH 1—2) and the mixture was filtered. The residual solid was triturated with portions of ethanol and was filtered again. The combined filtrates were evaporated at 35—40 °C to yield a white solid and non-volatile oil. This mixture was dissolved in acetone (30 cm^3) and petrol (b.p. 40—60 °C; 30 cm^3) containing toluene-*p*-sulphonic acid (100 mg) and was heated in a Dean–Stark apparatus for 72 h. The solvent was evaporated off and the residual oil was dissolved in ether (15 cm^3). The ethereal solution was shaken with saturated sodium carbonate solution (15 cm^3) and was dried (K_2CO_3). Solvent was removed and the residual oil was distilled *in vacuo*; yield: 2.06 g (11.8 mmol, 53%), b.p. 70—80 °C at 0.005—0.01 mmHg (Kügelrohr); n.m.r. (CCl_4) δ 1.26 (s, 3 H), 1.31 (s, 3 H), 1.35—1.70 (m, 6 H), 2.91 (s, 1 H), and 3.3—4.1 (m, 4 H); i.r. (film) 3 430br,

2 990, 2 940, 2 870, 2 140br, 1 380, and 1 370s cm^{-1}. Addition of $Eu_2(fod)_6$ to the sample resolved the multiplet at δ 3.3—4.1 into a triplet (*J* 6 Hz, CH_2OH) and an AB quartet from diastereotopic hydrogen atoms at C-5.

5,5-*Dideuterio*-4-(3′,3′-*dideuterio*-3′-*hydroxypropyl*)-2,2-*dimethyl*-1,3-*dioxolan*.—This compound was prepared from 1,1,5,5-tetradeuteriopentane-1,2,5-triol (864 mg, 7 mmol) in an analogous manner to that just described; yield: 902 mg (5.5 mmol, 79%), b.p. 60—66 °C at 0.01 mmHg (Kügelrohr); n.m.r. (CCl_4) δ 1.27 (s, 3 H), 1.32 (s, 3 H), 1.5—1.65 (m, 4 H), 3.1—3.35 (m, 1 H), and 4.0br (s, 1 H).

4-*Deuterio*-2,2-*dimethyl*-4-(4′-p-*tolylsulphonyloxybutyl*)-1,3-*dioxolan*.— 4-Deuterio-4-(4-hydroxybutyl)-2,2-dimethyl-1,3-dioxolan (1.16 g, 6.62 mmol) was dissolved in ice-cold pyridine (3.1 cm^3). A solution of toluene-*p*-sulphonyl chloride in pyridine (3.3 cm^3) was added over 10 min and the mixture was stirred for an additional 65 min at room temperature. The mixture was poured into 10 cm^3 of ice-cold 2M hydrochloric acid and additional acid (12.5 cm^3) was added to bring the pH to 1. The toluene-*p*-sulphonate was extracted with ether (3 × 25 cm^3), and the combined ether extracts were washed with 2M hydrochloric acid (10 cm^3), 10% sodium carbonate (10 cm^3), and brine (10 cm^3) and were finally dried (K_2CO_3–$MgSO_4$). The solvent was removed to yield a viscous oil (1.92 g, 5.84 mmol, 88%); n.m.r. (CCl_4) δ 1.23 (s, 3 H), 1.28 (s, 3 H) 1.25—1.95 (m, 6 H), 2.44 (s, 3 H), 3.2—4.2 (m, 4 H), and 7.2—7.95 (AB q, 4 H).

5,5-*Dideuterio*-4-(3′,3′-*dideuterio*-3′-p-*tolylsulphonyloxypropyl*)-2,2-*dimethyl*-1,3-*dioxolan*.—This compound was prepared in an analogous manner from 5,5-dideuterio-4-(3′,3′-dideuterio-3′-hydroxypropyl)-2,2-dimethyl-1,3-dioxolan in 80% yield; n.m.r. (CCl_4) δ 1.23 (s, 3 H), 1.27 (s, 3 H), 1.4—1.8 (m, 4 H), 2.44 (s, 3 H), 3.9br (t, 1 H), and 7.2—7.9 (AB q, 4 H).

5-*Deuterio*-5,6-*dihydroxyhexyl*(*pyridine*)*cobaloxime* (8f).—A solution of cobalt dichloride hexahydrate (2.38 g, 10 mmol) in methanol (30 cm^3) was degassed with bubbling argon for 15 min. Dimethylglyoxime (2.32 g, 20 mmol) was added and the suspension was stirred for 30 min under argon. Sodium hydroxide (20 mmol in 12.7M aq. solution) and pyridine (0.81 cm^3, 10 mmol) were added and the homogeneous solution was cooled to −15 °C and stirred for 15 min. Aqueous sodium hydroxide (10 mmol) and potassium hydroborate (135 mg, 2.5 mmol) in water (2 cm^3) were added and after stirring for 15 min, a solution of 4-deuterio-2,2-dimethyl-4-(4-*p*-tolysulphonyloxybutyl)-1,3-dioxolan (1.92 g, 5.83 mmol) in methanol (4 cm^3) was added. The mixture was stirred at 0 °C for 3 h, the argon supply was disconnected, and the suspension was kept at room temperature in the dark, in a stoppered flask for 72 h. The mixture was partly evaporated by blowing a gentle stream of air for 90 min and was then poured into water (130 cm^3) containing pyridine (0.2 cm^3). The yellow solid was filtered off and washed with cold water containing pyridine. The material was sucked dry on a sinter and was completely dried *in vacuo*; yield: 2.67 g (5.07 mmol, 87%). This product (2.67 g, 5.07 mmol) was stirred in absolute ethanol (20 cm^3) with 2M hydrochloric acid (3 cm^3). The solid slowly dissolved and after 2 h the reaction was complete as monitored by t.l.c. [silica gel, 10% MeOH–CH_2Cl_2; starting material R_F 0.63, (8f) R_F 0.12]. The mixture was evaporated to *ca.* 1 cm^3 at room temperature and pyridine (1 cm^3) was added, whereupon an orange solid precipitated. Excess of solvent was evaporated off. The solid was dissolved in 10% methanol–dichloromethane (6 cm^3) and filtered through silica gel (10 g) eluting with the same solvent mixture. A small fast-running yellow band (unchanged starting material) was rejected. The main eluate was evaporated to a small volume, pyridine (1 cm^3) was added, and the excess of solvent was removed by freeze-drying. The residual solid was recrystallised from 10% methanol–dichloromethane–0.1% pyridine at −20 °C; yield: 1.07 g (2.2 mmol, 43%); n.m.r. ($CDCl_3$), δ 0.6—1.8 (m, 8 H), 2.13 (s, 12 H), 3.49 (m, 2 H), and 7.2—8.8 (m, 5 H).

1,1,5,5-*Tetradeuterio*-4,5-*dihydroxypentyl*(*pyridine*)-*cobaloxime* (8e).—This compound was prepared in an analogous manner to (8f): n.m.r. ($CDCl_3$) δ 0.99 (m, 2 H), 1.32 (m, 2 H), 2,13 (s, 12 H), 3.64br (t, 1 H), 7.3 (m, 2 H), 7.7 (m, 1 H), and 8.5 (m, 2 H).

Photolysis of (8e).—For general directions see ref. 7. A solution of (8e) (237 mg) in 0.1M acetic acid (234 cm^3) was degassed by argon bubbling and photolysed until colourless (35 min). At this point DNP reagent was added and the reaction was worked up in the usual manner.[7] After column chromatography, the band of deuteriated pentanal DNP was collected and was further purified by preparative layer chromatography [20 × 20 × 0.5 cm silica gel plate, elution with ether–petrol (1 : 3)] to give deuteriated pentanal DNP (0.57% by u.v.–visible spectroscopy).

Isolation of Deuteriated Pentane-1,2-*diol and* 4,5-*Dihydroxypent*-1-*ene from Photolysis of* (8e).—After photolysis of (8e) (200 mg) in 0.1M acetic acid (250 cm^3) and treatment of the resulting solution with DNP reagent in the manner just described, the aqueous solution from extracting pentanal DNP with dichloromethane was continuously extracted for 48 h with ether. The ethereal extract was dried and evaporated and the residue was chromatographed on silica gel using methyl acetate as eluant. A fraction containing deuteriated pentane-1,2-diol and 4,5-dihydroxypent-1-ene was isolated and examined by ^1H n.m.r. spectroscopy (see text).

Photolysis of (8f).—For general directions see ref. 7. A solution of (8f) (55.8 mg) in 0.1M acetic acid (44.5 cm^3) was degassed by argon bubbling and photolysed until colourless (15 min). At this point DNP reagent (50 cm^3) was added and the mixture was stirred for 30 min. Extraction with dichloromethane (3 × 25 cm^3), drying of the combined extracts, and evaporation gave a residue that was triturated with ether–petrol (1 : 1); the ether was added first, the mixture was swirled briefly, and then an equal volume of petrol was added. The ether–petrol extract was filtered on a column of silica gel. Elution with chloroform gave a yellow fraction which was evaporated, leaving a mixture of deuteriated hexan-2-one and hexanal DNPs (4.1% by u.v.–visible spectroscopy).

In another experiment on the same scale as above, the colourless solution from photolysis was extracted with pentane. Careful concentration gave a solution of deuteriated hexan-2-one and hexanal in pentane which was examined by g.l.c. and g.l.c.–mass spectrometry. G.l.c. (Perkin-Elmer F11; QF-1; 30 °C) showed a ratio of deuteriated hexan-2-one to hexanal of 1 : 5. G.l.c.–m.s. was performed with a Pye 104 chromatograph containing 1.5% QF1 on Chromosorb W column (5 ft, 4 mm i.d.) at 30 °C coupled to an A.E.I. MS50 mass spectrometer. With a helium flow rate of 40 cm^3 min^{-1} the retention time of deuteriated hexanal was 4.0 min, and that of deuteriated hexan-2-one 5.4 min. M.s. scans around the profile of each g.l.c. peak gave for deuteriated hexan-2-one a $[^2H_1]$-content

of 40%, and for deuteriated hexanal a [$^2H_1$]-content of *ca.* 80%. An accurate figure for the aldehyde could not be obtained owing to the low abundance of its molecular ion and the existence of a peak at $(M - 1)^+$.

In a third experiment, deuteriated hexanal and hexan-2-one were extracted with carbon tetrachloride. The extract was concentrated to 0.5 cm^3 and was examined by ^{1}H n.m.r. spectroscopy (see text).

Preparation of Samples of Deuteriated Pentanal, Hexanal, and Hexan-2-one for ^{2}H *N.M.R. Spectroscopy.*—(a) [$^2H_4$]-*Pentanal.* Compound (8e) (253 mg) in 0.1M acetic acid (250 cm^3) was degassed and photolysed (10 min) in the usual manner. The resulting solution was poured into ice-cold DNP reagent (100 cm^3) and redistilled pentanal (10 μl) was added. The mixture was shaken and cooled in an ice-bath for 2½ h. The precipitate was removed by centrifugation and was dissolved in dichloromethane (30 cm^3). The supernatant liquid was extracted with dichloromethane (3 × 50 cm^3) and the combined dichloromethane solutions were dried and evaporated. The residue was triturated with ether (5 cm^3), petrol (5 cm^3) was added, and the resulting mixture was filtered through a short silica gel column, washing with 1 : 1 ether–petrol. The filtrate was evaporated and the yellow crystalline residue was examined by ^{2}H n.m.r. spectroscopy (see text).

(b) [^{2}H]*Hexanal.* Using the foregoing procedure with (8f) (250 mg) with addition of unlabelled hexanal (10 μl) after photolysis gave [^{2}H]hexanal DNP diluted with hexanal DNP.

(c) [^{2}H]*Hexan-2-one.* The foregoing procedure with (8f) (259 mg), with addition of unlabelled hexan-2-one (10 μl), after photolysis gave [^{2}H]hexan-2-one DNP, diluted with hexan-2-one DNP.

10,10-*Dimethyl*-9,11-*dioxabicyclo*[6.3.0]*undec*-4-*ene.*—Cyclo-oct-5-ene-*trans*-1,2-diol was prepared by treating *cis*,*cis*-cyclo-octa-1,5-diene with performic acid followed by alkaline hydrolysis;[25] {^{1}H}-^{13}C n.m.r. ($CDCl_3$) δ 22.0, 27.0, 31.8, 81.0, 107.3, and 129.6 p.p.m. The *trans*-diol (8.8 g, 60.5 mmol) in acetone (75 cm^3) and benzene (75 cm^3) containing toluene-*p*-sulphonic acid (57 mg) was heated in a Dean–Stark apparatus for 18 h. The solvent was evaporated off and the residue, dissolved in dichloromethane (15 cm^3), was washed with 2M aqueous sodium carbonate (5 cm^3) and brine (10 cm^3) and was then dried (Na_2CO_3–K_2CO_3). The solvent was evaporated off and the residue was distilled under reduced pressure to yield the title compound as an oil, (6.6 g, 38.6 mmol, 64%), b.p. 40—50 °C at 0.08—0.12 mmHg (lit.,[26] 66—68 °C at 2 mmHg).

10,10-*Dimethyl*-4-*hydroxy*-9,11-*dioxabicyclo*[6.3.0]*undecane.*—10,10-Dimethyl-9,11-dioxabicyclo[6.3.0]undec-4-ene (13.8 g, 75.7 mmol) was stirred in tetrahydrofuran (60 cm^3) at room temperature whilst a solution of mercury(II) acetate (27.8 g, 86.8 mmol) in water (95 cm^3) and glacial acetic acid (1 cm^3) was added dropwise. The mixture was stirred for 104 h and then 3M sodium hydroxide (50 cm^3) was added until a permanent yellow precipitate formed. The mixture was cooled in ice and a solution of sodium hydroborate (1.7 g, 45 mmol) in 3M sodium hydroxide (50 cm^3) was added. The mixture was then stirred for 10 min, the mercury was allowed to settle, and sodium chloride was added to saturate the aqueous phase. The pale yellow organic layer was separated and the aqueous layer was extracted with dichloromethane (100 cm^3). The combined organic extracts were dried ($MgSO_4$), the solvent was evaporated off, and the residue distilled to yield the title compound as an oil (9.8 g, 49 mmol, 65%), b.p. 109—111 °C at 0.1 mmHg; n.m.r. (CCl_4) δ 1.25—1.30 (m, 6 H), 1.2—2.5 (m, 10 H), 2.8br (s, 1 H, exchangeable with D_2O), and 3.7br (m, 3 H). The {^{1}H}-^{13}C n.m.r. spectrum of this compound shows it to be a mixture of diastereoisomers: δ 16.6, 20.7, 27.0, 27.2, 29.0, 30.2, 33.0, 33.4, 33.8, 34.3, 37.0, 69.7, 72.7, 80.0, 81.2, 106.6, and 106.8 p.p.m. Hydroboration of the dioxabicyclo[6.3.0]undecene with diborane in tetrahydrofuran, followed by oxidative cleavage with sodium hydroxide–hydrogen peroxide, gave the title compound in 55% yield.

Toluene-p-*sulphonates from* 10,10-*Dimethyl*-4-*hydroxy*-9-11-*dioxabicyclo*[6.3.0]*undecane.*—The alcohol (7.0 g, 35 mmol) was treated with toluene-*p*-sulphonyl chloride (8.1 g, 42.5 mmol) in dry pyridine as described.[7] After 16 h at 0 °C the mixture was worked up to yield a pale yellow, viscid oil (12.3 g, 99%), to which an equal volume of petrol (b.p. 40—60 °C) was added. The resulting homogeneous solution was cooled in ice to give a white solid, which was recrystallised from 1 : 1 dichloromethane–petrol at −20 °C. The resulting white crystals (m.p. 95—97 °C; 3.9 g, 31%) consisted of a single isomer according to spectral data: ^{1}H n.m.r. ($CDCl_3$) δ 1.3 (s, 6 H), 1.2—2.3 (m, 10 H), 2.43 (s, 3 H), 3.65br, (m, 2 H), 4.65br, (m, 2 H), and 7.25, 7.40, 7.70 and 7.85 (AB q, 4 H); {^{1}H}-^{13}C n.m.r. ($CDCl_3$) δ 16.8, 19.8, 21.6, 26.6, 26.9, 28.5, 29.7, 32.0, 33.0, 33.4, 34.0, 80.1, 81.8, 83.9, 106.8, 127.7, 129.9, 135.5, and 144.3 p.p.m. (Found: C, 61.1; H, 7.3; S, 9.1. $C_{18}H_{26}O_5S$ requires C, 61.0; H, 7.4; S, 9.1%).

The filtrate from the crystallisation from petrol was evaporated at room temperature to yield a white solid which on crystallisation from 1 : 1 dichloromethane–petrol gave white crystals, m.p. 65—66 °C (4.2 g, 34%); ^{1}H n.m.r. ($CDCl_3$) δ 1.35 (s, 6 H), 1.15—2.6 (m, 10 H), 2.48 (s, 3 H), 3.75br (m, 2 H), 4.75br, (m, 1 H), and 7.28, 7.53, 7.84, and 7.99 (AB q, 4 H); {^{1}H}-^{13}C n.m.r. ($CDCl_3$) δ 16.9, 21.6, 26.6, 27.0, 28.6, 32.1, 33.0, 80.1, 81.8, 106.9, 127.7, 129.9, 135.1, 141.0, and 150.9 p.p.m. (Found: C, 60.7; H, 7.4; S, 9.2%).

Reaction of either of the foregoing toluene-*p*-sulphonates with (pyridine)cobaloxime(I) [prepared either under Schrauzer's conditions[27] or by reducing bromo(pyridine)-cobaloxime with sodium hydroborate in ethanol] failed to yield an alkylcobaloxime.

10,10-*Dimethyl*-4-*iodo*-9,11-*dioxabicyclo*[6.3.0]*undecane.*—Treatment of the foregoing toluene-*p*-sulphonates with sodium iodide in acetone at either room temperature or 0 °C in the dark resulting in rapid darkening of the mixture. Work-up gave the title compound (mixture of diastereoisomers) contaminated with iodine and 10,10-dimethyl-9,11-dioxabicyclo[6.3.0]undec-4-ene. Purification was achieved either by column chromatography or low pressure distillation giving an initially pale yellow oil which rapidly darkened, even when stored in the dark at −20 °C; ^{1}H n.m.r. ($CDCl_3$) δ 1.39 (m, 6 H), 1.0—2.8br (m, 10 H), 3.65—4.1 (m, 2 H), and 4.1—4.9 (m, 1 H); {^{1}H}-^{13}C n.m.r. ($CDCl_3$) δ 20.9, 21.8, 23.3, 27.0, 31.3, 31.7, 32.8, 33.1, 43.1, 35.9, 37.7, 40.5, 79.0, 79.6, 80.0, 80.5, 106.2, 106.6, and 129.3 p.p.m.

5-*Iodocyclo-octane*-1,2-*diol.*–The foregoing iodo-acetal (6.5 g, 21.0 mmol) was dissolved in methanol (20 cm^3) and an equal volume of 2M aqueous hydrochloric acid was added. The homogeneous mixture was left at room temperature for 3 days to complete the deacetalisation. Aqueous sodium carbonate (2M) was added to neutralise the acid and

the dark mixture was evaporated to small volume. The residue was extracted with dichloromethane (2 × 10 cm³), and solvent was off evaporated to yield 5-iodocyclo-octane-1,2-diol as a brown oil (3.9 g, 14.5 mmol) which was used immediately.

4,5-*Dihydroxycyclo-octyl(pyridine)cobaloxime*.—This compound was prepared using cobalt dichloride hexahydrate (10 mmol) and crude 5-iodocyclo-octane-1,2-diol (14.5 mmol) following Schrauzer's procedure.[27] The crude cobaloxime was purified by chromatography on a column of silica gel eluting with dichloromethane–methanol–pyridine (9 : 1 : 0.1 v/v), followed by recrystallisation from dichloromethane containing 1% v/v pyridine at −20 °C; yield: 1.1 g (2.15 mmol, 21.5%); ^{1}H n.m.r. ($CDCl_3$) δ 0.7—2.0 (m, 10 H), 2.16 (s, 12 H), 3.1—3.7 (m, 2 H), 4.5—5.0 (m, 1 H), 7.26 (m, 2 H), 7.8 (m, 1 H), and 8.48 (m, 2 H) (Found C, 48.3; H, 6.4; N, 13.5. $C_{21}H_{34}CoN_4O_4$ requires: C, 49.3; H, 6.7; N, 13.7%).

Cyclo-octanone from Photolysis of (8g).—Anaerobic photolysis of (8g) in 0.1M aqueous acetic acid under previously described conditions [7] followed by treatment with DNP reagent and column chromatographic separation of DNPs gave cyclo-octanone DNP (30%), m.p. 171—174 °C (mixed m.p. 170—171 °C with authentic material of m.p. 177—179 °C). The ^{1}H n.m.r. spectrum of this product was identical to that of authentic cyclo-octanone DNP and its t.l.c. (silica gel, solvent systems: chloroform; 1 : 1 ether–petrol) showed a single spot with R_F identical to that of authentic standard.

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