Light-induced Conversion of Ethane-1,2-diol or 2-Aminoethanol into Acetaldehyde in the Presence of 8-Methoxy-5′-deoxy-5′-adenosylcobalamin or a Simpler Cobalt(III) Alkyl†

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Summary Anaerobic photolysis of the newly synthesised 8-methoxy-5′-deoxy-5′-adenosylcobalamin, methylcobalamin or methyl(aquo)cobaloxime (but not coenzyme B_{12}) causes the transformation of $HOCH_2CH_2X$ (X = NH_2 or OH) into MeCHO and the pH dependence of yield parallels that obtained in •OH induced reactions; the results are interpreted in terms of an initial hydrogen atom abstraction from substrate by a carbon-centred radical.

WE report results which may have a bearing on the mechanism of the 5′-deoxy-5′-adenosylcobalamin (AdoCbl-coenzyme B_{12})-controlled conversion of ethane-1,2-diol or 2-aminoethanol into acetaldehyde in the presence of the appropriate enzyme.

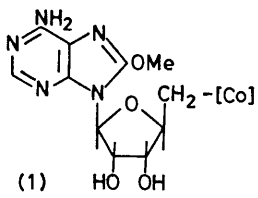
A coenzyme analogue, 8-methoxy-5′-deoxy-5′-adenosylcobalamin (**1**) (λ_{max} 534 nm) has been synthesised {in three steps from the nucleoside (**2**): (a) NaOMe–MeOH, (b) $SOCl_2$–hexamethylphosphoric triamide and (c) cob(I)alamin (B_{12s}); the intermediates, 8-methoxyadenosine and 8-methoxy-5′-chloro-5′-deoxyadenosine, were isolated and characterised; [Co] in (**1**) is such that [Co]-CN represents cyanocobalamin}, and shows a low activity in the ethanolamine ammonia-lyase system.[1] The results of a number [(i)—(iv)] of model (enzyme-free) experiments concerning anaerobic photolysis of a Co^{III} alkyl in the presence of substrate are summarised in the Table.

TABLE
Summary of photolysis experiments of substrate $HOCH_2CH_2X$ (X = NH_2 or OH) in presence of a Co^{III} alkyl showing % of MeCHO formed[a]

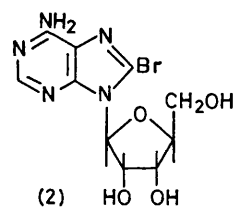
		Co^{III} alkyl			
Substrate	pH[b]	AdoCbl	(**1**)	(**3**)	(**4**)
1 M $HOCH_2CH_2OH$	2·0	0		11	32
"	7·4	0		8	17
"	11·2	4		36	35
9 M $HOCH_2CH_2OH$	2·0	3	13	34	73
"	7·4	8	21	17	17
"	11·2	10	64	46	95
Neat $HOCH_2CH_2OH$	—	0		0	6
1M $HOCH_2CH_2NH_2$	2·0	0		0	0
"	7·4	0[c]	11	29	25
"	11·2	2		0	0

[a] A $1·5 \times 10^{-3}$ M solution of the Co^{III} alkyl was photolysed for 3 h in the presence of substrate at 30 °C; yields (%) of MeCHO are based on photolysed cobalt and were determined spectrophotometrically at 340 nm using NADH and yeast-alcohol dehydrogenase (ref. 2); they are based on the mean of two or more measurements. Irradiation under N_2 was carried out in a Pyrex Schlenk tube using a 150 W Osram spotlight at a distance of 15 cm. [b] Buffered by HCl–KCl (pH, 2·0), $K_2H[PO_4]/KH_2[PO_4]$ (pH, 7·4), or $Na_2H[PO_4]/Na_3[PO_4]$ pH, 11·2). [c] 1 M $EtOCH_2CH_2NH_2$ also produced no MeCHO.

† No reprints available.

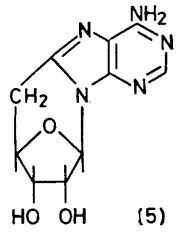


(1)



(2)

(i) Using compound (**1**), methylcobalamin (**3**), or methyl(aquo)cobaloxime (**4**), as the Co^{III} alkyl, significant conversion of substrate into acetaldehyde was achieved.
(ii) By contrast, contrary to an earlier assertion,[2] AdoCbl is essentially inactive towards either substrate or 2-amino-1-ethoxyethane; the dominant reaction is the intramolecular transformation of the nucleoside radical from AdoCbl into the 8,5′-*cyclic*-5′-deoxyadenosine (**5**), identified by t.l.c. in comparison with an authentic sample prepared[3] by anaerobic photolysis of substrate-free AdoCbl.



(5)

(iii) The pH dependence of the yield of MeCHO from $HOCH_2CH_2X$ (X = NH_2 or OH) using either of the Co^{III} methyls (**3**) or (**4**) parallels that obtained[4] using •OH (from Ti^{III}–H_2O_2 or pulse radiolysis), which was said to cause hydrogen atom abstraction and conversion of the resulting $\cdot CH(OH)CH_2X$ to $\cdot CH_2CHO$, both radicals being observed by e.s.r. spectroscopy.[4] This suggests that the conversion of substrate into MeCHO is cobalt-independent in our experiments.
(iv) We confirm that irradiation of a Co^{III} methyl in neat ethane-1,2-diol produces negligible acetaldehyde,[5] which we attribute to the failure of this medium to provide the general acid–base catalysis suggested by (iii).

Relevant to (iii), Golding and his co-workers[6] have reported a 10% conversion of $HOCH_2CH_2OH$ into MeCHO by anaerobic photolysis in the presence of (**4**) at pH 2. Under similar conditions, we also find MeCHO; the yields being 32% spectrophotometrically and by g.l.c. Furthermore, we observe a similar conversion at pH 11·2 by a preparative-scale experiment (forming the dimedone derivative of MeCHO).

As for (iii), our results are not due to formation of •OH *via* $\cdot CH_3$ because methylcobalamin (**3**) is apparently unaffected by exposure to light under conditions which cause its photolysis in the presence of *e.g.*, ethanediol. Moreover, in the presence of various alcohols, the rate of Co–CH_3 cleavage is dependent on the nature of ROH, *e.g.*, $Pr^i > Pr^n$;[7] this is attributed to the reversibility of the Co^{III}–CH_3 homolysis and the competition for the $\cdot CH_3$ formed, between hydrogen atom abstraction and recombination with the Co^{II} species. The formation of •OH *via* $\cdot CH_3$ is known to be relatively slow.[8]

The following control experiments relevant to (i)—(iv) were carried out: irradiation under various pH conditions of (a) each Co^{III} alkyl, (b) each substrate in the presence or absence of the appropriate Co^{II} compound [cob(II)alamin or diaquocobaloxime(II)], and (c) acetaldehyde. Additionally, (d), each mixture identical to that used in (i)—(iv) was stored in the dark at the same temperature (*ca.* 30 °C) for a similar period. In none of (a), (b), or (d) was MeCHO formed, except 4% for 9 M aqueous $HOCH_2CH_2OH$ at pH 11·2 in the presence of diaquocobaloxime(II) and in (c), there was negligible decomposition of MeCHO.

We conclude that (i) the formation of acetaldehyde from substrate $HOCH_2CH_2X$ (X = NH_2 or OH) in the photolysis experiments is initiated by a carbon-centred radical from the homolysis of the Co^{III} alkyl which abstracts a hydrogen atom giving $\cdot CH(OH)CH_2X$ (see also ref. 6), and (ii) the subsequent transformation of this substrate radical into MeCHO is cobalt-independent. It seems likely, (iii), that in the enzyme system the 8-position is 'protected' by the protein, so that cyclisation into (**5**) is prevented. Although we believe it is unwise to extrapolate from model experiments to enzyme systems, we note that (i) and (iii) are consistent with current ideas on mechanisms of AdoCbl-enzyme-controlled conversions of $HOCH_2CH_2X$ (X = NH_2 or OH) into MeCHO.[9]

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