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Photochemical Reactions of Vitamin B_{12} Derivatives

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Abstract:

The cobalt(III)corrins related to coenzyme B_{12} (**2**, R=5'-deoxyadenosyl) or to vitamin B_{12} (**1**, R=CN) are intensely coloured compounds and are known to undergo two types of light induced reactions: (light induced) loss of an axial ligand or sensitization of reactions with singlet oxygen. The former type of reaction provides an efficient entry to the production of alkyl radicals by the photolysis of the corresponding organometallic B_{12}-derivatives (such as **2**). New developments in the photochemistry of organometallic and other B_{12}-derivatives are delineated here.

1. INTRODUCTION

The cyano-Co(III)corrin vitamin B_{12} (**1**, R=CN), although without an apparent biological role itself, happened to be the first corrinoid isolated from a natural source (some 40 years ago) and to be structurally characterized [1]. The metabolically important organometallic cofactors themselves, such as coenzyme B_{12} (**2**, R=5'-adenosyl) or methylcobalamin (**3**, R = methyl, see Fig. 1), turned out to be remarkably sensitive to visible light, which impeded their isolation originally: in (aqueous) solution, from electronically excited methylcobalamin (**3**) as well as from thermally activated or electronically excited coenzyme B_{12} (**2**) cob(II)alamin (**4**) and an alkyl radical are set free [2]. The examination of this homolytic cleavage at the organometallic bond of organocobalamins, such as **2** or **3**, has found interest, not only due to the biological relevance of this type of reaction for the coenzyme **2** (see Fig. 2) [3,4], but also for synthetic purposes [5]. The photochemistry of organocobalamins, in particular, proved to be a versatile route to organic radicals.

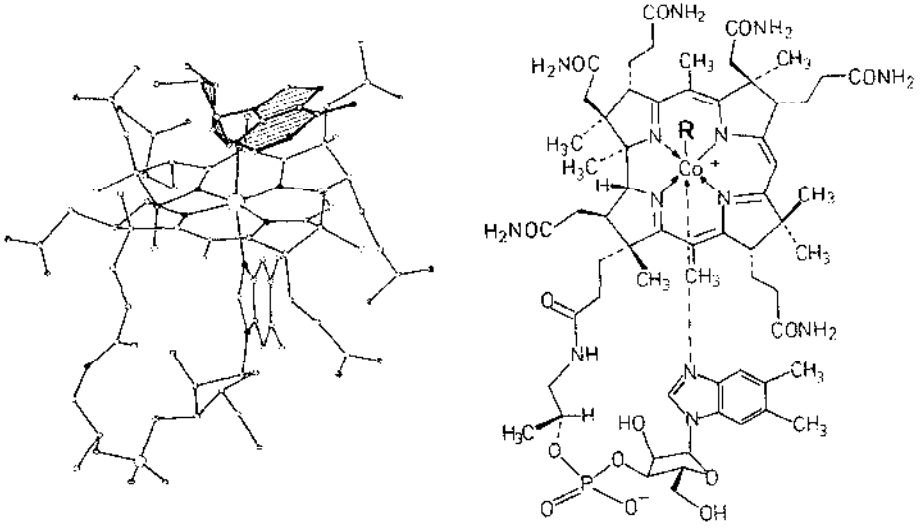

Figure 1: Structure of coenzyme B_{12} (**2**) according to X-ray analysis (Hodgkin et al.[1]) and structural formulae of vitamin B_{12} (**1**, R = CN), coenzyme B_{12} (**2**, R = 5'-adenosyl), methylcobalamin (**3**, R = methyl), cob(II)alamin (**4**, R = e) and other organocobalamins (R = alkyl, acyl).

Figure 2: Coenzyme B_{12} (**2**): its homolysis to cob(II)alamin (**4**) and 5'-deoxyadenosyl radical, as its biologically relevant reactivity [3,4].

The alkyl radicals and the radicaloid Co(II)corrin **4**, formed e.g. by photoinduced homolysis of **2** and **3**, in turn recombine at nearly diffusion controlled rate [6]: the thermally or photochemically induced Co-C-bond homolysis of **2** and **3** is thermally reversible in the absence of a radical

trap. Correspondingly the biologically relevant reactivities of the coenzyme **2** (a reversible source of a free alkyl radical by thermal homolysis of its Co-C-bond [4]) and of the radicaloid Co(II)corrin **4** (an excellent trap for alkyl radicals [6,7]) can be modelled profitably in particular by photochemical experiments in (aqueous) solutions, in the absence of oxygen. In the presence of oxygen, on the other hand, the photoinduced cleavage of the Co-C-bond of organometallic B_{12}-derivatives effectively becomes irreversible [2], due to the rapid reaction of molecular oxygen with alkyl radicals, as well as with the Co(II)corrin **4**.

2. A COBALT CORRIN AS SENSITIZER FOR REACTIONS WITH SINGLET OXYGEN

Some Co(III)corrins were observed recently to undergo a second type of light induced reaction: contrary to previous experiences with other Co(III)corrins [8], the dicyano-Co(III)-B-didehydrocorrinoid "pyrocobester" (**5**,[9]) turned out to be a good sensitizer for reactions with singlet oxygen ($\Phi(^1O_2)$ ca. 0.2) [10]. In oxygenated solution **5** is readily cleaved to yield the 5,6-dioxo-5,6-seco-B-didehydrocorrinoid **6** in a chemically uniform reaction (see Figure 3). This, and the (preliminary) observation of luminescence with **5**, indicate the photophysical behaviour of the B-didehydrocorrinoid **5** to deviate remarkably from that of the characteristically "nonluminescent" Co(III)corrins. This difference is a consequence of the conjugation of the additional double bond with the corrin π-system in **5**, which also causes a significant bathochromic shift of the absorbtion spectra (e.g. by ca.120 nm of the corresponding dicyano-Co(III)corrins).

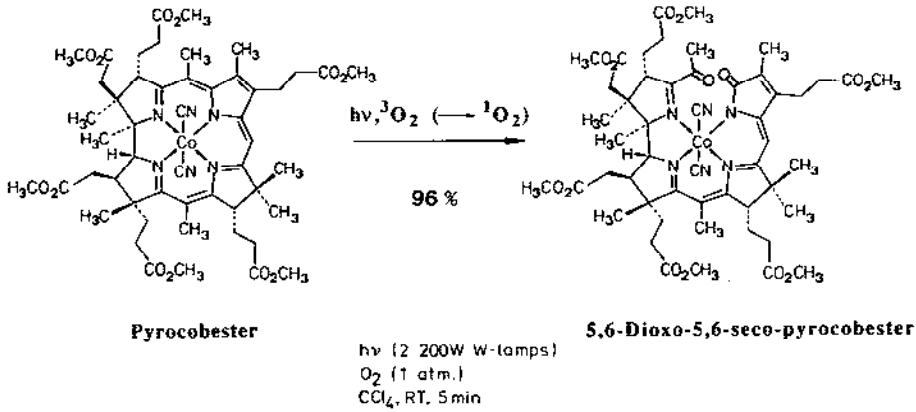

Figure 3: Light-induced oxygenolysis of the didehydrocorrinoid **5** [10].

3. PHOTOINDUCED CARBONYLATION OF A METHYLCORRIN

The examination of a possible access to acetylcobalamin (7) by way of an insertion of carbon monoxide into the Co-C-bond of methylcobalamin (3), of interest primarily in the context of the newly discovered pathway of carbon dioxide fixation in anaerobic bacteria [11], was rewarded with the development of an unprecedented (photo)process with organocorrinoids (see Fig. 4 [12]): the photoinduced carbonylation of a methylcorrin. This reaction presumably operates via the intermediacy of free methyl radicals and of cob(II)alamin (4) [12] where, accordingly, carbon monoxide would function as a non-oxidative trap for free methyl radicals.

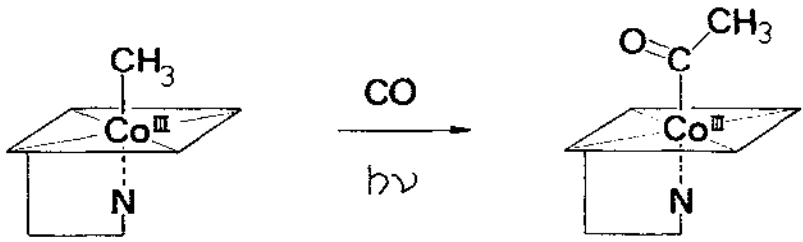

Figure 4: Preparation of acetylcobalamin (7) by photoinduced carbonylation of methylcobalamin (3) [12]

4. 1,ω-DI-[Coβ-COBYRINYL]-n-ALKANES AS "LATENT ALKYL-1,ω-DIRADICALS"

Coenzyme B_{12}, "a reversibly functioning carrier of alkyl radicals"[3,4], and some other organocobalamins, represent "latent alkyl radicals": visible light (or also thermal activation) can cleave them homolytically, to set free an alkyl radical. Similarly then, alkyl bridged dinuclear organocorrinoids, such as the 1,5-di-[Co-cobyrinyl]-n-pentane (8 [13]), could be viewed as "latent alkyl-1,ω-diradicals" (see Fig. 5).

We have recently synthesized and fully characterized a series of 1,ω-di-[Coβ-cobyrinyl]-n-alkanes (ω=4-6) [13], and examined their photochemistry in preliminary experiments [14]. Much earlier, also L.Smith et al. proposed to have synthesized a "halogen-free compound, presumed to be a 'dimer' [15], from the reductive alkylation of B_{12} with 1,4-dibromobutane or with Coβ-[4-bromobutyl]-cobalamin, while Schrauzer & Windgassen have reported on the preparation of an analoguous B_{12}-model compound, a "cobaloxime" [16] (reviewed in [17]).

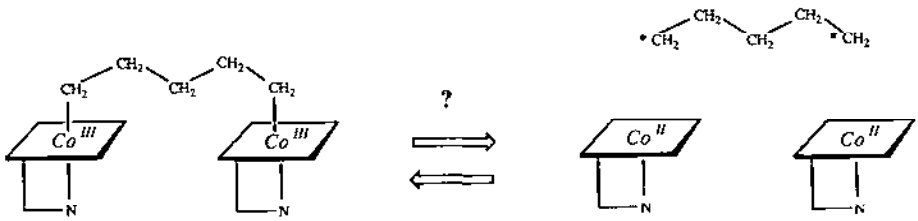

Figure 5: 1,5-Di-[Coβ-cobyrinyl]-n-pentane (8) as a "latent pentyl-1,5-diradical"

Would the photochemical reactivity at the corrin bound metal center be conserved in the dimers, in comparison to that in mononuclear organocobalamins, or altered, by virtue of the bridging alkyl ligand ?

When a deoxygenated solution of 8 in D_2O was exposed to sun-light at r.t., the UV/VIS-spectroscopically analyzed reaction mixture indicated the presence of Co(II)- and Co(I)-corrins, while the analysis of a $CDCl_3$-extract of the reaction mixture indicated olefins and a fraction (formed in ca. 15 % yield from 8), which, by ^{1}H-NMR and by GC/MS, exhibited identical characteristics as cyclopentane (see Fig. 6). The cycloalkane could potentially arise from a path via an alkyl-1,ω-diradical. More likely, under the conditions of our experiment, it comes from (hypothetical) intramolecular attack of the C-radical terminus of a cobalt-bound linear alkyl (radical) chain from a (sequential) cleavage of 8 at one of its Co-C-bonds on the remaining Co-C-bond. Interestingly, for the newly studied biosynthetic formation of C-C-bonds at unactivated alkylpositions in bacterial lipids, a reaction pathway has recently been considered, which would involve an intermolecular attack of an alkyl radical on a cobalt-bound alkyl group of an organocobalamin [18].

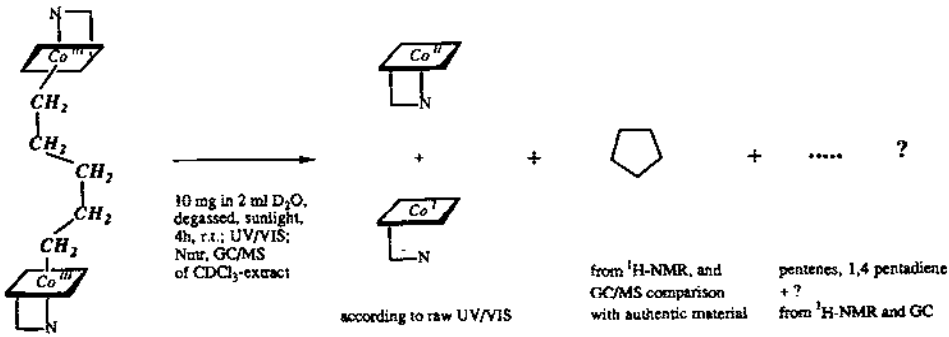

Figure 6: Formation of cyclopentane, pent(adi)enes, Co(I)- and Co(II)-cobalamin from photolysis of 1,5-di-[Coβ-cobyrinyl]-n-pentane (8) [14].

In conclusion, the photochemical reactivity of vitamin B_{12}-derivatives, exemplified here, comes about primarily by the intramolecular interaction of the corrin-bound cobalt center and the corrinoid ligand π-system, and is modified by the nature of the axial ligands. Visible light induced reactions with vitamin B_{12}-derivatives can provide a means of generating highly reactive species, such as alkyl radicals and "diradicaloids", or singlet oxygen, of interest to a wide range of fields, from physical chemistry (via biology) to medicine.

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