A New Model Compound for Vitamin B_{12} Coenzyme: Synthesis and Crystal Structure of a Tetraazamacrocyclic Alkylcobalt(III) Compound with a Pendant Coordinating Alkyl Arm

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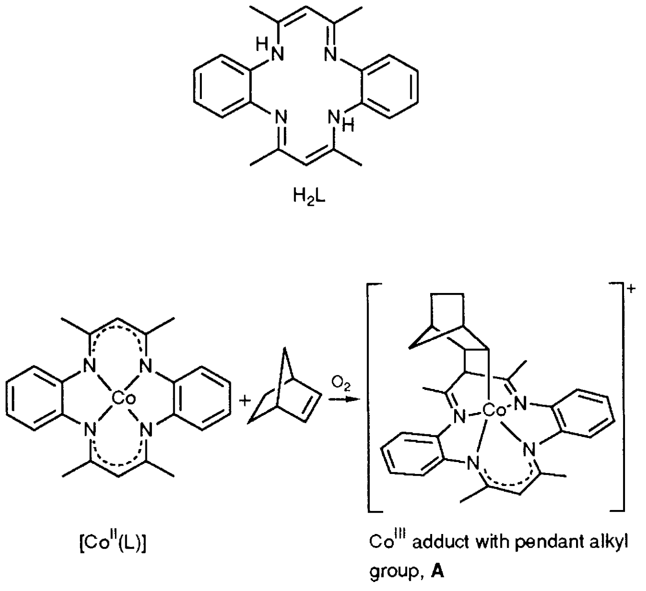
A novel reaction between norbornene and the cobalt(II) complex of the tetraazamacrocyclic ligand 5,14-dihydro-6,8,15,17-tetramethyldibenzo[*b,i*][1,4,8,11]tetraazacyclotetradecine (H_2L), in the presence of oxygen, gives the 5,16-dihydro-16-(*exo*-norbornane-2,3-diyl-κ C^2)-6,8,15,17-tetramethyldibenzo[*b,i*][1,4,8,11]tetraazadecinato-κ$^4N^{5,9,14,18}$cobalt(III) cation (**A**); this was isolated as [mono(acetone)-{5,16-dihydro-16-(*exo*-norbornane-2,3-diyl-κ C^2)6,8,15,17-tetramethyldibenzo[*b,i*[1,4,8,11]tetraazadecinato-κ$^4N^{5,9,14,18}$}cobalt(III)] tetraphenylborate, and its X-ray crystal structure establishes the presence of a pendant alkyl–cobalt bond.

In a number of coenzyme B_{12} (5′-deoxyadenosylcobalamin) dependent enzyme reactions, a radical intermediate has been detected by ESR spectroscopy.[1] Recently, radicals were detected upon addition of (*R,S*)-methylmalonyl-CoA to a solution of methyl-malonyl-CoA mutase and coenzyme B_{12}.[2] It is widely believed that homolysis of the cobalt–carbon bond of coenzyme B_{12}, generating a 5′-deoxyadenosyl radical and cob(II)alamin, is an essential step in enzymatic 1,2-rearrangements catalysed by coenzyme B_{12}.[1] However, a recent study using a model substrate containing a pentenyl group as an alkene radical trap indicates that a free radical pathway is unlikely in the methylmalonate to succinate rearrangement.[3]

Attempts to mimic the mechanism of coenzyme B_{12} dependent enzymatic reactions have involved the synthesis of model compounds containing an intramolecular cobalt(III)–carbon bond.[4,5] These permit a study of the properties of carbon-centred radicals which are forced to stay in close proximity to the cobalt(II) complex formed on homolysis of the cobalt(III)–carbon bond. Intramolecularly bound alkylcobalt(III) compounds derived from the open-chain ligands dimethylglyoximate[4] and bis(salicylaldehydato)ethane-1,2-diimine[5] have been reported.

In order to obtain a closer resemblance to the corrin ring of coenzyme B_{12}, we have chosen to use the tetraaza macrocycle 5,14-dihydro-6,8,15,17-tetramethyldibenzo[*b,i*][1,4,8,11]-tetraazacyclotetradecine (H_2L) as a precursor for forming alkylcobalt(III) compounds with an intramolecular cobalt(III)–carbon bond. The coordination chemistry of this ligand has recently been reviewed,[6] and Goedken and coworkers[7,8] have reported a cycloaddition of ethyne to $[Co(L)]^+$, giving a



Scheme 1

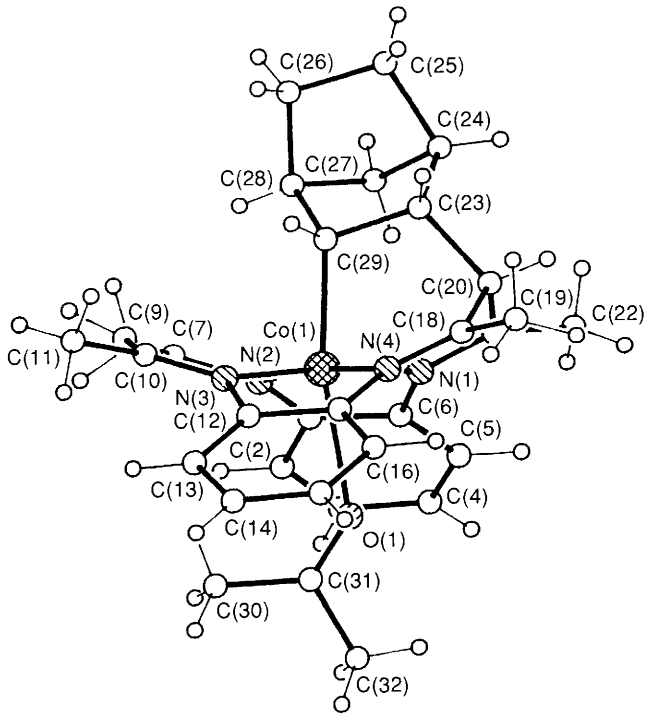


Fig. 1 Crystal structure and atomic numbering scheme for the cobalt complex cation **A**. Selected bond lengths (Å): Co–C(29) 2.04(2), Co–O(1) 2.30(2), Co–N(1) 1.87(2), Co–N(2) 1.88(2), Co–N(3) 1.86(2), Co–N(4) 1.90(1), N(3)–C(10) 1.33(2), C(9)–C(10) 1.37(3), N(4)–C(18) 1.28(2), C(18)–C(20) 1.52(3), C(20)–C(23) 1.59(3), C(23)–C(29) 1.52(2). Selected bond angles (°): C(29)–Co–N(4) 84.6(7), C(23)–C(29)–Co 111(1), C(20)–C(23)–C(29) 113(2), C(18)–C(20)–C(21) 117(2), C(7)–C(9)–C(10) 128(2).

pentadentate macrocyclic ligand with a vinyl group coordinated to the metal ion. However, it is not expected that a vinylcobalt(III) compound will be a good model for coenzyme B_{12}, especially because of the very different properties of vinyl radicals and alkyl radicals (or the respective carbanions). Attempts to prepare an analogous alkylcobalt(III) compound by cycloaddition of ethene to $[Co(L)]^+$ were unsuccessful.[7]

We have found it possible to synthesize analogous alkylcobalt(III) compounds by cycloaddition of alkenes which have compressive cisoid strain (*e.g.* norbornene, cyclobutene, cyclopropene and their derivatives). In the case of norbornene addition (Scheme 1), the geometry of the carbon atoms of the coordinated norbornyl group are close to tetrahedral, and a carbon-centred radical obtained by homolysis of the cobalt–carbon bond can be expected to have properties of a radical in a carbon skeleton *without* strain.

We report here the synthesis and crystal structure of [mono(acetone)-{5,16-dihydro-16-(*exo*-norbornane-2,3-diyl-κ C^2)-6,8,15,17-tetramethyldibenzo[*b*,*i*][1,4,8,11]tetrazadecinato-κ$^4N^{5,9,14,18}$}cobalt(III)] tetraphenylborate (**A**; Fig. 1). The macrocycle, H_2L, was prepared by a published method,[9] and $[Co^{II}(L)]$ was obtained by mixing equimolar amounts of ice-cold degassed solutions of cobalt(II) acetate tetrahydrate (0.73 g, 2.9 mmol) in methanol (10 cm^3), and H_2L (1.0 g; 2.9 mmol) in dichloromethane (15 cm^3). Addition of a large excess of norbornene (bicyclo[2.2.1]hept-2-ene; 5.0 g, 53 mmol) followed by slow air-oxidation of the cobalt(II) complex at 0 °C gives **A** [isolated as the tetraphenyl borate salt by addition of $Na[BPh_4]$ (1.5 g)] in good yield (2.3 g; 90%). The compound was recrystallised from acetone, giving the mono(acetone) complex. Fast atomic bombardment (FAB) mass spectrometry in *o*-nitrobenzyl alcohol shows peaks at *m/z* 495 (parent ion) and at *m/z* 401 corresponding to elimination of norbornene. Elemental analyses and ^1H and ^{13}C NMR spectra confirm the structure of **A**, which was established by X-ray crystallography. At higher temperatures **A** eliminates norbornene in dichloromethane solution as shown by ^1H NMR spectroscopy.

Crystals of **A** suitable for X-ray structural analysis were obtained from a toluene solution by liquid diffusion into heptane at −20 °C. The crystal structure† is shown in Fig. 1, together with selected bond lengths and angles. The pentadentate ligand coordinates as a dianion, the carbanion at C(29) being stabilised by coordination to cobalt(III). An acetone molecule is coordinated at the sixth coordination site, with a relatively long Co–O bond length (2.30 Å) due to the

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† *Crystal data* for **A**: $[C_{32}H_{38}CoN_4O]^+[C_6H_5)_4B]^- \cdot 3$ PhMe, M = 872.8 + 276.4, triclinic, space group $P\bar{1}$, a = 11.914(2), b = 12.593(3), c = 19.721(4) Å, α = 75.73(3), β = 86.86(3), γ = 83.91(3)°, U = 2 850 Å^3, Z = 2, D_c = 1.32 g cm^{-3}, Mo-Kα radiation, λ = 0.71069 Å, μ(Mo-Kα) = 0.33 mm^{-1}, T = 220 K, R = 0.087, R_w = 0.093 for 1 990 unique observed ($I/\sigma(I)$ > 2.0) reflections. Crystal character: dark-coloured thin plates, poorly diffracting. Data were collected with a Siemens R3m four-circle diffractomer in the β–2θ mode. The crystal was held at 220 K with an Oxford Cryosystems Cryostream Cooler. Maximum 2θ was 40°. Three standard reflections showed no change during data collection. The 5 432 reflections collected were processed using profile analysis to give 5 325 unique reflections, of which 1 990 were considered observed [$I/\sigma(I)$ > 2.0], this small proportion being indicative of the weakly diffracting crystals. These were corrected for Lorentz, polarisation but not absorption effects. Crystal dimensions were 0.05 × 0.1 × 0.2 mm. No systematic reflection conditions; space group $P\bar{1}$ was selected, and shown to be correct by the successful refinement. The structure was solved by direct methods using SHELXTL (TREF). A coordinated acetone and three toluene solvent molecules (two distorted on centres of symmetry) were also identifed. Anisotropic thermal parameters were used only for Co and N atoms. Hydrogen atoms were given fixed isotropic thermal parameters, U = 0.08 Å^2, and were inserted at calculated positions and not refined. Final refinement was on F by least-squares methods, refining 287 parameters. Largest positive and negative peaks on a final difference Fourier synthesis were of height ±0.5 e Å^3. A weighting scheme of the form $W = 1/(\sigma^2(F) + gF^2)$ with g = 0.0015 was used, and shown to be satisfactory by a weight analysis. The relatively poor final R was not unexpected in the light of the weakly scattering crystals, and the presence of disordered solvent. Atomic coordinates, bond lengths and angles, and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre. See Notice to Authors, Issue No. 1.

trans-influence of the carbanion. The crystal structure shows that **A** is formed by an *exo* addition of norbornene, which is the common stereochemistry upon addition of this strained alkene. The macrocycle attains a pronounced saddle-shape, which is typical for complexes of L^{2-}, and for derivatives of this ligand.[8] In **A** this saddle-shape is furthermore enforced by the bulky bridging norbornyl group. The C(23)–C(29) single bond length is 1.52 Å [compared to a C–C double bond length of 1.33 Å in the analogous vinylcobalt(III) compound[8]], the C(29)–Co(1)–N(4) angle is 84.6°, slightly smaller than the corresponding angle in the vinylcobalt(III) compound.[8] The cobalt–carbon bond length is 2.04 Å, which is typical of that found in other alkylcobalt(III) compounds. The cobalt–carbon bond length in the analogous vinylcobalt(III) compound is only 1.91 Å.[8] The significantly different thermal stability of the two compounds is reflected in the different cobalt–carbon bond strengths. For comparison the cobalt–carbon bond length of **A** is close to that found in 5′-deoxyadenosylcobalamin (2.05 Å).[10]

Further work is in progress with analogous reactions of other ring-strained alkenes, and we shall report on these studies at a later date.

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