Methyl-transfer by Methylcobalamin to Tetracyanoethylene

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Mixtures of methylcobalamin and tetracyanoethylene in CH_3OH-H_2O media display a sharp absorption band at 420 nm (ϵ = 1.1 × 10^4 l mol^{-1} cm^{-1} and formation constant = 3.9 × 10^2 l mol^{-1}, 23 °C), indicating the formation of a charge-transfer complex between the corrin π-orbitals and tetracyanoethylene prior to the methyl-transfer step; the relevance to Co–C bond cleavage is discussed.

The mechanisms of methyl-transfer from methylcobalamin (CH_3-B_{12}) to an electrophile are of considerable interest.[1] These reactions are generally thought to involve direct displacement of the cobalt by attack at the α(saturated) carbon. We show here the first example of the formation of a charge-transfer complex between the corrinoid and the attacking electrophile prior to Co–C bond cleavage.

In the presence of NH_4Cl, 3.0 × 10^{-5} M CH_3-B_{12} was quantitatively demethylated to H_2O-B_{12}^{+} by 5.0 × 10^{-4} M tetracyanoethylene (TCNE) in CH_3OH-H_2O (1 : 1). This reaction reached completion in *ca.*7 days (23 °C). Isosbestic points at 495 and 390 nm were observed. Demethylation does not occur in the absence of a proton donor. Spectrophotometric titration at 350 nm shows that the demethylation occurs with a 1 : 1 stoicheiometry. The ^{13}C n.m.r. examination of the reaction solution of $^{13}CH_3$-B_{12} (90% enriched) and TCNE shows that the ^{13}C resonance was shifted downfield from 9.1 p.p.m. (^{13}C–Co)[2] to 15.7 p.p.m. (neat Me_4Si). Based on these observations, the methyl-transfer product is tentatively proposed to be either $CH_3(CN)_2CC(CN)_2(H)$ or $CH_3-N=CH-C(CN)=C(CN)_2$.

The electronic spectra of CH_3-B_{12} in the presence and absence of TCNE (*ca.* 130-fold excess, in the absence of proton donor) are shown in Figure 1(a). A sharp new absorption band appears at 420 nm. A Benesi–Hilderbrand plot at this wavelength (Figure 2) yields ϵ = 1.1($\pm$0.15) × 10^4 l mol^{-1} cm^{-1} and a formation constant K_1 = 3.9($\pm$0.80) × 10^2 l mol^{-1} (23 °C). It should be noted that the charge-transfer bands of organometallic δ-donor [*e.g.* $(CH_3)_2Hg$]-TCNE complexes are broad (λ_{max} 345—437 nm) with rather small formation constants and molar absorptivities.[3] This sharp contrast indicates that the Co–C bond is not involved directly. Concurrent with the appearance of the new band at 420 nm, the π-π^* transition band of CH_3-B_{12} at 522 nm begins to shift to shorter wavelengths. This shift terminates at 466 nm at sufficiently high [TCNE]. Since 522 and 466 nm are the α-bands of the base-on and base-off CH_3-B_{12}, respectively,[4] this blue shift indicates clearly that the base-on CH_3-B_{12} is converted into the base-off form at high [TCNE]. A separate spectrophotometric titration at 522 nm gives the base-on $\rightleftharpoons$ base-off equilibrium constant K_2 *ca.* 40 l mol^{-1} (23 °C).

The 270 MHz ^1H n.m.r. spectra of CH_3-B_{12} (1.0 × 10^{-3} M in CD_3OD-D_2O) in the presence of a 10- and 80-fold excess of

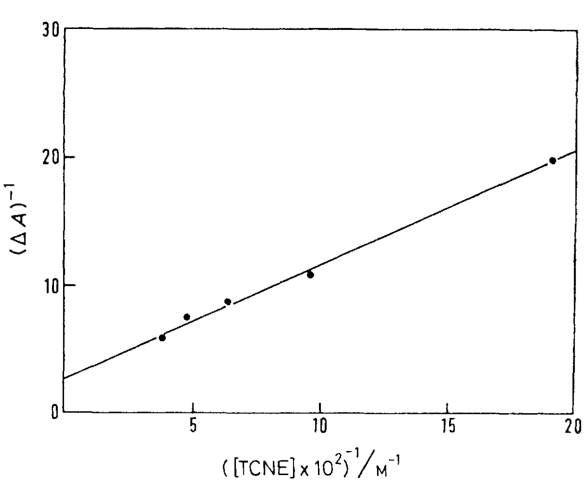


Figure 2. Benesi–Hilderbrand plot of the charge-transfer bands of CH_3-B_{12}–TCNE complexes in CH_3OH-H_2O (1 : 1). *A* = absorbance. Concentration of CH_3-B_{12} = 3.2 × 10^{-5} M; temperature: 23 °C; λ: 420 nm; light length: 1 cm.

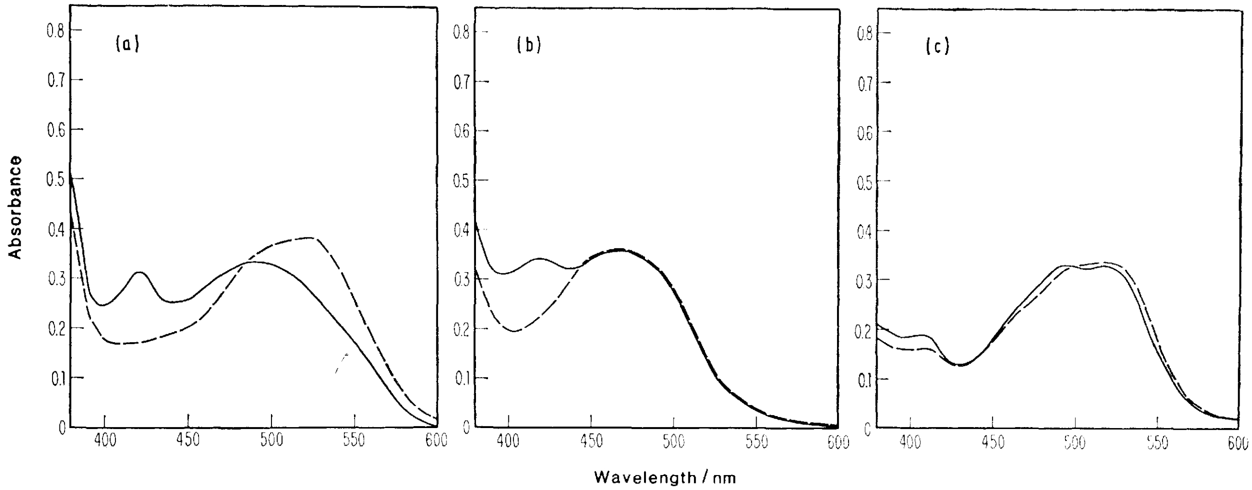


Figure 1. Electronic spectra of B_{12} compounds in the presence of TCNE in 1 : 1 CH_3OH-H_2O. An equal concentration of TCNE was used in the reference cell to eliminate the absorption of TCNE. (a) - - - - - : 3.2 × 10^{-5} M CH_3-B_{12}, ——— : 3.2 × 10^{-5} M CH_3-B_{12} + 4.1 × 10^{-3} M TCNE; (b) - - - - - : 3.2 × 10^{-5} M methylcobinamide, ——— : 3.2 × 10^{-5} M methylcobinamide + 4.1 × 10^{-3} M TCNE; (c) - - - - - : 3.8 × 10^{-5} M H_2O-B_{12}^{+}, ——— : 3.8 × 10^{-5} M H_2O-B_{12}^{+} + 4.1 × 10^{-3} M TCNE.

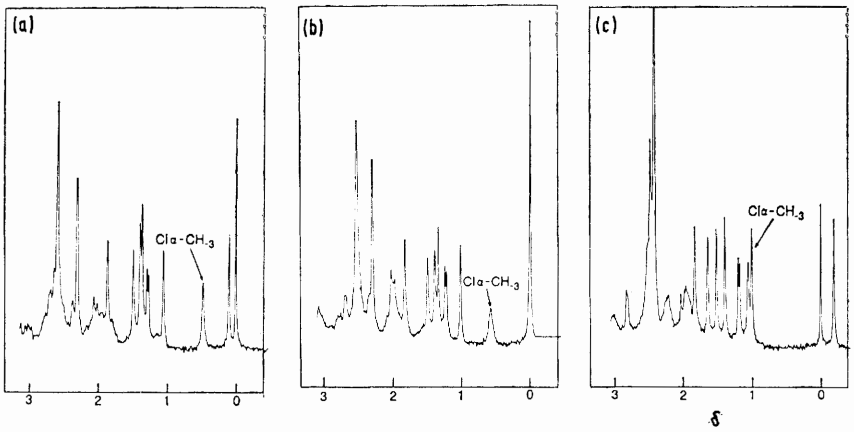
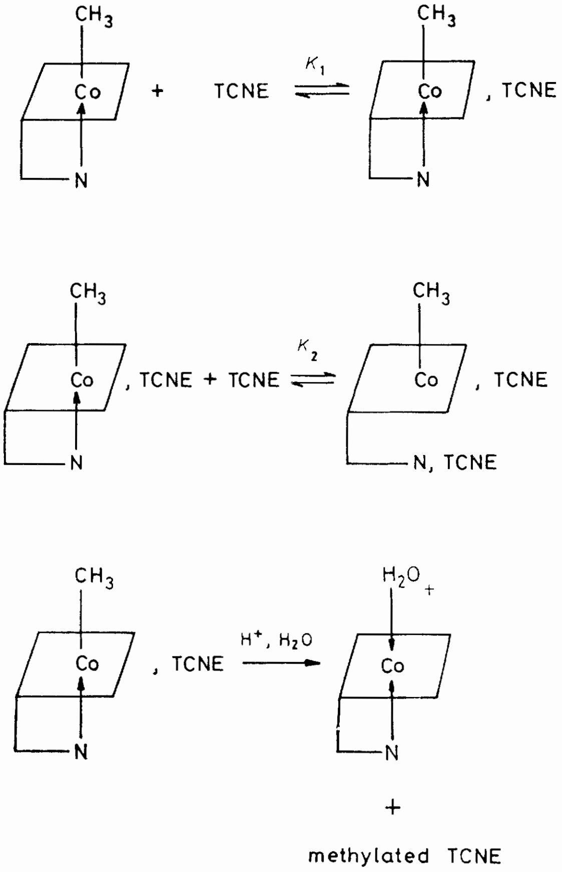


Figure 3. 270 MHz ^{1}H n.m.r. spectra of CH_3-B_{12} (1.0×10^{-3} M) in 1 : 1 CD_3OD–D_2O, 23 °C. (a) [TCNE] = 0; (b) [TCNE] = 1.0×10^{-2} M; (c) [TCNE] = 8.0×10^{-2} M.



Scheme 1

TCNE are shown in Figure 3 (only the parts at high field are shown). With an 80-fold excess of TCNE, CH_3-B_{12} appears largely in the base-off form. This is confirmed by the spectrum of 1.0×10^{-3} M CH_3-B_{12} in 0.1 M HCl. Note that the CH_3–Co resonance (the furthest upfield resonance) is shifted upfield on conversion from the base-on into the base-off form. Using 0.466 and 0.983 [internal sodium 3-(trimethylsilyl)tetradeuteriopropionate] as the chemical shifts of Clα-CH_3 for base-on and base-off CH_3-B_{12}, respectively,[5] and 0.575 with a 10-fold excess of TCNE, the rate constant for the base-on $\rightleftharpoons$ base-off conversion is estimated to be $>6 \times 10^4$ l mol^{-1} s^{-1} (23 °C).

The electronic spectra of methylcobinamide (CH_3-B_{12} without the 5, 6-dimethylbenzimidazole ribose moiety) and H_2O-B_{12}^+ in the presence of TCNE also display new absorption bands at 420 and 406 nm, respectively [Figures 1(b) and 1(c)]. These bands are broader than that of CH_3-B_{12}. Taken together, these data indicate that the signal at 420 nm is the charge-transfer band of CH_3-B_{12}, arising from the interaction of the corrin π-orbitals and TCNE. Neither the Co–C bond nor the 5,6-dimethylbenzimidazole is involved directly.

In summary, spectral studies provide evidence for the formation of a charge-transfer complex between the corrinoid and TCNE. At high [TCNE], a second TCNE interacts with the 5,6-dimethylbenzimidazole moiety resulting in a base-on into base-off conversion. The methyl transfer reaction occurs in the presence of a proton donor. The overall methyl-transfer reaction can be described by the mechanism shown in Scheme 1. However, it should be noted that the charge-transfer complex is not necessarily on the reaction co-ordinate for demethylation and may merely be a side alley. It is noteworthy that the base-on into base-off conversion is frequently observed in the methyl-transfer reactions from CH_3-B_{12} to an electrophile, such as Hg^{2+6} or $PdCl_4^{2-}$.[7] However, this is the first time that a charge-transfer complex between a corrin ring and an electrophile has been demonstrated. The significance of this observation is that it reveals that the methyl-transfer between CH_3-B_{12} and an electrophile can be discussed in terms of a charge-transfer complex and an electron-transfer reaction.

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References

1 G. Agnes, S. Bendle, H. A. O. Hill, F. R. Williams, and R. J. P. Williams, *J. Chem. Soc., Chem. Commun.*, 1971, 850; J. M. Wood, *Science*, 1974, **183**, 1049; M. D. Johnson, *Acc. Chem. Res.*, 1978, **11**, 57.

2 H. P. C. Hogenkamp, N. A. Kohlmiller, R. Hausinger, T. E. Walker, and N. A. Matwiyoff, *J. Chem. Soc., Dalton Trans.*, 1981, 1668.

3 J. Y. Chen, H. C. Gardner, and J. K. Kochi, *J. Am. Chem. Soc.*, 1976, **98**, 6150; S. Fukuzumi, K. Mochida, and J. K. Kochi, *ibid.*, 1979, **101**, 5961.

4 J. M. Pratt, 'Inorganic Chemistry of Vitamin B_{12},' Academic Press, London, 1972, p. 44.

5 O. D. Hensens, H. A. O. Hill, J. Thornton, A. M. Turner, and R. J. P. Williams, *Philos. Trans. R. Soc. London, Ser. B*, 1976, **273**, 353; O. D. Hensens, H. A. O. Hill, C. E. McClelland, and R. J. P. Williams, 'B_{12},' Vol. 1, ed. D. Dolphin, Wiley, New York, 1982, p. 463.

6 R. E. DeSimone, M. W. Penley, L. Charbonneau, S. G. Smith, J. M. Wood, H. A. O. Hill, J. M. Pratt, S. Ridsdale, and R. J. P. Williams, *Biochim. Biophys. Acta*, 1973, **304**, 851.

7 W. H. Scovell, *J. Am. Chem. Soc.*, 1974, **96**, 3451.