Thermolysis of Adenosylcobalamin: A Product, Kinetic, and Co–C5′ Bond Dissociation Energy Study

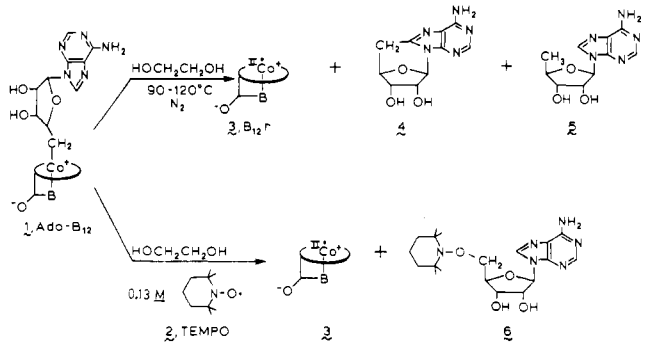
Sir:

Facile cobalt–carbon bond homolysis in vivo is the essential, biochemically unique, first step in the adenosylcobalamin (Ado-B_{12})-dependent rearrangement reactions.[1] In fact, recent evidence points to this homolysis as the key but only role played by the Ado-B_{12} cofactor.[2] However, in vitro and in the absence of light,[3] Ado-B_{12} (**1**) was previously reported to be stable (≤5% decomposition) for 5 h at 94 °C in water under argon.[4]

Herein we report the first product, kinetic, $\Delta H^{\ddagger}$, $\Delta S^{\ddagger}$, and Co–C5′ bond dissociation energy (BDE) data for the thermal homolysis of Ado-B_{12}. Our data also yield the insight that the Ado-B_{12}-dependent enzyme diol dehydratase must be providing *at least* a 14.7 kcal/mol lowering of the barrier for Co–C bond homolysis for a rate acceleration of *at least* 10^{10} and yield additional insights on other effects due to the enzyme.

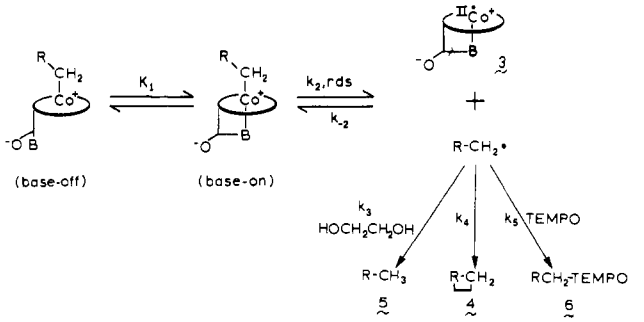
Thermolysis of Ado-B_{12} was achieved by employing the R·-selective nitroxide trapping technique we recently developed for the determination of Co–C BDE's[5] and simply by using higher temperatures (90–120 °C) and longer times ($t_{1/2}$ = 15.8 h, 90 °C) than those previously employed. Ethylene glycol proved to be the solvent system of choice following control experiments demonstrating that although $B_{12(r)}$ (Co(II)) reacts with the nitroxide 2,2,6,6-tetramethylpiperidinyl-1-oxy (Tempo) in H_2O, in ethylene glycol 2.0×10^{-4} M $B_{12(r)}$ (**3**) plus 1.0×10^{-2} M Tempo (**2**) are stable (<1% reaction over 4 h at 110 °C).

Unexpectedly, even in the absence of Tempo (**2**) the anaerobic thermolysis of Ado-B_{12} (**1**) in ethylene glycol with the exclusion of light proceeded at convenient rates at temperatures of 90–120 °C with isosbestic points at 391, 485, and 583 nm (Figure A, supplementary material). The observed products (eq 1) were 100 ± 2% $B_{12(r)}$ (**3**) (by comparison to



(1)

Scheme I



authentic material[6]), 52 ± 8% of isolated 8,5′-anhydro-5′-deoxyadenosine (**4**),[7] and 29 ± 8% of isolated 5′-deoxyadenosine (**5**).[8] The last two products were identified by TLC, IR, and 360-MHz ^{1}H NMR in comparison to authentic materials (details are available as supplementary material). Product studies in H_2O and Me_2SO show that the cyclization product **4** is the predominant product, although detectable amounts of **5** are present. These product studies rule out disproportionation between the 5′-deoxyadenosyl radical and its cyclized form as the major pathway to **4** and **5**. Consistent with this conclusion, product studies in $HOCD_2CD_2OH$ yielded more **4**, but less **5**, demonstrating that D· (H·) abstraction from $HOCD_2CD_2OH$ ($HOCH_2CH_2OH$) is occurring. With 1 equiv of Tempo (**2**) a new nucleoside product, 5′-deoxy-5′-[(2,2,6,6-tetramethyl-1-piperidinyl)oxy]adenosine (**6**), appeared.[9] Increasing the amount of Tempo (**2**) relative to 1.0×10^{-3} M Ado-B_{12} caused a decrease in the yield of **4** and **5** until only **4** and **6** were observed at 0.013 M (13 equiv) Tempo (**2**) and only **6** was observed at 0.13 M (130 equiv) Tempo (**2**) (eq 1).

Kinetic studies were carried out spectrophotometrically[10] by following the disappearance of (5–20) $\times 10^{-5}$ M Ado-B_{12} (**1**) at 520 nm. Precise (±3%) data and over 50 runs were required to detect, quantify, and reproduce with confidence the unusually small[5] dependence upon added Tempo and $B_{12(r)}$ (Co(II)).

In kinetic studies with ≥5×10^{-3} M (≥50 equiv Tempo (**2**), the rate was zero order in Tempo (**2**) (Figure B, supplementary material) and first-order plots exhibiting excellent linearity over 3 half-lives were observed with $k_{obsd,TEMPO}$(110.0 °C) = $(1.21 \pm 0.01) \times 10^{-4}$ s^{-1} (20 runs). In the absence of Tempo (**2**) the rate decreased by only 7.4%,[11] $k_{apparent}$(110.0 °C) = $(1.12 \pm 0.03) \times 10^{-4}$ s^{-1} (20 runs), and a slight curvature in the first-order plots over 3 half-lives (Figure C, supplementary material) was observed due to the buildup of $B_{12(r)}$ (Co(II)) and its slight inhibition via the RCH_2–Co ⇌ RCH_2· + Co(II)· equilibrium. A curve-fitting analysis of these data[12a] yielded

(1) Recent reviews include: (a) Dolphin, D., Ed. "B_{12}"; Wiley-Interscience: New York, 1982. (b) Zagalak, B., Friedrich, W., Eds. "Vitamin B_{12}, Proceedings of the 3rd European Symposium on Vitamin B_{12} and Intrinsic Factor"; Walter de Gruyter: New York, 1979. (c) Babior, B. M.; Krouwer, J. S. *CRC Crit. Rev. Biochem.* **1979**, *6*, 35. (d) Abeles, R. H.; Dolphin, D. *Acc. Chem. Res.* **1976**, *9*, 114. (e) Golding, B. T. In ref 1a, Chapter 15, p 543.

(2) (a) Finke, R. G.; Schiraldi, D. A.; Mayer, B. J. *Coord. Chem. Rev.* **1984**, *54*, 1. (b) Finke, R. G.; McKenna, W. P.; Schiraldi, D. A.; Smith, B. L.; Pierpont, C. *J. Am. Chem. Soc.* **1983**, *105*, 7592. (c) Finke, R. G.; Schiraldi, D. A. *J. Am. Chem. Soc.* **1983**, *105*, 7605.

(3) Photohomolysis of the Co–C bond of Ado-B_{12} is well-known: (a) Johnson, A. W.; Shaw, N.; Wagner, F. *Biochim. Biophys. Acta* **1963**, *72*, 107. (b) Rudakova, I. P.; Ershova, T. E.; Belokova, A. B.; Yurkevich, A. M. *J. Chem. Soc., Chem. Commun.* **1978**, 592. (c) Rudakova, I. P.; Chauser, E. G.; Yurkevich, A. M. *Bioorg. Khim.* **1975**, *1*, 616. (d) Joblin, K. N.; Johnson, A. W.; Lappert, M. F.; Nicholson, B. K. *J. Chem. Soc., Chem. Commun.* **1975**, 441.

(4) Hogenkamp, H. P. C.; Vergamini, P. J.; Matwiyoff, N. A. *J. Chem. Soc., Dalton Trans.* **1975**, 2628.

(5) (a) Finke, R. G.; Smith, B. L.; Mayer, B. J.; Molinero, A. A. *Inorg. Chem.* **1983**, *22*, 3677. (b) For other work in the area of Co–C BDE's see: Halpern, J. *Pure Appl. Chem.* **1983**, *55*, 1059 and references therein.

(6) Blaser, H. U.; Halpern, J. *J. Am. Chem. Soc.* **1980**, *102*, 1684.

(7) (a) Hogenkamp, H. P. C. *J. Biol. Chem.* **1963**, *238*, 477. (b) Duong, K. N. V.; Gaudemer, A.; Johnson, M. D.; Quillivic, R.; Zylber, J. *Tetrahedron Lett.* **1975**, *34*, 2997. (c) Matsuda, A.; Muneyama, K.; Nishida, T.; Sato, T.; Ueda, T. *Nucleic Acids Res.* **1976**, *3*, 3349.

(8) Shaw, S. J.; Desiderio, D. M.; Tsuboyama, K.; McCloskey, J. A. *J. Am. Chem. Soc.* **1970**, *92*, 2510.

(9) Isolated as a white solid. ^{1}H NMR (360 MHz, $(CD_3)_2SO$): δ 8.29 (s, 1 H, H-8), 8.13 (s, 1 H, H-2), 7.28 (s, 2 H, NH_2), 5.89 (d, 1 H, H-1′), 5.61 (d, 1 H, OH-2′), 5.26 (d, 1 H, OH-3′), 4.47 (m, 1 H, H-2′), 4.28 (m, 1 H, H-3′), 4.01 (m, 1 H, H-5′), 3.98 (m, 1 H, H-4′), 3.91 (m, 1 H, H-5′), 1.38 (m, 6 H, Tempo CH_2's), 1.08 (s, 6 H, Tempo CH_3's), 1.03 (s, 6 H, Tempo CH_3's).

(10) In order to avoid complications due to the effects of the temperature dependence of the axial base equilibrium upon the visible spectrum, thermolyses were carried out in an oil bath, but spectra were recorded following rapid cooling to 25.0 °C to quench the thermolysis reaction.

(11) This small decrease in rate is consistent with a report that the photohomolysis of Ado-B_{12} goes at the same rate with or without oxygen present: Brady, R. O.; Barker, H. A. *Biochem. Biophys. Res. Commun.* **1961**, *4*, 373.

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the ratio $m = k_{-2}/[(K_1k_2/(1 + K_1)) + k_3[HOCH_2CH_2OH] + k_4] = (7 \pm 3) \times 10^6$ M^{-1} in terms of the constants used in Scheme I. Separate experiments confirmed a small, 14% maximum, rate decrease, $k_{obsd,B_{12(r)}}(110.0\ °C) = (1.04 \pm 0.03) \times 10^{-4}$ s^{-1} (15 runs), in the presence of 2.7×10^{-4} M (4 equiv) $B_{12(r)}$, the maximum $[B_{12(r)}]$ experimentally accessible for reasonably precise kinetics due to overlapping $B_{12(r)}$ and Ado-B_{12} absorbances. However, within this 14% range an inverse, linear dependence upon $[B_{12(r)}]$ (0–2.7×10^{-4} M) was observed, unambiguously demonstrating for the first time in vitro the presence of the biochemically significant RCH_2–Co $\rightleftharpoons RCH_2\cdot$ + Co(II)· equilibrium. At 110.0 °C the appropriate[12b] $1/k_{obsd}$ vs. $[B_{12(r)}]$ plot (Figure D, supplementary material) yielded, in terms of the constants in Scheme I, the slope $m = k_{-2}/[(K_1k_2/(1 + K_1)) + k_3[HOCH_2CH_2OH] + k_4] = (4.6 \pm 0.3) \times 10^6$ M^{-1} and the intercept $1/(K_1k_2/(1 + K_1)) = 1/k_{obsd,Tempo} = 8310 \pm 60$ s, where 1/intercept = $k_{obsd,Tempo} = (1.20 \pm 0.01) \times 10^{-4}$ s^{-1}. These values are in good agreement with the independently determined $m = (7 \pm 3) \times 10^6$ M^{-1} and $k_{obsd,Tempo}(110.0\ °C) = (1.21 \pm 0.01) \times 10^{-4}$ s^{-1} values (vide supra) for these constants. Combining the slope with literature estimates for the H· abstraction, k_3,[13a] and cyclization, k_4,[13b] rate constants yields[13c] the *estimate* that $k_{-2} \simeq (4 \pm 3) \times 10^8$ M^{-1} s^{-1}, a value that is close to the diffusion limit and is in the known $(0.05–2.0) \times 10^9$ M^{-1} s^{-1} range of R· + Co(II)· recombination rate constants.[14]

The results clarify the observed insensitivity of the rate to added Tempo and $B_{12(r)}$ by demonstrating that H· abstraction and cyclization compete effectively with $RCH_2\cdot$ + $B_{12(r)}$ recombination even in the absence of Tempo, i.e. $(k_3 \times [HOCH_2CH_2OH] + k_4)/k_{-2}[Co^{II}] = 180–18$ for the range of $[Co^{II}] = 10^{-5}–10^{-4}$ M, respectively. In the presence of excess Tempo, $RCH_2\cdot$ + Co(II) recombination is noncompetitive and Co–C bond homolysis becomes rate determining. All of our results are consistent with and supportive of the mechanism shown in Scheme I. This scheme also incorporates Schrauzer and Grate's observation that homolysis from an alkylcobinamide (lacking the axial base) is negligible relative to that of the corresponding base-on alkylcobalamin ($k_{base\text{-}off} \simeq 10^{-3}k_{base\text{-}on}$).[15]

Having rigorously established conditions where Co–C bond homolysis is rate limiting, we measured the temperature dependence of $k_{obsd,Tempo}$ ($\geq 5.0 \times 10^{-3}$ M Tempo) at 5 °C intervals over a 30 °C range[16] to obtain $\Delta H^{\ddagger}_{obsd} = 30.6 \pm 0.3$ kcal/mol and $\Delta S^{\ddagger}_{obsd} = 2.9 \pm 0.7$ eu (Figure E, supplementary material). In order to obtain the desired activation parameters for the base-on homolysis step (k_2 (Scheme I)), it is necessary to correct the observed activation parameters for the temperature dependence of the axial base equilibrium, requiring that ΔH and ΔS for this equilibrium (K_1 (Scheme I)) be measured. This was accomplished by monitoring the absorbance of solutions of Ado-B_{12} ((0.65–2.75) $\times 10^{-4}$ M in ethylene glycol) as a function of temperature from 10 to 80 °C. Curve fitting of the appropriate equation[17a] to these data yielded $\Delta H = -7.6 \pm 0.2$ kcal/mol and $\Delta S = -20.2 \pm 0.7$ eu for the base-off to base-on equilibrium, in excellent agreement with the most recently obtained values for other alkylcobalamines.[17b] Following the correction of the observed activation parameters for the axial base temperature dependence,[18] the activation parameters for the base-on homolysis were determined, $\Delta H_2^{\ddagger} = 34.5 \pm 0.8$ kcal/mol and $\Delta S_2^{\ddagger} = 23.1 \pm 1.0$ eu. Since the Co–C BDE is equal to $\Delta H_2^{\ddagger} - \Delta H_{-2}^{\ddagger}$, a value for $\Delta H_{-2}^{\ddagger}$ is also required. Our estimate of k_{-2}(110 °C, $HOCH_2CH_2OH$) $\simeq (4 \pm 3) \times 10^8$ M^{-1} s^{-1}, the $(0.05–2.0) \times 10^9$ M^{-1} s^{-1} range of all known R· + Co(II)· rate constants,[14] Endicott's flash photolysis measurement of *in cage* 5′-deoxyadenosyl $RCH_2\cdot$ + $B_{12(r)}$ recombination,[14h] $k_{recomb}(\sim 25\ °C, H_2O) = (1.3 \pm 1.1) \times 10^9$ s^{-1}, and the only available measurement of a R· + Co(II)· recombination, $\Delta H^{\ddagger} \simeq 2$ kcal/mol (a diffusional barrier),[19] all indicate that the enthalpic barrier to $RCH_2\cdot$ + $B_{12(r)}$ recombination is $\Delta H_{-2}^{\ddagger} \lesssim 3 \pm 1$ kcal/mol. These observations provide the first estimate of the base-on, Ado-B_{12}, Co–C5′ BDE = $\Delta H_2^{\ddagger} - \Delta H_{-2}^{\ddagger} \simeq 31.5 \pm 1.3$ kcal/mol.

The results herein, $\Delta G^{\ddagger}_{obsd}(37\ °C) = 29.7$ kcal/mol, the fact that B_{12}-dependent enzymes such as diol dehydratase exhibit rates of ≥ 100 turnovers/(site s),[20] $\Delta G_{cat}^{\ddagger} \simeq 15$ kcal/mol,[20] and the fact that Co–C bond homolysis is not rate limiting in the enzyme[21] suggest that the enzymes provide at least a $\gtrsim 14.7$ kcal/mol lowering of the barrier for Co–C5′ homolysis for a rate enhancement of at least $\gtrsim 10^{10}$. It remains to be explained, however, exactly how this is accomplished.[22,23]

(12) (a) Assuming a rapidly established base-on/base-off equilibrium and a steady-state concentration for the 5′-deoxyadenosyl radical, the rate law for Scheme I (in the absence of Tempo) is given by $-d[Ado\text{-}B_{12}]/dt = \{(k_3[HOCH_2CH_2OH] + k_4)K_1k_2/(K_1 + 1)\}/\{k_3[HOCH_2CH_2OH] + k_4 + k_{-2}[B_{12(r)}]\}$. Rearrangement of the integrated rate law yields $t = \{(K_1 + 1)/K_1k_2 + m([Ado\text{-}B_{12}]_0 + [B_{12(r)}]_0)\} \ln ([Ado\text{-}B_{12}]_0/[Ado\text{-}B_{12}]) + m([Ado\text{-}B_{12}] - [Ado\text{-}B_{12}]_0)$, where $m = k_{-2}/\{(K_1k_2/(1 + K_1)) \times (k_3[HOCH_2CH_2OH] + k_4)\}$. This expression was fit to (time, absorbance) data via nonlinear regression by variation of the only unknown parameter, m ($[K_1 + 1]/(K_1/k_2) = 1/k_{obsd,Tempo}$ is a known quantity). (b) Under conditions of constant $[B_{12(r)}]$, the rate law becomes $-d[Ado\text{-}B_{12}]/dt = k_{obsd}[Ado\text{-}B_{12}]$ and $1/k_{obsd} = (K_1 + 1)/K_1k_2 + \{(K_1 + 1)k_{-2}[B_{12(r)}]\}/\{K_1k_2(k_3[HOCH_2CH_2OH] + k_4)\}$.

(13) (a) Thomas, J. K. *J. Phys. Chem.* **1967**, *71*, 1919. (b) The fact that the cyclic nucleoside product (**4**) is still detectable at 0.013 M Tempo coupled with the fact that the rates of trapping of alkyl radicals by nitroxides are known to be diffusion controlled[13d–i] indicate that this cyclization is rapid. This observation is consistent with product studies of the aerobic photolysis of Ado-B_{12}[13j–l] where cyclization competes successfully with trapping by O_2, another diffusion-controlled process.[13m,n] (c) Taking $k_{-2}/\{K_1k_2/(K_1 + 1)(k_3[HOCH_2CH_2OH] + k_4)\} = 4.6 \times 10^6$ M^{-1} (from the $1/k_{obsd}$ vs. $[B_{12(r)}]$ plot), estimating $k_3 = 10^3–10^4$ M^{-1} s^{-1} [13a] and $k_4 = 10^5–10^6$ s^{-1},[13b] and taking $K_1k_2/(K_1 + 1) = k_{obsd,Tempo} = 1.21 \times 10^{-4}$ s^{-1} yield $k_{-2} = (4 \pm 3) \times 10^8$ M^{-1} s^{-1}. (d) Brownlie, I. T.; Ingold, K. U. *Can. J. Chem.* **1967**, *45*, 2427. (e) Hill, C. L.; Whitesides, G. M.; *J. Am. Chem. Soc.* **1974**, *96*, 870. (f) Nigam, S.; Asmus, K. D.; Willson, R. L. *J. Chem. Soc., Faraday Trans. 1* **1976**, 2324. (g) Schmid, P.; Ingold, K. U. *J. Am. Chem. Soc.* **1978**, *100*, 2493. (h) Kinney, R. J.; Jones, W. D.; Bergman, R. G. *J. Am. Chem. Soc.* **1978**, *100*, 7902. (i) Espenson, J. H.; McDowell, M. S. *Organometallics* **1982**, *1*, 1514. (j) Johnson, A. W.; Shaw, N. *J. Chem. Soc.* **1962**, 4608. (k) Hogenkamp, H. P. C.; Ladd, J. N.; Barker, H. A. *J. Biol. Chem.* **1962**, *237*, 1950. (l) See ref 7a. (m) Miller, A. A.; Mayo, F. R. *J. Am. Chem. Soc.* **1956**, *78*, 1017. (n) Gordon, S.; Hart, E. J.; Matheson, M. S.; Rabani, J.; Thomas, J. K. *Discuss. Faraday Soc.* **1963**, *36*, 193.

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(15) Schrauzer, G. N.; Grate, J. H. *J. Am. Chem. Soc.* **1981**, *103*, 541.

(16) The $k_{obsd,Tempo}$ values (s^{-1}, ±3%) and temperatures (°C, ±0.2 °C) are respectively as follows: 1.22×10^{-5}, 90.0; 2.23×10^{-5}, 95.0; 4.11×10^{-5}, 100.0; 7.13×10^{-5}, 105.0; 1.21×10^{-4}, 110.0; 2.08×10^{-4}, 115.0; 3.34×10^{-4}, 120.0.

(17) (a) The following equation describes the absorbance of a solution of Ado-B_{12} as a function of temperature: $Abs = [Ado\text{-}B_{12}]_{total}[\epsilon_{base\text{-}off} + \epsilon_{base\text{-}on} \exp(\Delta S/R - \Delta H/RT)]/[1 + \exp(\Delta S/R - \Delta H/RT)]$. This equation was fit to the (absorbance, temperature) data by variation of the parameters ΔH, ΔS, and $\epsilon_{base\text{-}on}$ with use of nonlinear regression. (b) Brown, K. L.; Hakimi, J. M.; Nuss, D. M.; Montejano, Y. D.; Jacobsen, D. W. *Inorg. Chem.* **1984**, *23*, 1463.

(18) Under conditions where the rate is zero order in [Tempo], the temperature dependence of k_{obsd} is given by $d(\ln k_{obsd}/T))/d(1/T) = d(\ln (k_2/T))/d(1/T) + d[\ln (K_1/(1 + K_1)T)]/d(1/T)$.

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Finally, the resistance of the Co corrin to R· attack as previously noted,[24] the fact that enzyme-free Ado-B_{12} is resistant to the undesirable but established type of side reaction[15,19,25] of Co(II) + ·CH_2CHOCH(Ad)CH(OH)CH(OH) → Co—H + CH_2=COCH(Ad)CH(OH)CH(OH), and the fact that the enzyme must prevent cyclization of the 5′-deoxyadenosyl radical[26] are additional points worth noting.

Acknowledgment. We wish to thank Dr. C. E. Klopfenstein for his assistance in obtaining high-field NMR spectra. Financial support was provided by NIH Grant AM-26241. R.G.F. is a Dreyfus Teacher-Scholar (1982–1987) and Alfred P. Sloan Foundation Fellow (1982–1984).

Registry No. **1**, 13870-90-1; **3**, 14463-33-3; **4**, 3415-89-2; **5**, 4754-39-6; **6**, 89959-02-4.

Supplementary Material Available: Figures A–E of spectral changes during homolysis, $k_{obsd,Tempo}$ vs. [Tempo], the slightly curved first-order plots in the absence of Tempo, the $1/k_{obsd}$ vs. $[B_{12(r)}]$ plot, and the ln (k_{obsd}/T) vs. $1/T$ plot, respectively, and details on the characterization of the nucleoside products (6 pages). Ordering information is given on any current masthead page.

(22) (a) Jencks, W. P. In "Chemical Recognition in Biology"; Chapeville, F., Haenni, A.-L., Eds.; Springer-Verlag: New York, 1980; p 3. (b) Walsh, C. "Enzymatic Reaction Mechanisms"; W. H. Freeman: San Francisco, 1979; Chapter 2. (c) Fersht, A. "Enzyme Structure and Mechanism"; W. H. Freeman: San Francisco, 1977; pp 253–273.

(23) For suggestions based on enzymatic studies,[23a–d] crystallographic studies of B_{12},[23e] and model studies[23f–i] see: (a) Babior, B. M. "B_{12}"; Dolphin, D., Ed.; Wiley-Interscience: New York, 1982; Vol. 2, p 263. Krouwer, J. S.; Holmquist, B.; Kipnes, R. S.; Babior, B. M. *Biochim. Biophys. Acta* **1980**, *612*, 153. (b) Hollaway, M. R.; White, H. A.; Joblin, K. N.; Johnson, A. W.; Lappert, M. F.; Wallis, O. C. *Eur. J. Biochem.* **1978**, *82*, 143. (c) Toraya, T.; Krodel, E.; Mildvan, A. S.; Abeles, R. H. *Biochemistry* **1979**, *18*, 417. (d) Toraya, T.; Ushio, K.; Fukui, S.; Hogenkamp, H. P. C. *J. Biol. Chem.* **1977**, *252*, 963. Sando, G. N.; Grant, M. E.; Hogenkamp, H. P. C. *Biochim. Biophys. Acta* **1976**, *428*, 228. Anton, D. L.; Tsai, P. K.; Hogenkamp, H. P. C. *J. Biol. Chem.* **1980**, *255*, 4507. (e) Glusker, J. P. In ref 1a, Chapter 3, p 23. (f) Summers, M. F.; Toscano, P. J.; Bresciani-Pahor, N.; Nardon, G.; Randaccio, L.; Marzilli, L. G. *J. Am. Chem. Soc.* **1983**, *105*, 6259 and references therein. (g) Pratt, J. M. *J. Mol. Catal.* **1984**, *23*, 187. Baldwin, D. A.; Betterton, E. A.; Pratt, J. M. *J. Chem. Soc., Dalton Trans.* **1983**, 2217 (part 22; see also their earlier papers in this series). (h) Ng, F. T. T.; Rempel, G. L.; Halpern, J. *Inorg. Chim. Acta* **1983**, *77*, L165 and references therein. (i) See ref 15.

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(25) (a) Tsou, T.-T.; Loots, M.; Halpern, J. *J. Am. Chem. Soc.* **1982**, *104*, 623. (b) Gjerde, H. B.; Espenson, J. H. *Organometallics* **1982**, *1*, 435.

(26) The 8,5′-anhydro-5′-deoxyadenosine product can be isolated from deactivated enzyme following reaction with the relatively poor substrate ethylene glycol. Abeles, R. H. *Proc. Robert A. Welch Found. Conf. Chem. Res.* **1972**, *15*, 113.

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The Most Simple Type of a Manganese Dihalide Phosphine Adduct: $MnI_2(PEt_3)_2$

Sir:

The chemistry of transition-metal phosphine and arsine complexes is well-known and documented[1] with the exception of manganese(II). This must be ascribed to preparative difficulties, which have endured for quite some time. An early report by Naldini[2] on $MnX_2(PPh_3)_2$ has been questioned by McAuliffe et al.,[3] who obtained $MnX_2(OPPh_3)_2$ instead. Bennett et al.[4] fully characterized the first manganese dihalide phosphine adduct $MnCl_2(diphos)_2$. Similar compounds, $MnX_2(dmpe)_2$ (X = Br, I), have subsequently been made by Wilkinson et al.[5] Chelating phosphines seemed to be necessary to obtain stable adducts because, until very recently, compounds of composition $MnX_2(PR_3)$ have been mentioned but not well characterized.[6] Green et al.[7] even stated that they were unable to isolate such compounds. It was highly desirable to know more about this chemistry since some controversy arose about their uptake of dioxygen (and other small molecules).[6–8]

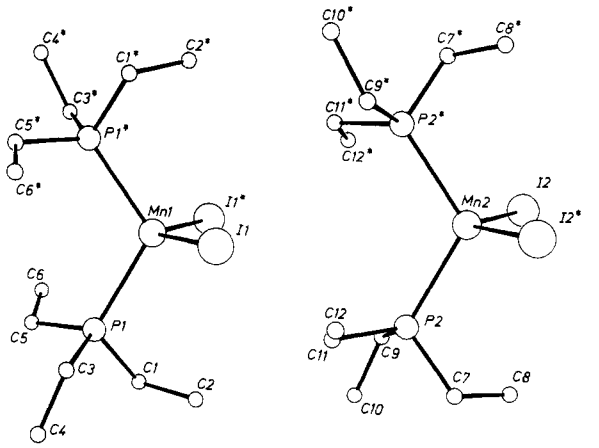

Figure 1.

During our studies on manganocenes and their reaction products such as halides and donor molecule adducts[9] we prepared $MnI_2(PEt_3)_2$, which is expected to simplify the complex situation and which we describe here. When this work was completed, McAuliffe et al.[10] could support their earlier results by a crystal structure of $[MnI_2(PPhMe_2)]_n$.

The title compound is obtained by reaction of anhydrous manganese diiodide[11] in ether with a small excess of triethylphosphine. Recrystallization from ether gives analytically pure[12] pink needles in 47% yield. The X-ray analysis[13] shows two molecuels, **1/2** (Figure 1), which are crystallographically different but very similar with respect to their structural pa-

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(12) Anal. Calcd for $C_{12}H_{30}I_2MnP_2$: C, 26.44; H, 5.55; I, 46.57; Mn, 10.07; P, 11.77. Found: C, 25.93; H, 5.47; I, 45.97; Mn, 10.25; P, 11.37.

(13) Crystal data: orthorhombic, *Pccn* (No. 56), a = 1732.6 (3) pm, b = 1730.2 (3) pm, c = 1470.2 (3) pm, V = 4407.28 × 10^6 pm^3, D_{expti} = 1.643 g cm^{-3} for Z = 8, μ(Mo Kα) = 34.80 cm^{-1}, $F(000)$ = 2104, T = 22 °C. Data collection, structure solution, and refinement: 2897 unique reflections (λ = 71.069 pm, ω scans, $1 \le \vartheta \le 22.5°$, empirical absorption correction, Syntex $P2_1$), heavy-atom methods, R = 0.050, R_w = 0.050 ($\omega = K/\sigma^2(F_o)$), K = 2.64 in last cycle for 155 parameters and 1866 observed reflections $F > 4\sigma(F)$ (SHELX 76).

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