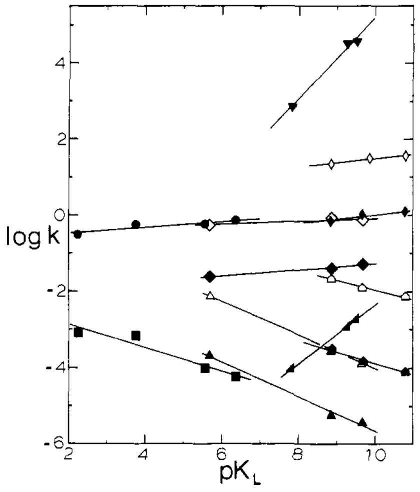

Figure 6. Plots of the logarithms of the rate constants for ligand association and dissociation with (carboxyalkyl)cobaloximes (solid symbols) and their conjugate bases (open symbols) vs. pK_L, the pK_a of the conjugate acid of the ligand: (carboxymethyl)cobaloximes, k_{on}, 4-X-py (●), R–NH$_2$ (◇, ◆), RS$^-$ (▼), k_{off}, 4-X-py (■), R–NH$_2$ (△, ▲), RS$^-$ (◢); (1-carboxyethyl)cobaloxime, k_{on}, R–NH$_2$ (◊, ♦), k_{off}, R–NH$_2$ (⌂, ☗). The solid lines are least-squares fits; slopes and intercepts are given in Table V.

to this average value (Table V), those for the (1-carboxyalkyl)cobaloximes themselves are significantly higher. Hence an enhancement of the interaction of β-effect cobalt centers with purely σ-donating primary amine ligands may indeed be operating, at least for the more basic members of the amine series. A similar, but more striking effect can be seen in the k_{off} correlations for the primary amine ligands. In this case, the slopes of the correlations for all the β-effect cobaloximes are quite similar in sign and magntiude to those previously determined for other organocobaloximes but the intercepts for the (1-carboxyalkyl)cobaloximes (and *not* their conjugate bases) are at least 1.5 log units lower. This would tend to indicate a substantial effect of σ–π conjugation on the kinetic stability of the primary amine complexes, although it is not completely clear how much of this effect should be attributed to the inductive effect of the organic ligands involved.[42,43]

We conclude, then, that there appears to be an effect of depletion of cobalt electron density by σ–π conjugation in (1-carboxyalkyl)cobaloximes on reactivity of the cobalt center, but it is difficult to accurately assess its extent with the current data.

Acknowledgment. This research was supported by the Robert A. Welch Foundation, Houston, TX (Grant Y-749), and the Organized Research Fund of The University of Texas at Arlington.

Registry No. $HOOCCH_2Co(D_2H_2)(OH_2)$, 60193-28-4; $HOOCCH_2Co(D_2H_2)$((2-methylthio)ethanol), 81956-62-9; $HOOCCH_2Co(D_2H_2)$(methyl (methylthio)acetate), 82010-07-9; $HOOCCH_2Co(D_2H_2)$(4-cyanopyridine), 81970-32-3; $HOOCCH_2Co(D_2H_2)$(4-(carboxamido)pyridine), 81956-63-0; $HOOCCH_2Co(D_2H_2)$(pyridine), 14641-02-2; $HOOCCH_2Co(D_2H_2)$(4-methylpyridine), 81956-64-1; $HOOCCH_2Co(D_2H_2)$(4-aminopyridine), 81970-33-4; $HOOCCH_2Co(D_2H_2)$(2,2,2-trifluoroethylamine), 81956-65-2; $HOOCCH_2Co(D_2H_2)$(glycine ethyl ester), 81956-66-3; $HOOCCH_2Co(D_2H_2)$(2,2-dimethoxyethylamine), 81956-67-4; $HOOCCH_2Co(D_2H_2)$(2-methoxyethylamine), 81956-68-5; $HOOCCH_2Co(D_2H_2)$(*n*-propylamine), 81956-69-6; $HOOCCH_2Co(D_2H_2)$(methyl thioacetate), 81956-70-9; $HOOCCH_2(Co(D_2H_2)$(methyl thiopropionate), 81956-71-0; $HOOCCH_2Co(D_2H_2)$(2-thioethanol), 81956-72-1; $HOOCCH(CH_3)Co(D_2H_2)(OH_2)$, 14637-38-8; $HOOCCH(CH_3)Co(D_2H_2)$((2-methylthio)ethanol), 81956-73-2; $HOOCCH(CH_3)Co(D_2H_2)$(methyl (methylthio)acetate), 81956-74-3; $HOOCCH(CH_3)Co(D_2H_2)$(4-cyanopyridine), 81956-75-4; $HOOCCH(CH_3)Co(D_2H_2)$(4-(carboxamido)pyridine), 81956-76-5; $HOOCCH(CH_3)Co(D_2H_2)$(pyridine), 14643-12-0; $HOOCCH(CH_3)Co(D_2H_2)$(4-methylpyridine), 81956-77-6; $HOOCCH(CH_3)Co(D_2H_2)$(4-aminopyridine), 81956-78-7; $HOOCCH(CH_3)Co(D_2H_2)$(2,2,2-trifluoroethylamine), 81956-79-8; $HOOCCH(CH_3)Co(D_2H_2)$(glycine ethyl ester), 81956-80-1; $HOOCCH(CH_3)Co(D_2H_2)$(2,2-dimethoxyethylamine), 81956-81-2; $HOOCCH(CH_3)Co(D_2H_2)$(2-methoxyethylamine), 81956-82-3; $HOOCCH(CH_3)Co(D_2H_2)$(*n*-propylamine), 81956-83-4; $HOOCCH(CH_3)Co(D_2H_2)$(methyl thioacetate), 81956-84-5; $HOOCCH(CH_3)Co(D_2H_2)$(methyl thiopropionate), 81956-85-6; $HOOCCH(CH_3)Co(D_2H_2)$(2-thioethanol), 81956-86-7; $HOOCCH_2CO_2^-$, 1000-88-0; CH_3COOH, 64-19-7; $C_6H_5CH_2COOH$, 103-82-2; CH_3SCH_2COOH, 2444-37-3; CH_3OCH_2COOH, 625-45-6; $C_6H_5OCH_2COOH$, 122-59-8; ICH_2COOH, 64-69-7; $BrCH_2COOH$, 79-08-3; $ClCH_2COOH$, 79-11-8; $NCCH_2COOH$, 372-09-8; $CH_3CH(CO_2^-)COOH$, 69858-36-2; $CH_3CH(CH_3)COOH$, 79-31-2; $CH_3CH(C_6H_5)COOH$, 492-37-5; $CH_3CH(CH_3S)COOH$, 58809-73-7; $CH_3CH(C_6H_5O)COOH$, 1701-77-5; $CH_3CH(Br)COOH$, 598-72-1; $CH_3CH(Cl)COOH$, 598-78-7; $CH_3CH(H_3N)COOH^+$, 17806-36-9.

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Reactions of B_{12r} with Aliphatic Free Radicals: A Pulse-Radiolysis Study[1]

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Abstract: The spectra of the intermediates formed in the reactions of B_{12r} with the free radicals $Br_2^-\cdot$, $CO_2^-\cdot$, $\cdot CH_2C(CH_3)_2OH$, $\cdot C(CH_3)_2OH$, $\cdot CH_2CHO$, and $\cdot CH(OH)CH_2OH$ are reported. The results indicate that $Br_2^-\cdot$ oxidizes B_{12r} to B_{12a}, via an inner-sphere mechanism, and $CO_2^-\cdot$ reduces B_{12r} to B_{12s}. All the aliphatic free radicals studied, $\cdot R$, react with B_{12r}, yielding as the first product a pseudocoenzyme denoted Co^{III}–R. Co^{III}–$CH_2C(CH_3)_2OH$ is stable for over a second in the pH range 3–10 as is Co^{III}–CH_2CHO. The latter compound hydrolyzes in acid solutions to yield B_{12a} and CH_3CHO. Co^{III}–$C(CH_3)_2OH$ and Co^{III}–$CH(OH)CH_2OH$ decompose heterolytically to yield mainly B_{12s}; a side reaction that probably yields Co^{III}–H via a β-hydride shift is also observed. The kinetics of decomposition of Co^{III}–$CH(OH)CH_2OH$ in neutral solutions are reported. No water elimination from the latter intermediate occurs. The reasons for the latter observation are discussed.

There is growing evidence that the mechanism of reaction of enzymes containing the coenzyme derivative of vitamin B_{12} involves free-radical reactions. The mechanism of reaction seems[3-6] to involve first the homolytic Co–C bond cleavage in the coenzyme

$$\text{Co–R} \rightleftarrows \text{Co}^{\text{II}} + \text{R}\cdot \qquad (1)$$

where the coenzyme and its ligand are denoted as Co–R. The free radical attacks the substrate, SH.

$$\text{R}\cdot + \text{SH} \rightleftarrows \text{RH} + \text{S}\cdot \qquad (2)$$

This reaction is followed schematically by one of the following reaction sequences:

Sequence I

$$\text{Co}^{\text{II}} + \text{S}\cdot \rightleftarrows \text{Co–S} \qquad (3)$$

$$\text{Co–S} \rightarrow \text{Co–P} \qquad (4)$$

$$\text{Co–P} \rightleftarrows \text{Co}^{\text{II}} + \text{P}\cdot \qquad (5)$$

Sequence II

$$\text{Co–S} \rightleftarrows \text{Co}^{\text{I}} + \text{S}^{+} \qquad (6)$$

$$\text{S}^{+} \rightleftarrows \text{P}^{+} \qquad (7)$$

$$\text{P}^{+} + \text{Co}^{\text{I}} \rightleftarrows \text{Co–P} \qquad (8)$$

Sequence III

$$\text{Co–S} \rightleftarrows \text{Co}^{\text{III}} + \text{S}^{-} \qquad (9)$$

$$\text{S}^{-} \rightleftarrows \text{P}^{-} \qquad (10)$$

$$\text{P}^{-} + \text{Co}^{\text{III}} \rightleftarrows \text{Co–P} \qquad (11)$$

Sequence IV

$$\text{S}\cdot \rightleftarrows \text{P}\cdot \qquad (12)$$

$$\text{P}\cdot + \text{Co}^{\text{II}} \rightleftarrows \text{Co–P} \qquad (13)$$

where PH is the product, formed via $\cdot\text{P} + \text{RH} \rightarrow \text{PH} + \text{R}\cdot$, and Co–P decomposes via eq 5.

Alternatively an outer-sphere redox process involving the cobalt center might occur.

Sequence V

$$\text{Co}^{\text{II}} + \text{R}\cdot \rightleftarrows \text{Co}^{\text{I}} + \text{R}^{+} \qquad (14)$$

$$\text{Co}^{\text{II}} + \text{R}\cdot \rightleftarrows \text{Co}^{\text{III}} + \text{R}^{-} \qquad (15)$$

and

$$\text{R}^{\pm} + \text{SH} \rightleftarrows \text{RH} + \text{S}^{\pm} \qquad (16)$$

or

Sequence VI

$$\text{Co}^{\text{II}} + \text{S}\cdot \rightleftarrows \text{Co}^{\text{I}} + \text{S}^{+} \qquad (17)$$

$$\text{Co}^{\text{II}} + \text{S}\cdot \rightleftarrows \text{Co}^{\text{III}} + \text{S}^{-} \qquad (18)$$

It was suggested that the radicals $\cdot CH(OH)CH_2OH$ and $\cdot CH_2C(CH_3)_2OH$ oxidize B_{12r} via an outer-sphere mechanism to give B_{12a}[7] and that $\cdot C(CH_3)_2OH$ reduces it to B_{12s}[8-10] via the same mechanism. The latter results are used to support sequences IV, V, and VI over sequences I, II, and III.[6,11] However, experimental data available suggest that relatively stable Co–S compounds are formed in reaction 3[12-15] when the substrate S does not contain a functional group that causes hydrolysis or redox processes.[13] Furthermore, most aliphatic free radicals are not expected to be efficient outer-sphere redox reagents, due to the large reorganization energies required in these processes.[15-18]

Considering these arguments, we have predicted[15] recently that the reactions of $\cdot CH_2C(CH_3)_2OH$, $\cdot CH(OH)CH_2OH$, and $\cdot C(CH_3)_2OH$ with B_{12r} involve the formation of the pseudocoenzymes $Co–CH_2C(CH_3)_2OH$, $Co–CH(OH)CH_2OH$, and $Co–C(CH_3)_2OH$, which then rearrange, when required, to the stable products via sequences I, II, or III. We wish to report experimental results, obtained by the pulse-radiolysis technique, that support these predictions.

Experimental Section

Materials. Solutions of B_{12r} were prepared by reduction of B_{12a} (Sigma) with hydrogen over Adams' catalyst.[8] The solutions thus prepared were handled by the syringe technique to avoid contact with air. All other chemicals were AR grade and were used without further treatment. Solutions were prepared with triple-distilled water.

Spectra of Transients. Spectra of the transients were recorded with the streak camera.[19] The streak duration was 200 μs, and when spectra at longer times after the pulse were required, a delay circuit, which starts the streak time at the required time after the pulse, was used. The solutions were contained in Suprasil cells with an optical path of 1 or 2 cm. The B_{12r} concentration was 6×10^{-5} M and the radical concentration formed by the pulse was ca. 1×10^{-5} M, but for the HCO_2^- and Br^- solutions, where the free-radical concentration was ca. 3×10^{-5} M. The large concentration of radicals is required in order to obtain accurate spectra also in regions where the spectral changes are small. However, as clearly radical–radical reactions in competition with the desired $B_{12r} + \cdot R$ reaction occurred, no absolute absorption coefficients were determined.

The streak camera records the spectra over a range of 180 nm. The spectra from 340 to 600 nm were recorded with two pulses, the first with the streak center at 430 nm and the second with the center at 510 nm. Thus, an overlap over a range of 100 nm between the two experiments was obtained.

Kinetics of Reaction. The kinetics were measured at wavelengths where large optical changes occur; thus smaller pulses, yielding $(1–5) \times 10^{-6}$ M of free radicals, were used. These experiments were carried out both at the linear accelerator at Argonne National Laboratory and at the Hebrew University of Jerusalem. The experimental setups have been described elsewhere in detail.[20,21]

Preparation of Free Radicals. The radiation chemistry of water and dilute aqueous solutions can be summed up by the equation[22]

$$\text{H}_2\text{O} \xrightarrow{\gamma,\text{e}^-} \text{e}^-_{\text{aq}}, \cdot\text{H}, \cdot\text{OH}, \text{H}_2\text{O}_2, \text{H}_2, \text{H}_3\text{O}^+_{\text{aq}} \qquad (19)$$

The yields of these primary products, which are homogeneously distributed in the solution within less than 10 ns, are $G_{e^-_{aq}} = G_{OH} = 2.65$, $G_H = 0.60$, $G_{H_2O_2} = 0.75$, $G_{H_2} = 0.45$ in units of molecules per 100 eV absorbed in the solution.[22]

In N_2O-saturated solutions (2×10^{-2} M), the following reactions have to be considered.

$$\text{e}^-_{\text{aq}} + \text{N}_2\text{O} \xrightarrow{\text{H}_2\text{O}} \cdot\text{OH} + \text{N}_2 + \text{OH}^- \qquad (20)^{23}$$

$$k = 8.7 \times 10^9\ \text{M}^{-1}\ \text{s}^{-1}$$

$$\text{e}^-_{\text{aq}} + \text{H}_3\text{O}^+ \rightarrow \text{H}\cdot \qquad (21)^{23}$$

$$k = 2.3 \times 10^{10}\ \text{M}^{-1}\ \text{s}^{-1}$$

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Thus, in neutral and alkaline N_2O-saturated solution, the free radicals present are $\cdot OH$ and $\cdot H$, the latter contributing ca. 10% of the free-radical concentration.

Reactions with $Br_2^-\cdot$. In N_2O-saturated solutions containing 0.01 M NaBr, the following reactions occur.[24]

$$\cdot OH + Br^- \rightarrow \cdot Br + OH^- \qquad (22)$$

$$k_{22} \geq 10^9 \ M^{-1} \ s^{-1} \text{ at pH} < 9$$

$$\cdot Br + Br^- \rightleftarrows Br_2^-\cdot \qquad (23)$$

$$K_{23} = 2 \times 10^5 \ M^{-1}$$

Thus, in these solutions, the major reacting free radical formed is $Br_2^-\cdot$.

Reactions with $CO_2^-\cdot$. In N_2O-saturated solutions containing 0.1 M HCO_2Na, the following reactions occur.

$$\cdot OH/H + HCO_2^- \rightarrow CO_2^-\cdot + H_2O/H_2 \qquad (24)$$

$$k_{OH + HCO_2^-} = 3 \times 10^9 \ M^{-1} \ s^{-1} \ {}^{25}$$

$$k_{H + HCO_2^-} = 1.3 \times 10^8 \ M^{-1} \ s^{-1} \ {}^{26}$$

Reactions with $\cdot C(CH_3)_2OH$. In N_2O-saturated solutions containing 0.1 M 2-propanol, the following reactions occur.[27]

$$\cdot OH/H + (CH_3)_2CHOH \xrightarrow{85.5\%} \cdot C(CH_3)_2OH + H_2O/H_2$$
$$\xrightarrow{13.3\%} \cdot CH_2CH(CH_3)OH + H_2O/H_2 \qquad (25)$$

$$k_{OH + (CH_3)_2CHOH} = 2.3 \times 10^9 \ M^{-1} \ s^{-1} \ {}^{25}$$

$$k_{H + (CH_3)_2CHOH} = 7.8 \times 10^7 \ M^{-1} \ s^{-1} \ {}^{26}$$

(The percents of yield of the two reactions are for the hydroxyl radical reactions.)

Reactions with $\cdot CH_2C(CH_3)_2OH$. In N_2O-saturated solutions containing 0.1 M $(CH_3)_3COH$, the $\cdot OH$ radicals react via the following mechanism:

$$\cdot OH + (CH_3)_3COH \rightarrow \cdot CH_2C(CH_3)_2OH + H_2O \qquad (26)$$

$$k = 4.2 \times 10^8 \ M^{-1} \ s^{-1}$$

However, the rate of reaction of H atoms with *tert*-butyl alcohol is rather low;[26] thus some H atoms remain to react with substrates present even at low concentrations.

Reactions with $\cdot CH(OH)CH_2OH$ and $\cdot CH_2CHO$. In N_2O-saturated solutions containing 0.1 M $CH_2(OH)CH_2OH$, the following reactions occur.

$$\cdot OH/H + CH_2(OH)CH_2OH \rightarrow \cdot CH(OH)CH_2OH + H_2O/H_2 \qquad (27)$$

$$k_{OH + CH_2OHCH_2OH} = 1.5 \times 10^9 \ M^{-1} \ s^{-1} \ {}^{25}$$

$$k_{H + CH_2OHCH_2OH} = 2.1 \times 10^7 \ M^{-1} \ s^{-1} \ {}^{26}$$

The latter radicals are dehydrated in acid- and base-catalyzed reactions.[28,29]

$$\cdot CH(OH)CH_2OH \xrightarrow{H_3O^+} \cdot CH_2CHO + H_2O \qquad (28)$$

$$\cdot CH(OH)CH_2OH \xrightarrow{OH^-} \cdot CH_2CHO + H_2O \qquad (29)$$

Results and Discussion

In order to identify the intermediates formed in the reaction of $\cdot CH_2C(CH_3)_2OH$, $\cdot CH(OH)CH_2OH$, $\cdot CH_2CHO$, and $\cdot C(CH_3)_2OH$ with B_{12r}, we first carried out two reference experiments. We determined the spectrum of B_{12a} formed in the reaction sequence:[30]

$$B_{12r} + Br_2^-\cdot \rightarrow Co^{III}\text{–}Br + Br^- \qquad (30)$$

$$Co^{III}\text{–}Br \rightarrow B_{12a} + Br^- \qquad (31)$$

Figure 1. Difference spectra between transients and B_{12r}. Solution composition: 6×10^{-5} M B_{12r}, 1×10^{-2} M NaBr, pH 6.1, 5×10^{-3} M phosphate buffer, N_2O saturated. Pulse intensity, 6×10^3 rad, 1-cm optical path. (- - -) 150 μs after pulse attributed to Co^{III}–Br; (···) 10 ms after pulse attributed to B_{12a}.

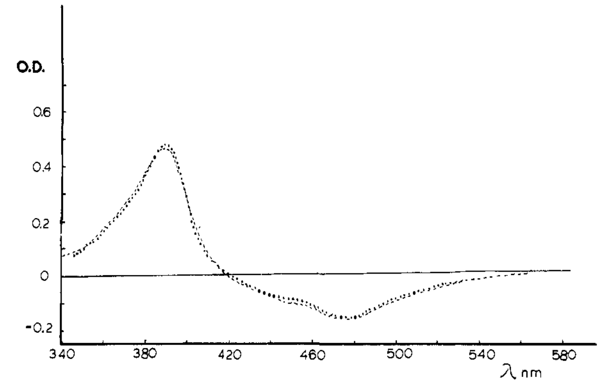

Figure 2. Difference spectra between transients and B_{12r}. Solution composition: 6×10^{-5} M B_{12r}, 5×10^{-2} M HCO_2Na, pH 6.1, 5×10^{-3} M phosphate buffer, N_2O saturated. Pulse intensity, 6×10^3 rad; 1-cm optical path. (- - -) 50 μs after pulse; (···) 10 ms after pulse both attributed to B_{12s}.

The results are plotted in Figure 1. The spectrum after 150 μs is attributed to Co^{III}–Br[30] and after 10 ms to B_{12a}.[30] The latter spectrum does not change for at least a second. It should be noted that the spectra plotted are the difference spectra between those of the products and that of B_{12r}. The spectrum of B_{12a} is characterized by a strong absorption band around 350 nm and a weaker one around 520 nm.

The second blank was the determination of the spectrum due to B_{12s} formed in the reaction[8]

$$B_{12r} + CO_2^-\cdot \rightarrow B_{12s} + CO_2 \qquad (32)$$

$$k = 8.2 \times 10^8 \ M^{-1} \ s^{-1}$$

The results, seen in Figure 2, suggest the formation of B_{12s} as an intermediate with a strong absorption band around 390 nm as expected. After a second, the absorption changes disappeared, indicating that B_{12r} is the final product. This observation is in agreement with expectation due to the following reactions.

$$B_{12s} + N_2O \xrightarrow{H_2O} B_{12a} + N_2 + 2OH^- \qquad (33)$$

$$k = 1.6 \times 10^2 \ M^{-1} \ s^{-1}, \text{ pH } 8^{31}$$

$$B_{12s} + B_{12a} \rightarrow 2B_{12r} \qquad (34)$$

$$k = 1.5 \times 10^7 \ M^{-1} \ s^{-1}, \text{ pH} < 6^{32}$$

Next we measured the spectra obtained under conditions where $\cdot CH_2C(CH_3)_2OH$ radicals are the major reactant; ca. 10% of H

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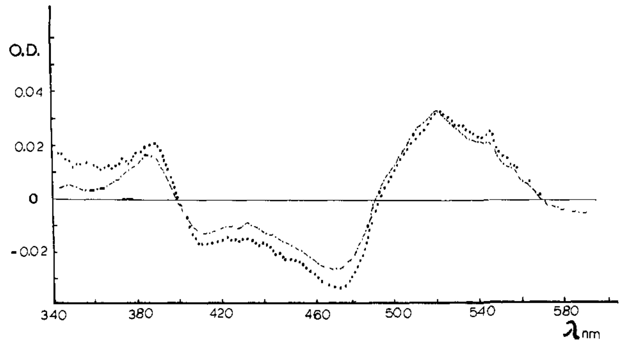

Figure 3. Difference spectra between transients and B_{12r}. Solution composition: 6×10^{-5} M B_{12r}, 0.1 M *tert*-butyl alcohol, pH 5.8, 5×10^{-3} M phosphate buffer, N_2O saturated. Pulse intensity, 4000 rad, 1-cm optical path. (···) 1 ms after pulse; (-···) 1 s after pulse both attributed to Co^{III}–$CH_2C(CH_3)_2OH$.

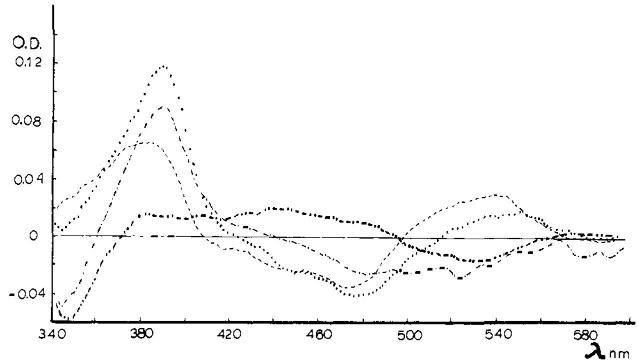

Figure 4. Difference spectra between transients and B_{12r}. Solution composition: 6×10^{-5} M B_{12r}, 0.1 M 2-propanol, 5×10^{-3} M phosphate buffer pH 5.8, N_2O saturated. Pulse intensity, 4000 rad, 1-cm optical path. (---) 50 µs after pulse attributed to Co^{III}–$C(CH_3)_2OH$; (···) 1 ms after pulse; (-···) 10 ms after pulse attributed to B_{12s} plus some products of a side reaction, probably Co^{III}–H; and (-···) 1 s after pulse attributed to B_{12r} plus some decomposition products.

atoms are present (see above). The results obtained at pH 5.8 are plotted in Figure 3. The nature of the product in this system clearly differs from that observed in the reference experiments. The product observed is stable for over a second in N_2O-saturated solution, thus indicating that it is not B_{12s}. The absorption spectrum of the product, seen in Figure 3, differs considerably from that of B_{12a} (Figure 1). These results suggest that a pseudocoenzyme is formed in the reaction

$$B_{12r} + \cdot CH_2C(CH_3)_2OH \rightarrow Co^{III}\text{–}CH_2C(CH_3)_2OH \qquad (35)$$

When the experiment was repeated at pH 10.7, the results were nearly identical with those observed at pH 5.8. At pH 3.1, a slightly different absorption spectrum was observed; however, its features also suggest the formation of a pseudocoenzyme. Our observations are in disagreement with those reported by Blackburn et al.[7] in neutral solutions. We feel that the results obtained by the streak camera are more accurate mainly for systems in which the reaction of the free radicals with the substrate competes with radical dimerization reactions. Furthermore, our experimental setup enabled spectral measurements up to a second after the pulse, whereas that of Blackburn et al. was limited to 1 ms.

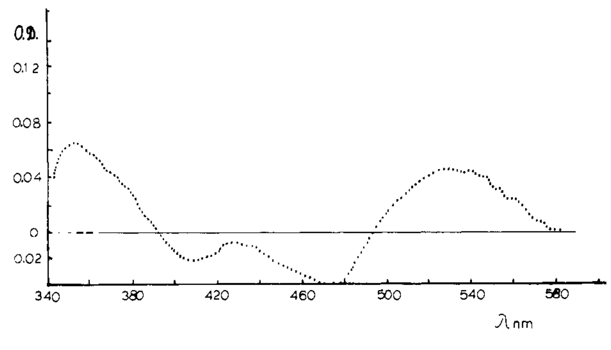

Figure 5. Difference spectrum between product and B_{12r}. Solution composition: 6×10^{-5} M B_{12r}, 0.5 M $(CH_2OH)_2$, pH 10.6, N_2O saturated. Pulse intensity, 4000 rad, 1-cm optical path. Spectrum measured 150 µs after the pulse attributed to Co^{III}–CH_2CHO.

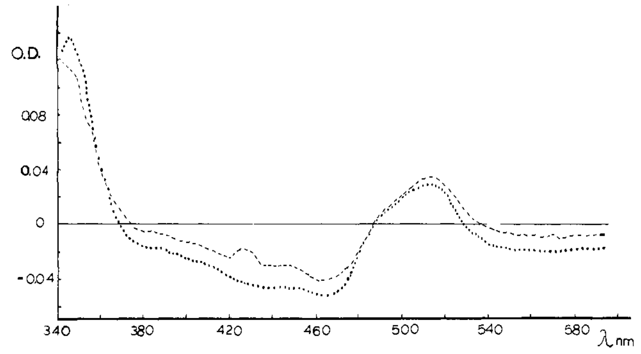

Figure 6. Difference spectra between transients and B_{12r}. Conditions as in Figure 5 but pH 1.0. (---) 150 µs after pulse, attributed to Co^{III}–CH_2CHO; (···) 1 s after pulse, attributed to B_{12a}.

The reaction of B_{12r} with $\cdot C(CH_3)_2OH$ radicals was reported to result in the formation of B_{12s}.[8] In Figure 4 are plotted the spectra observed at different times after the pulse under conditions where the only radicals formed are $\cdot C(CH_3)_2OH$ and $\cdot CH_2CH(CH_3)OH$. (The latter radical concentration is ca. 13% of the total radical concentration.[27]) The results clearly indicate that the system is complicated and cannot be explained by the reaction[35]

$$\cdot C(CH_3)_2OH + B_{12r} \rightarrow B_{12s} + (CH_3)_2CO + H_3O^+ \qquad (36)$$

followed by reactions 33 and 34 only. The spectrum observed after 50 µs is similar to that observed on the *tert*-butyl alcohol system (Figure 3). This observation suggests that the first intermediate formed is a pseudocoenzyme; i.e., the reaction occurring is

$$\cdot C(CH_3)_2OH + B_{12r} \rightarrow Co^{III}\text{–}C(CH_3)_2OH \qquad (37)$$

probably accompanied by the formation of some Co^{III}–$CH_2CH(CH_3)OH$. The spectrum after 1 ms resembles that of B_{12s} (Figure 2), though still some absorption around 540 nm is observed. After 10 ms, no absorption around 540 nm is observed, in agreement with the spectrum of B_{12s}; however, a bleaching around 350 nm is observed, which indicates that B_{12s} is not the only product at this stage. After a second, only minor optical changes at $\lambda > 370$ nm are observed, as expected when B_{12s} is formed (see above). However, the bleaching observed around 350 nm indicates that an unidentified product is formed, at least as a byproduct of a side reaction. This product has an absorption spectrum different from that of B_{12s}, B_{12r}, B_{12a}, and a pseudocoenzyme. As to the nature of this product and its mechanism of formation, we can only speculate; one plausible mechanism is

$$Co^{III}\text{–}C(CH_3)_2OH \xrightarrow[\text{shift}]{\beta\text{-hydride}} Co^{III}\text{–}H + CH_3C(OH){=}CH_2 \qquad (38)$$

followed by attack of the hydride on the corrin ring. Similar hydride shifts were suggested as an explanation of an analogous system involving a cobalt macrocycle complex[15] and as the mechanism of decomposition of secondary alkylcobalamins.[6,33]

Reactions of $\cdot CH_2CHO$ with B_{12r} were measured at pH 10.6 and 1.0; the results are plotted in Figures 5 and 6, respectively. The spectrum of the product at pH 10.6, which is stable for at least a second, resembles that observed in the *tert*-butyl alcohol system and is, therefore, attributed to the pseudocoenzyme formed in the reaction

$$B_{12r} + \cdot CH_2CHO \rightarrow Co^{III}\text{–}CH_2CHO \qquad (39)$$

This conclusion is in agreement with the observations of Blackburn

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[33] Grate, J. H.; Schrauzer, G. N. *J. Am. Chem. Soc.* **1979**, *101*, 4601.

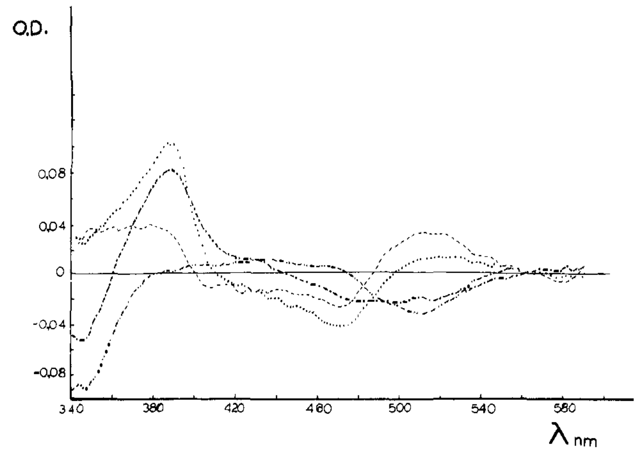

Figure 7. Difference spectra between transients and B_{12r}. Solution composition: 6×10^{-5} M B_{12r}, 0.5 M $(CH_2OH)_2$, 5×10^{-3} M phosphate buffer, pH 5.8, N_2O saturated. Pulse intensity, 4000 rad, 1-cm optical path. (---) 50 μs after pulse attributed to Co^{III}–$CH(OH)CH_2OH$; (···) 1 ms after pulse; (-···) 10 ms after pulse attributed to B_{12s} plus some products of a side reaction, probably Co^{III}–H; (--·) 1 s after pulse, attributed to B_{12r} plus some decomposition products.

et al.[7] At pH 1.0, the final spectrum resembles that of B_{12a}, seen in Figure 1, again in agreement with Blackburn et al.[7] However, the observation that the spectrum of the initial product differs from the final one suggests that B_{12a} is formed via reaction 39 followed by reaction 40. This conclusion is in agreement with

$$Co^{III}\text{–}CH_2CHO + H_3O^+ \rightarrow B_{12a} + CH_3CHO \qquad (40)$$

$$k = 4.3\ M^{-1}\ s^{-1}\,{}^{34}$$

the idea that aliphatic free radicals of this type are bad outer-sphere redox reagents, even when the free energy gain in the reaction is large, due to the large rearrangement energies required.[15-18]

The spectra of the intermediates obtained in the reaction of B_{12r} with $\cdot CH(OH)CH_2OH$ radicals at pH 5.8 are plotted in Figure 7. Similar results were obtained at pH 3.1, though a pH effect on the spectra was observed. The spectra at pH 5.8 (Figure 7) are nearly identical with those observed in the 2-propanol system at the same pH (Figure 4). Thus, the results seem to suggest that the following sequence of reactions best describes this system:

$$Co^{II} + \cdot CH(OH)CH_2OH \rightarrow Co^{III}\text{–}CH(OH)CH_2OH \qquad (41)$$

$$Co^{III}\text{–}CH(OH)CH_2OH \rightarrow Co^{I} + CH_2OHCHO + H_3O^+ \qquad (42)$$

$$Co^{III}\text{–}CH(OH)CH_2OH \rightarrow Co^{III}\text{–}H\ CH(OH){=}CHOH(CH_2OHCHO) \qquad (43)$$

followed by reactions 33 and 34 and some decomposition products of Co^{III}–H.

Finally, we measured the kinetics of reaction of $\cdot CH(OH)CH_2OH$ with B_{12r} in neutral solutions (pH 5.9) by following the rate of change of the absorption as a function of time at several wavelengths; i.e., λ = 370, 390, 430, and 520 nm. We obtain $k_{41} = (1.8 \pm 0.4) \times 10^8\ M^{-1}\ s^{-1}$, in good agreement with the results of Blackburn et al.[7] The following two reactions are not well separated in time, and the results at the different wavelengths could be fitted to one rate law with a rate ranging between 7×10^2 and $4 \times 10^3\ s^{-1}$, depending on the wavelength. These results suggest that k_{42} (or $k_{42} + k_{43}$) $\sim 1 \times 10^3\ s^{-1}$ and that a further reaction follows with $k \sim 7 \times 10^2\ s^{-1}$ (probably the decomposition of Co^{III}–H). Finally, the last reaction observed has a rate of $3.9 \pm 0.5\ s^{-1}$, and if this reaction is attributed to reaction 33 (see above), then $k_{33} \simeq 2 \times 10^2\ M^{-1}\ s^{-1}$, in very good agreement with the results of Swallow et al.[31]

Conclusions

The results of this study demonstrate that the mechanism of reaction of saturated aliphatic radicals with B_{12r} involves the formation of cobalt(III)–carbon bonds even in systems where the latter bond is unstable and decomposes heterolytically. This finding is in agreement with expectations, as outer-sphere redox processes would yield the unstable cation R^+ or anion R^-, reactions 14 and 15, respectively, and not the stable products ROH or RH. Thus, though reactions 44 and 45 are exothermic, reactions 14

$$Co^{II} + R\cdot + H_2O \rightarrow Co^{I} + ROH + H_3O^+ \qquad (44)$$

$$Co^{II} + R\cdot + H_2O \rightarrow Co^{III} + RH + OH^- \qquad (45)$$

and 15 are endothermic.[35] The reported redox potentials of the free radicals are for the couples $R\cdot/ROH$ or $R\cdot/RH$ and not for $R\cdot/R^+$ or $R\cdot/R^-$.[38] Indeed for the free radicals for which polarographic half-wave potentials were measured, large overpotentials were observed as expected.[38] In terms of the Marcus theory, these arguments are equivalent to stating that the rate of electron exchange via the outer-sphere mechanism between $R\cdot$ and ROH or RH is very slow.

Finally, it should be noted that we observe that Co^{III}–$CH(OH)CH_2OH$ decomposes heterolytically (reaction 42) and not via β-OH elimination, as expected from the free-radical mechanism for the B_{12} activity in diol dehydrase[4,39-44] and as reported for a naive model system.[15,45] However, as recent results indicate that the stability and mechanism of decomposition of the cobalt–carbon bond in alkylcobalamins depend on steric factors,[6,46,47] it is plausible that the enzymatic reaction follows a different route than that reported here. In the enzyme, the cobalt–carbon bond is probably also located in a less protic environment than in the present study. This might also affect the mode of decomposition of the cobalt–carbon bond.

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Registry No. $B_{12\gamma}$, 14463-33-3; $Br_2^{-}\cdot$, 12595-70-9; $CO_2^{-}\cdot$, 14485-07-5; $\cdot CH_2C(CH_3)_2OH$, 5723-74-0; $\cdot C(CH_3)_2OH$, 5131-95-3; $\cdot CH_2CHO$, 4400-01-5; $\cdot CH(OH)CH_2OH$, 3250-66-6.

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(35) One of the referees pointed out that reaction 45 was positively demonstrated for ethyl and methyl radicals[36,37] by use of isotope labeling. However, it was pointed out in these studies[36] that reaction 3 is the major route and that reaction 45 occurs only as a side reaction. Furthermore, these studies are based on measurements of the isotopic composition of ethane and methane formed as final products. It was not shown that no transient complex between the free radicals and the ligands of the divalent cobalt is formed prior to the evolution of the final products.

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