the other hand, the results of coenzyme tritium labeling studies[10] can be readily interpreted[11] in terms of our mechanism,[1] which is uniquely supported by stoichiometric and catalytic model reactions, as well as by the N_2O inhibition experiments described in this communication.

In applying N_2O as a potential inhibitor to other coenzyme B_{12} dependent enzyme reactions we have to date been unable to observe inhibiting effects with ribonucleotide reductase from *Lactobacillus leichmannii* and with methylmalonyl-CoA mutase from *Propionibacterium shermanii*.[12] In contrast to dioldehydrase, which is inactivated by oxygen, these enzymes operate aerobically just as well as anaerobically. The absence of an inhibiting effect of N_2O thus does not rule out the possibility that the Co(I) nucleophile is present in the active form of the enzyme; it may be that the active site is merely more protected against oxidation by either O_2 or N_2O.

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(10) P. A. Frey, M. K. Essenberg, R. H. Abeles, and S. S. Kerwar, *J. Amer. Chem. Soc.*, **92**, 4488 (1970).

(11) (a) The principal objection raised[10] against our mechanism[1] is derived from the results of tritium labeling experiments. The tritium incorporation from labeled substrate into the enzyme-bound coenzyme increases the radioactivity of the coenzyme 200–700 times compared to the activity of product propionaldehyde in the reaction solution. This rules out equilibration between product propionaldehyde in the solution with enzyme-bound coenzyme under the reaction conditions. We assume, however, that the H–T exchange takes place between the enzyme-bound coenzyme and newly formed propionaldehyde at the active site, *prior* to equilibration with propionaldehyde outside the enzyme.

(12) Inhibition experiments were performed by Dr. D. Jacobsen (Scripps Clinic and Research Foundation, La Jolla, Calif.) and Dr. J. D. Brodie, State University of New York at Buffalo.

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Hydridocobaloximes

Sir:

Hydridocobaloximes, H–Co(dmg)$_2$B (dmg = dimethylglyoximato monoanion, B = axial base), are the Brønsted acids corresponding to the cobaloxime(I) nucleophiles, and are postulated intermediates in certain cobaloxime reactions under neutral reducing conditions.[1-4] In previous attempts at synthesis, only the corresponding cobaloxime(II) derivatives were obtained, suggesting that hydridocobaloximes are inherently unstable species. We have now found that the stability of hydridocobaloximes is sensitively influenced by the nature of the axial base component B. Whereas hydridocobaloximes in which the axial ligands are predominantly σ-bonding nitrogen bases are indeed short-lived and difficult to isolate, relatively stable hydrides are formed if the axial ligands are π-bonding trialkylphosphines. The hydride H–Co(dmg)$_2$P(n-C$_4$H$_9$)$_3$, **1**, for example, is obtained by reducing Cl–Co(dmg)$_2$P(n-C$_4$H$_9$)$_3$ with excess $NaBH_4$ in pH 7 phosphate-buffered 50% (volume) aqueous methanol.[5] The black, oxygen-sensitive crystals of **1** precipitate out of the reaction solution with methanol of crystallization. *Anal.* Calcd for $C_{20}H_{42}N_4O_4PCo \cdot 2CH_3OH$: C, 47.37; H, 9.05; N, 10.07; P, 5.56; Co, 10.74. Found: C, 47.95; H, 9.65; N, 9.78; P, 5.68; Co, 10.95. The compound loses the methanol on heating *in vacuo* to 75° and starts to decompose with hydrogen evolution at 150°. *Anal.* Calcd for the methanol-free **1**, $C_{20}H_{42}N_4O_4PCo$: C, 48.77; H, 8.59; N, 11.37; Co, 11.96. Found: C, 48.32; H, 8.21; N, 11.20; Co, 11.32. The hydride **1** is also formed on careful acidification of alkaline solutions of the corresponding cobaloxime(I) nucleophile. Prepared in this fashion, **1** was apparently in our hands in 1965, but was at this time considered to be a cobaloxime(II) derivative.[1] It is now apparent that cobaloximes(II) with P(n-C$_4$H$_9$)$_3$ as the axial base disproportionate readily even in neutral solution. Unlike the Co(I) nucleophile, **1** is freely soluble in nonpolar hydrocarbon solvents and may be *quantitatively extracted into n-hexane or benzene*. The pK_a of **1** was estimated to be 10.5 by phase-distribution measurements between 50% aqueous methanol and n-hexane and is in agreement with the result of a previous indirect determination.[1] The constitution of **1** is supported by infrared and nmr measurements. In the infrared spectrum (Nujol mull) a band at 2240 cm^{-1} is assigned to the Co–H stretch; the Co–D stretch in the deuteride occurs at 1680 cm^{-1}. The hydride and deuteride bands disappear upon exposure of the infrared disks to air. Similar bands were found to be absent in the infrared spectra of a variety of cobaloxime(II) and alkylcobaloxime derivatives. In the ^{1}H nmr spectrum in n-hexane a broad signal of relative intensity 1 at δ 6.0 ppm is assigned to the resonance of the cobalt-bound hydrogen, consistent with the polarization H$^{\delta+}$–Co$^{\delta-}$ of the cobalt–hydrogen bond. The Co–H signal is absent in the spectrum of the deuteride and disappears on passing air through the nmr sample solution containing the hydride. The signal of the dmg methyl protons occurs at 1 ppm and coincides with the signals of the tributylphosphine ligand. The anomalously high chemical shift of the dmg protons indicates a partial negative charge of the Co(dmg)$_2$ moiety.

In the reduction of halocobaloximes(III) with $NaBH_4$ in neutral buffered solution transient blue species are frequently observed, indicating the formation of unstable hydridocobaloximes under these special conditions of reduction. Utilizing the solubility of

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(2) G. N. Schrauzer, and R. J. Windgassen, *J. Amer. Chem. Soc.*, **89**, 1999 (1967).

(3) E. N. Sal'nikova and M. L. Khidekel', *Izv. Akad. Nauk, Ser. Khim.*, 1, 223 (1967).

(4) M. Naumburg, K. N.-V. Duong, and A. Gaudemer, *J. Organometal. Chem.*, **25**, 231 (1970).

(5) In a typical experiment, 5 g of Cl–Co(dmg)$_2$P(n-C$_4$H$_9$)$_3$ [see G. N. Schrauzer, *Inorg. Syn.*, 11, 62 (1968)] was suspended in 250 ml of 50% (v/v) aqueous methanol. A total of approximately 15 g of solid primary and tertiary sodium phosphate was added to adjust the pH close to 7. After most of the alkali phosphate dissolved a freshly prepared solution of 1.5 g of $NaBH_4$ in 25 ml of water was added gradually over a period of 30 min. Occasionally, small amounts of methanol had to be added to reduce excessive foaming. During the last 15 min of $NaBH_4$ addition the reaction solution was kept anaerobic by a blanket of nitrogen. A nearly black solid precipitates which was collected by filtration under nitrogen gas. The hydride was washed with water to remove inorganic salts and dried *in vacuo* at 75° for 12 hr. The isolated yield was 4.3 g of dry hydride, or 92%, based on cobaloxime starting material. The product slowly oxidizes on contact with air, but may be stored for at least several days in argon-filled ampoules. Decomposition was noted on prolonged storage.

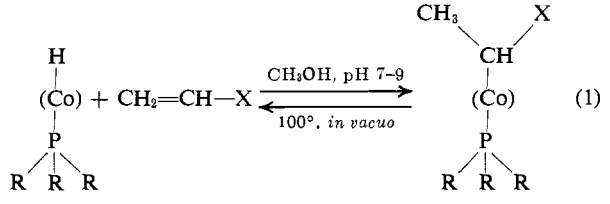
Table I. Wavelengths and Intensities of the CT Absorption of Hydridocobaloximes in Three Solvents

In-plane ligand[a]	Axial base	λ_{max}, mμ (ε)[c] *n*-Hexane	C_6H_6	CH_3OH
dmg	$P(n\text{-}C_4H_9)_3$	565 (6.0 × 10³)	592 (5.8 × 10³)	614 (5.0 × 10³)
dmg	$P(C_2H_5)_2C_6H_5$	565 (6.2 × 10³)	564 (6.0 × 10³)	620 (5.2 × 10³)
dmg	$P(C_6H_5)_3$	*b*	587 (4.0 × 10³)	607 (4.5 × 10³)
dmg	$C_6H_{11}NC$	*b*	617 (4.5 × 10³)	614 (3.0 × 10³)
$dmgB_2F_4$	$P(n\text{-}C_4H_9)_3$	*b*	522 (4.0 × 10³)	650 (4.0 × 10³)
$dmgB_2F_4$	$P(C_2H_5)_2C_6H_5$	*b*	600 (5.0 × 10³)	617 (4.8 × 10³)
$dmgB_2F_4$	$P(C_6H_5)_3$	617 (6.0 × 10³)	587 (4.0 × 10³)	607 (5.0 × 10³)
$dmgB_2F_4$	Pyridine	*b*	637 (3.0 × 10³)	613 (3.8 × 10³)
dpg	$P(C_6H_5)_3$	*b*	637 (4.2 × 10³)	640 (3.9 × 10³)

[a] dmg = dimethylglyoxime; dmg B_2F_4 = dmg ligand in which the oxime protons are substituted by BF_2 groups; dpg = diphenylglyoxime. [b] Hydride insoluble or unstable in *n*-hexane. [c] Values of ε approximate.

hydridocobaloximes in nonpolar solvents, several were characterized in solution by their optical absorption spectra. All hydridocobaloximes exhibit an intense, solvent-dependent charge-transfer absorption in the visible region. Values of λ_{max} (ε) for a number of hydrides are given in Table I. The dark violet H–Co(dmg)₂py is formed on reducing Cl–Co(dmg)₂py with excess $NaBH_4$ in a pH 7 phosphate-buffered 50% aqueous methanolic suspension at 20°, but decomposes slowly at room temperature. The hydridocobaloximes with imidazole or benzimidazole as the axial ligands, however, are already too unstable to be isolated even at low reaction temperatures.

All hydridocobaloximes react with alkyl halides in protic media to produce alkylcobaloximes at rates comparable to those observed[6] with the free Co(I) nucleophiles. In carefully dried and methanol-free *n*-hexane or benzene, **1**, surprisingly, is *unreactive* with alkyl halides, ethylene oxides, ethyl acrylate, or acrylonitrile. The $3d_{z^2}$ orbital in **1** thus is effectively screened by the proton. In aqueous methanol **1** reacts with vinylogs such as acrylonitrile or acrylates to yield the α-substituted ethylcobaloxime derivatives. This reaction is characteristic of hydridocobaloximes[2] and hydridorhodoximes;[7] with the free nucleophiles the corresponding β-substituted ethylcobaloximes are formed.[2] On heating, the reverse reaction occurs, providing an example for a hydride elimination in cobaloxime chemistry (eq 1; X, *e.g.*, CN or COOR). The thermolysis at



(1)

100° *in vacuo* of α-cyanoethyl(tributylphosphine)-cobaloxime represents a convenient laboratory method for the synthesis of solvent-free **1** in essentially quantitative yield, and in analytical purity. (*Anal.* Calcd for **1**: C, 48.77; H, 8.59; N, 11.37; Co, 11.96. Found: C, 48.39; H, 8.21; N, 11.52; Co, 11.40.) The product is also identical in every respect with the solvent-free hydride obtained by the alternative method described above, and exhibits the ir Co–H stretch at 2240 cm^{-1} (Nujol mull under N_2). The reverse reaction of **1** with acrylonitrile in CH_3OH at pH 7–9 affords the known[2] α-cyanoethyl(tributylphosphine)cobaloxime in 80% isolated yield (the reaction is best conducted employing a 20-fold excess of acrylonitrile, maintaining strictly anaerobic conditions). The same compound may be obtained by generating the hydridocobaloxime *in situ*, using methods described in ref 2. The formation of **1** is also observed on heating higher alkylcobaloximes containing hydrogen in the β position and $P(n\text{-}C_4H_9)_3$ as the axial base. Hydride elimination reactions may be important in cobamide coenzyme catalyzed processes and are presently being investigated.[8]

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Iodine as an Exceptionally Favorable Inhibitor for the Reaction of Oxygen with Trialkylboranes. Evidence for a Very Slow Initiation Step in the Autoxidation of Organoboranes

Sir:

The very rapid reaction of trialkylboranes in tetrahydrofuran (THF) solution with oxygen[1] is strongly inhibited by the presence of small amounts of elemental iodine. Indeed, the presence of iodine in appreciable concentration, 0.2 *M*, effectively prevents the uptake of oxygen by 0.5 *M* solutions of representative organoboranes over periods as long as several days. Consequently, the reaction of oxygen with trialkylboranes must involve a relatively slow rate of radical initiation, with a very fast rate of chain propagation.

The facile autoxidation of organoboranes was long believed to be a nonradical process because many of the usual radical inhibitors, such as hydroquinone, had no apparent effect upon the reaction.[2] The oxidation of optically active 1-phenylethylboronic acid gave racemic product and this was considered to be suggestive of a process involving radicals.[3] Indeed, it was observed that the autoxidation of this boronic acid exhibits a remarkable induction period in the presence of added inhibitors, such as copper(II) *N*,*N*-dibutyldithiocarbamate and galvinoxyl.[3] It was then discovered

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