Exploratory Studies on Reactions of Cobaloxime π-Cations with C-Nucleophiles: Irreversible Alkene Decomplexation versus Nucleophilic Capture

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(β-Hydroxyalkyl)- and (β-acetoxyalkyl)cobaloximes can undergo facile acid-catalyzed β-heteroatom exchange with oxygen and nitrogen nucleophiles in an S_N1-like mechanism via cationic metal−alkene π-complex intermediates (cobaloxime π-cations). The reaction of cobaloxime π-cations with carbon nucleophiles has not been previously reported. The results reported in this paper demonstrate that cobaloxime π-cations are reasonably good electrophiles. They are sufficiently reactive to add to the electron-rich sp^2 centers in allyltrimethylsilane and pyrrole. A major side reaction for intermolecular reactions is irreversible alkene decomplexation. An intramolecular pyrrole cyclization (**22** to **23**, 83% yield) significantly raised the yield for nucleophilic addition compared to that of the analogous intermolecular couplings (**12b** to **13b**, 32% yield and **17** to **18**, 29% yield). The results of these studies provide a foundation for the design and evaluation of modified cobalt ligands with the goal of suppressing alkene decomplexation and enhancing reaction of cobaloxime π-cations with C-nucleophiles.

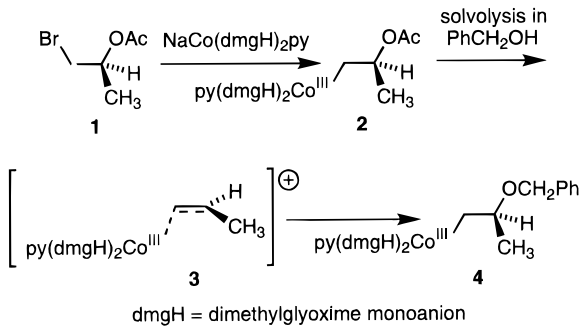
(β-Hydroxyalkyl)- and (β-acetoxyalkyl)cobaloximes are known to undergo facile acid-catalyzed β-heteroatom exchange with oxygen and nitrogen nucleophiles.[1] Golding[2] discovered that the solvolysis of homochiral (2-acetoxypropyl)cobaloxime (**2**, Scheme 1) with benzyl alcohol to produce **4** proceeded with retention of configuration, although no yield was given. Several studies by Brown,[3] Silverman and Dolphin,[4] and others have investigated the mechanism of this reaction. Brown used low-temperature ^{13}C NMR to directly observe the cobaloxime π-cation of ethene, formed by acid treatment of (2-hydroxyethyl)- and (2-alkoxyethyl)cobaloximes.[3b] At −30 °C there were two ^{13}C resonances, 41 ppm apart, for the ethene carbons. These results indicated that even a symmetrical alkene such as ethene forms an unsymmetrical rapidly equilibrating cobaloxime π-cation (Scheme 2).

We became interested in the possibility of using (β-hydroxyalkyl)cobaloximes for carbon−carbon bond formation via cobaloxime π-cations as shown in Scheme 3. In such a scheme, the cobalt−carbon bond would play multiple roles in bond constructions, displaying ionic reactivity in the cobaloxime π-cation step (**7**−**9**) and radical reactivity in further synthetic transformations via radical processes.[5] The likelihood of success for the sequence of reactions shown in Scheme 3 hinges on the reactivity of cobaloxime π-cations as electrophiles. The studies described in this paper were designed to determine whether cobaloxime π-cations are sufficiently electrophilic to react with alkenes in C−C bond constructions.

Results and Discussion

Initial studies focused on the cobaloxime π-cation of ethene (shown in Scheme 2) since it is the simplest possible cobaloxime π-cation and its properties and reactions can be used as a key reference standard for comparison with other cobaloxime π-cations. Reaction of ethylene oxide (**10a**) with $NaCo(dmgH)_2py$ provided (β-hydroxyethyl)cobaloxime, a known compound,[6] in 69% isolated yield. Acetylation of (β-hydroxyethyl)cobaloxime with Ac_2O and pyridine in CH_2Cl_2 provided (2-acetoxyethyl)cobaloxime (**12a**) in 81% isolated yield. Reaction of **12a** with allyltrimethylsilane and $BF_3{\cdot}Et_2O$ in CH_2-

Scheme 1



dmgH = dimethylglyoxime monoanion

(5) For some representative examples or reactions of B_{12} and B_{12}-like alkylcobalt complexes see: (a) Okabe, M.; Tada, M. *Chem. Lett.* **1980**, 831. (b) Scheffold, R.; Rytz, G.; Walder, L. In *Modern Synthetic Methods*; Scheffold, R., Ed.; John Wiley & Sons: New York, 1983; Vol. 3, pp 355−440. (c) Johnson, M. D. *Acc. Chem. Res.* **1983**, *16*, 343. (d) Ladlow, M.; Pattenden, G. *Tetrahedron Lett.* **1984**, *25*, 4317. (e) Torii, S.; Inokuchi, T.; Yukawa, T. *J. Org. Chem.* **1985**, *50*, 5875. (f) Baldwin, J. E.; Li, C. S. *J. Chem. Soc., Chem. Comm.* **1987**, 166. (g) Branchaud, B. P.; Meier, M. S.; Choi, Y. *Tetrahedron Lett.* **1988**, *29*, 167. (h) Gupta, B. D.; Roy, S. *J. Chem. Soc., Perkin Trans. 2* **1988**, 1377. (i) Pattenden, G. *Chem. Soc. Rev.* **1988**, *17*, 361. (j) Ghosez, A.; Göbel, T.; Giese, B. *Chem. Ber.* **1988**, *121*, 1807. (k) Branchaud, B. P.; Meier, M. S. *J. Org. Chem.* **1989,** *54,* 1320. (l) Branchaud, B. P.; Detlefsen, W. D. *Tetrahedron Lett.* **1991**, *32*, 6273. (m) Clark, A. J.; Jones, K. *Tetrahedron* **1992**, *48*, 6875. (n) Giese, B.; Carboni, B.; Göbel, T.; Muhn, R.; Wetterich, F. *Tetrahedron Lett.* **1992**, *33*, 2673. (o) Giese, B.; Erdmann, P.; Göbel, T.; Springer, R. *Tetrahedron Lett.* **1992**, *33*, 4545. (p) Martin, O. R.; Xie, F.; Kakarla, R.; Benhamza, R. *Synlett* **1993**, 165. (q) Auer, L.; Weymuth, C.; Scheffold, R. *Helv. Chim. Acta* **1993**, *76*, 810. (r) Fry, A. J.; Sirisoma, U. N. *J. Org. Chem.* **1993**, *58*, 4919. (s) Zhang, D. Z.; Scheffold, R. *Helv. Chim. Acta* **1993**, *76*, 2602.

(6) Schrauzer, G. N.; Windgassen, R. J. *J. Am. Chem. Soc.* **1967**, *89*, 143.

[⊗] Abstract published in *Advance ACS Abstracts,* December 15, 1995.

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(2) Golding, B. T.; Sakrikar, S. *J. Chem. Soc., Chem. Commun.* **1972**, 1183.

(3) (a) Brown, K. L.; Ramamurthy, S.; Marynick, D. S. *J. Organomet. Chem.* **1985**, *287*, 377−94. (b) Brown, K. L.; Ramamurthy, S. *Organometallics* **1982**, *1*, 413−15.

(4) Silverman, R. B.; Dolphin, D. *J. Am. Chem. Soc.* **1976**, *98*, 4626.

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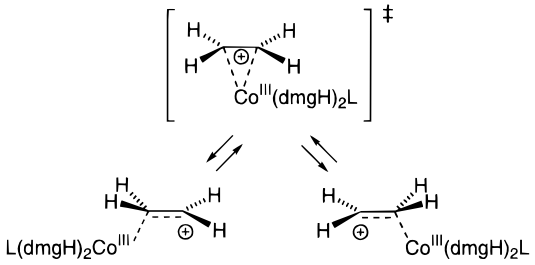
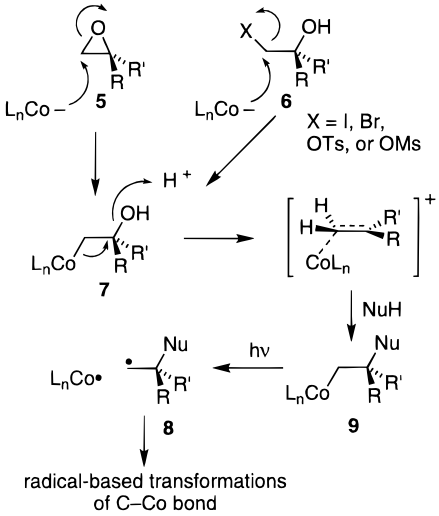
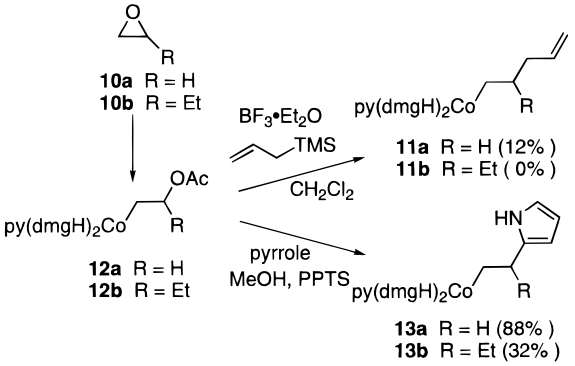
Scheme 2



Scheme 3



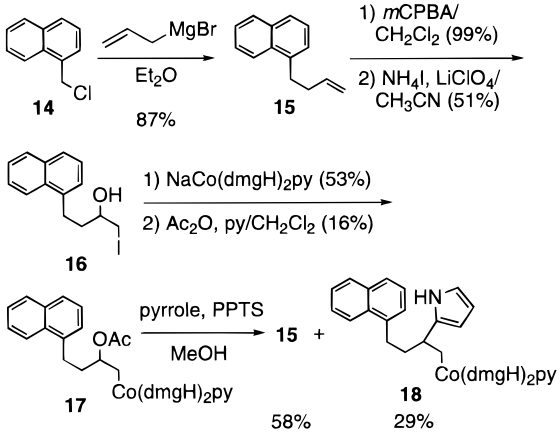
Scheme 4



Cl_2 provided **11a** in 12% isolated yield; these are the best conditions found for this reaction after exploring several Lewis acid, solvent, and temperature parameters. Experimentation with other carbon nucleophiles led to the discovery that pyrrole, a more electron-rich nucleophile, reacted with **12a** in methanol using pyridinium *p*-toluenesulfonate (PPTS) as a catalyst to form **13a** in 88% yield (Scheme 4).

To test the effect of an alkyl substituent, (2-acetoxybutyl)cobaloxime (**12b**) was examined. Direct reaction of NaCo(dmgH)$_2$py with **10b** proceeded in low yields. Conversion of **10b** to 1-iodobutan-2-ol was accomplished in 98% yield using NH_4I and $LiClO_4$ in acetonitrile by the method of Chini et al.[7] Reaction of 1-iodobutan-2-ol with NaCo(dmgH)$_2$py provided (2-hydroxybutyl)cobaloxime (63%) which was acetylated with Ac_2O and pyridine in CH_2Cl_2 to provide (2-acetoxybutyl)cobaloxime (**12b**) in 54% yield (33% overall yield for three steps from **10b**).

Scheme 5



Reaction of **12b** with allyltrimethylsilane and $BF_3{\cdot}Et_2O$ in CH_2Cl_2 failed to provide any of the carbon-coupled product **11b**, although **12b** was completely consumed in the reaction. Coupling of **12b** with the more nucleophilic pyrrole in methanol using PPTS as a catalyst was successful, providing **13b**, with complete regioselectivity for C−C bond construction at the more substituted carbon, in a modest 32% yield.

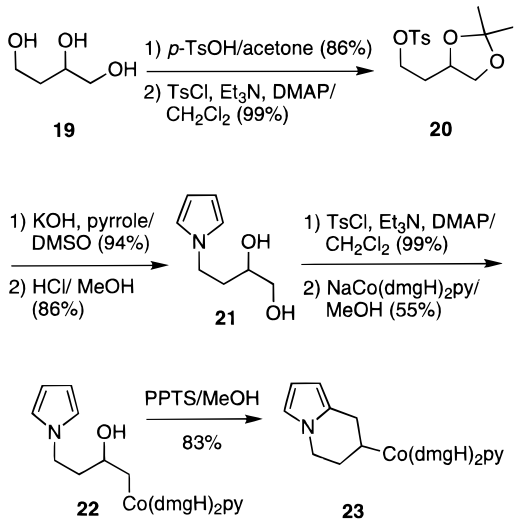
The most plausible interpretation of the results with **12a** and **12b** is that the cobaloxime π-cations have two possible fates: trapping with C-nucleophile or irreversible alkene decomplexation.[3] Since the alkene products from reactions of **12a** and **12b** are too volatile to conveniently isolate and quantitate, a larger substrate with a less volatile alkene elimination product was studied. In Scheme 5, (α-chloromethyl)napthalene (**14**) was coupled with allylmagnesium bromide to provide 4-(1-naphthyl)-1-butene (**15**) in 87% yield.[8] The alkene moiety in **15** was epoxidized with *m*-chloroperoxybenzoic acid (*m*CPBA) to provide 1,2-epoxy-4-(1-naphthyl)butane in essentially quantitative yield. Reaction of the epoxide with NH_4I and $LiClO_4$ in acetonitrile, again by the method of Chini et al.,[7] provided iodide **16** in 51% yield. Reaction of **16** with NaCo(dmgH)$_2$py in methanol provided a 53% yield of the β-hydroxy cobaloxime which was reacted with Ac_2O and pyridine in CH_2Cl_2 to provide **17** in 16% yield. The yield of **17** is low because it is unstable and decomposes during chromatographic purification on silica gel. Reaction of **17** with pyrrole in methanol using PPTS as a catalyst led to the production of **18** in 29% yield, with complete regioselectivity for C−C bond construction at the more substituted carbon, and alkene **15** in 58% yield. These results demonstrate that alkene decomplexation from the transient cobaloxime π-cation is the major side reaction limiting the efficiency of intermolecular coupling.

Since intermolecular pyrrole couplings with alkyl-substituted systems such as **12b** (to form **13b** in 32% yield) and **17** (to form **18** in 29% yield) were feasible, albeit in low yield, an analogous cyclization reaction was expected to be much more favorable and high-yielding. To examine this issue, a (β-hydroxyalkyl)cobaloxime with an attached pyrrole moiety (**22**) was synthesized (Scheme 6). Selective 1,2-diol protection of 1,2,4-butanetriol (**19**) using *p*-toluenesulfonic acid (*p*TsOH) in acetone[9] proceeded in 86% yield to provide 1,2-*O*-isopropylidenebutane-1,2,4-triol which was converted to tosylate **20** using

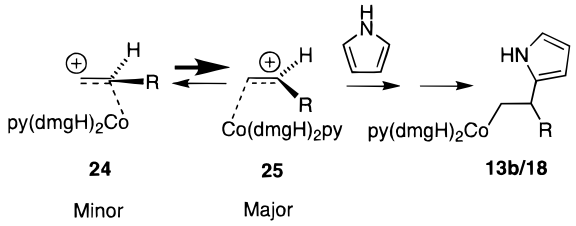
(7) Chini, M.; Crotti, P.; Gardelli, C.; Macchia, F. *Tetrahedron* **1992**, *48*, 3805.

(8) Lambert, J. B.; Fabricius, D. M.; Hoard, J. A. *J. Org. Chem.* **1979**, *44*, 1480.

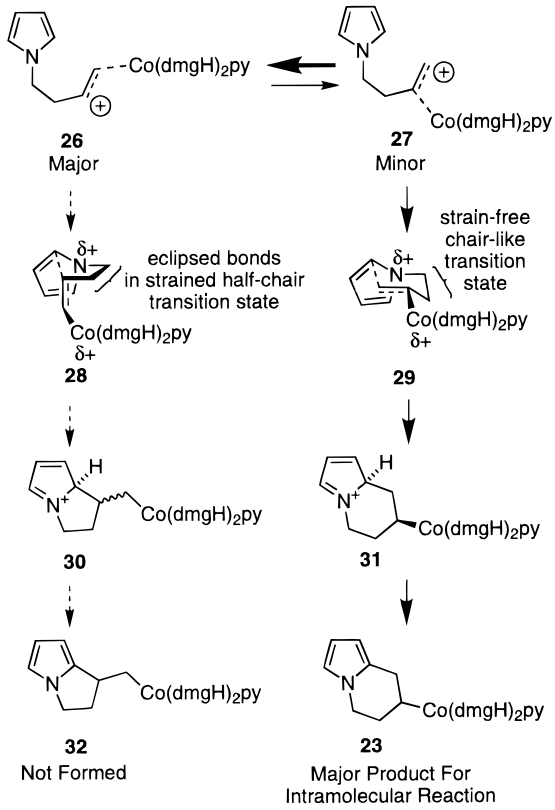
Scheme 6



Scheme 7

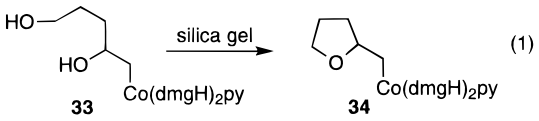


Scheme 8



p-toluenesulfonyl chloride (TsCl), triethylamine, and 4-(dimethylamino)pyridine (DMAP) in CH_2Cl_2 in essentially quantitative yield. *N*-Alkylation of the potassium salt of pyrrole anion [formed by reaction of pyrrole with KOH in dimethyl sulfoxide (DMSO)][10] proceeded in 94% yield, and subsequent acid-catalyzed cleavage of the acetonide group provided **21** in 86% yield (81% overall for two steps from **20**). Selective tosylation of the primary alcohol moiety in **21** using TsCl, Et_3N, and DMAP in CH_2Cl_2 (essentially quantitative) followed by reaction with $NaCo(dmgH)_2py$ in MeOH (55%) provided (2-hydroxy-4-*N*-pyrrolylbutyl)cobaloxime (**22**) in 54% overall yield for two steps from **21**. Mild acid catalysis using PPTS in MeOH smoothly and efficiently converted **22** into cyclized product **23** in 83% yield.

Interestingly, the intramolecular pyrrole reaction (**22** to **23**) provided exactly the opposite regiochemistry to the analogous intermolecular pyrrole reactions (**12b** to **13b** and **17** to **18**). The intermolecular reactions apparently result from nucleophilic capture of the more stable isomer of the hyperconjugated cobaloxime π-cation (**25** in Scheme 7). Attack at the more substituted center can be rationalized as a charge effect in which the nucleophile is attracted to the most positive center (the most substituted center in **25**). For the intramolecular reaction, ring strain, eclipsing interactions, and possibly some stereoelectronic effects apparently become dominant. Hand-held molecular models and simple molecular mechanics modeling of possible intermediates **30** (either diastereomer) and **31** clearly show that endo cyclization to form intermediate **31** and then product **23** can proceed through a relatively strain-free and low-energy 6-membered ring transition state (**29**), as shown in Scheme 8. Exo cyclization, however, to form intermediate **30** would have to proceed through a high-energy 5-membered ring transition state (**28**) which has much ring strain and numerous eclipsing interactions on the incipient 5-membered ring. Much of this strain is almost certainly the result of the necessity of maintaining the planarity of the pyrrole ring with the CH_2 directly attached to the pyrrole nitrogen since a more conformationally flexible cyclization to form a cyclic ether (**33** to **34**, eq 1) is known to proceed with exclusively exo regiochemistry via nucleophilic attack at the more substituted carbon to provide **34** in 70% yield.[1b]



(1)

Conclusion

The results reported in this paper demonstrate that cobaloxime π-cations are reasonably good electrophiles and are sufficiently reactive to add to electron-rich sp^2 centers. It might be possible to exploit this interesting and potentially useful reactivity for applications in organic synthesis. Unfortunately, the cobaloxime π-cations derived from the simple dimethylglyoxime-based cobaloximes used in the present study undergo facile and apparently irreversible alkene decomplexation in competition with the desired reaction with nucleophiles. Intramolecular cyclization instead of intermolecular coupling significantly raises the yield for nucleophilic addition in competition with alkene decomplexation, but focusing solely on cyclizations limits the potential scope of the reaction and is only a partial solution to the problem. It should be possible to alter the steric and electronic properties of cobaloxime ligands or the ligands

(9) Hayashi, H.; Nakanishi, K.; Brandon, C.; Marmur, J. *J. Am. Chem. Soc.* **1973**, *95*, 8749.

(10) Heaney, H.; Ley, S. V. *J. Chem. Soc., Perkin. Trans. 1* **1973**, 499.

in other coenzyme B_{12} model complexes to both suppress the alkene decomplexation reaction and enhance the reactivity with nucleophiles. One possible solution to both problems would be to make the cobaloxime moiety more electron deficient, thus the more electrophilic cobalt-containing moiety should more strongly bond with the alkene, enhancing its lifetime, and it should also simultaneously make the complexed alkene more reactive with nucleophiles. Ongoing and future studies will address these fundamental issues and also explore the development of new synthetic methodology and potential synthetic applications.

Experimental Section

Materials and Methods. All reactions were performed under a N_2 atmosphere and were stirred with a magnetic stir bar. All chromatography was performed on silica gel unless otherwise noted; gravity chromatography was performed with Mallinckrodt silica gel (60−230 mesh), and flash chromatography was performed with EM Science silica gel 60 (finer than 230 mesh). Commercial reagent grade solvents and chemicals were used unless otherwise noted. CH_2Cl_2 was dried by passage through a column of neutral or basic Al_2O_3 (Aldrich: activated, Brockmann I, ~150 mesh) into a nitrogen-filled flask or storage vessel. TsCl was purified by washing an Et_2O solution with saturated $NaHCO_3$ repeatedly, drying the organic layer over $MgSO_4$, then suction filtering through Celite, slightly concentrating the solution, and then crystallizing by cooling over dry ice to obtain pure TsCl. In all reactions with cobaloximes, solvents were deoxygenated by bubbling with N_2 for 1 min/mL of solution unless otherwise noted. Since alkylcobaloximes are somewhat air sensitive in solution, chromatography fractions were concentrated in vacuo as soon as possible with the water bath temperature not exceeding 40 °C during rotary evaporation. Decomposition points of cobaloximes are not reported since the temperature range of decomposition for metal−1,2-dioxime complexes varies with conditions.[11] ^1H and ^{13}C NMR spectra were recorded at 300 and 75 MHz, respectively, in $CDCl_3$; the residual $CHCl_3$ was defined as 7.26 and 77.00 ppm, respectively. Coupling constants are reported in hertz. Due to anisotropic effects, more than two ^{13}C NMR signals associated with dimethylglyoxime monoanion ligands of alkylcobaloximes are often observed, thus providing more ^{13}C signals than might be expected for an apparently symmetric metal−ligand system. Alkylcobaloximes have a broad ^{13}C NMR resonance for the carbon attached to cobalt due to quadrapolar relaxation of the carbon by the cobalt.[12] Attached proton tests (APT) were performed at 75 MHz, but with a shorter data acquisition time than the decoupled ^{13}C; therefore the carbon attached to the cobalt was not detected. Optically active (*S*)-1,2,4-butanetriol was used in the synthesis of compound **23** because the possibility of an exo cyclization on **22** (instead of the endo cyclization that produced **23**) would have provided some interesting stereochemical results. Since the endo cyclization to produce **23** occurred, optical rotation data on **20**, **21**, **22**, and other intermediates in its synthesis were not collected because that information was no longer relevant to this study.

(2-Hydroxyethyl)cobaloxime.[6] $CoCl_2 \cdot 6H_2O$ (3.0 g, 12.6 mmol) was added to deoxygenated MeOH (20 mL), and the solution was deoxygenated for an additional 5 min followed by the addition of dimethylglyoxime (3.0 g, 25.8 mmol), 50% NaOH (2.4 g, 30 mmol), and pyridine (1.10 mL, 13.6 mmol). The brown solution was cooled to −5 °C, and then $NaBH_4$ (1.6 g, 42.3 mmol) was added followed by stirring for 10 min (greenish-black mixture). Ethylene oxide (0.75 mL, 15 mmol), which had been condensed into a Schlenk tube at −78 °C, was transferred via cannula into the reaction mixture. Gas was evolved, and the mixture grew lighter in color. The reaction mixture was kept at or below 0 °C for 3.5 h and then was allowed to warm to rt slowly overnight. The mixture was partially neutralized with 1.0 M HCl to pH 8, dried over Na_2SO_4 for 2 h, and then filtered with suction through a fritted glass funnel. This crude reaction mixture was adsorbed onto 15 g of silica gel and was purified by gravity column chromatography (0−100% EtOAc/hexanes and then 0−10% EtOH/EtOAc). The orange product band was collected in a N_2-filled flask. Removal of solvents in vacuo provided 3.64 g of an orange powder (69% yield). ^1H NMR δ 1.69 (t, J = 6, 2 H), 2.15 (s, 12 H), 3.03 (t, J = 6, 2 H), 7.33 (t, J = 6.3, 2 H), 7.74 (t, J = 7.2, 1 H), 8.57 (d, J = 5.4, 2 H), 18.19 (O−H−O bridge, br s); ^{13}C NMR δ 12.09, 65.38 , 125.28, 137.61, 149.74, 150.00; IR (KBr, cm^{-1}) 3409 (br, s), 2945 (m), 2910 (m), 1553 (s), 1441 (m), 1237 (s); MS (FAB) m/z 414 (M + 1), 334 (M − py), 289 [Co(dmgH)$_2$]; HRMS calcd for $CoC_{15}H_{25}N_5O_5$ (M + 1) 414.1187, found 414.1190.

(2-Acetoxyethyl)cobaloxime (12a). A flame-dried reaction vessel was charged with (β-hydroxyethyl)cobaloxime (1.03 g, 2.5 mmol), dry CH_2Cl_2 (~40 mL), Ac_2O (1.0 mL, 10.6 mmol, distilled), and pyridine (1.0 mL, 12.4 mmol, distilled), and then the solution was deoxygenated for 30 min followed by stirring at rt for 24 h. Additional pyridine (0.6 mL, 7.4 mmol) was then added, and the reaction was followed by TLC until all starting material was consumed; the solvent was then removed in vacuo. The crude product was purified by flash column chromatography (0−100% EtOAc/hexanes) to provide 0.92 g of **12a** as an orange powder (81% yield): ^1H NMR δ 1.54 (t, J = 8.1, 2 H), 1.95 (s, 3 H), 2.14 (s, 12 H), 3.73 (t, J = 8.1, 2 H), 7.32 (t, J = 6.6, 2 H), 7.72 (t, J = 7.5, 1 H), 8.55 (d, J = 5.1, 2 H), 18.19 (br s); ^{13}C NMR δ 12.00, 21.09, 22.63 (br), 66.70, 125.20, 137.60, 149.85, 149.79, 170.75; IR (KBr) cm^{-1} 3430 (br, w), 2924 (w), 1729 (s), 1560 (m), 1230 (s); MS (FAB) m/z 456 (M + 1), 376 (M − py), 289; HRMS calcd for $CoC_{17}H_{27}N_5O_6$ (M + 1) 456.1293, found 456.1300.

1-Iodobutan-2-ol. This compound was synthesized according to the method of Chini et al.[7] $LiClO_4$ (1.53 g, 14.4 mmol) and NH_4I (2.0 g, 13.8 mmol) were placed in a flask and purged with N_2. Acetonitrile (~20 mL, distilled) and 1,2-epoxybutane (0.82 mL, 9.5 mmol) were added via syringe. The mixture was protected from light and stirred at rt for 3 h. Half of the solvent was then removed in vacuo, and the residue was diluted with water. This mixture was extracted with Et_2O (3×), and then the combined Et_2O layers were washed with water and saturated NaCl, dried over $MgSO_4$, gravity filtered, and concentrated in vacuo to provide 1.86 g of a pale yellow oil (98%): ^1H NMR δ 0.97 (t, J = 7.5, 3 H), 1.59 (m, 2 H), 1.85 (br s, 1 H), 3.24 (dd, J = 6.6, 10.2, 1 H), 3.42 (dd, J = 10.2, 1 H), 3.45 (m, 1 H); ^{13}C NMR δ 9.87, 15.91, 29.47, 72.19; IR (neat, cm^{-1}) 3372 (br s), 2963 (s), 2934 (s), 2876 (s); MS (EI) m/z 200 (M), 183 (M − OH); HRMS calcd for C_4H_9IO 199.9700, found 199.9708.

(2-Hydroxybutyl)cobaloxime. $CoCl_2 \cdot 6H_2O$ (2.85 g, 12 mmol), dimethylglyoxime (2.74 g, 23.6 mmol), 50% NaOH (1.74 g, 22 mmol), and pyridine (1.0 mL, 12.4 mmol) were added to deoxygenated MeOH (65 mL), and the mixture was deoxygenated for 10 min. The solution was then cooled over an ice bath, $NaBH_4$ (0.64 g, 16.9 mmol) was added in two aliquots, and the mixture was stirred for 10 min (greenish-brown color). A solution of 1-iodobutan-2-ol (2.5 g, 12.5 mmol) in deoxygenated MeOH (10 mL) was transferred via cannula into the reaction. After the mixture was stirred for 2 h over an ice bath, $NaBH_4$ (0.2 g, 5.3 mmol) was added. After an additional hour, the reaction mixture was adsorbed onto silica gel. A layer of sand, silica gel (~100 g), and the silica adsorbed with the product were placed (listed bottom to top) in a 600 mL fritted glass funnel. The column was eluted under aspirator vacuum with CH_2Cl_2 and then EtOAc until the eluent ran almost colorless to yield 3.32 g of an orange powder (63% yield). Gravity chromatography (0−100% EtOAc/hexanes) provided a sample suitable for spectral analysis. ^1H NMR δ 0.80 (t, J = 7.5, 3 H), 1.11 (t, J = 9.6, 1 H), 1.32 (m, 2 H), 2.13 (s, 12 H), 2.19 (m, overlapping with a peak at 2.13 ppm), 2.36 (impurity, s), 2.81 (m, 1 H), 7.34 (t, J = 6.6, 2 H), 7.75 (t, J = 7.2, 1 H), 8.55 (d, J = 4.8, 2 H); ^{13}C NMR δ 10.55, 12.13, 30.66, 36.99 (br), 75.46,

(11) Schrauzer, G. N.; Windgassen R. J. *J. Am. Chem. Soc.* **1966**, *88*, 3738.

(12) Brown, K. L.; Satyanarayana, S. *Inorg. Chem.* **1992**, *31*, 1366 and references therein.

125.26, 137.58, 149.89, 150.10; IR (KBr, cm^{-1}) 3494 (br, m), 2945 (m), 2896 (m), 1553 (s), 1230 (s); MS (FAB) *m/z* 443 (M + 2), 442 (M + 1), 363 (M − py), 289; HRMS calcd for $CoC_{17}H_{30}N_5O_5$ (M + 2) 443.1579, found 443.1580.

(2-Acetoxybutyl)cobaloxime (12b). (2-Hydroxybutyl)-cobaloxime (1.35 g, 3.1 mmol) was acetylated according to the procedure for **12a** above, except that 6.25 equiv of Ac_2O and 24 equiv of pyridine were used. The reaction time was 40.5 h at which time the starting material was still present (as determined by ^1H NMR). The silica gel used for chromatography was first deactivated by swirling the silica with 5% pyridine/MeOH (enough to make a homogeneous slurry) and then removing the volatiles in vacuo until the silica was a powder. Gravity chromatography (0−95.5% EtOAc/hexanes containing 0.5% pyridine) yielded 0.52 g of a bright yellow−orange powder (43% isolated yield, 54% calculated yield as determined by ^1H NMR and based on recovered starting material): ^1H NMR; δ 0.76 (t, J = 7.5, 3 H), 1.38−1.67 (m, 4 H), 2.01 (s, 3 H), 2.12, 2.15 (singlets, 12 H total), 3.86 (m, 1 H), 7.30 (t, J = 6.9, 2 H), 7.71 (t, J = 7.5, 1 H), 8.58 (d, J = 5.7, 2 H) 18.19 (br s); ^{13}C NMR δ 9.87, 11.95, 21.45, 28.37, 28.40, 77.37, 125.06, 137.45, 149.51, 149.80, 149.87, 170.78; IR (KBr, cm^{-1}) 3431 (br, w), 2966 (m), 2917 (m), 1729 (s), 1560 (s), 1244 (s); MS (FAB) *m/z* 484 (M + 1), 404 (M − py), 289; HRMS calcd for $CoC_{19}H_{31}N_5O_6$ (M + 1) 484.1606, found 484.1630.

Allyltrimethylsilane Coupling Conditions. (2-Acetoxyalkyl)cobaloxime was added to a reaction flask, and the flask was purged with N_2. Dry CH_2Cl_2 (to make the solution 0.02 M in cobaloxime) was transferred via cannula, allyltrimethylsilane (22 equiv) was added via syringe, and the mixture was deoxygenated. $BF_3{\cdot}Et_2O$ (1.2 equiv, Aldrich Sure Seal) was added via syringe. The reaction mixture immediately changed from orange to dark orange in color. The mixture was stirred ∼14 h at rt, the solvents were removed in vacuo, and the residue was flash chromatographed (0−100% EtOAc/hexanes). Reactions were carried out with 0.09−0.25 mmol of cobaloxime.

4-Pentenylcobaloxime (11a). This compound was produced from the reaction of (2-acetoxybutyl)cobaloxime and allyltrimethylsilane according to the general procedure above and was isolated as an orange solid in 12% yield: ^1H NMR δ 1.00 (m, 2 H), 1.60 (t, J = 8, 2 H), 1.96 (q, J = 7.5, 2 H), 2.11 (s, 12 H), 4.83 (dd, J = 10.5, 18, 2 H), 5.72 (m, J = 6.6, 9.9, 17.1, 1 H), 7.29 (t, J = 6.6, 2 H), 7.69 (t, J = 7.8, 1 H), 8.58 (d, J = 5.1, 2 H), 18.22 (s); ^{13}C NMR δ 11.97, 11.99, 29.67, 30.00, 34.66, 113.60, 125.11, 137.34, 139.03, 149.10, 149.86, 150.03; IR (KBr, cm^{-1}) 3431 (broad, w), 2917 (s), 2854 (m), 1560 (s), 1237 (s); MS (FAB) *m/z* 438 (M + 1), 358 (M − py), 289; HRMS calcd for $CoC_{18}H_{29}N_5O_4$ (M + 1) 438.1551, found 438.1542.

Pyrrole Coupling Conditions. MeOH (volume adjusted so that cobaloxime is ∼7.6 mM) was deoxygenated. The cobaloxime (1 equiv), pyrrole (125 equiv), and PPTS (2 equiv) were added, and the solution was deoxygenated an additional 5 min. The solution was stirred while protected from ambient light for 18 h. The reaction mixture was then transferred, concentrated in vacuo, taken up in CH_2Cl_2, and poured through a fritted glass funnel containing a thin layer of sand, silica gel (2.5 g), and another thin layer of sand (listed bottom to top) using additional CH_2Cl_2 as needed for quantitative transfer. The silica gel was eluted under aspirator vacuum with EtOAc (30 mL), and the solution was concentrated in vacuo to give a product mixture. Product yield was quantitated by ^1H NMR using Ph_3CH as an internal standard. Reactions were carried out with 0.07−0.4 mmol of cobaloxime. Reported yields are an average of three reactions.

(2-(α-Pyrrolyl)ethyl)cobaloxime (13a). This compound was produced from reaction of (2-acetoxyethyl)cobaloxime (**12a**) with pyrrole according to the general procedure for pyrrole coupling. Flash chromatography (0−100% EtOAc/hexanes) yielded an orange powder: ^1H NMR δ 1.78 (t, J = 9, 2 H), 2.09 (s), 2.19 (t, 14 H together), 5.83 (s, 1 H), 6.04 (m, 1 H), 6.57 (m, 1 H), 7.32 (t, J = 6.9, 2 H), 7.72 (t, J = 7.2, 1 H), 8.62 (d, J = 5.7, 2 H), 18.25 (br s); ^{13}C NMR δ 11.96, 27.95, 104.26, 108.00, 115.54, 125.17, 132.84, 137.46, 149.18, 149.54, 149.83, 150.00; IR (KBr, cm^{-1}) 3275 (m), 2910 (m), 1553 (s), 1229 (s); MS (FAB) *m/z* 462 (M^+), 383 (M − py), 289; HRMS calcd for $CoC_{19}H_{27}N_6O_4$ 462.1425, found 462.1440.

(2-(α-Pyrrolyl)butyl)cobaloxime (13b). This compound was produced from reaction of (2-acetoxybutyl)cobaloxime (**12b**) with pyrrole according to the general procedure for pyrrole coupling. Flash chromatography (0−100% EtOAc/hexanes) yielded a yellow−orange powder: ^1H NMR δ 0.71 (t, J = 7.2, 3 H), 1.36 (m, 2 H), 1.58 (impurity, br s), 1.96, 2.00 (s, 12 H), 2.17 (m, J = 8.7, ∼2 H), 2.33 (t, J = 8.7, 1 H), 5.70 (br s, 1 H), 6.00 (d, J = 2.7, 1 H), 6.52 (br s, 1 H), 7.30 (t, J = 6.3, 2 H overlapped with $CHCl_3$), 7.71 (t, J = 7.5, 1 H), 8.22 (br s, 1 H), 8.53 (d, J = 5.4, 2 H), 18.20 (s); ^{13}C NMR (peak assignments are based on an APT NMR experiment) δ 11.91 (CH_3, dmgH CH_3), 32.10 (CH_2), 33.45 (absent on APT, br s),[14] 41.02 (CH), 102.50 (CH), 107.57 (CH), 114.91 (CH), 125.05 (CH), 137.32 (CH), 138.47 (quaternary C), 149.81 (CH), 149.93 (CH), 149.97 (CH), 150.03 (quaternary C); IR (KBr, cm^{-1}) 3413 (br, m), 2960 (w), 2924 (w), 2361 (vw), 2296 (vw), 1684 (m), 1560 (s), 1232 (s); MS (FAB) *m/z* 191 (M + 1); HRMS calcd for $CoC_{21}H_{32}N_6O_4$ (M + 1) 491.1817, found 491.1831.

4-(1-Naphthyl)-1-butene (15). Caution: Stench. This compound was synthesized by the procedure of Lambert et al.[8] A commercial solution of allylmagnesium bromide in Et_2O was used, and 6.65 g of **15** was obtained as a pale yellow oil (87% yield). Gravity chromatography (0−5% CH_2Cl_2/hexanes) yielded a sample suitable for spectral analysis: ^1H NMR δ 2.60 (q, J = 7.8, 2 H), 3.24 (t, J = 7.8, 2 H), 5.11 (d, J = 10.2, 1 H), 5.18 (d, J = 17.1, 1 H), 6.03 (m, J = 6.6, 10.2, 17.1, 1 H), 7.38−7.60 (m, 4 H), 7.78 (d, J = 8.1, 1 H), 7.92 (d, J = 7.5, 1 H), 8.11 (d, J = 7.8, 1 H); ^{13}C NMR δ 32.44, 34.78, 114.89, 123.70, 125.39, 125.45, 125.50, 125.73, 125.88, 125.90, 126.62, 128.76, 131.84, 133.87, 137.88, 138.21; IR (neat, cm^{-1}) 3066 (m), 2936 (m), 1640 (w), 1597 (w), 1510 (w), 1396 (w), 796 (s); MS (EI) *m/z* 182 (M), 141 (naph − CH_2^+); HRMS calcd for $C_{14}H_{14}$ 182.1096, found 182.1099.

1,2-Epoxy-4-(1-naphthyl)butane. *m*CPBA (8.52 g, 80−85% purity, ∼39.5 mmol) was added to a solution of 4-(1-naphthyl)-1-butene (**15**) (4.51 g, 24.7 mmol) in CH_2Cl_2 (∼300 mL) and stirred. White precipitate was present during the reaction. After 6.5 h, the reaction was complete as determined by TLC. The reaction mixture was then concentrated in vacuo, taken up in Et_2O, washed with saturated $NaHCO_3$, water, and saturated NaCl, dried over $MgSO_4$, suction filtered through Celite, and concentrated in vacuo to give a pale yellow powder which contained *m*CPBA. It was then taken up in CH_2Cl_2 and stirred vigorously with saturated $Na_2S_2O_3$ for 45 min. The layers were then separated, and the organic layer was washed with saturated $Na_2S_2O_3$ and saturated $NaHCO_3$. The drying steps were repeated, and the product was concentrated in vacuo to give 4.87 g of an orange oil (99% yield). Flash chromatography (0−40% EtOAc/hexanes) gave a sample suitable for spectral analysis: ^1H NMR δ 1.89−2.01 (m, 1 H), 2.03−2.15 (m, 1 H), 2.54 (dd, J = 2.7, 4.8, 1 H), 2.80 (t, J = 4.5, 1 H), 3.02−3.08 (m, 1 H), 3.18−3.40 (m, 2 H), 7.38−7.47 (m, 2 H), 7.49−7.58 (m, 2 H), 7.77 (d, J = 7.8, 1 H), 7.89 (d, J = 8.7, 1 H), 8.08 (d, J = 8.1, 1 H); ^{13}C NMR δ 29.21, 33.50, 47.11, 51.86, 123.53, 125.47, 125.85, 125.95, 126.83, 128.78, 131.70, 133.88, 137.27; IR (neat, cm^{-1}) 3046 (m), 2926 (m), 2989 (m), 1600 (m), 1510 (m); MS (EI) *m/z* 198 (M), 141 (naph − CH_2^+); HRMS calcd for $C_{14}H_{14}O$ 198.1045, found 198.1044.

1-Iodo-4-(1-naphthyl)butan-2-ol (16). This compound was synthesized from 1,2-epoxy-4-(1-naphthyl)butane according to the methodology of Chini et al.[7] as described above for the preparation of 1-iodobutan-2-ol. The reaction time was 12 h; 1.89 g of the iodide was obtained. Gravity chromatography (0−100% Et_2O/hexanes) and then recrystallization from Et_2O/hexanes/CH_2Cl_2 gave 1.05 g of pale yellow 0.25 in. needles (51% yield): mp 102.5−105.5 °C; ^1H NMR δ 2.01 (dd, J = 7.5, 15, 2 H), 2.15 (d, J = 5.4, 1 H), 3.09−3.20 (m, 1 H), 3.25−3.41 (overlapped m, 3 H), 3.64 (br d, J = 3.9, 1 H), 7.35−7.44 (m, 2 H), 7.47−7.57 (m, 2 H), 7.74 (d, J = 7.8, 1 H), 7.88 (d, J = 7.5, 1 H), 8.08 (d, J = 8.1, 1 H); ^{13}C NMR δ 16.42, 29.05, 37.47, 70.52, 123.65, 125.54, 125.93, 126.11, 126.89, 128.83, 131.70, 133.93, 137.43; IR (KBr, cm^{-1}) 3398 (br, s), 3354 (br, s), 2947

(m), 2915 (w); MS (EI) *m/z* 326 (M), 141 (naph − CH_2^+); HRMS calcd for $C_{14}H_{15}IO$ 326.0169, found 326.0166.

(2-Hydroxy-4-(1-naphthyl)butyl)cobaloxime. $CoCl_2 \cdot 6H_2O$ (2.18 g, 9.2 mmol), dimethylglyoxime (2.14 g, 18.4 mmol), 50% NaOH (1.46 g, 18.3 mmol), and pyridine (0.75 mL, 9.3 mmol) were added to deoxygenated MeOH (35 mL). The mixture was deoxygenated an additional 10 min and then cooled over an ice bath. Two aliquots of $NaBH_4$ (0.69 g total, 18.2 mmol) were added over a 30 min period, and the mixture was stirred. Iodide **16** (2.15 g, 6.6 mmol) was then added as a deoxygenated solution in MeOH and THF (15 and 10 mL, respectively), and the reaction mixture was allowed to warm to rt and stirred for 2 h. $NaBH_4$ (0.15 g, 4 mmol) was added, and the reaction mixture was stirred for 4 h. $NaBH_4$ (0.15 g, 4 mmol) was again added, and the reaction mixture was stirred for an additional hour. The crude reaction mixture was adsorbed directly onto silica gel. Gravity chromatography was performed with deoxygenated solvents (0−100% EtOAc/hexanes). The orange product band was collected in a N_2-filled flask and concentrated in vacuo to give 1.97 g of an orange foam (53% yield). Repeated gravity chromatography gave a sample suitable for spectral analysis: ^{1}H NMR δ 1.17 (t, J = 9.6, 1 H), 1.73 (m, 1 H), 1.89 (m, 2 H), 2.03/2.04 (two s, 12 H), 2.20 (d, J = 9.3, 1 H), 2.84 (m, 2 H), 3.15 (m, 2 H), 7.31−7.36 (m, 4 H), 7.43−7.50 (m, 2 H), 7.67 (m, 2 H), 7.80 (d, J = 7.5, 1 H), 8.08 (d, J = 8.1, 1 H), 8.53 (d, J = 5.1, 2 H), 18.20 (very broad); ^{13}C NMR δ 11.97, 29.00, 37.00, 38.45, 72.54, 124.25, 125.22, 125.38, 125.55, 126.05, 128.41, 132.04, 133.75, 137.57, 138.91, 149.71, 149.81, 150.08, 150.13; IR (KBr, cm^{-1}) 3475 (br, m), 1957 (w), 2916 (w), 1559 (s), 1446 (s), 1241 (s); MS (FAB) *m/z* 568 (weak M + 1), 289.

(2-Acetoxy-4-(1-naphthyl)butyl)cobaloxime (17). (2-Hydroxy-4-(1-naphthyl)butyl)cobaloxime (1.04 g, 1.8 mmol) was acetylated as previously described for compound **12b** with 10 equiv of Ac_2O and 11 equiv of pyridine in dry CH_2Cl_2. The reaction was complete after 41.5 h as determined by TLC. Gravity chromatography with deoxygenated solvents (0−80% EtOAc/hexanes) gave 0.18 g of an orange solid (16% yield). Repeated gravity chromatography on neutral Al_2O_3 (Aldrich: activated, Brockmann I, ~150 mesh) gave a sample suitable for spectral analysis: ^{1}H NMR δ 1.28 (EtOAc), 1.54−1.89 (m, 4 H), 1.989 (EtOAc), 2.04 (s, 3 H), 2.11 (s, 12 H), 2.37 (impurity), 2.98 (t, J = 8.1, 2 H), 4.16 (m, 1 H), 7.30−7.51 (m, 6 H), 7.68 (m, 2 H), 7.81 (d, J = 7.8, 1 H), 8.05 (d, J = 8.4, 1 H), 8.57 (d, J = 5.1, 2 H), 18.24 (s); ^{13}C NMR δ 12.04/12.11, 21.58, 29.35, 36.55, 76.30, 124.07, 125.17−126.35 (6 peaks), 128.54, 131.93, 133.83, 137.53, 138.41, 149.76−150.05 (4 peaks), 170.92; IR (KBr, cm^{-1}) 3438 (br, w), 3052 (w), 2928 (w), 1726 (m), 1560 (m), 1235 (s), 1089 (m); MS (FAB) *m/z* 609 (weak M + 1), 530 (M − py), 289.

(4-(1-Naphthyl)-2-(α-pyrrolyl)butyl)cobaloxime (18). This compound was produced from reaction of **17** with pyrrole according to the general procedure for pyrrole coupling except that the reaction time was 15 h. The yields of **15** and **18** were quantitated by ^{1}H NMR using Ph_3CH as an internal standard. Reported yields are an average of three reactions. Gravity chromatography (0−100% EtOAc/hexanes) gave an orange solid: ^{1}H NMR δ 1.26 (EtOAc), 1.48 (d, impurity), 1.75−1.82 (m, 4 H), 1.93/1.97 (two s, 12 H), 2.33−2.44 (β-CH, impurity, m, 2 H), 2.88 (m, 2 H), 5.84 (s, 1 H), 6.06 (d, J = 2.4, 1 H), 6.58 (s, 1 H), 7.20−7.33 (m, 4 H), 7.41 (m, 2 H), 7.65 (m, 2 H), 7.78, (m, 2 H), 7.41 (br s, 1 H), 8.54 (d, J = 5.4), 18.20 (s); ^{13}C NMR δ 11.87, 14.17 (impurity), 20.93 (impurity), 29.66 (impurity), 30.87, 34.00 (br), 39.64, 40.40, 60.29 (impurity), 102.99, 107.84, 115.21, 124.05, 125.05, 125.21, 125.51, 125.62, 126.14, 128.51, 131.95, 133.87, 137.34, 138.07, 139.21, 149.93, 150.11, 150.06; IR (KBr, cm^{-1}) 3423 (br, w), 2931 (m), 1569 (m), 1241 (s); HRMS (FAB) calcd for $CoC_{31}H_{38}N_6O_4$ (M + 1) 617.2286, found 617.2298.

1,2-*O*-Isopropylidenebutane-1,2,4-triol. This compound was prepared according to the procedure of Hayashi et al. using 19.46 g of 1,2,4-butanetriol (183.4 mmol).[9] A 22.99 g sample of 1,2-*O*-isopropylidenebutane-1,2,4-triol was obtained as a pure, colorless oil without purification (86% yield): ^{1}H NMR δ 1.25 (s, 3 H), 1.30 (s, 3 H), 1.70 (m, 2 H), 2.99 (s, 1 H), 3.44 (t, J = 7.5), 3.64 (m, 2 H), 3.97 (dd, J = 6.3, 8.1, 1 H), 4.16 (m, 1 H); ^{13}C NMR δ 25.45, 26.66, 35.75, 59.66, 69.24, 74.31, 108.67; IR (neat, cm^{-1}) 3427 (br, s), 2991 (s), 2936 (s), 2882 (s), 1382 (s), 1225 (s), 1061 (s).

1,2-*O*-Isopropylidenebutane-1,2,4-triol 4-*p*-Toluenesulfonate (20). This compound was previously prepared by Tanis et al.[13] TsCl (9.78 g, 51.3 mmol) was added to a flame-dried reaction flask. Dry CH_2Cl_2 (~250 mL) was transferred via cannula into the flask, Et_3N (13 mL, 93.3 mmol, stored over molecular sieves) was added via syringe, and the white gas given off was purged from the flask with N_2. DMAP (~10 mg, 0.08 mmol) was added. The reaction mixture was cooled over an ice bath, and 1,2-*O*-isopropylidenebutane-1,2,4-triol (7.1 g, 48.6 mmol) was added as a solution in dry CH_2Cl_2 via cannula. The mixture was stirred for 3.5 h at 0−5 °C and then allowed to warm to rt after which it was stirred an additional 6 h, and the reaction was determined to be complete by TLC. The reaction mixture was then transferred and concentrated in vacuo. The residue was taken up in EtOAc (250 mL), washed with saturated $NaHCO_3$ and saturated NaCl, dried over $MgSO_4$, suction filtered through Celite, and concentrated in vacuo to give 14.49 g of an orange oil (99% yield). Gravity chromatography (0−100% Et_2O/hexanes) gave a sample suitable for spectral analysis: isolated as a yellow oil; ^{1}H NMR δ 1.29 (s, 3 H), 1.34 (s, 3 H), 1.56 (impurity), 1.89 (m, 2 H), 2.45 (s, 3 H), 3.51 (t, J = 7.5, 1 H), 4.02 (dd, J = 6, 8.1, 1 H), 4.10−4.18 (m, 3 H), 7.36 (d, J = 8.1, 2 H), 7.80 (d, J = 8.4, 2 H); ^{13}C NMR δ 21.32, 25.31, 26.62, 32.96, 67.24, 68.83, 72.10, 108.73, 127.64, 129.66, 133.50, 144.61; IR (neat, cm^{-1}) 2995 (m), 2940 (m), 2884 (m), 1607 (m), 1370 (s), 1188 (s); MS (EI) *m/z* 301 (M + 1), 243 (M − acetone), 155, 139; HRMS calcd for $C_{14}H_{21}SO_5$ (M + 1) 301.1110, found 301.1120.

4-*N*-Pyrrolyl-1,2-*O*-isopropylidenebutane-1,2-diol. This compound was peviously prepared by Tanis et al.[13] A flame-dried reaction flask was charged with powdered KOH (12.33 g, 220 mmol) and dry DMSO (~150 mL) and cooled in an ice bath. Pyrrole (15 mL, 216 mmol, distilled) was added, and the ice bath was removed after 5 min. The mixture was stirred for an additional 45 min. Tosylate **20** (42.4 g, 141 mmol) was added as a solution in DMSO dropwise via cannula over a 45 min period. The color gradually changed from light green to brown. After the addition of **20** was complete, no tosylate remained (as determined by TLC). The reaction mixture was cooled in an ice bath, and water (100 mL) was added slowly. The mixture was poured into a separatory funnel, more water (150 mL) and Et_2O (300 mL) were added, and the layers were separated. The organic layer was washed with saturated NaCl, dried over $MgSO_4$, suction filtered through a small pad of silica over Celite, and concentrated in vacuo to yield 25.99 g of a yellow oil (94% yield). Gravity chromatography (0−50% Et_2O/hexanes) gave a sample suitable for spectral analysis; isolated as a yellow oil; ^{1}H NMR δ 1.35 (s, 3 H), 1.43 (s, 3 H), 1.98 (q, J = 6.6, 2 H), 3.47 (t, J = 7, 1 H), 3.96 (dd, J = 3.3, 6, 1 H), 4.02 (overlapping m, 3 H), 6.14 (t, J = 2, 2 H), 6.66 (t, J = 2, 2 H); ^{13}C NMR δ 25.40, 26.82, 35.49, 45.95 65.76, 72.92, 108.01, 108.71, 120.28; IR (neat, cm^{-1}) 2991 (s), 2936 (s), 2875 (m), 2371 (w), 2336 (w), 1505 (s), 1389 (s), 1218 (s); MS (EI) *m/z* 195 (M), 137, 120, 81, 80 (pyrrole − CH_2^+); HRMS calcd for $C_{11}H_{17}NO_2$ 195.1260, found 195.1260.

4-*N*-Pyrrolylbutane-1,2-diol (21). This compound was previously prepared by Tanis et al.[13] Deprotection was accomplished by the method of Hayashi et al.[9] 4-*N*-Pyrrolyl-1,2-*O*-isopropylidenebutane-1,2-diol (5.26 g, 26.9 mmol) was dissolved in MeOH (270 mL) and deoxygenated for 2 h. HCl (0.1 M, 84 mL) was added, and the solution was further deoxygenated for 45 min. The reaction mixture was protected from light and stirred for 25 h; a white floating solid appeared. MeOH (60 mL) and water (20 mL) were added, and it was determined by TLC that no starting material was present. Volatiles were removed in vacuo. The residue was taken up in EtOAc (450 mL), washed with saturated $NaHCO_3$ and saturated NaCl, dried over $MgSO_4$, suction filtered through Celite, and concentrated in vacuo to a brown oil. The aqueous layers were then re-extracted with EtOAc, and the organic

(13) Tanis, S. P.; Raggon, J. W. *J. Org. Chem.* **1987**, *52*, 819.

layers were combined and worked up in the same manner to give a total of 3.6 g of a brown oil (86% yield). Flash chromatography (0−100% EtOAc/hexanes then 0−10% EtOH/EtOAc) gave a sample suitable for spectral analysis: isolated as a yellow oil; ^{1}H NMR δ 1.83 (m, 2 H), 2.77 (br s, 1 H), 3.01 (br s, 1 H), 3.40 (dd, J = 8, 11.1, 1 H), 3.54 (d, J = 9.6, 2 H), 4.05 (t, J = 6.9, 2 H), 6.15 (d, J = 2, 2 H), 6.68 (d, J = 2, 2 H); ^{13}C NMR δ 34.34, 45.60, 66.47, 69.06, 108.01, 120.48; IR (neat, cm^{-1}) 3386 (br, s), 2936 (m), 2882 (m), 2371 (w), 2343 (w), 2248 (w), 1505 (s), 1293 (s), 1096 (s); MS (EI) m/z 155 (M), 81 (pyrrole − CH_2^+); HRMS calcd for $C_8H_{13}NO_2$ 155.0946, found 155.0951.

4-*N*-Pyrrolylbutane-1,2-diol 1-*p*-Toluenesulfonate. This compound was previously prepared by Tanis et al.[13] The tosylate was synthesized from compound **21** (1.04 g, 6.7 mmol) according to the procedure for the preparation of compound **20.** Reaction time at 0−5 °C was 1.5 h before the reaction was allowed to reach rt. The reaction mixture was then transferred and concentrated in vacuo. The slushy yellow−white mixture was taken up in EtOAc, washed with saturated $NaHCO_3$ and saturated NaCl, dried over $MgSO_4$, suction filtered through Celite, and concentrated in vacuo to give 2.03 g of an orange−brown oil (99% yield). Gravity chromatography (0−100% EtOAc/hexanes) gave a sample suitable for spectral analysis: isolated as a colorless oil which gave white crystals when a chloroform solution of the oil was concentrated in vacuo; mp 79.2−83 °C; ^{1}H NMR δ 1.82 (m, 2 H), 2.30 (d, J = 3.6, 1 H), 2.46 (s, 3 H), 2.76 (m, 1 H), 3.85 (dd, J = 6.9, 10.2, 1 H), 3.93 (dd, J = 3.0, 10.2, 1 H), 4.03 (t, J = 6.9, 2 H), 6.12 (t, J = 2, 2 H), 6.62 (d, J = 2, 2 H), 7.25 (d, J = 8.1, 2 H), 7.78 (d, J = 8.7, 2 H); ^{13}C NMR δ 21.47, 34.11, 45.13, 66.33, 73.55, 108.08, 120.40, 127.75, 129.85, 132.23, 145.05; IR (KBr, cm^{-1}) 3570 (sharp, m), 3106 (w), 2957 (w), 1355 (s), 1184 (s), 959 (s); MS (EI) m/z 310 (M + 1); HRMS calcd for $C_{15}H_{19}NSO_4$ 309.1035, found 309.1028.

(4-*N*-Pyrrolyl-2-hydroxybutyl)cobaloxime (22). $CoCl_2 \cdot 6H_2O$ (5.81 g, 24.4 mmol), dimethylglyoxime (5.65 g, 48.7 mmol), 50% NaOH (3.9 g, 48.8 mmol), and pyridine (2.0 mL, 24.7 mmol, distilled) were added to deoxygenated MeOH (84 mL), and the solution was deoxygenated for 7 more min. The reaction mixture was cooled in an ice bath, $NaBH_4$ (1.5 g, 40 mmol) was added in two aliquots, and the dark brown mixture was stirred for 20 min. 4-*N*-Pyrrolylbutane-1,2-diol 1-*p*-toluenesulfonate (4.37 g, 14.1 mmol) as a deoxygenated solution in MeOH was added via cannula. After 7 h at rt, the solution was dark orange−red. The crude reaction mixture was then filtered through a pad of silica gel, and the column was eluted with EtOAc until the eluent ran light yellow. The orange solution was concentrated in vacuo, then adsorbed onto silica, placed on a fritted glass funnel, and eluted with EtOAc; the orange solution was concentrated in vacuo to give 3.95 g of an orange powder (55% yield). Gravity chromatography (0−100% EtOAc/hexanes) on deactivated silica gel (5% pyridine/MeOH as described above) yielded an orange powder suitable for spectral analysis: ^{1}H NMR δ 1.03 (t, J = 9.6, 1 H), 1.73 (m, 2 H), 2.07, 2.08 (two s, 13 H), 2.54 (m, 1 H), 2.83−3.99 (two m, 2 H), 6.03 (s, 2 H), 6.58 (s, 2 H), 7.31 (t, J = 6.6, 2 H), 7.72 (t, J = 7.5, 1 H), 8.51 (d, J = 5.4, 2 H), 18.01 (br s); ^{13}C NMR δ 12.04, 12.09, 35.88 (br), 38.95, 45.96, 69.59, 107.35, 120.67, 125.23, 137.62, 149.69, 149.81, 150.20, 150.37; IR (KBr, cm^{-1}) 3470 (br, m), 2954 (w), 2926 (m), 1572 (s), 1454 (s), 1237 (s), 1097 (s); MS (FAB) m/z 507 (M + 1); HRMS calcd for $CoC_{21}H_{32}N_6O_5$ (M + 1) 507.1766, found 507.1749.

Cobaloxime 23. Cobaloxime **22** (0.84 g, 1.7 mmol) was dissolved in MeOH (~40 mL), and the solution was deoxygenated for 35 min. PPTS (0.509 g, 2 mmol) was added, and the reaction mixture was stirred for 20 h while protected from ambient light. The product precipitated out of solution as a bright yellow solid which was separated from the solution by centrifugation at 10 °C (in centrifuge tubes topped off with argon) followed by a MeOH rinse (MeOH deoxygenated with argon). The tubes containing the yellow solid were purged with N_2 overnight. The yellow−orange powder was then transferred, and the residual volatiles were removed in vacuo, providing 0.67 g of a yellow powder (83% yield): ^{1}H NMR δ 1.51 (m, 1 H), 1.75 (m, 1 H), 2.12 (s, 14 H), 2.40 (less than 1 H, imp), 2.95 (m, 1 H), 3.81 (m, 2 H), 5.71 (s, 1 H), 6.04 (s, 1 H), 6.40 (s, 1 H), 7.31 (t, J = 6.6, 2 H), 7.71 (t, J = 7.5, 1 H), 8.60 (d, J = 5.1, 2 H), 18.01 (br s); ^{13}C NMR (peak assignments are based on an APT NMR experiment) δ 12.02 (CH_3), 12.06 (CH_3), 32.48 (CH_2), 32.54 (CH_2), 38.55 (not detected in APT experiment),[14] 46.08 (CH_2), 102.89 (CH), 107.70 (CH), 117.52 (CH), 125.11 (CH), 130.85 (quaternary C), 137.40 (CH), 149.72 (quaternary C), 149.96 (quaternary C), 150.02 (CH); IR (KBr, cm^{-1}) 3440 (br, m), 2922 (w), 2875 (w), 2363 (w), 2336 (w), 1559 (s), 1449 (s), 1238 (s), 1090 (s); MS (FAB); 290 [Co(dmgH)$_2$]; HRMS calcd for $CoC_{21}H_{30}N_6O_4$ (M + 1) 489.1660, found 489.1647.

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Supporting Information Available: ^{1}H and ^{13}C NMR spectra of all compounds (43 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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(14) See Materials and Methods in Experimental Section.