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Substituent Effect of Chelated Cobalt. 3. Acidities of (2-Carboxyethyl)(ligand)cobaloximes[1,2]

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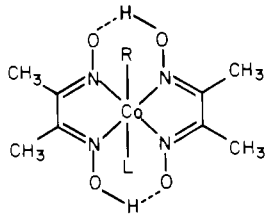
pK_a's for carboxyl proton dissociation from (carboxyethyl)(ligand)cobaloximes with 15 different axial ligands, including *S*-methyl sulfides, primary amines, substituted pyridines, and thiolate anions, have been determined. The observed pK_a values vary from 4.71 to 5.11 although the proton basicity of the axial ligands varies by about 16 orders of magnitude. These values have been correlated with those of ten 2-substituted propionic acids to provide values of σ_I, the inductive substituent parameter, for the cobaloxime chelated cobalt centers. The resulting values of $-\sigma_I$ are found to be directly proportional to the measured proton basicity of the trans axial ligands, although the values for the primary amine ligated cobaloximes fall on a different correlation than those for pyridine and thiolate anion ligated cobaloximes. These results are discussed in the light of recent studies on the saponification of cobaloxime-substituted methyl benzoates from which an inverse dependence of $-\sigma_I$ on axial ligand basicities for primary amine ligands was obtained.

Introduction

Organocobaloximes (**1**)[3] have been widely studied as models



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for organocobalamines. Because of the importance of the carbon–cobalt bond in vitamin B_{12} biochemistry we have been interested in studying the inductive and resonance substituent effects of chelated cobalt centers as a means both to establish an experimental basis for understanding the carbon–cobalt bond and to acquire predictive capability for the reactivities of functional groups on cobalt-bound organic ligands.

In recent reports[1,4] we have attempted to address the question of the electronic substituent effect of cobaloxime chelated cobalt centers on covalently bound organic groups by application of the Taft dual-substituent parameter equation[5] to the base-catalyzed hydrolysis kinetics of cobaloxime-substituted methyl benzoates (i.e., ((carbomethoxy)phenyl)cobaloximes). Although such an analysis seems generally to provide consistent and reasonable results, it is impossible to tell if this approach properly separates inductive and resonance effects without independent determinations of either the inductive (σ_I) or delocalization (σ_R) parameters obtained for the cobaloxime substituents. Furthermore, when using kinetic data for such correlations it is important to test the implicit assumption that the mechanism of the reaction investigated remains the same for the basis set compounds and the compounds containing the substituent to be evaluated. This is particularly true when the available basis set substituents differ markedly in nature and substituent effect from the substituents under investigation, as in the present case. The need to consider such complications is implied by our apparently anomalous observation[1] that inductive electron donation by the substituent $-Co(D_2H_2)L$ appears to decrease linearly with the proton basicity of the axial ligand for L = RNH_2, a result contrary to other observations[6] as well as reasonable chemical intuition. It was consequently desirable to study the inductive substituent effect of cobaloxime chelated cobalt centers in a system in which π interactions of the detecting group with the cobalt center are not possible and by use of an equilibrium parameter to obviate the complication of mechanistic considerations. To this end we now report our study of the acidities of (carboxyethyl)(ligand)cobaloximes and their relation to the acidities of other 2-substituted propionic acids.

In addition it has been previously pointed out that (carboxymethyl)cobalt complexes are extremely weak Brønsted acids,[4,7-9] an apparent consequence of the β effect[10] or $\sigma \rightarrow \pi$ conjugation[11] in organocobalt chemistry. The current data will also provide a basis for our forthcoming analysis of the β effect in (carboxymethyl)- and (1-carboxyethyl)cobaloximes.[12]

Experimental Section

Materials. Dimethylglyoxime, cobaltous acetate, sodium borohydride, sodium and potassium phosphates, methanol, buffer components, and inorganic salts and acids were obtained in the highest purity commercially available and used without further purification.

All axial ligands except *S*-methyl methyl mercaptoacetate and all substituted propionic acids except *S*-methyl-2-mercaptopropionic acid were purchased commercially and recrystallized or redistilled under argon before use.

Mercaptoacetic acid was methylated with dimethyl sulfate according to the procedure of Schmolka and Spoerri:[13] yield 51%; NMR (neat) δ_{Me_4Si} (external) 2.18 (S, 3 H), 3.27 (S, 1.94 H), 10.53 (S, 1.02 H). *S*-Methylmercaptoacetic acid was esterified with methanol by the procedure of Mooradian et al.:[14] yield 41%; bp 185 °C; NMR (neat) δ_{Me_4Si} (external) 2.03 (S, 3 H), 3.08 (s, 2.03 H), 3.56 (S, 3.05 H).

2-Mercaptopropionic acid was similarly methylated with dimethyl sulfate[13] to give *S*-methyl-2-mercaptopropionic acid: yield 38%; bp 129–131 °C (18 torr); NMR (neat) δ_{Me_4Si} (external) 2.30 (S, 3 H), 2.91 (S, 4.07 H); NMR (0.58 M NaOD/D_2O) δ_{Me_4Si} (external) 2.26

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(1) Part 2: Brown, K. L.; Awtrey, A. W. *J. Organomet. Chem.* **1980**, *195*, 113–122.
(2) Abbreviations: $RCo(D_2H_2)L$ = alkyl(ligand)bis(dimethylglyoximato)cobalt(III) = alkyl(ligand)cobaloxime.
(3) Cobaloximes are bis(dimethylglyoximato)cobalt complexes. For a description of their chemistry and structure see: Schrauzer, G. N. *Acc. Chem. Res.* **1968**, *1*, 97–103.
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Table I. Equilibrium Constants for Axial Ligation and Deprotonation Equilibria of (Carboxyethyl)cobaloximes with Sulfur-Containing Ligands[a]

L	pK_L[b]	$K_f^{A^-}$ data: pH	$K_f^{A^-}$, M^{-1}	K_f^{AH} data: pH	K_f^{AH}, M^{-1}	pK_a^L	method[c]	σ_I[d]
S-methyl-2-mercaptoethanol		7.50 ± 0.02	44.6 ± 2.6	2.85 ± 0.01	29.5 ± 0.8	4.71 ± 0.03	I	−0.045
S-methyl methyl mercaptoacetate		7.55 ± 0.05	6.31 ± 0.36	2.92 ± 0.03	4.48 ± 0.33	4.74 ± 0.05	I	−0.065
methyl mercaptoacetate	7.83 ± 0.01[e]		(1.06 ± 0.02) × 10^5		(1.55 ± 0.03) × 10^5	5.06 ± 0.02	III	−0.271
methyl mercaptopropionate	9.27 ± 0.01[f]		(2.31 ± 0.08) × 10^5		(3.62 ± 0.19) × 10^5	5.09 ± 0.04	III	−0.291
2-mercaptoethanol	9.51 ± 0.01[e]		(2.59 ± 0.06) × 10^5		(4.27 ± 0.11) × 10^5	5.11 ± 0.03	III	−0.304

[a] 25.0 ± 0.1 °C; ionic strength 1.0 M. [b] pK_a of the conjugate acid of the ligand. [c] See text. [d] Calculated from eq 18 and the values of pK_a^L. [e] Reference 21. [f] This work.

Table II. Equilibrium Constants for Axial Ligation and Deprotonation of (Carboxyethyl)cobaloximes with 4-Substituted Pyridine Ligands[a]

L	pK_L[b]	pH	α_L[c]	K_f^{app}, M^{-1}	K_f^{AH}, M^{-1}	$K_f^{A^-}$, M^{-1}	pK_a^L	method[d]	σ_I[e]
4-cyano-pyridine	2.24 ± 0.02[f]	7.50 ± 0.01	1.000	161 ± 4		161 ± 4	4.84 ± 0.03	I	−0.132
		2.87 ± 0.03	0.812 ± 0.013	118 ± 2	145 ± 4				
4-carboxamido-pyridine	3.77 ± 0.01[f]	7.50 ± 0.01	1.000	420 ± 4		420 ± 4	4.88 ± 0.03	I	−0.155
		2.85 ± 0.02	0.107 ± 0.005	41.7 ± 0.9	406 ± 10[g]				
		2.52 ± 0.03	0.0532 ± 0.0003	22.4 ± 1.4					
pyridine	5.56 ± 0.01[h]					1200 ± 70[h]	4.99 ± 0.04	I	−0.226
		2.82 ± 0.01	(1.80 ± 0.06) × 10^{-3}	2.48 ± 0.08	1510 ± 120[g]				
		2.79 ± 0.02[h]	(1.70 ± 0.09) × 10^{-3}[h]	2.80 ± 0.23[h]					
4-methyl-pyridine	6.36 ± 0.02				2750 ± 90	1990 ± 80	5.03 ± 0.03	III	−0.252
4-amino-pyridine	9.40 ± 0.02[f]	8.44 ± 0.01	0.0988 ± 0.0021	578 ± 15	9530 ± 800[i]	5880 ± 200[g]	5.10 ± 0.04	II[j]	−0.297
		8.27 ± 0.01	0.0690 ± 0.0033	407 ± 13					

[a] 25.0 ± 0.1 °C; ionic strength 1.0 M. [b] pK_a of the conjugate acid of the ligand. [c] Calculated from eq 10 and pK_L. [d] See text. [e] Calculated from eq 18 and the values of pK_a^L. [f] Reference 22. [g] Average of two determinations. [h] Reference 4. [i] Calculated from eq 11. [j] Stopped flow.

(S, 3 H), 2.48–2.97 (m, 4.02 H).

(Carboxyethyl)(aquo)cobaloxime was prepared by reductive alkylation of diaquocobaloxime(II) (prepared in situ) with 2-bromopropionic acid by the method of Crumbliss and Gaus[15] as modified by Brown.[16]

Methods. All work with organocobaloximes was performed in dim light, and solutions were covered with aluminum foil. Glass-distilled, deionized water was used throughout, and ionic strength was maintained at 1.0 M with KCl. EDTA (10^{-4} M) was employed to retard air oxidation of thiolate anions.

NMR measurements were made on a Varian T-60 NMR spectrometer. UV–visible spectra were recorded on a Cary 14 or a Cary 219 recording spectrophotometer. Single-wavelength absorbance measurements were made on a Cary 219 or a Gilford Model 250 spectrophotometer. pH measurements were made on a Radiometer PHM 64 pH meter with samples and standards incubated at 25.0 ● 0.1 °C.

Glycine ethyl ester, methyl mercaptopropionate, and all substituted propionic acids were titrated potentiometrically at 25.0 ± 0.1 °C at 0.01 or 0.02 M. pK_a values were determined from least-squares fits of the data to eq 1,[17] were [AH] and [A^-] are the "stoichiometric"

$$pH = pK_a + \log \{([A^-] + [H^+])/([AH] - [H^+])\} \quad (1)$$

concentrations of the weak acid and its conjugate base at each point in the titration.

Equilibrium constants, K_f^{app}, for axial binding to (carboxyethyl)-cobaloxime and/or its conjugate base (eq 2 and 3) were determined

$$RCo(D_2H_2)OH_2 + L \rightleftharpoons^{K_f^{app}} RCo(D_2H_2)L \quad (2)$$

$$K_f^{app} = [RCo(D_2H_2)L]/[RCo(D_2H_2)OH_2][L] \quad (3)$$

spectrophotometrically at 450–460 nm for all ligands except RS^- (for which λ = 340 nm was utilized[18]) by the method previously described.[19,20]

Measurements of ligand dissociation rate constants were made spectrophotometrically after dilution of solutions of preformed organo(ligand)cobaloximes with the final concentrations and pHs adjusted to ensure that the ligand dissociation reaction proceeded >90% to completion.[4,19] Least-squares fits of semilogarithmic plots of the absorbance vs. time data thus obtained provided values for the apparent ligand dissociation rate constants k_{off}^{obsd}.

Results. Determinations of the acid dissociation constants of $HOOCCH_2CH_2Co(D_2H_2)L$, pK_a^L (eq 4), were made in conjunction

$$K_a^L = [^-OOCCH_2CH_2Co(D_2H_2)L][H^+]/[HOOCCH_2CH_2Co(D_2H_2)L] \quad (4)$$

with Scheme I and the previously determined value of K_a^{HOH}[4] (eq 5, $K_a^{HOH} = (1.29 \pm 0.06) \times 10^{-5}$). Because of the variety of axial

$$K_a^{HOH} = [^-OOCCH_2CH_2Co(D_2H_2)OH_2][H^+]/[HOOCCH_2CH_2Co(D_2H_2)OH_2] \quad (5)$$

ligands used, with proton basicities varying by about 16 orders of magnitude, several different means were used to obtain the values of pK_a^L.

Method I involved measurement of $K_f^{A^-}$ (eq 6) and K_f^{AH} (eq 7) at pH >6.9 and pH <2.9, respectively, where the (carboxyalkyl)co-

$$K_f^{A^-} = [^-OOCCH_2CH_2Co(D_2H_2)L]/[^-OOCCH_2CH_2Co(D_2H_2)OH_2][L] \quad (6)$$

$$K_f^{AH} = [HOOCCH_2CH_2Co(D_2H_2)L]/[HOOCCH_2CH_2Co(D_2H_2)OH_2][L] \quad (7)$$

baloxime is >99% as its conjugate base or free acid species, respectively.

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Table III. Equilibrium Constants for Axial Ligation and Deprotonation of (Carboxyethyl)cobaloximes with Primary Amines[a]

L	pK_L[b]	pH	α_L[c]	K_f^{app}, M^{-1}	$K_f^{A^-}$, M^{-1}	K_f^{AH}, M^{-1}	pK_a^L	method[d]	σ_I[e]
2,2,2-trifluoroethylamine	5.68 ± 0.01[f]				30.4 ± 0.8	23.4 ± 1.3	4.78 ± 0.03	III	−0.090
glycine ethyl ester	7.86 ± 0.01[g]	7.08 ± 0.01	0.142 ± 0.004	57.4 ± 1.4	402 ± 15	322 ± 19[h]	4.79 ± 0.04	II	−0.097
2,2-dimethoxyethylamine	8.86 ± 0.01[f]	8.86 ± 0.01	0.500 ± 0.008	337 ± 7	675 ± 18	585 ± 30[h]	4.83 ± 0.02	II	−0.123
2-methoxyethylamine	9.68 ± 0.02[f]	8.90 ± 0.02	0.143 ± 0.008	174 ± 2	1230 ± 50	1100 ± 80[h]	4.85 ± 0.01	II	−0.136
n-propylamine	10.80 ± 0.02[f]	9.75 ± 0.01	0.0818 ± 0.0039	252 ± 4	3080 ± 160	2960 ± 250[h]	4.87 ± 0.02	II	−0.149

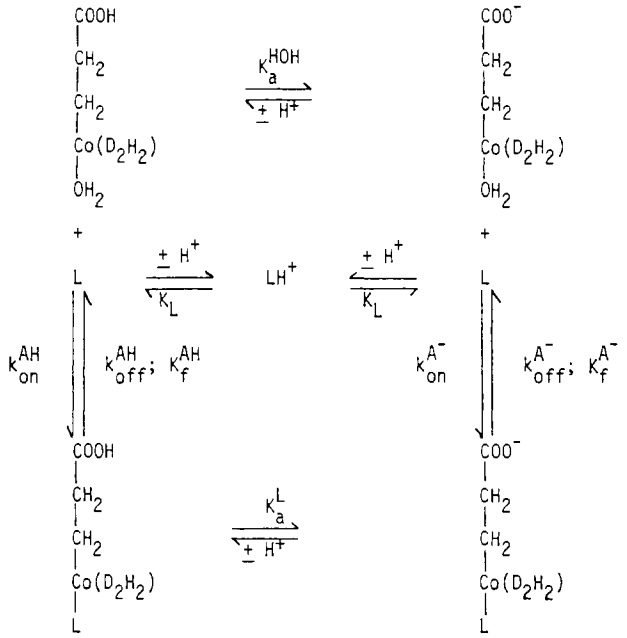
[a] 25.0 ± 0.1 °C; ionic strength 1.0 M. [b] pK_a of the conjugate acid of the ligand. [c] Calculated from eq 10 and pK_L. [d] See text. [e] Calculated from eq 18 and the values of pK_a^L. [f] Reference 22. [g] This work. [h] Calculated from eq 11.

Table IV. Forward and Reverse Rate Constants for Association of Primary Amines with (Carboxyethyl)(aquo)cobaloxime and Its Conjugate Base[a]

L	k_{off}^{AH}, s^{-1}	$k_{off}^{A^-}$, s^{-1}	k_{on}^{AH},[b] M^{-1} s^{-1}	$k_{on}^{A^-}$,[c] M^{-1} s^{-1}
glycine ethyl ester	(2.83 ± 0.03) × 10^{-2}	(6.18 ± 0.16) × 10^{-2}	9.12 ± 0.55	24.8 ± 1.1
2,2-dimethoxyethylamine	(1.25 ± 0.04) × 10^{-2}	(3.26 ± 0.10) × 10^{-2}	7.31 ± 0.44	22.0 ± 0.6
2-methoxyethylamine	(6.63 ± 0.32) × 10^{-3}	(1.72 ± 0.01) × 10^{-2}	8.60 ± 0.71	21.1 ± 1.0
n-propylamine	(4.06 ± 0.21) × 10^{-3}	(1.13 ± 0.03) × 10^{-2}	12.0 ± 1.0	34.9 ± 1.8

[a] 25.0 ± 0.1 °C; ionic strength 1.0 M. [b] Calculated from eq 13 and the values of K_f^{AH} in Table III. [c] Calculated from eq 14 and the values of $K_f^{A^-}$ in Table III.

Scheme I



This method was satisfactory for the weakly basic ligands *S*-methyl-2-mercaptoethanol, *S*-methyl methyl mercaptoacetate, 4-cyanopyridine, 4-carboxamidopyridine, and pyridine. When necessary, the observed ligand binding constants, K_f^{app}, were corrected for ligand protonation by eq 8 (pH <2.9) or eq 9 (pH >6.9),[19] where α_L is the

$$K_f^{AH} = K_f^{app}/\alpha_L \quad (8)$$

$$K_f^{A^-} = K_f^{app}/\alpha_L \quad (9)$$

fraction of ligand as the unprotonated species (Scheme I), as calculated from the pK_a of the conjugate acid of the ligand and eq 10. Values

$$\alpha_L = K_L/(K_L + [H^+]) \quad (10)$$

of K_a^L (Scheme I) were then calculated from eq 11 based on the cyclic

$$K_a^L = K_a^{HOH}K_f^{A^-}/K_f^{AH} \quad (11)$$

nature of the equilibria in Scheme I. Data obtained in this manner are listed in Tables I and II.

For ligands of moderate to strong proton basicity but with relatively slow rates of dissociation from the cobalt center, values of pK_a^L were determined by method II, using the pH dependence of the ligand dissociation rate. Ligands in this class included 4-aminopyridine, glycine ethyl ester, 2,2-dimethoxyethylamine, 2-methoxyethylamine, and *n*-propylamine. From the law of mass action and Scheme I, one can readily show that the pH dependence of the observed first-order rate constant for ligand dissociation is given by eq 12. Exemplary

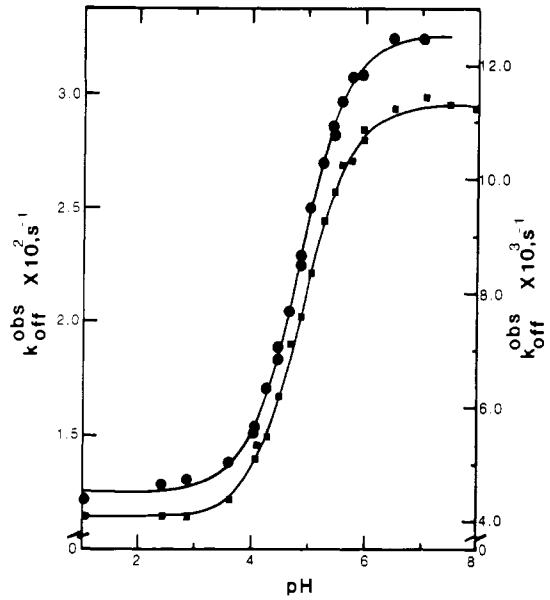


Figure 1. Plots of k_{off}^{obsd} vs. pH for (carboxyethyl)(ligand)cobaloximes (25.0 ± 0.1 °C; ionic strength 1.0 M). The solid lines were calculated from eq 12 and the least-squares values of the equilibrium and rate constants: (●) L = 2,2-dimethoxyethylamine, left ordinate, pK_a^L = 4.83 ± 0.02, k_{off}^{AH} = 0.0125 ± 0.0004 s^{-1}, $k_{off}^{A^-}$ = 0.0326 ± 0.0010 s^{-1}; (■) L = *n*-propylamine, right ordinate, pK_a^L = 4.87 ± 0.02, k_{off}^{AH} = 0.00406 ± 0.00021 s^{-1}, $k_{off}^{A^-}$ = 0.0113 ± 0.0003 s^{-1}.

data of this kind are shown in Figure 1. Values for the rate constants and K_a^L were obtained by a least-squares fit of the data to eq 12. In such cases, values of $K_f^{A^-}$ were determined spectrophotometrically as described above and the values of K_f^{AH} were calculated from eq 11. Equilibrium constants obtained in this manner are listed in Tables II and III. Values of k_{off} determined in this manner are listed in Table IV, along with those for ligand association which were calculated from eq 13 and 14.

$$k_{off}^{obsd} = (k_{off}^{AH}[H^+] + k_{off}^{A^-}K_a^L)/(K_a^L + [H^+]) \quad (12)$$

$$k_{on}^{AH} = k_{off}^{AH}K_f^{AH} \quad (13)$$

$$k_{on}^{A^-} = k_{off}^{A^-}K_f^{A^-} \quad (14)$$

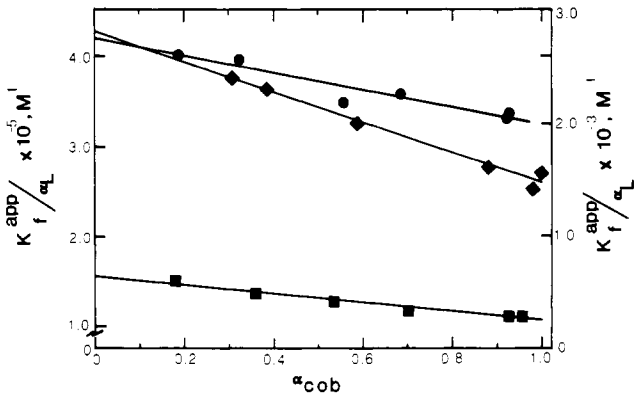


Figure 2. Plots of ligand binding constants, corrected for ligand ionization, K_f^{app}/α_L, vs. α_{cob}, the fraction of (carboxyethyl)(aquo)-cobaloxime as the anionic conjugate base (25.0 ± 0.1 °C; ionic strength 1.0 M). The solid lines are least-squares fits of the data to eq 17: (●) L = 4-methylpyridine, right ordinate, intercept = 2750 ± 80 M^{-1}, slope = −755 ± 120 M^{-1}; (■) L = methyl mercaptoacetate, left ordinate, intercept = (1.55 ± 0.03) × 10^5 M^{-1}, slope = (−4.85 ± 0.47) × 10^4 M^{-1}; (♦) L = 2-mercaptoethanol, left ordinate, intercept = ± 0.11) × 10^5 M^{-1}, slope = (−1.68 ± 0.14) × 10^5 M^{-1}.

Table V. pK_a's of Substituted Propionic Acids, XCH_2CH_2COOH[a]

X	pK_a[b]	σ_I[c]	X	pK_a[b]	σ_I[c]
$(CH_3)_3Si$	4.74	−0.10	I	3.91	0.39
CH_3	4.68	−0.04	Br	3.89	0.44
H	4.74	0.00	Cl	3.96	0.46
C_6H_5	4.57	0.10	NH_3^+	3.75	0.60[d]
CH_3S	4.25	0.23	NO_2	3.69	0.65

[a] 25.0 ± 0.1 °C; ionic strength 1.0 M. [b] All standard deviations <0.01. [c] Reference 5, except as noted. [d] Reference 23.

Values of pK_a^L for the remaining ligands (4-methylpyridine, 2,2,2-trifluoroethylamine, 2-mercaptoethanol, methyl mercaptoacetate, and methyl mercaptopropionate) were determined by method III, the pH dependence of the apparent ligand binding constant, K_f^{app}. From Scheme I and eq 3–7, one can show that K_f^{app} is given by eq 15 where

$$K_f^{app} = K_f^{AH}(1 - \alpha_{cob})\alpha_L + K_f^{A^-}\alpha_{cob}\alpha_L \quad (15)$$

α_{cob} is the fraction of (carboxyethyl)(aquo)cobaloxime as the anionic conjugate base species (eq 16) and α_L is defined in eq 10. Typical

$$\alpha_{cob} = K_a^{HOH}/(K_a^{HOH} + [H^+]) \quad (16)$$

data, plotted according to the rearranged eq 17, are shown in Figure

$$K_f^{app}/\alpha_L = K_f^{AH} + (K_f^{A^-} - K_f^{AH})\alpha_{cob} \quad (17)$$

2 for representative ligands. Equilibrium constants obtained in this manner are listed in Tables I–III.

Finally, Table V shows the values of the pK_a's of ten substituted propionic acids (determined potentiometrically) along with the values of the polar substituent constant, σ_I, for the substituents. All of these data gave excellent linear plots when plotted according to eq 1, and all slopes were within a few percent of 1.000.

Discussion

Kinetics and Equilibria of Axial Ligand Exchange. The binding constants for the various ligands to both $HOOCCH_2CH_2Co(D_2H_2)OH_2$ and its conjugate base show excellent linear free energy relationships with pK_L within each isosteric series of ligands (Figure 3), as was the case for $CH_3Co(D_2H_2)OH$.[22] Furthermore, the same kind of selectivity and

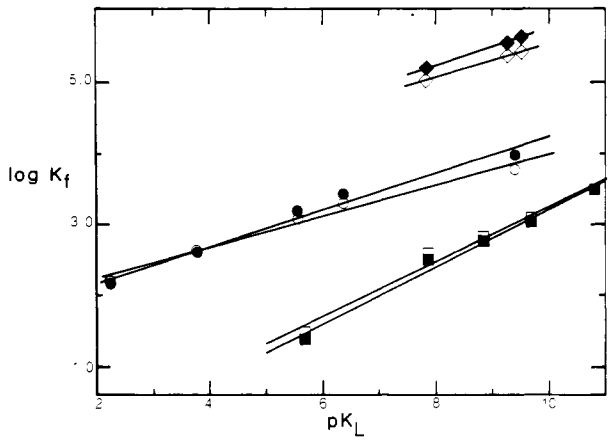


Figure 3. Plots of log K_f^{AH} (solid symbols) and log $K_f^{A^-}$ (open symbols) vs. pK_L for $HOOCCH_2CH_2Co(D_2H_2)OH_2$ and $^-OOCCH_2CH_2Co(D_2H_2)OH_2$, respectively. The solid lines are least-squares fits: (●, ○) L = X-py, K_f^{AH} intercept = 1.663 ± 0.133 and slope = 0.258 ± 0.022, $K_f^{A^-}$ intercept = 1.794 ± 0.110 and slope = 0.220 ± 0.018; (■, □) L = RNH_2, K_f^{AH} intercept = −0.824 ± 0.264 and slope = 0.403 ± 0.030, $K_f^{A^-}$ intercept = −0.594 ± 0.287 and slope = 0.384 ± 0.033; (♦, ◇) L = RS^-, K_f^{AH} intercept = 3.154 ± 0.042 and slope = 0.260 ± 0.005, $K_f^{A^-}$ intercept = 3.205 ± 0.034 and slope = 0.233 ± 0.004.

sensitivity for ligands is found as for $CH_3Co(D_2H_2)OH_2$, the absolute affinities increasing rather markedly in the order RNH_2 < X-py < RS^- but the slopes of the correlations of log K_f^{AH} and log $K_f^{A^-}$ decreasing in the order RNH_2 < X-py ~ RS^-. As discussed previously[22] both of these trends indicate substantial metal-to-ligand π donation, a phenomenon now well established for organocobaloximes.[18,22,26,27]

Table VI contains a collection of slopes and intercepts of correlations of ligand affinities and ligand association and dissociation rate constants with pK_L for several organocobaloximes. The most extensive data are for primary amines for which log K_f vs. pK_L correlations show little or no change in slope over a wide range of trans organic ligands (σ^*[24] varying from 0 to +0.90). The average value of this slope (N = 5) is 0.394 ± 0.016 so that all but one of the values are contained within ±1.0 standard deviation of the mean. Hence, for these representative non-π-accepting ligands the sensitivity of ligand affinity to proton basicity of the ligand is apparently independent of the electron inductive effect of the organic ligand. This is not the case for the π-accepting ligands X-py and RS^- for which, within the limits of the less extensive data, the slopes of the correlations of log K_f appear to increase monotonically with increasing electron-withdrawing ability of the organic ligand. Interestingly, the intercepts of these correlations monotonically decrease with increasing electron withdrawal by the organic group, suggesting that an increase in sensitivity of K_f to ligand proton basicity is accompanied by a decrease in absolute affinity.

The ligand association and dissociation rate constants for primary amines also correlate reasonably well with pK_L as shown in Figure 4. Both k_{on} and k_{off} for primary amine ligands can be seen to increase by factors of 2–3 upon proton dissociation of (carboxyethyl)cobaloxime. This is consistent with our previous demonstration[19] of inverse dependencies of both log k_{off} and log k_{on} for 2,2-dimethoxyethylamine on electron-withdrawing ability of the organic ligand and the fact that the σ^* value for the carboxyethyl ligand is substantially decreased upon deprotonation. Again, these observations confirm the dissociative nature of the ligand substitution

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Table VI. Slopes and Intercepts of log K_f, log k_{on}, and log k_{off} vs. pK_L Correlations for Various Alkylcobaloximes, $RCo(D_2H_2)OH_2$, and Various Ligands[a]

R	σ*	parameter correlated	L	slope	intercept	N[b]	ref
CH_3	0.00[c]	K_f	RNH_2	0.38 ± 0.01	−0.43 ± 0.04	5	22
CH_3	0.00[c]	K_f	X-py	0.21 ± 0.01	2.09 ± 0.07	5	22
CH_3	0.00[c]	K_f	RS^-	0.18 ± 0.01	3.66 ± 0.06	3	22
$^-OOCCH_2CH_2$	0.02[d]	K_f	RNH_2	0.38 ± 0.03	−0.59 ± 0.29	5	this work
$^-OOCCH_2CH_2$	0.02[d]	K_f	X-py	0.22 ± 0.02	1.79 ± 0.11	5	this work
$^-OOCCH_2CH_2$	0.02[d]	K_f	RS^-	0.23 ± 0.01	3.21 ± 0.03	3	this work
$HOOCCH_2CH_2$	0.38[d]	K_f	RNH_2	0.40 ± 0.03	−0.82 ± 0.26	5	this work
$HOOCCH_2CH_2$	0.38[d]	K_f	X-py	0.26 ± 0.02	1.66 ± 0.13	5	this work
$HOOCCH_2CH_2$	0.38[d]	K_f	RS^-	0.26 ± 0.01	3.15 ± 0.04	3	this work
m-$CH_3OOCC_6H_4$	0.85[e]	K_f	RNH_2	0.42 ± 0.05	−0.66 ± 0.41	4	1
p-$CH_3OOCC_6H_4$	0.90[e]	K_f	RNH_2	0.39 ± 0.05	−0.56 ± 0.46	4	1
CH_3	0.00[c]	k_{on}	RNH_2	0.04 ± 0.02	0.41 ± 0.14	5	22
CH_3	0.00[c]	k_{off}	RNH_2	−0.33 ± 0.02	0.75 ± 0.19	5	22
$^-OOCCH_2CH_2$	0.02[d]	k_{on}	RNH_2	0.05 ± 0.05	0.96 ± 0.42	4	this work
$^-OOCCH_2CH_2$	0.02[d]	k_{off}	RNH_2	−0.26 ± 0.03	0.78 ± 0.24	4	this work
$HOOCCH_2CH_2$	0.38[d]	k_{on}	RNH_2	0.05 ± 0.04	0.54 ± 0.37	4	this work
$HOOCCH_2CH_2$	0.38[d]	k_{off}	RNH_2	−0.29 ± 0.03	0.68 ± 0.28	4	this work

[a] All data at 25.0 ± 0.1 °C; ionic strength 1.0 M. [b] Number of points in the correlation. [c] Reference 24. [d] Calculated from ref 23. [e] Reference 25.

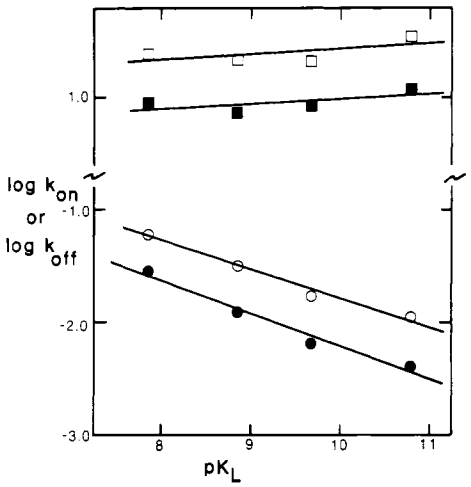

Figure 4. Logarithmic plots of the rate constants for primary amine association and dissociation with (carboxyethyl)cobaloxime and its conjugate base vs. pK_L. The solid lines are least-squares fits: (●) log k_{off}^{AH} intercept = 0.684 ± 0.284 and slope = −0.289 ± 0.030; (○) log $k_{off}^{A^-}$ intercept = 0.783 ± 0.244 and slope = −0.256 ± 0.026; (■) log k_{on}^{AH} intercept = 0.539 ± 0.369 and slope = 0.045 ± 0.039; (□) log $k_{on}^{A^-}$ intercept = 0.962 ± 0.426 and slope = 0.047 ± 0.045.

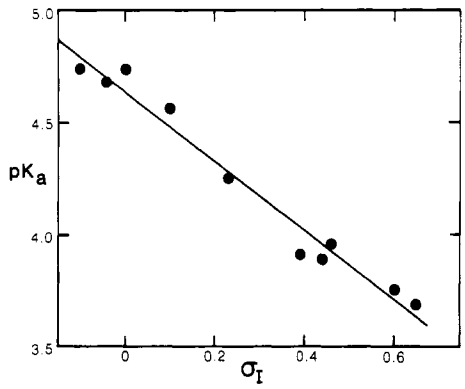

Figure 5. Plot of the pK_a's of substituted propionic acids vs. σ_I for the substituent (Table V). The solid line is a least-squares fit with slope = −1.547 ± 0.095, intercept = 4.640 ± 0.036, and f = 0.105.

mechanism.[19,26,28-31] And again, a comparison of the slopes of the log k_{on} and k_{off} correlations with those for $CH_3Co(D_2H_2)OH_2$ (Table VI) shows little or no dependence of the slope on the inductive effect of the organic ligand.

Inductive Effect of Cobaloxime Cobalt Centers. Values of the proton dissociation constant of (carboxyethyl)(ligand)cobaloximes, pK_a^L, are given in Tables I–III. These values can be seen to vary over a fairly narrow range of about 2.5-fold in acidity, despite a large variation of proton basicity of the ligands. That this is a consequence of the insulation of the carboxyl group from the cobalt center by two methylene groups rather than an inability of the cobalt atom to transmit the electronic effect of the trans axial ligand is adequately demonstrated by the work of Fox et al.,[16] who showed that fully two-thirds of the electronic effect of substituted pyridines could be transmitted by the cobalt atom to the trans organic ligand in methylcobaloximes.

So that the electronic effect of the cobaloxime group could be expressed on the σ_I scale, the values for the pK_a's of ten substituted propionic acids (Table V) have been fit to eq 18

$$pK_a = \rho_I\sigma_I + pK_a^\circ \qquad (18)$$

to provide the values ρ_I = 1.547 ± 0.095 and pK_a° = 4.640 ± 0.036. The slope of this very good correlation (N = 10, f = 0.11[5]) is in excellent agreement with that obtained from literature values for 2-substituted propionic acids[32] (N = 11, ρ_I = −1.566 ± 0.109, f = 0.10). With use of these values and eq 18, σ_I values for the cobaloxime chelated cobalt centers have been calculated and are listed in Tables I–III. These values can be seen to range from −0.045 for L = *S*-methyl-2-mercaptoethanol to −0.304 for L = 2-mercaptoethanol (corresponding to a range of σ* = −0.28 to −1.89[23]) making the cobaloxime chelated cobalt centers by far the most electron-donating substituents so far quantitated.

Figure 6 shows a plot of $-\sigma_I$ for $Co(D_2H_2)L$ vs. the pK_a of the conjugate acid of the axial ligand, L, from which it can be seen that excellent correlations can be obtained. Interestingly, the purely σ-donating RNH_2 ligands correlate separately from the π-accepting RS^- and X-py ligands, but the

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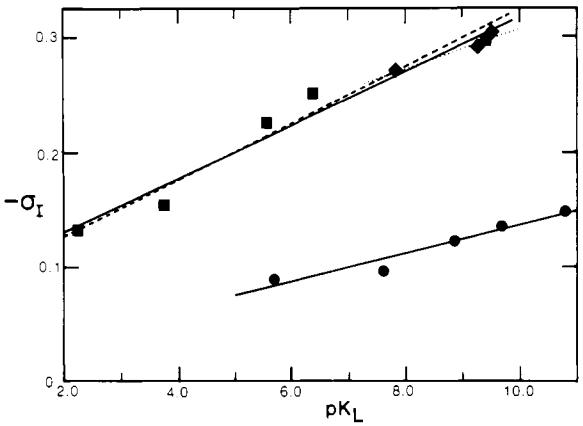

Figure 6. Plots of $-\sigma_I$ for the chelated cobalt centers, $Co(D_2H_2)L$, vs. the pK_a of the conjugate acid of the ligand, pK_L. The solid, dashed, and dotted lines are least-squares fits: (●) L = RNH_2, lower solid line, slope = 0.0123 ± 0.0023, intercept = 0.0135 ± 0.0200, f = 0.057; (■) L = X-py, dashed line, slope = 0.0246 ± 0.0031, intercept = 0.0782 ± 0.0183, f = 0.058; (♦) L = RS^-, dotted line, intercept = 0.132 ± 0.043, slope = 0.0176 ± 0.0049, f = 0.012. The upper solid line is a correlation including L = RS^- and X-py, intercept = 0.0828 ± 0.0127, slope = 0.0235 ± 0.0018, and f = 0.045.

latter afford cobaloximes which are more electron donating than the former. This is surprising since one might expect that significant metal-to-ligand π donation would decrease the ability of the cobalt atom to release electron density to the organic ligand. It is also surprising to note that although the data for the anionic RS^- and neutral X-py ligands may be independently correlated (dashed and dotted lines in Figure 6; slopes, intercepts, and f values given in the figure legend), they may be treated as a single data set to give an excellent correlation (upper solid line, Figure 6; slope = 0.0235 ± 0.00176, intercept 0.0828 ± 0.0127, f = 0.045). This could possibly be due to fortuitous compensation of the charge difference for the increased π-accepting ability of the RS^- ligands.

The *S*-methyl sulfides, *S*-methyl-2-mercaptoethanol and *S*-methyl methyl mercaptoacetate, represent an interesting contrast to the other ligand series. They are extremely weak proton bases[33] and presumably weak σ donors to organocobaloxime cobalt centers, being very weakly bound (Table I) although stable adducts to organocobaloximes are known.[28,34,35] Presumably the major bonding is via cobalt-to-sulfur π donation. In contrast to the RS^- and X-py π acceptors (which are also excellent σ donors), *S*-methyl sulfide–cobaloxime adducts have the lowest values of $-\sigma_I$ (Table I). However, if one assumes a pK_a of about −5.4 for these ligands,[33] the σ_I values for the $Co(D_2H_2)S(CH_3)R$ centers are in excellent agreement with both the upper and lower correlations (solid lines) in Figure 6 (σ_I = −0.053 from the RNH_2 correlation, σ_I = −0.044 from the combined RS^- and X-py correlation; observed values −0.045 and −0.065).

The positive slope for the correlation of $-\sigma_I$ for the $Co(D_2H_2)H_2NR$ centers with the pK_a of RNH_3^+ is in direct contradiction to results previously obtained for the same ligands by application of the Taft dual-substituent parameter equation to the rates of saponification of *p*- and *m*-$CH_3OOCC_6H_4Co(D_2H_2)H_2NR$.[1] The source of the conflict must lie with the interpretation of the previous results since it is difficult to see how the current analysis could go astray. As pointed out in the Introduction, the use of kinetic data for determination of substituent constants mandates the implicit assumption that both the mechanism and the rate-determining step of the reaction investigated remain the same for the basis set compounds and the compounds whose substituents are to be evaluated. In the current case of hydroxide ion catalyzed methyl benzoate hydrolysis, either problem could arise. With the assumption that saponification of methyl benzoates occurs via a two-step mechanism, either attack of hydroxide ion to form a tetrahedral addition intermediate (a step which must be aided by electron-withdrawing substituents) or expulsion of methoxide ion from the intermediate (a step which must be aided by electron-donating substituents) could be rate determining.[36] Unfortunately, the observation of positive ρ values for the basis set compounds[4] does not allow this distinction to be made. If, but only if, expulsion of methoxide ion is rate-determining for the basis set compounds, then the extremely electron-donating cobaloxime substituents could sufficiently speed methoxide expulsion and retard hydroxide ion attack to cause a change in rate-determining step. However, since a two-step mechanism with rate-determining hydroxide ion attack should also be characterized by positive ρ values, it is unlikely that the observed inverse dependence of $-\sigma_I$ on pK_L could be obtained. The possibility of a change of mechanism, of course, remains. The cobaloxime-substituted methyl benzoates could presumably undergo saponification by concerted displacement on the sp^2 carbonyl carbon. Unfortunately, it is not possible to predict the expected sign of the ρ values for such a mechanism which has often been proposed but a mechanism for which no direct evidence has been obtained.[36]

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Registry No. $HOOCCH_2CH_2Co(D_2H_2)$(*S*-methyl-2-mercaptoethanol), 76448-23-2; $HOOCCH_2CH_2Co(D_2H_2)$(*S*-methyl methyl mercaptoacetate), 76448-22-1; $HOOCCH_2CH_2Co(D_2H_2)$(methyl mercaptoacetate), 76448-21-0; $HOOCCH_2CH_2Co(D_2H_2)$(methyl mercaptopropionate), 76448-20-9; $HOOCCH_2CH_2Co(D_2H_2)$(2-mercaptoethanol), 76448-19-6; $HOOCCH_2CH_2Co(D_2H_2)$(4-cyanopyridine), 76448-18-5; $HOOCCH_2CH_2Co(D_2H_2)$(4-carboxamidopyridine), 76448-17-4; $HOOCCH_2CH_2Co(D_2H_2)$(pyridine), 14783-99-4; $HOOCCH_2CH_2Co(D_2H_2)$(4-methylpyridine), 76448-16-3; $HOOCCH_2CH_2Co(D_2H_2)$(4-aminopyridine), 76448-15-2; $HOOCCH_2CH_2Co(D_2H_2)$(glycine ethyl ester), 76448-14-1; $HOOCCH_2CH_2Co(D_2H_2)$(2,2,2-trifluoroethylamine), 76448-13-0; $HOOCCH_2CH_2Co(D_2H_2)$(2,2-dimethoxyethylamine), 76448-12-9; $HOOCCH_2CH_2Co(D_2H_2)$(2-methoxyethylamine), 76448-11-8; $HOOCCH_2CH_2Co(D_2H_2)$(*n*-propylamine), 76448-10-7; $HOOCCH_2CH_2Co(D_2H_2)$(aquo), 76448-09-4; $(CH_3)_3SiCH_2CH_2COOH$, 5683-30-7; $CH_3CH_2CH_2COOH$, 107-92-6; CH_3CH_2COOH, 79-09-4; $C_6H_5CH_2CH_2COOH$, 501-52-0; $CH_3SCH_2CH_2COOH$, 646-01-5; ICH_2CH_2COOH, 141-76-4; $BrCH_2CH_2COOH$, 590-92-1; $ClCH_2CH_2COOH$, 107-94-8; $H_3N^+CH_2CH_2COOH$, 21029-88-9; $NO_2CH_2CH_2COOH$, 504-88-1; *S*-methyl methyl mercaptoacetate, 16630-66-3; *S*-methylmercaptoacetic acid, 2365-48-2; *S*-methyl-2-mercaptopropionic acid, 58809-73-7; glycine ethyl ester, 459-73-4; 2,2-dimethoxyethylamine, 22483-09-6; 2-methoxyethylamine, 109-85-3; *n*-propylamine, 107-10-8; methyl mercaptopropionate, 53907-46-3.

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