Use of Intraligand CH Coupling Constants to Assess Binding in Organometallic Compounds. Insight into Electronic and Steric Properties of Monodentate P-Donor Ligands

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In a series of methylcobaloximes ($LCo(DH)_2CH_3$, where DH = monoanion of dimethylglyoxime), the influence of P-donor ligands (L) on $^1J_{CH}$ values of the $Co-CH_3$ moiety correlated well with the pK_a of L except when L was bulky (Cy_3P and *i*-Pr_3P). In contrast, no single steric parameter of those known for the trivalent P donors examined could be used to describe the variance of $^1J_{CH}$. The results indicate that the dominant property of L influencing this $^1J_{CH}$ is electron donation. Although poor, the best correlation with a steric parameter was found with calculated cone angles (CCA) determined by experimental methods on methanol-coordinated cobaloximes. Since the single parameter fits with pK_a indicated a steric effect, multiparameter regressions were performed using various combinations of electronic and steric terms. Terms reflecting only σ-donor ability (e.g., pK_a) gave better correlations than terms reflecting combinations of σ-donor and π-acceptor properties (e.g., $\Sigma\chi$). CCA values also resulted in better multiparameter fits of the data than other reported steric terms. Using a multiparameter approach also allowed for the simultaneous fit of data for L = phosphine and phosphite ligands. Correlations of this type were poor with single parameter fits. The sensitivity of $^1J_{CH}$ to trans ligand electronic and steric effects indicates that small changes in the hybridization of the $Co-CH_3$ moiety occur. This method allows us to probe the nature of Co−C bonding in the ground state. The other experimental methods for probing this bond (e.g., X-ray crystallography, FT-Raman spectroscopy, etc.) indicate that this bond is relatively insensitive to the trans ligand in the ground state. Thus, $^1J_{CH}$ values may be a useful general method for examining B_{12} systems and also hold promise for other types of organometallic compounds.

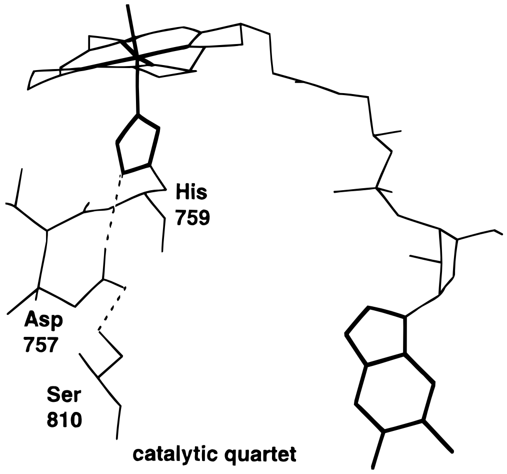
Introduction

Recent crystal structures of the methylcobalamin (MeB_{12})-dependent methionine synthase[1] and the adenosylcobalamin ($AdoB_{12}$)-dependent methylmalonyl-coenzyme A (CoA) mutase[2] have shed new light on the nature of bound B_{12} cofactors. The most striking feature observed in these structures is the coordination of a histidine imidazole trans to the alkyl in the position occupied by the tethered benzimidazole of the unbound cofactor (e.g., methionine synthase, Chart 1). This imidazole forms a link in the hydrogen bonding network known as the catalytic quartet. Protein-mediated electron donation by the trans imidazole is now hypothesized to be a significant component in catalysis.[1−3]

In organocobalt compounds, the trans influence of the R group on the L ligand can be readily explained because of the large dependence of axial metal-to-ligand distance on the nature of R. Parameters such as NMR shifts and L ligand dissociation rates have been found to be useful solution measurements that depend significantly on R.[4−6] Furthermore, we recently reported a spectroscopic method utilizing one-bond proton-carbon coupling constants ($^1J_{CH}$) obtained with a modified NMR pulse sequence to probe the induced electronic changes in a neutral ligand resulting from the variation of the negative trans ligand.[7] The complexes studied were cobaloximes (Chart 2). In cobaloximes, the influence of negative axial ligands with a range of electron donor abilities is well understood.[7,8]

In contrast to the array of methods for assessing the influences of the negative ligand (R) on the neutral axial ligand (L), there

Chart 1



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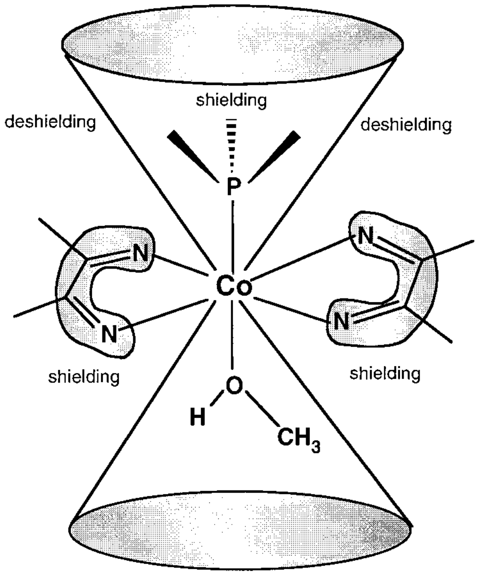
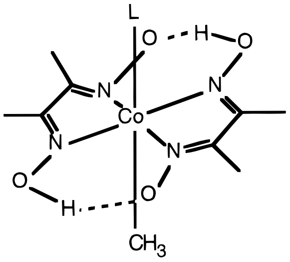


Figure 1. Typical anisotropic shielding cones for B_{12} model complexes demonstrated on the methanol-coordinated P-donor complex used for CCA determination.

Chart 2



LCo(DH)$_2$CH$_3$

is no simple means for probing how the variation of L through a range of electron donors influences the linkage between R and Co. Analysis of X-ray crystal structures has suggested that changes in the Co$-$C bond length are mainly steric and not electronic in nature.[9] Thus, structural data are not so useful in probing the electronic effect of L on R. Furthermore, no significant changes in the Co$-$C stretching frequency were detectable in near-IR FT-Raman spectra of cobalamins and methylcobinamides containing imidazole and imidazolate ligands.[3] Typically, a conjugated L (e.g., py, 1,5,6-trimethylbenzimidazole) permits interpretation of chemical shifts of L carbon atoms well removed from the metal center.[8,10] The difficulties in interpreting NMR shift data in the proximity of the anisotropic metal center are also well established for these systems (Figure 1).[7,8,11] The lack of conjugation in R groups of biological interest precludes the use of shifts. High resolution coupling constant information circumvents problems arising from through-space contributions to chemical shift such as metal center anisotropy. The Fermi contact term, which depends on the probability of an electron being at the nucleus, usually dominates the spin$-$spin coupling for directly bound nuclei (^1J).[12] Because electron density at the nucleus occurs only in s orbitals, only the contribution of valence atomic s electrons to molecular orbitals is important in the description of the coupling interactions.[12] Hence, the $^1J_{CH}$ values for the Co$-$CH$_3$ moiety can be used as a probe of changing s orbital contribution in the CH bond in response to changes in cobalt mediated by the other ligands.

Model complexes such as the cobaloximes have been well characterized and utilized successfully in interpreting the spectra of cobalamin species.[5,6] Phosphorus donor ligands, namely phosphines and phosphites, encompass a wide range of electron-donating ability and steric bulk. Thus we have examined methylcobaloximes containing abiological P-donor ligands as the most suitable candidates for this initial study probing the response of the Co$-$CH$_3$ moiety to changes in the trans ligand.

Experimental Section

Materials. Me$_3$P (1.0 M in toluene), Et$_3$P, *n*-Bu$_3$P, (NCCH$_2$CH$_2$)$_3$P, EtPh$_2$P, Et$_2$PhP, Me$_2$PhP, (PhO)$_3$P, (MeO)$_3$P, and (*i*-PrO)$_3$P (Aldrich) and *i*-Pr$_3$P, Cy$_3$P, Bz$_3$P, Ph$_3$P, (*p*-ClPh)$_3$P, (*p*-FPh)$_3$P, (*p*-MePh)$_3$P, (*p*-MeOPh)$_3$P, (*p*-Me$_2$NPh)$_3$P, *i*-PrPh$_2$P, and (NCCH$_2$CH$_2$)$_2$PhP (Strem) were used without further purification. Deuterated chloroform was purchased from Cambridge Isotope Laboratories. H$_2$OCo(DH)$_2$CH$_3$, (4-NCpy)Co(DH)$_2$Cl, and (4-NCpy)Co(DH)$_2$CH$_3$ were prepared as previously described.[13,14]

Syntheses. LCo(DH)$_2$Cl (L = Et$_3$P, Et$_2$PhP, *i*-PrPh$_2$P, (NCCH$_2$CH$_2$)$_2$PhP, (*p*-CH$_3$OPh)$_3$P, *n*-Bu$_3$P, Ph$_3$P) were prepared by the addition of L (1.18 mmol) to a brown suspension of (4-NCpy)Co(DH)$_2$Cl (1.19 mmol) in CH$_2$Cl$_2$ (25 mL). The solution became clear red before the product precipitated as a red-brown powder, which was collected by filtration.

Ph$_3$PCo(DH)$_2$CH$_3$ was prepared by alkylating Ph$_3$PCo(DH)$_2$Cl according to a previously reported method.[14,15] The analogues with L = Me$_3$P and Et$_3$P were prepared by addition of L (1.12 mmol) to H$_2$OCo(DH)$_2$CH$_3$ (0.40 g, 1.24 mmol) in methanol (20 mL) under N$_2$. After the suspension was stirred overnight, the resulting yellow solution was filtered to remove the excess of H$_2$OCo(DH)$_2$CH$_3$. The solvent and any remaining free ligand were removed under vacuum.

Et$_2$PhPCo(DH)$_2$CH$_3$ was prepared by the addition of Et$_2$PhP (0.224 mL, 1.29 mmol) to (4-NCpy)Co(DH)$_2$CH$_3$ (0.50 g) in CH$_2$Cl$_2$ (25 mL). After the solution was stirred for 2 h, the solvent was removed, and the remaining residue was suspended in Et$_2$O. The yellow product was removed on a filter and washed with Et$_2$O.

i-Pr$_3$PCo(DH)$_2$CH$_3$ was prepared *in situ.* After the addition of *i*-Pr$_3$P (0.5 μL, 0.0025 mmol) to an NMR tube containing a suspension of H$_2$OCo(DH)$_2$CH$_3$ (0.0315 g, 0.098 mmol) in CDCl$_3$ (0.60 mL), the ^{1}H NMR spectra ($^5J_{PH}$ and $^3J_{PH}$ coupling to the oxime methyl and Co$-$CH$_3$ signals) indicated formation of the desired product.

The remaining LCo(DH)$_2$CH$_3$ complexes [L = *n*-Bu$_3$P, Cy$_3$P, Bz$_3$P (where Bz = benzyl), (NCCH$_2$CH$_2$)$_3$P, (MeO)$_3$P, (PhO)$_3$P, Me$_2$PhP, EtPh$_2$P, *i*-PrPh$_2$P, (NCCH$_2$CH$_2$)$_2$PhP, (*p*-ClPh)$_3$P, (*p*-FPh)$_3$P, (*p*-MePh)$_3$P, (*p*-MeOPh)$_3$P, (*p*-Me$_2$NPh)$_3$P] were prepared by the addition of L (1.40 mmol) to a suspension of H$_2$OCo(DH)$_2$CH$_3$ (1.55 mmol) in CH$_2$Cl$_2$ (25 mL). After the red suspension was stirred for 2 h, the resulting yellow solution was filtered to remove unchanged H$_2$OCo(DH)$_2$CH$_3$, and the solvent was removed under reduced pressure. To remove unchanged L, the residue was suspended in a minimal amount of Et$_2$O and the suspension filtered to isolate the product. When the complex was Et$_2$O soluble, it was recrystallized from MeOH/H$_2$O.

C, H, and N analyses (Atlantic Microlabs, Inc., Norcross, GA) and yields of the new complexes are presented in the Supporting Information.

Spectral Measurements. All data were collected using 50$-$100 mM samples on a General Electric GN-600 Omega spectrometer and

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referenced to TMS. 1D ^{1}H spectra were acquired at 599.64 MHz with a 30° pulse width and 32K data points. A large window (~12 500 Hz) was necessary to observe the O- - -H−O signal at ~18−19 ppm.

2D single bond ^{1}H−^{13}C HMQC[16] (heteronuclear multiple quantum coherence) spectra were collected at 25 °C for assignment of the Co−CH$_3$ ^{13}C shift. Matrices were 256 × 2K data points with 32−64 acquisitions per t_1. Four dummy scans were applied at the beginning of the experiment, and a relaxation delay of 800 ms to 1.5 s was used prior to each scan. A square sine-bell filter was applied in both dimensions with a 45° phase shift. The second dimension was zero-filled to 2K data points prior to Fourier transformation.

^{1}H−^{13}C coupling constants were measured with the JHMQC (*J*-coupled heteronuclear multiple quantum coherence) method (spectral window of ~2000−7000 Hz, 32K data points, and 500−1000 scans).[7] The data sets were processed, and the coupling constants with a maximum error of ±0.20 Hz were determined as described previously.[7]

Calculated Cone Angles (CCA). CCA's were determined with the reported method[17] for Et$_3$P, Et$_2$PhP, *i*-PrPh$_2$P, (NCCH$_2$CH$_2$)$_2$PhP, and (*p*-CH$_3$OPh)$_3$P; CCA's for *n*-Bu$_3$P and Ph$_3$P were redetermined for comparison to reported values.[17] A mixture of AgNO$_3$ (0.24 mmol) and LCo(DH)$_2$Cl (0.2 mmol) in CH$_3$OH (10 mL) was stirred for 1−2 h and passed through Celite. The brown residue left after the solvent was removed under reduced pressure was dissolved in CH$_3$OH (1.7 mL), and the ^{1}H NMR spectrum was recorded at 23 °C. The CCA was then determined from the coordinated methanol shift (δ, ppm) by using the equation CCA (deg) = 178(10 − δ) − 1157.

Statistical Analysis. Data were analyzed using the program JMPIN (version 3.1.5, SAS Institute, Inc.) to generate least-squares regressions of the general form $Y = a_1X_1 + a_2X_2 + a_3X_3 + c$ [where Y = experimentally measured dependent variable; c = constant; a_1, a_2, a_3 = coefficients; X_1, X_2, X_3 = independent variables (i.e., electronic and steric parameters)]. When only a single electronic or steric parameter was involved, a_2 and a_3 were set to zero, leaving a standard linear equation. Likewise, for a dual-parameter fit, a_3 was set to zero. In the case of Drago's E_B−C_B parameters, weighting factors were sometimes used in fitting the data to give equations of the general form $Y = a_1(wE_B) + a_2(wC_B) + a_3X_3 + c$ [where w = weight assigned to a particular set of E_B−C_B parameters]. Coefficients of determination (r^2) were adjusted[18] to reflect the number of data points (n) according to the equation $r_a^2 = 1 - (1 - r^2)(n - 1)/(n - 2)$. As n increases, r_a^2 approaches r^2, which indicates the fraction of the total variance of the data set that is represented by the least-squares fit of the data. When weighted data are employed, n is defined as the sum of the weights assigned to the terms. During the preliminary screening of parameter combinations, those combinations producing $r_a^2 < 0.80$ were eliminated from further consideration. Although values of $r_a^2 \approx 0.80$ are not indicative of good correlations, such a demarcation was useful in determining which fits of the data required further analysis.

The analyses also included ANOVA (analysis of variance) tables and effect tests. The ANOVA tables included F tests for the overall least-squares equation, indicating the significance level or the probability (p) that one of the terms is not significant.[18] Values of $p \leq 0.0010$ were interpreted as significant, while values of $p < 0.0001$ were interpreted as highly significant. The effect tests consisted of an F test of each individual parameter, producing a p value for the significance of that term in the least-squares equation. The p values were used in combination with the r_a^2 values to assess the quality of each data fit. The F tests utilized in these studies should not be confused with the f values (which are an alternative to r_a^2 values) used by Taft and co-workers. Both the r_a^2 and p values are employed to judge the ability of our regression equations to account in a statistically significant manner for the change in $^1J_{CH}$ through the series of ligands studied.

Results

Spectroscopic data for LCo(DH)$_2$CH$_3$ complexes and relevant steric and electronic parameters are given in Tables 1 and 2 and in the Supporting Information. In general, both Co−CH$_3$ $^1J_{CH}$ values and ^{1}H shifts for the complexes displayed a weak trend, decreasing as the pK_a of the phosphine increased. The $^1J_{CH}$ for the *i*-Pr$_3$P and Cy$_3$P complexes were notable exceptions, showing larger couplings than anticipated from this trend (Figure 2). The $^1J_{CH}$ data for the three phosphite complexes did not integrate into these trends. The ^{1}H shifts exhibited a poor correlation with pK_a when using all of the phosphines and phosphites and improved when only the phosphines were used (Supporting Information). ^{13}C NMR shifts for the Co−CH$_3$ moiety show no obvious trends.

Table 1. NMR Data in CDCl$_3$ for LCo(DH)$_2$CH$_3$ and Steric Parameters for L

	L	Co−CH$_3$ $^1J_{CH}$ (Hz)	TCA (deg)[a]	CCA (deg)[b]	E_r (kcal/mol)[c]
1	Me$_3$P	137.06	118	115	39
2	Et$_3$P	137.82	132	130	61
3	*n*-Bu$_3$P	137.70	132	131	64
4	*i*-Pr$_3$P	139.01	160	164	109
5	Cy$_3$P	139.06	170	171	116
6	Bz$_3$P	138.38	165	136	82
7	(NCCH$_2$CH$_2$)$_3$P	139.70	132	134	
8	Ph$_3$P	139.51	145	160	75
9	(*p*-ClPh)$_3$P	140.26	145[d]	160[d]	74
10	(*p*-FPh)$_3$P	139.98	145[d]	160[d]	74
11	(*p*-MePh)$_3$P	139.47	145[d]	160[d]	74
12	(*p*-MeOPh)$_3$P	139.28	145[d]	157	76
13	(*p*-Me$_2$NPh)$_3$P	138.58	145[d]	160[d]	
14	EtPh$_2$P	138.64	140	145	66
15	*i*-PrPh$_2$P	139.26	150	166	75
16	Et$_2$PhP	137.82	136	137	57
17	Me$_2$PhP	137.55	122	125	44
18	(NCCH$_2$CH$_2$)$_2$PhP	139.24	136	142	
19	(PhO)$_3$P	139.00	128	119	65
20	(MeO)$_3$P	138.15	107	115	52
21	(*i*-PrO)$_3$P	137.96	130	121	74

[a] Tolman cone angle (ref 21). [b] Calculated cone angle (ref 17). [c] Ligand repulsive energy (ref 27). [d] Value estimated from Ph$_3$P.

Table 2. Electronic Parameters for P-Donor Ligands

	L	pK_a[a]	$E°$(**I**)[b]	E_B[c]	C_B[c]	weight[c]
1	Me$_3$P	8.65	0.400	0.250	5.81	1.0
2	Et$_3$P	8.69	0.393	0.270	6.11	1.0
3	*n*-Bu$_3$P	8.43	0.377	0.290	5.90	1.0
4	*i*-Pr$_3$P	9.30[d]		0.350	5.91	0.5
5	Cy$_3$P	9.70	0.310	0.370	5.91	1.0
6	Bz$_3$P	6.00[e]		0.307	3.77	0.2
7	(NCCH$_2$CH$_2$)$_3$P	1.37[d]				
8	Ph$_3$P	2.73	0.510	0.301	4.07	1.0
9	(*p*-ClPh)$_3$P	1.03[f]	0.593	0.282	3.55	1.0
10	(*p*-FPh)$_3$P	1.97		0.288	3.81	0.6
11	(*p*-MePh)$_3$P	3.84	0.490	0.308	4.37	1.0
12	(*p*-MeOPh)$_3$P	4.57	0.478	0.307	4.52	1.0
13	(*p*-Me$_2$NPh)$_3$P	8.65		0.342	5.05	0.4
14	EtPh$_2$P	4.90	0.475	0.274	4.85	1.0
15	*i*-PrPh$_2$P	5.00				
16	Et$_2$PhP	6.25	0.444	0.288	5.43	1.0
17	Me$_2$PhP	6.50	0.436	0.273	5.27	1.0
18	(NCCH$_2$CH$_2$)$_2$PhP	3.20				
19	(PhO)$_3$P	−2.00[e]	0.860	0.090	3.36	1.0
20	(MeO)$_3$P	2.60	0.680	0.131	4.83	1.0
21	(*i*-PrO)$_3$P	4.08[e]	0.620	0.211	4.59	0.7

[a] Reference 33. [b] $E°$ for η-MeCp(CO)$_2$MnL (**I**) from ref 24. [c] Reference 25. [d] Reference 30. [e] Reference 34. [f] Reference 35.

Simple Linear Regression. Electronic Parameters. The general trend of decreasing $^1J_{CH}$ with increasing pK_a was investigated in greater detail. Correlations with other commonly used terms for σ-donor and π-acceptor parameters such as Bodner's $\Sigma\sigma$,[19] Kabachnik's parameter ($\Sigma\sigma^{\phi}$),[20] Tolman's $\Sigma\chi$

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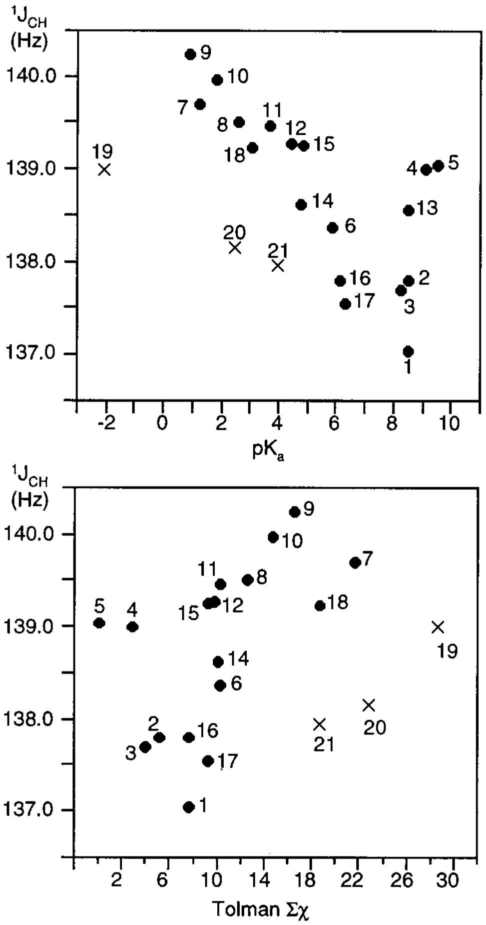

Figure 2. Plots of $^1J_{CH}$ (Hz) for phosphine and phosphite complexes against pK_a (top) and Tolman's $\Sigma\chi$ values (bottom). See Tables 1 and 2 for P-donor numbering scheme (● = phosphine, × = phosphite ligand).

(original[21] and Bartik's modified values[22,23]), $E°$ values of Giering, *et al.*,[23,24] and Drago's E_B-C_B parameters[25] were also investigated. Complexes with the bulky ligands (Cy_3P and i-Pr_3P) were not considered in these early screenings since a large steric influence was obvious from the initial plots (Figure 2).

A simple linear regression of $^1J_{CH}$ as a function of $\Sigma\sigma^{\phi}$ revealed a very poor correlation ($r_a^2 = 0.5645$, $n = 14$). The remaining nine electronic terms were screened by using the data for the complexes for which each parameter was available [i.e., $n = 8$, L = Et_3P, n-Bu_3P, Ph_3P, (p-ClPh)$_3$P, (p-MeOPh)$_3$P, $EtPh_2P$, Et_2PhP, Me_2PhP]. Because r_a^2 was <0.8, $\Sigma\chi$ (Tolman's and Bartik's values), $\Sigma\sigma$, and three of Giering's four sets of $E°$ were eliminated from further consideration (Supporting Information).

The remaining three terms were considered with the addition of the data for complexes with L = Me_3P and (p-MePh)$_3$P (Supporting Information). The weaker correlation compared to the other two parameters as well as the limited data available led us to exclude $E°$(**I**) from further examination. The data set was expanded again to $n = 13$ by adding the L = Bz_3P, (p-FPh)$_3$P, and (p-Me$_2$NPh)$_3$P complexes. The pK_a values produced a regression equation, $^1J_{CH} = -0.34\text{p}K_a + 140.51$, with an excellent score for significance but a low r_a^2. The weighted E_B-C_B values produced a fit better than pK_a, whereas the absence of weighting factors produced a poorer fit. However, all three fits were comparable. Because of the dual-component nature of the E_B-C_B description of σ-donation, the significance of each term was investigated via effect tests. The C_B parameter appeared to be primarily responsible for the good correlations. Therefore, C_B was tested as a single-parameter effect for the variance of $^1J_{CH}$; C_B generated a fit comparable to $^1J_{CH}$ vs pK_a.

It is instructive to consider the relationship between pK_a and the E_B-C_B parameters since these two parameters have been reported to correlate well.[25,26] A fit of $\text{p}K_a = a_1wE_B + a_2wC_B + c$ using the data available for relevant phosphines ($n = 15$) generated regression statistics indicative of a significant relationship (Supporting Information). A fit of C_B as a single parameter vs pK_a for all 15 ligands generated a fit with a moderately good r_a^2 with high significance (Supporting Information).

Steric Parameters. Because the Cy_3P and i-Pr_3P data did not fit in the initial analysis of $^1J_{CH}$ vs pK_a (Figure 2), we assessed the contribution of a steric trans influence. Ligands of the type (p-RPh)$_3$P, where R ≠ H, were omitted from the initial regression analyses since some of the steric parameters in Table 1 were only estimates. The coupling constants are plotted against the steric parameters in Figure 3. Attempts to fit a linear least-squares equation for $^1J_{CH}$ versus cone angles (CCA and TCA) and Brown's ligand repulsive energy (E_r)[27] resulted in moderate to poor correlations (Table 3) using data for the complexes of the 11 L's for which all three steric terms were available. Inclusion of L = (p-RPh)$_3$P with the estimated cone angles resulted in similar fits of the data. Regardless of the use or omission of the estimated cone angles, CCA proved to be clearly the best single steric parameter for modeling the variance of the coupling constants.

Multicomponent Analysis. Multiparameter systems combining electronic and steric terms were investigated in an effort to fit the coupling data for the complexes with bulky ligands into a single equation. Initially, all possible combinations of electronic and steric parameters were investigated. The analyses were carried out using phosphine data alone and in combination with phosphite data as well as with and without L having estimated cone angles.

TCA's fit poorly regardless of the electronic parameter chosen. E_r was a significant contributor to the data fit in a small number of cases. However, CCA values were the most successful steric parameters in multiparameter equations (Table 4). The correlations generally improved when estimated CCA's were used for the missing L = (p-RPh)$_3$P data. Including the data for the three phosphite complexes also improved the correlation statistics.

The σ-donation parameters, pK_a and E_B-C_B, generally produced the best regression statistics (Table 4). Giering's $E°$(**I**) generated an excellent fit when CCA was the steric parameter. However, the small number of $E°$(**I**) values limits its usefulness. The weighted E_B-C_B parameters produced good fits of the data as assessed by r_a^2 and overall p; however, effect tests suggested low statistical significance for the E_B-C_B parameters ($p > 0.02$) when the phosphites were omitted from

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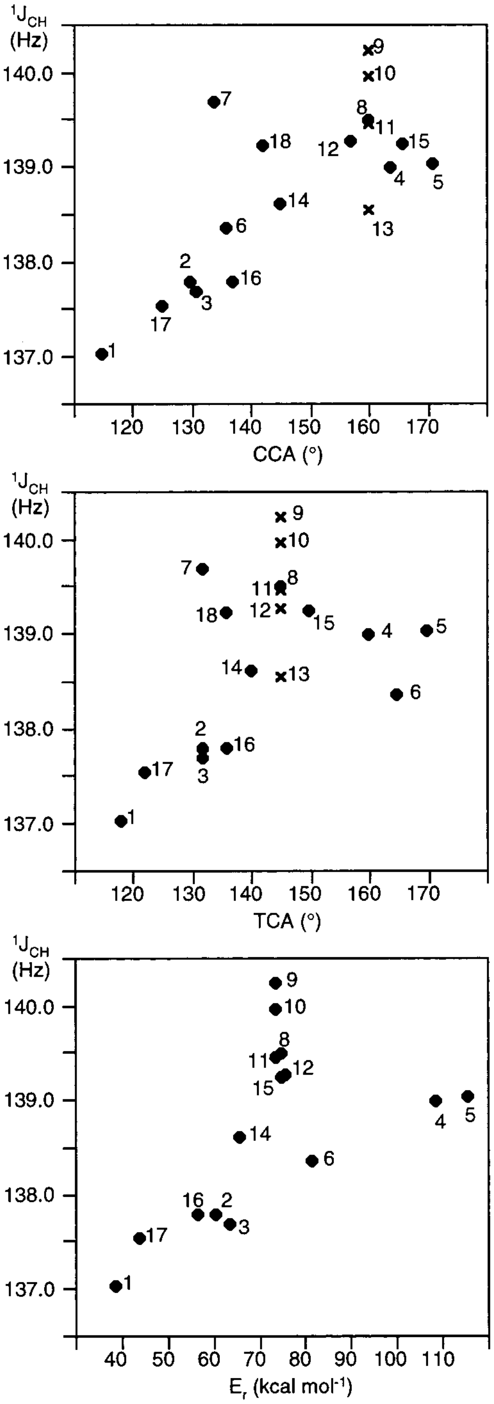

Figure 3. Plots of phosphine complex $^1J_{CH}$ (Hz) values against steric parameters. The estimated steric parameters for $(p\text{-RPh})_3P$ ligands (where R ≠ H) are represented with an ×.

the regression. Weighted C_B values produced better fits than E_B-C_B with and without the phosphites in the data set.

Discussion

As L in our range of $LCo(DH)_2CH_3$ compounds becomes a poorer donor through a combination of electronic and steric effects, the $^1J_{CH}$ values of $Co-CH_3$ change measurably. Using the relationship $^1J_{CH}$ (Hz) $= 500\rho_{C-H}$ (where ρ_{C-H} is the fraction of s character in the C hybrid orbital of the CH bond),[28] we find that the percentage of s character in the $Co-CH_3$ CH bond increases from 27.4% (L = Me_3P) to 28.1% (L = $(p\text{-ClPh})_3P$). These values are between those for a pure sp^3 system (25%) and an sp^2 system (33.3%). According to Bent's rule,[29] the greater p character in the C hybrid orbital of the CoC bond indicates that the substituent on C (*i.e.*, $Co(DH)_2L$) becomes more electronegative. In this discussion we consider the quantitative aspects of these changes in $^1J_{CH}$.

Table 3. Regression Analysis of $^1J_{CH}$ with Steric Parameters

	without $(p\text{-RPh})_3P$ estimates		with $(p\text{-RPh})_3P$ estimates	
	r_a^2	p	r_a^2	p
CCA	0.8784	<0.0001	0.7778	<0.0001
TCA	0.5357	0.0066	0.2935	0.0216
E_r	0.5108	0.0081	0.2729	0.0266

Electronic Parameters. The electronic parameters considered in this study have been widely applied to other transition metal systems to describe either σ-donation or a combination of σ-donor and π-acceptor effects. Both pK_a and Drago's E_B-C_B parameters have been reported to describe primarily σ-donor properties,[25,30] whereas the remaining parameters have been reported to represent a combination of σ and π effects.[30,31]

The σ-donation terms utilized in this study generated comparable least-squares fits of the $^1J_{CH}$ values. The E_B component was shown to be statistically insignificant in many of the fits. We suggest that in the case of cobaloximes the dual parametrization of the σ-donation term is not necessary. This is supported by the strong correlation found between pK_a and E_B-C_B parameters (Supporting Information) as well as between pK_a and C_B alone. The largest discrepancies between the two sets of parameters were found for the Bz_3P and $(p\text{-Me}_2NPh)_3P$ complexes; these were assigned low weights in the E_B-C_B method because of the limited data available for their determination.[25] Therefore, we consider pK_a the best available electronic donation parameter for the description of the change in the trans methyl group $^1J_{CH}$ when steric effects are minimized.

Steric Parameters. Several measures of ligand size (CCA, TCA, E_r) have been used in past studies. The substantial deviation of data for complexes with L = $i\text{-Pr}_3P$ and Cy_3P in the electronic parameter analyses suggested a possible steric influence on the observed $^1J_{CH}$ values. These two ligands have the largest steric bulk according to two (TCA, E_r) of the three steric parameters considered. TCA values are more numerous because of the simple nature of the calculation. Some of their limitations have been noted.[32] In particular, TCA values are determined from the CPK models with a fixed metal−phosphorus bond distance and are based on the entire ligand. The more recent parameter, E_r, was designed to account for such a problem since the value depends on the variation in the van der Waals repulsive force with changing metal−ligand distances.[27,32]

Another consideration is the ability of the ligand substituents to adopt more or less constrained conformations relative to the conformation utilized by Tolman. The TCA approach utilizes the entire ligand in its smallest conformation without taking into account neighboring ligand environments.[21] The E_r method calculates a minimized structure of L bound to the metal center

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Table 4. Summary of Multiparameter Fits Using $^1J_{CH} = a_1X_1 + a_2X_2 + a_3X_3 + c$[a]

electronic term	a$_1$	a$_2$	a$_3$	c	*n*[b]	r_a^2	electronic term significance (*p*)
Phosphines Only, No Cone Angle Estimates							
pK_a	0.04	−0.10		133.37	10	0.9444	0.0077
E_B-C_B	0.05	−0.21	−7.57	134.13	8.7	0.9700	0.0759 (*E*), 0.0637 (*C*)
C_B	0.04	−0.33		134.64	8.7	0.9546	0.0056
Phosphines Only, with Cone Angle Estimates							
pK_a	0.04	−0.15		133.49	14	0.9552	<0.0001
E_B-C_B	0.06	−0.27	−11.05	134.49	12.3	0.9714	0.0206 (*E*), 0.0294 (*C*)
C_B	0.04	−0.50		135.48	12.3	0.9544	<0.0001
With Phosphites, No Cone Angle Estimates							
pK_a	0.04	−0.15		134.13	13	0.9177	<0.0001
E_B-C_B	0.05	−0.21	−7.25	134.17	11.4	0.9761	<0.0001 (*E*), 0.0070 (*C*)
C_B	0.03	−0.56		136.88	11.4	0.8606	0.0001
With Phosphites, with Cone Angle Estimates							
pK_a	0.04	−0.17		133.94	17	0.9544	<0.0001
E_B-C_B	0.05	−0.33	−6.35	134.56	15	0.9692	0.0007 (*E*), 0.0006 (*C*)
C_B	0.03	−0.55		136.40	15	0.9280	<0.0001

[a] This table compares regressions involving only those complexes with ligands common to the pK_a, E_B-C_B, CCA, TCA, and E_r data sets. All cases reported here employ CCA as the steric term (a_1X_1). The a_2X_2 term represents either pK_a or C_B, and a_3X_3 represents E_B when it is employed. Both overall regression analysis and steric term significance resulted in $p \leq 0.0001$ for all cases reported here except when using E_B-C_B with phosphines only and no cone angle estimates ($p = 0.0004$). All E_B-C_B regressions presented in this table employed weighted data. [b] For E_B-C_B analyses, $n = \Sigma$(weights).

at a fixed distance and then uses that fixed structure of L while varying the metal−P distance.[27] Using an octahedral model complex is an added benefit to this approach since it allows for "interweaving" of L with the other ligands. However, the Cr(CO)$_5$ complex utilized in the E_r method is less sterically constrained and less rigid than the equatorial (DH)$_2$ unit of the cobaloximes.

In contrast to the above-mentioned steric parameters, CCA values were determined experimentally for this specific class of complex; therefore, the M−P bond distance and the ligand conformation reflect the time-averaged value. In general, the $^1J_{CH}$ data were fit better by the CCA parameter than by other steric parameters (Table 3). In the cobaloximes, the steric interaction between the axial P ligand and the equatorial ligands will arise from the local environment of the P and not the outer periphery of the substituents on P. The spectroscopic nature of the CCA approach parametrizes this local steric interaction for cobaloximes. The Bz$_3$P ligand exemplifies this situation. In both the TCA and E_r approaches, Bz$_3$P has a larger steric parameter than Ph$_3$P, the only difference in the structures being the addition of a linking CH$_2$ group between the Ph rings and the P in Bz$_3$P. The CCA approach produces a cone angle 24° smaller for Bz$_3$P compared to Ph$_3$P. The smaller CCA can be attributed to the positioning of the Ph groups away from the local metal−P bond environment. Along these same lines, *i*-PrPh$_2$P was found to have a CCA between the values for *i*-Pr$_3$P and Cy$_3$P (Table 1); however, the $^1J_{CH}$ value for the *i*-PrPh$_2$P complex was fit better than those for the *i*-Pr$_3$P and Cy$_3$P complexes in the regressions with electronic parameters (Figure 2).

The new CCA values reported here suggest the existence of small and previously undetected electronic influences on the shift of the coordinated methanol (Figure 1) used in calculating CCAs. For instance, the CCA of 160° reported[17] for Ph$_3$P was confirmed here. Previously, since TCA measurements do not change between complexes with (*p*-RPh)$_3$P ligands and those with Ph$_3$P, the CCA values for both types were assumed to be the same. However, our experiments give the new value of 157° for (*p*-MeOPh)$_3$P. In the case of the L = Et$_3$P complex, we have determined a CCA of 130°, which is 4° smaller than the CCA reported for the seemingly analogous complex with L = (NCCH$_2$CH$_2$)$_3$P (134°). Therefore, it appears that the electron-donating MeO substituent slightly decreases the observed CCA, whereas the electron-withdrawing CN substituent increases the observed CCA.

Indeed, the interdependence of electronic and steric characteristics of the P ligands has been noted.[21,31] A small bias due to an electronic influence may account in part for the substantially better correlation of $^1J_{CH}$ with CCA compared to TCA or E_r, although none of the steric terms alone could be used to describe the changes in $^1J_{CH}$. Changing CCA by 3−4° (e.g., using 160° and 134° as estimates of CCA for (*p*-MeOPh)$_3$P and (NCCH$_2$CH$_2$)$_3$P, respectively) does not does not significantly affect the $^1J_{CH}$ multiparameter regression analysis results, since CCA is not the dominant factor in the regression. It would be interesting to use CCA methods to examine this interdependence of electronic and steric effects in some future study directed at assessing steric parameters.

Multicomponent Models. Regression analyses involving pK_a and CCA consistently produced excellent statistical scores for significance when fitting $^1J_{CH} = a_1\mathrm{p}K_a + a_2\mathrm{CCA} + c$ (Table 4). Using all available pK_a and CCA data ($n = 21$), we obtained a good fit of high statistical significance with the equation, $^1J_{CH} = -0.18\mathrm{p}K_a + 0.04\mathrm{CCA} + 134.37$ ($r_a^2 = 0.9116$, $p < 0.0001$, Figure 4). The ready availability of these two parameters for L makes them a suitable choice for describing the influence of the trans ligand in the methylcobaloxime system. Although excellent fits were obtained with the E_B-C_B parameters, the complexity associated with their determination and the apparent lack of necessity for a multicomponent description of σ-donation (vide supra) suggest that pK_a is the better electronic parameter for describing $^1J_{CH}$, as shown by the consistently lower *p* values for the pK_a term (Table 4). The ability to fit data from bulky ligand complexes with the relationship $^1J_{CH} = a_1\mathrm{p}K_a + a_2\mathrm{CCA} + c$ seems to indicate that the σ-donation and steric bulk of L are the primary factors influencing the changes in hybridization of the C of the Co−CH$_3$ moiety as reflected in $^1J_{CH}$. The inability of combined σ-donor and π-acceptor terms to describe the changes in $^1J_{CH}$ in the multiparameter approach supports our conclusion from the simple linear fits that π interactions with Co are not important or not observable with the current approach.

Interestingly, the three phosphite complexes studied did not integrate into the simple analyses with the electronic terms.

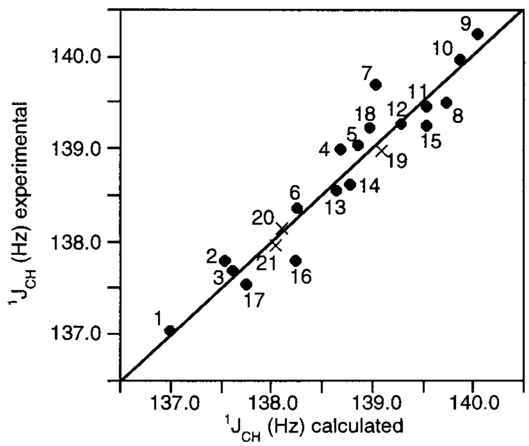

Figure 4. Plot of experimentally determined $^1J_{CH}$ vs calculated $^1J_{CH}$ ($^1J_{CH} = -0.18\text{p}K_a + 0.04\text{CCA} + 134.37$ ($n = 21$, $r_a^2 = 0.9116$, $p < 0.0001$), ● = phosphine, × = phosphite ligand).

However, once steric effects were included in the data fitting procedures, the phosphite data were found to contribute to the resulting least-squares fits. The $^1J_{CH}$ values for Co$-$CH$_3$ in these complexes are lower than would be expected from the fit of nonbulky phosphines with pK_a ($^1J_{CH} = -0.34\text{p}K_a + 140.51$, $n = 13$), whereas the bulky phosphines have higher values than predicted from the same equation. The lower $^1J_{CH}$ values for the phosphite complexes are most likely a result of the broad Co$-$CH$_3$ signals (relative to the phosphine complex signals, Figure 5), which suggest complications from either ligand exchange or electronic effects. The ability to fit the phosphite complex data with the multiparameter regressions involving CCA's further suggests that the CCA values may be affected to a slight extent by factors other than steric bulk. We did not extend this study beyond the three phosphite complexes used here since these are relatively poor ligands in cobaloximes.

Conclusions

Our results further support the structural and FT-Raman results, which suggest that variations in the ground state of the Co$-$CH$_3$ moiety are small as the trans ligand is varied. Nevertheless, the variations in $^1J_{CH}$ with changes in L are much larger than the accuracy of our experimental method. Our regression analyses of $^1J_{CH}$ with electronic parameters reveal stronger statistical relationships between $^1J_{CH}$ and σ-donation parameters, rather than combined σ-donor/π-acceptor parameters. Moreover, we found that pK_a is the best available electronic donation parameter for describing the change in the trans methyl group $^1J_{CH}$ when L was nonbulky. Adding a steric term to the equations allowed for simultaneous fits of all the ligands used, including bulky phosphines and phosphites, with the best fit of $^1J_{CH}$ obtained with the pK_a and CCA combination. The excellent r_a^2 and significance level obtained for the description of $^1J_{CH}$ with a σ-donation and steric parameter suggest that π interactions between Co and P may not be important in these systems. Analysis of $^1J_{CH}$ values is a viable method for probing the cobalt-bound methyl group for changes in hybridization resulting from changes in electron donation by the trans neutral ligand.

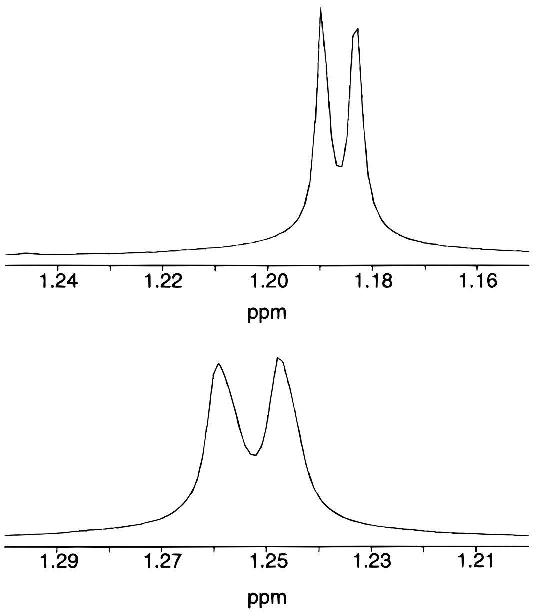

Figure 5. Co$-$CH$_3$ region of ^{1}H NMR spectra of Ph$_3$PCo(DH)$_2$CH$_3$ (top) and (PhO)$_3$PCo(DH)$_2$CH$_3$ (bottom). The doublet results from three-bond coupling to the P of the trans ligand.

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Supporting Information Available: Tables of elemental analyses and yields, of NMR data including Co$-$CH$_3$ ^{1}H, ^{13}C NMR shifts, $^3J_{PH}$, $^1J_{CH}$, and $^5J_{PH}$ values, O- - -H$-$O ^{1}H shifts, additional electronic parameters for L, regression analysis results for simple linear fits with electronic terms and the regression analysis of pK_a vs E_B-C_B (including plot), and plots of $^1J_{CH}$ vs $\Sigma\sigma$, $\Sigma\sigma^{\phi}$, and $E°$(**I**) and of Co$-$CH$_3$ ^{1}H NMR shift vs pK_a (6 pages). Ordering information is given on any current masthead page.

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