Comments on Coupling Graphical and Regression Analyses of Ligand Effect Data

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Received July 24, 1995[⊗]

In this paper we show how graphical analysis of ligand effect data for families of ligands should be combined with regression analysis in order to gain a more self-consistent interpretation of regression results. If a steric threshold shows up in the graphical analysis of the data for the trialkyl ligands (AR_3), then the threshold must show up in regression analysis of the full set of data. Similarly, the dependence of the data for the isosteric ligands $A(p\text{-}XC_6H_4)_3$ must have the same dependence on the electronic parameter χ that we find for the regression analysis for the full set of data. Finally, graphical analysis for both AR_3 and $A(p\text{-}XC_6H_4)_3$ families shows vividly whether steric effects and/or aryl effects belong in the full analysis. Thus, for results of any regression analysis to be acceptable, they must be consistent with the results of graphical analysis.

Introduction

Quantification of ligand effect data is necessary for rationally predicting reactivity, stereoselectivity, and regioselectivity of stoichiometric and catalytic reactions. Furthermore, quantification serves as a probe of reaction mechanism, gives us insight into the nature of metal−ligand bonding, provides a target for theorists, and leads to improved pedagogy by obviating the need for vague and qualitative stereoelectronic arguments to explain trends in reactivity and structure. For the past 10 years our group[1−3] together with the Poë group[4] have been exploring how to analyze ligand effect data. As a result of this work, we have developed a method, which we call the quantitative analysis of ligand effects or QALE.

We have found that a number of physiochemical properties are related via eq 1 to the stereoelectronic properties of ligands of the type AR_3, AR_xPh_{3-x}, and $A(p\text{-}XC_6H_4)_3$.[5] Equation 1 is a general form of the QALE equation for systems that might contain up to one observable steric threshold.

$$\text{property} = a(\chi) + b\theta + b'(\theta - \theta_{st})\lambda + c(E_{ar}) + d \quad (1)$$

In eq 1, χ[6] is an electronic parameter;[7−9] *the response of the property to* χ is assumed to be linear over the entire range of ligands. The steric parameters are θ and $(\theta - \theta_{st})\lambda$, where θ is Tolman's cone angle[10] and θ_{st} is the steric threshold. The response of the property to the steric parameter $(\theta - \theta_{st})\lambda$ is not linear: λ, which is a switching function, is zero for θ less than θ_{st}, λ is unity for θ greater than θ_{st}. E_{ar}[1] is the aryl effect parameter, which depends on the number of pendent aryl groups of AR_xPh_{3-x} and $A(p\text{-}XC_6H_4)_3$. Equation 1 allows for non zero steric effects below the steric threshold (the $b(\theta)$ term) with a different steric effect above the steric threshold (the $b'(\theta - \theta st)\lambda$ term). If there is no observable steric threshold then the "b'" term is set to zero.

Via eq 1, we have analyzed successfully a large body of kinetic and stereoselectivity data; thermodynamic data (pK_a values, $E°$ values, heats of reaction, equilibrium constants), bond lengths, and NMR, IR, UV/vis, photoelectron, and Mossbauer spectroscopic data.[5] In addition, we have found that the phosphorus(III) stereoelectronic parameters (χ, θ, E_{ar}) are transferable to other systems including silyl groups,[3] arsines,[5] alkyl groups,[5] nitriles,[11] and even thioethers[12] where the third pendent group has been replaced by a nonbonding pair of electrons.[13]

In the QALE eq (1) there are up to six quantities that have to be assigned nonzero values (a, b, b', c, d, and θ_{st}). With such a large number of variables the question arises as to whether one can get meaningful results from linear regression using this equation alone.[14] By using graphical methods and examining families of ligands we will show that we can get independent information that can be used to verify the results of a regression analysis. First, we consider the graphical analysis of data for separate families of ligands within a larger

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

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(6) Bartik, T.; Himmler, T.; Schulte, H.; Seevogel, K. J. *J. Organomet. Chem.* **1984**, *272*, 29.

(7) In this paper we use χ, θ, and E_{ar} as our stereoelectronic parameters, but, in principle, other stereoelectronic parameters (i.e., pK_a values of HPR_3^+, Brown's E_R values,[8] or Coville's solid angle values[9]) could also be employed. We have found that the use of χ, θ, and E_{ar} tends to give the highest quality analyses of the data based on eq 1.

(8) White, D. P.; Brown, T. L. *Inorg. Chem.* **1995**, *34*, 2718 and references therein.

(9) White, D.; Coville, N. J. *Adv. Organomet. Chem.* **1994**, *36*, 95 and references therein.

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(11) Fernandez, A. L.; Prock, A.; Giering, W. P. *Organometallics* **1994**, *13*, 2767.

(12) Tracey, A. A.; Eriks, K.; Prock.; Giering, W. P. *Organometallics* **1990**, *9*, 1399.

(13) We have excluded from our analyses data for ligands containing bonds to heteroatoms or ligands that appear to exhibit unusual electronic effects ($A(CH_2CH_2CN)_3$ and $A(o\text{-}MeOC_6H_4)_3$).

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experimental set and show the kinds of information that can be obtained from these restricted sets of data. We then go on to do a complete graphical and regression analysis of a set of data that includes the families of ligands, AR_3, AR_xPh_{3-x} and $A(p\text{-}XC_6H_4)_3$.

The Search for a Steric Threshold. Analysis of the Data for Trialkyl Ligands, AR_3

An important feature of QALE is the provision for a steric threshold.[15−17] In the following discussion we consider only the cases where the property of interest involves the difference in energy (log k and $-\Delta H_{rx}$) between two states. The observation of steric thresholds then depends on a number of factors.[17]

(A) No steric thresholds will be observed if, (a) for each state, steric effects are either linearly operative or absent or, (b) for each state, equivalent steric effects (steric thresholds and sensitivities[18]) are present.

(B) One steric threshold will be observed if (a) a steric threshold is present in one state and steric effects are either absent or linearly operative in the other state or (b) there are equivalent steric thresholds but different steric sensitivities in each state.

(C) Two steric thresholds will be observed if both states have different steric thresholds.

(D) Between zero and four steric thresholds might appear in a set of data for a system where two competitive reactions (e.g., stereoselectivity) are involved.

The analysis of data for the trialkyl ligands, AR_3, allows us to determine the number and position of steric thresholds. For these trialkyl derivatives E_{ar} is zero and θ and χ are linearly correlated (Figure 1).

If a plot of a property versus either θ or χ shows a break, then because of this linear correlation, we can ascribe this break to a change in steric effects only. The reader should recall that the QALE model requires that the response of the property to electronic effects must be continuous and linear. *It is advantageous to make the plot of data in terms of θ because the position of the break is the steric threshold.* We illustrate this manner of detection of a steric threshold for Poë's kinetic data for the first order dissociation of CO from $LRu(CO)_4$ (eq 2),[19,20] and for the kinetic data of the second order associative reaction between $H-SiR_3$ and Br_2 (eq 3).[21]

$$LRu(CO)_4 \xrightarrow{k} LRu(CO)_3 + CO \qquad (2)$$

$$R_3Si-H + Br_2 \xrightarrow{k} HBr + R_3Si-Br \qquad (3)$$

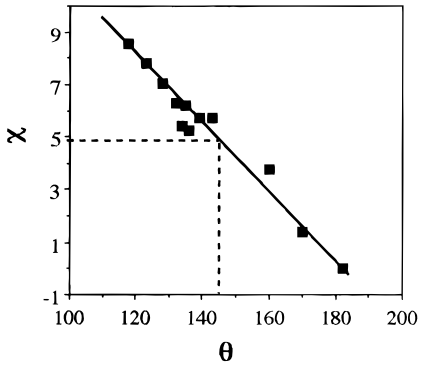

Figure 1. Plot of χ versus θ for commonly encountered trialkyl ligands of the type AR_3 and AR_2R'. In order of increasing size, the ligands are AMe_3, AMe_2Et, $AMeEt_2$, AEt_3, APr_3, AMe_2Cy, ABu_3, $AMe_2(t\text{-Bu})$, $A(i\text{-Bu})_3$, $A(i\text{-Pr})_3$, ACy_3, and $A(t\text{-Bu})_3$. The point of intersection of the dotted lines shows that a hypothetical triaryl ligand $[A(p\text{-}XPh)_3]$ with θ of 145° would lie on this line if its χ value were 4.8. Thus, in the absence of an aryl effect, this hypothetical ligand would behave like a trialkyl ligand. See Figures 4 and 5.

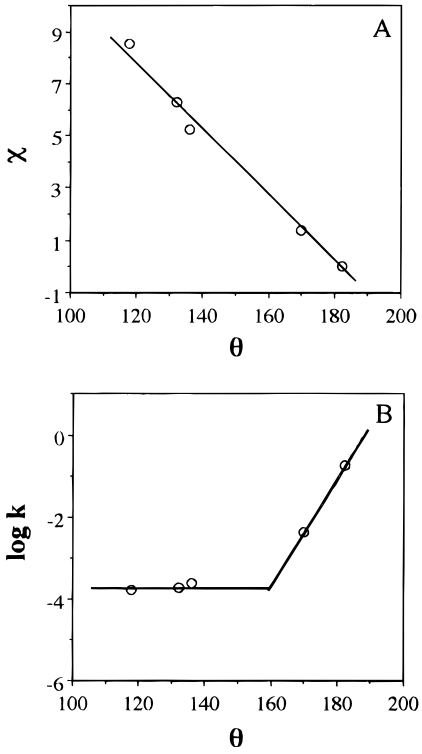

Figure 2. (A) Plot of χ versus θ for the PR_3 ligands used in reaction 2. (B) Plot of log k for PR_3 versus θ showing a steric threshold near 160°, after which the rate of the dissociative reaction increases.

In Figure 2A, we show the high correlation of χ with θ for the PR_3 ligands used in reaction 2. Thus, in the absence of a steric threshold, we would expect the plot of log k versus θ to be linear. The actual plot (Figure 2B) shows a steric threshold around 160°.

A similar analysis of reaction 3 again shows a linear relationship between χ and θ, this time for SiR_3 (Figure 3A). A plot of the data versus θ shows a break in the curve about 135°, indicating a steric threshold at this point.

Because of the linear relationship between θ and χ for AR_3, it is not possible to separate the contributions

(14) Conventional wisdom states that the more parameters the greater the value of r^2. We have observed that this is only true when a given set of parameters gives an incomplete description of the property and the addition of extra parameters completes the description. If these extra parameters are extraneous and there is a sufficiently large set of data, then the inclusion of these extraneous parameters in the regression analysis has little effect on the r^2 value and the coefficients of the extraneous parameters have unacceptably large standard errors.

(15) Golovin, M. N.; Rahman, M. M.; Belmonte, J. E.; Giering, W. P. *Organometallics* **1985**, *4*, 1981.

(16) Dahlinger, K.; Falcone, F.; Poë, A. J. *Inorg. Chem.* **1986**, *25*, 2654.

(17) Eriks, E.; Liu, H.-L.; Prock, A.; Giering, W. P. *Inorg. Chem.* **1989**, *28*, 1759.

(18) Steric sensitivity is defined as the derivative, d(property)/dθ, after the steric threshold.

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(21) Hetflejes, J.; Mares, F.; Chvalovsky, V. *Collect. Czech. Chem. Commun.* **1972**, *37*, 1713.

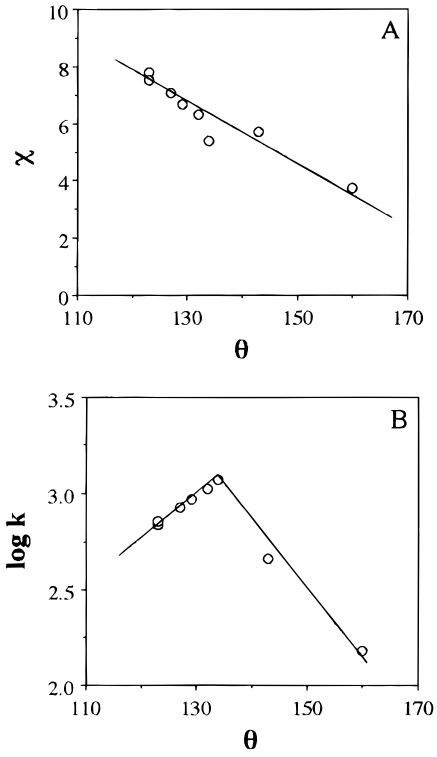

Figure 3. (A) Plot of χ versus θ for the SiR_3 groups used in reaction 3. (B) Plot of log k for SiR_3 versus θ. The plot shows a steric threshold around 135° after which the rate of the associative reaction decreases.

of the two parameters based on the data for AR_3 alone. In general, a linear regression analysis restricted to AR_3 will produce large standard errors for the coefficients of the QALE equation despite the large r^2 which might be obtained. However, there is a special condition (e.g., entering ligand dependent reactions) where (a) a steric threshold exists and (b) steric effects are not operative for ligands below the steric threshold (making coefficient "*b*" in eq 1 vanish). Thus, we are left with the parameter $(\theta - \theta_{st})\lambda$, which is *not* linearly related to χ, and we can obtain meaningful coefficients for the QALE equation. In general, it is usually necessary to employ additional families of ligands so as to reduce the correlation between parameters in order to obtain meaningful values of the coefficients of eq 1.[1]

Analyses virtually identical to that for AR_3 can be performed for either the $APhR_2$ or APh_2R families of ligands, since within each family E_{ar} is a constant and χ and θ are linearly correlated. These analyses must show the same steric threshold as observed in the analysis of AR_3 as well as in the regression analysis of the full set of data.

For reactions involving spectator ligands there can be up to two steric thresholds and three regions of different steric effects.[17] In principle, the steric thresholds can be detected by the analysis of the data for AR_3 as described above. In practice, we have found no clear cut example of a system with two steric thresholds where only AR_3 are involved.[22] Thus, we restrict our attention to the analysis of systems with one or no steric threshold.

(22) Rahman, M. M.; Liu, H.-L.; Prock, A.; Giering, W. P. *Organometallics* **1987**, *6*, 650.

Estimation of the Coefficient of χ: Analysis of the Data for $A(p\text{-}XC_6H_4)_3$

In the past, in order to overcome the high correlation between χ and θ for PR_3, the data for the mixed alkyl/phenyl phosphines were included along with the data for PR_3 ($r^2 = 0.429$ for the correlation between χ and θ). However, when we include the second electronic parameter, E_{ar}, we find an excellent correlation of χ with θ and E_{ar} ($r^2 = 0.990$). Hence, when E_{ar} is included, it is not generally possible to separate the individual contributions of the three parameters when the analysis is restricted to this group of ligands.[1] Only when the data for a set of isosteric ligands (i.e. $A(p\text{-}XC_6H_4)_3$) are included, can the correlation between parameters be sufficiently reduced to allow a full QALE analysis.

In the QALE model, both E_{ar} and θ are constant for $A(p\text{-}XC_6H_4)_3$. Thus, a plot of the data versus χ for $A(p\text{-}XC_6H_4)_3$, affords an estimate of the coefficient of χ in the QALE equation[1] for the full set of data. This estimate must be statistically indistinguishable from the value obtained for the coefficient of χ via regression analysis of the total set. Indeed, this is what we observe in the analyses of all suitable sets of data. The equivalence of the χ coefficients then serves as a check on the full analysis.

Estimation of the Importance of the Aryl Effect and Steric Effects.

Insight into the importance of aryl and steric effects can be obtained through plots of the data for AR_3 together with the data for $A(p\text{-}XC_6H_4)_3$ versus the electronic parameter, χ. First, for illustrative purposes we consider the graphical analyses of hypothetical kinetic data *in which there is no aryl effect or steric threshold*, Figure 4. An important consequence of the linear correlation between χ and θ for AR_3 is that when there is no aryl effect, the line for the isosteric $A(p\text{-}XC_6H_4)_3$ ligands with $\theta = 145°$ will cross the line for AR_3 at $\chi = 4.8$, corresponding to $\theta = 145°$. Since the line for the isosteric ligands, $A(p\text{-}XC_6H_4)_3$ has a negative slope, we see that log k increases with increasing electron donor capacity of the ligands, i.e., decreasing χ.

With this information in hand we are now ready to see how the relative slopes of the AR_3 and $A(p\text{-}XC_6H_4)_3$ lines give us information about steric effects. If there is no steric effect or aryl effect then the data for AR_3 and $A(p\text{-}XC_6H_4)_3$ will fall along coincident (and thus parallel) lines (Figure 4A—this figure serves as a point of comparison for the rest of this discussion). If the reaction is sterically accelerated, then since χ and θ are inversely related, we get a larger negative slope of the line for AR_3 (Figure 4B). If the reaction is slightly inhibited sterically such that electronic effects still predominate, the slope of the line for AR_3 is still negative but smaller than that for $A(p\text{-}XC_6H_4)_3$ (Figure 4C). If steric inhibition just balances the electronic effect, the resulting line for AR_3 is horizontal (Figure 4D). Finally, if steric inhibition is the dominant effect then the line for AR_3 has a positive slope (Figure 4E).

If there is an aryl effect, then the lines for the AR_3 and $A(p\text{-}XC_6H_4)_3$ data intersect at a point other than χ

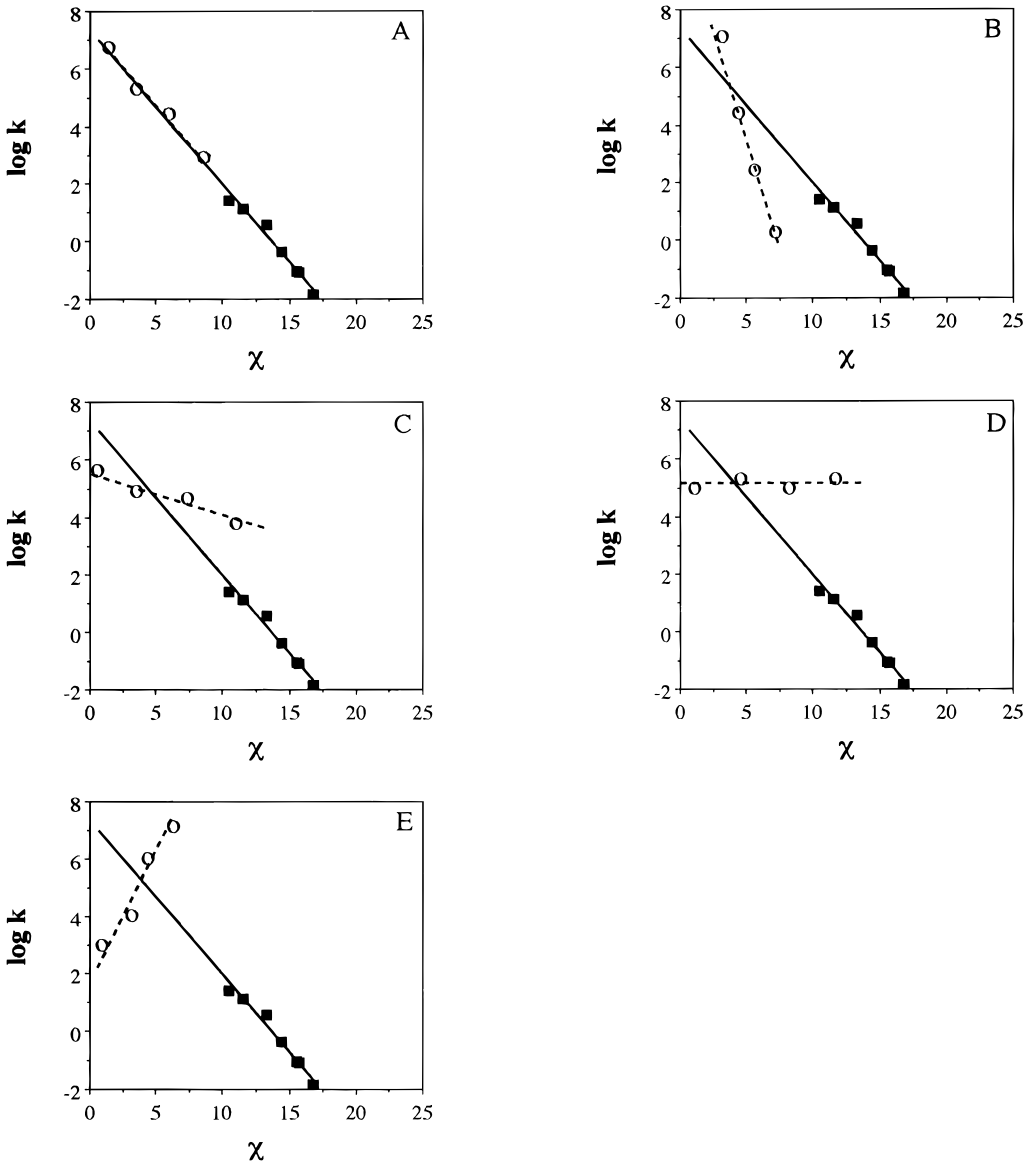

Figure 4. Plots of hypothetical kinetic data (log k) versus χ for a system with neither an aryl effect nor a steric threshold. See the text for a description of each plot. Data for AR_3 and $A(p\text{-}XC_6H_4)_3$ are shown by open circles and filled squares, respectively.

= 4.8. The magnitude of this deviation is a measure of the aryl effect.

In Figure 5, we show the analyses of some literature data. We start with an analysis of Bodner's δ values (relative ^{13}C chemical shifts for the carbonyl ligands of $LNi(CO)_3$)[23] (Figure 5A). When we plot the data for PR_3 and $P(p\text{-}XC_6H_4)_3$ versus χ, we see that the data lie along a single line. This indicates that neither steric effects (same slope) nor the aryl effect (no separation of the curves) are operative in this set of data. In the second example (Figure 5B), we plot the first vertical ionization potentials[24−31] of PR_3 and $P(p\text{-}XC_6H_4)_3$ versus χ. Here, we see two separate but parallel curves for PR_3 and $P(p\text{-}XC_6H_4)_3$, which shows that there is a significant aryl effect but again no steric effect.

Our third example is the graphical analysis (Figure 5C) of the kinetic data for the second-order reaction (4) as reported by Herrick.[32] The negative slope of the line for $P(p\text{-}XC_6H_4)_3$ indicates that the reaction is accelerated as the phosphines become better electron donors (smaller χ).

$$\eta\text{-CpFe(CO)}(\eta^3\text{-Bz}) + \text{L} \xrightarrow{k} \eta\text{-CpFe(CO)(L)(Bz)} \quad (4)$$

Since the slopes of the curves for the PR_3 and $P(p\text{-}XC_6H_4)_3$ differ in sign, we see that there is a large and dominant steric effect for PR_3. Finally, since the two

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(28) Bock. H. *Pure Appl. Chem.* **1975**, *44*, 343.
(29) Ikuta S.; Kebarle, P.; Bancroft, G. M.; Chan, T.; Puddephatt, R. J. *J. Am. Chem. Soc.* **1982**, *104*, 3699.
(30) Stelzer, O.; Unger, E. *Chem. Ber.* **1975**, *108*, 1246.
(31) Puddephatt, R. J.; Dignard-Bailey, L.; Bancroft, G. M. *Inorg. Chim. Acta* **1985**, *96*, L91.
(32) Herrick, R. S.; Duff Jr., R. R.; Frederick, A. B. *J. Coord. Chem.* **1994**, *32*, 103. The datum for $P(p\text{-}FC_6H_4)_3$, which lies well off the line determined by the other $P(p\text{-}FC_6H_4)_3$ ligands, is treated as an outlier and is not included in this analysis.

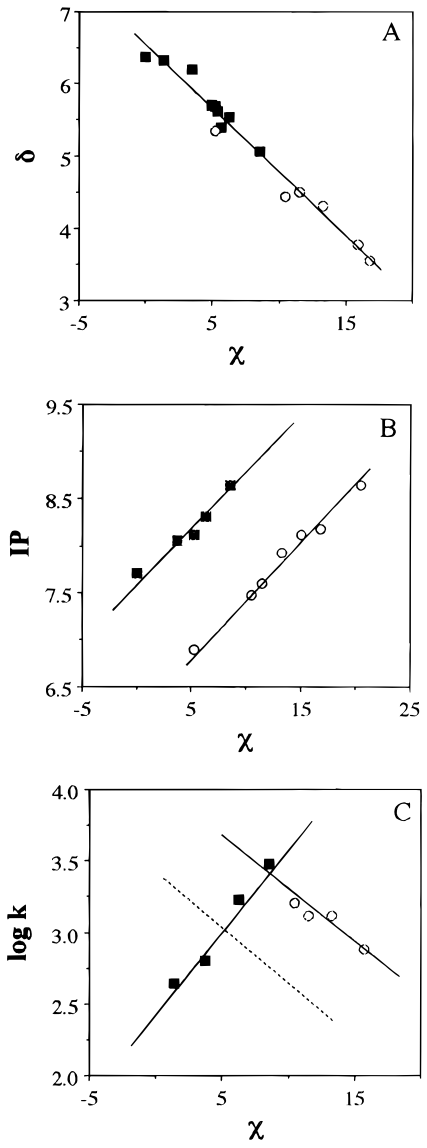

Figure 5. (A) Plot of Bodner's δ values for PR_3 and for $P(p\text{-}XC_6H_4)_3$ versus χ. (B) Plot of the first vertical ionization potentials (IP) versus χ. (C) Plot of log k versus χ for reaction 4. Data for PR_3 and $P(p\text{-}XC_6H_4)_3$ are shown by filled squares and open circles, respectively. The dashed line shows the expected behavior of $P(p\text{-}XC_6H_4)_3$ in the absence of an aryl effect.

curves cross at approximately $\chi = 8$ there must be a significant aryl effect. This aryl effect enhances the reactivity of $P(p\text{-}XC_6H_4)_3$ as compared to PR_3. All these observations are consonant with an entering ligand dependent reaction.

Illustrative Full Analysis of a Set of Ligand Effect Data.

Heats of reaction 5 as reported by Nolan[33] provide a particularly useful set of data for illustrating a complete QALE analysis. This is a system where steric effects are manifest in only one state (the product). Hence, if there is a steric threshold, then in the region below the steric threshold there can be no steric effect (i.e., the coefficient "*b*" in eq 1 is zero). *Notice that the data set is a thermodynamic one and not a kinetic one and is therefore independent of mechanism—the observation of a steric threshold must be attributed to nonlinear steric effects and not a change in mechanism.*

$$(BDA)Fe(CO)_3 + 2L \rightarrow L_2Fe(CO)_3 + BDA + \Delta H \quad (5)$$

BDA = benzylideneacetone

A plot of χ versus θ for the trialkyl phosphines, PR_3, shows a high correlation (Figure 6A). A plot of the $-\Delta H_{rx}$ versus θ shows a steric threshold near 135° (Figure 6B). We complete the graphical part of the analysis by plotting together the data for PR_3 and $P(p\text{-}XC_6H_4)_3$ versus χ (Figure 6C). From the plot for $P(p\text{-}XC_6H_4)_3$ we get an estimate (eq 6) of the coefficient of χ

$$\text{for } P(p\text{-}XC_6H_4)_3 \qquad -\Delta H_{rx} = -0.71(\chi) + 36.8 \quad (6)$$

(−0.71), which must be, and is, statistically indistinguishable from the coefficient of χ (−0.73 ± 0.10) obtained by regression analysis of the full set of data. This negative coefficient indicates that $-\Delta H_{rx}$ increases as the phosphines become better electron donors (smaller χ). The curve for PR_3 in Figure 6C shows the break attributable to the steric threshold. Since there are no steric effects for the small PR_3 ($\theta < 135°$), the points for these small ligands lie along a line that appears to be parallel to that for $P(p\text{-}XPh)_3$, as they should be in the QALE model. The curve for the $P(p\text{-}XC_6H_4)_3$ data ($\theta = 145°$, which lies beyond the steric threshold at 135°) intersects the curve for the large PR_3 ($\theta > 135°$) at approximately $\chi = 4.0$. This indicates a small but significant aryl effect that diminishes $-\Delta H_{rx}$. (If there were no aryl effect then the intersection would occur at $\chi = 4.8$.)

The regression analysis (eq 7) of the full set of data is in agreement with the graphical analysis. The standard errors associated with each coefficient are shown below the coefficient.[34]

$$-\Delta H = \underset{\pm 0.10}{-0.73(\chi)} - \underset{\pm 0.026}{0.461(\theta - 135)\lambda} - \underset{\pm 0.34}{1.68E_{ar}} + \underset{\pm 0.8}{46.3} \quad (7)$$

$$r^2 = 0.964 \qquad n = 16$$

Generation of Steric and Electronic Profiles

We find it useful to display the results of a QALE analysis as steric and electronic profiles, which show the response of the data to changes in only one variable. We generate these profiles by subtracting terms of the regression equation, excluding the one variable of interest, from the experimental data as shown below in eqs

(33) Li, C.; Stevens, E. D.; Nolan, S. P. *Organometallics*, **1995**, *14*, 3791. We have analyzed these data using Brown's E_R values as the steric parameter along with χ and E_{ar} according to eq 1 with coefficient *b* set to zero. With or without a steric threshold, the analysis is not as good as that obtained with θ as the steric parameter.

(34) We determine the value of a particular steric threshold, θ_{st}, through linear regression analysis as the value which minimizes the standard deviation (maximizes r^2). Thus, we are applying linear regression to a nonlinear problem. However, we show in ref 1 via a simulation method that for the large enough values of r^2 that we normally encounter, the error in θ_{st} is small. Moreover, the 95% confidence limits determined by the simulation agree quite well with those obtained by the simpler treatment where we maximize r^2. The coefficients and their 95% confidence limits are $a = -0.73 \pm 0.22$, $b' = -0.461 \pm 0.057$, $c = -1.69 \pm 0.75$, and $d = 46.3 \pm 1.8$.

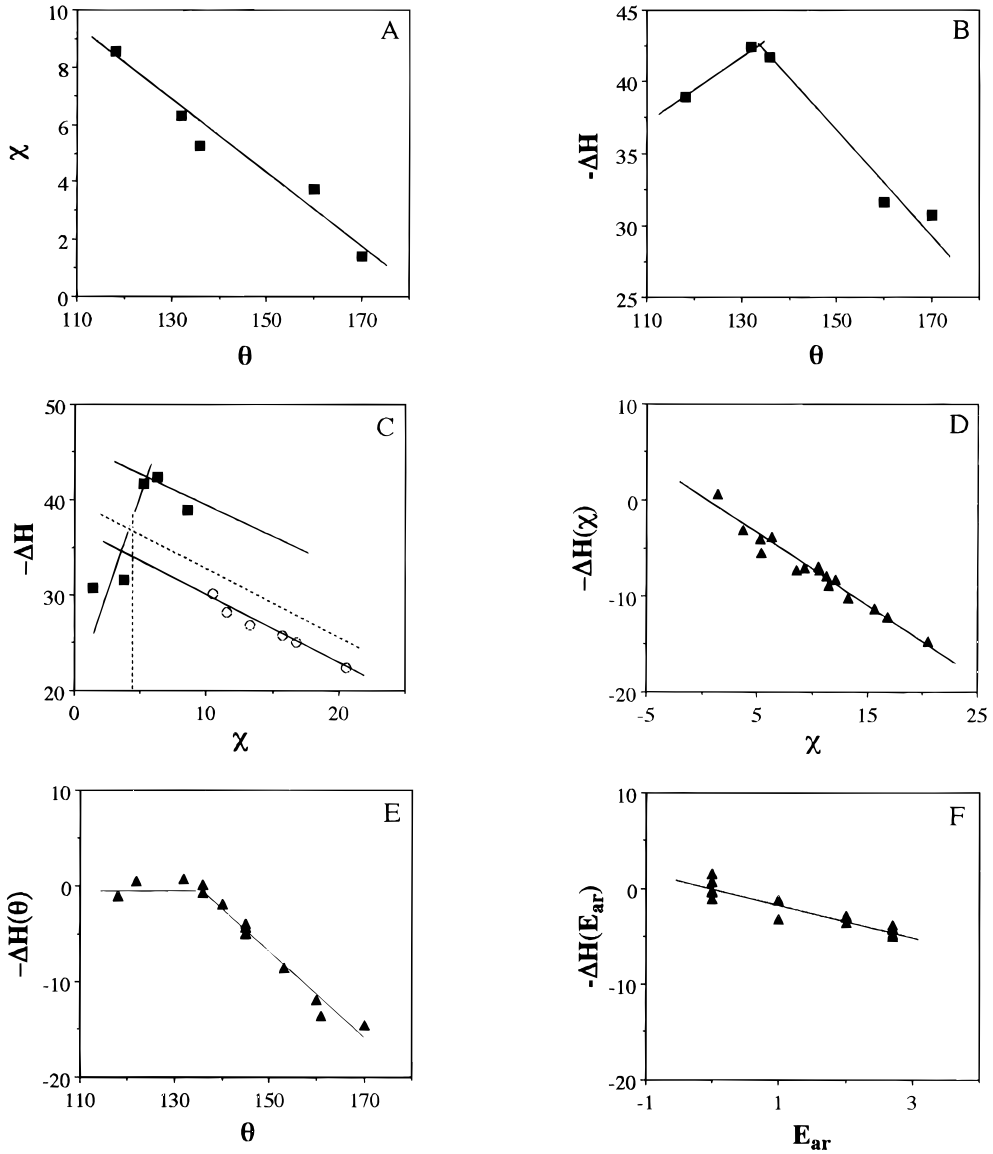

Figure 6. Graphical analysis of $-\Delta H_{rx}$ for reaction 5. (A) Plot of χ versus θ for the trialkyl phosphines (PR_3) used in reaction 5. (B) Plot of $-\Delta H_{rx}$ versus θ for PR_3. (C) Plot of $-\Delta H_{rx}$ for PR_3 and $P(p\text{-}XC_6H_4)_3$ versus χ. The dashed line shows the expected position of the line for $P(p\text{-}XC_6H_4)_3$ if there were no aryl effect. (D) χ profile. (E) Steric (θ) profile. (F) E_{ar} profile. Data for PR_3 and $P(p\text{-}XC_6H_4)_3$ in parts A–C are shown by filled squares and open circles, respectively.

8–10.

$$\text{property}(\theta) = \text{property(exp)} - a\chi - cE_{ar} - d \quad (8)$$

$$\text{property}(\chi) = \text{property(exp)} - b(\theta - \theta_{st})\lambda - cE_{ar} - d \quad (9)$$

$$\text{property}(E_{ar}) = \text{property(exp)} - a\chi - b(\theta_{st})\lambda - d \quad (10)$$

We display these profiles for reaction 5 in Figure 5D–F. We find it convenient to use the same vertical scales for the three profiles. This allows for easy visual comparison of the importance of each of the three parameters. Because of the way these profiles are constructed, each displays the total error in the analysis.

We see that the results of the graphical analysis and the regression analysis are in harmony. They both show a steric threshold at 135°, they both show the same coefficient for χ, and they both show that the aryl effect diminishes $-\Delta H_{rx}$.

Rogue Points

When doing an analysis, we must be on guard for an apparent steric threshold owing to the presence of a rogue point—one that does not correlate with the rest of the data. This rogue point might be attributed to experimental problems or it might reflect a phenomenon that is not accounted for by the model on which the analysis is based. The question arises as to how we can identify such a point and justify its exclusion from the analysis. We illustrate one graphical solution to this problem by considering the analysis of the data for the displacement of iodide by phosphine from iodoethane (eq 11).[35]

$$EtI + L \xrightarrow{k} Et{-}L^{+} + I^{-} \quad (11)$$

A plot of χ versus θ (Figure 7A) for the PR_3 used in this study shows a linear relationship, which means all

(35) Henderson, W. A.; Buckler, S. A. *J. Am. Chem. Soc.* **1960**, *82*, 5794.

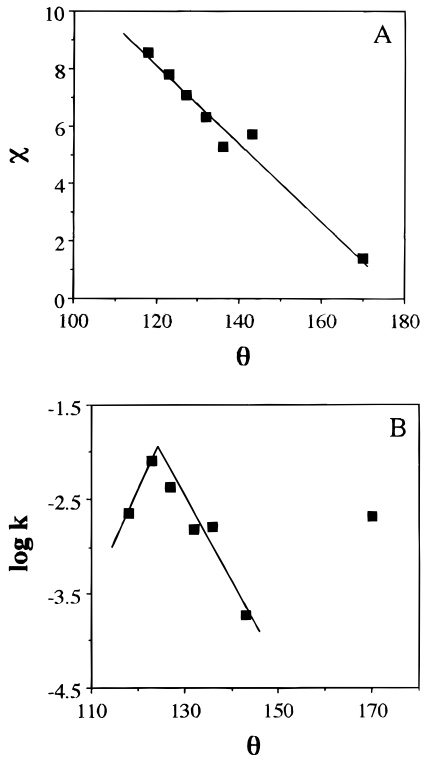

Figure 7. (A) Plot of χ versus θ for PR_3 used in the study of reaction 11. (B) Plot of log k versus θ for PR_3 used in reaction 11.

the PR_3 data can be used to locate the steric threshold. *Since the first interaction between the nucleophile and the substrate occurs in the transition state of this entering ligand dependent reaction, there can only be one kinetic steric threshold and the rate must diminish beyond the steric threshold.* Thus, a plot of log k versus θ can show no more than one break. A plot of experimental log k versus θ (Figure 7B) for PR_3 shows two points (PMe_3 and PCy_3) lying off the line determined by the remainder of the data. Either the point for PMe_3 or the point for PCy_3 must be an outlier. Figure 7B is best viewed as having a steric threshold near 125°, leaving the datum for PCy_3 lying well off the resulting curve, i.e., PCy_3 is far too reactive for its size. Thus, for some reason the PCy_3 point does not fit the model. Lacking additional data, we have no choice but to exclude it from the QALE analysis.

Conclusion

In this paper we have called attention to the importance of coupling graphical with numerical analysis when employing the QALE method. We have shown that a sufficient number of each family of AR_3 and $A(p\text{-}XC_6H_4)_3$ must be included in an experiment so that a graphical analysis of the resulting data will be meaningful. This graphical analysis tells us (a) if we need additional data before we go on to the full regression analysis and (b) if there is a steric threshold in the data and (c) serves as a check on the consistency and reasonableness of the results of the regression analysis.

Acknowledgment. We thank Professors Anthony Poë and Steven Nolan for allowing us to use unpublished data from their laboratories.

OM950564P