Coordination Chemistry Reviews, 33 (1980) 251—277
Elsevier Scientific Publishing Company, Amsterdam — Printed in The Netherlands

THE INTERPRETATION OF REACTIVITY IN CHEMICAL AND BIOLOGICAL SYSTEMS WITH THE *E* AND *C* MODEL

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(Received 14 March 1980)

CONTENTS

A. INTRODUCTION

The measurement of coordinate bond strengths ($-\Delta H$) has led to a data set that can be quantitatively correlated with the *E* and *C* equation $-\Delta H = E_AE_B + C_AC_B$. The information from this correlation provides valuable insights into the large number of systems in which Lewis acid—base interactions dominate the chemistry. Illustration of these applications of the *E* and *C* model are presented in this article. A procedure is offered which permits one to use the information from this correlation in place of pK_B data for interpretations of chemical reactivity and spectroscopic changes. Arguments are presented to establish the *E* and *C* parameters for molecular acids and bases as the norm for inherent scales of Lewis acid—base strength.

Lewis acid—base interactions have become recognized as having fundamental significance in most chemical reactions that occur in chemical and biological systems. Earlier reports from this laboratory [1—3], concerned

0010-8545/80/0000—0000/$05.40

with the fundamental nature of this interaction, led to the proposal of the E and C equation. This equation has excellent correlative and predictive capabilities with regards to the acid—base bond strength. The equation is

$$-\Delta H = E_A E_B + C_A C_B \quad (1)$$

where $-\Delta H$ is an enthalpy of adduct formation measured in the gas phase or a poorly solvating solvent, the subscripts A refer to acid and B to base, E is an empirical parameter related to the tendency to undergo electrostatic bonding and C is a parameter related to the tendency to undergo covalent bonding. There are several important consequences of this relationship which have not been emphasized. It is the purpose of this article to demonstrate that, as a reliable indicator of sigma bond strength, the E and C equation should serve as the fundamental basis for the design and interpretation of any studies probing structure—reactivity relationships. The information contained in the parameters can be used as a guide to the interpretation of qualitative findings in all areas of chemistry (biochemistry, catalysis, organic, organometallic, etc.). The sigma bond strength contribution to observed spectral changes also can be probed using the E and C parameters. Indeed, any property that has previously been correlated with pK_B or Donor numbers [4] can be more properly interpreted using the E and C parameters. The purpose of this article is to illustrate procedures for using, and insights provided by, the E and C model as a fundamental tool for rationalizing and understanding chemical reactivity.

B. EARLY APPROACHES TO INTERPRETING REACTIVITY

Development of acid—base chemistry in the 1950's and early 1960's used pK_B (or pK_A) values as the norm for sigma donor (or acceptor) strength [5]. When a basicity order toward a new substrate arose that was different from the pK_B order, some qualitative quantum mechanical type of explanation (for example, steric effects, π-backbonding, π-antibonding, hyperconjugation, etc.) was invoked to account for the discrepancy. There are several problems with this approach.

1. The pK_B values contain contributions from solvation energies. Solvation energies and the donor—acceptor bond energies must be factored so their effect on reactivity can be treated independently. Only then can both effects be understood.

2. The pK_B data contain contributions to both solvation and bond energies from entropy and enthalpy terms. Quantum mechanical contributions are manifested in ΔE which for certain systems are best approximated by ΔH. The pK_B values often do not even parallel the ΔH values for aqueous basicity.

3. The Mulliken treatment of charge transfer complexes [6] proposes that there are two independent contributions to a coordinate bond energy; a covalent contribution, described by the wave function ψ_{cov}, and an electro-

static wave function, described by ψ_{el}. The bond in the adduct, ψ^0, is a combination of these two effects

$$\psi^0 = a\ \psi_{el} + b\ \psi_{cov} \tag{2}$$

where a and b are constants that illustrate the relative importance of the two effects in the adduct bond [7]. A largely electrostatic interaction, $a >> b$, occurs when highly charged, small electron pair acceptors and donors interact. A largely covalent interaction, $b >> a$ occurs when there is effective overlap and good energy matching of the acceptor and donor orbitals. Different orders of donor (or acceptor) strength result toward an acceptor (or donor) in which the electrostatic term dominates than toward an acceptor in which the covalent term dominates. The point that there is no inherent order of donor strength is the essence of the Class A and B [8] as well as the hard—soft [9] classifications of acids and bases.

The points listed above are worth further discussion because they continue to be overlooked even in the literature of the 1970's. There is a tacit violation of all three points whenever a pK_B plot is employed to interpret reactivity. In a typical scenario some reactivity or spectral property of a system is measured as a function of base (or acid) variation. This property for the various base (or acid) adducts is plotted against the pK_B (or pK_A) value. A line is drawn through the points for the "well behaved", often very similar type of bases (similar C/E ratios, vide infra). When the measured property for a particular base produces a point that falls above the line, π-stabilization is proposed. When the value for this property falls below the line, π-antibonding or steric effects are offered as the cause. When the above procedure does not work, the authors limit the data correlated by drawing separate lines through families of compounds. Chances of success are improved with the families because the bases are similar. However, in addition to the pi-bonding and steric considerations offered above, the entropy and solvation effects described in the first two points presented at the beginning of this section are present in pK_B values and could cause a plot of the measured property to deviate from a linear relation with pK_B. So many effects are included in a pK_B value that it becomes impossible to understand why a correlation does or does not exist. Even if monotonic solvation and entropy effects were present in the series of bases selected, the trend in the pK_B values would offer a single scale basicity order (a violation of point 3 above). A plot of data for bases interacting with a more covalent acid than hydronium ion vs. pK_B would not be linear. Positive deviations from such a plot occur for covalent bases (the C_AC_B product is large) and these deviations have been incorrectly attributed to π-backbonding stabilization. Negative deviations are incorrectly attributed to steric or π-antibonding effects. Often the incorrect logic of a pK_B plot takes a more subtle form. Although not explicitly stated, the pK_B values are used to establish a norm for basicity and explanations are then offered when a measured property of a series of base adducts deviates from this order. It would be embarrassing to list the number of times that the procedures described above have, for example, appeared in American Chemical Society journals in the 1970's and 1980's. Two illustrative examples will suffice. Data for the binding of bases and dioxygen to cobalt(II) complexes have been plotted vs. pK_B and incorrect inferences [10,11] drawn about the bonding of *N*-methylimidazole [12]. Trends in the coordinating tendencies of various bases to methyl cobaloxime were shown [13] to provide an incorrect assessment of the covalent nature of the cobalt center in this acid and vitamin B-12.

C. A VIABLE, MODERN APPROACH TO ACID—BASE CHEMISTRY

From the above discussion, it becomes apparent that if chemists are to understand chemical reactivity, they must have a way of determining what is normal in a simple, sigma bonded, donor—acceptor interaction. This objective can be accomplished by determining a mathematical equation for bond strength and testing this equation with experimental data. Ideally, one would like to derive the equation and parameters from theory but a quantum mechanical calculation of the energy of acid—base adduct formation is not yet feasible. The alternative is an empirical solution to the problem that can subsequently be justified with quantum mechanics.

The data used to develop the model should involve enthalpies of interaction with minimal solvation contributions, for these quantities are a measure of bond strength. A simple system should be investigated first and one that has been extensively studied is indicated by the general reaction

$$A + B \rightleftharpoons AB \tag{3}$$

where A is the Lewis acid, B the Lewis base and AB the adduct. Initially, acids and bases should be selected in which the interaction involves sigma bond formation. In the empirical approach, the mathematical equation must be determined along with the parameters to be used in it.

The equation to be employed must be consistent with what is known about Lewis acid—base reactions. According to the Mulliken formulation [1] there must be at least two contributions; covalent and electrostatic. Furthermore, to obtain scrambled donor orders with acid variation at least two terms are needed in the equations. For example the order $R_3N > R_2O > R_2S$ pertains for the enthalpy of adduct formation with the acid phenol and the order $R_3N > R_2S > R_2O$ is obtained with the acid iodine [14]. The total covalent contribution is a function of the acid covalent bond forming tendencies, C_A, and the base covalent bond forming tendency C_B. The total electrostatic contribution is a function of the acid electrostatic bond forming tendency E_A and the base electrostatic bond forming tendency E_B. If a base fragment in the adduct has an appreciable dipole moment but the acid fragment it interacts with does not, the electrostatic contribution will be small. A product type function, as is involved in a dipole—dipole type interaction, will accomplish this so we write E_AE_B for the electrostatic contribution.

TABLE 1

E and *C* numbers for various acids and bases [a]

Formula	*E*	*C*	W^b	*C*/*E*
Acids [c]				
1 I_2	1.00 *	1.00 *		1
2 ICl	5.10	0.830		0.16
3 C_6H_5SH	0.99	0.198		0.20
4 C_6H_5OH	4.33	0.422		0.10
5 *p*-$CH_3C_6H_4OH$	4.18	0.404		0.10
6 *p*-FC_6H_4OH	4.17	0.446		0.11
7 *m*-FC_6H_4OH	4.42	0.506		0.11
8 *p*-$C1C_6H_4OH$	4.34	0.478		0.11
9 *m*-$CF_3C_6H_4OH$	4.48	0.530		0.12
10 $(CH_3)_3COH$	2.04	0.300		0.15
11 CH_3CH_2OH	3.88	0.451		0.12
12 $(CF_3)_2CHOH$	5.93	0.623	1.10	0.11
13 C_4H_4NH	2.54	0.295		0.12
14 $CHCl_3$	3.02	0.159		0.05
15 $(CH_3)_3SnCl$	5.76	0.03		0.01
16 $BF_3(g)$	9.88	1.62		0.16
17 $B(CH_3)_3(g)$	6.14	1.70		0.28
18 $Al(CH_3)_3$	16.9	1.43		0.08
19 SO_2	0.920	0.808		0.88
20 $Cu(hfac)_2$	3.46	1.32		0.38
21 H_2O	1.64	0.571		0.35
22 $CH_3Co(DMG)_2$	9.14	1.53		0.17
23 $Zn\{N[Si(CH_3)_3]_2\}_2$	5.16	1.07		0.21
24 $Ni(TFACCAM)_2$	3.38	0.640		0.19
25 NiSMDPT	3.94	0.500		0.13
26 π-allyl PdCl	3.41	0.980	3.1	0.29
27 RhCODCl	4.93	1.25	6.3	0.25
28 $Rh(CO)_2Cl$	8.72	2.02	11.3	0.23
29 ZnTPP	5.15	0.620		0.12
30 CoTPP	4.44	0.58		0.13
Bases [c]				
31 NH_3	1.15	4.75		4.1
32 CH_3NH_2	1.30	5.88		4.5
33 $(CH_3)_2NH$	1.09	8.73		8.0
34 $(CH_3)_3N$	0.808	11.54		14.2
35 CH_3CN	0.886	1.34		1.5
36 $(CH_3)_2NCN$	1.10	1.81		1.7
37 $CH_3CON(CH_3)_2$	1.32 *	2.58		2.0
38 $CH_3COOC_2H_5$	0.975	1.74		1.8
39 $(CH_3)_2CO$	0.937	2.33		2.5
40 $(C_2H_5)_2O$	0.936	3.25		3.5
41 $O(CH_2)_4O$	1.09	2.38		2.2
42 $(CH_2)_4O$	0.978	4.27		4.4
43 $HC(S)N(CH_3)_2$	0.76	8.19		10.8
44 $(CH_3)_2SO$	1.34	2.85		2.1
45 $(CH_2)_4O$	1.38	3.16		2.3
46 $(CH_3)_2S$	0.343	7.46		21.8

TABLE 1 (continued)

Formula	*E*	*C*	*C/E*
47 $(C_2H_5)_2S$	0.339	7.40 *	21.8
48 C_5H_5NO	1.34	4.52	3.4
49 4-$CH_3C_5H_4NO$	1.36	4.99	3.7
50 $(CH_3)_3P$	0.838	6.55	7.8
51 C_6H_6	0.280	0.590	2.1
52 $C_9H_{18}NO$ (TMPNO)	0.915	6.21	6.8
53 $HC(C_2H_4)_3N$	0.700	13.2	18.9
54 $C_6H_{10}O$ (bridged ether)	1.08	3.76	3.5
55 $(CH_3)_2Se$	0.217	8.33	38.4
56 $C_2H_5C(CH_2O)_3P$	0.548	6.41	11.7
57 $[(CH_3)_2N]_3PO$	1.52	3.55	2.3
58 C_5H_5N	1.17	6.40	5.5
59 $CH_3C_4H_4N$	1.26	6.47	5.1
60 *N*-methyl imidazole	0.934	8.96	9.6

[a] For a more complete list see refs. 3 and 51. Error limits for the parameters are also given in these articles.

[b] Systems for which a W is reported should be used in the equation $-\Delta H + W = E_AE_B + C_AC_B$, vide infra.

[c] For acid 20 hfac is hexafluoroacetylacetonate, for 22 DMG is dimethylglyoximate, for 24 TFACCAM is trifluoroacetylcamphorato (ref. 15), for 29 and 30 TTP is tetraphenylporphine, for base 52 $C_9H_{18}NO$ is the free radical 2,2,6,6-tetramethylpiperidine-*N*-oxyl, for 54 $C_6H_{10}O$ is 7-oxabicyclo[2.2.2]heptane.

Structural formulae are readily written for the acids and bases from the information given.

Similarly if the base readily donates electron density but the acid does not readily accept density, the covalent contribution will be small. The covalent contribution is thus written as C_AC_B and the equation [1—3] for the total enthalpy of adduct formation is that given earlier (eqn. 1): $-\Delta H = E_AE_B + C_AC_B$. The data set, selected according to the criteria stated above, determines whether this equation or a different one should be used to reproduce the enthalpies of formation of the donor—acceptor adduct.

By considering all combinations of many acids and bases, one can determine many more enthalpies than there are unknown values to be determined for the parameters E_A, C_A, E_B and C_B. The large number of simultaneous equations that can be written for each different donor—acceptor pair are solved by computer [2] to produce values [15] of E_A, E_B, C_A and C_B for each acid and base that give the best least squares fit of the calculated and experimental enthalpies of adduct formation (see Table 1). Substitution of the values for a particular acceptor and the values for a particular donor into eqn. (1) predicts, upon multiplication and addition, an enthalpy usually within ±0.1 kcal mole^{-1} of the experimental value. Nearly 400 enthalpies have been correlated by this approach. A total of 2000 can be predicted. By substituting the appropriate parameters from Table 1 into eqn. (1) the

TABLE 2

F-Strain systems (ΔH in kcal mole^{-1})

Acid	Base	$-\Delta H$ (E and C)	$-\Delta H$ (exp.)
$B(CH_3)_3$	$(CH_3)_3N$	24.5	17.6
$B(CH_3)_3$	$(C_2H_5)_3N$	26.0	10.0
$B(CH_3)_3$	$HC[CH_2CH_2]_3N$	26.7	19.9

scrambled donor strength ($-\Delta H$) orders $(CH_3)_2NH > (C_2H_5)_2O > (CH_3)_2S$ for phenol and $(CH_3)_2NH > (CH_3)_2S > (C_2H_5)_2O$ for iodine are obtained. If these accomplishments of the model are not convincing enough, further strong support comes from the proof [2] that the Hammett equation is a special (more restrictive) case of the E and C equation. Thus, this vast data base provides additional, quantitative support for eqn. (1).

Of even more interest than the systems that fit eqn. (1) are those that do not fit. If physical meaning can be attributed to the discrepancy between the calculated and experimental value, then we can be confident that the model has inherent meaning incorporated into it and is not simply using enough variables to reproduce the set of data. The F-strain systems reported by Brown [17] demonstrate this point. Since the strain is a function of the geometry of the adduct and not an inherent property of the acid or base, information about this effect will not be contained in the E and C numbers. Table 2 illustrates the difference between experimental and calculated enthalpies on these systems.

The discrepancy between the calculated and experimental enthalpies for the $(CH_3)_3BN(CH_3)_3$ system, which we attribute to steric strain, is in excellent agreement with the 7.8 kcal mole^{-1} of strain estimated by Brown from the heat of combustion of the analogous hydrocarbon [17]. These predictions of the E and C model are gratifying and suggest that inherent meaning regarding the enthalpy of interaction is contained in the parameters.

D. APPLICATIONS OF THE E AND C APPROACH

The main advantages to quantifying any body of data are the new insights provided by such an exercise. Obtaining a quantitative method for determining the existence and magnitude of steric effects in intermolecular interactions by use of the E and C model has already been discussed as an illustration of this idea. In this section other insights that can be obtained by this approach will be presented. One can conclude that since E and C indicates what is normal in sigma, coordinate bond formation, any experiments designed to probe bonding or structural effects on the reactivity of a chemical system (that is any bond strength related question) should be carried out in the framework of these studies. The use of the E and C model for understanding structure—reactivity relations will be illustrated in (i) synthetic studies in coordination and organometallic chemistry, (ii) quantitative studies of chemical reactivity and coordinate bond strengths, (iii) detection of various stabilization and destabilization effects in coordinate bond formation, (iv) determining thermodynamic quantities for steps in a chemical reaction that cannot be measured directly, (v) presenting a viable alternative to pK_B and donor number correlations, (vi) predicting the enthalpies of O_2 binding, a spin-pairing interaction, (vii) understanding the factors enhancing catalytic activity and selectivity.

(i) Synthetic studies in coordination and organometallic chemistry

It is important to emphasize that not all applications of the E and C model require an evaluation of $-\Delta H$ in non-polar solvents. Any situation in which an investigator previously would have used a qualitative hard—soft acid—base (HSAB) explanation of reactivity is amenable to an electrostatic—covalent rationalization. It has been shown that the two factors influencing coordinate bond formation are not related to each other in the way that hard is related to soft [18]. The hard—soft explanation fails to account for the E and C data set in a quantitative or qualitative way. Referring to the two effects as covalent and electrostatic eliminates the either/or aspect of the HSAB description and enables certain materials (e.g., CH_3NH_2) to be described as both strong electrostatic and covalent donors or acceptors. Nothing is both hard and soft [19]. In the qualitative rationalization of reactivity most of the essential conclusions of HSAB remain unchanged except those in which it was concluded that a substance is hard because it is not soft. Covalent and electrostatic properties are not mutually exclusive. If the E and C parameters are not known for a substance, all of the factors previously mentioned [9] as contributing to softness (low ionization potential, polarizable donor and large size) can be used to make predictions of covalency for relative comparisions. A strong electrostatic species is a molecule with high polarity or an ion with high charge and small size.

In this qualitative rationalization of reactivity it is important to emphasize that a great many factors besides bond strength considerations could contribute to the observation. Entropy effects, kinetic effects and solvation are often important considerations. One thus determines if the results parallel bond strength considerations and rationalizes them on this basis if they do. In this after-the-fact type of rationalization, it is very important to have an approach that does not work when solvation or entropy effects dominate. We shall next illustrate how the E and C parameters in Table 1 can be used in a qualitative way to insure that the rationalizations do not violate established trends.

The quantitative E and C parameters are very important in both the design and interpretation of any set of experiments involving acid or base variation.

If one is qualitatively attempting to characterize the reactivity of a new acid, for example the metal center in a model biological compound or a metal cluster, the binding of the bases trimethyl amine ($C = 11.5; E = 0.81$), pyridine ($C = 6.4; E = 1.2$), cage phosphite (or trimethyl phosphite) ($C = 6.4$; $E = 0.55$), tetrahydrofuran ($C = 4.3; E = 0.98$), and diethyl sulfide ($C = 7.4$; $E = 0.34$) should be investigated. If a reactivity order pyridine > tetrahydrofuran > $(CH_3)_3N$ > cage phosphite > diethyl sulfide were found, this would indicate an electrostatic acid because this order parallels the trend in E values. Other bases in Table 1 could be investigated to confirm this rationalization. If an order $(CH_3)_3N$ > diethyl sulfide > pyridine ~ phosphite > tetrahydrofuran were found this would indicate a covalent order. An improper selection of bases can lead to results that do not permit any conclusions to be drawn about the nature of the acid. This will be shown in the next section.

For most applications the base order will be dominated by both E and C. Cramer and Bopp [20] have devised a clever graphical scheme for illustrating the different donor (or acid) orders that can be obtained as the covalent and electrostatic nature of the acid (or base) is varied. Factoring and rearranging [19] eqn. (3) leads to

$$\frac{-\Delta H}{C_A + E_A} = \frac{C_B + E_B}{2} + \left(\frac{C_B - E_B}{2}\right)\left(\frac{C_A - E_A}{E_A + C_A}\right) \tag{4}$$

If one plots $-\Delta H/(C_A + E_A)$ vs. $(C_A - E_A)/(E_A + C_A)$ a straight line will result for the interaction of a given base with various acids. The line for any base in the E and C correlation can be constructed by calculating $-\Delta H$ for this base interacting with iodine and phenol. Substituting the enthalpy for the iodine adduct into eqn. (4) along with the appropriate E and C values gives one point on the line. Repeating the procedure for the phenol adduct leads to the second point to permit drawing of the line. This procedure has been carried out for a series of bases leading to Fig. 1. The quantity $-\Delta H/(C_A + E_A)$ on the vertical axis can be viewed as an inherent donor strength normalized (by the denominator) for interaction with various acids. We shall abbreviate this fraction as S_B. The horizontal axis is a scale that indicates the relative importance of the covalent or electrostatic nature of the acid. The range is from +1 for a purely covalent acid ($E_A = 0$) to −1 for a purely electrostatic acid ($C_A = 0$). This fraction $(C_A - E_A)/(C_A + E_A)$ will be abbreviated as R_A. If the value of R_A is known, the donor strength order can be read from the graph. If the donor order is known, the approximate R_A value (that is the relative importance of covalent and electrostatic interaction) can be deduced. Accordingly, this plot will be referred to as a donor order plot. The donor order for iodine is obtained by reading the bases on the S_B axis at $R_A = 0$ (for I_2, $C_A = 1$ and $E_A = 1$): $CH_3CN < NH_3 <$ THF < cage phos < $C_5H_5N < (C_2H_5)_2S < (CH_3)_3N$.

In a qualitative application, determination of a basicity order with a few key experiments permits one to locate the position of the acid on the R_A

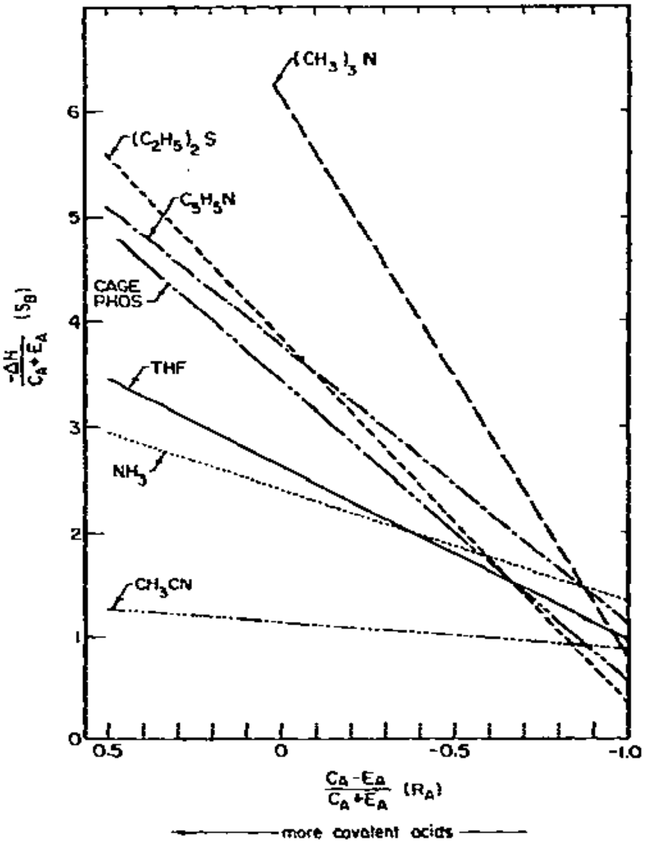

Fig. 1. A plot showing various base orders (vertical axis) as the covalent—electrostatic properties of the acid (horizontal axis) change.

axis. Predictions of the donor order of other bases can be read from the plot. Any base whose E_B and C_B parameters are known can be readily added to this plot. We also see from Fig. 1, that in order for base donor orders to reverse with change of acid, the plotted lines must cross. The many different orders that can be obtained are illustrated by the large number of intersecting lines. Since the THF line is above and does not cross CH_3CN, the result $CH_3CN > THF$ would indicate that an unusual stabilization effect (not sigma bonding) must exist in the CH_3CN compound (for example, π-backbonding) or a destabilizing effect exists in the THF compound (e.g., a steric effect).

We note by examining the respective E_B and C_B numbers or by looking at Fig. 1, that in a sigma interaction, pyridine will be a stronger donor than phosphite. If a result obtained is phosphite > pyridine, stabilization from π-backbonding is suggested because neither domination by the C number nor the E number would lead to this result. The base $CH_3(CO)N(CH_3)_2$ will always be stronger than $CH_3COOC_2H_5$ because both the E and C number of the former is larger. If a series of bases is selected for study whose donor order lines do not intersect, one cannot infer anything about the R_A property of the acid. Such strategy amounts to very poor experiment design. An order in which steric effects are absent and which makes no sense in terms of the above types of considerations for a series of bases in Table 1 (that is, the order can't be found in a plot like Fig. 1) would suggest a dominance of the chemistry by an effect other than donor strength.

Similar plots [10] can be made to give acid orders and these plots will be referred to as acceptor order plots.

The above discussion illustrates that in this type of qualitative application, the *E* and *C* approach (electrostatic—covalent) has many more similarities to HSAB than there are differences. This point can be missed by reading the literature for the tendency has been to focus on the differences that exist in the two approaches. Indeed if one uses the terms soft (for the *C* value) and charged (for the *E* value) the description is valid in the covalent—electrostatic context.

The next set of qualitative applications are some in which the *E* and *C* advantage of predicting relative magnitudes of interaction are important. Consider first the kinetic *trans* effect order : [21] CO, $C_2H_4 > PR_3, SR_2 > NH_3$, Py $> H_2O$. With CO a weak sigma donor appearing as the strongest base, the order indicates a pronounced dependence on π effects which are present in the CO, PR_3 and C_5H_5N adducts. Referring to Fig. 1 (with H_2O added) the order $R_2S > NH_3 > H_2O$ suggests that the sigma bonding component of the *trans* effect has considerable covalency in the interaction with an R_A value of -0.5 or more. (Most first-row metal complexes have an R_A value of -0.75 or less.) Using the *E* and *C* values to add other bases to Fig. 1, we predict a *trans* effect order for sigma donors of: $R_3N > RNH_2 > NH_3 >$ THF $> Et_2O >$ DMA $> CH_3C(O)OCH_3$.

Fowkes has pioneered [22] the qualitative and semiquantitative application of the *E* and *C* model to problems of adhesion. Predictions of the best polymer supports for binding substrates (for example, polymer tapes to bind iron oxide) have been made by estimating interactions for the functional groups in the polymer with the substrate by using model compounds in the *E* and *C* list. The same approach can be used to select supports to be used in high pressure liquid chromatography separations. A retention order of bases by the support can be used to estimate the support R_A value. Predictions of the binding order of other bases with functional groups in the *E* and *C* correlation can then be made. Selection of a support that maximizes the difference in the S_B value should improve the separation. Many factors exist that could lead to reversals in the prediction of small differences. However, this procedure does provide a rational approach to a complicated problem.

With these examples, we see unique ways in which the quantitative studies leading to the *E* and *C* formulation can be used to reach important conclusions for the qualitative understanding of structure—reactivity relations. In the context of the total picture of structure—reactivity relations, the following types of applications are also unique to the *E* and *C* approach.

(ii) Quantitative studies of chemical reactivity and coordinate bond strengths

As previously mentioned, the E and C approach can be used to predict the enthalpies of interaction of 2000 acid—base pairs (50 base parameters and 40 acid parameters). In terms of the following type of displacement reaction

$$AB + B' \rightarrow AB' + B \text{ or } AB + A' \rightarrow A'B + A$$

over 176,000 enthalpies can be predicted (the general formula is $nm(n + m - 2)$ where n is the number of acids and m the number of bases). Enthalpies for 1,911,000 (the general formula is $\frac{1}{2}nm[(nm) - (n + m - 1)]$) displacement reactions of the form

$$AB + A'B' \rightarrow A'B + AB'$$

can be predicted. The above analysis constitutes a conservative estimate of the predictive power of the E and C method. For example, the difference between the E or C values of analogous methyl and ethyl substituted compounds is slight. Subtracting 3% of the C value and 5% of the E value from $(C_2H_5)_3S$ or $(C_2H_5)_3N$ (if the ethyl derivative is most accurately known) leads to reasonable predictions of the enthalpies of the analogous methyl compound. Larger alkyl substituents than ethyl bound to a functional group have E and C values comparable to those of the ethyl derivatives and, in the absence of steric effects, donors with ethyl or larger alkyl group have comparable enthalpies of interaction with Lewis acids. As a result of this similarity, the parameters for an ethyl derivative can be used to predict the donor strength of a functional group in a polymer.

Using Hammett substituent constants, one is in a position to use reported procedures [2] to calculate the E and C parameters for any substituted phenyl derivative of an acid or base if E and C parameters are known for the unsubstituted phenyl derivative. Thus, the parameters in Table 1 are applicable to an even larger number of systems than are indicated there.

New acids or bases are readily incorporated into the scheme. Recommended solvents [3] should be employed for enthalpy measurements to insure that complications from solvation are minimal. In certain cases, corrections can be made that permit study in more polar solvents [23]. To incorporate a new acid, one would measure four or more enthalpies of adduct formation using bases with known E_B and C_B values with as wide a range in the ratio of C_B/E_B as possible. The four or more simultaneous equations of the form of eqn. (1) are solved for the two unknowns E_A and C_A. One must be careful to select systems that involve normal sigma bond formation without F-strain to obtain meaningful parameters. A graphical representation of the solution of the simultaneous equations is referred to as an E vs. C plot and serves to illustrate the quality of the fit. Rearranging eqn. (1) we obtain

$$-E_A = C_AC_B/E_B + \Delta H/E_B \qquad (5)$$

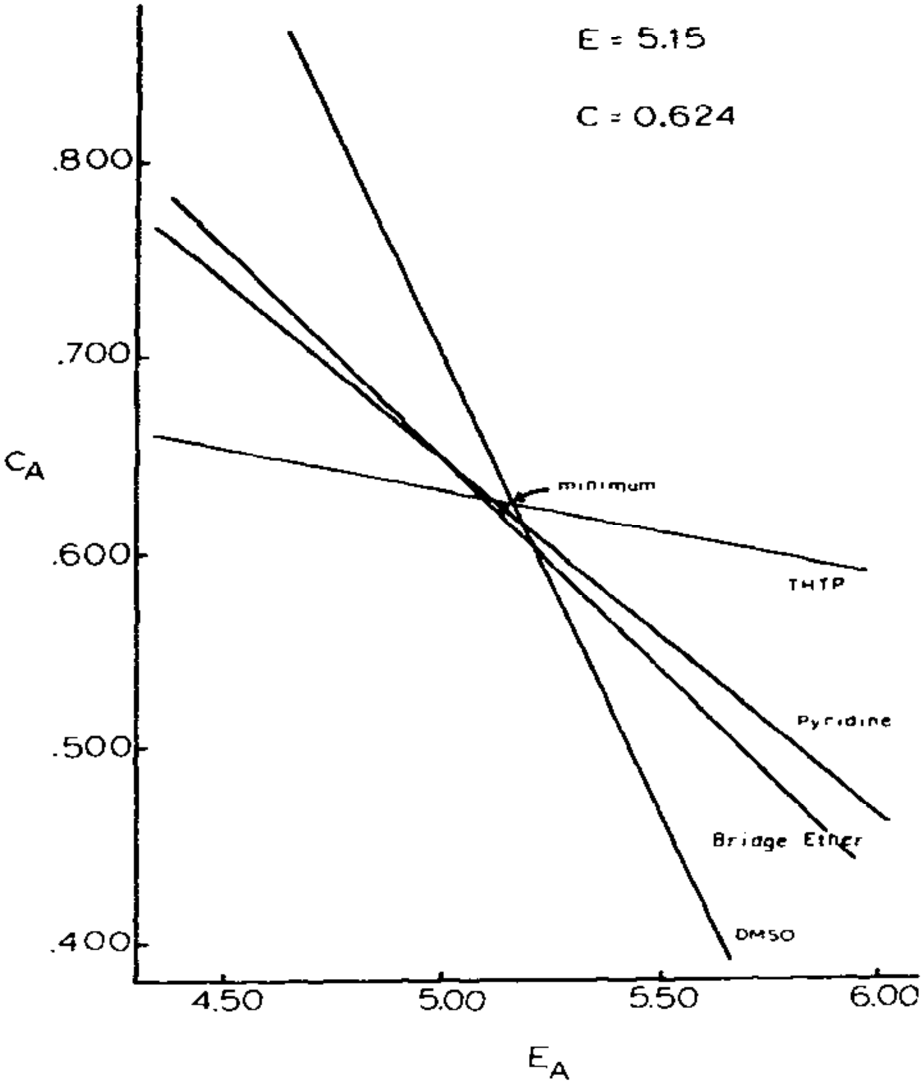

Fig. 2. An E vs. C plot for zinc tetraphenylporphine.

Measuring enthalpies of adduct formation of the new acid with bases whose E_B and C_B values are known, leaves E_A and C_A as the only unknowns in this equation. Selecting various values of C_A one can calculate the corresponding value of E_A. This procedure is illustrated with the enthalpy data reported by Vogel and Stahlbush [24] for zinc(II) tetraphenylporphine. Plotting various values of E_A corresponding to selected C_A values produces a line in Fig. 2. The same procedure employing a second base produces a second line whose intersection with the first line is the solution of the two simultaneous equations. Note the slope of these lines, given by C_B/E_B, should differ as much as possible. When data for several bases are plotted, the slopes should vary and the intersections should occur in a small region. (See Fig. 2 for an excellent data set.) A least-squares technique is employed to determine E_A and C_A as well as their error limits. New bases can be incorporated by a similar procedure.

If one is interested in a quantitative understanding of the coordination tendencies of a system, enthalpy data must be obtained. The data in Table 1 should be used in the design of the experiments to select acids or bases with a varying C/E ratio. When the C/E ratios of the acids or bases used are similar, the plot of eqn. (5) leads to parallel lines and no information of value in characterizing the reactivity of an acid is obtained. Many literature reports suffer from this shortcoming.

There are reported studies [25] in which data have been measured in poorly solvating solvents, but no check has been made to see if the results obey the E and C equation. Some of the systems reported are very similar to those in the E and C analysis, but the reported data do not obey eqn. (1). In all reported instances to date where this kind of discrepancy exists, the experimental data have been found to be glaringly deficient either in terms of experimental design or analysis. A quick check of the lack of consistency of the enthalpy data with eqn. (1) and a reexamination of the quality of the data and design of the experiment would have prevented the publication of incorrect results in these cases. Real deviations from eqn. (1) will exist and when they are discovered, independent spectroscopic or other experiments can be designed to elucidate unusual bonding contributions (see section D(iii)). At any rate, the E and C approach is established as an indispensable tool for the design of experiments and interpretation of thermodynamic data related to coordination.

(iii) Detection of various stabilization and destabilization effects in coordinate bond formation

Chemical reactivity and intermolecular interactions are much more complicated than normal sigma bond formation between a Lewis acid and base. Thus, it does not detract from the E and C model when exceptions are found. Indeed, an important strength of the model is its ability to provide a quantitative basis for recognizing stabilizing and destabilizing effects in chemical bonds.

The E and C equation has been used to detect the presence of steric effects in several systems besides those used in Table 1. One does not simply relate a deviation between calculated and observed enthalpy to a steric effect. For example, a steric effect for an acid toward $(C_2H_5)_2O$ as a donor is indicated when the discrepancy between the calculated and experimental enthalpy is larger for this donor than for tetrahydrofuran. Such a result was obtained for the adducts of $(CH_3)_3SnCl$ with these oxygen donors [26].

Since the limitations of the *E* and *C* model have not been established rigorously, one should not attribute any miss of a calculated value to some bonding effect. Spectroscopic or other experiments should be designed to probe the suspected source of the discrepancy. This approach is illustrated in a recent article [27] in which it was demonstrated that metal—metal bonding in the acid $Rh_2(RCO_2)_4$ enhances the tendency for π-back-bonding into the coordinated base B of $Rh_2(RCO_2)_4 \cdot B$. Extra stabilization over that expected from the σ-bond *E* and *C* prediction was found for the donors pyridine and CH_3CN and was suspected to arise from metal to ligand π-back-bonding. This was confirmed electrochemically. Oxidation of $Rh_2(RCO_2)_4$—B involves removal of the π^* (essentially metal) electron and this removal is more difficult than expected on the basis of the σ-interaction in those systems in which the π^* orbitals were suspected of being involved in back-bonding.

Other confirming types of experiments that can be carried out to detect unusual effects parallel those described above for detecting steric effects. A series of systems in which varying contributions from the suspected effect exist would be studied. The magnitude of the discrepancy between the calculated (*E* and *C*) and measured enthalpies should parallel the expected trends in the magnitude of the effect. For example, a greater discrepancy from metal to ligand back-honding should result when the base $(RO)_3P$ is studied than that when R_3P is studied (where R is alkyl). A series of experiments of this type are needed to confirm the suspected [13] π-stabilization in the interaction of a phosphite donor with methylcobaloxime.

There are many systems in inorganic chemistry in which a donor—acceptor interaction is accompanied by an antiferromagnetic coupling of unpaired electrons on the donor and acceptor. For example, in the bonding of nitric oxide to a transition metal forming a linear nitrosyl, electron pair donation from an *sp* orbital on nitrogen is accompanied by a pairing up of the unpaired electron in the π-orbital of nitric oxide with a metal electron. Similar interactions occur in complexes [28] of stable free radical nitroxides, R_2NO, in which electron pair donation from an *n* orbital on oxygen is accompanied by an antiferromagnetic coupling of the nitroxide unpaired electron with a metal electron. The essential orbital interactions for a simple case are shown in Fig. 3. Specific examples involve the adduct formed between $Cu(hfac)_2$ or $VO(hfac)_2$ and TMPNO (see Table 1). To what extent, if any, is the metal—ligand bond in these systems stabilized by the antiferromagnetic exchange interaction? In order to answer this question for the nitroxide systems described above, the E_A and C_A parameters of $Cu(hfac)_2$ and $VO(hfac)_2$ were determined by studying their enthalpies of adduct formation with diamagnetic bases. The E_B and C_B parameters for the free radical base were determined by studying its enthalpy of adduct formation with diamagnetic acids. All three systems gave an excellent fit to the *E* and *C* equation. The contribution to the stability of the $VO(hfac)_2 \cdot$ TMPNO [29] or $Cu(hfac)_2 \cdot$ TMPNO adduct [30] from the antiferromagnetic interaction would be reflected as a larger experimental value for the enthalpy of formation of

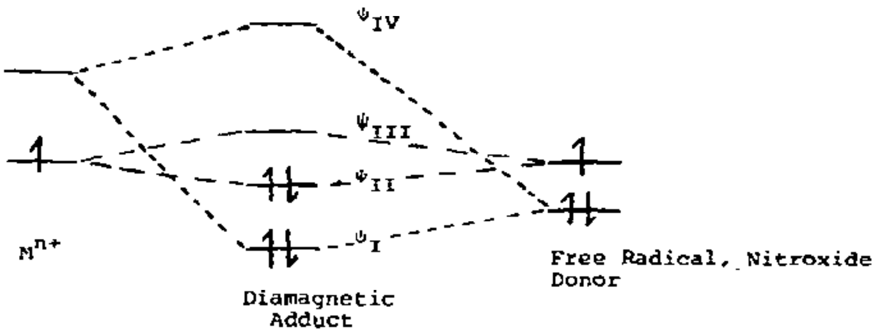

Fig. 3. A molecular orbital description of an antiferromagnetic interaction.

these adducts than that predicted by substituting the E and C parameters, determined on systems where this effect is absent, into eqn. (1). No extra stability was detected. The antiferromagnetic interaction was attributed more to a destabilization of the vacant molecular orbital associated with this interaction (ψ_{III} of Fig. 3) than to a bond stabilization (lowering ψ_{II} of Fig. 3) [29].

(iv) Determining thermodynamic quantities for steps in a chemical reaction that cannot be directly measured

Most chemical reactions are more complex than the simple reaction type

$$A + B \rightleftharpoons AB \tag{6}$$

treated above. A next stage in complexity would be reactions

$$A_2 + 2\ B \rightarrow 2\ AB \text{ (with B varied)} \tag{7}$$

or

$$AB + B' \rightarrow AB' + B \tag{8}$$

where A is held constant in a series of reactions with varying donors B′. These two, and many other reactions, are characterized by having a constant energy step involved in the reaction in addition to the varying energies associated with coordinating different donor molecules. In the first reaction type shown (eqn. (7)), the constant energy is associated with cleavage of the dimeric acid A_2 and in the second reaction type (eqn. (8)) displacement of B (cleavage of the A—B bond) is the common step. There is no way that this constant energy contribution can be incorporated into the E_A and C_A parameters. For example an equation of the following type, where k and k' are attempts to incorporate the constant contribution, would give a variable contribution as the base C_B and E_B values are changed.

$$-\Delta H = (E_A - k)E_B + (C_A - k')C_B = E_AE_B + C_AC_B - kE_B - k'C_B$$

Instead this constant energy term must be written into the equation as a constant.

$$-\Delta H + W = E_A E_B + C_A C_B \tag{9}$$

For a new acid A_2, enthalpies for the reaction in eqn. (7) can be determined for several bases whose C_B and E_B values are known. The resulting simultaneous equations can be solved for E_A, C_A and W. This procedure, referred to as the constant W approach, was checked [31] on several systems in which the W value is known. It has been used to provide enthalpies of dissociation of the chlorobridged dimers, $[(CO)_2RhCl]_2$ [32], $[(COD)RhCl]_2$ [33] (where COD represents cyclooctadiene) and $[(\pi\text{-allyl})PdCl]_2$ [34] of 22.6, 12.6 and 6.2 kcal mole^{-1} respectively. The resulting E_A and C_A parameters pertain to the monomeric fragments. The constant W approach can be used to factor out the constant energy associated with any particular step that exists in a series of adduct formation reactions.

(v) A viable alternative to pK_B *and donor number correlations*

In literature articles, the motivation for reporting plots of pK_B or donor numbers vs. some measured property is to determine if the property varies in a systematic way with sigma bond strength as a base (or acid) is changed in a series of experiments. The measured property often involves equilibrium constants, rate constants, thermodynamic parameters measured in polar solvents or some spectral change. In view of the reasons presented at the beginning of this article, pK_B's and donor numbers are not reliable estimates of sigma bond strengths so it becomes ludicrous to interpret deviations from these correlations with bonding arguments. The E and C correlation, as a reliable indicator of sigma bond strengths, affords an excellent standard for this type of application. This standard overcomes all three of the objections to pK_B data cited earlier. The approach will be demonstrated with a series of general spectral changes, $\Delta\nu$, for an acid coordinating to a base. In order to determine if these changes are dominated by sigma bonding considerations, one would write for those systems where only sigma contributions exist

$$\Delta\nu + W = \text{“}E_A\text{”}E_B + \text{“}C_A\text{”}C_B \tag{10}$$

where W can be zero.

The quotation marks indicate that “E_A” includes any conversion factors needed to convert E_B to a frequency in addition to the response in $\Delta\nu$ caused by coordination of the base. As a result, “E_A” and “C_A” cannot be used to predict enthalpies and their use must be specified. This equation allows for the entire range of base donor orders encompassed in the E and C analysis (Fig. 1). For each base studied, one of a series of simultaneous equations is written. The set is solved for the two unknowns “E_A” and “C_A” [35].

To illustrate this approach, an attempt was made to correlate the differ-

TABLE 3

Experimental and "E_A", "C_A" calculated chemical shifts for $CHCl_3$ adducts

	Exp. $\Delta\nu$ (ppm)	Calc. $\Delta\nu$ [a]	Difference
Quinuclidine	1.15 ± 0.1	1.24	+0.09
Cage phosphite	0.19 ± 0.05	0.73	+0.54
$[-CH_2CH_2-]S$	0.75 ± 0.03	0.69	+0.06
$(C_3H_5)_3N$	1.51 ± 0.04	1.29	−0.22
$(C_2H_5)_2O$	0.605 ± ?	0.76	+0.15
THF	0.84 ± 0.02	0.86	+0.02
C_5H_5N	1.36 ± 0.07	1.12	−0.24
CH_3CN	0.48 ± 0.04	0.63	+0.15
$(CH_3)_2CO$	0.96 ± 0.01	0.76	−0.20
$(C_2H_5)_2S$	0.77 ± 0.09	0.66	−0.11
$CH_3COOC_2H_5$	0.66 ± 0.06	0.71	+0.05

[a] $\Delta\nu = \nu_{B-HCCl_3} - \nu_{HCCl_3}$. Calc. $\Delta\nu$ is obtained by substituting $W = 0$, "E_A" = 0.62, "C_A" = 0.061 into eqn. (10) along with reported E_B and C_B values.

ence in the chemical shift of free chloroform and a series of Lewis base adducts, $\Delta\nu$, with the E_B and C_B parameters of the base. The original data from ref. 36 is summarized in Table 3 along with the frequencies calculated by using the best fit parameters of "E_A" = 0.62, "C_A" = 0.0609 and $W = 0$. Compared to the accuracy of the numbers, the differences between the calculated and experimental values of $\Delta\nu$ is large and the fit unacceptable. When W is non-zero and is allowed to vary, the improvement is slight and still unacceptable. The absence of a correlation between the chemical shift and the sigma bonding properties of the donors is in agreement with the literature interpretation of the data [36]. Donor anisotropic contributions to the proton shifts resulted in the lack of correlation.

On the other hand, when the shift in the O—H stretching frequency of *t*-butanol upon hydrogen bonding to a series of bases [37] is analyzed, the data are well fit with "E_A" = 165.5, "C_A" = 27.3 and $W = 125$ cm^{-1}. This correlation is not too surprising since ΔH and $\Delta\nu$ are linearly related for the bases selected. However, it should be emphasized that eqn. (10) could permit a correlation of a spectral shift that did not parallel $-\Delta H$. If, for example, covalency should be weighted more in terms of influencing the spectroscopy than it is for $-\Delta H$, this fact can be incorporated into the "C_A" parameter.

The widely publicized donor number approach [4] involves a basicity scale determined from the enthalpies of interaction of donors with $SbCl_5$ in 1,2-dichloroethane. This is a single scale basicity order and suffers the limitations previously described for such approaches. Furthermore, it has been shown [38] that there are extensive solvation contributions to enthalpies measured in this solvent for the $SbCl_5$ adducts [38] and adducts of other acids [39]. When attempts [40] are made to fit donor numbers to an

E, C and W analysis; DN = "E_A"E_B + "C_A"C_B, further evidence for solvation contributions is obtained. Reference 40 can be consulted as an example of how an E and C analysis on a system can provide insights regarding the existence of effects other than sigma bond contributions. Conditions are described which could lead to linear plots of DN vs. some measured properties. These conditions, like parallel lines in an E vs. C plot, result in no information about the domination of sigma bond strengths on the measured property.

The red shifts in the Soret band of zinc tetraphenylporphyrin upon base coordination [41,42] have also been recently analyzed by the E and C approach [40]. No general correlation was obtained indicating that the differences could not be attributed to sigma bond strengths. When a limited data set was utilized a good correlation could be obtained in which the trend was dominated by the base electrostatic term. The limited data set probably reflects a minor trend of a more complex phenomenon. More systems that do not conform to the correlation are needed in order to detect patterns in the exceptions. An earlier analysis [42] of this data set based on a combination of parameters that include solvation and other effects concluded that polarizability (our C-term) dominated the trend observed for the limited data set. This serves to illustrate the point that there are enough parameters in the literature which when taken in combination can fit most anything. However, if the parameters include contributions from many effects (solvation, entropy, etc.), there is no fundamental significance of meaning to the existence of a correlation.

When one attempts to correlate complicated phenomena (ΔG's, $\Delta\nu$'s, etc.) with bond strengths, it should be no surprise to find the absence of a correlation. The phenomena could be dominated by considerations not related to bond strength (entropy effects, solvation and other factors). It is also possible that electrostatic and covalent effects have a different functional dependence on the property being measured than they do on bond strengths and this would lead to a lack of correlation. At any rate, the approach described in this section does provide valid insights of the type one would have incorrectly hoped to obtain with a pK_B (or pK_a) or donor number plot in the past.

(vi) Predicting the enthalpies of O_2 binding — a spin-pairing interaction

The binding of dioxygen to transition metal ions has been studied extensively in view of the importance of this interaction in hemoglobin and other biological systems. It is now widely accepted that the interaction involves the pairing up of unpaired electron(s) on O_2 with unpaired electron(s) on the metal forming a bonding molecular orbital(s) [43]. As such it is not a Lewis acid—base interaction. Thermodynamic data relevant to this interaction have been obtained. Enthalpies of formation of a series of base adducts of cobalt(II) protoporphyrin(IX) dimethylester [Co(II)(por)] have been reported [12].

$$\mathrm{Co(II)(por)} + \mathrm{B} \rightleftharpoons \mathrm{B{-}Co(por)} \tag{13}$$

The Lewis acid Co(II)(por) obeys the E and C equation with E_A and C_A parameters of 4.44 and 0.58 respectively. Data for several of these five coordinate base adducts binding O_2 *trans* to the base to form six coordinate complexes have also been determined [12].

$$\mathrm{B{-}Co(por)} + \mathrm{O_2} \rightleftharpoons \mathrm{B{-}Co(por){-}O_2} \tag{14}$$

The adducts are stable only at low temperatures and/or high pressures so the measurements are very difficult and time consuming. It would be of interest to be able to predict the enthalpy of O_2 binding for bases that have not been measured. This system is not directly amenable to an E and C treatment because the cobalt—B complex is changed for each O_2 complexation reaction. Furthermore, O_2 coordination involves spin pairing and not electron pair donation as in the other systems contained in E and C. It is possible to view the formation of an O_2 adduct (in a thermodynamic sense) by the following series of steps

$$\mathrm{Co(por)} + \mathrm{O_2} \rightleftharpoons \mathrm{Co(por){-}O_2} \tag{15}$$

$$\mathrm{Co(por)\,O_2} + \mathrm{B} \rightleftharpoons \mathrm{B{-}Co(por){-}O_2} \tag{16}$$

The first step can be considered a constant W process and the second a coordination of the base to the Lewis acid, Co(por)O_2. A mathematical derivation based on these steps has been reported [12] which indicates that the enthalpies of oxygen binding (eqn. (14)) can be fit to an equation of the form

$$-\Delta H_{O_2} = -W + \Delta E_A E_B + \Delta C_A C_B \tag{17}$$

where W is the constant enthalpy corresponding to eqn. (15), $\Delta E_A = E_A(2) - E_A(1)$, $\Delta C_A = C_A(2) - C_A(1)$, $E_A(1)$ and $C_A(1)$ are values for the Lewis acid Co(por) (eqn. (13)) while $E_A(2)$ and $C_A(2)$ are values for the Lewis acid Co por—O_2 reacting with bases (eqn. (16)). The fit of the experimental enthalpy data is shown in Table 4. Values of $W = -1.5$, $\Delta E_A = 2.9$ and $\Delta C_A = 0.6$ are obtained. Substitution of these values into eqn. (17) along

TABLE 4

Enthalpies of dioxygen binding to Co(por)B as a function of axial base variation

Axial base	$-\Delta H_{O_2}$ (exp.)	$-\Delta H_{O_2}$ (E, C and W)
1-Methylimidazole	10.0	9.8
Pyridine	8.0	8.9
$\mathrm{O{-}P[N(CH_3)_2]_3}$	8.9	8.1
N,*N*-dimethylacetamide	6.6	6.9
Tetrahydrothiophene	7.6	7.4

with the reported E_B and C_B values for the more than 50 bases in this correlation, enables the calculation of the enthalpies of dioxygen binding for all these systems. The W value, that is the enthalpy of eqn. (15), is consistent with the fact that axial base is required for O_2 binding to Co(por) at −40°C. In these systems the entropy of O_2 binding is about 40 eu so a larger enthalpy would be required to produce a negative ΔG. The values of ΔE_A and ΔC_A provide some interesting insights. Since E_A (1) and C_A (1) were found to be 4.44 and 0.58 respectively from the thermodynamic data determined for eqn. (13), E_A (2) and C_A (2) are calculated to be 7.3 and 1.2 respectively from the ΔE_A and ΔC_A values. The acidity of the cobalt is approximately doubled by coordination of the dioxygen to form Co(por)—O_2. By comparing the fractional contribution of the $\Delta C_A C_B$ term (eqns. (14) and (17)) to the total enthalpy of dioxygen binding with the fractional contribution of $C_A C_B$ to the enthalpy of base adduct formation (eqns. (3) and (13)), covalency is seen to be slightly more important in influencing the trends for the former interaction.

(vii) Application of the E *and* C *equation to problems in catalysis*

The E and C approach has considerable potential as an important tool for the understanding of catalytic processes. Since data are not available to illustrate this application, this section will deal with a formulation of the basic approach. Many catalytic reactions can be described by the following general reaction type.

$$\mathrm{A + B \rightleftharpoons AB} \tag{18}$$

$$\mathrm{AB + S \rightarrow ABS \rightarrow D + A} \tag{19}$$

The net reaction involves the catalysis by A of B plus S to produce D. The species A can be a conventional Lewis acid or an acidic site on a solid surface. Often a competing reaction to form products other than D can occur. A very large number of catalytic reactions are encompassed by these general equations. Accordingly, the importance of understanding the coordination step is also illustrated. The methods described in earlier sections indicate the approach to understanding the first step (eqn. (18)) of the reaction. More data involving small molecule binding are needed for systems in which small molecule activation occurs. The E and C studies can also be readily extended to the interactions of substrates with solid Lewis acid (base) catalysts. Successful correlations can be anticipated for sigma donors (acceptors) with solid acids (donors) if the interactions of this acid center with neighbor atoms in the condensed phases are the same prior and subsequent to coordination. If the interactions in the solid phase change upon coordination, the E and C model will apply if the change parallels the strength of binding. If two sites exist in the system with comparable acidity or basicity (close enough so as not to be distinguished in the experimental measurement of chemisorption) the model will work and average E and C parameters will result. In a homogeneous $Cu(hfac)_2$ system, a similar problem arose [44] when two isomeric adducts were found to exist. Because of the similarity in the strength and nature of the acid—base interaction in both instances, the same E_A and C_A parameters applied to both adducts.

The next step in extending the E and C model to catalysis involves measuring the reactivity imparted by coordination (the second step, eqn. (19)). In the past, the catalytic activity of A has been interpreted in terms of the strength of the A—B interaction. Knowing that this interaction is dominated by both electrostatic and covalent interactions it is reasonable to expect that the perturbation made on B causing it to be susceptible to reaction with S will also be dominated by both effects. Once a quantitative measure of the reactivity has been selected, the E and C formulation of the problem now becomes comparable to the approach used in the previous section on dioxygen binding. The reaction of S + B is treated (in a thermodynamic sense) as a constant with the observed reactivity being dominated by a varying A plus SB interaction. E_B and C_B values could be determined for SB as described for $Co—O_2$ in the previous section. The relative importance of the covalent or electrostatic properties of the acids in influencing catalysis can then be deduced by systematic variation of A. It is conceivable in processes involving competing reactions, that the relative importance of the two paths depends upon the C or E nature of perturbation made by the catalyst upon the substrate. Information relative to catalyst design for enhanced selectivity would result. Clearly, the collection of experimental data that will permit this type of analysis provides a systematic way to approach the design of catalysts with improved efficiency and selectivity.

The activation of dihydrogen is a fundamental step in hydrogenation reactions. Important information can be obtained from an E, C and W analysis. For example, in the rhodium(I) system, we are in the process of obtaining thermodynamic information on the following reactions.

$$[P_2RhCl]_2 + 2\,B \rightarrow 2\,P_2RhClB \qquad (20)$$

$$P_2RhCl \cdot B + H_2 \rightarrow P_2RhH_2Cl \cdot B \qquad (21)$$

As shown earlier, study of reactions similar to that in eqn. (20), provide the bridge cleavage energy in addition to E_A and C_A parameters for "P_2RhCl". The enthalpy data for eqns. (20) and (21) can be treated analogous to the dioxygen binding system with the following reaction corresponding to the constant W process.

$$P_2RhCl + H_2 \rightarrow \text{“}P_2RhClH_2\text{”} \qquad (22)$$

The enthalpy of base coordination to this species compared to that toward P_2RhCl will provide quantitative insight into the modifications that have occurred in the acidity of the rhodium center as a result of the oxidative addition. It will also provide very important quantitative data on the influence of metal—base coordination on the stability of the metal—hydrogen bond. It should be emphasized that detailed insights and interpretations of the type just discussed could not be extracted from the thermodynamic data without the *E*, *C* and *W* model.

E. MEANING OF THE PARAMETERS AND A THEORETICAL JUSTIFICATION FOR THE *E* AND *C* EQUATION

It has been shown that the approach employed by Mulliken in the analysis of the charge transfer spectra of Lewis acid—base adducts can be used to derive the *E* and *C* equation [45] providing theoretical justification for the empirical success of eqn. (3). Using a vacant orbital on the acid and the lone pair orbital on the base as the basis set, a two by two secular determinant is solved for the energy change upon adduct formation. Introducing assumptions invoked in doing perturbation theory, one can derive an expression which has the same form as the *E* and *C* equation (eqn. (3)). The one center terms in the derived equation are the counterpart of the electrostatic interaction in the ionic—covalent model and the two center terms correspond to covalency [45].

Hudson and Klopman [46] derived an expression for the initial change in the energy of a system upon incipient adduct formation that also consists of an electrostatic term and a covalent term. The former depends upon charge densities and radii of the donor and acceptor atoms and the latter on overlap, symmetry and orbital energies of the donor (HOMO) and acceptor (LUMO).

The Mulliken-based analysis is a simplified one that does not include, for example, the change in geometry that invariably occurs in the acid or base upon coordination. Energy is required for these perturbations and this energy is provided by the increased strength in the donor—acceptor bond in the adduct. In several systems it has been shown that these changes are directly proportional to the enthalpy of adduct formation. Upon hydrogen bond formation an infrared study shows that the X—H force constant decreases in direct proportion to the enthalpy of adduct (X—H ··· B) formation [47]. An nmr study of the changes in $J_{\mathrm{Sn-H}}$ in a series of $(CH_3)_3$ SnCl adducts indicates that the Sn—C hybridization change is proportional to the enthalpy of adduct formation [48]. The B—F distance lengthens and the F—B—F angle decreases more for BF_3 adducts of strong donors than for weak ones [49].

It can be demonstrated mathematically that any effect, *k*, that is proportional to the strength of the donor—acceptor interaction is readily incorporated into the *E* and *C* equation. The *E* and *C* parameters are in effect $E = E' - k$ and $C = C' - k$; here E' and C' would be the parameters in the absence of an energy requirement and *k* relates to the proportional energy requirement. The incorporation of this proportional effect can be seen by expanding the *EE* term. For the base, the term $-k_BE_A$ corresponding to rearrangement of the base is incorporated into E_B as an effect that is proportional to the strength of the acid E_A. Thus both acid and base polarizations that are directly proportional to the strength of the interaction are readily included [50] in the E_AE_B term as either a positive or negative quantity (usually a net stabilizing effect results). A similar contribution can be incorporated into the C_AC_B term. Clearly any effect in an acid or base whose magnitude is proportional to the strength of interaction is readily incorporated into the E and C parameters. This situation is to be contrasted to the constant energy contribution discussed in the section on the constant W approach. We can conclude that if the acid—base rearrangement energies were a constant, the system would not obey the E and C equation.

In a complete quantum mechanical analysis of an acid—base interaction one can list many factors involved in the interaction. The mathematical analysis involved in the E and C model clearly shows that only two independent effects are required for the interpretation and prediction of bond energies for the adducts in the correlation. Thus the many different contributions are not independent but interrelated to form two groups. Should our knowledge increase to the point where the independent factors can be evaluated quantitatively and grouped into two independent terms, a procedure for carrying out a matrix transformation to accommodate this new model has been reported. In the meantime, a solution has been selected which models our qualitative ideas about the importance of ionic and covalent contributions to adduct stability.

The general concept of a bond consisting of electrostatic and covalent contributions is at best a semi-quantitative idea that makes it convenient for chemists to discuss bonding. For this reason, as well as the other factors discussed above that can be incorporated into the parameters, we do not expect our parameters to give a quantitative break-up of the enthalpy into these quantities. Since the parameters do mirror our qualitative ideas about the covalent and ionic nature of the interaction, they provide a basis for this qualitative type of discussion.

In solving the data set that led to the E and C values, two of the four parameters fixed were $C_A = 1.00$ and $E_A = 1.00$ for iodine. Thus it is not possible to make a direct comparison of the C value and the E value for a given acid or base. We can only compare trends in the C values or the E values for a series of acids or bases. For example, phenol with an E_A value of 4.33 is much more electrostatic in its interactions with bases than iodine with E_A = 1.00. Similarly, diethylsulfide ($C_B = 9.40$) is more covalent and less electrostatic ($E_B = 0.339$) in its interaction than diethylether ($C_B = 3.25$ and $E_B = 0.990$). The causes for the changes in the donor orders of $(CH_3)_3N$, $(CH_3)_2S$ and $(CH_3)_2O$ towards iodine and phenol can be seen to be consistent with earlier qualitative explanations for the trends by calculating and comparing the trends in the C_AC_B products for the six adducts with each other.

One additional factor complicating the quantum mechanical interpretation of the E and C parameters involves potential solvation contributions. If specific interactions with the solvent are absent, these effects are expected to be minimal in non-polar solvents. This was demonstrated by obtaining constant enthalpies for the displacement reaction

$$BA + B' \rightarrow B'A + B \qquad (23)$$

in a series of non-polar solvents [23] and by studying adduct formation reactions in benzene [51]. Factors may exist that cause the system in these non-polar solvents to be different from those in the gas phase. For example, the base could be aggregated in the non-polar solvent so the reaction studied is

$$B_n + A \rightarrow B_nA \qquad (24)$$

The E_B and C_B numbers would apply to B_n. Clearly, more accurate gas phase data are needed for a full understanding of chemical reactivity but it is entirely possible that the "solvent minimized" data will be as (or probably more) important as the gas phase results for understanding chemical reactivity in solution.

It is well established that entropies for gas phase reactions are very different than those for the same reaction in solution. This fact must be borne in mind when comparing gas phase and solution results for molecules with two potential donor sites; for example, acetone with donor n and π oxygen electrons. Domination by entropy differences could lead to different donor—acceptor interactions (that is different donor sites) under the different sets of conditions. Furthermore, the influence of the surface of the container on the measurements being carried out on a gas phase system are non-trivial [52] and have often been overlooked. A rapid, accurate method for obtaining data on the gas phase equilibria of neutral acids and bases is sorely needed for there is little doubt that this information will add greatly to our understanding of chemical reactivity in solution.

ACKNOWLEDGEMENT

The author acknowledges the National Science Foundation for their partial support of this research. Helpful discussions with Prof. G.C. Vogel are also appreciated.

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