Cross-interaction Constants in the Nucleophilic Reactions of Carbonyl Compounds Involving a Tetrahedral Intermediate

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Cross-interaction constants, ρ^r_{XY}, ρ_{YZ} and ρ_{XZ} are defined using observed rate constant, $k_N = (k_1/k_{-1})k_2 = Kk_2$, for the stepwise carbonyl addition reactions involving the rate-limiting breakdown of a tetrahedral intermediate ($T^{\pm}$). Abundant experimental evidence in the literature enables us to determine signs for the three constants for such mechanism. $\rho^r_{XY} > 0$, $\rho_{YZ} < 0$ and $\rho_{XZ} > 0$. These are in contrast to those for the concerted $S_N 2$ mechanism, $\rho_{XY} < 0$, $\rho_{YZ} > 0$ and $\rho_{XZ} \gtrless 0$, and provide useful mechanistic criteria. In the light of these criteria, mechanisms of some nucleophilic reactions of carbonyl compounds are re-examined.

Introduction

It has been shown that the cross-interaction constants, ρ_{ij} and β_{ij} in eqs. 1,[1] are activation parameters ($\Delta\rho^*_{ij}$ and $\Delta\beta^*_{ij}$)[2] representing the changes in the intensity of interaction from initial state, ρ^o and β^o,

$$\log\ (k_{ij}/k_{HH}) = \rho_i\sigma_i + \rho_j\sigma_j + \rho_{ij}\sigma_i\sigma_j \quad (1a)$$

$$\log\ (k_{ij}/k_{HH}) = \beta_i pK_i + \beta_j pK_j + \beta_{ij} pK_i pK_j \quad (1b)$$

to transition state (TS), ρ^* and β^*:

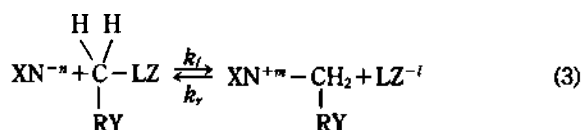$$\rho_{ij}(\equiv\Delta\rho^*_{ij}) = \rho^*_{ij} - \rho^o_{ij} \quad (2a)$$

$$\beta_{ij}(\equiv\Delta\beta^*_{ij}) = \beta^*_{ij} - \beta^o_{ij} \quad (2b)$$

In these expressions, i and j denote X, Y or Z fragment comprising the TS, Scheme 1. The magnitude of ρ^*_{ij} (or ρ^o_{ij}) represents the intensity of interaction between σ_i and σ_j through the respective reaction centers R_i and R_j in the TS (or in the initial state), whereas the magnitude of β^*_{ij} (or β^o_{ij}) represents the intensity of direct interaction between the respective reaction centers, R_i and R_j in the TS (or in the initial state)[1]. Since the signs of the two, ρ_{ij} ($\equiv\Delta\rho^*_{ij}$) and β_{ij} ($\equiv\Delta\beta^*_{ij}$), are always the same, the same interpretation of the significance of the sign will apply to the both constants[3]; thus in the following we will only deal with the ρ_{ij} ($\equiv\Delta\rho^*_{ij}$).

Whenever two separate species or reactants react, there is no interaction initially and hence $\rho^o_{XY} = \rho^o_{XY} = 0^2$, in contrast, however, ρ^o_{YZ} is the value within a covalent bonded system, ρ_{YZ}^{cov}, and will have a large magnitude[4].

Cross-interaction Constants in the Equilibrium Process. Let us first consider a normal concerted $S_N 2$ process Eq. 3, where $n = m + l$ and X, Y and Z are

$$\underset{RY}{XN^{-n}} + \overset{\overset{H\ H}{\diagdown\diagup}}{\underset{\underset{RY}{|}}{C}} - LZ \underset{k_r}{\overset{k_f}{\rightleftharpoons}} XN^{+m} - CH_2 + LZ^{-l} \quad (3)$$

the substituents in the nucleophile, substrate and leaving group, respectively (Scheme 1).

Various cross-interaction constants can be defined from Eq. 1a and Scheme 1.[1]
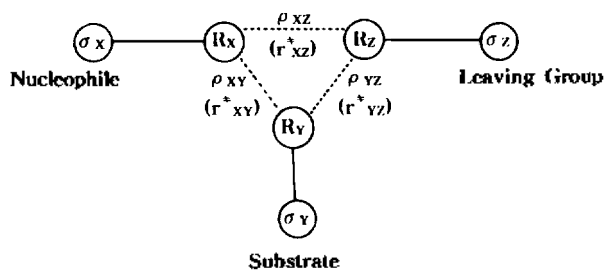
Scheme 1. A Typical $S_N 2$ TS.

$$\rho_{XY}(\equiv\Delta\rho^*_{XY}) = \left(\frac{\partial^2\log\ k}{\partial\sigma_X\cdot\partial\sigma_Y}\right)_Z = \left(\frac{\partial\rho_Y}{\partial\sigma_X}\right)_Z = \left(\frac{\partial\rho_X}{\partial\sigma_Y}\right)_Z \quad (4a)$$

Similarly

$$\rho_{YZ}(\equiv\Delta\rho^*_{YZ}) = \left(\frac{\partial\rho_Z}{\partial\sigma_Y}\right)_X = \left(\frac{\partial\rho_Y}{\partial\sigma_Z}\right)_X \quad (4b)$$

$$\rho_{XZ}(\equiv\Delta\rho^*_{XZ}) = \left(\frac{\partial\rho_Z}{\partial\sigma_X}\right)_Y = \left(\frac{\partial\rho_X}{\partial\sigma_Z}\right)_Y \quad (4c)$$

From Eq. 2a, using $\rho^o_{XY} = \rho^o_{XZ} = 0$ and $\rho^o_{YZ} = \rho_{YZ}^{cov}$,

$$\rho_{XY}(\equiv\Delta\rho^*_{XY}) = \rho^*_{XY} - \rho^o_{XY} = \rho^*_{XY} \quad (5a)$$

$$\rho_{XZ}(\equiv\Delta\rho^*_{XZ}) = \rho^*_{XZ} - \rho^o_{XZ} = \rho^*_{XZ} \quad (5b)$$

$$\rho_{YZ}(\equiv\Delta\rho^*_{YZ}) = \rho^*_{YZ} - \rho^o_{YZ} = \rho^*_{YZ} - \rho_{YZ}^{cov} \quad (5c)$$

The intensity of interaction between any two substituents (or reaction centers) is inversely distance dependent[1] so that a greater degree of bond formation (shorter r^*_{XY} in Scheme 1) leads to a larger magnitude of ρ_{XY}^*. On the other hand, the interaction between Y and Z will be the greatest in a covalent-bonded system so that ρ_{YZ}^{cov} will be greater than ρ^*_{YZ}; moreover as the degree of bond cleavage increases the magnitude of ρ^*_{YZ} will decrease, but in contrast, the magnitude of ρ_{YZ} ($\equiv\Delta\rho^*_{YZ}$) = $\rho^*_{YZ} - \rho_{YZ}^{cov}$ should increase. Thus the magnitude of ρ_{YZ} ($\equiv\Delta\rho^*_{YZ}$) reflects the degree of bond cleavage[2]. The magnitude of ρ_{XY} and ρ_{YZ} is proportional to the extent of bond-making and -breaking, respectively, in the TS of a concerted $S_N 2$ process.

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Now for the equilibrium of Eq. 3,

$$K = \frac{k_f}{k_r} \tag{6}$$

Thus, representing forward and reverse processes between i and j as ρ_{ij} and ρ_{ji}, respectively, and using Eqs. 5 and 6, we arrived at the following relation.[4]

$$
\begin{aligned}
\rho'_{XY} &= \Delta\rho^*_{XY} - \Delta\rho^*_{YX} \\
&= \rho^*_{XY} - \rho^*_{YX} + \rho^o_{YX} \\
&= \rho^o_{YX} = \rho_{XY}{}^{cov}
\end{aligned} \tag{7}
$$

Here ρ^*_{XY} is equal to ρ^*_{YX} based on the principle of microscopic reversibility[5].

This relation indicates that the equilibrium cross-interaction constant, ρ'_{XY}, in a normal concerted S_N2 process represents the intensity of interaction within a covalent-bonded system, $\rho_{XY}{}^{cov}$.[4]

Likewise, since $\rho'_{XZ} = \rho'_{ZX} = 0$ and $\rho^*_{XZ} = \rho^*_{ZX}$,

$$
\begin{aligned}
\rho'_{XZ} &= \Delta\rho^*_{XZ} - \Delta\rho^*_{ZX} = \rho^*_{XZ} - \rho^o_{XZ} - \rho^*_{ZX} \\
&+ \rho^o_{ZX} = \rho^*_{XZ} - \rho^*_{ZX} = 0
\end{aligned} \tag{8}
$$

This is reasonable since there is no species or complex in which X and Z are covalent-bonded in the equilibrium, Eq. 3.

Similarly, since $\rho'_{ZY} = 0$ and $\rho^*_{YZ} = \rho^*_{ZY}$,

$$
\begin{aligned}
\rho'_{YZ} &= \Delta\rho^*_{YZ} - \Delta\rho^*_{ZY} \\
&= \rho^*_{YZ} - \rho^o_{YZ} - \rho^*_{ZY} + \rho^o_{ZY} \\
&= -\rho^o_{YZ} = -\rho_{YZ}{}^{cov}
\end{aligned} \tag{9}
$$

Note that both ρ'_{XY} and ρ'_{YZ} represent the intensity of interaction within a covalent-bonded system but may have different signs.

Results of our studies have shown[1] that in the concerted S_N2 processes,

$$\rho_{XY}(\equiv \Delta\rho^*_{XY}) < 0 \tag{10a}$$

$$\rho_{YZ}(\equiv \Delta\rho^*_{YZ}) > 0 \tag{10b}$$

and $\rho_{XZ}(\equiv \Delta\rho^*_{XZ})$ can be either positive or negative[1].

The signs of ρ_{XY} (<0) and ρ_{YZ} (>0) for the concerted S_N2 processes can be rationalized MO theoretically. Since an electron withdrawing substituent in the substrate ($\delta\sigma_Y > 0$) lowers frontier orbital levels[6], especially the σ^*_{C-LZ} LUMO, charge transfer from the HOMO of the nucleophile, which is a nonbonding orbital n_N, into this σ^*_{C-LZ} level is facilitated as the charge transfer stabilization energy, $E_{ct}(\cong Hn\sigma^*/\Delta\varepsilon_{FMO})$, is inversely related to the interfrontier level gap, $\Delta\varepsilon_{FMO} = \sigma^*_{C-LZ} - n_N$[7]. The facile charge transfer should lead to a greater degree of bond formation ($\delta\rho_X < 0$) as well as to a greater degree of bond cleavage ($\delta\rho_Z > 0$) in a concerted S_N2 process; thus $\rho_{XY} = (\partial\rho_X/\partial\sigma_Y) < 0$ and $\rho_{YZ} = (\partial\rho_Z/\partial\sigma_Y) > 0$.

It is also found that $\rho'_{XY} = \rho_{XY}{}^{cov}$ has a large negative value; ρ'_{XY} has the same sign as ρ_{XY} but the magnitude is much greater. For the reactions of benzyl and benzoyl compounds with aniline nucleophiles, $\rho_{XY} \cong -0.5 \sim -0.8^1$ whereas $\rho'_{XY} \cong -1.40^4$.

Cross-interaction Constants in the Stepwise Nucleophilic Reactions of a Carbonyl Compound Involving a Tetrahedral Intermediate. Let us consider a ty-
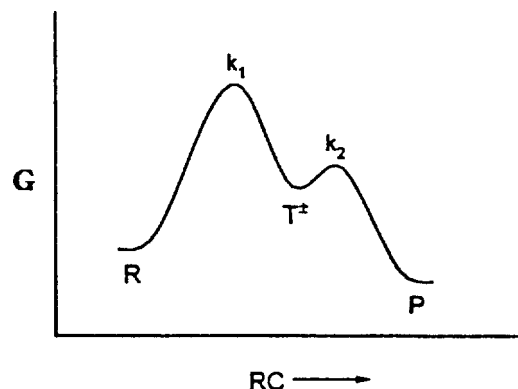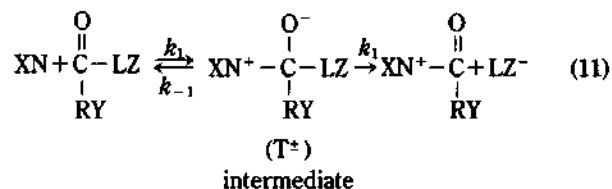

Figure 1. Energy (G) profile along reaction coordinate (RC) for a reaction with rate-limiting formation of $T^{\pm}$.

pical stepwise nucleophilic reaction of carbonyl compound with a neutral nucleophile, Eq. 11.

$$
XN + \overset{\overset{\text{O}}{\|}}{\underset{\underset{\text{RY}}{|}}{C}} - LZ \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} XN^+ - \overset{\overset{\text{O}^-}{|}}{\underset{\underset{\text{RY}}{|}}{C}} - LZ \overset{k_2}{\rightarrow} XN^+ - \overset{\overset{\text{O}}{\|}}{\underset{\underset{\text{RY}}{|}}{C}} + LZ^- \tag{11}
$$

$$(T^{\pm})$$
intermediate

Steady-state treatment to the zwitterionic tetrahedral addition intermediate, $T^{\pm}$, leads to

$$k_{obsd} = k_o + k_N [\text{N}] \tag{12}$$

where $\qquad k_N = \dfrac{k_1 k_2}{k_{-1} + k_2} \tag{13}$

(i) For the rate-limiting formation of the tetrahedral intermediate, $T^{\pm}$, (Fig. 1) the following relations hold.

$$k_N = k_1, \text{ since } k_{-1} \ll k_2 \text{ in Eq. 13.} \tag{14}$$

In this case,

$$\left(\frac{\partial^2 \log k_N}{\partial\sigma_X \cdot \partial\sigma_Y} \right)_Z = \left(\frac{\partial^2 \log k_1}{\partial\sigma_X \cdot \partial\sigma_Y} \right)_Z = \rho_{XY}(\equiv \Delta\rho^*_{XY}) \tag{15a}$$

$$\left(\frac{\partial^2 \log k_N}{\partial\sigma_Y \cdot \partial\sigma_Z} \right)_X = \left(\frac{\partial^2 \log k_1}{\partial\sigma_Y \cdot \partial\sigma_Z} \right)_X = \rho_{YZ}(\equiv \Delta\rho^*_{YZ}) \cong 0.0 \tag{15b}$$

Similarly ρ_{XZ} can be defined.

The sign and magnitude of $\rho_{XY}(\equiv \Delta\rho^*_{XY})$ will be similar to those for the ρ_{XY} values of the forward reaction of concerted S_N2 processes, Eq. 3. The sign of ρ_{XZ} can be either positive or negative but the magnitude will be somewhat greater than that in the case of Eq. 3. The main difference between the forward concerted processes in Eq. 3 and the rate-limiting adduct formation in Eq. 11 is that in the latter ρ_{YZ} is zero[1] since there is practically no change in the intensity of interaction between Y and Z in the activation process ($\rho^*_{YZ} \cong \rho^o_{YZ}$), so that $\rho_{YZ}(\equiv \Delta\rho^*_{YZ}) = \rho^*_{YZ} - \rho^o_{YZ} \cong 0^4$. Thus the two processes, k_f in Eq. 3 and k_1 in Eq. 11, can be distinguished by the magnitude of ρ_{YZ}; it will be zero in the latter (k_1) whereas it will be a nonzero positive value in the former process (k_f).

(ii) For the rate-limiting breakdown of $T^{\pm}$ to products, (Fig. 2), the overall observed rate constant, k_N, can be given as,
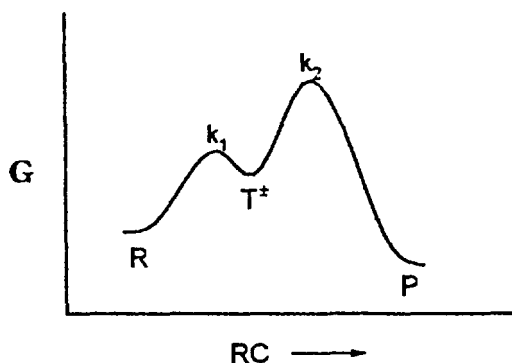
Figure 2. Energy (G) profile along reaction coordinate (RC) for a reaction with rate-limiting breakdown of $T^{\pm}$.

$$k_N = \frac{k_1}{k_{-1}} k_2 = K \cdot k_2 \tag{16}$$

since $k_{-1} > k_2$ in Eq. 13.

Thus, $k_N(X, Y, Z) = K(X, Y, Z) \cdot k_2(X, Y, Z)$ (17)

$$\log k_N = \log K + \log k_2 \tag{18}$$

Various cross-interaction constants can be defined using the observed rate constant, k_N, as follows.

$$\left(\frac{\partial^2 \log k_N}{\partial \sigma_X \cdot \partial \sigma_Y} \right)_Z = \left(\frac{\partial^2 \log K}{\partial \sigma_X \cdot \partial \sigma_Y} \right)_Z + \left(\frac{\partial^2 \log k_2}{\partial \sigma_X \cdot \partial \sigma_Y} \right)_Z$$
$$= \rho'_{XY}(T^{\pm}) \tag{19}$$

$$\left(\frac{\partial^2 \log k_N}{\partial \sigma_Y \cdot \partial \sigma_Z} \right)_X = \left(\frac{\partial^2 \log K}{\partial \sigma_Y \cdot \partial \sigma_Z} \right)_Z + \left(\frac{\partial^2 \log k_2}{\partial \sigma_Y \cdot \partial \sigma_Z} \right)_X$$
$$= \rho_{XY}(T^{\pm}) \tag{20}$$

These simplifications apply because in the rate-determining step, k_2, the change in the intensity of interaction between X and Y is insignificant (*i.e.*, the second term of Eq. 19 is zero), whereas in the adduct formation equilibrium, K, the intensity of interaction between Y and Z stays practically constant (*i.e.*, the first term of Eq. 20 is zero).

On the other hand,

$$\left(\frac{\partial^2 \log k_N}{\partial \sigma_X \cdot \partial \sigma_Z} \right)_Y = \left(\frac{\partial^2 \log K}{\partial \sigma_X \cdot \partial \sigma_Z} \right)_Y + \left(\frac{\partial^2 \log k_2}{\partial \sigma_X \cdot \partial \sigma_Z} \right)_Y$$

$$\rho_{XZ(obsd)}(\equiv \Delta \rho^*_{XZ}) = \rho'_{XZ}(T^{\pm}) + \rho_{XZ}(T^{\pm}) \tag{21}$$

In this case, the effect of interaction between X and Z on $\log k_N$ is complex, but $\rho'_{XZ}(T^{\pm})$ is expected to be a large positive quantity since it is for the bonded system in $T^{\pm}$ in contrast to that in the TS ($\rho_{XZ}(T^{\pm})$) which will be a smaller magnitude of plus or minus sign; overall the net effect will result in a positive observed ρ_{XZ} value.

Examples of Carbonyl Addition Reactions. The aminolysis reactions of carbonyl compounds usually exhibit the nonlinear Brønsted-type plots showing a break from a large ($\beta = 0.8$-1.0) to a small ($\beta \approx 0.1$-0.3) rate dependence on basicity of the attacking amine as the basicity of nucleophile increases. The break of this type has been attributed to a change in the rate-determining step from breakdown to formation of a tetrahedral intermediate, $T^{\pm}$, in the reac-

tion path. Such rate-limiting breakdown of $T^{\pm}$ has been reported, for example, in the reactions of methyl chloroformate with pyridines[8], substituted diphenyl carbonates with quinuclidines[9], 2,4-dinitrophenyl acetate and methyl carbonate with pyridines[10], acetic anhydride with pyridines[11], 2,4-dinitrophenyl benzoate and p-nitrobenzoate with pyridines[12], phenyl and p-nitrophenyl thiolacetates with amines[13], 2,4-dinitrophenyl acetate with secondary alicyclic amines[14], 2,4-dinitrophenyl and 2,4,6-trinitrophenyl thiolacetates with amines[15] and 2,4-dinitrophenyl methyl carbonate with secondary alicyclic amines[16]. The results of these experimental studies provided following evidence for the rate-limiting breakdown mechanism of the zwitterionic tetrahedral intermediate, $T^{\pm}$:

(i) The partitioning of the tetradedral intermediate, $T^{\pm}$, favors amine expulsion, 1, relative to leaving group (LZ) which is normally OR or SR type, 2, as the group that remains behind (RY) becomes more electron withdrawing ($\delta \sigma_Y > 0$).

This means that the bond between N and C in 1 is rather long and weak so that ρ_X is less negative ($\delta \rho_X > 0$).
Thus,

$$\left(\frac{\partial \rho_X}{\partial \sigma_Y} \right)_Z = \rho'_{XY}(T^{\pm}) > 0 \tag{22}$$

Alternatively, electron donating substituents ($\delta \sigma_Y < 0$) in the group which does not leave favor the expulsion of the leaving group, LZ, ($\delta \rho_Z > 0$) relative to amine, ($\delta \rho_X < 0$).
Thus,

$$\left(\frac{\partial \rho_Z}{\partial \sigma_Y} \right)_X = \rho_{XZ}(T^{\pm}) < 0 \tag{23}$$

whereas

$$\left(\frac{\partial \rho_X}{\partial \sigma_Y} \right)_Z = \rho'_{XY}(T^{\pm}) > 0 \tag{22}$$

Geminal interactions between two σ bonds are known to be destabilizing since the delocalization is σ-σ* antibonding, which is in contrast to the well-known π-π* bonding and stabilizing delocalization in π-conjugated systems.[17] In the $T^{\pm}$ intermediate, there are two acceptor σ bonds, $C-N^+X$ and C-LZ, whereas $C-O^-$ can be a strong donor and C-RY can be either an acceptor (if Y is electron withdrawing) or a donor (if Y is electron donating) bond. A strong donor, σ$_{C-O}$, and a strong acceptor, σ*$_{C-N^+X}$, can interact geminally to destabilize the σ*$_{C-N^+X}$ and cleave the $C-N^+X$ bond leading to the kinetically observable result of $k_{-1} > k_2$. However, when Y is an electron donating substituent ($\delta \sigma_Y < 0$), *i.e.*, the RY group is an electron donor, σ-σ* interaction between σ$_{C-R}$ and σ*$_{C-LZ}$ can supplement the σ-σ* between $C-O^-$ and C-LZ bonds to result in the favorable expulsion of the LZ group ($\delta \rho_Z > 0$). Thus, $\rho_{XZ} = \partial \rho_Z / \partial \rho_Y < 0$. Since in this case, the amine product in 2 is stabilized, the expulsion of N^+X is disfavored relative to that of LZ.

(ii) The amine expulsion from $T^{\pm}$ is favored ($\sigma \rho_X > 0$) by elec-

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Table 1. Summary of the Signs of Cross-interaction Constants

Mechanism	Sign[a]
S_N1[18]	$\rho_{XY}=0$, $\rho_{YZ}>0$, $\rho_{XZ}=0$
Concerted S_N2:	$\rho_{XY}<0$, $\rho_{YZ}>0$, $\rho_{XZ}^{\neq}{}_{<0}$, $\rho_{XY}{'}<0$
Stepwise Carbonyl Addition-Elimination:	
Formation of T$^{\neq}$:	$\rho_{XY}<0$, $\rho_{YZ}\cong0$, $\rho_{XZ}^{>0}{}_{<0}$
Breakdown of T$^{\neq}$:	$\rho_{XY}{'}>0$, $\rho_{YZ}<0$, $\rho_{XZ}>0$

[a]The same signs apply for the corresponding β_{ij} and $\beta{'}_{ij}$.

tron-withdrawing substituents ($\delta\sigma_Z>0$) in the leaving group.
Thus,

$$\left(\frac{\partial\rho_X}{\partial\sigma_Z}\right)_Y = \rho_{XZ}(\mathrm{T}^{\neq})>0 \qquad (24)$$

(iii) The enthalpy of activation, ΔH^*, is relatively low (≤15 kcal/mol) whereas the entropy of activation, ΔS^*, has a larger negative value ($\approx-24\sim-44$ calK^{-1}mol^{-1}) in the rate determining expulsion of leaving group, **2**, compared to that of amine, **1**.

The results are summarized in Table 1. We note that $\rho_{XY}{'}$ (T$^{\neq}$) (Eq. 19) is positive whereas ρ_{YZ}(T$^{\neq}$) (Eq. 20) is negative, in contrast to a negative $\rho{'}_{XY}$ (Eq. 7) and positive ρ_{YZ} (Eq. 4b) in the concerted S_N2 processes. The signs of cross-interaction constants, therefore provide criteria for distinguishing mechanisms between concerted S_N2 and the carbonyl addition involving a tetrahedral intermediate, T$^{\neq}$, (Table 1). These criteria are, however, necessary conditions and can not be sufficient conditions.

In the light of mechanistic criteria listed in Table 1 we will now discuss some of the experimental results reported in which the effects of substituents, X, Y and/or Z, on rates are explicitly examined so that the cross-interaction constants, ρ_{XY} (or $\rho{'}_{XY}$), ρ_{YZ} and/or ρ_{XZ} are determinable as summarized in Table 2.

The first two entries, A and B, in this table[19,20] are quite interesting cases; the reactions have been shown to proceed *via* two pathways, the second-order, k_2, and the third-order, base-catalyzed, k_3, paths. The signs of ρ_{YZ} in Table 2 predict that the k_2 path for A but in contrast the k_3 path for B are consistent with the mechanism in which the expulsion of leaving group is the rate determining step *i.e.*, $\rho_{YZ}<0$ in Table 1. On the other hand, the k_2 path for B are predicted to proceed by a concerted S_N2 mechanism ($\rho_{YZ}>0$), since if the mechanism were stepwise with rate-limiting formation of the tetrahedral intermediate ρ_{YZ} should have been zero. The lower ΔH^* values and the larger negative ΔS^* values observed for the k_3 process in reaction B[20] support the predicted mechanism by the negative sign of ρ_{YZ}, *i.e.*, the rate-limiting expulsion of the leaving group from a putative tetrahedral intermediate.

For reaction C,[21] the authors suggested originally a concerted S_N2 type of mechanism. However, the signs of ρ_{XY}, ρ_{YZ} and ρ_{XZ} are all consistent with those predicted for a stepwise mechanism in which the rate determining step is the expulsion of leaving group from a zwitterionic tetrahedral intermediate, T$^{\neq}$. Furthermore the magnitude of $\rho_{XY}(\equiv\rho{'}_{XY})$ and ρ_{YZ} are quite large, suggesting that the amine is tightly bound in T$^{\neq}$ whereas the bond cleavage of the leaving group, $^-$SC$_6$H$_5$Z, from T$^{\neq}$ is quite advanced in the TS. The positive sign of ρ_{XZ} is also in line with the stepwise mechanism predicted.

Table 2. Some examples of the cross-interaction constants for reactions involving the rate-limiting leaving group expulsion step from a tetrahedral intermediate (T$^{\neq}$)

Entry	Reaction	ρ_X	ρ_Y	ρ_Z	ρ_{XY}	ρ_{YZ}	ρ_{XZ}	Ref.
A	YC$_6$H$_4$COOC$_6$H$_4$Z + pyrrolidine $\xrightarrow{\text{MeCN}}_{25.0\,°C}$; k_2	—	1.0	6.2	—	-1.0	—	19
B	YC$_6$H$_4$NHCOOC$_6$H$_4$Z + n-BuNH$_2$ $\xrightarrow{\text{dioxane}}_{31.0\,°C}$; k_2	—	1.6	3.6	—	1.0	—	20
	; k_3		1.5	4.2	—	-4.0	—	
C	YC$_6$H$_4$COSC$_6$H$_4$Z + XC$_6$H$_4$NH$_2$ $\xrightarrow{\text{MeOH}}_{55.0\,°C}$	-5.11	1.41	4.47	1.48	-1.38	0.56	21
D	YC$_6$H$_4$CSSC$_6$H$_4$Z + XC$_6$H$_4$NH$_2$ $\xrightarrow{\text{MeCN}}_{55.0\,°C}$	-2.86	0.83	2.26	0.66	-0.81	0.60	22
E	YC$_6$H$_4$COOCOC$_6$H$_5$ + XC$_6$H$_4$NH$_2$ $\xrightarrow{\text{MeOH}}_{45.0\,°C}$	-3.14	1.31	—	0.54	—	1.19	23
F	YC$_6$H$_4$COCH$_2$OSO$_2$C$_6$H$_4$Z + XC$_6$H$_4$NH$_2$ $\xrightarrow{\text{MeOH}}_{45.0\,°C}$	-1.99	0.61	1.24	0.11	-0.66	0.32	24
G	YC$_6$H$_4$COCH$_2$OSO$_2$C$_6$H$_4$Z + XC$_6$H$_4$CH$_2$NH$_2$ $\xrightarrow{\text{MeOH}}_{45.0\,°C}$	-0.76	0.54	1.02	0.03	-0.52	0.12	25
H	YC$_6$H$_4$COCH$_2$Br + XC$_6$H$_4$NH$_2$ $\xrightarrow{\text{MeOH}}_{45.0\,°C}$	-1.81	0.61	—	0.11	—	—	26
I	YC$_6$H$_4$COCH$_2$Br + XC$_6$H$_4$CH$_2$NH$_2$ $\xrightarrow{\text{MeOH}}_{45.0\,°C}$	-0.88	0.37	—	0.05	—	—	27
J	YC$_6$H$_4$COCH$_2$OSO$_2$C$_6$H$_4$Z + (CH$_3$)$_2$NC$_6$H$_4$X $\xrightarrow{\text{MeOH}}_{55.0\,°C}$	-1.95	0.64	1.18	0.11	-0.59	0.28	28

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Based on the signs of the cross-interaction constants, reactions D[22] and E[23] are also predicted to proceed by a stepwise elimination mechanism. We note that the magnitudes of both ρ_{XY} and ρ_{YZ} are smaller than those for reaction C[21]; thus in these reactions the amines are somewhat loosely bound in $T^{\pm}$ and the extent of bond cleavage of the leaving group from $T^{\pm}$ is rather low. These trends are quite opposite to those for reaction C. This shows that under similar conditions the $-\overset{\overset{S}{\|}}{C}-$ group favors amine expulsion in contrast to the $-\overset{\overset{O}{\|}}{C}-$ group which favors the leaving group ($^{-}SC_6H_4Z$) expulsion.

The most interesting and unexpected mechanistic assignments based on the signs in Table 1 are for the aminolysis reaction of phenacyl compounds, reactions F-J[24-28] According to the signs of ρ_{XY} (>0) in all cases and also of ρ_{YZ}(<0) and ρ_{XZ}(>0) for reaction J[28], these reations are predicted to proceed by a stepwise mechanism in which the expulsion of leaving group from a putative tetrahedral intermediate, $T^{\pm}$, is rate limiting. These reactions were originally reported to proceed by a concerted S_N2 mechanism.

Winstein *et al.*,[29] and Bunton[30] have indeed proposed contribution of a tetrahedral intermediate of the type 3 in a stepwise carbonyl addition mechanism for the nucleophilic substitution reactions of phenacyl compounds.

3   4
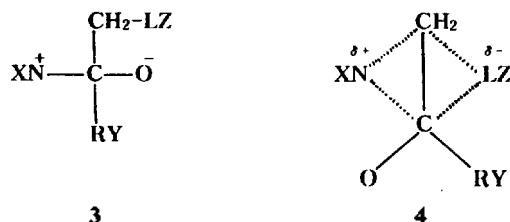
However in recent works on such systems the consensus is in favor of a concerted S_N2 mechanism. Especially structure 3 is incompatible with the symmetry required for the identity reactions (XN=LZ)[31]; for the necessary symmetry is to be achieved the structure like 4 must be predicted as a TS, which is not suggested in theoretical studies[32].

However, in the light of the mechanistic criteria based on the signs of ρ_{XY}(>0) (and also the signs of ρ_{YZ}(<0) and ρ_{XZ}(>0) for reaction J) in all the aminolysis reactions of phenacyl compounds listed in Table 2, a stepwise mechanism with the rate-limiting expulsion of leaving group rom $T^{\pm}$, 3, cannot be summarily dismissed. On the contrary, further experimental as well as theoretical works on the mechanism of aminolysis of phenacyl compounds may prove that the predictions made based on the signs of the cross-interaction constant turn out to be correct. Obviously, much well designed works to this end are necessary to settle this controversial problem.

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Synthesis and Reaction Chemistry of Some Ferrocene-Containing Chelate Ligands with Dirhodium Acetate: X-ray Crystal Structure of (η¹-(S,R)-CPFA)₂Rh₂(OAc)₄

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New ferrocene-based chelate amines, $Fe[C_5H_4CH(Me)NMe_2]_2$ (3), $Fe[C_5H_3(CH(Me)NMe_2)(PPh_2)-1,2]_2$ (4), $(C_5H_5)Fe(C_5H_3(CH_2NMe_2)(CH(CN)NMe_2)-1,2)$ (6), and $(C_5H_5)Fe(C_5H_3(CH_2NMe_2)(CH(Me)NMe_2-1,2))$ (7) have been prepared. The reaction and the coordination chemistry of 4 and other related compounds (S,R)-(1-N,N-dimethylaminoethyl)-2-dicyclohexyl-phosphino)ferrocene (CPFA) and 1,1'-bis-(diphenylphosphino)ferrocene (BPPF) with $Rh_2(OAc)_4(MeOH)_2$ were investigated. The reaction of the chiral ligand (S,R)-CPFA forms a complex of the type $(η^1-(S,R)-CPFA-P)_2Rh_2(OAc)_4$ (8) in which the ligand is coordinated to both rhodium centers in a monodentate fashion through phosphorus. In contrast, the bisphosphine analogues such as BPPF and 4 afford chelate complexes of the type $(η^2-PP)Rh_2(OAc)_4$ (9 & 10) where both ligands act as a chelate bidentate to a single rhodium atom. All these complexes were characterized by microanalytical and spectroscopic techniques. In one case, the structure of 8 was determined by X-ray crystallography. Crystals are monoclinic, space group C2 (No. 5), with $a=26.389$ (3), $b=12.942$ (1), $c=11.825$ (1) Å, $β=111.22$ (1)°, $V=3964.7$ (8) Å³, $Z=4$, and $D_{calc}=1.58$ g cm⁻³. Two Rh(II) centers are bridged by four AcO⁻ groups in the $η^1:η^1$ mode across a Rh-Rh single bond, and octahedral coordination at Rh(1) and Rh(1') is completed by axially coordinating (S,R)-CPFA and a briding AcO⁻, respectively.

Introduction

Dimeric rhodium(II) complexes[1,2], notably those with bridging carboxylate ligands[3], have been the subject of considerable study in the past two decades. Their interesting structural and spectroscopic properties, along with observed catalytic[4], and antitumor activities[5], have led to numerous investigations of the rhodium-rhodium and rhodium-ligand interactions. These complexes contain a rhodium-rhodium single bond with four equatorial bridging carboxylate ions, which are relatively inert to substitution[6]. The two axial positions may be occupied by donor solvents that can undergo rapid ligand exchange to yield adducts with a variety of ligand species[3]. In this connection, much attention has recently been focused on the nature of the rhodium-ligand bonding interactions, i.e., cyclometallation reaction.[7-13]

As part of our ongoing project on the synthesis and application of rhodium complexes incorperating ferrocene-containing ligands in homogeneous catalysis[14], we have prepared some ferrocenylphosphines including those new series of aminoferrocenes 3, 4, 6, and 7 described in Schemes 1 & 2 and their dirhodium acetate complexes 8-10 to investigate not only the coordination behavior of these ligands with Rh₂(OAc)₄(MeOH)₂ but catalytic potentiality of the resulting complexes. One such area would be asymmetric cyclopropanation[15-19] as represented by equation (1).

In this paper are described the synthesis and structural

$$(1)$$
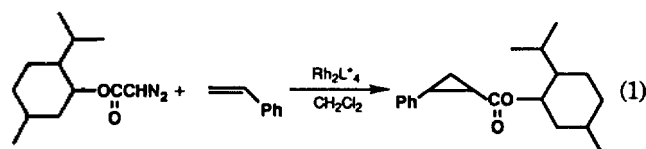
characterization of these new ferrocene-based ligands. Also are described the reaction and coordination chemistry of Rh₂(OAc)₄ with the ligand 4 and other related compounds BPPF and CPFA as presented in Scheme 3.

Experimental

Reagent and Instruments. All manipulations were carried out under an argon atmosphere using a double manifold vacuum system and Schlenk techniques. All commercial reagents were used as received unless otherwise mentioned. Solvents were purified by standard methods[19], and were freshly distilled prior to use. Microanalyses were performed by The Center for Instrumental Analysis, Kyungpook National University. ¹H and ³¹P NMR spectra were recorded on a Bruker AM-300 spectrometer operating at 300 and 121.5 MHz, respectively. ¹H shifts are reported relative to external TMS (δ=0 ppm) and ³¹P shifts relative to 85% H₃PO₄. IR spectra were recorded on a Mattson FT-IR Galaxy 6030E. Melting points were determined using Thomas-Hoover melting point apparatus and reported without correction. The