Theoretical studies on cross interactions in the protonation equilibria of diaryl ketones

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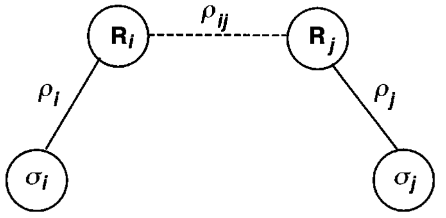
Cross interactions in the protonation equilibria of diaryl ketones have been studied MO theoretically at the MP2/6-31G*//RHF/6-31G* level. The susceptibility parameters, S, defined by $\Delta d_X = S_X \times \Delta\sigma_X^+$ and $\Delta d_Z = S_Z \times \Delta\sigma_Z^+$, where d is the length of the bond linking the ring to the carbonyl carbon (C_α), are all positive. However the cross-interaction terms $S_{XZ} = \frac{\Delta S_X}{\Delta\sigma_Z^+} > 0$ and $S_{ZX} = \frac{\Delta S_Z}{\Delta\sigma_X^+} < 0$, have different signs indicating that the resonance interaction modes of the two rings in the equilibria are different; the X-ring interacts by π-polarization whereas the Z-ring by through-conjugation in the protonated state (**P**). These two different modes of resonance interactions are supported by the natural population analysis (NPA). The Hammett cross-interaction constants (CIC), ρ_{XZ}, are all negative and the magnitude is of a similar order to that of the susceptibility change, ΔS_Z, upon protonation for the 5-membered heteroaromatic ring. The two different modes of resonance interactions within the X- and Z-rings are also reflected in the two different σ scales (σ_X and σ_Z^+) that give the best fits to the general equation defining the CICs ρ_{XZ} using the reaction energy for the protonation reaction, ΔE°_{XZ}. The magnitude of the CIC for an equilibrium process is in general large, especially when the reaction center has a strong cationic charge in the product state.

Introduction



Scheme 1

Cross interactions between two systems, i and j in Scheme 1, in a reaction have been a subject of intensive studies in our laboratory.[1] The two systems with substituents, σ_i and σ_j, may be two reactants, or two fragments within a molecule, interacting through the reaction centers, R_i and R_j respectively. It has been shown that a Taylor series expansion of log k_{ij} (or log K_{ij}) around $\sigma_i = \sigma_j = 0$ leads to a simple expression, eqn. (1a). The

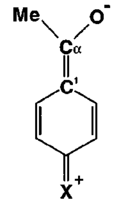
$$\log(k_{ij}/k_{HH}) = \rho_i\sigma_i + \rho_j\sigma_j + \rho_{ij}\sigma_i\sigma_j \qquad (1a)$$

cross-interaction constant ρ_{ij}, which can be alternatively defined by eqn. (1b), is an activation (with k_{ij}) or reaction (with K_{ij})

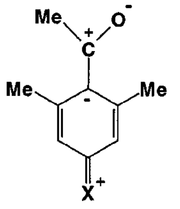
$$\rho_{ij} = \frac{\partial\rho_j}{\partial\sigma_i} = \frac{\partial\rho_i}{\partial\sigma_j} \qquad (1b)$$

parameter and its sign and magnitude provide valuable mechanistic information. For example, the magnitude represents the change in the intensity of interaction between the two fragments in an activation or equilibrium process.[1,2]

Recently there has been considerable interest in the two remarkably different modes of resonance interactions observed in the *para*-substituted nitrobenzenes and aromatic carbonyl compounds.[3] The observed ^{13}C chemical shifts of the carbonyl carbon (C_α) indicated that through-conjugation predominates in 4-X-acetophenones (**A**) while π-polarization (charge alternated form) prevails in 4-X-2,6-dimethylacetophenones (**B**).[3g] An electron donor ($\Delta\sigma_X < 0$) reduces positive charge on C_α ($\Delta q_\alpha^+ < 0$) in the "normal" resonance interaction in **A**, whereas it increases positive charge on C_α ($\Delta q_\alpha^+ > 0$) causing a down-field ^{13}C NMR chemical shift in the so-called "reverse" resonance effect in **B**.[3g]



A

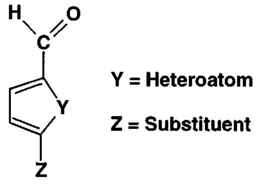


B

In general, resonance effects can be regarded as a blend of conjugation and π-polarization. The former mode is favored in a coplanar, and/or in a protonated, but not entirely coplanar, system in which conjugation may be enforced by the strong requirement for stabilization of the positive charge on C_α, whereas the latter mode prevails in a non-coplanar and/or in a system with a strong donor substituent on the carbonyl carbon (*e.g.* NH_2, OMe, OPh, *etc.* instead of Me in **A**) which reduces the positive charge on C_α and consequently leads to a much reduced resonance electron demand from the substituted ring.[1]

Theoretical as well as experimental studies have shown that a stronger donor ($\Delta\sigma_X < 0$) leads to (i) an increase in negative charge on the *ipso* carbon (C^1) and the carbonyl oxygen, and (ii) contraction of the bond linking the ring to the carbonyl carbon in both through-conjugation (**A**) and π-polarization interaction modes (**B**). In the latter mode, though the bond is drawn as a single bond, it was reported that such an ionic bond is almost as short as a double bond.[3b,4] The only way to discriminate between the two modes is by the variation of charge on the carbonyl carbon (C_α^+): a stronger donor ($\Delta\sigma_X < 0$) leads to an increase in positive charge ($\Delta C_\alpha^+ > 0$) by π-polarization in contrast to a decrease in positive charge ($\Delta C_\alpha^+ < 0$) by through-conjugation.

On the other hand, in a recent theoretical work[5] on the protonation equilibria of 5-membered heteroaromatic aldehydes (5MHAs), **C**, we have shown that the susceptibility, $-\rho_Z^+$, of the

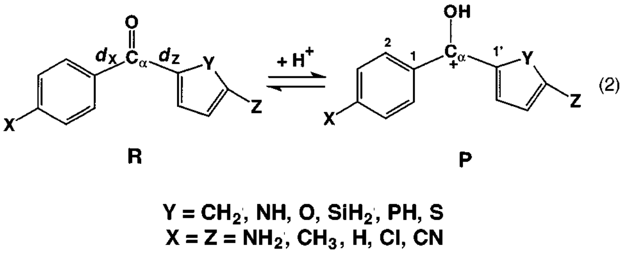


C

carbonyl moiety to substituent (Z) changes is in the reverse order of the delocalizability of lone-pair (or pseudo) π electrons (n_π(Y)) on the heteroatom Y; the greater the delocalizability of n_π(Y), the weaker is the cationic charge on C_α, and hence the weaker is the resonance electron demand, *i.e.*, the smaller is the magnitude of ρ_Z^+.

In this work, we investigated cross interactions between the two aromatic rings of diaryl ketones in the protonation equilibria, eqn. (2), theoretically at the MP2/6-31G*//RHF/6-31G* level.[6]

We have determined two types of cross-interaction constants: (i) $S_{XZ} = \frac{\Delta S_X}{\Delta\sigma_Z^+}$ and $S_{ZX} = \frac{\Delta S_Z}{\Delta\sigma_X^+}$ (in general $S_{XZ} \neq S_{ZX}$) where $S_X = \frac{\Delta d_X}{\Delta\sigma_X^+}$ and $S_Z = \frac{\Delta d_Z}{\Delta\sigma_Z^+}$ (d_X and d_Z are defined in eqn. (2)), and (ii) ρ_{XZ} (= ρ_{ZX}) in eqn. (3), where ΔE^o_{XZ} is the reaction energy for reaction (2).



(2)

Y = CH$_2$, NH, O, SiH$_2$, PH, S
X = Z = NH$_2$, CH$_3$, H, Cl, CN

$$-\frac{\Delta E^o_{XZ}}{2.3RT} = \rho_X\sigma_X + \rho_Z\sigma_Z^+ + \rho_{XZ}\sigma_X\sigma_Z^+ \qquad (3)$$

The purposes of this work are to show explicitly that (i) there are two different modes of resonance interaction and the two modes can be operating concurrently within a molecule, through-conjugation in the Z-ring and π-polarization in the X-ring, and (ii) to identify the factors that determine the magnitude of the cross-interaction constants, ρ_{XZ}, as Y is varied.

Calculations

Since a large number of reactions (>150 protonation equilibria) involving relatively large reaction systems (>15 heavy atoms) are examined, the computational level was kept at the MP2/6-31G*//RHF/6-31G*. Vibrational frequency calculations were carried out to confirm the stationary states at the RHF/3-21G*//RHF/3-21G* level. All structures were fully optimized without any restriction. Natural population analyses (NPA)[7] were carried out using NBO 4.0 interfaced to GAUSSIAN94. The GAUSSIAN92 and 94 series of programs[8] were used throughout in this work.

Results and discussion

Structures

The two (X- and Z-) rings are not in general coplanar. Torsional angles with respect to the carbonyl group, dihedral angles $\angle OC_\alpha C^{1'}Y$ and $\angle OC_\alpha C^1C^2$, are summarized in Table 1. As in the 5MHAs, the heteroatom Y is *syn* to the CO groups in all cases with one exception of Y = O.† Interestingly the *anti* form of Y = O (**R**) and its protonated form (**P**) have a relatively small distortion of the two rings. The planarity is better for the Z-ring than the X-ring.

Table 1 Torsional angles (in degrees) for X = Z = H

	Y =	CH$_2$	NH	O	SiH$_2$	PH	S
Z-Ring							
($\angle OCC^{1'}Y$)	(**R**)	16.7	9.9	9.2	18.1	21.5	16.0
	(**P**)	8.6	6.5	5.4	10.7	14.7	10.8
X-Ring							
($\angle OCC^1C^2$)	(**R**)	31.6	32.3	23.1	30.7	32.3	33.7
	(**P**)	41.6	41.3	30.7	40.5	41.5	39.8

Bond lengths d_O (d_{CO}), d_X and d_Z for **R** and **P** are listed in Table 2. Since the phenyl ring is remote and distorted out of the plane defined by $OC_\alpha C^1C^{1'}$ more than the 5-membered heteroaromatic rings, effects of the heteroatom, Y, on the bond length of d_X will be smaller than those on d_Z; differences in d_Z between the shortest (Y = NH) and the longest (Y = PH for **R** and Y = SiH$_2$ for **P**) values are *ca.* 0.01 and 0.03 Å for **R** and **P** respectively, whereas they are an order of magnitude smaller for d_X than the corresponding values of d_Z. In general, effects of the Z-ring are much greater than those of the X-ring; because the Z-rings are, in general, more electron rich than the X-ring, *i.e.*, the Z-ring would be more electron donating with a more coplanar structure than the X-ring. Thus the d_Z values are much shorter than the d_X values, and Δd_Z (= $d_P - d_R$) is *ca.* twice as large (~0.08 Å) as Δd_X (~0.04 Å). The relatively coplanar structure of Y = O (Table 1) is evident in large decreases in d_X, reflecting the enhanced resonance bond contraction of the d_X.

The NPA charges[7,9] are shown in Table 3. Here again the stronger effects of the Z-ring are reflected in the relative positive charge present within the two rings; π-electron flow from a ring towards the carbonyl moiety is *ca.* 2 times greater for the Z-ring than for the X-ring so that the Z-ring is overall much more positive than the X-ring. The Z-ring for Y = O is relatively more positive (in fact the most positive among various Y). This is again due to the near coplanarity of the two rings for Y = O (Table 1).

Susceptibility and cross-interaction constants based on resonance bond contraction

The effects of the substituents at the *para* position, X and Z, are transmitted directly to the carbonyl moiety and are reflected in the bond length contraction of d_X and d_Z respectively. We have determined the susceptibility constant, *S*, from the slope of the plot of Δd (× 10^2) against σ^+, eqn. (4a) and (4b). In both **R** and **P** states, Δd_X as well as Δd_Z correlated better with σ^+ than with σ. The *S* values are collected in Table 4.

$$\Delta d_X = S_X \times \sigma_X^+ \qquad (4a)$$

$$\Delta d_Z = S_Z \times \sigma_Z^+ \qquad (4b)$$

Since a stronger donor ($\Delta\sigma^+ < 0$) leads to a greater bond

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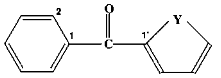
† As a starting point for the calculation, we first computed *anti* and *syn* conformers for Y = O at the RHF/3-21G* level of theory (not listed in this paper) and chose the most stable conformer in the discussion. In the case of the reactant, the *syn* conformer is 5.96 kcal mol^{-1} more stable than the *anti* conformer. In the product, however, the hydrogen-bonded conformer (*anti* form) is more stable than the *syn* conformer. Formation of the *anti* product from the *syn* reactant requires rotation around the C–C bond connecting the carbonyl carbon and the Z-ring upon protonation. Since we did not consider this rotation process, the *anti* conformer was not included in the analysis.

Table 2 Bond lengths (X = Z = H, in Å)



Y		CH_2	NH	O	SiH_2	PH	S
$d_O(C_\alpha$–O)	**R**	1.2007	1.2037	1.1992	1.2010	1.1995	1.1979
	P	1.2981	1.3090	1.2988	1.2959	1.2944	1.2941
$d_Z(C_\alpha$–$C^{1'})$	**R**	1.4795	1.4698	1.4806	1.4826	1.4841	1.4832
	P	1.3942	1.3745	1.3962	1.4049	1.4038	1.4000
	Δd_Z	−0.0853	−0.0953	−0.0844	−0.0777	−0.0803	−0.0832
$d_X(C_\alpha$–$C^1)$	**R**	1.5010	1.4964	1.4971	1.5016	1.5002	1.4994
	P	1.4661	1.4654	1.4533	1.4650	1.4645	1.4617
	Δd_X	−0.0349	−0.0310	−0.0438	−0.0366	−0.0357	−0.0377

Table 3 NPA Charges (X = Z = H, in electron units)

		CH_2	NH	O	SiH_2	PH	S
C_α	**R**	0.662	0.656	0.639	0.667	0.664	0.661
	P	0.708	0.649	0.675	0.732	0.727	0.713
	Δq	0.046	−0.007	0.036	0.065	0.063	0.052
O[a]	**R**	−0.641	−0.666	−0.638	−0.641	−0.635	−0.630
	P	−0.690 (+0.540)	−0.714 (+0.542)	−0.692 (+0.543)	−0.688 (+0.541)	−0.687 (+0.543)	−0.687 (+0.545)
	Δq	−0.049	−0.048	−0.054	−0.047	−0.052	−0.057
Z-Ring	**R**	0.005	0.025	0.003	−0.001	−0.009	−0.016
	P	0.336	0.416	0.317	0.306	0.302	0.300
	Δq	0.331	0.391	0.314	0.307	0.311	0.316
X-Ring	**R**	−0.026	−0.015	−0.004	−0.025	−0.020	−0.015
	P	0.106	0.107	0.157	0.109	0.115	0.129
	Δq	0.132	0.122	0.161	0.134	0.135	0.144

[a] Charge of hydrogen bonded to the carbonyl oxygen in **P** is shown in parentheses.

Table 4 Susceptibility constants[a]

	R		**P**	
Y	S_X (Z = H)	S_Z (X = H)	S_X (Z = H)	S_Z (X = H)
CH_2	0.73	1.08	2.40	2.94
NH	0.72	1.07	2.11	2.17
O	0.80	1.15	2.70	3.11
SiH_2	0.76	0.98	2.66	3.09
PH	0.75	1.05	2.77	3.05
S	0.73	1.02	2.65	2.79

[a] S_X and S_Z values are calculated in the case of Z = H and X = H, respectively.

Table 5 Cross-interaction constants, S_{XZ} and S_{ZX}, based on bond contractions of d_X and d_Z

	R		**P**	
Y	S_{XZ}	S_{ZX}	S_{XZ}	S_{ZX}
CH_2	0.08	0.06	0.94	−0.57
NH	0.07	0.06	0.82	−0.60
O	0.08	0.04	0.68	−0.39
SiH_2	0.08	0.08	0.97	−0.53
PH	0.08	0.06	0.99	−0.56
S	0.07	0.05	0.80	−0.44

contraction ($\Delta d < 0$), S is positive in all cases, and the susceptibilities are considerably stronger, and hence the S values are much greater, in the protonated (**P**) state than those in the reactant (**R**) state due to a much stronger cationic charge on the carbonyl carbon (C_α) in the **P** state. Somewhat larger S values obtained for the Y = O system must reflect higher degrees of coplanarity of the X- and Z-rings with the carbonyl group. The transmission of the substituent effect is also more efficient through the 5-membered heteroaromatic ring (Z-ring) than through the phenyl ring (X-ring), $S_Z > S_X$ (*vide supra*).

Cross-interaction constants, S_{XZ} and S_{ZX}, are determined both for the **R** and **P** states using eqn. (5a) and (5b) as summarized in Table 5.

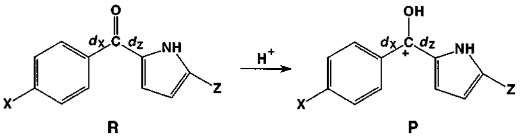
$$S_{XZ} = \frac{\Delta S_X}{\Delta \sigma_Z^+} \tag{5a}$$

$$S_{ZX} = \frac{\Delta S_Z}{\Delta \sigma_X^+} \tag{5b}$$

An illustrative example is given for Y = NH in Table 6. We note that the magnitude of the cross-interaction constants is much larger for **P** than for **R** as anticipated from a stronger cationic charge center, C_α^+, in **P** leading to a much stronger cross-interaction of the two substituents X and Z in the two rings through the common reaction center, C_α. Surprisingly, however, the sign of S_{ZX} for **P** is negative in contrast to the positive signs for all other cross-interaction constants, S_{XZ} and S_{ZX} in **R** and S_{XZ} in **P**.

In order to find out the factors determining the sign of the cross-interaction constants, we have carried out natural population analysis (NPA). The results showed that a stronger donor X (or Z) invariably leads to an increase in the negative

Table 6 Cross-interaction between the two rings (Y = NH)



	R		P	
X or Z	S_X	S_Z	S_X	S_Z
p-NH$_2$	0.68	1.02	1.11	3.10
p-CH$_3$	0.70	1.05	1.80	2.33
H	0.72	1.07	2.11	2.17
p-Cl	0.75	1.09	2.19	2.16
p-CN	0.82	1.15	2.71	1.97
	$S_{XZ} = +0.07$	$S_{ZX} = +0.06$	$S_{XZ} = +0.82$	$S_{ZX} = -0.60$

Table 7 NPA charges (in electronic charge units) of the carbonyl carbon ($q_{C_\alpha}^+$) for the protonated state (**P**) with Y = O

	X = NH$_2$	H	CN	Mode[a]
Z = NH$_2$	0.5484	0.5393	0.5230	π-Polariz.
H	0.6057	0.6506	0.6463	?
CN	0.5958	0.6625	0.6628	Conjug.

[a] Question mark (?) represents mixture of the two modes.

charge on the carbonyl oxygen atom and the *ipso* carbon (C^1 or $C^{1'}$). In contrast, however, the positive charge of the carbonyl carbon (C_α^+) increases when a stronger donor transmits resonance electrons by π-polarization whereas the C_α^+ decreases when resonance electrons are transmitted by through-conjugation. Thus, the two different modes of resonance electron transmission can be distinguished according to whether the C_α^+ increases (π-polarization) or decreases (conjugation) with a stronger donor substituent. Overall, the π-polarization mode was found to be preferred in the X-ring in **R** but the through-conjugation mode prevailed in the Z-ring in **P**. For the Z-ring in **R** and the X-ring in **P**, a blend of the two modes was operative so that it was difficult to assign a clear-cut single mode. However in the former, the π-polarization mode was predominant overall, whereas in the latter π-polarization prevailed only when Z is a strong donor, Z = NH$_2$.

This analysis indicates that for all Y in **R** substituent effects are transmitted by the π-polarization mode both in the X- and Z-rings, whereas in the protonated state (**P**) transmission of substituent effect in the Z-ring is by conjugation but a blend of the two modes are operative in the X-ring. An interesting example is the resonance interaction in the phenyl ring (X-ring) of the protonated state with Y = O (Table 7). A strong donor in the Z-ring (Z = NH$_2$) leads to a π-polarization mode in the X-ring ($\Delta\sigma_X < 0 \rightarrow \Delta C_\alpha^+ > 0$), whereas a strong acceptor Z (Z = CN) reverses it to conjugation ($\Delta\sigma_X < 0 \rightarrow \Delta C_\alpha^+ < 0$). This is a result of the conjugative interaction within the Z-ring ($\Delta\sigma_Z < 0 \rightarrow \Delta C_\alpha^+ < 0$ and $\Delta\sigma_Z > 0 \rightarrow \Delta C_\alpha^+ > 0$): a strong donor Z reduces the positive charge on C_α sufficient to induce π-polarization interaction in the X-ring, while a strong acceptor Z enhances the positive charge on C_α allowing through-conjugation in the X-ring.

It was found that the resonance bond contraction, $-\Delta d$, is much greater by through-conjugation than by π-polarization. For example with Y = NH in **R**, $d_X = 1.48$–1.50 and $d_Z = 1.46$–1.48 Å so that $\Delta d(\mathbf{R}) = d_X(\mathbf{R}) - d_Z(\mathbf{R}) \cong 0.02$ Å whereas in **P**, $d_X = 1.41$–1.48 and $d_Z = 1.34$–1.42 Å leading to $\Delta d(\mathbf{P}) \cong 0.06$ Å. It is notable that the difference in bond length, $\delta d = d_X - d_Z$, increases in **P** to *ca.* 3 times that in **R**, and also the bond contraction of d_Z upon protonation is greater by 2–3 times than that of d_X, $\Delta d_Z = 2$–$3\ \Delta d_X$ where $\Delta d = d_P - d_R$. These comparisons indicate that bond contraction upon protonation is much greater in d_Z than in d_X, which in turn implies that bond contraction incurred by through-conjugation is much greater than that by π-polarization.

Table 8 The Hammett constants,[a] ρ_X and ρ_Z^+, for the gas-phase protonation processes (MP2/6-31G*//RHF/6-31G*)

		Z				
	Y	NH$_2$	CH$_3$	H	Cl	CN
ρ_X[b]	CH$_2$	−6.78	−8.81	−9.43	−8.91	−9.82
	NH	−6.96	−8.62	−9.18	−8.98	−9.62
	O	−7.54	−9.63	−10.23	−9.83	−10.74
	SiH$_2$	−6.57	−9.03	−9.68	−9.00	−9.98
	PH	−6.88	−8.93	−9.54	−8.99	−9.94
	S	−7.24	−8.98	−9.54	−9.15	−9.93
ρ_Z^+[c]	CH$_2$	−8.60	−9.98	−10.32	−10.27	−10.72
	NH	−6.76	−7.99	−7.79	−8.23	−8.62
	O	−6.69	−8.28	−8.63	−8.48	−8.95
	SiH$_2$	−8.75	−10.27	−10.64	−10.61	−11.23
	PH	−8.18	−9.60	−9.93	−9.87	−10.31
	S	−6.85	−8.16	−8.46	−8.35	−8.76

[a] Regression coefficients (*r*) are better than 0.97 in all cases. [b] Each entry of ρ_X value is calculated using a standard σ in eqn. (6) in varying the X group while keeping Y and Z constant. [c] Each entry of ρ_Z^+ value is calculated using σ^+ in eqn. (6) and varying the Z group while keeping X and Y constant.

It should noted here again that the conjugative mode of resonance interaction is favored by a stronger positive charge ($\Delta C_\alpha^+ > 0$), whereas π-polarization is favored by a weaker positive (or stronger negative) charge ($\Delta C_\alpha^+ < 0$) on the carbonyl carbon.

It can be shown that when the resonance interaction modes within the two rings are the same, the cross-interaction constants, S_{XZ} and S_{ZX}, are positive. For example, in **R** with Y = NH, as X is varied from NH$_2$ to CN ($\Delta\sigma_X^+ > 0$) S_Z changes from 1.33 to 1.41 ($\Delta S_Z > 0$) which gives a positive S_{ZX} (> 0). In this case, the resonance interaction occurs in both rings by the π-polarization mode. In contrast, in **P** as Z is varied from NH$_2$ to CN ($\Delta\sigma_Z^+ > 0$) S_X changes from 1.22 to 2.53 ($\Delta S_X > 0$) so that $S_{XZ} > 0$ as result of conjugative interaction in both rings. Bond contraction of d_X is in this case predominantly influenced by the conjugative mode. However, in **P** as X is varied from NH$_2$ to CN ($\Delta\sigma_X^+ > 0$) S_Z decreases from 2.74 to 1.78 ($\Delta S_Z < 0$) resulting in a negative S_{ZX} (< 0). Clearly this is due to a π-polarization interaction in the X-ring ($\Delta\sigma_X^+ > 0 \rightarrow \Delta C_\alpha^+ < 0$) in contrast to a conjugative mode of interaction in the Z-ring ($\Delta C_\alpha^+ < 0 \rightarrow \Delta S_Z < 0$). Thus the charge on C_α is determined by π-polarization, whereas the resonance bond contraction of d_X is predominantly influenced by conjugation, *i.e.*, the transmission mode of the resonance effect in the X-ring is a blend of the two, π-conjugation and through-conjugation, and the former controls the charge polarization whereas the latter prevails in the bond contraction of d_X.

Susceptibilities and cross-interaction constants based on the reaction energies

The protonation energies, $\Delta E^\circ = E_P - E_R$, are used to derive Hammett ρ values for the two ring systems separately, eqn. (6). The results are shown in Table 8.

$$-\frac{\Delta E^\circ}{2.3RT} = \rho\sigma \qquad (6)$$

The best fits were obtained with the σ^+ scale for the Z-ring as expected from the essentially conjugative nature of the interaction between the 5-membered heteroaromatic ring and the protonated carbonyl group. In contrast, however, the ordinary σ scale was required for the better correlation of eqn. (6) for

Table 9 ρ_X (Z = H), ρ_Z^+ (X = H) and ρ_{XZ} values at various levels of theory

		Y					
	Method[a]	CH_2	NH	O	SiH_2	PH	S
ρ_X[b]	A	−9.89	−10.35	−11.99	−10.20	−10.24	−10.36
	B	−9.92	−9.21	−10.97	−10.33	−10.34	−10.47
	C	−10.31	−10.05	−10.41	−10.52	−10.34	−10.45
	D	−9.44	−8.75	−10.69	−9.86	−9.90	−9.97
	E	−9.43	−9.18	−10.23	−9.68	−9.54	−9.54
ρ_Z^+[c]	A	−12.16	−11.16	−10.57	−12.26	−11.73	−10.43
	B	−11.62	−10.96	−10.88	−11.43	−11.16	−10.21
	C	−10.51	−9.40	−9.75	−10.58	−10.04	−8.98
	D	−11.35	−10.09	−10.08	−11.32	−10.89	−9.72
	E	−10.32	−7.79	−8.63	−10.64	−9.93	−8.46
ρ_{XZ}[d]	A	−1.91	−1.43	−2.49	−2.03	−1.96	−1.81
	B	−1.89	−1.43	−2.35	−2.04	−1.98	−1.84
	C	−1.68	−1.16	−1.29	−1.70	−1.45	−1.21
	D	−2.01	−1.65	−2.46	−2.14	−2.11	−2.02
	E	−1.58	−1.39	−1.66	−1.77	−1.58	−1.40

[a] The following abbreviations are used for the calculational method; A: RHF/3-21G*//RHF/3-21G*, B: RHF/6-31G*//RHF/3-21G*, C: RMP2/6-31G*//RHF/3-21G*, D: RHF/6-31G*//RHF/6-31G*, E: RMP2/6-31G*//RHF/6-31G*. [b] Each ρ_X entry is calculated using a standard σ in eqn. (6) and varying the X group while keeping Y and Z (= H) constant. [c] Each ρ_Z^+ entry is calculated using σ^+ in eqn. (6) and varying the Z group while keeping X (= H) and Y constant. [d] Regression coefficients (*r*) are better than 0.97 in all cases.

the X-ring,[‡] which suggests a prevalently non-conjugative, or π-polarization, mode of interaction for the X-ring.[3g]

Interestingly, the magnitude of ρ_X is similar to, or slightly greater than, that of ρ_Z^+; this is in contrast to the general trend that enhanced substituent constants such as σ^+ lead to increased susceptibility constants (ρ^+). A similar enhanced susceptibility with σ rather than with σ^+ was reported for the basicity (pK_{BH^+}) dependence on the substituent effect in 4-X-acetophenones ($\rho^+ = 1.2$) (**A**) and 4-X-2,6-dimethylacetophenones ($\rho = 5.3$) (**B**), for which through-conjugation and π-polarization modes of interaction, respectively, have been predicted.[3g] Examination of Table 8 reveals that for the diaryl ketones where Y = NH, O or S, and Z = NH_2 the magnitude of ρ_X is larger in the X-ring whereas that of ρ_Z^+ is smaller (for all X) in the Z-ring than those corresponding values for Y = CH_2, SiH_2 and PH. As has been stressed above, a weaker positive charge on C_α (C_α^+ is low for Y = NH, O and S with Z = NH_2 due to (i) the stronger delocalizability of the lone-pair π electron on the heteroatoms and (ii) a strong donor substituent on the Z-ring, Z = NH_2) leads to an increased susceptibility by π-polarization (larger magnitude of ρ_X) in the X-ring, in contrast to a decreased susceptibility by through-conjugation (smaller magnitude of ρ_Z^+) in the Z-ring. However, the ρ_X values with other weaker electron donors and electron acceptors in the Z-ring exhibit a strong levelling effect, particularly for Z = H, the ρ_X values are almost the same for the various Y substituents. This may be again due a blend of π-polarization and through-conjugation modes operating within the X-ring.

It should be pointed out that separate determination of the cross-interaction constants, ρ_{XZ}, for the two stationary states, **R** and **P**, is not possible since ρ_{XZ} is a reaction parameter. This means also that, unlike the cross-interaction constants S_{XZ} and S_{ZX} based on the bond contractions of d_X and d_Z, separate determination of $\rho_{XZ} = \dfrac{\Delta\rho_X}{\Delta\sigma_Z}$ and $\rho_{ZX} = \dfrac{\Delta\rho_Z}{\Delta\sigma_X}$ for **R** or **P** is impossible, and $\rho_{XZ} = \rho_{ZX}$[1] since the reaction energy, $\Delta E°$, cannot be separated into two component parts, $\Delta E^\circ \not\longrightarrow \Delta E^\circ(X) + \Delta E^\circ(Z)$, for each reaction energy determined.

The cross-interaction constants, ρ_{XZ} derived from eqn. (3), are summarized in Table 9. We note that the effect of basis sets on the magnitude of ρ_{XZ} is relatively small. By contrast, however, the effect of electron correlation (MP2) is substantial. Especially the magnitude of ρ_{XZ} for Y = O has been greatly reduced so that the order of increasing magnitude (O1) is

$$NH < S < CH_2 \cong PH < O < SiH_2 \qquad (O1)$$

similar to that of the changes in the positive charge on C_α (ΔC_α^+) and in the susceptibility of substituent effects (ΔC_α^+ and ΔS are in the order $NH < S < O < CH_2 < PH < SiH_2$) within the 5-membered heteroaromatic aldehyde ring upon protonation.[5] The exceptionally large magnitude of ρ_{XZ} for Y = O seems to reflect the greatest degree of coplanarity of the two rings for Y = O. The energy lowering by incorporation of the electron correlation effect ($\Delta E = E_{MP} - E_{RHF} < 0$) was greater for the reactants (**R**) than for the protonated (**P**) states by 7–9 kcal mol^{-1} in all the systems studied. It was also found that the lowering ($-\Delta E$) is greater, the stronger the electron donating power of substituent Z ($\Delta\sigma_Z^+ < 0$). These results simply show that electron correlation is greater in an electron localized system (**R**) than in a delocalized state (**P**). It has been shown that correlated treatments lead to higher resonance delocalization and this tendency of electron correlation to enhance delocalization is a general effect.[9] The results of this energy lowering, especially for systems with a stronger donor substituent, are reflected in the reduced magnitude of ρ_Z^+ and ρ_{XZ}. On the other hand, the energy lowering by improvement of the basis set from 3-21G* to 6-31G* (here again the lowering was greater in **R** than in **P**) was rather small (0–2 kcal mol^{-1}) as reflected in the relatively small effect of the basis set on ρ_{XZ}.

The fact that the order of ρ_{XZ} for the diaryl ketone systems with various heteroatoms Y (O1) is similar to that of the susceptibility of independent 5-membered heteroaromatic ring systems indicates that the effect of the X-ring is small and contributes almost a constant term to the overall cross-interaction in the protonation equilibria. The size of ρ_{XZ} ranging from *ca.* −1.4 to −1.8 is relatively large and is an indication that there is a relatively strong interaction within a molecule between the two rings upon protonation.[1]

The cross-interaction constants for equilibrium processes are in general large when in the product state the two fragments interacting are covalently bonded, and especially when a positive charge center is involved. An experimental example is the equilibrium cross-interaction constant determined for the

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[‡] Bond length changes seem to be more susceptible to resonance electron donation (Δd *vs.* σ_X^+) in eqn. (4a) and (4b) since the susceptibility, *S*, is separately determined from **R** and **P**. However the Hammett reaction constant, ρ, reflects the change ($\Delta E°$) from **R** to **P**. Thus the bond length and energy changes could be correlated differently with σ_X^+ and σ, respectively, for the X-ring.

Table 10 Comparison of the two types of cross-interaction constants for the protonation equilibria (for $\delta\Delta d = d_P - d_R$; $\delta\Delta d_X = S_X \times \sigma_Z$ *etc.*)

Y	S_{XZ}	S_{ZX}	ρ_{XZ}(MP2)
CH_2	0.86	−0.63	−1.58
NH	0.75	−0.60	−1.39
O	0.61	−0.43	−1.66
SiH_2	0.89	−0.61	−1.77
PH	0.91	−0.62	−1.58
S	0.73	−0.48	−1.40
reg. coeff. (*r*)	>0.96	>0.99	>0.97

nucleophilic substitution reactions of benzyl bromides with *N*,*N*-dimethylanilines (DMA),[10] eqn. (7).

$$XC_6H_4N(CH_3)_2 + YC_6H_4CH_2Br \xrightarrow[45.0\,^{\circ}C]{MeCN} \underset{(QA^+)}{XC_6H_4N^+(CH_3)_2CH_2C_6H_4Y} + Br^- \qquad (7)$$

In this case, the cross-interaction constant ($\rho_{XY} = -1.45$) is that between X and Y within the quaternary ammonium ion (QA^+), since the two reactants are non-interacting in the initial state. The two interacting fragments in QA^+ are covalently bonded and the reaction center is positively charged so that the magnitude of the cross-interaction constant is large.

Another experimental example of a strong interaction between two rings is found in the solvolysis of X,Z-disubstituted benzhydryl compounds, XC_6H_4–$C(CF_3)(C_6H_4Z)$–Tos, in MeOH at 25 °C, for which $\rho_{XZ} = -6.03 \pm 0.05$ ($r = 0.973$) was obtained.[11] The magnitude of ρ_{XZ} is extremely large, in fact is the largest ever observed, since a very strong positive charge develops at the reaction center in the transition state (TS) due to a strong electron acceptor group, CF_3, attached to the reaction center carbon, C_α.[12] Although ρ_{XZ} corresponds in this case to an activation parameter, the development of positive charge is believed to be nearly complete in the TS. The positive charge developed in the TS is so strong that the interaction of the two substituents, X and Z, at the cationic center is the strongest every observed.[11]

We have compared in Table 10 the ρ_{XZ} values (MP2) with the corresponding ΔS_{XZ} and ΔS_{ZX} values defined by eqn. (8a)–(8c).

$$\Delta S = \delta\Delta d/\Delta\sigma = S(\mathbf{P}) - S(\mathbf{R}), \text{ where } \delta\Delta d = d_P - d_R \qquad (8a)$$

$$\Delta S_{XZ} = \Delta S_X/\Delta\sigma_Z = S_{XZ}(\mathbf{P}) - S_{XZ}(\mathbf{R}) \qquad (8b)$$

$$\Delta S_{ZX} = \Delta S_Z/\Delta\sigma_X = S_{ZX}(\mathbf{P}) - S_{ZX}(\mathbf{R}) \qquad (8c)$$

We note that the magnitudes of the cross-interaction constants, ΔS_{XZ}, ΔS_{ZX} and ρ_{XZ}, for the systems with Y = NH, S and O (except for ρ_{XZ} with Y = O, for which coplanarity of the two rings are the greatest) are smaller than those for the other systems (Y = PH, CH_2 and SiH_2). This suggests that both ΔS_{XZ} (and ΔS_{ZX}) and ρ_{XZ} are of the same origin although the former is based on bond contractions (Δd_X and Δd_Z) whereas the latter is based on the reaction energies ($\Delta E°$).

Table 11 DSP analysis for protonation equilibria with Z or X = H[a]

	X-Ring (Z = H)			Z-Ring (X = H)		
Y	f^b	r^b	*f*/*r*	f^c	r^c	*f*/*r*
CH_2	−4.61	−3.01	1.53	−3.54	−5.71	0.62
NH	−4.57	−2.91	1.57	−5.46	−3.90	1.40
O	−4.55	−3.37	1.35	−4.23	−4.58	0.92
SiH_2	−4.54	−3.14	1.45	−2.53	−6.05	0.42
PH	−4.43	−3.10	1.43	−3.25	−5.51	0.59
S	−4.45	−3.10	1.44	−4.36	−4.46	0.98

[a] Regression coefficients (*r*) are better than 0.99 in all cases. [b] Each row of *f* and *r* is calculated by varying the X group while keeping Y and Z (= H) constant. [c] Each row of *f* and *r* is calculated by varying the Z group while keeping X (= H) and Y constant.

Finally we have subjected the reaction energies to the dual substituent parameter (DSP) analysis,[13] Table 11. A notable trend is that field effect is predominant, *f*/*r* > 1.0, in the X-ring in contrast to the dominant resonance effect, *f*/*r* < 1.0, in the Z-ring (except for Y = NH which has the lowest magnitude of *r* and the largest size of *f*). This is again a manifestation of the predominance of π-polarization in the X-ring and through-conjugation in the Z-ring. The relatively larger *f*/*r* values for the systems with Y = NH, O and S are again an indication of a weaker conjugative interaction accompanied by a stronger π-polarization component due to the lower positive charge on the carbonyl carbon ($\Delta C_\alpha^+ < 0$) as a result on the stronger delocalization of the lone-pair π-electrons of the heteroatoms. The delocalizability of the lone-pair π or pseudo π-electrons (Y = CH_2 and SiH_2) on the heteroatoms Y has been shown to be in the order NH > O > S > PH > CH_2 > SiH_2, which in turn leads to a reverse order of the positive charge on the carbonyl carbon, C_α^+.[5]

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