A Frontier Orbital Study of Substituent Effects in the Deamination of *N*-Substituted Quinone Di-imines *

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The substituent effects on the rate constants of the acid and alkaline deamination of quinone di-imines are explained, using the frontier orbital (FO) perturbation theory. The main contributions to the perturbation energy are electrostatic and orbital interactions. The alkaline deamination is both orbital and charge controlled, whereas the acid deamination is only an orbital-controlled reaction.

In previous papers[1] the kinetics and mechanism of the deamination of *N*-substituted quinone di-imines were discussed. From the rate constants and activation parameters and their dependence on the pH it was concluded that in alkaline solutions OH^- attacks the C(1) atom after a pre-equilibrium with H_2O, whereas the acid deamination starts by an attack of H_2O at the C(4) atom. It is proposed that these attacks determine the rate constants k_1 and k_3 of the acid and alkaline deamination. The proposed reaction schemes of both attacking nucleophiles are represented in Figure 1.

This paper reports that the measured substituent dependency of the deamination rate can be explained quantitatively by the perturbation FO theory using e.s.r. data.

Theory and Method of Calculation

In the frontier orbital approach only the interactions of the highest occupied molecular orbitals (HOMO), the lowest unoccupied molecular orbital (LUMO), and the non-bonding molecular orbital (NBMO) are employed.[2,3] For the deamination of quinone di-imines the orbital diagram in Figure 2 is valid. The MO energy levels of the various quinone di-imines were found by Hückel MO calculations.[4] The attacking nucleophiles OH^- and H_2O are represented by their non-bonding electron pairs. As shown in Figure 2 the nucleophile interacts with the neighbouring energetically empty orbitals of the quinone di-imine. During the approach of the reacting molecules their energies are shifted, which can be treated with a perturbation calculation.[5]

For the deamination, two main energy terms contribute to the perturbation energy, ΔE_{FO}: the electrostatic interaction ΔE_{el} and the stabilization energy ΔE_S, equation (1). For reactions

$$\Delta E_{FO} = \Delta E_{el} + \Delta E_S \qquad (1)$$

with comparable transition states it is assumed that the perturbation energy, ΔE_{FO}, is proportional to the activation energy, $\Delta E^{\neq}$, and therefore to log k, equation (2).

$$\Delta E_{FO} \sim \Delta E^{\neq} \qquad (2)$$

Using the Hückel approximation, the electrostatic interaction is expressed in terms of charge densities, $e_o q_i^\pi$, of the various centres i reacting with each other, equation (3), where N is the nucleophile.

$$\Delta E_{el} = \frac{q_i^\pi q_N e_o^2}{4\pi\varepsilon_o \varepsilon r_{iN}} \qquad (3)$$

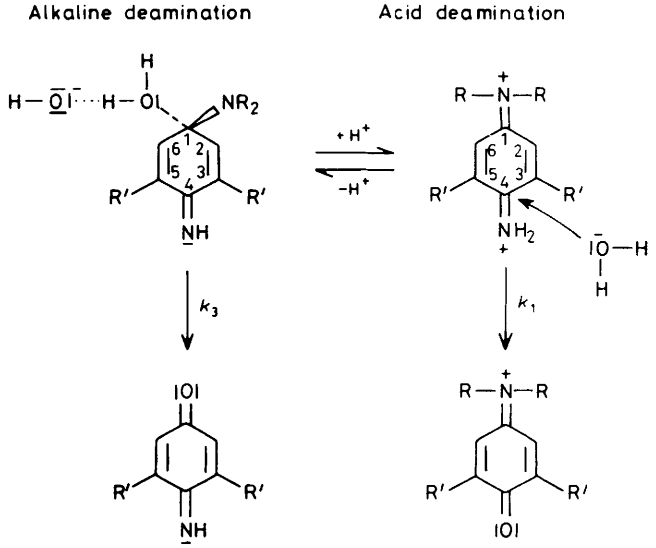

Figure 1. Reaction scheme of the acid and alkaline deamination of quinone di-imines (ref. 1)

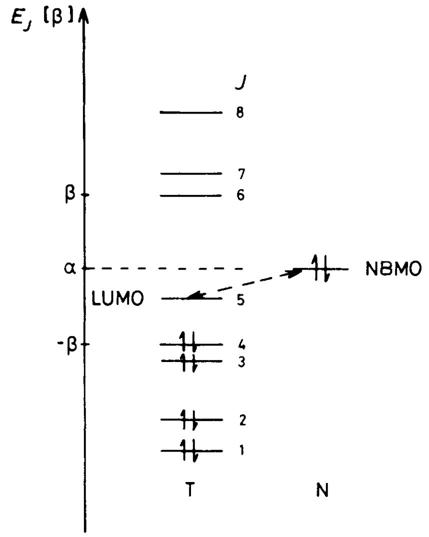

Figure 2. Orbital diagram for the deamination of quinone di-imines (T), with hydroxy ion (N)

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* For previous papers in this series, see ref. 1.

The q_i^π value is given by equation (4),[6] where b_J denotes the number of electrons distributed in each orbital J ($b_J = 0$, 1, or 2), and c_{Ji} is the coefficient of the LCAO-MO orbitals.

$$q_i^\pi = \sum_{J=1}^{n} b_J c_{Ji}^2 \qquad (4)$$

For the nucleophile OH^- $q_N = -1$, and for H_2O $q_N = 0$.

In general, the stabilization energy ΔE_S between a doubly occupied NBMO (φ_N) and a LUMO (φ_J) is given by equation (5), provided φ_N and φ_J are not degenerate. E_N and E_J denote the corresponding orbital energies.

$$\Delta E_S = \frac{2\langle\varphi_N|\mathscr{H}|\varphi_J\rangle^2}{E_N - E_J} \qquad (5)$$

Applying the LCAO-MO approximation and considering only neighbouring energy levels (see Figure 2, LUMO of T and NBMO of N) equation (5) becomes equation (6), with the

$$\Delta E_S = \frac{2(c_N{}^2 c_{Ji}{}^2 \beta_{iN})^2}{E_N - E_J} \qquad (6)$$

resonance integral β_{iN} representing the interaction between atom i of the quinone di-imine and the attacking nucleophile N.

As the nucleophile always attacks the same carbon atom,[7] β_{iN} can be regarded as equal for all structurally related compounds investigated in this paper. Within the HMO approximation the energies E_J and E_N are expressed by the corresponding energy eigenvalue coefficients, x_J and x_N, as $E_J = \alpha_c + x_J\beta_{cc}$. The constants α_c and β_{cc} denote the coulomb and the resonance integrals, respectively. If the reaction distance r_{iN} in equation (3) is regarded as being approximately constant and considering that for a non-bonding orbital $c_N{}^2 = 1$ and $x_N = 0$, equation (1) for the quinone di-imines being discussed gives equation (7), with $J = 5$ and $i = 1$ or 4.

$$\Delta E_{FO} = \frac{q_i^\pi q_N e_o{}^2}{4\pi\varepsilon_o\varepsilon r_{iN}} + \frac{2c_{5i}{}^2\beta_{iN}{}^2}{x_5\beta_{cc}} \qquad (7)$$

The various LCAO coefficients c_{5i} are obtained either by MO calculation[8] or experimentally from e.s.r. spin densities ρ_{iN},[6] which in a first approximation are equal to the squares of the LCAO coefficients,[6] equation (8). The spin densities ρ_i^π of

$$c_J{}^2 = \rho_i^\pi \qquad (8)$$

the centre i are related to the experimental e.s.r. coupling constants a_i by the McConnel relation, equation (9). The

$$a_i = |Q_i|\rho_i^\pi \qquad (9)$$

different spin-polarization parameters Q_i for various semiquinone di-imines were determined by e.s.r. studies.[4,9] Unfortunately, the C(4) and C(1) atoms where nucleophiles attack in acid or alkaline medium have no nuclear spin. (The ^{13}C coupling cannot be resolved in these many-line e.s.r. spectra.) Therefore their spin densities, $c_{54}{}^2$ and $c_{51}{}^2$, are not represented by e.s.r. coupling constants and can only be found by MO calculations. As usual the coulomb perturbation parameters h_{NX_2} of the various amino functions were obtained by the correlation of experimental e.s.r. coupling constants and computed spin densities.[4] The calculations were carried out by a McLachlan procedure (POL-2) modified for radical cations.[10] For the different perturbation parameters the following values were found: $h_{NH_2} = 1.26$; $h_{NMe_2} = 0.99$; and $h_{NEt_2} = 0.88$. The methyl group was considered to be an inductive perturbation by $h_{CMe} = -0.3$.

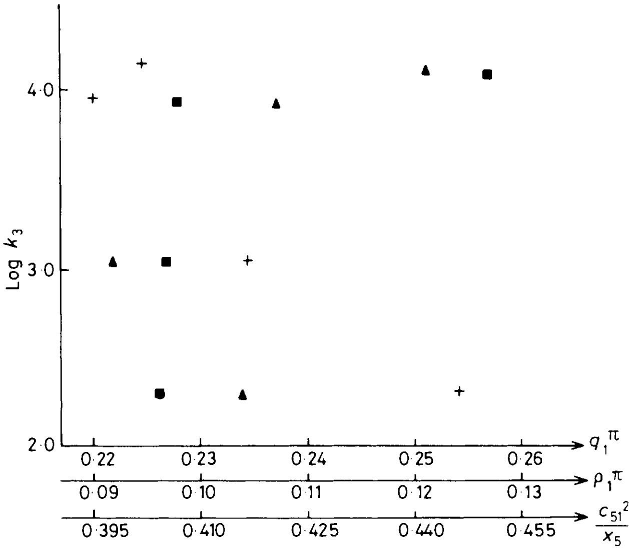

Figure 3. Log k_3 as a function of charge density q_i^π (■), spin density ρ_i^π (▲), and the orbital factor $c_{51}{}^2/x_5$ (+)

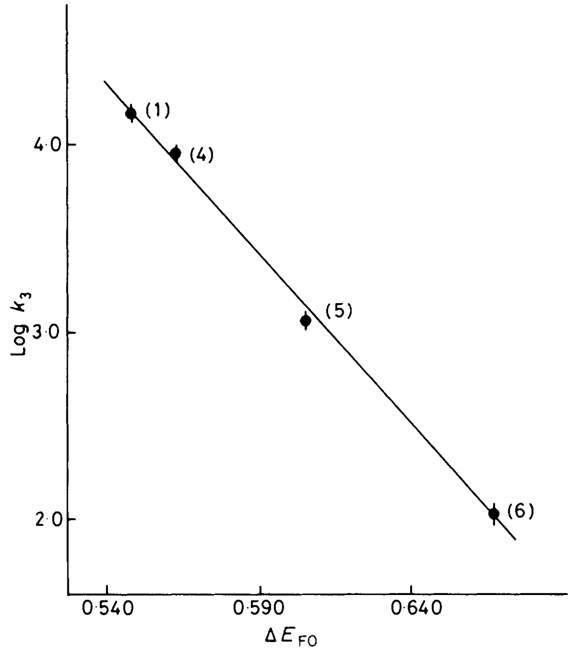

Figure 4. Alkaline deamination: rate constants log k_3 as a function of the perturbation energy ΔE_{FO}. For identification of compounds (**1**), (**4**), (**5**), and (**6**) see Tables 1 and 2

Discussion

The Alkaline Deamination.—The kinetic studies show that OH^- attacks the carbon atom C(1). Table 1 lists the rate constants log k_3 of the alkaline deamination, the energy eigenvalue coefficients x_5, the charge densities q_1^π, and the spin densities $c_{51}{}^2$ as well as the perturbation energies ΔE_{FO} calculated according to equation (7). As shown in Figure 3 log k_3 can be correlated with neither the charge density q_i^π nor with the spin density ρ_i^π nor the orbital factor $c_{51}{}^2/x_5$, as was assumed formerly. However, a very good linear dependency of log k_3 on ΔE_{FO} is found (see Figure 4).

Table 1. Alkaline deamination of quinone di-imines: charge densities q_1^{π}, LCAO coefficients c_{51}^2 of the quinone di-imines (LUMO), energy eigenvalue coefficients x_5, perturbation energies ΔE_{FO}, and rate constants k_3

Quinone di-imine	log k_3[1]	q_1^{π}	c_{51}^2	x_5	ΔE_{FO}
(**1**) *NN*-Dimethyl-*p*-quinone di-imine	4.15	0.257	0.121	0.301	0.547
(**4**) *NN*-Diethyl-*p*-quinone di-imine	3.95	0.228	0.107	0.271	0.562
(**5**) 3-Methyl-*NN*-diethyl-*p*-quinone di-imine	3.04	0.227	0.105	0.253	0.606
(**6**) 3,5-Dimethyl-*NN*-diethyl-*p*-quinone di-imine	2.30	0.226	0.104	0.233	0.667

Table 2. Acid deamination of quinone di-imines: LCAO coefficients c_{54}^2 of the quinone di-imines (LUMO), energy eigenvalue coefficients x_5, perturbation energies ΔE_{FO}, and rate constants k_1

Quinone di-imine	log k_1[1]	c_{54}^2	x_5	ΔE_{FO}
(**1**) *NN*-Dimethyl-*p*-quinone di-imine	−1.959	0.146	0.301	0.970
(**2**) 3-Methyl-*NN*-dimethyl-*p*-quinone di-imine	−1.432	0.164	0.279	1.176
(**3**) 3,5-Dimethyl-*NN*-dimethyl-*p*-quinone di-imine	−1.356	0.183	0.259	1.414
(**4**) *NN*-Diethyl-*p*-quinone di-imine	−1.824	0.143	0.271	1.056
(**5**) 3-Methyl-*NN*-diethyl-*p*-quinone di-imine	−1.509	0.161	0.252	1.278

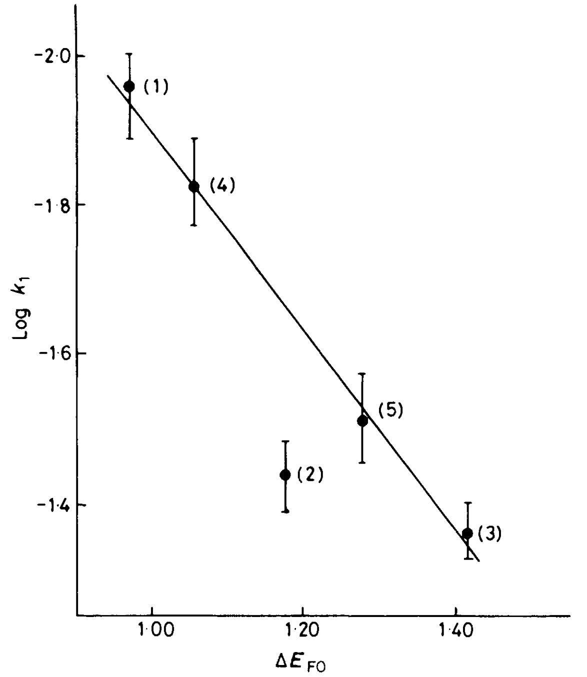

Figure 5. Acid deamination: rate constants log k_1 as a function of the perturbation energy ΔF_{FO}. For identification of compounds (**1**)—(**5**) see Table 2

The Acid Deamination.—The C(4) atom of the quinone di-imine is attacked by an uncharged water molecule, therefore the electrostatic interaction term ΔE_{el} in equations (1) and (7) disappears. Thus, the reaction is entirely orbital controlled.

The rate constant of the acid deamination, log k_1, and the spin densities, c_{54}^2, are quoted in Table 2. A linear correlation between log k_1 and ΔE_{FO} also exists here, as shown in Figure 5. The deviation with substance (**2**) probably is due to experimental difficulties.[11]

Conclusions

The substituent effects on the rate constants of acid and alkaline deamination of various quinone di-imines is interpreted using the frontier orbital theory and a perturbation approach. The perturbations are caused mainly by a charge density term ΔE_{el} and an orbital interaction term ΔE_S. Other interactions such as polarization and repulsion effects can be disregarded as they are either small or can be considered being constant for the reaction investigated.

The results of the frontier orbital calculations are in good agreement with the mechanisms deduced from kinetic data proposed in the earlier papers.[1] The advantage of this approach lies in the fact that it allows predictions to be made in the case of deamination where chemical intuition is insufficient to make correct predictions.

Acknowledgements

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