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NUCLEOPHILICITIES OF COMPOUNDS WITH INTERACTING ELECTRON PAIRS. DIAZINE-CATALYZED ESTER HYDROLYSIS

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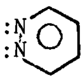
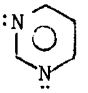
Pair-pair electron repulsion has been suggested to be an important factor responsible for the abnormally high reactivity of nucleophiles such as $R\ddot{\underset{..}{O}}\ddot{\underset{..}{O}}^{-}$ toward some electrophiles.[1] Recently, it has been suggested that widely separated electron pairs may interact strongly. Thus, molecular orbital calculations[2] and photoelectron spectroscopy[3,4] indicate that the unshared electron pairs of the diazines pyridazine (I),pyrimidine (II) and pyrazine (III) interact strongly. Interactions are transmitted both through space and through bonds.


I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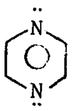
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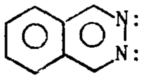
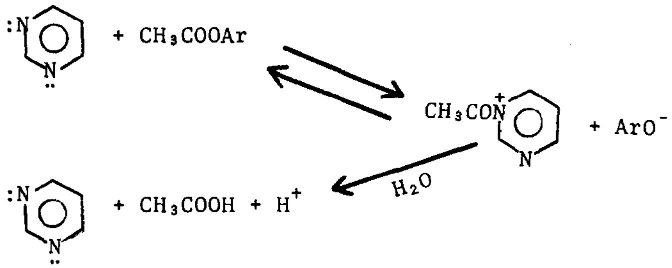

IV

This recent evidence for electron pair repulsion prompted us to determine whether the diazines and a benzolog, phthalazine (IV), would show an enhanced reactivity toward 2,4-dinitrophenyl acetate (DNPA); these compounds are expected to act as nucleophilic catalysts for the hydrolysis of this ester.[5] A representative hydrolysis pathway is shown in Scheme 1. This ester was selected for study because it was expected to react with the compounds of interest at convenient rates and because it is known to show large rate enhancements[5] in its reactions with nucleophiles such as $R\ddot{\underset{..}{O}}\ddot{\underset{..}{O}}^{-}$.

Scheme 1



The approach adopted is a standard one. The reactivities of I-IV were estimated from their pKa values using an established[5] Brønsted reactivity-basicity correlation. The estimated reactivities then were compared with experimental reactivities obtained under similar experimental conditions. Differences between observed and estimated nucleophilicities provide a measure of rate enhancements.

The reference Brønsted correlation was established using known rate constants for the reactions of DNPA with 4-methylpyridine (V), pyridine (VI) and nicotinamide (VII) in water at 25.0° and 1.0 M ionic strength.[5] (In order to check our method, the reactivity of nicotinamide toward DNPA was determined. Our second order rate constant is only 6% less than the reported value.)

The reactivities of I-IV toward DNPA at 25.0° were measured spectrophotometrically at 400 nm in 1:1 acetic acid-acetate ion buffers ($3.2\text{-}20 \times 10^{-3}$ M, total buffer) maintained at 1.0 M ionic strength with KCl. The concentration of DNPA was varied over the range $1\text{-}15 \times 10^{-5}$ M. Pseudo-first rate plots were linear over at least 4 half-lives and second-order rate constants, k_2, were not dependent on the initial concentration of DNPA, showing that the reverse of the first step in Scheme 1 is kinetically unimportant. Rate constants were calculated according to equation 1. Corrections for acetate ion and water catalyzed ester hydrolyses were made using known rate constants;[5] they were ≤ 13% of $k\psi$. The

$$k\psi = k_2[B]_t \cdot \frac{Ka}{[H] + Ka} + 3.4 \times 10^{-2}\,[CH_3CO_2^-] + 1.2 \times 10^{-5}[H_2O] \qquad (1)$$

concentration of nucleophile in the free base form was calculated from a knowledge of the total concentration of nucleophile, $[B]_t$, its Ka and a measured pH. Titrations were used to obtain pKa values for I and IV at 25.0° and 1.0 M ionic strength; values for II and III are taken from the literature.[6] Results are summarized in Table 1.

Table 1. Conditions and Results of the Hydrolysis of DNPA at 25.0°.

Compound	pKa	No. of Runs	Free Nucleophile Concn. Range, M	k_2, M^{-1} min^{-1}
I	2.44	6	0.00493-0.0257	4.35±0.26
II	1.23	4	0.216-0.648	$2.84 \pm 0.30 \times 10^{-2}$
III	0.65	3	0.260-0.520	$1.68 \pm 0.08 \times 10^{-2}$
IV	3.54	6	0.000470-0.00182	50.6 ±3.4

Figure 1 shows the Bronsted plot of nucleophilic reactivity vs pKa established by pyridine nucleophiles. The results for diazines II and III lie on this line and do not show an enhanced reactivity toward DNPA. But diazines I and IV show rate enhancements by a factor of 12. (Rate and equilibrium constants for the diazines are statistically corrected to reflect reaction at two equivalent nitrogen atoms, i.e., $k_2/2$ and 2Ka are used in Figure 1.)

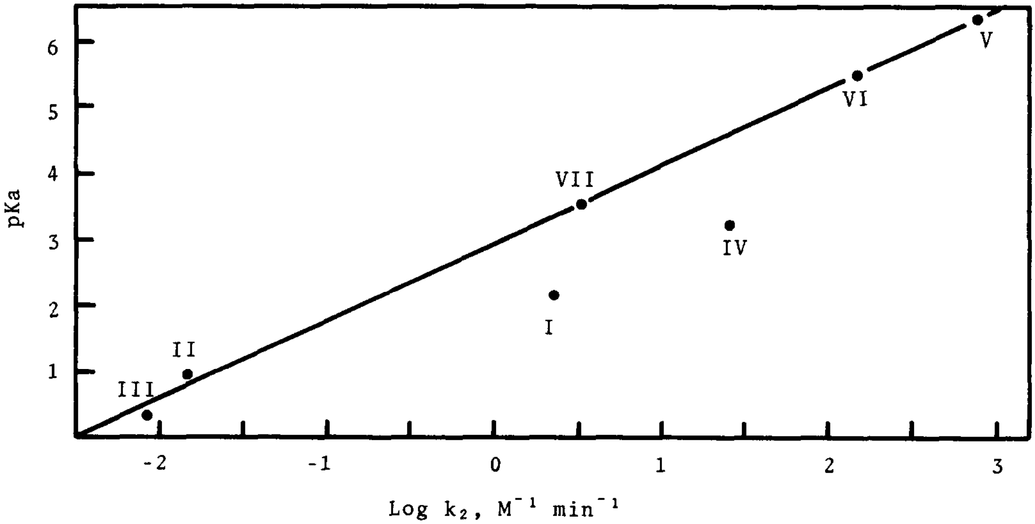


Figure 1. Brønsted plot of pKa vs log k_2 for diazines I-IV and pyridines V-VII reacting with DNPA.

It is clear from our results that I and IV can show reactivities which exceed those predicted by their basicities but it is curious that no special nucleophilicities are found for II and III. It will be of interest to determine whether rate enhancements can be demonstrated for II and III toward other electrophiles.

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