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ELECTRONIC NATURE OF THE AZA SUBSTITUENT OF PYRIDYL AND QUINOLYL GROUPS FOR REACTIVITIES IN AN INSULATED SYSTEM[1)]

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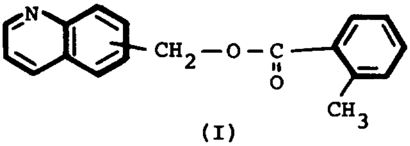
abstract: A new set of σ^o values was determined for all positions of pyridyl and quinolyl groups, reliably excluding steric effect by peri-hydrogen, on the basis of the rates of the alkaline hydrolysis of substituted 2-methylbenzoates and pyridylmethyl and quinolylmethyl 2-methylbenzoates in 70% aq acetone.

Nitrogens in N-containing heteroaromatics and their onium ions can affect organic and bioorganic reactivities quite importantly. One of the fundamenta points needing quantitative clarification is that of intramolecular effects of neutral mono-nitrogen in N-heteroaromatics such as pyridine and quinoline.[2)] Attempts to evaluate such electronic effects have been made by using various reactions such as pyrolysis of 1-(quinolyl)ethyl acetates[3)] and hydrolysis of methyl quinolinecarboxylates[4)] among others.[5)] These attempts, however, involve considerable uncertainties due to small ρ values,[3,6)] peculiarity of solvent-free conditions,[3)] complications by steric effects of peri-hydrogen,[4)] and tautomerism.[5)]

We wish to report here that a set of σ^o-type reactivities for pyridyl and quinolyl groups derived from the alkaline hydrolysis of arylmethyl 2-methylbenzoates (I) in 70%(V/V) aqueous acetone at 25 °C [7)] allows the desired electronic effects to be analysed in detail. The system possesses intrinsic advantages in that (i) the reaction center (C=O) is insulated far from the aryl group by a methylene and an oxygen, which brings about negligible


(I)

contribution of steric effects by peri-hydrogen ($\sigma^o_{1\text{-naph}} \approx \sigma^o_{2\text{-naph}}$),8) and (ii) nevertheless, the ρ value is large enough to evaluate a new set of σ^o constants within the usual limits of precision ($\rho_m \approx 1.0$).9) The methyl group at the ortho position of the benzoate moiety acts to reduce the hydrolysis rates by a factor of about ten and allows one to follow the rates for electron attracting pyridyl and quinolyl derivatives by ordinary titration methods.

Table 1 shows the second order rate constants and the σ^o values calculated from the rates relative to the rate for benzyl 2-methylbenzoate (Ph) by using ρ_m=0.989 determined from meta and para substituents (n=4). These σ^o values agree well with those reported by Deady and Shanks for the pyridyl group,10) but disagree with Taylor's for the quinolyl group,3) especially at the B ring positions. The present order of σ^o values in the quinoline series is 4Q>2Q>3Q>5Q>7Q≈6Q>8Q>Ph; in the first three groups, the sequence and the relative magnitudes are nearly equal to those in the pyridine series obtained (4P>2P>3P>Ph). All positions in the pyridyl and quinolyl groups have considerable electron attracting character, as expected from the electronic effects of nitrogen located in the parent ring.

Table 1. The Rate Constants and the σ^o Values from the Alkaline Hydrolysis of Arylmethyl 2-Methylbenzoates (70% aq acetone, 25°)

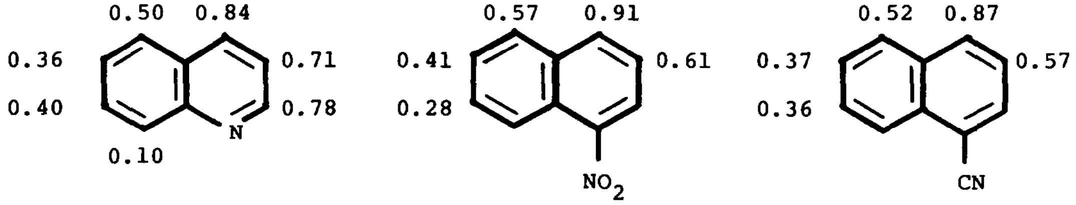
Aryl	$10^3k_2(s^{-1}M^{-1})$	σ^o a)	σ^o b)	σ^o_{corr} c)
Phenyl (Ph)	0.886 ± 0.019	0.00	0.00	
4-Chlorophenyl	1.72 ± 0.01	0.29	0.28	
3-Chlorophenyl	2.07 ± 0.05	0.37	0.37	
3-Nitrophenyl	4.47 ± 0.10	0.71	0.71	
2-Pyridyl (2P)	5.06 ± 0.09	0.76		
3-Pyridyl (3P)	4.58 ± 0.09	0.72		
4-Pyridyl (4P)	7.58 ± 0.07	0.94		
1-Naphthyl			0.05	
2-Naphthyl			0.06	
2-Quinolyl (2Q)	5.97 ± 0.03	0.84		0.78
3-Quinolyl (3Q)	5.10 ± 0.11	0.77		0.71
4-Quinolyl (4Q)	6.46 ± 0.05	0.89		0.84
5-Quinolyl (5Q)	3.11 ± 0.05	0.55		0.50
6-Quinolyl (6Q)	2.30 ± 0.02	0.42		0.36
7-Quinolyl (7Q)	2.55 ± 0.04	0.46		0.40
8-Quinolyl (8Q)	1.25 ± 0.02	0.15		0.10

a) Derived by $(k_X/k_{ph})/0.989$. b) Taken from Refs. 8 and 9b. c) $\sigma^o_{corr} = \sigma^o_{quino} - \sigma^o_{1\text{-}}$ or $_{2\text{-naph}}$.

By analogy with substituent effects in the naphthalene system,[11,12] the σ^o_{corr} values, derived by subtracting σ^o for the corresponding parent hydrocarbon from the σ^o for the quinoline system, must represent electronic effects of the aza substituent. The σ^o_{corr} values may be compared with some physical quantities, but could not be simply accounted for in terms of, for example, pi-charge differences calculated with the CNDO/2 MO method by Bloor and others available.[13]

Recently, we have noted that the contribution of the inductive effect of substituents in the naphthyl system is correlated fairly well by Dewar's function of $1/r$, possibly indicating a field effect.[12] Actually, the present aza effects can be interpreted to some extent with such a simplified function, where r is a distance between the carbon at which the reacting side-chain is attached and the nitrogen. We note the marked deviations of 4Q and 4P in the plot of σ^o_{corr} vs $1/r$, suggesting the importance of another pi-electronic (attracting) effect in such conjugated positions;[14] the 2Q, 2P, and 8Q are out of considerations, because the N-C distance is too short to apply the simple $1/r$ approximation and the effect of conformational preference may be involved.

The comparison of the σ^o_{corr} of quinolyl groups with the apparent $\bar{\sigma}_{corr}$ values derived from ΔpK_a for the dissociation of 1-nitronaphthalenecarboxylic acids and 1-cyanonaphthalenecarboxylic acids in 50% aq EtOH[15] is very instructive (Chart 1), where $\rho=1.38$ for 1-naphthalenecarboxylic acid series[12b] and $\rho=1.51$ for 2-naphthalenecarboxylic acid series[12a] are employed for calculation.[12c]



σ^o_{corr} values $\bar{\sigma}_{corr}$ values $\bar{\sigma}_{corr}$ values

Chart 1.

The NO_2 group in 1-nitronaphthyl derivatives is twisted out of the plane of the ring, and must have a reduced pi-electronic ability compared with a normal untwisted NO_2 group ($\sigma_i=0.46$, $\sigma^-_\pi=0.33$).[16] The overall figures in Chart 1 are explicable in terms of the following characters of inductive(σ_i) and pi-electronic(σ^-_π) effect for the aza substituent as a kind of a modified NO_2 in the naphthalene ring.[17]

$$\sigma_{i,aza} > \sigma_{i,NO_2} \simeq \sigma_{i,CN}(0.42)^{16)}$$

$$\sigma^-_{\pi,aza} < \sigma^-_{\pi,NO_2}(\text{twisted}) \simeq \sigma^-_{\pi,CN}(0.23)^{16)}$$

The large aza inductive ability may arise from the near location of N and the small pi-electronic ability may be understood in terms of the absence of an effective route by which accumulated electron density on N can be dispersed to outside unsaturated bonds as for NO_2. These are supported by the numerical values of σ^o (=0.94) and $\Delta\bar{\sigma}_R^-$ (=0.19) for the 4-pyridyl group[19] derived from the LArSR approach,[9b,18] independently.

References and Notes

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17) These sequences were evaluated from the relative magnitude of C_i and C_π values derived by using the statistical method for the three sets: $\sigma = (1/r)C_i + (\Delta q)C_\pi$ and $\sigma = \rho_i C_i + \rho_\pi C_\pi$. As a scale of transmission efficiency of pi-electronic effect, Forsyth's charge difference value (Δq)[20] were attempted to be employed in the former, although such Δq's at conjugated positions were considered to be overestimated in the present system. While, in the latter, ρ_i and ρ_π values were taken from the transmission coefficients for the basicities of substituted quinolines by means of the LSFE analysis.[1]
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