Tetrahedron Letters,Vol.22,No.47,pp 4733-4736,1981 0040-4039/81/474733-04$02.0(
Printed in Great Britain

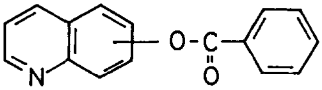
TOTAL REACTIVITY OF PYRIDINE AND QUINOLINE VIA THE REACTIONS OF ARYLBENZOATES WITH HYDROXIDE ION. APPARENT SUBSTITUENT CONSTANTS FOR SOME N-HETEROAROMATIC GROUPS

Masami SAWADA,* Masaharu ICHIHARA, Takashi ANDO, Yasuhide YUKAWA
The Institute of Scientific and Industrial Research,
Osaka University, Suita, Osaka 565, Japan
Yuho TSUNO*
Department of Chemistry, Faculty of Science,
Kyushu University, Hakozaki, Fukuoka 812, Japan

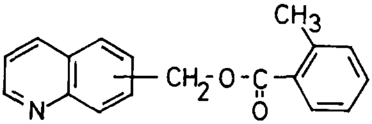
abstract: A new set of apparent σ values was evaluated for the aza substitution of all positions in pyridyl and quinolyl groups on the basis of the alkaline hydrolysis of aryl benzoates. The enhanced reactivities of 4-pyridyloxy- and 4-quinolyloxy- groups were first estimated quantitatively.

The electronic effects of pyridyl and quinolyl groups or more exactly, those of aza substituent at various positions in aromatic rings have not been well understood yet.[1] Apart from some fragmentary data, there are few kinetic studies for N-heteroaromatics, especially for quinolyl groups, with high precisions in a systematic fashion.[1] Previously, we reported a new set of σ^{o} values for pyridyl and quinolyl groups in an ordinary aqueous organic solvent .[2] The applicability of the resulted σ^{o} values must be then tested for other reactions containing such N-heteroaromatic groups.

The reaction of a series of pyridyl and quinolyl benzoates (I) with hydroxide anion was chosen as an appropriate reaction system. Compared with the previous insulated system (II), the present N-heteroaromatics in (I) are close to the reaction center (C=O) by a CH_2 group, which may bring about appreciable contributions of steric effects by peri-hydrogen and of additional electronic effects by ether oxygen linked directly to the N-heteroaromatics. The present report aims at establishing validity of the previous σ^{o} values and evaluating additional electronic and steric effects operated in the present system (I).



(I)



(II)

The alkaline hydrolysis rates were followed by two methods to get more reliable data: conductivity measurement in 56%(W/W) aq acetone at 5 °C (56A),[3,5] and spectrophotometric one in 33%(V/V) aq acetonitrile at 25 °C (33AN).[4,6] The second order rate constants are summarized in Table 1. The results can be satisfactorily combined with those of substituted-phenyl benzoates available under the same conditions.[3,4]

The analysis of meta and para substituent effects by means of our LArSR equation[8] gives the following relationships. The r^- value is approximately

in 56A at 5 °C; $\log k/k_o = 1.93\ (\sigma^o + 0.25\Delta\bar{\sigma}_R^-) - 0.04$ [9]

in 33AN at 25 °C; $\log k/k_o = 1.35\ (\sigma^o + 0.18\Delta\bar{\sigma}_R^-) - 0.03$ [10]

0.2 in both cases, indicating weak but existing additional resonance interactions with para pi-acceptor substituents, as mentioned by Humffray and Ryan.[3] Mechanistic evidence for the alkaline hydrolysis of such esters, which have been accumulated by using various LFER [4,11] and KIE [12] approaches indicates that the rate determining step is in the formation of the tetrahedral adduct. Therefore, the r^- value may be ascribed to the relative importance of the phenolic oxygen resonance with pi-acceptor aromatics (cross conjugation) in the transition state. The apparent $\bar{\sigma}$ values for the aza replacement or

Table 1. Rate Constants for the Reactions of Aryl Benzoates with OH^-

Aryl[a]	Rate Constant 56A, 5°C 10^2k_2 $(s^{-1}M^{-1})$	(n)[b]	33AN, 25°C 10^2k_2 $(s^{-1}M^{-1})$	(n)[b]
Phenyl(Ph)	0.707 ± 0.015[c]	(2)	5.52 ± 0.17[d]	(5)
p-COMe-Ph			27.5 ± 0.40	(4)
m-NO_2-Ph	14.8 ± 0.20[e]	(2)		
1-Naphthyl			4.21 ± 0.07	(3)
2-Naphthyl			5.33 ± 0.08	(3)
2-Pyridyl	8.81 ± 0.12	(4)		
3-Pyridyl	19.7 ± 0.30	(3)		
4-Pyridyl			200 ± 6	(2)
2-Quinolyl	13.1 ± 0.1	(2)		
3-Quinolyl	17.8 ± 0.4	(3)		
4-Quinolyl	57.0 ± 0.3	(3)	133 ± 3	(3)
5-Quinolyl	4.15 ± 0.03	(2)		
6-Quinolyl	3.97 ± 0.05	(2)		
7-Quinolyl	4.63 ± 0.06	(2)		
8-Quinolyl			2.99 ± 0.03	(2)

a) See Ref. 7 for mp of the compounds. b) Number of kinetic runs.
c) Reported as 0.793.[3] d) Reported as 5.58.[4] e) Reported as 14.8.[3]

benzaza substitution in the present N-heteroaromatics are calculated based on the above ρ_m value[13)] for substituted phenyl derivatives (Table 2).

The reactivity sequence of (I) apparently differs from the sequence of (II). The following interesting facts are noted in the difference $\Delta\sigma=\bar{\sigma}-\sigma^o$ (in Table 2). The $\bar{\sigma}$ values for the 3P, 3Q, 6Q, and 2N are reasonably equal to the corresponding σ^o values, indicating their non-conjugative characters. The $\bar{\sigma}$ for the conjugative 7Q also fits well with the σ^o. This reflects reduced pi-electron attraction of the nitrogen in the second ring of the naphthalene. The retardation $\Delta\sigma=-0.13$ attributable to the peri-hydrogen steric effect is evidently observed for 5Q and 1N. Very interestingly, the retardation effect $\Delta\sigma=-0.33$ caused by the nitrogen lone pair is significant in 8Q. The repulsive interaction with reaction site is clearly more effective than the above peri-hydrogen effect.

The most remarkable is the large rate acceleration observed for the conjugative 4P and 4Q. When the correction, -0.13 obtained for 5Q, is applied to the peri-hydrogen steric effect in 4Q, the $\Delta\sigma$ values of 4P and 4Q amount to 0.26 (averaged), twice as much as the $\Delta\sigma$ value for strong acceptors p-NO_2 and p-CN groups. Even though the nitrogen 4 position in the naphthalene ring has been considered of not as good a pi-electron acceptor as p-NO_2 group,[1)] this significant acceleration suggests that the particular stabilization interaction

Table 2. Apparent $\bar{\sigma}$ Values Derived from the Reaction of Aryl Benzoates

Aryl	$\bar{\sigma}$ a)	σ^o b)	$\Delta\sigma$ c)	Aryl	$\bar{\sigma}$ a)	σ^o d)	$\Delta\sigma$ c)
Phenyl(Ph)	(0.000)	(0.00)	(0.00)	p-Me-Ph	-0.143	-0.124	-0.02
1-Naphthyl(1N)	-0.066	0.05	-0.12	m-Cl-Ph	0.327	0.373	-0.05
2-Naphthyl(2N)	0.010	0.06	-0.04	p-Cl-Ph	0.282	0.281	0.01
2-Pyridyl(2P)	0.595	0.76	-0.17	m-COMe-Ph	0.381	0.376	0.01
3-Pyridyl(3P)	0.779	0.72	0.06	p-COMe-Ph	0.540	0.491	0.05
4-Pyridyl(4P)	1.18	0.94	0.24	p-COOEt-Ph	0.498	0.453	0.05
2-Quinolyl(2Q)	0.686	0.84	-0.15	p-COPh-Ph	0.532	0.490	0.04
3-Quinolyl(3Q)	0.756	0.77	-0.01	m-CN-Ph	0.635	0.615	0.02
4-Quinolyl(4Q)	1.04^{ave}	0.89	0.15	p-CN-Ph	0.786	0.653	0.13
5-Quinolyl(5Q)	0.423	0.55	-0.13	m-NO_2-Ph	0.710^{ave}	0.710	0.00
6-Quinolyl(6Q)	0.412	0.42	-0.01	p-NO_2-Ph	0.897^{ave}	0.800	0.10
7-Quinolyl(7Q)	0.447	0.46	-0.01				
8-Quinolyl(8Q)	-0.176	0.15	-0.33				

a) Present study. See Note 13. b) Ref. 2. c) $\Delta\sigma = \bar{\sigma} - \sigma$. d) Ref. 14.

exists between the ether oxygen and the pyridine or quinoline probably due to the contribution from stable pyridone and quinolone structures. This may further suggest a large σ^- value as well as large $\Delta\bar{\sigma}_R^-$ value for the 4-aza substituent. On the other hand, in the case of 2P or 2Q, the apparent retardation is observed as -0.16 σ-unit. If the quinoidal stabilization effect is assumed to be the same in both cases of 2 and 4 aza derivatives, the retardation arising from the proximity of the nitrogen lone pair at ortho position to the reaction site in 2P or 2Q would be estimated to be as much as -0.4 σ-unit.

References and Notes

1) For recent review, M. Charton,"Correlation Analysis in Chemistry", Plenum Press(1978), Chap. 5.
2) M. Sawada, M. Ichihara, T. Ando, Y. Yukawa, and Y. Tsuno, Tetrahedron Lett. 21, 4917(1980).
3) A. A. Humffray and J. J. Ryan, J. Chem. Soc., B, 1967, 468.
4) J. F. Kirsch, W. Clewell, and A. Simon, J. Org. Chem., 33, 127(1968).
5) At 5.00±0.01 °C. $[\mathrm{NaOH}]_0=2[\mathrm{ester}]_0=5\times10^{-3}$ M. The Tobey's method with $\Delta t\simeq\tau$ was employed for the rate calculations; S. W. Tobey, J. Chem. Educ., 39, 473(1962).
6) At 25.00±0.03 °C in a 5 cm-length cell. KOH was used ($\mu=0.3$ M with KCl). The observed relationship ($\mathrm{pH}=0.952\log[\mathrm{OH}^-]+14.58$) was used for triethylamine buffer solution. A non-linear method was employed to get the pseudo 1st order rate constants; C. D. Ritchie et al., J. Am. Chem. Soc., 97, 1163(1975).
7) C. J. Cavallito and T. H. Hasbell, J. Am. Chem. Soc., 66, 1166(1944); J. I. G. Cadogan, J. Chem. Soc., 1959, 2844.
8) Y. Tsuno, M. Fujio, Y. Takai, and Y. Yukawa, Bull. Chem. Soc. Jpn., 45, 1519(1972); Y. Tsuno, Y. Kusuyama, M. Sawada, T. Fujii, and Y. Yukawa, 48, 3337(1975). References cited therein.
9) R=0.9926, s=±0.067, n=10 (H, m-Cl, m-Ac, m-CN, m-NO_2, p-Ac, p-COPh, p-COOEt, p-CN, p-NO_2).
10) R=0.9953, s=±0.058, n=6 (H, p-Me, p-Cl, m-NO_2, p-Ac, p-NO_2).
11) C. D. Ritchie, J. Am. Chem. Soc., 97, 1170(1975); W. P. Jencks and M. Gilchrist, ibid., 90, 2622(1968).
12) M. H. O'Leary and J. F. Marlier, J. Am. Chem. Soc., 101, 3300(1979); I. M. Korach, J. P. Elrod, and R. L. Schowen, ibid., 102, 7530(1980).
13) For 56A, 5 °C: $\log k/k_0=1.895\sigma_m-0.032$ (r=0.9953, s=±0.058, n=5).
For 33AN, 25 °C: $\log k/k_0=1.345\sigma_m-0.029$ (r=0.9989, s=±0.027, n=4).
14) M. Sawada, M. Ichihara, Y. Yukawa, T. Nakachi, and Y. Tsuno, Bull. Chem. Soc. Jpn., 53, 2055(1980).

(Received in Japan 18 August 1981)