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Substituent Effects on Dissociation Constants of 4- and 6-Styryl-2-aminotropones

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The dissociation constants of two series of 4- and 6-styryl-2-aminotropones were measured spectrophotometrically in 50% aqueous methanol at 20°C. It was found that Hammett's free energy relationship is applied to the analysis of substituent effects, with $\rho=0.59$ and 0.40, respectively, and that there is a difference between the electronic effects of the two isomers.

The transmission of electronic effects from one aromatic ring to another through the linkage between them has recently aroused considerable interest. For stilbenes which have an ethylene linkage between two benzene rings, the dissociation constants of various 4-aminostilbenes[1] and 4-hydroxystilbenes[2] and the chemical shifts of 4-fluorostilbenes[3] were measured. It was found that the electronic effect of the substituent in one ring is transmitted through the ethylene linkage to the *p*-substituent in another ring and is correlated by the Hammett equation.

One of the authors (H. M.) investigated the reactions of 4-styryltropolone and its derivatives, which have a similar ethylene linkage, with various nucleophilic reagents.[4] In order to examine the reactivities quantitatively, we measured the dissociation constants of some 4-[5] and 5-styryltropolones[6] (Fig. 1). We found that the electronic effects of substituents in the benzene ring are transmitted through the ethylene linkage to tropolone nucleus, though the effects are small as in the case of stilbenes.[1,2]

In 4-styryltropolone, there are two tautomeric forms, *viz.*, 2-hydroxy-4-styryltropone and 2-hydroxy-6-styryltropone. The dissociation constants of 4-styryltropolones are, therefore, a combination of two nonequivalent tautomeric forms evidenced by the different ultraviolet absorption spectra of 4- and 6-styryl-2-hydroxytropones[7] and the substituent effects in these two forms should differ.

In order to determine the difference of substituent effects between the 4- and 6-(substituted styryl)tropones, the dissociation constants of 4- and 6-styryl-2-aminotropones (Fig. 1) were measured spectrophotometrically. It was shown that a difference in the electronic effect between the two forms actually exists.

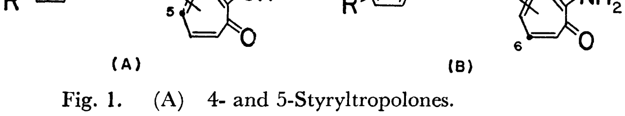

Fig. 1. (A) 4- and 5-Styryltropolones.
(B) 4- and 6-Styryl-2-aminotropones.

Results and Discussion

Dissociation Constants. The dissociation constants of two series of 2-aminotropones, *viz.*, 2-amino-4-styryltropones and 2-amino-6-styryltropones with substituent in the benzene ring, were determined spectrophotometrically in 50% aqueous methanol at 20°. The results expressed in terms of pK_a values are summarized in Table 1. Since activity coefficients were not introduced into the calculations, the dissociation constants do not represent thermodynamic terms, giving only a relative measure of base strength.

Table 1. Dissociation constants of 2-amino-4- and 6-styryltropones

No.	R	pK_a 4-Styryl	pK_a 6-Styryl
1	*p*-OCH$_3$	2.71	2.69
2	*p*-CH$_3$	2.64	2.65
3	H	2.54	2.57
4	*p*-Cl	2.39	2.51
5	*p*-Br	2.34	2.50
6	*m*-Cl	2.33	2.42
7	*m*-NO$_2$	2.14	—
8	*p*-NO$_2$	2.08	—

Numbering of substituents refers to that given in Figs. 2 and 3.

The dissociation constants are comparable to the pK_a value (2.17) of 2-aminotropone.[8] Further, the 4- and 6-styryl-2-aminotropones show the pK_a values between 2.08 [4-(*p*-nitrostyryl)] and 2.71 [4-(*p*-methoxystyryl)], and are less basic than *p*-(substituted styryl)-anilines (*i.e.* 3′- and 4′-substituted 4-aminostilbenes [pK_a 3.43 (*p*-nitro) to 3.86 (*p*-methoxy)]).[1] This is attributed to the electron-withdrawing effect of the carbonyl group adjacent to the amino group in tropone nucleus.

Substituent Effects. When the pK_a values of 2-amino-4-styryltropones are plotted against the Hammett

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[1] H. Veschambre and A. Kergomard, *Bull. Soc. Chim. Fr.*, **1966**, 336.

[2] H. Veschambre, G. Dauphin, and A. Kergomard, *ibid.*, **1967**, 2846.

[3] R. G. Pews and N. D. Ojha, *J. Amer. Chem. Soc.*, **91**, 5769 (1969).

[4] H. Matsumura, *Nippon Kagaku Zasshi*, **77**, 300 (1956); **78**, 669 (1957); **81**, 1763 (1960); **82**, 623, 775 (1961); H. Matsumura and S. Nagamura, *ibid.*, **85**, 901 (1964).

[5] K. Imafuku, S. Nakama, and H. Matsumura, *Tetrahedron*, **26**, 1821 (1970).

[6] K. Hamada, S. Nakama, K. Imafuku, K. Kurosawa, and H. Matsumura, *ibid.*, **27**, 337 (1971).

[7] H. Matsumura, Ph. D. Thesis, Tohoku University (1961).

[8] T. Hiratsuka and S. Seto, presented at 1 st Symposium on Nonbenzenoid Aromatic Chemistry, Sendai (1966).

substituent constants, σ,[9] of the substituent in the benzene ring, the plot gives the line shown in Fig. 2, and the following equation is obtained by the least square method.

$$\mathrm{p}K_a = 2.53 - 0.59\,\sigma \quad (r=0.993)$$

For the 2-amino-6-styryltropones, a similar Hammett plot is given (Fig. 3) and the following equation is obtained.

$$\mathrm{p}K_a = 2.58 - 0.40\,\sigma \quad (r=0.992)$$

Thus, it was found that the electronic effects of the substituents in the benzene ring are transmitted through the ethylene linkage to the amino group in the tropone nucleus and are correlated by the Hammett equation. However, the effects are small and considered to be inductive, since the styryl group in these 4- and 6-styryl-2-aminotropones is located at such a position that the resonance interaction between the styryl group and the reaction centre of tropone nucleus is inhibited.

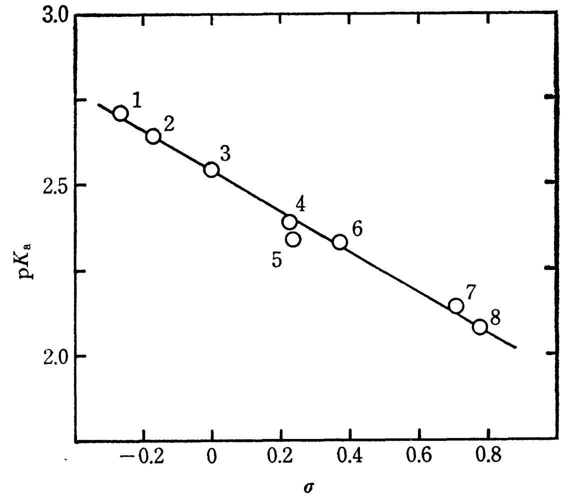

Fig. 2. The Hammett plot of pK_a's of 2-amino-4-styryltropones.

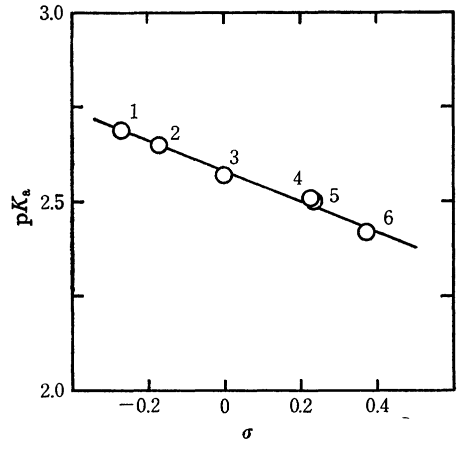

Fig. 3. The Hammett plot of pK_a's of 2-amino-6-styryltropones.

When the 4-styryl and 6-styryl derivatives are compared with each other, the reaction constant (0.59) of 4-styryl isomers is larger than that of 6-styryl isomers (0.40) because of the difference in distance between the styryl group and the amino group. However, both of them are comparable to the ρ value of the dissociation of 4-aminostilbenes (0.42 in 50% aqueous ethanol at 20°).[1]

Experimental

Materials. The 2-amino-4-styryltropones and 2-amino-6-styryltropones were prepared by the method des-

Table 2. 2-Amino-4-styryltropones and 2-amino-6-styryltropones

Styryl group	Substituent	Mp (°C)	Analysis (%) Found C	H	N	Calcd C	H	N
4-Styryl	H	194—195[a]						
	p-OCH_3	194—196	75.61	5.98	5.58	75.87	5.97	5.53
	p-CH_3	190—193	81.09	6.41	5.95	80.98	6.37	5.90
	p-Cl	211—213	70.16	4.68	5.26	69.91	4.69	5.43
	m-Cl	170—171	69.82	4.77	5.71	69.91	4.69	5.43
	p-Br	215—216	59.52	4.10	4.62	59.62	4.00	4.64
	p-NO_2	265—267	67.24	4.60	10.44	67.15	4.51	10.44
	m-NO_2	222—225			10.29			10.44
6-Styryl	H	137—138[b]						
	p-OCH_3	151—153			5.26			5.53
	p-CH_3	175—176	80.69	6.20	6.12	80.98	6.37	5.90
	p-Cl	183—184	69.96	4.68	5.48	69.91	4.69	5.43
	m-Cl	202—204	69.63	4.66	5.35	69.91	4.69	5.43
	p-Br	199—201	59.63	4.13	4.88	59.62	4.00	4.64

a) Mp. 194.5—195°C (Ref. 10).
b) Mp. 137—138°C (Refs. 10 and 11).

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[9] H. H. Jaffé, *Chem. Revs.*, **53**, 191 (1953).

[10] H. Matsumura, *Nippon Kagaku Zasshi*, **81**, 1763 (1960).

[11] D. S. Tarbell, K. I. H. Williams, and E. J. Sehm, *J. Amer. Chem. Soc.*, **81**, 3443 (1959).

cribed elsewhere.[12]

4-Styryltropones[13] were treated with an excess of diazomethane in chloroform to give two isomers, *viz.*, 2-methoxy-4-styryltropones and 2-methoxy-6-styryltropones. The two isomers were separated by preparative thin layer chromatography.

Each methyl ether was ammonolyzed with ammonia in absolute ethanol in a sealed tube to give the desired 2-amino-4-styryltropones or 2-amino-6-styryltropones. They were purified by recrystallization from ethanol or benzene.

Their melting points and analytical data are listed in Table 2.

Measurements of the Dissociation Constants. The dissociation constants of the 2-amino-4-styryltropones and 2-amino-6-styryltropones were measured spectrophotometrically in 50% aqueous methnol at 20° by the method of Flexer *et al.*[14]

These constants were obtained by using the equation

$$pK_a = pH - \log\frac{\varepsilon_{BH^+} - \varepsilon}{\varepsilon - \varepsilon_B}$$

where ε_B and ε_{BH^+} are the molar extinction coefficients of the base and conjugate acid, respectively. As an example, the spectral change of 2-amino-4-styryltropone upon pH change of medium is shown in Fig. 4.

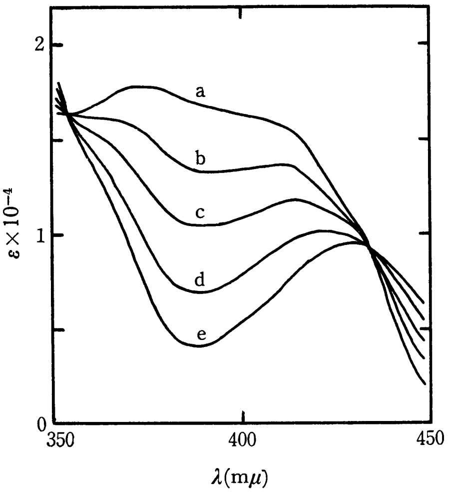

Fig. 4. Electronic Spectra of 2-Amino-4-styryltropone in 50% aqueous methanol.
a: pH 1.03 (conjugate acid), b: pH 2.15, c: pH 2.52, d: pH 3.09, e: pH 6.34 (free base)

The absorption spectra were taken on a Hitachi EPS-3T spectrophotometer, and the pH values were measured by a Hitachi-Horiba F-5 pH meter.

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[12] K. Imafuku and H. Matsumura, This Bulletin, **46**, 199 (1973).

[13] S. Nakama, K. Imafuku, and H. Matsumura, *ibid.*, **43**, 3265 (1970).

[14] L. A. Flexer, L. P. Hammett, and A. Dingwall, *J. Amer. Chem. Soc.*, **57**, 2103 (1935).