Substituent Effects on Dissociation Constants of *trans*-3-Hydroxy-6-styryl-4-pyrones

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The dissociation constants of 6-substituted 3-hydroxy-4-pyrones and *trans*-6-(substituted styryl)-3-hydroxy-4-pyrones were measured spectrophotometrically in 50% aqueous methanol at 25 °C. The results are correlated to the substituent constants σ, the following equations being obtained: $pK_a=8.57-1.53\,\sigma$ and $pK_a=8.54-0.23\,\sigma$. The transmission coefficient through the styryl group was found to be 0.150 for the 3-hydroxy-6-styryl-4-pyrone system.

Choux and Benoit[1] measured the dissociation contants of 6-substituted 3-hydroxy-4-pyrones in water at 25 °C, and obtained the following Hammett equation:

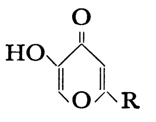
$$pK_a = 8.01 - 1.63\sigma \quad (r=0.978). \qquad (1)$$

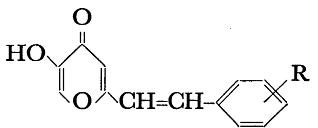
However, little is known about the substituent effects for 3- or 5-hydroxy-4-pyrones. We report herewith on the substituent effects of 3-hydroxy-4-pyrones having styryl groups in the 6-position.

Studies were made on the substituent effects on dissociation constants of 4- and 5-styryltropolones.[2,3] The transmission of electronic effects from one aromatic ring to another through the ethylene linkage between them has been investigated in detail. It is of interest to compare the reaction constants of 4- and 5-styryltropolones with that of 3-hydroxy-6-styryl-4-pyrones. We found that the electronic effects of substituents in the benzene ring are transmitted through the ethylene linkage to 4-pyrone nucleus, the effects being comparable to those of 4-hydroxystilbenes.

Results and Discussion

Dissociation Constants. The dissociation constants of 6-substituted 3-hydroxy-4-pyrones (I) and 6-(substituted styryl)-3-hydroxy-4-pyrones (II) were determined spectrophotometrically in 50% aqueous methanol at 25 °C. The results are summarized in Tables 1 and 2.


(I)


(II)

Ia R=H
Ib R=CH_3
Ic R=COOH
Id R=CH_2Cl

IIa R=H
IIb R=p-OCH_3
IIc R=p-CH_3
IId R=3′,4′-$(OCH_3)_2$
IIe R=p-Cl
IIf R=m-NO_2
IIg R=p-NO_2

TABLE 1. DISSOCIATION CONSTANTS OF 6-SUBSTITUTED 3-HYDROXY-4-PYRONES

R	σ	pK_a
CH_3	−0.17[a]	8.84
H	0.00	8.55
COO-	0.13[b]	8.38
CH_2Cl	0.18[a]	8.29

a) Ref. 5. b) Ref. 6.

TABLE 2. DISSOCIATION CONSTANTS OF 6-(SUBSTITUTED STYRYL)-3-HYDROXY-4-PYRONES

No.[a]	R	σ[b]	pK_a
1	p-OCH_3	−0.27	8.60
2	p-CH_3	−0.17	8.58
3	3′,4′-$(OCH_3)_2$	−0.15	8.57
4	H	0.00	8.55
5	p-Cl	0.23	8.52
6	m-NO_2	0.71	8.37
7	p-NO_2	0.78 (1.27)[c]	8.26

a) Numbers correspond to those in Fig. 1.
b) Ref. 5. c) σ^- Value.

The pK_a values of these 4-pyrones are smaller than those of phenols (pK_a=10.02 for phenol),[4] since the carbonyl group of 4-pyrones causes a decrease in the pK_a values by its electron withdrawing effect.

Substituent Effects. The pK_a values of 6-substituted 3-hydroxy-4-pyrones (I) and 6-(substituted styryl)-3-hydroxy-4-pyrones (II) were plotted against the Hammett substituent constants σ.[5,6] As an example, the Hammett plot of the latter is shown in Fig. 1. The following Eqs. 2 and 3 were obtained by the least squares method for systems (I) and (II), respectively (except for the p-nitro group in Eq. 3).

$$pK_a = 8.57 - 1.53\sigma \quad (r=0.998), \qquad (2)$$

$$pK_a = 8.54 - 0.23\sigma \quad (r=0.983). \qquad (3)$$

The plot of the p-nitro group deviates from the straight line given by Eq. 3 (Fig. 1). The deviation might be

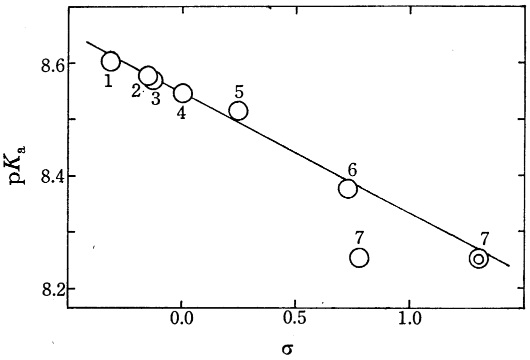


Fig. 1. The Hammett plot of pK_a's of 3-hydroxy-6-styryl-4-pyrones.
◎; Plotted against σ^- (1.27).

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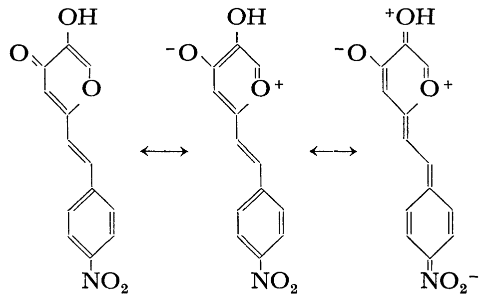
attributed to the resonance interaction between the *p*-nitro group and the hydroxyl group in the 3-hydroxy-4-pyrone. Application of the σ^--value (1.27)[6] for the *p*-nitro group gives good linearity (Fig. 1). A similar resonance effect was also observed in the dissociation of *trans*-*p*-nitro-4-hydroxystilbene.[7] In 4- and 5-styryltropolones, the resonance effect might be present only in 5-styryltropolones, but this was not confirmed since 5-(*p*-nitrostyryl)tropolone was not available.



Reaction Constants. The reaction constants of 6-substituted 3-hydroxy-4-pyrones (I) and 6-(substituted styryl)-3-hydroxy-4-pyrones (II) are 1.53 and 0.23, respectively. These values are comparable to those of phenols (2.55)[8] and 4-hydroxystilbenes (0.37),[7] respectively. The reaction constant of 3-hydroxy-6-styryl-4-pyrones lies between 0.13 and 0.60 constants of 4- and 5-styryltropolones, respectively. The difference can be attributed to the tautomerism of tropolones.

Transmission Coefficients. When the reaction constants for the same reaction of two series of aromatic compounds, which are parents, and styryl-substituted compounds are denoted by ρ_M and ρ_S, respectively, the transmission coefficient π of the styryl group can be defined as follows:

$$\pi = \rho_S/\rho_M.$$

The transmission coefficients π for several systems are given in Table 3. The π-value of 3-hydroxy-6-styryl-4-pyrone system is 0.150, and comparable to that of 4-hydroxystilbenes. We found that the electronic effects of the substituents in the benzene ring are transmitted through the styryl group in the order, 4-styryltropolones $<$ 4-hydroxystilbenes $\fallingdotseq$ 3-hydroxy-6-styryl-4-pyrones $<$ 5-styryltropolones.

Table 3. Reaction constants and transmission coefficienis

System	Solvent	Temp (°C)	ρ	π
Phenols	49% EtOH	20—22	2.55[a]	
4-Hydroxystilbenes	50% EtOH	20	0.37[b]	0.145
Tropolones	H_2O	25	2.68[c]	
4-Styryltropolones	50% MeOH	20	0.13[d]	0.049
5-Styryltropolones	50% MeOH	20	0.60[e]	0.224
3-Hydroxy-4-pyrones	50% MeOH	25	1.53[f]	
3-Hydroxy-6-styryl-4-pyrones	50% MeOH	25	0.23[f]	0.150

a) Ref. 8. b) Ref. 7. c) N. Yui, *Sci. Repts. Tohoku Univ., I*, **40**, 102, 114 (1956). d) Ref. 2. e) Ref. 3. f) Results in this work.

Experimental

All the melting points were measured on a Yanagimoto micromelting point apparatus and are uncorrected. The IR spectra were taken on a JASCO IRA-1 spectrophotometer, and the NMR spectra on a Hitachi-Perkin-Elmer R-24 spectrometer (60 MHz).

The pK_a values of 4-pyrones were measured spectrophotometrically in 50% aqueous methanol at 25 °C by the method of Albert and Serjeant.[9] The UV spectra were taken on a Hitachi EPS-3T spectrophotometer, while the pH values were measured with a Hitachi-Horiba F-7 pH meter.

Materials. All 6-substituted 3-hydroxy-4-pyrones were prepared according to the method given in references: Ia, mp 117—118 °C (lit,[10] 118 °C); Ib, mp 152 °C (lit,[11] 152—153 °C); Ic, mp 270 °C (lit,[12] 273—274 °C); Id, mp 166—167 °C (lit,[13] 166—167 °C).

6-(Substituted styryl)-3-hydroxy-4-pyrones were obtained by the Wittig reaction. Phosphonium salt was prepared by the reaction of 5-hydroxy-2-chloromethyl-4-pyrone[13] with triphenylphosphine in benzene, 58% yield. Phosphonium salt (1.1 mmol) and benzaldehyde (1 mmol) were added to a sodium ethoxide (2 mmol) solution, and the resulting mixture was stirred for 2 h at room temperature under nitrogen atmosphere. After 2 M hydrochloric acid had been poured into the reaction mixture, the products were extracted with chloroform. Chloroform was evaporated off and the residue was chromatographed on silica gel column [Wakogel C-100 (60 g) and B-10 (10 g)] with chloroform to afford 3-hydroxy-6-styryl-4-pyrones, which were recrystallized from benzene. The yields, mp's spectral and analytical data are as follows: IIa; Yield, 34%; mp 183—185 °C; IR (KBr) 3180, 1660, 970 cm^{-1}; NMR ($CDCl_3$) δ: 7.85 (s, 1H), 7.7—7.2 (m, 6H), 6.66 (d, 1H, J=17.3 Hz), 6.45 (s, 1H), 8.3—7.6 (br, 1H). Found: C, 73.18; H, 4.77%. Calcd for $C_{13}H_{10}O_3$: C, 72.89; H, 4.71%. IIb: Yield, 32%; mp 187.5—189 °C; IR (KBr) 3100, 1655, 975 cm^{-1}; NMR ($CDCl_3$) δ: 7.79 (s, 1H), 7.35 (d, 1H, J=15.3 Hz), 7.5—6.8 (m, 4H), 6.49 (d, 1H, J=15.3 Hz), 6.36 (s, 1H), 3.82 (s, 3H), 8.0—7.5 (br, 1H). Found: C, 68.98; H, 4.95%. Calcd for $C_{14}H_{12}O_4$: C, 68.84; H, 4.95%. IIc: Yield, 25%; mp 216.5—217.5 °C; IR (KBr) 3200, 1660, 965 cm^{-1}; NMR ($CDCl_3$) δ: 7.31 (s, 1H), 7.5—7.0 (m, 5H), 6.58 (d, 1H, J=15.6 Hz), 6.38 (s, 1H), 2.36 (s, 3H), 8.0—7.5 (br, 1H). Found: C, 73.54; H, 5.32%. Calcd for $C_{14}H_{12}O_3$: C, 73.67; H, 5.30%. IId, Yield; 21%; mp 175—175.5 °C; IR (KBr) 3230, 1655, 955 cm^{-1}; NMR ($CDCl_3$) δ: 7.79 (s, 1H), 7.5—6.4 (m, 5H), 6.42 (s, 1H), 3.91 (s, 3H), 3.89 (s, 3H), 6.7—6.0 (br, 1H). Found: C, 65.52; H, 5.07%. Calcd for $C_{15}H_{14}O_5$: C, 65.69; H, 5.15%. IIe; Yield; 31%; mp 232 °C (dec); IR (KBr) 3250, 1660, 960 cm^{-1}; NMR (CF_3COOH) δ: 8.65 (s, 1H), 7.95 (d, 1H, J=15.7 Hz), 7.7—7.4 (m, 4H), 7.63 (s, 1H), 7.10 (d, 1H, J=15.7 Hz). Found: C, 62.87; H, 3.74%. Calcd for $C_{13}H_9O_3Cl$: C, 62.79; H, 3.65%. IIf: Yield, 20%; mp 250 °C (dec); IR (KBr) 3230, 1665, 965 cm^{-1}; NMR (CF_3COOH) δ: 8.78 (s, 1H), 8.7—7.2 (m, 6H), 7.56 (s, 1H), Found: C, 59.73; H, 3.63; N, 5.16%. Calcd for $C_{13}H_9NO_5$: C, 60.23; H, 3.50; N, 5.40%. IIg; Yield, 11%; mp 245—247 °C (dec); IR (KBr) 3200, 1655, 970 cm^{-1}; NMR (CF_3COOH) δ: 8.63 (s, 1H), 8.5—7.7 (m, 5H), 7.46 (s, 1H), 7.21 (d, 1H, J=16.7 Hz). Found: C, 60.36; H, 3.50; N, 5.32%. Calcd for $C_{13}H_9NO_5$: C, 60.23; H, 3.50; N, 5.40%.

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