BULLETIN OF THE CHEMICAL SOCIETY OF JAPAN, VOL. 46, 1425—1428 (1973)

Transmission of Substituent Effects through Oxygen and Sulfur Atoms. III. The Ionization Equilibrium Constants of Ring-substituted *cis*-β-Phenoxyacrylic Acids

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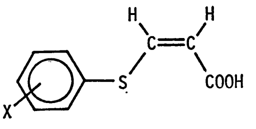
(Received October 7, 1972)

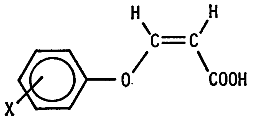
cis-β-Phenoxyacrylic acid and several of its ring-substituted derivatives were prepared, and their ionization constants were determined in 50% ethanol–water at 25 °C. The Hammett ρ value for the ionization of these acids, 0.439, is smaller than that reported for *cis*-β-phenylthioacrylic acids, 0.531. The greater efficiency of the sulfur atom in transmitting the substituent effects is explainable in terms of the "through-conjugation" of the sulfur atom in the thioacrylate anions formed.

In the preceding two papers,[1,2] we treated the effects of substituents on the ^{1}H and ^{13}C chemical shifts of phenyl vinyl ether and sulfide. It was found that the sulfur atom behaves as a more efficient transmitter of substituent effects than does oxygen when it is interposed between two unsaturated groups. This finding offered strong evidence for the presence of a "through-conjugation" in sulfur bondings.[3] In this paper we will examine the ρ values for acid ionization, since ionization equilibria are fundamental to Hammett's ρσ relationship.

Hogeveen[4] reported the ionization constants of *cis*-β-phenylthioacrylic acids (I, abbreviated as *cis*-β-PSA hereafter).[5] For the purpose of comparison, we prepared *cis*-β-phenoxyacrylic acid (II, abbreviated as *cis*-β-POA) and its *p*-CH$_3$O, *m*-CH$_3$O, *p*-CH$_3$, *m*-CH$_3$, *p*-Cl, and *m*-Cl derivatives, and measured their ionization constants, K_a. The ρ-value for *cis*-β-PSA was found to be greater than that for *cis*-β-POA.



I



II

Experimental

Synthesis of cis-β-*Phenoxyacrylic Acids.* The *cis*-β-phenoxyacrylic acids were prepared by the direct *trans* addition of a substituted phenol to propiolic acid in aqueous potassium hydroxide.

$$XC_6H_4OH + HC{\equiv}CCOOH \xrightarrow{OH^-} II$$

The procedure for preparation was analogous to that used for the base-catalyzed addition of thiophenol to propiolic acid.[6] A substituted phenol (0.1 mol) was dissolved in 60 ml of 4N potassium hydroxide, and then the solution was heated to 60—70°C under stirring. After 0.1 mol of propiolic acid had been added, the mixture was stirred for 2—3 hr at 70—80 °C and then cooled. On acidifying the solution with hydrochloric acid, a sol layer was separated out. The liquid layer, together with the sol layer, was subjected to extraction with ether. A 5% aqueous potassium hydroxide was added to the extract, and the aqueous layer was carefully neutralized, and then separated from the ethereal layer. The subsequent acidification of the aqueous layer with hydrochloric acid gave a solid product. It was isolated by filtration and recrystallized from ligroin. The products were identified by elemental analysis and by NMR spectral measurements (Table 1).

In preparing *cis*-β-POA, we at first followed Gottesman's method:[7]

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[1] T. Fueno, O. Kajimoto, K. Izawa, and M. Masago, This Bulletin, **46**, 1418 (1973).

[2] O. Kajimoto, M. Kobayashi, and T. Fueno, *ibid.*, **46**, 1422 (1973).

[3] C. C. Price and S. Oae, "Sulfur Bonding," Ronald Press, New York, N. Y. (1962).

[4] H. Hogeveen, *Rec. Trav. Chim.*, **83**, 813 (1964); H. Hogeveen, G. Maccagnani, and F. Taddei, *ibid.*, **83**, 937 (1964).

[5] In this paper we refer to the ethylenic carbon atoms at the positions α and β with respect to the –COOH group as the α and β carbons, respectively. Therefore, care must be taken when one compares the properties of these carbon atoms with those of the α and β carbons in phenyl vinyl ether or thioether.

[6] F. Montanari and A. Negrini, *Gazz. Chim. Ital.*, **87**, 1073 (1957).

[7] E. Gottesman, *Ber.*, **66**, 1168 (1933).

TABLE 1. MELTING POINTS, ELEMENTAL ANALYSIS DATA AND PROTON CHEMICAL SHIFTS OF *cis*-β-PHENOXYACRYLIC ACIDS

Substituent	Mp	Calcd %		Found %		Chem. shift (τ)		$J_{\alpha\beta}$
	°C	C	H	C	H	α	β	cps
p-CH_3O	125	61.85	5.19	62.12	5.16	4.865	3.101	7.0
p-CH_3	118	67.41	5.66	67.49	5.66	4.843	3.059	7.1
m-CH_3	83	67.41	5.66	67.44	5.74	4.826	3.025	7.0
H	79	65.85	4.91	66.20	4.74	4.811	3.039	7.2
	(127)	(65.85)	(4.91)	(65.71)	(4.85)	(4.46)	(2.09)	(12.5)[a]
m-CH_3O	89	61.85	5.19	61.79	5.23	4.800	3.014	7.2
p-Cl	132	54.43	3.55	54.20	3.43	4.780	3.089	6.8
m-Cl	116	54.43	3.55	54.63	3.47	4.765	3.065	7.0

a) The figures in parentheses are for *trans*-β-phnoxyacrylic acid.

$$C_6H_5ONa + HC{\equiv}CCOOEt \xrightarrow[H_2O]{OH^-} \text{II}$$

He reported that the product had a mp of 129 °C and concluded it to be a *cis*-acid. Our NMR measurement, however, revealed that it was a *trans* isomer. For the *p*-Cl derivative, also, a mixture of *cis* and *trans* isomers was formed. No doubt, his identification was erroneous.

Determination of the Ionization Constants. The pK_a values were determined potentiometrically with a Hitachi-Horiba Model F-5 pH meter at 25±0.5 °C by the ordinary method.[8] A 25 ml portion of 0.01N acid in aqueous ethanol (50% by volume) was titrated with a 0.1N potassium hydroxide solution under a nitrogen flow. The pK_a values were then calculated by the following equation:

$$pK_a = pH + \log\frac{[HA]-[H^+]}{[A^-]+[H^+]}$$

where [HA] is the concentration of acid, [A^-] is the stoichiometric concentration of ionized acid, which can be regarded as equal to the concentration of KOH added, and [H^+] is the hydrogen-ion concentration as determined from the measured pH, which can be neglected when the pH is above 5.

In practice, the pK_a of each acid was determined as an average value of eight data measured in the pH range of 4.7—6.3. The scatters of the measured data from the average value did not exceed ±0.02.

NMR Measurements. The details were described in a previous paper.[1] Samples, 10% in $CDCl_3$, were examined at room temperature. The experimental errors were no greater than ±0.5 Hz.

IR Measurements. The IR spectra of β-POA's were recorded on a Hitachi Perkin-Elmer 225 spectrometer as 5×10^{-3} mol/l CCl_4 solutions in a 1 cm quartz cell. On the dilution of the solution, the associated OH stretching peak of *cis*-β-POA did not change in its intensity relative to the free OH peak. Evidently this peak originates from intramolecular hydrogen bonding.

Results

The apparent ionization constants of substituted *cis*-β-POA measured by the above method are given in Table 2, together with those of *cis*-β-PSA reported by Hogeveen.[4] The Hammett relationship was found to hold, as is shown in Fig. 1. The least-squares fit gave ρ=0.439, with the correlation coefficient of 0.974. The ρ value is smaller than that of 0.531 which was reported by Hogeveen for *cis*-β-PSA.

TABLE 2. IONIZATION CONSTANTS (pK_a) OF *cis*-β-PHENOXYACRYLIC AND *cis*-β-PHENYLTHIOACRYLIC ACIDS

Substituent	*cis*-β-POA	*cis*-β-PSA[4]
p-CH_3O	6.09	6.01
p-CH_3	6.08	5.98
m-CH_3	6.05	—
H	6.02	5.93
	(5.86)[a]	(5.78)[a]
m-CH_3O	5.98	—
p-Cl	5.91	5.76
m-Cl	5.81	—
m-NO_2	—	5.55
p-NO_2	—	5.44

a) The pK_a values for the *trans* acids.

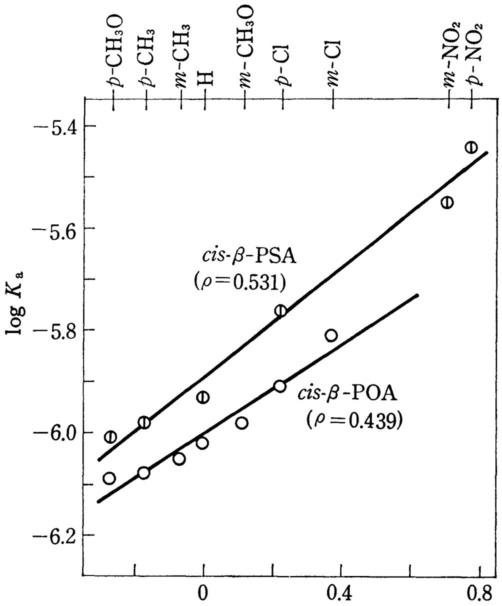

Fig. 1. Hammett plots of ionization equilibrium constants for *cis*-β-phenoxyacrylic acids (*cis*-β-POA) and *cis*-β-phenylthioacrylic acids (*cis*-β-PSA).

The chemical shifts of the α-proton of *cis*-β-POA are plotted against the Hammett σ-values in Fig. 2; this

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[8] A. Albert and E. P. Serjeant, "Ionization Constants of Acids and Bases. A Laboratory Manual," Methuen and Co. Ltd. (1962).

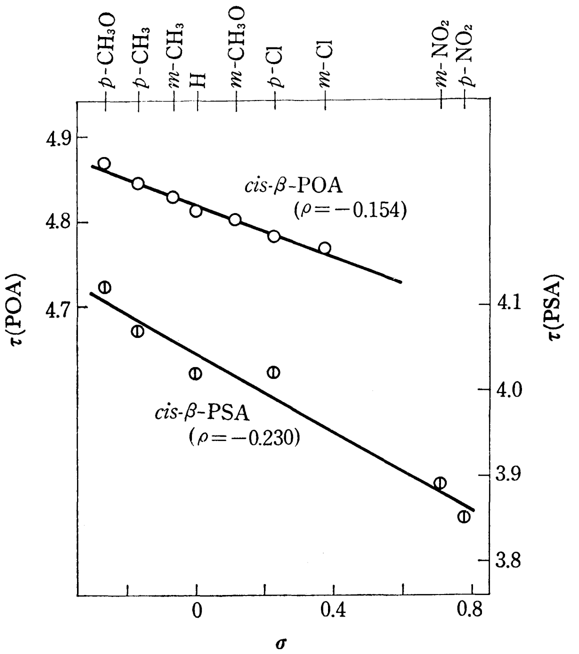


Fig. 2. Hammett plots of the α-proton chemical shifts of *cis*-*β*-phenoxyacrylic acids (*cis*-*β*-POA) and *cis*-*β*-phenylthioacrylic acids (*cis*-*β*-PSA).

plot gives the ρ value of $-0.154\ \tau/\sigma$. The corresponding value for *cis*-*β*-PSA[4] was found to be −0.230.

Discussion

(A) Transmission of Substituent Effects. We will compare the relative efficiencies of oxygen and sulfur atoms in transmitting the electronic effects of substituents on the ionization constants of $XC_6H_4YCH_2COOH$ and $XC_6H_4YCH{=}CHCOOH$.

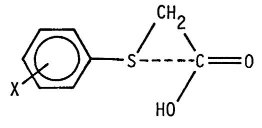
Behaghel and Rollmann[9] measured the ionization constants of $C_6H_5OCH_2COOH$, $C_6H_5SCH_2COOH$, $C_6H_5SeCH_2COOH$, and some of their derivatives. However, recent measurements of pK_a by Pasto *et al.*[10] for substituted phenylthioacetic acids have revealed that the data obtained by those workers are not reliable. Hence, we have evaluated the ρ value on the basis of the pK_a data reported by the latter workers. Fortunately, the ionization constants of phenoxyacetic acids have also been extensively examined in aqueous solution by Hayes and Branch.[11] For the sake of fair comparisons, we selected the CH_3O, CH_3, H, Cl, and NO_2 derivatives and evaluated the ρ-values with respect to only these substituents. The results are summarized in Table 3.

Table 3. ρ-Values and the related quantities for the ionization equilibria

	$X{-}C_6H_4{-}Y{-}CH_2COOH$		$X{-}C_6H_4{-}Y{-}CH{=}CHCOOH$(*cis*)	
	O[11]	S[10]	O	S[4]
ρ	0.312	0.296	0.439	0.531
r	0.985	0.980	0.974	0.991
s	0.021	0.021	0.046	0.035
n[a]	9	8	7	6
pK_a(X=H)	3.17	3.53	6.02	5.93

a) The number of substituents.

Phenoxyacetic acids show a slightly larger ρ value (0.312) than phenylthioacetic acids (0.296)—*i.e.*, O>S. Conversely, with the acrylic type of acids, the result is O<S, as has already been described. Thus, there is an enhanced transmission by the sulfur atom interposed between two unsaturated groups. This fact reinforces the validity of the concept of the "through-conjugative" behavior of the sulfur atom.[1,2] The conjugation is considered to be involved more favorably in the anions formed than in the undissociated acids.



III

A comparison of the ρ values of the acetic acid derivative gives us additional information of interest. For ^1H chemical shifts, the ρ value varied by a factor of 2 on going from aniosles (−0.270) to thioanisoles (−0.115).[1] In acid dissociation, the diminution in the ρ value is very small. This distinction can be understood by considering the nonbonding interaction[12] between the sulfur atom and the carbonyl group in phenylthioacetic acids III. That is, the acids are provided with two routes for the transmission of the substituent effects, one through σ-bonds and the other through direct nonbonding interaction. The dependence of pK_a on the substituents can thus become greater than would be expected simply from the inefficient transmission through the σ-bonds alone.

The ^1H chemical shifts observed for *cis*-*β*-POA deserve special attention. The shifts of the α-proton in the *cis*-acids were found to conform to the Hammett relationship, with $\rho=-0.154$. The ρ value obtained is smaller in magnitude than that for the sulfur analogs, −0.230. These results are in line with our previous observations with phenyl vinyl ethers and sulfides.[1,5]

(B) Relative Acid Strengths of Unsubstituted Acids. The pK_a values of the unsubstituted acids of interest are listed at the bottom of Table 3. Phenoxyacetic acid is more acidic than phenylthioacetic acid, whereas *cis*-phenoxyacrylic acid is a weaker acid than its sulfur

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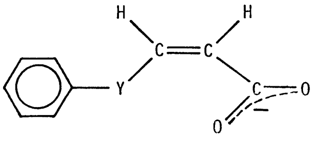
9) O. Behaghel and M. Rollmann, *J. Prakt. Chem.*, **114**, 287 (1926).

10) D. J. Pasto, D. McMillan, and T. Murphy, *J. Org. Chem.*, **30**, 2688 (1965).

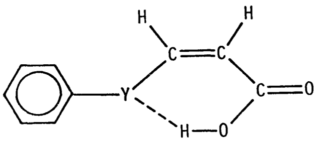
11) N. V. Hayes and G. E. K. Branch, *J. Amer. Chem. Soc.*, **65**, 1555 (1943).

12) Such an interaction has also been proposed by Oae and Yano.[13] They investigated the effect of ring-substituents on the E2 elimination of 3-phenylthio-propyl chlorides and their oxygen analogs. Rate of elimination for the phenylthio derivatives showed Hammett type dependence with the reaction constant of 0.37, while, for oxygen analogs, no noticeable substituent dependence could be found. From this fact, they suggested that the nonbonding interaction may be operative between sulfur atom and terminal two carbons at the transition state.

13) S. Oae and Y. Yano, 23th Annual Meeting of the Chemical Society of Japan (1970); Preprint III, p. 1374.



IV



V

analog. This contrast may be explained by considering the anionic form of these acids. With β-phenylthioacrylic acid, the anion, IV, is much stabilized by the electron-accepting conjugation of the sulfur atom. As the acid dissociation equilibria are controlled by the stability of the resulting anion, the thioacrylic acid may well show a greater acidity than its oxygen analog. By contrast, in the case of saturated acids, no such conjugation can occur, resulting in the greater acidity of the oxygen-containing acid because of the greater electronegativity of the oxygen atom.

In addition, the acidity of *trans*-β-POA is greater than that of its *cis* isomer, contrary to the case of cinnamic acids.[14] Such a trend has already been pointed out for β-PSA by Hogeveen, but he gave no explanation.[4] It might be explained in terms of hydrogen-bonded six-membered ring in the *cis*-acids. The hydrogen bonding in V should prevent the ionization, thus decreasing its acidity. This is not the case for *trans*-acid.

The IR measurements of *cis*- and *trans*-β-POA confirm the above interpretation. *cis*-β-POA shows two peaks, at 3543 and 3483 cm^{-1}; the former corresponds to free OH stretching, while the latter corresponds to the intramolecular associated OH stretching.[15,16] By contrast, the *trans* isomer gives only one peak of free OH, at 3546 cm^{-1}. For β-PSA, we have no data, but the situation is probably the same as in β-POA. In fact, a report is available which shows that the electron-donating ability of ethereal sulfur is nearly the same as, or a little greater than, that of oxygen in the hydrogen bonding.[17]

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[14] J. F. J. Dippy and J. E. Page, *J. Chem. Soc.*, **1938**, 357.

[15] M. Ōki and M. Hirota, This Bulletin, **33**, 119 (1960).

[16] M. Davies and D. M. F. Griffiths, *J. Chem. Soc.*, **1955**, 132.

[17] B. B. Wayland and R. S. Drago, *J. Amer. Chem. Soc.*, **86**, 5240 (1964).