Emanuele Maccarone, Antonino Mamo, Giancarlo Perrini and Michele Torre

Istituto Dipartimentale di Chimica e Chimica Industriale,
Università, Viale Andrea Doria, 6, 95125 Catania, Italy
Received September 30, 1980

The dissociation equilibrium constants of some E-α-phenyl-β-arylacrylic acids (Ar = 2-pyridyl, 3-pyridyl, 4-pyridyl, 1-naphthyl, 2-naphthyl, anthracen-9-yl) have been measured in 80% aqueous 2-methoxyethanol at 25°. The pKa values of these acids, together with those of p-substituted phenyl, 2-furyl, 2-thienyl and selenophen-2-yl derivatives, have been rationalized by an equation involving separate contributions of polar, conjugative and steric effects of heterocycles. The pKa values of some E-α-phenyl-β-alkylacrylic acids (alk = methyl; ethyl; n-propyl; i-propyl; n-butyl; i-butyl) are also reported.

Acidities of series of substituted acrylic acids appear to provide data of great potential use in the quest for separation of overall substituent effects, particularly in heterocycle containing compounds. In previous work we noticed that differences in the acidities of some E and Z-α,β-diarylacrylic acids **1** and **2** result from differences in stereochemistry; the pKa values depend on polar and steric effects in the Ar group (1).
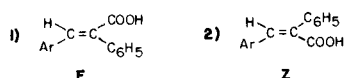

The dissociation constants of E- and Z-α-phenyl-β-p-X-substituted-phenylacrylic acids (X = OCH₃, CH₃, H, Cl, NO₂) were linearly correlated by the simple Hammett equation, because of the constancy of the steric effects among the benzene series. However, a more general equation 1, involving separate contributions of polar (σ_{BA}) and steric effects (θ) was tested for both benzene and heterocyclic derivatives (Ar = 2-furyl, 2-thienyl, selenophen-2-yl) whose internal angles are markedly different from that of the benzene ring.

$$1) \quad pKa = pKa_o + \varrho\sigma_{BA} + \psi\theta$$

Nevertheless, the regression analysis was based on few data, and some criticism could be made about the generality of the correlation. We have measured the pKa of new E-acids (**1**: Ar = 2-pyridyl, 3-pyridyl, 4-pyridyl, 1-naphthyl, 2-naphthyl, anthracen-9-yl), with the aim of determining what structural effects are responsible for the observed pKa values, using a more extended range of substrates.

In this work we also report the pKa values of the E-α-phenyl-β-alkylacrylic acids (**3**).
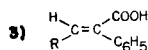
R = methyl; ethyl; n-propyl; i-propyl; n-butyl; i-butyl

The pKa of the acids in Table I were measured in 80% aqueous 2-methoxyethanol at 25°, because of the poor solubility in pure water. The usual potentiometric pro-

cedure was used (2). These dissociation constants are not thermodynamic quantities, but it has been argued that they can be analyzed analogously by free energy relationships (3). Table I also reports the ir stretching frequencies of the carbonyl group, and Figure I shows the correlation between the pKa and ν_{CO} values.

The linear plot indicates that both properties measure the same electronic effects on the functional group and provides evidence for conjugative interactions between the Ar and COOH groups. Particularly, the low values of the CO frequency in the five-membered heterocyclic derivatives confirm the single-bond character of the CO group (4).

However, if the pKa values are plotted against the σ_{BA} constants of the heteroatoms (5) or of the polycyclic ring systems (6) a scattered plot is observed, and only the pKa of the 2-naphthyl derivative falls on the line defined by benzene derivatives (Figure II).

The contributions of other structural effects, such as mesomeric and/or steric effects, could justify the lack of correlation. Particularly, the different size of the aromatic cycles can stabilize different conformations among the members of the considered series. In fact, the high positive deviations (lower acidities) are associated with the pKa of five-membered heterocycles containing acids, in which the cycle internal angle, on which the side chain is bonded (X -C₂-C₃), is remarkably less than the 120° angle of the benzene ring (7). A negative deviation from linearity is observed for the pKa of the 2-pyridyl derivative, in which the N-C₂-C₃ angle is about 124° (8).

Thus, the possibility of an almost planar structure in the five-membered heterocycle derivatives would favor the electron releasing effects from the heteroatom and, of course, would weaken the acid strength, as observed.
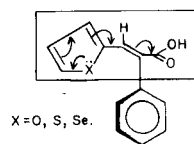

X = O, S, Se.

Table I

pKa Values of E-α-Phenyl-β-arylacrylic Acids
in 80% Aqueous 2-Methoxyethanol at 25°

No.	Ar	pKa (a)	ν CO (cm^{-1})(b)
1	Phenyl (c)	7.03	1673 (d)
2	p-Methoxyphenyl (c)	7.28	1670 (d)
3	p-Methylphenyl (c)	7.31	1671 (d)
4	p-Chlorophenyl (c)	6.95	1678 (d)
5	p-Nitrophenyl (c)	6.32	1680 (d)
6	2-Furyl (c)	7.36	1665
7	2-Thienyl (c)	7.35	1665
8	Selenophen-2-yl (c)	7.30	1660
9	1-Naphthyl	6.93	1670
10	2-Naphthyl	7.04	1675
11	Anthracen-9-yl	6.76	1685
12	2-Pyridyl	5.80	1725
13	3-Pyridyl	6.62	1690
14	4-Pyridyl	6.41	1710

(a) The maximum error was ± 0.04 pK units for all compounds. (b) In potassium bromide disk. (c) Reference 1. (d) C. W. Bird and E. M. Briggs, *J. Chem. Soc. C*, 1265 (1967).

This is consistent with previous spectroscopic results which pointed out the coplanarity of the 2-heteroaryl rings with the carboxyl group in E-acids (9) in comparison with the corresponding benzene derivative (10). A combination of polar, conjugative and steric effects may underlie the acidity of these compounds.

To operate a detailed analysis of these structural effects on the pKa values, we applied the following three-parameters equation 2 which includes the separate contributions of polar (σ_{BA}), resonance (σ^+) and steric effects (θ),

$$2) \quad pKa = pKa_o + \varrho\sigma_{BA} + \varrho^+\sigma^+ + \psi\theta$$

where the σ_{BA} values are the above explained polar constants (5,6), the σ^+ values are the electrophilic endocyclic constants, derived in most cases from the extended selectivity treatment (11,12), and the θ values represent the differences between the internal angle of the aromatic cycle (on which the side chain is bonded) (7,8,13) and the 120° of the benzene ring. The ϱ, ϱ^+ and ψ parameters are the sensitivities of the equilibrium to polar, resonance and

Table II

Analysis of the Structural Effects on the pKa Values by Equation 2

Data Imput:

No.	pKa (Experimental)	σ_{BA}	σ^+	θ	pKa (Calcd.)
1	7.03	0.00	0.00	0.00	7.03
2	7.28	− 0.27	− 0.78	0.00	7.35
3	7.31	− 0.17	− 0.31	0.00	7.20
4	6.95	0.23	0.11	0.00	6.87
5	6.32	0.78	0.79	0.00	6.40
6	7.36	1.04	− 0.93	− 9.32	7.26
7	7.35	0.67	− 0.79	− 8.53	7.41
8	7.30	0.60	− 0.88	− 8.44	7.46
9	6.93	0.50	− 0.51	0.25	6.80
10	7.04	0.04	− 0.51	0.52	7.07
11	6.76	0.77	− 1.25	1.00	6.71
12	5.80	0.88	0.75	3.88	6.05
13	6.62	0.74	0.54	− 1.47	6.58
14	6.41	1.11	1.16	− 1.67	6.25

Data Output:

Selections of the Variables	σ_{BA}	σ^+	θ	$\sigma_{BA}\sigma^+$	$\sigma_{BA}\theta$	$\sigma^+\theta$	$\sigma_{BA}\sigma^+\theta$
Degrees of Freedom	12	12	12	11	11	11	10
100 R^2	24.3	58.5	36.3	66.5	87.4	67.8	93.2
Coefficients of the Variables	−0.51	−0.47	−0.069	−0.30	−0.77	−0.38	−0.63
				−0.42	−0.096	−0.039	−0.19
							−0.076
Standard Errors of the Coefficients	0.26	0.11	0.026	0.19	0.12	0.12	0.10
				0.11	0.013	0.022	0.06
							0.012
Constant Term	7.14	6.80	6.77	6.96	7.11	6.75	7.03
Overall F-Test	3.8	16.9	6.8	10.9	38.2	11.6	45.6

steric effects, respectively. The pKa_o constant term represents the calculated pKa of the unsubstituted benzene derivative, because σ_{BA}, σ^+ and θ values are zero for the benzene ring, by definition.

Table III

pKa Values of *E-α-Phenyl-β-alkylacrylic Acids* in 80% Aqueous 2-Methoxyethanol at 25°

No.	R	pKa (a)	pK RCOOH (b)	ν CO (c)
1	methyl	7.43	4.76	1660 (d)
2	ethyl	7.34	4.87	1670 (d)
3	*n*-propyl	7.23	4.82	1685
4	*i*-propyl	7.30	4.85	1670
5	*n*-butyl	7.26	4.86	1690
6	*i*-butyl	7.36	4.77	1680

(a) The maximum error was ±0.04 pK units for all compounds. (b) In water at 25°: G. Kortum, W. Vogel and K. Andrussow, "Dissociation Contants of Organic Acids in Aqueous Solution", Butterworth, London, 1961. (c) In potassium bromide disk. (d) Reference 25.
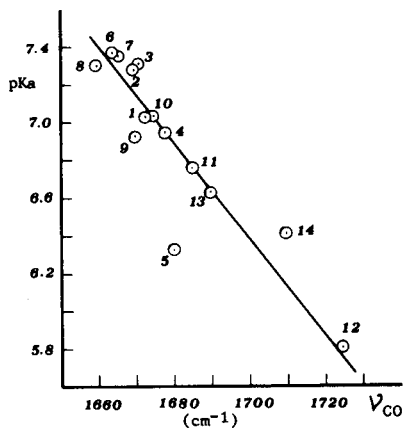

Figure I. Plot of the pKa values of *E-α-phenyl-β-aryl-* acrylic acids against the ir stretching frequencies of the carbonyl group. Key for numbers as in Table I.
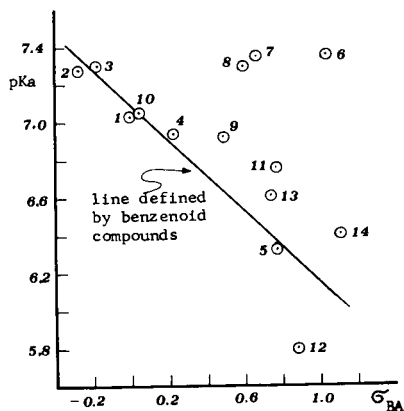

Figure II. Plot of the pKa values of *E-α-phenyl-β-aryl-* acrylic acids against σ_{BA} values. Key for numbers as in Table I.
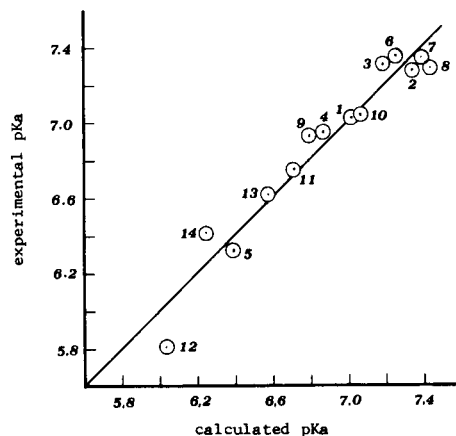

Figure III. Correlation between the experimental and calculated pKa values. Key for numbers as in Table I.

The equation 2 and its reduced forms have been already applied in kinetic studies of Schiff's reaction (14) and of acidic isomerization of *E-α,β-diarylacrylonitriles* (15), besides the previous work on the dissociation equilibria of *E-* and *Z-α,β-diarylacrylic acids* (1).

The regression analysis by equation 2 has been made by a computer program. The used data and the statistical results are reported in Table II.

The best solution is given by the following empirical equation 3,

3) $pKa = 7.03 - (0.63 \pm 0.10)\sigma_{BA} - (0.19 \pm 0.06)\sigma^+ - (0.076 \pm 0.012)\theta$

which explain 93.2% of the observed variations. The F-test (45.6) from 14 observations and 10 freedom degrees is significant above the 99% confidence level. The single- and two-parameters selections provide less significant F-tests and higher standard errors of the variable coefficients (Table II). The good correlation between the observed and calculated pKa, by equation 3 is shown in Figure III.

The negative signs of ϱ, ϱ^+ and ψ coefficients are in agreement with the expected effects on the acidity. In fact, the positive (negative) σ_{BA}, σ^+ and θ values decrease (increase) the pKa values. Particularly, the negative θ values of the five membered heterocycles allow the display of $+M$ conjugation from the heteroatoms to the carboxyl group, weakening the proton dissociation. So, the expected acid strengthening effects on the pKa, due to negative polar contribution ($\varrho\sigma_{BA}$) are overcome by the positive contributions of conjugative and steric effects ($\varrho^+\sigma^+ + \psi\theta$); and higher pKa values are observed in comparison with the benzene derivative.

The dominating contribution in the pKa of polycyclic and pyridyl derivatives is given by the polar effects. In the α-phenyl-β-2-pyridylacrylic acid, where each structural effect cooperates to decrease the pKa, the $\varrho\sigma_{BA}$ contribu-

tion explains about 60% of the pKa variation with respect to the standard compounds (ΔpKa = -1.23).

The pKa values of E-α-phenyl-β-alkylacrylic acids are reported in Table III together the pKa values of the corresponding alkanoic acids. A comparison of pKa of both series points out the small effects of the alkyl groups, in most cases within experimental errors.

These results do not allow a reliable rationalization by some free energy treatments, *i.e.*, by Taft-Pavelich (16) or Charton equations (17).

EXPERIMENTAL

The E-α-phenyl-β-arylacrylic acids, apart from the 2-pyridyl derivative, were synthesized by Perkin condensation of the appropriate arenecarboxaldehyde and phenylacetic acid in acetic anhydride with triethylamine as catalyst, following a procedure already described (1,18). The E-α-phenyl-β-2-pyridylacrylic acid was prepared by hydrolysis of the corresponding acrylonitrile with 65% sulfuric acid (19) [Ar, m.p. °C, λ max (95% ethanol) (log ϵ)]: 1-naphthyl, 164-165° from ethanol (20), 226 nm (4.53), 317 nm (3.96); 2-naphthyl, 208° from ethanol (21) 228 nm (4.42), 269 nm (4.38), 312 nm (4.31); anthracen-9-yl, 263° from ethanol (22), 256 nm (5.02); 2-pyridyl, 170-172° from DMSO-ethanol (19), 224 nm (4.04), 305 nm (4.44) (19); 3-pyridyl, 200° from ethanol (23), 257 nm (4.04), 280 sh nm (4.00); 4-pyridyl, 273° from acetic acid (24), 262 nm (4.12).

The E-α-phenyl-β-alkylacrylic acids were also prepared by Perkin condensation; but the reaction mixtures were refluxed for 10 hours [R, m.p. (°C), λ max (95% ethanol) (log ϵ)]: methyl, 137° from water (25), 234 sh nm (3.74); ethyl, 63° from petroleum ether (25), 235 sh nm (3.80); n-propyl, 68-69° from petroleum ether; 235 sh nm (3.76) (24); i-propyl, 128-129° from petroleum ether; 235 sh nm (3.75) (24); n-butyl; 30-31° from petroleum ether; 235 sh nm (3.78) (24); i-butyl, 76-78° from petroleum ether; 235 sh nm (3.82) (24).

2-Methoxyethanol (AnalaR grade) and doubly distilled water (carbon dioxide free) were used to prepare 80% (v/v) aqueous 2-methoxyethanol. The pKa measurements were performed in duplicate or triplicate runs by a potentiometric apparatus, following a procedure requiring correction for the hydrogen ion concentration, as already described (1,2).

REFERENCES AND NOTES

(1) E. Maccarone, A. Mamo, D. Sciotto and M. Torre, *J. Chem. Soc.,*
Perkin Trans. 2, 161 (1980).

(2) A. Albert and E. P. Serjeant, "Ionization Constants of Acids and Bases", Methuen, London, 1962, chapter 2.

(3) W. Simon, *Angew. Chem., Int. Ed. Eng.,* **13**, 661 (1964).

(4) M. S. C. Flett, *Trans. Farad. Soc.,* **44**, 767 (1948).

(5) P. Tomasik and C. D. Johnson, *Adv. Heterocyclic Chem.,* **20**, 1 (1976).

(6) σ_{BA} = (pKa ArCOOH $-$ pKa PhCOOH)/ϱ, (ϱ = 1.00 in water at 25°) [Ar, pKa ArCOOH (water 25°), σ_{BA}]: 1-naphthyl, 3.70, 0.50; 2-naphthyl, 4.16, 0.04 (G. Kortum, W. Vogel and K. Andrussow, "Dissociation Constants of Organic Acids in Aqueous Solution", Butterworths, London, 1961); σ_{BA} (anthracen-9-yl) = (5.76-4.56)/1.52 = 0.77 (from pKa values in 50% aqueous ethanol at 50°); G. L. Anderson, R. C. Parish and L. M. Stock, *J. Am. Chem. Soc.,* **93**, 6984 (1971).

(7) F. Fringuelli, G. Marino and A. Taticchi, *Adv. Heterocyclic Chem.,* **21**, 121 (1977); and references therein.

(8) B. Bak, L. Hansen-Nygaard and J. Rastrup-Andersen, *J. Mol. Spectrosc.,* **2**, 361 (1958).

(9) S. Fisichella, G. Scarlata and D. Sciotto, *Ann. Chim. (Rome),* **63**, 55 (1973); S. Fisichella, G. Mineri, G. Scarlata and D. Sciotto, *ibid.,* 779 (1973); *Tetrahedron,* **31**, 2445 (1975).

(10) H. E. Zimmermann and L. Abramjian, *J. Am. Chem. Soc.,* **81**, 2086 (1959).

(11) G. Marino, *Adv. Heterocyclic Chem.,* **13**, 276-280 (1971).

(12) L. M. Stock and H. C. Brown, *Adv. Phys. Org. Chem.,* **1**, 117 (1963).

(13) "Interatomic Distances Supplement", Spec. Publ. No. 18, The Chemical Society, London, 1965.

(14) E. Maccarone, A. Mamo and G. Perrini, submitted for publication.

(15) E. Maccarone, A. Mamo, G. Scarlata and M. Torre, *J. Org. Chem.,* **44**, 2896 (1979).

(16) R. W. Taft, Jr., "Steric Effects in Organic Chemistry", M. S. Newman, Ed., Wiley, New York, N.Y., 1956, chapter 13.

(17) M. Charton, *J. Am. Chem. Soc.,* **97**, 1552, 3691 (1975); *J. Org. Chem.,* **41**, 2906 (1976).

(18) R. Ketcham and D. Jambotkar, *J. Org. Chem.,* **28**, 1034 (1963).

(19) P. L. Kumler and R. A. Dybas, *J. Org. Chem.,* **35**, 125 (1970).

(20) P. Ruggli and R. Preuss, *Helv. Chim. Acta,* **24**, 1345 (1941).

(21) J. L. Everett and G. A. R. Kon, *J. Chem. Soc.,* 1601 (1948); B. B. Datta and J. C. Bardhan, *ibid.,* 3974 (1962.

(22) G. Drefahl and K. Ponsold, *Chem. Ber.,* **93**, 472 (1960).

(23) F. H. Clarke, G. A. Felock, G. B. Silverman and C. M. Watnik, *J. Org. Chem.,* **27**, 533 (1962).

(24) This work. Satisfactory combustion analytical data for C, H ($\pm$ 0.3%) were found. Moreover, the ^{1}H nmr spectrum confirms the structure.

(25) K. Nilsonn, *Acta Chem. Scand.,* **19**, 612 (1965).