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MOUNT VERNON, IOWA

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, THE UNIVERSITY OF TEXAS]

Transmission of Electronic Effects by the Cyclopropane Ring. Ionization Constants of *m*- and *p*-Substituted β-Phenylpropionic, *cis*- and *trans*-2-Phenylcyclopropanecarboxylic Acids in 50% Ethanol

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Ionization constants of three series of *m*- and *p*-substituted acids have been measured in 50% ethanol: β-phenylpropionic, *cis*- and *trans*-2-phenylcyclopropanecarboxylic. Hammett rho constants are 0.344, 0.436, and 0.473, respectively, which, by contract with previous measurements in water, suggests that the cyclopropane ring transmits electronic effects somewhat better than does the dimethylene group.

The "double bond character" of the cyclopropane ring in simple electrophilic addition reactions and hydrogenation has been recognized for many years. More recently nucleophilic addition[2a] to cyclopropylcarbonyl compounds and Diels-Alder addition to the vinylcyclopropane linkages[2b] have been observed. During the past fifteen years a considerable body of evidence from spectra,[3] dipole moments,[3a] and chemical reactivity[2] has supported the idea of cyclopropane conjugation. The cyclopropane ring shows strong conjugation with a cationic carbon atom.[4] Two proposed molecular-orbital structures of cyclopropane[5] attribute to it a considerable degree of pi bond character. Stereochemical requirements for conjugation with three-membered rings have been examined.[6]

Controverting this are several reports of the failure of the cyclopropane ring to transmit conjugative effects in an excited state (ultraviolet spectra[7]), in reactions involving carbanion formation,[7] and (presumably in the ground state) in the ionization process of a series of *m*- and *p*-substituted 2-phenylcyclopropanecarboxylic acids.[8] More recently the measurement of rates of alkaline hydrolysis of *cis*-[9] and *trans*-[3a,9] ethyl *m*- and *p*-substituted 2-phenylcyclopropanecarboxylates has led to the conclusion that the three-membered ring transmits electronic effects considerably better than does the dimethylene (—CH_2CH_2—) group of the ethyl β-phenylpropionates.

The conflicting conclusions based on ionization constant data[8] and rate data[3a,9] have suggested a further examination of the former. The choice of 50% ethanol, rather than water,[8] as the medium results in small but uniform deviations from thermodynamic values of K_i. Certain advantages meanwhile accrue, including enhanced substituent effects and solubility of the compounds. The ionization constants are listed in Table I for the β-phenylpropionic acids and for the *cis*- and *trans*-2-phenylcyclopropanecarboxylic acids.

An examination of Hammett equation rho values (Table II) reveals some of the differences between ester hydrolysis and K_i in water data, and between K_i data in water and in 50% ethanol.

In ester hydrolysis rho increases as the transmitting linkage is varied in the order —CH_2CH_2— < *trans*-cyclopropane < *cis*-cyclopropane < *cis*-—CH=CH— < *trans*—CH=CH—. The K_i data in water show *trans*-cyclopropane $\lesssim$ —CH_2CH_2— <-*trans* —CH=CH—. In 50% ethanol the K_i order is —CH_2CH_2— < *cis*-cyclopropane < *trans*-cyclopropane, in agreement with spectral evidence.[4,9] Considering only the work herein reported, one

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[1] (a) Based, in part, on the Ph.D. dissertation of C. A. K., The University of Texas, 1962. (b) Department of Chemistry, University of Oklahoma, Norman, Okla.

[2] (a) See, for example, R. W. Kierstead, R. P. Linstead, and B. C. L. Weedon, *J. Chem. Soc.*, 3616 (1952); (b) S. Sarel and E. Breuer, *J. Am. Chem. Soc.*, **81**, 6522 (1959).

[3] (a) See references in R. Fuchs and J. J. Bloomfield, *J. Am. Chem. Soc.*, **81**, 3158 (1959); (b) M. F. Hawthorne, *J. Org. Chem.*, **21**, 1523 (1956); (c) G. W. Cannon, A. A. Santilli, and P. Shenian, *J. Am. Chem. Soc.*, **81**, 1660 (1959); R. J. Mohrbacker and N. H. Cromwell, *J. Am. Chem. Soc.*, **79**, 401 (1957).

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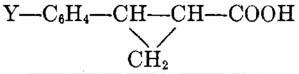
[9] R. Fuchs and J. J. Bloomfield, manuscript in preparation.

TABLE I

IONIZATION CONSTANTS OF *m*- AND *p*-SUBSTITUTED β-PHENYLPROPIONIC, *cis*- AND *trans*-2-PHENYLCYCLOPROPANECARBOXYLIC ACIDS IN 50% ETHANOL AT 25°

Substituent	σ[a]	pK_a of[b] $Y—C_6H_4CH_2CH_2COOH$	 $Y—C_6H_4—\underset{CH_2}{CH—CH}—COOH$ *cis*	*trans*
4-NO_2	+0.778	5.554		5.333
3-NO_2	0.710		5.961	5.415
3,4-Cl_2	0.525	5.690	6.123	5.492
3-Br	0.391			5.614
3-Cl	0.373	5.772	6.215	5.612
4-Br	0.232			5.635
4-Cl	0.227	5.781	6.222	5.629
Unsubstituted	0.000	5.877	6.331	5.783
3,4-CH_2O_2	−0.159		6.358	5.783
4-CH_3	−0.170	5.930	6.433	
4-OCH_3	−0.268	5.911	6.405	5.849
3,4(CH_3)$_2$	−0.303			5.888

[a] Hammett equation substituent constants from H. H. Jaffé, *Chem. Revs.*, **53,** 191 (1953). [b] Each value is the average of two to five determinations at 25.00 ± 0.02°; average mean deviation of ±0.003. The values are uncorrected for the presumably uniform error due to junction potential in the partially nonaqueous medium.

TABLE II

COMPARISON OF RHO VALUES

Series	Ester Hydrolysis	$K_i(H_2O)$	K_i(50% C_2H_5OH)
β-Phenylpropionic	0.489[a]	0.212[a]	0.344[c,d]
trans-2-Phenylcyclopropane	0.812[b,e]	0.182[g]	0.473[c,h]
cis-2-Phenylcyclopropane	1.014[f]		0.436[c,i]
trans-Cinnamic	1.301[j]	0.466[a]	
cis-Cinnamic	1.122[j]		

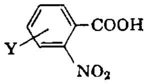
[a] Table I, footnote *a*. [b] Ref. 9. [c] This work. [d] Std. dev. ±0.023; corr. coeff. 0.9746. [e] Ref. 3a. [f] Ref. 9. [g] Ref. 8. [h] Std. dev. ±0.018; corr. coeff. 0.9829. [i] Std. dev. ±0.028; corr. coeff. 0.9775. [j] J. J. Bloomfield and R. Fuchs, *J. Org. Chem*, **26,** 2991 (1961).

might be willing to attribute the moderately better ability of the three-membered ring to transmit electronic effects to a two-path inductive effect. Typically the introduction of an addition methylene group between substituent and reaction site diminishes the rho value to about 40% of the original. This is almost exactly the magnitude of rho which the *trans*-phenylcyclopropanecarboxylic acids show above that of the β-phenylpropionic acids. Considering *all* of the available information, it becomes necessary to attribute to the cyclopropane ring the ability to transmit resonance effects *via* a pi bond system provided a sufficient demand is made at the reaction site due to the nature of the reaction, the medium, the functional group, and the electronic properties of the remainder of the molecule.

In a number of series of structurally related acids and in a variety of solvents rho parallels −log k_0, the pK_a of the unsubstituted compound. As a working hypothesis it is suggested that resonance effects increase considerably, and possibly inductive effects, slightly, with demand. Jaffé[10] has considered the ionization of $ArB(OH)_2$, ArCOOH, $ArAsO(OH)_2$, and $ArPO(OH)_2$ and has related rho in each series to the ionic refractivity (or polarizability) of the central atom. An equally good relationship holds for rho and −log K_0 for each series (Table III). A similar statement can be made for the benzoic acids in various ethanol–water mixtures, and for the series of *m*- and *p*-substituted benzoic acids with *o*-H *vs.* *o*-NO_2 groups. Undoubtedly other factors contribute to the observed ρ. Apparent exceptions occur, for example, in cases such as the 2,6-dimethylbenzoic acids wherein steric factors have a pronounced effect on −log K_0. The high correlation coefficients of almost all of these series rule out variable sigma values of a few substituents, and suggest instead a genuine variation in the transmitting effectiveness of the benzene ring.

TABLE III

THE RELATIONSHIP OF RHO AND $-pK_0$ FOR THE IONIZATION OF ACIDS

Reaction Series	ρ[a]	−log K_0
$ArB(OH)_2$	2.53	9.7
ArCOOH	1.00	4.2
$ArAsO(OH)_2$	0.95	3.5
$ArPO(OH)_2$	0.76	1.8
	0.91	2.2
ArCOOH 50% ethanol	1.60	5.5
70% ethanol	1.74	6.2
90% ethanol	1.87	6.9
100% ethanol	1.96	7.2

[a] For reference see Table I, footnote *a*.

In the three series of acids of the present study a solvent change from water to 50% ethanol may increase the transmission of electronic effects by the benzene ring in all cases, and by the three-

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[10] H. H. Jaffé, L. D. Freedman, and G. O. Doak, *J. Am. Chem. Soc.*, **75,** 2209 (1953).

TABLE IV

PHYSICAL PROPERTIES OF *m*- AND *p*-SUBSTITUTED β-PHENYLPROPIONIC, *cis*- AND *trans*-2-PHENYLCYCLOPROPANECARBOXYLIC ACIDS

Substituent	M.P.[a]	Calcd. C, %	Calcd. H, %	Found C, %	Found H, %
	β-PHENYLPROPIONIC ACIDS				
4-NO_2	165.4–166.2 (166–167)[b]				
3,4-Cl_2	95.8–96.8	49.34	3.68	49.51	3.84
3-Cl	71.6–72.5 (77)[c]	58.55	4.91	58.44	4.79
4-Cl	120.9–121.9 (122–123)[b]				
Unsubstituted	47.8–48.6 (48–49)[b]				
4-CH_3	115.8–116.7 (116.5–117)[b]				
4-OCH_3	103.1–103.8 (107–108)[b]				
	cis-2-PHENYLCYCLOPROPANECARBOXYLIC ACIDS				
3-NO_2	178.7–179.7	57.97	4.38	58.20	4.26
3,4-Cl_2	179.2–180.2	51.97	3.49	51.97	3.47
3-Cl	113.4–114.4	61.08	4.61	60.84	4.64
4-Cl	128.1–129.1	61.08	4.61	61.35	4.71
Unsubstituted	105.0–105.6 (105.5–106.5)[b]				
3,4-CH_2O_2	145.0–145.6	64.07	4.89	64.35	4.79
4-CH_3	101.3–102.2	74.98	6.87	74.97	6.89
4-OCH_3	100.8–101.0	68.74	6.30	68.86	6.23
	trans-2-PHENYLCYCLOPROPANECARBOXYLIC ACIDS				
4-NO_2	199.0–200.0 (197–199)[b]				
3-NO_2	154.7–155.6 (155.5–156.5)[b]				
3,4-Cl_2	141.7–142.3	51.97	3.49	51.93	3.56
3-Br	117.6–118.0	49.82	3.76	49.82	3.80
3-Cl	108.2–108.6 (108–109)[b]				
4-Br	126.0–126.7	49.82	3.76	50.01	3.84
4-Cl	115.8–116.7 (115.5–116.5)[b]				
Unsubstituted	90.8–91.4 (92–93)[b]				
3,4-CH_2O_2	124.0–124.8	64.07	4.89	64.08	4.80
4-OCH_3	113.2–114.2 (112–113)[b]				
3,4-$(CH_3)_2$	99.5–100.0	75.76	7.42	75.47	7.29

[a] All melting points are uncorrected. [b] Ref. 8. [c] J. F. J. Dippy and J. E. Page, *J. Chem. Soc.*, 357 (1938).

membered ring in the phenylcyclopropanecarboxylic acids. In view of the relationship between equilibrium constants (here for acid ionization) and the free-energy difference (ΔF) between equilibrated species, this is, in effect, a suggestion that ρ in a number of acid series is dependent on ΔF, especially when differences in ρ are due primarily to enthalpy, rather than entropy, differences. A change from water to a less polar medium presumably acts to diminish solvation of the carboxylate ion relative to the carboxylic acid, thus increasing the free energy of ionization.

EXPERIMENTAL

Preparation of acids. The acids were prepared from the corresponding esters[3a,9] by acid-catalyzed hydrolysis in aqueous ethanol. The physical properties and analyses are listed in Table IV.

Measurement of pK_a. Solvent (50.0% ethanol–50.0% water by volume) was prepared in large quantity; density measurements agreed with published values. Samples of each acid ($8.89 \pm 0.01 \times 10^{-3}$ mole) were dissolved in 100 ml. of solvent, the titration flask was purged with nitrogen and the acid solution was titrated with a 0.26 *N* sodium hydroxide solution in the solvent. Measurements of the *p*H were made with a Beckman GS meter after each small addition of base. Especially small increments (0.01 ml.) were added around the equivalence point. The *p*K_a was taken as equal to the *p*H at half-neutralization determined graphically, and making use of a differential plot to establish the neutralization point. A more exact calculation established that a correction of as much as 0.001 *p*H unit was necessary only for *p*K_a's of less than 5.5. Essentially identical *p*K_a values were calculated from the *p*H at one-fourth and three-fourths neutralization in sample cases.

Apparatus. The neutralization was carried out in a 250-ml. spherical flask with four necks bearing a glass electrode, a calomel electrode, a nitrogen inlet tube, and a rubber septum. Base was added from a calibrated 5 ml. × 0.01 ml. buret through a syringe needle which pierced the septum and delivered titrant underneath the surface of the acid solution. Prepurified nitrogen saturated with 50% ethanol and maintained under positive pressure, was led into the titration flask and the buret. During the process of dissolving the acid sample and the contents of the flask was mixed by a magnetic bar driven by a submarine magnetic stirrer. The titration flask was immersed in a water bath at 25.00 ± 0.02°.

Additional precautions. Several different glass and reference electrodes were used during this work without appreciable variation in measured values of *p*H. In general duplicate determinations were carried out at widely separated times and with different electrodes. Each new batch of commercial phthalate buffer (stated *p*H 4.01 ± 0.01 at 25°) was compared with previous samples before use. The buret and titrant were maintained at ± 1° during each complete determination. The amount of base required for neutralization was in all cases close to the calculated amount; this rules out contamination of the samples by appreciable quantities of neutral impurities or acids of grossly different equivalent weight.

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[Contribution from the Department of Chemistry of the University of Wisconsin]

Relative Rates of Base-Catalyzed Racemization and Deuterium Exchange of Aryl 2-Octyl Sulfones[1]

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The rates of base-catalyzed (sodium methoxide) racemization (k_{rac}) and exchange of deuterium for hydrogen (k_{exc}) of phenyl and *p*-tolyl 2-octyl-2-*d* sulfone in methanol at 100° have been determined. The phenyl sulfone racemizes and exchanges more rapidly than the *p*-tolyl analog. With each sulfone, exchange exceeds racemization—*e.g.*, k_{exc}/k_{rac} is 17 for the phenyl sulfone and 14 for the *p*-tolyl sulfone. Thus exchange occurs for the most part with preservation of optical configuration. This shows that carbanions stabilized by sulfone groups are nonplaner; *i.e.*, enantiomeric sulfones give enantiomeric carbanions.

Recent preliminary reports[3] concerning the relative rates of base-catalyzed racemization and deuterium exchange of optically active 2-octyl-2-*d* phenyl sulfone prompt us to report the results of a similar investigation. Because of work in progress in other laboratories[3,4] we have discontinued our research in this area and report herein results obtained to date which are complementary to those reported in ref. 3.[5] In the present work we determined the pseudo first-order rates of racemization of (−)phenyl and (−)*p*-tolyl 2-octyl sulfone and the rates of racemization and deuterium exchange of the deuterated analogs in methanol containing sodium methoxide.

Our interest in the stereochemical behavior of carbanions stabilized by sulfone functions stems from an investigation of elimination reactions of cyclic β-chloro sulfones.[6] In that work it was suggested that base-promoted *cis*-elimination of *trans*-chloro sulfones to give α,β-unsaturated sulfones may involve a two-step process (removal of the acidic α-hydrogen atom followed by conversion of the intermediate carbanion to product) rather than a concerted process.[7] The primary objective of the present work was to determine if the properties of α-sulfonyl carbanions are consistent with this view.

RESULTS AND DISCUSSION

Optically pure (−)-phenyl and (−)-*p*-tolyl 2-octyl sulfone were prepared from (−)-2-octanol.[8] The alcohol was converted to the *p*-toluenesulfonate derivative,[9] which was reacted with sodium thiophenolate or sodium *p*-thiocresolate to form the desired active aryl 2-octyl sulfide. The sulfide was converted to the corresponding sulfone by oxidation with hydrogen peroxide in glacial acetic acid.[10] The aryl 2-octyl-2-*d* sulfones were prepared in a similar manner from (−)-2-octanol-2-*d*, which was obtained by reduction of 2-octanone with lithium aluminum deuteride.

Kinetic data for the base-catalyzed racemization and exchange of deuterium for hydrogen of phenyl and *p*-tolyl 2-octyl sulfone in methanol at 100° are presented in Table I. Optically pure undeuterated sulfones were used in experiments 1–4 and 6–10. In these experiments the reactions were followed to about 75% completion, and the loss of optical activity was complete. Good pseudo first-order behavior (first order in methoxide ion and sulfone) was observed. The infrared spectra of the racemic products (isolated after ten half-periods) were indistinguishable from those of the optically pure reactants.

Optically pure phenyl and *p*-tolyl 2-octyl-2-*d* sulfone were used in experiments 5 and 11. In these experiments the same reaction solution was used to determine the rates of racemization and deuterium exchange.

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[1] This work was supported in part by the Research Committee of the Graduate School with funds given by the Wisconsin Alumni Research Foundation.

[2] (a) Du Pont Summer Research Fellow, 1959. (b) Du Pont Summer Research Fellow 1957.

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