tinct difference from that workhorse of benzylic oxidations, activated manganese dioxide,¹⁰ and its more powerful relative, nickel peroxide.¹¹

In order to examine the bismuthate reaction products, 2,4,6-tri-tert-butylphenol was treated with sodium bismuthate to give the corresponding stable phenoxyl radical. This reaction with excess of the phenol was used to completely exhaust the oxidizing power of a bismuthate sample. After benzene and water washings, the remaining residue was Bi₂O₃. Titration of the washes indicated amounts of sodium hydroxide almost equivalent to the initial sodium bismuthate. These results suggest that the stoichiometry of bismuthate oxidations is $2NaBiO_3 + 4(H) \rightarrow H_2O +$ $Bi_2O_3 + 2NaOH$. It should be borne in mind that the formula of the bismuthate does not fully express its structure. Commercial bismuthate usually has a 5-6% water content as determined by benzene azeotrope. Bismuthates with or without this water are equally effective in xylenol polymerization. Azetropic distillation has little effect on "chemical hydration" as indicated by ir bands at 2.95 and 5.95 μ .¹² The structure of the bismuthate undergoes a substantial change in refluxing acetic acid, wherein the 2,6-xylenol oxidation products are 2-acetoxy-2,6-dimethylcyclohexadien-3,5-one (63%) and diphenoquinone (III, 15%). No polymer was formed. Without the xylenol the sodium bismuthate in refluxing acetic acid evolves oxygen, as demonstrated by trapping the oxygen by a nitrogen sweep into a separate flask containing the 2,4,6-tri-tert-butylphenoxyl radical. Acidity causes a drop in active oxygen content. Commercial sodium bismuthate possesses an active oxygen content of 3.1×10^{-3} g-atoms of oxygen per gram. This is indicative of 91% purity, if correction is made for 5% water. The value for bismuthate treated with 10% sulfuric acid is 1.2×10^{-3} g-atoms of oxygen per gram. The sodium bismuthate, however, does not change in oxidizing power on standing in acetic acid at room temperature for several days.

Other phenols which have been polymerized by sodium bismuthate are durenol and 2,6-dimethoxyphenol. The durenol (2,3,5,6-tetramethylphenol) was treated with a 2 molar excess of bismuthate in refluxing benzene for 2 hr to give a 64% vield of a polymer (mp 215-230°) whose ir and NMR spectra were identical with those reported by Price and Nakagawa.¹³ A similar treatment of 2,6-dimethoxyphenol afforded a polymer VII which adhered strongly to the bismuthate surface. Soxhlet extraction with chloroform was used to obtain a 66% yield of a polymer melting at 205-210°. Its NMR spectrum had two singlet peaks at 3.7 (6 H) and 6.3 ppm (2 H) relative to $(CH_3)_4Si$. Significant ir bands were at 8.2, 8.35, 10.1, 10.6, 11.3, and 12.1μ .

Experimental Section

Materials and Instruments. Phenols were obtained from Aldrich Chemical Co. and were used without further purification. Sodium bismuthate was obtained from J. T. Baker Chemical Co., Fisher Scientific Co., and Allied Chemical Co. Spectral determinations were determined as follows: infrared, Perkin-Elmer Model 137; nuclear magnetic resonance, Varian Associates Model A-60; mass spectra, Varian Associates Model M-66. Melting points were determined on a Thomas-Hoover Unimelt apparatus. The thermometer was calibrated against melting point standards supplied by A. H. Thomas Co.

An Oxidation Procedure. Sodium bismuthate (33.0 g. 0.118 mol) was added to a solution of 2,6-xylenol (4.1 g, 0.033 mol) in 100 ml of benzene. The mixture was refluxed for 2 hr with magnetic stirring. After being cooled to 20° the mixture was filtered and the residual sodium bismuthate was washed with 150 ml of benzene. The combined benzene solutions were washed with a 5% solution of NaOH. Acidification of the basic layer did not yield any organic matter. The dried benzene solution was evaporated to give a crude polymer, which was dissolved in 25 ml of chloroform. The latter solution was poured into 200 ml of methanol to coagulate the polymer, which was then filtered and dried. It weighed 3.05 g and melted at 186-215°. The alcoholic mother liquor was concentrated to near dryness and yielded 0.047 g of diphenoquinone (III), as determined by superimposition of its infrared spectrum with that of an authentic sample. A portion of the dried recovered sodium bismuthate-bismuth oxide mixture was dissolved in concentrated hydrochloric acid without any residue.

Registry No.—I, 576-26-1; II repeating unit, 24938-67-8; II ho-mopolymer, 25134-01-4; III, 4906-22-3; IV, 527-60-6; V homopolymer, 30140-67-1; VI, 91-01-1; VII repeating unit, 25667-13-4; VII homopolymer, 25511-61-9; NaBiO₃; 12125-43-8; 2,6-di-tert-butylphenol, 128-39-2; tetra-tert-butyldiphenoquinone, 2455-14-3; 4hydroxy-3,5-dimethylbenzaldehyde, 2233-18-3; 2-acetoxy-2,6-di-methylcyclohexadien-3,5-one, 7218-21-5; durenol, 527-35-5.

References and Notes

- A. S. Hay, Adv. Polym. Sci., 4, 496 (1967).
 B. O. Lindgren, Acta Chem. Scand., 14, 1203 (1960).
 E. McNelis, J. Org. Chem., 31, 1255 (1966).
 H. D. Becker, U. S. Patent 3,390, 125 (June 25, 1968).
 G. D. Conpert M. S. Placetard O. S. Constant, 14, 1203 (1968).
- (5) G. D. Cooper, H. S. Blanchard, G. F. Endres, and H. Finkbeiner, J. Am. Chem. Soc., 87, 3996 (1965).
- (6) W. J. Mils, O. E. Van Lohuizen, J. Bussink, and L. Vollbracht, *Tetrahedron*, 23, 2253 (1967).
 (7) D. G. Hewitt, J. Chem. Soc. C, 1750 (1971).
 (8) C. C. Price and N. S. Chu, J. Polym. Sci., 61, 136 (1962).
 (9) E. McNelis, J. Am. Chem. Soc., 88, 1074 (1968).

- B. M. Evans, G. Rev., Chem. Soc. 13, 61 (1959).
 K. Nakagawa, R. Konaka, and T. Nakata, J. Org. Chem., 27, 1597 (1962).
- (12) A. Miller and C. H. Wilkins, Anal. Chem., 24, 1253 (1952).
- (13) C. C. Price and K. Nakaoka, Macromolecules, 4, 363 (1971).

Ionization Constants of Substituted 2-Aminoacetanilides and Benzylamines. Transmission of Electronic Effects through Amide Links

Frances B. Peters and H. W. Johnson, Jr.*

Department of Chemistry, University of California at Riverside, Riverside, California 92502

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Previous papers in this series have reported the effect of aromatic ring substituents on the rates of reaction at the methylene group adjacent to the carbonyl in substituted anilides.¹ A typical study was the displacement rate of 4nitrophenoxide with 2-bromoacetanilides.^{1d} The reaction center was immediately adjacent to the carbonyl group, and Hammett ρ values²⁻⁷ appeared to indicate efficient transfer of activation effects through the amide link. Two studies have indicated low transmission efficiencies through the amide functionality: the ionization constants of 4-substituted 4'-aminobenzanilides⁸ and the ¹⁹F chemical shifts in substituted trifluoroacetanilides.⁹

In a continuation of these studies, and because of possible interest from the biochemical area, we have prepared a group of ring-substituted 2-aminoacetanilides and have measured the pK's in water solution. For comparison the pK's of a group of ring-substituted benzylamines have been determined; previous determinations^{3,10–12} of the Hammett ρ for these amines gave values ranging from $0.72^{3,10}$ to 1.06^{11} to 1.13 (data from ref 12 fit to the Hammett equation in this work; r = 0.987). Values of ρ refer to eq 1. It was

$$\mathbf{B}\mathbf{H}^+ \rightleftharpoons \mathbf{B} + \mathbf{H}^+ \tag{1}$$

thought desirable to remeasure the benzylamines to ensure consistency of measurement with the 2-aminoacetanilides.

The benzylamines and their hydrochlorides are known compounds; they were purchased or prepared by reported

Table I pK Values of the 2-Aminoacetanilide Hydrochlorides in Water at 23 ± 1°

Substituent	pK	σα		
4'-CH ₃	7.99	-0.17		
4'-H	7.96	0.00		
$3'-OCH_3$	7.92	0.12		
4'-C1	7.88	0.23		
3'-C1	7.89	0.37		
$4' - CF_3$	7.83	0.54		
3'-NO2	7.78	0.71		
4'-NO2	7.76^{b}	0.78		
$\rho = 0.23$; $r = 0.960;^c s =$	= 0.027.		

^a Reference 4. ^b Determined at 0.001 M because of limited solubility in water. ^c The somewhat low r value is caused primarily by the small slope of the regression line when compared with the normal error of ± 0.02 .

Table II pK Values of the Benzylamine Hydrochlorides in Water at $23 \pm 1^{\circ}$

Registry no.	Substituent	(this study)	p <i>K</i> (other work)	σđ
26177-45-7	4-CH ₃	9.74	9,54ª	-0.17
3287-99-8	4-H	9.54	9,38ª	0.00
			9.34^{b}	
			9.62^{c}	
42365-43-5	4-C1	9.31	9.14^{a}	0.23
			$9,18^{b}$	
42365-42-4	3-C1	9.09	9.01^{a}	0.37
			8.99^{b}	
18600-42-5	$4 - NO_2$	8,58	8.50^{a}	0.78
	-		8.38^{b}	
ρ	= 1.23; r =	= 0.998; s	= 0.025.	

 a pK values at 25°, ref 11. b pK values at 25°, ref 12. c pK at 25°: R. J. Bruehlman and F. H. Verkock, J. Am. Chem. Soc., 70, 140 (1948). d Reference 4.

methods. The 2-aminoacetanilides and their hydrates are known compounds;¹³ the hydrochlorides appear to be unreported except for the parent compound.^{13a,14} The most common method of synthesis of the 2-aminoacetanilides is the ammonolysis of the 2-chloroacetanilides; it was found most convenient to use the Sheehan–Frank¹⁴ route involving reaction of N-phthaloylglycyl chloride with the aniline followed by hydrazinolysis of the protecting group.¹⁵ The 2-aminoacetanilide hydrochlorides had satisfactory infrared spectra and elemental analyses.

The pK's were determined by potentiometric titration of 0.02 M amine hydrochloride with 0.08 M sodium hydroxide in water at 23 ± 1°.¹⁶ The pK values were reproducible to 0.02 pK units in different titrations; at least three independent titrations were conducted for each compound, and the average is reported. The pK values refer to eq 1. Table I reports pK values with the selected Hammett σ constant⁴ for the eight 2-aminoacetanilide hydrochlorides used in this work. Table II reports identically determined pK values and σ constants for five benzylamine hydrochlorides; Table II also contains previous workers' pK values.

The pK values for the 2-aminoacetanilide hydrochlorides gave a ρ value of 0.23 (r = 0.960).³ Irrespective of model compound comparison, the ring substituent has only a small effect on the dissociation constant of the ammonium group. Presumably the same low effect would be noted for differing substituents in peptides if steric and/or secondary-tertiary structural effects are absent. The ρ value for dissociation of the benzylamine hydrochlorides from this work was 1.23 $(r = 0.998)^3$ using five compounds in water at $23 \pm 1^\circ$. This value is near the 1.13 calculated from the data of Litvinenko et al.,¹² somewhat higher than the 1.06 of Blackwell et al.,¹¹ and substantially higher than the first report of 0.72.³ In this equilibrium reaction the amide link is transmitting substituent effects with 20–25% efficiency, measured by $\rho(\text{anilide})/\rho(\text{ben$ $zylamine})$. In the reactive site was adjacent to the carbonyl group, the transmission efficiencies appeared to be 70–100%.¹

This work suggests that the amide group functions as a relatively efficient transmitter of substituent effects when the reactive site or transition state has the potential to conjugate with the carbonyl carbon atom. The pK measurements of Kadin¹⁷ on 2-methyl-1,3(2H,4H)-dioxoisoquinol-ine-4-carboxanilides (ρ 1.25), the ¹⁹F NMR measurements of Pews¹⁸ on 3- and 4-substituted 4'-fluorobenzanilides as contrasted with our measurements of trifluoroacetanilides,⁹ as well as our previous kinetic results¹ fit the pattern. The pK measurements of Menger⁸ with 4-substituted 4'-aminobenzanilides (ρ = 0.06) remain to be explained unless a directional effect¹⁸ is operative. The work of Pews¹⁷ and Kadin¹⁸ seems to eliminate ground-state vs. transition-state substituent sensitivity as the major contributor to the explanation.

Experimental Section

General. Melting ranges were determined with a Thomas-Hoover capillary apparatus and are uncorrected. Infrared spectra were obtained using a Perkin-Elmer Model 621 spectrophotometer. Titration curves were obtained using a Corning Model 7 pH meter (No. 475007) with glass electrode (No. 476022) and reference electrode (No. 476002).

Mallinckrodt BuffAR standard buffer solutions, pH at 25° of 4.01, 7.00, and 10.00, were used to standardize the pH meter prior to each run.

Microanalyses were performed by C. F. Geiger, Ontario, Calif., and Elek Microanalytical Laboratories, Harbor City, Calif.

Chemicals. The benzylamines, benzyl chlorides, N-phthaloylglycine, and thionyl chloride used in this study were obtained from Aldrich Chemical Co. The anilines and hydrazine hydrate were obtained from Mallincrodt Chemical Works, Matheson Coleman and Bell, and Sigma Chemical Co.

Preparation of the 2-Aminoacetanilide Hydrochlorides. The general method is a modification of a literature procedure^{14,15} and can be illustrated by the preparation of 2-aminoacetanilide hydrochloride.

Thionyl chloride (24.0 g, 0.2 mol) and N-phthaloylglycine (20.5 g, 0.1 mol) were refluxed together for 2.5 hr. Excess $SOCl_2$ was removed in a stream of N₂. The crude product was dissolved in benzene to make 200 ml of solution. Phthaloylglycyl chloride (100 ml benzene solution, 0.05 mol) was slowly added to 500 ml of benzene solution containing aniline (9.2 g, 0.1 mol). The precipitate of crude phthaloylglycine anilide was collected, rinsed with water, and recrystallized twice from absolute methanol, yield 11.4 g (0.04 mol), 80%. Phthaloylglycine anilide (5.6 g, 0.02 mol) as a slurry in 250 ml of absolute ethanol was refluxed for 1.5 hr with 99% hydrazine hydrate (1.19 g, 0.022 mol). Ethanol was removed from the reaction mixture using a Roto-vap evaporator. The residue was treated with 150 ml of 2 N HCl and the mixture was heated at 60° for 15 min and allowed to cool to room temperature. Phthalhydrazide (3.2 g, 0.02 mol dry material) was removed by filtration. Water and HCl were removed on the Roto-vap, yield of crude product 3.4 g (0.018 mol), 82%. The solid was crystallized from ethanol into three fractions. The middle fraction (mp 190-195°) was recrystallized from ethanol and used for pK determinations (mp 190-250° dec). Melting ranges of the 2-aminoacetanilide hydrochlorides are included in Table III. All the compounds except for the 4'-NO2 and 3'-NO2 derivatives evolve gas, melt, and decompose over a long temperature range.

Preparation of the Benzylamine Hydrochlorides. Five benzylamine hydrochlorides were prepared from the amines and HCl or by reaction of phthalimide, K_2CO_3 , and the appropriate substi-

Table III				
Melting Characteristics of the				
2-Aminoacetanilide Hydrochlorides ^a				

Registry no,	Substituent	Melting range, °C	
4801-39-2	Н	190-250 dec	
54643-64-0	4'-CH3	200–260 dec	
54643-65-1	$4'-NO_2$ 273-274 (darkens 2		
54643-66-2	3'-NO ₂	246–248 (darkens 240)	
54643-67-3	4'-C1	235-290 dec	
54643-68-4	3'-Cl	210–2 80 dec	
54643-69-5	3'-OCH ₃	210–225 dec	
54643-70-8	4'-CF ₃	235-245 dec	

^a Satisfactory analytical data for C, H, Cl (±0.35%) were reported for the compounds in this table. Ed.

tuted benzyl chloride, followed by hydrazinolysis. Two recrystallizations of the crude products from ethanol yielded the benzylamine hydrochlorides melting with some decomposition: 4-methyl-benzylamine, mp 240-243° (lit. mp 235°);^{19a} benzylamine, mp 263-264° (lit. mp 260°);^{19b} 4-chlorobenzylamine, mp 263-265° (lit. mp 259°);^{19c} 3-chlorobenzylamine, mp 225-227° (lit. mp 225°);^{19c} 4-nitrobenzylamine, mp 269-270° with decomposition from 260° (lit. mp 256° dec).^{19c}

Potentiometric Determination of pK Values. Solutions (0.02 M) of each of the 2-aminoacetanilide hydrochlorides and benzylamine hydrochlorides in water were prepared. Three 25.0-ml aliquots of each were titrated at $23.0 \pm 1^{\circ}$ with 0.08 M NaOH and the pH of the solutions was measured at intervals using glass and saturated calomel electrodes.^{16,20,21} Values of pK were computed from the equation $pK = pH + \log [BH^+]/[B]$. The ionic strength was constant (0.02) throughout each titration. The pK's determined are the so-called "mixed" constants.¹⁰ Scatter within individual runs ranged from 0.02 to 0.09 pK units, depending upon the purity of the compound. Agreement between average pK values among the three titrations for each compound ranged from 0.00 to 0.02.

Values of ρ were determined from pK values and the respective σ constants⁴ using an Olivetti Underwood Programma 101 leastsquares program.²²

Registry No.-Thionyl chloride, 7719-09-7; N-phthaloylglycine, 4702-13-0; phthaloylgylcyl chloride, 6780-38-7; phthaloylglycine anilide, 2017-94-9.

References and Notes

- (a) H. W. Johnson, Jr., and M. P. Schweizer, J. Org. Chem., 26, 3666 (1961);
 (b) H. W. Johnson, Jr., E. Ngo, and V. A. Pena, *ibid.*, 34, 3271 (1969);
 (c) H. W. Johnson, Jr., Y. Iwata, E. Ngo, and R. Stafford, Ab-stracts, 158th National Meeting of the American Chemical Society, New York, N.Y., Sept 1969, No. ORGN 31; (d) H. W. Johnson, Jr., and Y. Iwata, J. Org. Chem., 36, 1921 (1971).
 L. P. Hammett, "Physical Organic Chemistry", 2nd ed, McGraw-Hill, New York, N.Y., 1970, p 355.

- New YOR, N.Y., 1970, p 355.
 (3) H. H. Jaffe, Chem. Rev., 53, 191 (1953).
 (4) C. D. Ritchie and W. F. Sager, Prog. Phys. Org. Chem., 2, 323 (1964).
 (5) S. Ehrenson, Prog. Phys. Org. Chem., 2, 195 (1964).
 (6) P. R. Wells, S. Ehrenson, and R. W. Taft, Prog. Phys. Org. Chem., 6, 1477 (1969).
- 147 (1968).
- (7) C. D. Johnson and K. Schofield, J. Am. Chem. Soc., 95, 270 (1973).
 (8) J. A. Donohue, R. M. Scott, and F. M. Menger, J. Org. Chem., 35, 3035 (1970).
- (9) H. W. Johnson, Jr., and Y. Iwata, J. Org. Chem., 35, 2822 (1970).
 (10) D. D. Perrin, "Dissociation Constants of Organic Bases in Aqueous So-
- Iution'', Butterworths, London, 1965, pp 116–119; W. A. Carothers, C. G. Bickford, and G. J. Hurwitz, J. Am. Chem. Soc., 49, 2908 (1927).
 (11) L. F. Blackwell, A. Fischer, I. J. Miller, R. T. Topson, and J. Vaughn, J.
- Chem. Soc., 3588 (1964). (12) L. M. Litvinenko, V. A. Dadali, A. M. Volovin and E. T. Titov, Reakts.
- Sposobn. Org. Soedin, 3, 75 (1966); Chem. Abstr., 69, 5699 (1968).
- Sposobn. Org. Soedin, 3, 75 (1966); Chem. Abstr., 69, 5699 (1968).
 (13) (a) A. J. Hill and E. B. Kelsey, J. Am. Chem. Soc., 42, 1704 (1920); (b) A. J. Hill and E. B. Kelsey, *Ibid.*, 44, 2357 (1922); (c) P. Pfeiffer and S. Suare, J. Prakt. Chem., 157, 97 (1941); (d) H. Tuppy, U. Wiesbauer, and E. Wintersberger, *Hoppe-Seyler's Z. Physiol. Chem.*, 329, 278 (1962).
 (14) J. C. Sheehan and V. S. Frank, J. Am. Chem. Soc., 71, 1856 (1949).
 (15) H. R. Ing and H. F. Manske, J. Chem. Soc., 2348 (1926).
 (16) A. Albert and E. P. Sergeant, "Ionization Constants of Acids and Bases", Wiley, New York, N.Y., 1962, Chapter 2.
 (17) R. G. Pews, Chem. Commun., 458 (1971).
 (18) S. Kadin. J. Org. Chem. 38, 1150 (1971).

- (18) S. B. Kadin, J. Org. Chem., 36, 1160 (1971).

- (a) T. Curtius, Ber., 35, 3232 (1902); (b) A. E. Martell and R. M. Herbst, J. Org. Chem., 6, 878 (1941); (c) T. Curtius, J. Prakt. Chem., 89, 508 (1914).
- H. Rossotti, "Chemical Applications of Potentiometry", D. Van Nostrand (20)Co., Ltd., London, 1969, p 117. M. M. Davis and H. B. Hetzer, *J. Phys. Chem.*, **61**, 123 (1957).
- (21)
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The Capability and Nature of the Amide Bond as a Transmitter of Electronic Effects¹

John P. Idoux* and Rudolfo Zarrillo

Department of Chemistry, Florida Technological University, Orlando, Florida 32816

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The planarity and restricted rotation which has been observed about amide bonds has been attributed to the importance of a dipolar resonance contributor such as II, and, in fact, based on contribution from such a form, Pauling²



has estimated that this carbon-nitrogen bond should have ca. 40% double-bond character. As a result, it has been assumed for some time that the amide bond can function as a transmitter of conjugative effects. Recently, however, a number of conflicting reports have appeared³⁻⁸ concerning the amide bond's capability as a transmitter of electronic effects, and in particular questions have arisen relative to the manner and magnitude of this transmission⁵⁻⁸ and of its dependence on the location of a substituent relative to the amide nitrogen.^{7,8} In an effort to clarify some of these questions and to investigate the validity of using either a nonreaction property (in the form of NMR chemical shifts) or a reaction property (in the form of pK_a data) as a probe of substituent effects, we report here studies on the transmission of electronic effects through two closely related amide bond containing systems. These studies involve comparisons of pK_a data for a simple monosubstituted biphenylamine system (III) with those for a related, perturbed biphenylamine system (IV) and NMR chemical shift data for 4-substituted biphenyls (V) and 4'-substituted 4-biphenylacetanilides (VI). Since the 1,1' bond in bi-



phenyl can conjugatively transmit electronic effects, although at a much diminished intensity relative to a single benzene ring,⁹⁻¹² we felt that comparisons of reaction and nonreaction properties of biphenyl and perturbed biphenyl systems would provide a rather severe test of the amide bond's conjugative ability.