hydrochloride with little change in a sealed ampoule for three months.

Experimental Section

Microanalyses were performed in the laboratory of Dr. F. Gautschi, Firmenich et Cie., Geneva. Boiling points are uncorrected. Vapor phase chromatography was performed on a F & M 720 instrument. The following spectrometers were used: nmr, Varian T-60 and HA-100; ir, Perkin-Elmer Models 237 and 247; uv, Cary Model 14; mass spectrum, Hitachi RMU6D.

Hydrogenation of 2-Acetylpyridine (3).—A solution of 8.4 g (69 mmol) of 2-acetylpyridine in 75 ml of absolute ethanol was hydrogenated in the presence of 1.5 g of 5% rhodium on alumina. Absorption was complete after uptake of 6490 cm^3 of H_2 [22° (760 mm), 3.9 equiv]. The mixture was filtered through Celite, evaporated, and distilled to give 6.94 g (78%) of alcohol **4**: bp 48° (0.1 mm) [lit.^{6} bp 101–102° (23 mm)]; ir ($CHCl_3$) 2400–3650 cm^{-1}; nmr (CCl_4) δ 1.0 (3 H, d, J = 7 Hz), 0.8–3.2 (9 H, m), 3.3 (1 H, s, disappears on exchange with D_2O), 3.4 (1 H, s, disappears on exchange with D_2O), 3.4 (1 H, m).

Oxidation of Alcohol 4.—A stirred suspension of silver carbonate on Celite (prepared^5 from 50 g of Celite, 60 g of silver nitrate, and 37 g of sodium bicarbonate), 7.0 g (54 mmol) of alcohol **4**, and 400 ml of benzene was heated at reflux for 20 hr under nitrogen. Filtration, evaporation *in vacuo*, and distillation afforded 3.84 g (57%) of approximately a 2:1 mixture of ketones **1** and **2** (nmr): bp 35–40° (0.1 mm); vpc (2-ft TCEP and 6-ft silicon gum rubber) 1 peak; ir ($CHCl_3$) 1650, 1670, 1695, 3430 cm^{-1}; uv (EtOH) 308 nm (ϵ 2450); uv (pentane) 312 nm (ϵ 3360); nmr (100 MHz, C_6D_6) enamine tautomer δ 1.5 (2 H, m), 1.9 (2 H, m), 2.0 (3 H, s), 2.8 (2 H, t, J = 2.5 Hz), 4.3 (1 H, broad, disappears on exchange with D_2O), 5.2 (1 H, t, J = 2.5 Hz); nmr imine tautomer δ 1.2 (4 H, m), 2.2 (2 H, m), 2.3 (3 H, s), 3.4 (2 H, m); mass spectrum (70 eV) m/e (rel intensity) 125 (58), 43 (100).

Anal. Calcd for $C_7H_{11}NO$: C, 67.17; H, 8.86. Found: C, 67.25; H, 9.29.

Hydrochloride of 1 and 2.—To an ice-cold solution of 603 mg (4.8 mmol) of the amines **1** and **2** in 20 ml of dry ether was added dropwise a slight excess of HCl in dry ether. The solid was filtered, washed with ether, and dried in a desiccator at 10 mm to give 664 mg (86%) of the hydrochloride: mp 112–119°; ir ($CHCl_3$) 1675, 1690, 1735, 2000–3600 cm^{-1}.

Regeneration of the Free Base.—A mixture of 427 mg (2.64 mmol) of the hydrochloride, 20 ml of methylene chloride, and 2 g of sodium bicarbonate was stirred at room temperature for 20 min. Filtration followed by evaporation and distillation of the residue yielded 217 mg (66%) of the amines **1** and **2**, bp ~35° (0.1 mm).

Registry No.—**1**, 25343-57-1; **1** HCl, 27300-26-1; **2**, 27300-27-2; **2** HCl, 27300-28-3.

Acknowledgment.—We are indebted to Firmenich et Cie., Geneva, for generous financial support.

[6] G. R. Clemo, R. Raper, and H. J. Vipond, *J. Chem. Soc.*, 2095 (1949).

Further Evidence for the Validity of the Overlap Indicator Method. Correlation of pK_a's of Corresponding Aniline and 2-Nitroaniline Derivatives

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Katritzky and coworkers[1] and Arnett and coworkers[2,3] have recently reported that good linear enthalpy–free-energy correlations serve to support the validity of the Hammett overlap indicator method[4] for estimating pK_a's of very weak bases. In the former instance,[1] ionization constants of a number of aniline indicators were determined over a range of temperatures,[5] and ΔF values were shown to be linear with enthalpies of ionization. The latter reports[2,3] involved comparisons of pK_a's for a variety of amine types with partial molal heats of transfer from carbon tetrachloride or tetrachloroethane to fluorosulfuric or sulfuric acid solvents.

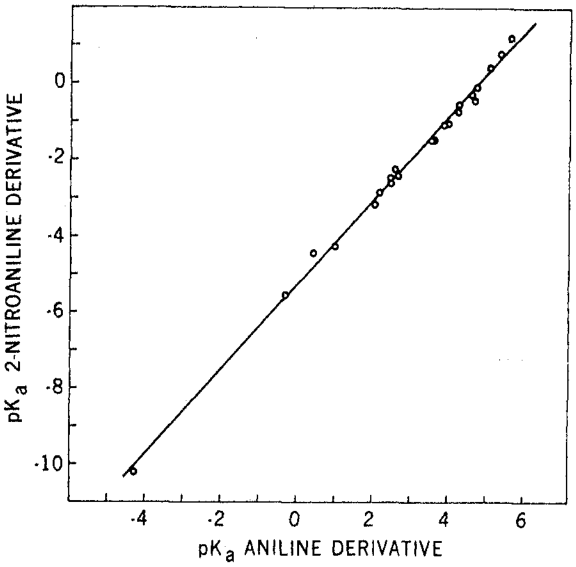

Figure 1.—Variation in pK_a's of 2-nitroaniline derivatives with those of correspondingly substituted anilines.

We wish now to describe an extended pK_a range linear free-energy correlation which serves as additional supporting evidence to confirm the reliability of more recent H_0 acidity function extrapolations for primary aniline indicators and therefore the overlap indicator method in general. Our evidence differs in nature from Arnett's and Katritzky's in that they compared related thermodynamic properties of same materials, whereas we correlate same properties of related materials.[6]

We have compared literature values for pK_a's of ortho- meta-, para-, and polysubstituted anilines (reaction series A) with those of corresponding 2- (or 6-) nitroaniline derivatives (series B) in water at 25 ± 3°; the data are listed in Table I. A plot (Figure 1) shows excellent linear correlation between the two series; least-squares analysis leads to the equation

$$\text{p}K_a\ (\text{series B}) = -5.32 + 1.11\ \text{p}K_a\ (\text{series A}) \qquad (1)$$

r (correlation coefficient) = 0.998
s (standard deviation) = 0.16 pK unit

For the more basic compounds, the pK_a determinations in both series were carried out in standard buffer solutions; at intermediate basicities, the pK_a's in

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[1] P. D. Bolton, C. D. Johnson, A. R. Katritzky, and S. A. Shapiro, *J. Amer. Chem. Soc.*, **92**, 1567 (1970).

[2] E. M. Arnett and J. J. Burke, *ibid.*, **88**, 4308 (1966).

[3] E. M. Arnett, R. P. Quirk, and J. J. Burke, *ibid.*, **92**, 1260 (1970).

[4] L. P. Hammett, "Physical Organic Chemistry," McGraw-Hill, New York, N. Y., 1940; E. M. Arnett, *Progr. Phys. Org. Chem.*, **1**, 233 (1963).

[5] C. D. Johnson, A. R. Katritzky, and S. A. Shapiro, *J. Amer. Chem. Soc.*, **91**, 6654 (1969).

[6] In a sense, the present correlation represents an application of a generalization regarding constant effects of ortho substituents first suggested by H. H. Jaffé, *Science*, **118**, 246 (1953); *Chem. Rev.*, **53**, 191 (1953).

TABLE I

pK_a's OF CORRESPONDING ANILINE AND 2-NITROANILINE DERIVATIVES IN WATER AT 25 ± 3°

No.	Substituent	Aniline pK_a	ref	2- (or 6-) Nitroaniline pK_a	ref	ΔpK_a, exptl − calcd (eq 1)
1	Unsubstituted	4.60	*a*	−0.29	*b*	0.10
2	4-CH$_3$O–	5.34	*a*	0.77	*c*	−0.14
3	4-CH$_3$–	5.08	*a*	0.43	*c*	−0.09
4	4-F–	4.65	*a*	−0.44	*c*	0.30
5	4-Cl–	3.98	*a*	−1.03	*c*	0.14
6	4-Br–	3.86	*a*	−1.05	*c*	0.03
7	4-CF$_3$–	2.57	*d*	−2.25	*c*	−0.21
8	4-CH$_3$OCO–	2.46	*e*	−2.61	*c*	0.03
9	4-NO$_2$–	1.00	*b*	−4.27	*l*	0.06
10	4-CH$_3$CO–	2.19	*f*	−2.85	*c*	−0.03
11	4-HO–	5.60	*f*	1.20	*g*	−0.28
12	3-CH$_3$–	4.73	*a*	−0.09[h]	*i*	0.04
13	3-CH$_3$O–	4.23	*a*	−0.72[h]	*i*	0.11
14	3-Cl–	3.52	*a*	−1.48[h]	*i*	0.08
15	3-Br–	3.58	*a*	−1.48[h]	*i*	0.15
16	3-NO$_2$–	2.46	*a*	−2.49[h]	*i*	−0.09
17	3-HO–	4.25	*f*	−0.55[h]	*j*	−0.03
18	2-Cl–	2.65	*a*	−2.41	*b*	0.04
19	2-NO$_2$–	−0.29	*b*	−5.56	*b*	−0.09
20	2,4-Cl$_2$–	2.05	*k*	−3.16	*k*	0.12
21	4-CH$_3$-2-NO$_2$–	0.43	*c*	−4.45	*k*	−0.39
22	2,4-(NO$_2$)$_2$–	−4.27	*l*	−10.23	*b*	0.15

[a] A. I. Biggs and R. A. Robinson, *J. Chem. Soc.*, 388 (1961). [b] Reference 1. [c] J. O. Shreck, C. K. Hancock, and R. M. Hodges, *J. Org. Chem.*, **30**, 3504 (1965). [d] J. D. Roberts, R. L. Webb, and E. A. McElhill, *J. Amer. Chem. Soc.*, **72**, 408 (1950). [e] R. A. Robinson and A. I. Biggs, *Aust. J. Chem.*, **10**, 128 (1957). [f] J. M. Vandenbelt, C. Henrich, and S. G. Vanden Berg, *Anal. Chem.*, **25**, 726 (1954). [g] H. G. Hansson, *Acta Chem. Scand.*, **16**, 1956 (1962). [h] 3-Substituted 6-nitroanilines. [i] C. K. Hancock, R. A. Brown, and J. P. Idoux, *J. Org. Chem.*, **33**, 1947 (1968). [j] J. W. Eastes, M. H. Aldridge, and M. J. Kamlet, *J. Chem. Soc. B*, 922 (1969). [k] E. Hogfeldt and J. Bigeleisen, *J. Amer. Chem. Soc.*, **82**, 15 (1960). [l] Reference 5.

series A were in standard buffers and those in series B in H_0 solutions; at the lower pK_a's, the overlap indicator method was used to determine basicities in both series. The excellent linearity, extending from the buffer range completely through the H_0 range, therefore serves to confirm both the accuracy of the latter measurements and the validity of the method. Considering the diverse sources of the data, and the fact that determinations in the H_0 range involved hydrochloric, perchloric, and sulfuric acid solutions, it is significant that the measured pK_a for 2,4,6-trinitroaniline (22B of Table I), which involves the greatest H_0 extrapolation, fits the correlation equation to within a single standard deviation, and that only one value (a relatively older measurement for 21B) differs from the calculated by as much as two standard deviations.

It is also worth comment that the 1.11 slope in the correlation equation implies that the base-weakening effect of the 2-nitro group in series B is not quite constant (*i.e.*, no straightforward additivity of substituent effects) but rather increases slightly the greater the electron-withdrawing ability of additional substituents. We rationalize this on the basis that intramolecular amine → nitro hydrogen bonding in 2-nitroanilines serves toward stabilization of the free bases relative to the corresponding anilinium ions and that inductive or mesomeric electron withdrawal from the amine nitrogens tends toward an increase in the strength of these amine → nitro hydrogen bonds.[7]

It should be noted that the 2- (or 6-) nitro substituents in series B are always unhindered and most likely essentially coplanar. The correlation would probably break down in situations where the nitro were adjacent to a second ortho substituent which might tend to force it toward noncoplanarity, *e.g.*, in 3-substituted 2-nitroanilines.

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[7] Jaffé's generalization[6] would have required a 1.00 slope in eq 1. The slightly higher observed value, attributable to the hydrogen-bonding effect, represents a refinement of the earlier statements but not a significant or inexplicable difference.

Synthesis and Cyclization of S-(2-Propynyl)-L-cysteine S-Oxide and S-Dioxide

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1-Alkenylcysteine *S*-oxides and *S*-dioxides in the presence of base undergo an internal addition of the amino function to the double bond to yield cyclic sulfoxides and sulfones.[1] It was of interest to determine if acetylenic cysteine *S*-oxides and *S*-dioxides would react in a similar manner. McDowell and Stirling[2] have shown that in the addition of a secondary amine to 1-alkynyl-, 2-alkynyl-, or the corresponding allenyl-*p*-tolyl sulfone, the same addition product is formed in each case with the double bond appearing *α,β* to the sulfur. These investigators also obtained evidence from kinetic studies that 2-alkynyl sulfones first isomerize to allenes which then add amine in a rate-determining step.

S-(2-Propynyl)-L-cysteine *S*-dioxide (**1**) was prepared by oxidation of *S*-(2-propynyl)-L-cysteine with hydrogen peroxide in acetic acid at 50°. Oxidation with the same reagent under milder conditions yielded a mixture of diastereomeric sulfoxides which were separated by fractional crystallization into (+)-*S*-(2-propynyl)-L-cysteine *S*-oxide, $[\alpha]^{26}\text{D}$ +72.5° (water), and the (−) *S*-oxide, $[\alpha]^{25}\text{D}$ −110° (water). With the expectation of comparing the cyclization of 1-propynyl and 2-propynyl derivatives, the oxidation of *S*-1-propynyl-L-cysteine[3] was attempted. Neither sulfoxide nor sulfone could be obtained by reaction with hydrogen peroxide in acetic acid or with aqueous sodium metaperiodate. Cystine and starting material were the only recoverable products. We have no explanation for the failure of 1-propynylcysteine to form sulfoxides or sulfones under conditions where the 1-propenyl and the 2-propynylcysteines oxidize.[4]

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(1) J. F. Carson, L. E. Boggs, and R. E. Lundin, *J. Org. Chem.*, **33**, 3739 (1968); J. F. Carson, R. E. Lundin, and L. E. Boggs, *ibid.*, **34**, 1996 (1969).

(2) S. T. McDowell and C. J. M. Stirling, *J. Chem. Soc. B*, 351 (1967).

(3) J. F. Carson and L. E. Boggs, *J. Org. Chem.*, **30**, 895 (1965).

(4) Truce and Markley[5] have recently reported the preparation of aliphatic 1-propynyl sulfoxides and sulfones by oxidation of the corresponding sulfides with *m*-chloroperbenzoic acid in chloroform at 0° with no difficulty.

(5) W. E. Truce and L. D. Markley, *ibid.*, **35**, 3275 (1970).