The correlation is much improved by use of this equation, as shown in Table I and Figure 3. The standard deviation is only 0.06 pK unit.

Further study will be needed to determine whether the value of 2.46 instead of 2.82 for the "relative raw net hydration energy"[14] is uniquely characteristic of secondary hydrazines. It could be so because of water of hydration at the adjacent nitrogen.[1] Alternatively, the value 2.82, derived for secondary aliphatic amines, may need modification. It is based on a choice of amines with "minimum steric requirements".[2,15] Use of 2.46 instead of 2.82 would not seriously impair the correlation of the base strengths of secondary aliphatic amines described in paper II of this series,[2] because there are already some rather large deviations from that correlation. (See Figure 1, ref. 2).

(14) This term, defined in the preceding paper of this series, is the net hydration energy relative to an arbitrary zero for tertiary amines and without refinement by a term in σ^*.

Acknowledgments. The author is indebted to the National Science Foundation as explained before[1] and to Dr. R. W. Taft, Jr., for advice in the choice of a σ^* constant for the amino groups.

(15) H. K. Hall, Jr., *J. Am. Chem. Soc.*, 79, 5441 (1957).

The Influence of Hydration on Base Strength. IV. Hindered Bases

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It is suggested that steric hindrance to hydration may be responsible for alterations in base strength as follows: 2,6-di-t-butylpyridine, −2.20 pK units; 2,4,6-tri-t-butylaniline, −4.11 pK units; 2,4,6-tri-t-butyl-N-methylaniline, −4.60 pK units; 2-methyl-4,6-di-t-butyl-N,N-dimethylaniline, −6.42 pK units; 2,4,6-tri-t-butylphenylhydrazine, −2.92 pK units; and 2,4,6-tri-t-butylphenoxide ion, +4 to 9 pK units. Except in the case of the N,N-dimethylaniline, these alterations are less than might be expected for 100% effectiveness of steric hindrance to hydration on the basis of previous estimates of the influences of hydration on base strength. The value for the N,N-dimethylaniline, however, is close to 100% of a previous estimate and therefore tends to confirm the previous estimates.

Previous work[1] has provided estimates of the effects of hydration on the equilibrium in aqueous solution (eq. 1).

$$R_1R_2R_3NH^+ + H_2O \rightleftharpoons R_1R_2R_3N + H_3O^+ \qquad (1)$$

These estimates are expressed as "net hydration energies" (defined as the difference between the hydration energies of amine and ammonium ion) and are expressed in pK units. The net effect of hydration is generally unfavorable to the dissociation shown and therefore is base strengthening, since the hydration energy of the ion is larger than that of the amine.

The study of bases in which there may be steric hindrance to hydration at the functional group can provide an indication of the magnitude of hydration effects. If the hindrance were completely effective, the resulting decrease in base strength would be a true measure of the effect of hydration on the strength of a comparable unhindered base, provided, of course, that some other phenomenon (such as steric strain[2]) were not responsible for the decrease in base strength.

Wepster and co-workers[3] have studied a large number of aniline derivatives with bulky substituents in *ortho* positions and have reported values of δpK_a, an apparent decrease in base strength attributable to steric hindrance to hydration. Bartlett[4] has suggested that steric hindrance to hydration may be responsible for the greatly reduced acidity of phenols with bulky *ortho* substituents.[5] It is of interest, therefore, to compare the apparent magnitudes of these effects with the estimates of hydration effects obtained in previous work.

Six representative bases have been chosen for consideration. These are shown in Table I and are 2,6-di-*t*-butylpyridine,[2] 2,4,6-tri-*t*-butylaniline,[3,4] 2,4,6-tri-*t*-butyl-N-methylaniline,[3] 2-methyl-4,6-di-*t*-butyl-N,N-dimethylaniline,[3] 2,4,6-tri-*t*-butylphenylhydrazine,[6] and 2,4,6-tri-*t*-butylphenoxide ion.[5]

For each of these, an estimate of the inductive effects of the substituents on the ring was made. In three cases, an estimate of the effect of steric inhibition of resonance was made. The results are presented in the table, and the methods of estimation are described below.

For 2,6-di-*t*-butylpyridine, the inductive effect of the two *t*-butyl groups was estimated from the following considerations. In aqueous solution, the effect of a 4-*t*-butyl is about the same as the effect of a 4-methyl substituent on the pK_a of pyridine, and the effect of

(1) (a) F. E. Condon *J. Am. Chem. Soc.*, 87, 4481 (1965); (b) *ibid.*, 87, 4485 (1965); (c) *ibid.*, 87, 4491 (1965).

(2) H. C. Brown and B. Kanner, *ibid.*, 75, 3865 (1953).

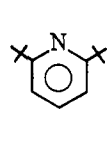
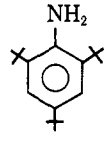
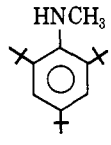
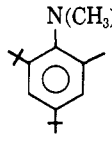
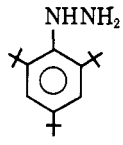
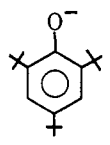
(3) (a) B. M. Wepster, *Rec. trav. chim.*, 76, 357 (1957); (b) J. Burgers, M. A. Hoefnagel, P. E. Verkade, H. Visser, and B. M. Wepster, *ibid.*, 77, 491 (1958).

(4) P. D. Bartlett, M. Roha, and R. M. Stiles, *J. Am. Chem. Soc.*, 76, 2349 (1954).

(5) H. Stillson, D. W. Sawyer, and C. K. Hunt, *ibid.*, 67, 303 (1945); 68, 722 (1946).

(6) F. E. Condon and G. L. Mayers, *J. Org. Chem.*, in press.

Table I. Effects of Steric Hindrance to Solvation on the pK_a Values of Some Sterically Hindered Bases at 25°

						
Solvent	50% EtOH	50% EtOH	50% EtOH	50% EtOH	50% EtOH	H_2O
pK_a of parent base	4.38[a]	4.26[b]	4.29[b]	4.39[b]	5.09[c]	9.85[d]
Inductive effects[e]	+1.40	+2.05	+2.05	+1.95	+0.71	+1.25
Steric inhibition of resonance			+1.83[b]	+2.85[b]	+0.78[e]	
pK_a calcd. with hydration	5.78	6.31	8.17	9.19	6.58	11.10
pK_a obsd.	3.58[a]	2.20[b]	3.57[b]	2.77[b]	3.66[c]	15–20[f]
δpK_a obsd.	−2.20	−4.11	−4.60	−6.42	−2.92	+4–9
Minimum δpK_a calcd.[e]	−5.22	−8.32	−6.59	−5.27	−9.55	+6.6
Maximum effectiveness, %	42	49	70	122	31	...

[a] Reference 2. [b] Reference 3. [c] Reference 6 (30°). [d] H. H. Jaffé, *Chem. Rev.*, **53**, 191 (1953). [e] See text. [f] Estimate based on the fact the phenol is insoluble in aqueous alkali of any strength but forms a salt with sodium amide in liquid ammonia (ref. 5).

a 2-methyl is about the same as that of a 4-methyl.[7] In 50% ethanol, in which the pK_a of 2,6-di-*t*-butylpyridine was measured, all the substituent effects are smaller,[2] and it was assumed that the effect of a 2-*t*-butyl would be (in the absence of steric effects) the same as that of a 2-methyl[8] (0.70 pK unit, average[2]). Brown and Kanner[2] estimated the effect of the two *t*-butyl groups in 2,6-di-*t*-butylpyridine as twice the effect of the one in 2-*t*-butylpyridine (0.30 pK unit). As their estimate reflected steric effects of the one *t*-butyl, it was rejected for present purposes.

For the other five compounds in Table I, the inductive effects of the ring substituents were estimated by use of the Hammett $\sigma\rho$ relationship.[9,10] The σ_{para} for *t*-butyl (−0.197) and for methyl (−0.170) were used and were assumed to apply for an *ortho* substituent in the absence of steric effects.[11]

The following ρ values were used. For 2,4,6-tri-*t*-butylaniline in 50% ethanol, ρ = 3.463, by linear interpolation between values given by Jaffé[10] for 30% ethanol (3.435) and 100% ethanol (3.535). This value was used also for 2,4,6-tri-*t*-butyl-N-methylaniline and for 2-methyl-4,6-di-*t*-butyl-N,N-dimethylaniline. For 2,4,6-tri-*t*-butylphenylhydrazine in 50% ethanol, the ρ = 1.21 for arylhydrazines in water was used.[12] For 2,4,6-tri-*t*-butylphenoxide ion in water, ρ = 2.113.[10] A 10% error in any one of these values would make a difference no larger than 0.20 pK unit.

The estimates of the effects of steric inhibition of resonance on the pK_a values of 2,4,6-tri-*t*-butyl-N-methylaniline and 2-methyl-4,6-*di*-*t*-butyl-N,N-dimethylaniline were taken from the work of Wepster.[3] They are based in part on spectroscopic evidence[13] that the inhibition is about 61% effective in the N-methylaniline and 95% effective in the N,N-dimethylaniline, and in part on an estimate of −3.00 pK units for the entire resonance effect of a phenyl group in the anilines.[14] It should be noted there appears to be no steric inhibition of resonance in anilines with bulky *ortho* substituents but without substituents on nitrogen.[3]

A 61% effectiveness of steric inhibition of resonance was adopted for 2,4,6-tri-*t*-butylphenylhydrazine, which is isoelectronic with 2,4,6-tri-*t*-butyl-N-methylaniline; but the entire resonance effect of the phenyl group in phenylhydrazine was estimated as −1.27 pK units, as follows.

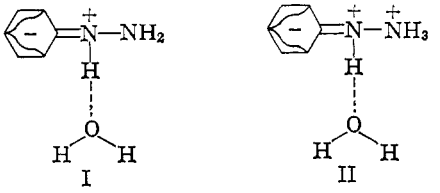
The change in pK_a on going from NH_2NH_2 (pK_a = 8.09)[15] to $C_6H_5NHNH_2$ (pK_a = 5.27)[12] at 25°, after suitable statistical corrections,[16] is −2.52 pK units; and this is due to inductive and resonance effects.[16a] The inductive effect may be like that observed on going from CH_3NH_2 (pK_a = 10.62)[17] to $C_6H_5CH_2NH_2$ (pK_a = 9.37),[18] which is −1.25 pK units. If so, the resonance effect of the phenyl group is −2.52 − (−1.25) = −1.27 pK units. Assuming steric inhibition of resonance to be 61% effective, as in 2,4,6-tri-*t*-butyl-N-methylaniline,[3] leads to the value, 0.78 pK unit, for the effect in 2,4,6-tri-*t*-butylphenylhydrazine.

Each estimated inductive effect and effect of steric inhibition of resonance was combined with the pK_a of the corresponding parent base (that is, the base without any ring substituents) to give what may be regarded as the pK_a expected if there were no other effect of the ring substituents. The differences between

(7) (a) H. C. Brown and R. Mihm, *J. Am. Chem. Soc.*, 77, 1723 (1955); (b) A. Gero and J. J. Markham, *J. Org. Chem.*, **16**, 1835 (1951).
(8) *Cf.* Wepster, *et al.*, ref. 3.
(9) (a) L. P. Hammett, *Chem. Rev.*, 17, 125 (1935); (b) "Physical Organic Chemistry," McGraw-Hill Book Co., Inc., New York, N. Y., 1940, p. 184.
(10) See Table I, footnote *d*.
(11) See R. W. Taft, Jr., in "Steric Effects in Organic Chemistry," M. S. Newman, Ed., John Wiley and Sons, Inc., New York, N. Y., 1956, p. 593; see also ref. 3.
(12) H. Stroh and G. Westphal, *Ber.*, **96**, 184 (1963).
(13) See also W. R. Remington, *J. Am. Chem. Soc.*, **67**, 1838 (1945).
(14) B. M. Wepster, *Rec. trav. chim.*, 71, 1171 (1952).
(15) (a) G. Schwartzenbach, *Helv. chim. Acta*, **19**, 178 (1936); (b) R. L. Hinman, *J. Org. Chem.*, **23**, 1587 (1958). The value shown is an average of values at 20 and 30°.
(16) S. W. Benson, *J. Am. Chem. Soc.*, **80**, 5151 (1958); R. P. Bell, "Acids and Bases," John Wiley and Sons, Inc., New York, N. Y., 1952, p. 61.
(16a) NOTE ADDED IN PROOF. This statement is incorrect, for there will be also changes in the hydration effects, as follows: (i) the change from a hydrazine for which m = 2 to one for which m = 1, −0.43 pK unit from eq. 5 of ref. 1c; (ii) the presence in $C_6H_5NHNH_2$ of the aniline-like hydration effects pictured in Figure 3 of ref. 1b, +A(unknown) −1.66(av.) pK unit; and (iii) the absence in $C_6H_5NHNH_2$ of the dehydration phenomenon pictured in Figure 1 of ref. 1c, +1.46 pK unit. For A = 0.75 pK unit (a value used elsehwere in this paper), the hydration effects almost wholly cancel one another; and the resulting resonance effect is not significantly different from the one computed in the text above.
(17) D. H. Everett and W. F. K. Wynne-Jones, *Proc. Roy. Soc.* (London), **A177**, 499 (1941).
(18) W. H. Carothers, C. F. Bickford, and C. J. Hurwitz, *J. Am. Chem. Soc.*, **49**, 2908 (1927).

this "pK_a calculated with hydration" and the pK_a observed (labeled "δpK_a observed") must be explained by some other effect of the ring substituents, presumably steric hindrance to hydration. They should be compared with the figures in the next to last line of the table ("minimum δpK_a calculated") which are based on previous papers of this series.

The "δpK_a calculated" for 2,6-di-*t*-butylpyridine is the value for tertiary aliphatic amines (actually trimethylamine) from eq. 9 of paper II of this series.[1b] The values for the next three compounds are based on eq. 16 of that paper. The value for the phenylhydrazine is the value for primary aliphatic amines (actually methylamine) based on eq. 9 (*loc. cit.*) The effect of resonance on the hydration at the secondary nitrogen is difficult to estimate; but the contribution to the total hydration energy from this source may be the same in a phenylhydrazine (I) and phenylhydrazinium ion



I II

(II). If so, the effect of steric hindrance to hydration would receive no contribution from this source.

The phenoxide ion was, for simplicity, treated as an N-methylaniline. A phenol, having one hydrogen on oxygen and (because of resonance III) one residual

III IV

pair of electrons, may be hydrated most similarly to an N-monosubstituted aniline,[1b] while a phenoxide ion (IV), which because of resonance has two residual electron pairs on oxygen, may be hydrated most similarly to an N-monosubstituted anilinium ion, which has two hydrogens attached to nitrogen. It is supposed that each electron pair on the oxygen atom of the phenol or phenoxide ion plays the same role in hydrogen bonding with solvent water as a hydrogen attached to nitrogen in the aniline or anilinium ion. The effects on pK_a are opposite in direction, however, because the electrical charge is found in the base, rather than in the conjugate acid.

The "δpK_a calculated" is a minimum value in most cases for two reasons: (i) each is based on a mathematical extrapolation, and alternative extrapolation formulas give values as much as 1.67 pK units larger[1b]; and (ii) the net hydration energies for anilines do not include a contribution from resonance-diminished hydration of the free base, designated by A and described in paper II of this series.[1b] Indeed, use of the value -3.00 pK units above for the resonance effect of the phenyl group on the pK_a of aniline implies a value of about 0.75 pK unit for the quantity A. If this amount is added to the net hydration energies for anilines, the δpK_a calculated is still too low by 0.4 pK unit to account for the δpK_a observed in the case of 2-methyl-4,6-di-*t*-butyl-N,N-dimethylaniline. This may be the fault of the mathematical extrapolation chosen. The correspondence, however, is such as to confirm the order of magnitude of the extrapolated result.

Steric hindrance to hydration appears to operate with different degrees of effectiveness among the compounds considered, as shown by the percentage figures in the last line of the table. These are maximum values, for the reasons just discussed. Among the anilines, the effectiveness increases with increasing substitution on the nitrogen, which is reasonable. It is smaller in the case of the phenylhydrazine because the hydration center is one atom removed from the bulky substituents.

That steric hindrance to hydration by two *o*-*t*-butyl groups is not 100% effective in pyridine finds a parallel in the fact that 1,3,5-tri-*t*-butylbenzene is nitrated more rapidly than benzene, even though each available position is flanked by two *t*-butyl groups.[6] In fact, it can be shown, as follows, that the steric effect of the two *o*-*t*-butyl groups in the nitration is about the same as the steric effect of the two *t*-butyl groups on the pK_a of 2,6-di-*t*-butylpyridine.

t-Butylbenzene is nitrated 15.7 times as rapidly as benzene; and the product is 12.0% *o*-, 8.5% *m*-, and 79.5% *p*-nitro-*t*-butylbenzene.[19] The partial rate factors (rates relative to that for any one position in benzene) are therefore: *ortho*, 5.6; *meta*, 4.0; and *para*, 75. If it be assumed that the *ortho* and *para* partial rate factors would be identical if it were not for steric hindrance, the steric effect of one *o*-*t*-butyl is such as to reduce the rate by a factor of $^{5.6}/_{75}$; and the effect of two *t*-butyl groups[20] would be $(^{5.6}/_{75})^2$, which is $^{1}/_{134}$. Now log ($^{1}/_{134}$) = -2.13, which may be compared with the -2.20 pK units for the observed effect of steric hindrance to hydration in 2,6-di-*t*-butylpyridine (Table I). Evidently, the steric requirements for the $HCNO_2^+$, in the transition state for the nitration, and those for the $NHOH_2^+$, in the hydrated pyridinium ion, are quite similar.

Acknowledgment. The author is indebted to the National Science Foundation as explained before.[1]

(19) H. Cohn, E. D. Hughes, M. H. Jones, and M. G. Peeling, *Nature*, 169, 291 (1952).
(20) F. E. Condon, *J. Am. Chem. Soc.*, 70, 1963 (1948).