

The Influence of Hydration on Base Strength.

III. Alkylhydrazines

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It is shown that the apparently anomalous base strengths of methyl- and ethylhydrazines can be correlated by means of Taft's substituent constants (σ^*) if it is postulated that hydration by hydrogen bonding at both nitrogens is important in determining base strength. The correlation provides evidence that protonation of an unsymmetrical hydrazine takes place at the nitrogen bearing the greater number of alkyl groups, because the alternative assumption does not allow a correlation.

In paper I of this series,¹ the effects of hydration of amine and ammonium ion on the equilibrium (eq. 1) were



considered. A general equation was presented for relating the net hydration energy (defined as the difference between the hydration energies of ammonium ion and amine) to the nature and number of the substituents, R_i . In paper II,² net hydration energies of aliphatic amines and N-substituted anilines were estimated with the aid of available pK_a data.³

The base strengths of alkylhydrazines have been considered anomalous because they are all weaker bases than hydrazine itself, which is just the opposite of what would be expected from the inductive effect of alkyl groups.⁴ Tetramethylhydrazine ($pK_a = 6.30$), for example, is the weakest of all and is almost 2 pK units weaker than hydrazine ($pK_a = 8.07$).^{3,4}

In this paper, it is shown that the base strengths of the alkylhydrazines can be correlated with the substituent constants, σ^* , devised by Taft,⁵ if it be postulated that hydration by hydrogen bonding at both nitrogens is important in determining base strength. In accordance with this postulate, replacement of hydrogen on either nitrogen by an alkyl group would have a base-weakening effect, which would cancel to some extent the base-strengthening inductive effect.

In applying the postulate, the question arises as to which of the nitrogens is protonated in the case of an unsymmetrical hydrazine (the one bearing the greater number of alkyl groups or the one bearing the greater number of hydrogens?). Fortunately, no *a priori* answer to this question must be given, for reasons that will become apparent in what follows. It is found, however, that a much better correlation is achieved by assuming that protonation of an unsymmetrical hydrazine occurs at the nitrogen bearing the greater number of alkyl groups, rather than the alternative.

(1) F. E. Condon, *J. Am. Chem. Soc.*, **87**, 4481 (1965).

(2) F. E. Condon, *ibid.*, **87**, 4485 (1965).

(3) pK_a is the negative logarithm of the equilibrium constant of reaction 1.

(4) R. L. Hinman, *J. Org. Chem.*, **23**, 1587 (1958).

(5) R. W. Taft in "Steric Effects in Organic Chemistry," M. S. Newman, Ed., John Wiley and Sons, Inc., New York, N. Y., 1956, p. 556 ff.

The correlation to be presented remains inconclusive with regard to the magnitude of a conceivable "dehydration" effect pictured in Figure 1. Any hydrazine base may be hydrated at both nitrogens by the type of interaction in which the nitrogen acts as hydrogen acceptor (electron pair donor) and the water is hydrogen donor. When one nitrogen is protonated, however, as in the hydrazinium ion, the other nitrogen must be a much poorer hydrogen acceptor, because of the positive charge on the ion. The requirement that dehydration accompany protonation would have a base-weakening effect on all the aliphatic hydrazines.⁶

The magnitude of the dehydration effect pictured in Figure 1 cannot be given with certainty; and it is treated here as a disposable parameter. The base strengths of the alkylhydrazines can be correlated about as well by assuming it is negligible as by assuming it is large. What makes this possible is an uncertainty in the σ^* values for the amino and alkylamino groups. Here, however, a σ^* value of 0.62 is adopted for all amino and alkylamino groups.⁷ This choice leads, as will be shown, to an estimate of -1.46 pK units for the effect of the dehydration phenomenon pictured in Figure 1.

With the aid of these parameters, the following equation was developed for alkylhydrazines at 30°.

$$pK_a = 9.50 + (10.92 - 0.778n) \log n - 1.46 + \\ (0.16 + 0.77m) \log (m + 1) + \\ 0.08m \sum_{j=1}^2 \sigma_j^* - (3.38 - 0.08n - \\ 0.016m) \sum_{i=1}^3 \sigma_i^* - \log (n/s) \quad (2)$$

The correlation by this equation is shown in Figure 2 and Table I.

(6) In arylhydrazines, the picture is complicated by resonance.

(7) The value is based on reported σ_1 constants and the relationships (i) $(\sigma_1)_X = 0.45\sigma^*_{XCH_3}$ and (ii) $\sigma^*_X = 2.8\sigma^*_{XCH_3}$ (see ref. 5, and 8a and b). The σ_1 for NH_2 is variously reported as 0.10^{8c,d} and 0.01,^{8e} while the σ_1 for NMe_2 is reported as 0.10 in two places.^{8e,f} A $(\sigma_1)_X$ of 0.10 leads to a σ^*_X of 0.62 by means of the relationships i and ii above. For H and alkyl groups, however,^{8b} (iii) $\sigma^*_X = 4.9\sigma^*_{XCH_3}$ and use of this in place of ii above leads to a σ^*_X of 1.09, which could account for all of the difference in the base strengths of trimethylamine and tetramethylhydrazine, without need for the dehydration effect pictured in Figure 1. A σ^* value of 0.62 was used here for all the amino and alkylamino groups, even though it seems to this author that some small variation would be expected among them, analogous to the variation among the σ^* constants of the alkyl groups, which are isoelectronic with the amino and alkylamino groups. For a contrary opinion, however, see ref. 8b.

(8) (a) C. D. Ritchie and W. F. Sager in "Progress in Physical Organic Chemistry," Vol. II, S. G. Cohen, A. Streitwieser, Jr., and R. W. Taft, Ed., Interscience Publishers, Inc., New York, N. Y., 1964; (b) C. D. Ritchie, *J. Phys. Chem.*, **65**, 2091 (1961); (c) R. W. Taft, Jr., *ibid.*, **64**, 1805 (1960); (d) R. W. Taft, Jr., *J. Am. Chem. Soc.*, **79**, 1045 (1957); (e) R. W. Taft, Jr., E. Price, I. R. Fox, I. C. Lewis, K. K. Anderson, and G. T. Davis, *ibid.*, **85**, 709 (1963); (f) R. W. Taft, Jr., and H. D. Evans, *J. Chem. Phys.*, **27**, 1427 (1957).

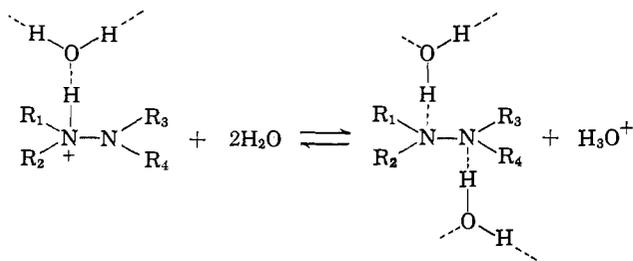


Figure 1. Dehydration accompanying protonation of a hydrazine.

Equation 2 was developed from eq. 2 of the preceding paper of this series^{2,9}; and most of the terms have the same meaning as before: pK_a is the negative logarithm of the dissociation constant in water of the hydrazinium ion as shown in Figure 1; n is the number of hydrogens attached to the protonated nitrogen in the hydrazinium

Table I. Correlation Parameters for the Alkylhydrazines^a

Base	pK_a		n	m	s	$\Sigma\sigma_i^*$	$\Sigma\sigma_j^*$
	Exptl. ^b	Eq. 2 (5)					
NH ₂ NH ₂	8.07	7.96 (8.10)	3	2	2	1.60	0.98
MeNHNH ₂	7.87	7.99 (7.77)	2	2	1	1.11	0.98
Me ₂ NNH ₂	7.21	6.98 (7.12)	1	2	1	0.62	0.98
MeNHNHMe	7.52	7.62 (7.50)	2	1	2	1.11	0.49
Me ₂ NNHMe	6.56	6.32 (6.56)	1	1	1	0.62	0.49
Me ₂ NNMe ₂	6.30	6.30 (6.30)	1	0	2	0.62	0
EtNHNH ₂	7.99	8.30 (8.08)	2	2	1	1.01	0.98
Et ₂ NNH ₂	7.71	7.63 (7.77)	1	2	1	0.42	0.98
EtNHNHEt	7.78	7.93 (7.81)	2	1	2	1.01	0.39
Et ₂ NNHEt	...	6.97 (7.21)	1	1	1	0.42	0.39
Et ₂ NNEt ₂	...	6.95 (6.95)	1	0	2	0.42	-0.20

^a Based on protonation of an unsymmetrical hydrazine at the nitrogen bearing the greater number of alkyl groups. ^b Reference 4.

ion; m is the number of hydrogens attached to the adjacent nitrogen, only singly protonated hydrazinium ions being considered; $\Sigma\sigma_i^*$ is a sum of substituent constants,⁵ one for each of the groups (or hydrogen atoms) attached to the proton-accepting nitrogen in the hydrazine; $\Sigma\sigma_j^*$ is the same for the adjacent nitrogen, but excluding a constant for the amino group, which becomes an ammonio group in the hydrazinium ion; and s is a statistical factor, which is two for a symmetrical hydrazine and unity for all others.¹⁰

In developing eq. 2 from eq. 2 of ref. 2, account had to be taken first of the fact that the base strengths of the alkylhydrazines were determined at 30°, whereas the previous equation was for amines at 25°. An estimate had to be made of the effect of raising the temperature 5°. Heats of dissociation in water of NH₄⁺ and its methyl derivatives at 298°K. are about 9–13 kcal./mole.¹¹ These values were assumed to be typical; and by means of the thermodynamic relationship, $dpK_a/dT = -\Delta H^\circ_T/2.3RT^2$, the temperature coefficient was estimated to be -0.02 to -0.03 pK unit per degree. Accordingly, the leading term in eq. 2 of ref. 2 was reduced from 9.61 to 9.50. Small changes would

(9) Equations 3, 6, or 7 of ref. 2 might have been used as a starting point also; but the choice of eq. 2 avoids a decision as to which, if any of the extrapolations contained in the other three is correct.

(10) S. W. Benson, *J. Am. Chem. Soc.*, **80**, 5151 (1958).

(11) (a) D. H. Everett and W. F. K. Wynne-Jones, *Trans. Faraday Soc.*, **35**, 1380 (1939); (b) *Proc. Roy. Soc. (London)*, **A177**, 490 (1941).

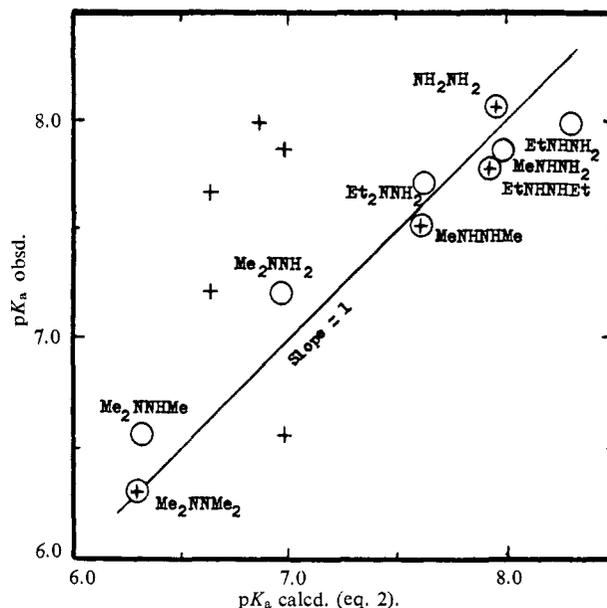


Figure 2. Correlation of base strengths of alkylhydrazines: O, based on protonation of an unsymmetrical hydrazine at the nitrogen bearing the greater number of alkyl groups; +, based on protonation at the nitrogen bearing the greater number of hydrogens.

be expected also in the other constants of the equation, but no effort was made to evaluate these changes. For aliphatic amines at 30°, therefore

$$pK_a = 9.50 + (10.92 - 0.778n) \log n - (3.38 - 0.08n) \sum_{i=1}^3 \sigma_i^* - \log(n/s) \quad (3)$$

An expression of the form of eq. 4 was then added to

$$(F + Gm) \log(m + 1) + 0.08m \sum_{j=1}^2 \sigma_j^* + 0.016m \sum_{i=1}^3 \sigma_i^* \quad (4)$$

eq. 3. This expression is designed to represent the supplementary net hydration energy of a hydrazine arising out of hydration at a second nitrogen directly attached to the proton-accepting one. The constants F and G were evaluated as described below. A term in "log $(m + 1)$ " was selected because it vanishes when $m = 0$ and because its logarithmic form is consistent with the definitions of pK and σ^* and with other terms already in the equation.¹² The term in $\Sigma\sigma_j^*$ measures changes in the net hydration energy resulting from modification of the substituents attached to this second nitrogen. Its numerical coefficient, 0.08, is the same as that before an analogous term relating to the other nitrogen. The term in $\Sigma\sigma_i^*$ measures effects of modification of the substituents attached to the other nitrogen. Its numerical coefficient, 0.016, resulted from application to 0.08 of a loss factor, $1/4.9$, which appears to hold for the transmission of the inductive effects of alkyl groups and hydrogen through an intermediate atom.^{8b}

Equation 2 is a combination of eq. 3, the expression 4 with the constants F and G evaluated, and a term,

(12) The polynomial, $0.155m + 0.125m^2$, would serve as well as the log $(m + 1)$ term in eq. 2.

-1.46, for the dehydration effect of Figure 1. The latter term results from consideration of the pK_a of tetramethylhydrazine and use of a σ^* constant of 0.62 for the dimethylamino group.

Tetramethylhydrazine can be regarded as trimethylamine in which one methyl is replaced by a dimethylamino group; and the whole of the apparent reduction in base strength might be attributed to an electron-withdrawing inductive effect of the dimethylamino group. The apparent reduction is 3.50 pK units; for if the pK_a of tetramethylhydrazine were calculated by eq. 3 (or by eq. 2 without the term -1.46) on the assumption the dimethylamino group is equivalent to a methyl group ($\sigma^* = 0$), the result would be 9.80 (0.30 unit higher than that for trimethylamine because of the statistical correction) and the pK_a is given as 6.30. For such a reduction in base strength, the σ^* constant for the dimethylamino group would have to be 1.06. A σ^* constant^{7,8} of only 0.62 can account for only about 59% of the apparent reduction in base strength, or 2.04 pK units. Some other effect must be involved. This may be the dehydration effect pictured in Figure 1. A value of -1.46 pK units is assigned to it on this basis, and the same value is used with all the hydrazines considered here.¹³

In preliminary work, the constants F and G in the expression 4 were evaluated by use of the pK_a data for the two symmetrical hydrazines NH_2NH_2 and $MeNHNHMe$. The results were therefore independent of which nitrogen accepts the proton when an unsymmetrical hydrazine acts as a base. A resulting form of eq. 2 was then used to calculate pK_a values for the remaining six alkyhydrazines (one symmetrical and five unsymmetrical) for which data are available, firstly assuming protonation of an unsymmetrical hydrazine at the nitrogen bearing the greater number of alkyl groups, and secondly assuming protonation at the nitrogen bearing the greater number of hydrogens. Only the first assumption gave an acceptable correlation, as seen also in Figures 2 and 3.

For the present correlation, however, the constants F and G were chosen so as to minimize the sum of the squares of the differences between observed and calculated pK_a values. To do this, the compounds were divided into groups according to whether $m = 1$ or $m = 2$; and an average value of the term, $(F + Gm) \log(m + 1)$, was computed for each group by finding the differences between each observed pK_a and the pK_a calculated by eq. 2 without the term, $(F + Gm) \log(m + 1)$. From the two numbers thus obtained, the constants F and G could be evaluated by solution of simultaneous equations.¹² The results are shown in eq. 2.

The pK_a values calculated by eq. 2 are compared with observed values in Table I and Figure 2. The circled points in the figure are based on protonation at the

(13) The experimental pK_a for tetramethylhydrazine shown in Table I was determined not by Hinman but by J. B. Class, J. G. Aston, and T. S. Oakwood, *J. Am. Chem. Soc.*, 75, 2937 (1953), at an unspecified temperature, perhaps 20°. The latter authors reported for trimethylhydrazine a pK_a of 6.78 at an unspecified temperature, while Hinman reported 6.56 at 30°. The pK_a of tetramethylhydrazine at 30° may be 6.08, therefore, rather than 6.30. If so, a value of -1.68 pK units would be assigned to the dehydration effect. The constants F and G in expression 4 would be 1.15 and 0.50, respectively, instead of 0.16 and 0.77 as shown in eq. 2. Then the calculated pK_a values would be the same as shown for eq. 2 in Table I, excepting tetramethylhydrazine (6.08) and tetraethylhydrazine (6.73).

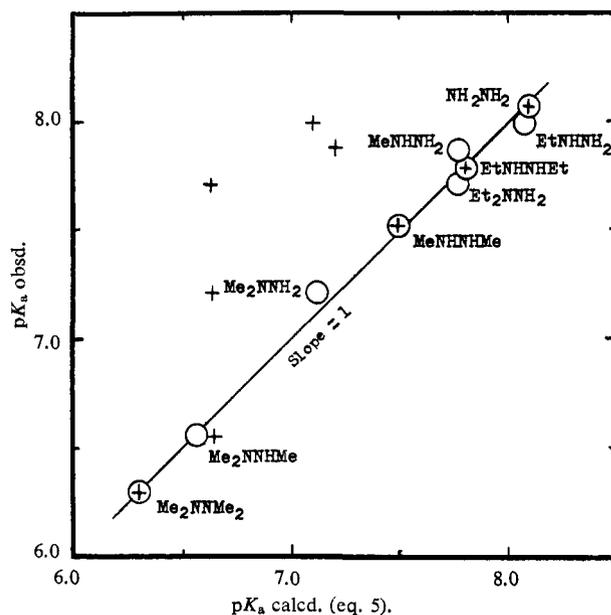


Figure 3. Correlation of base strengths of alkyhydrazines (for legend, see Figure 2).

nitrogen bearing the greater number of alkyl groups, while the crosses are based on the alternative assumption. The line of unit slope represents perfect correlation. For the circled points, the root mean square (standard) deviation from the line is 0.174 pK unit. The figure provides strong evidence that protonation of an unsymmetrical hydrazine takes place at the nitrogen bearing the greater number of alkyl groups, rather than the alternative.

An Improved Correlation. Close examination of Figure 2 shows that the points for secondary hydrazines (those for which $n = 2$) are displaced as a group with respect to the points for primary and tertiary hydrazines (excepting the point for tetramethylhydrazine, which is required to fall on the line by the choice of constants for eq. 2). Such a displacement could be caused by an incorrect value for the effect of hydration at the protonated nitrogen in the case of secondary hydrazines. The value used is that established for secondary aliphatic amines in the preceding paper of this series. It is 2.82 pK units (relative to an arbitrary 0 for tertiary amines). The average displacement of the points for secondary hydrazines was found to be 0.36 pK unit. That is, it appears that for secondary hydrazines hydration at the protonated nitrogen is base-strengthening by 2.46 pK units (relative to an arbitrary 0 for tertiary hydrazines) instead of 2.82 pK units. Adoption of this value (and retention of the value 4.10 pK units for the single primary hydrazine, NH_2NH_2) leads to the following modification of eq. 2.

$$pK_a = 9.50 + (7.34 + 0.42n) \log n - 1.46 + (1.47 + 0.26m) \log(m + 1) - 0.08m \sum_{j=1}^2 \sigma_j^* - (3.38 - 0.08n - 0.016m) \sum_{i=1}^3 \sigma_i^* - \log(n/s) \quad (5)$$

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

(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^* .

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).

Acknowledgments. The author is indebted to the National Science Foundation as explained before¹ 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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Contribution from the Department of Chemistry, The City College of the City University of New York, New York, New York. Received March 27, 1965

*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 work¹ has provided estimates of the effects of hydration on the equilibrium in aqueous solution (eq. 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

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

some other phenomenon (such as steric strain²) were not responsible for the decrease in base strength.

Wepster and co-workers³ 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. Bartlett⁴ 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

(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.