19-Oxoandrost-5-ene-3β,17β-diol (IX).—A stirred suspension of 5.0 g. (0.0167 mole) of VIII and 2.5 g. of powdered lithium aluminum hydride in 750 ml. of anhydrous tetrahydrofuran was boiled under reflux for 120 hr., chilled in an ice bath, and the excess hydride was decomposed with ethyl acetate. After acidification with 20% hydrochloric acid, the mixture was refluxed for 3 hr. The solution was clarified, if necessary, by addition of acid and was evaporated under reduced pressure until heavy precipitation occurred. Water was added to effect further precipitation. The solid was filtered and washed with water, and, after recrystallization from aqueous ethanol, gave 2.95 g. (60%) of IX, m.p. 184–190°. The analytical sample recrystallized from acetone–hexane had m.p. 185–188°, $\mu_{\max}^{\mathrm{KBr}}$ 3.00 (strong), 3.73 (sh), 5.84 (strong), loss of –CN band at 4.5, $[\alpha]^{25}\mathrm{D}$ −247° (*c*, 1% in MeOH).

Anal. Calcd. for $C_{19}H_{28}O_3$: C, 74.96; H, 9.27. Found: C, 74.80; H, 9.13.

19-Oxoandrost-5-ene-3β,17β-diol Diacetate.—A solution of IX in pyridine and acetic anhydride was kept at 27° for 18 hr. and poured into ice–water. Filtration of the precipitate gave the crude product, which on recrystallization from aqueous ethanol, had m.p. 150–153°, $\mu_{\max}^{\mathrm{KBr}}$ 3.68 (sh), 5.80, 8.03, $[\alpha]^{25}\mathrm{D}$ −252° (*c*, 1% in $CHCl_3$), n.m.r.: 0.75 (C(18)-H), 2.00, 2.03 (acetate methyls), 258–293 c.p.s. (broad hump) (3αH, 17α–H), 345–363 c.p.s. (broad hump) (6–H), 9.75 (19–H).

Anal. Calcd. for $C_{23}H_{32}O_5$: C, 71.10; H, 8.30. Found: C, 71.02; H, 8.27.

Androst-5-ene-3β,17β,19-triol (X).—A solution of 0.4 g. (0.00145 mole) of IX and 0.4 g. of sodium borohydride in 50 ml. of methanol was kept at 27° for 1 hr. and acidified with 10% hydrochloric acid to pH 1. The clear solution was concentrated under reduced pressure, diluted with water, and filtered to give 0.35 g. (87%) of X, m.p. 229–230°. The analytical sample, recrystallized from acetonitrile, had m.p. 232–233°, $\mu_{\max}^{\mathrm{KBr}}$ 3.03, 9.50, 9.70, $[\alpha]^{25}\mathrm{D}$ −48° (*c*, 0.5% in MeOH).

Anal. Calcd. for $C_{19}H_{30}O_3$: C, 74.47; H, 9.87. Found: C, 74.62; H, 9.81.

The product could also be prepared by reduction of IX with lithium aluminum hydride in boiling tetrahydrofuran solution for 1 hr.

19-Hydroxyandrost-4-ene-3,17-dione (XI).—A mixture of 10 ml. of cyclohexanone and 15 ml. of toluene was heated to boiling and 4 ml. of distillate was collected and discarded. Then 0.35 g. (0.00145 mole) of X was quickly dissolved in the hot anhydrous solution and 1.0 g. of powdered redistilled aluminum isopropoxide was added. The mixture quickly was brought to reflux and maintained there for 10 min. The mixed solvent was removed *in vacuo* at 70–75°, and the residue was taken up in 200 ml. of chloroform which was washed with 1 *N* sulfuric acid (100 ml.) and water and dried over sodium sulfate. Evaporation of the chloroform left a syrupy residue containing some cyclohexanone. The residue was chromatographed on 10.0 g. of neutral alumina; the following eluents were used: (4 × 5 ml.) ether; (4 × 5 ml.) methanol–ether (1%); (4 × 5 ml.) methanol–ether (2%); (4 × 5 ml.) methanol–ether (4%); (4 × 5 ml.) methanol–ether (8%); (4 × 5 ml.) methanol–ether (16%); (4 × 5 ml.) methanol–ether (32%). From the 2% methanol–ether fractions, a trace of what was apparently 19-norandrostenedione was isolated in crystalline form, m.p. 160–167 (reported[15] m.p. 171–172°), $\lambda_{\max}^{\mathrm{EtOH}}$ 240 mμ, $\mu_{\max}^{\mathrm{KBr}}$ 5.75, 6.00, 6.18 (absence of —OH band). From the 8% methanol–ether fractions, 0.09 g. (26%) of colorless crystals of XI was isolated, which, after recrystallization from acetone–hexane had m.p. 168–170°, $\lambda_{\max}^{\mathrm{EtOH}}$ 243 mμ, log *E* 4.18, $[\alpha]^{25}\mathrm{D}$ +195° (*c*, 0.9% in chloroform), $\mu_{\max}^{\mathrm{KBr}}$ 2.95, 5.75, 6.04, 6.18, (reported[16] m.p. 168–170°, $\lambda_{\max}^{\mathrm{MeOH}}$ 242 mμ, log *E* 4.18, $[\alpha]^{30}\mathrm{D}$ +178 ± 4° (chloroform), $\mu_{\max}^{\text{solid film}}$ 2.94, 5.80, 6.06, 6.17).[17]

Anal. Calcd. for $C_{19}H_{26}O_3$: C, 75.46; H, 8.67. Found: C, 75.05; H, 8.65.

From the 16% MeOH–ether fractions there was obtained 0.01 g. of what is probably 19-hydroxytestosterone, m.p. 199–201°, (reported[5] 201–203°), $\lambda_{\max}^{\mathrm{EtOH}}$ 243 mμ, $\mu_{\max}^{\mathrm{KBr}}$ 3.05, 6.10, 6.19.

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Solvent Effects in the Menschutkin Reaction

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The rates of the reaction of pyridine with ethyl bromide and ethyl iodide have been determined in benzene, chlorobenzene, bromobenzene, and iodobenzene. The rate constant increase is proportional to the polarizability of the solvent, and is attributed to the interaction of the solvent with the leaving halide in the transition state.

The effect of the solvent upon the rate of the Menschutkin reaction had been shown to be important by many workers.[3–8] The reaction, in which ions are formed from electrically neutral reagents, proceeds more rapidly in solvents of high dielectric constant.

Attempts to correlate the solvent effect with physical properties of the solvent have been made by several authors. Eagle and Warner[8] correlated the reaction rate constant with the dielectric constant in the mixed solvent alcohol–water. Kosower[9] demonstrated that the rate constant for pure alcohol solvents correlate well with *Z*. A plot of log *k vs. Z* gave a linear relationship. Kerr[10] attempted to correlate the dipole moment with the reaction rate constant, but acknowledged that he had achieved only limited success. Grim, Ruf, and Wolf[11] showed that the rate constant varied with dielectric constant for solvents with a large range of *D* (dielectric constant), but could not demonstrate a quantitative relationship. A frequently used relationship between *D* and the rate constant is given in equation 1.[12]

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[2] Support of the URP program of the National Science Foundation is gratefully acknowledged.

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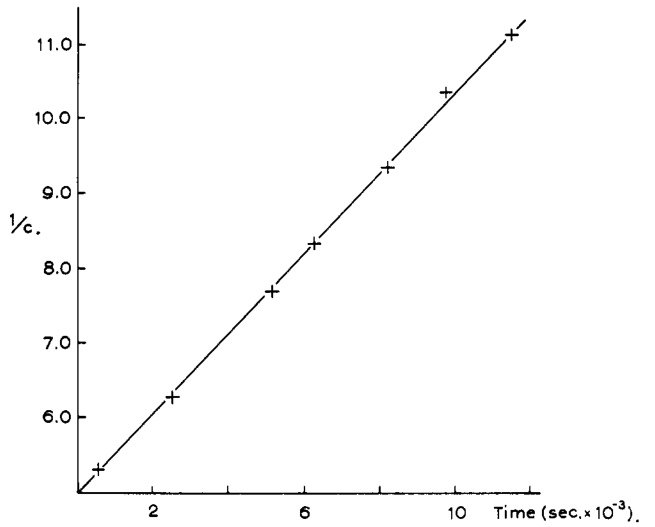

Fig. 1.—Ethyl iodide + pyridine in the solvent bromobenzene at 99.85°.

$$\ln k_2 = \ln k_0 - \frac{1}{kT}\left[\frac{(D-1)}{(2D+1)}\left\{\frac{\omega_A{}^2}{r_A{}^3} + \frac{\omega_B{}^2}{r_B{}^3} - \frac{\omega_*{}^2}{r_*{}^3}\right\}\right] + \sum \frac{\phi}{kT} \quad (1)$$

where k_2 is the rate constant in the solvent 2; k_0 is the rate constant at $D = 1$; ω_A, ω_B and ω_* are the dipole moments of the reagents A and B and the transition state; r_A, r_B, and r_* are the radii of the reagents and the transition state, respectively; ϕ is the contribution of nonelectrostatic forces.

Tommila[13] has showed that this relationship may be used to express the effect of the mixed solvents acetone–water, acetone–benzene, acetone–dioxane, and acetone–tetrahydrofuran on the reaction rate. He assumed that ϕ was negligible with respect to electrostatic forces, and plotted ln k *vs.* $(D - 1)/(2D + 1)$. The result was a series of straight lines of different slopes.

Two other workers have suggested that this equation does not have universal applicability. Wanatabe and Fuoss[14] have investigated the use of this equation for the reaction of butyl bromide with pyridine and 4-picoline in 5 solvents of relatively high D. The usual assumption that ϕ is negligible was showed to be untenable. These investigators suggested that the transition state probably is a solvated complex. An investigation by Caldin and Peacock[15] also showed that electrostatic forces alone cannot explain solvent effects. They demonstrated that "simple electrostatic theory fails to account for the solvent effects" by calculating the activation energy and the frequency factor from an equation similar to equation 1 and comparing their results with the observed data. Their literature survey of five reactions, one of which was the Menschutkin reaction, led to a classification into three categories, namely aliphatic, aromatic, and hydroxylic solvents. The rate constants for the reactions in aromatic solvents were higher than those in aliphatic solvents. They attributed this to the high polarizabilities of the aromatic solvents.

The present paper reports the results of an investigation to determine if the polarizability of the solvent has a significant influence on the reaction rate constant of the Menschutkin reaction.

Experimental

Ethyl iodide and ethyl bromide, Fisher reagent grade, were dried over Drierite, distilled over copper, and stored over copper metal. All distillations were performed in a 24-in. silvered, vacuum-jacketed column packed with glass helices. Pyridine, Fisher reagent, was dried over potassium hydroxide and distilled. The solvents were refluxed with pyridine, washed with sulfuric acid, then with water. They were dried over Drierite and then distilled through the 24-in. column. The purity of the solvents was confirmed by boiling point range, refractive index, and gas chromatography.

Procedure.—All burets and pipets were calibrated and the thermometers were compared with a thermometer which was calibrated at the National Bureau of Standards. A sealed ampoule technique was used for the kinetic experiments, with seven to nine samples analyzed in each run. The rates were followed by a determination of the ion concentration by means of a potentiometric titration. The rate constants were reckoned from the slope of a plot of $1/(\mathrm{Cl}^-)$ *vs.* time, for the concentrations of the reagents were made equal. In all the experiments, the initial concentrations were 0.200 M. The rate constants were corrected for solvent expansion. The products crystallized from the cold reaction mixture and were isolated by filtration. The ethylpyridinium iodide that was isolated had m.p. 85–86°; lit.[16] m.p. 90.5°.

Discussion and Results

Pyridine was treated with ethyl iodide and ethyl bromide in benzene, chlorobenzene, bromobenzene, and iodobenzene. These solvents were chosen, for they give a large variation in polarizability of the substituent group and a small change in D. The rate constants were determined at 80 and 100° with equal molar concentrations for the amine and alkyl halide. The reactions were run with initial concentrations of 0.20 M. Good straight lines were obtained for the plot of $1/C$ *vs.* time, and the duplicate rate constants were reproducible to ±2%. A typical plot is given in Fig. 1 and the rate data and thermodynamic properties are presented in Table II. Comparison of our data with those of Winkler and Hinshelwood[17] showed that the rate constant does not vary greatly with initial concentration. They reported 7.25 and 25.0 $\times 10^{-4}$ l./mole sec. for the reaction of ethyl bromide and pyridine at 80 and 100°. Our values were 7.44 and 28.4 $\times 10^{-4}$ l./mole sec. for the same reactions at twice the initial concentrations. Norris and Prentiss[4] have reported initial rate constants for the reaction of ethyl iodide and pyridine in acetone, nitrobenzene, methyl alcohol, ethyl alcohol, and other aliphatic alcohols. Their initial concentrations varied from 0.37 to 0.69 for acetone, 0.23 to 1.00 for nitrobenzene, and 0.4 to 0.68 for benzene. The largest variations in initial rate constant with initial concentration occurred with benzene, where k increased from 25 to 28, or about 10%. There was a similar increase with acetone and nitrobenzene, but the per cent increase was smaller. They also observed a slight drift in their rate constants with time. Our plots of $1/C$ *vs.* time showed no evidence of curvature, nor was this mentioned by Winkler and Hinshelwood.

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TABLE I

RATE CONSTANTS FOR THE MENSCHUTKIN REACTION IN VARIOUS SOLVENTS

Ethyl iodide + triethylamine[a] at 100°

Solvent	R,[b] cc./mole	Z[d]	D[c]	k, l./mole sec.
Benzene	1.10	..	2.27	4.0×10^{-4}
Chlorobenzene	6.03	..	5.62	13.8
Bromobenzene	8.80	..	5.40	16.0
Iodobenzene	13.94	..	4.62	26.5
Nitrobenzene	...	..	34.8	138
Ethyl iodide + pyridine[e] at 25°				
Benzene	...	..	2.27	7.9×10^{-7}
n-Propyl alcohol	...	78.3	20.1	8.6
Ethanol	...	79.6	24.3	10.8
Methanol	...	83.6	32.6	19.4
Acetone	...	65.7	20.7	100
Nitrobenzene	...	..	34.8	197

[a] Data from ref. 11. [b] Atomic refraction constants for the substituent group on benzene for H_α line. Data from ref. 26. [c] C. P. Smythe, "Dielectric Behavior and Structure," McGraw-Hill Book Co., New York, N. Y., 1955. N. A. Lange, "Lange's Handbook of Chemistry," 9th Ed., Handbook Publishers, Inc., Sandusky, Ohio, p. 1222. [d] Data from ref. 9. [e] Data from ref. 4.

TABLE II

THE RATES AND THERMODYNAMIC PROPERTIES FOR THE REACTION OF EtX AND PYRIDINE IN VARIOUS SOLVENTS

Reagent EtBr at 79.3°

Solvent	$k \times 10^5$, l./mole sec.	ΔS^*, cal./deg./mole	ΔE^*, kcal./mole
Benzene	0.744	34.5	17.5
Chlorobenzene	2.72, 2.72	35.2	16.45
Bromobenzene	3.22, 3.28	34.9	16.30
Iodobenzene	5.22, 5.32	33.2	16.70
Reagent EtBr at 99.4°			
Benzene	2.84	34.8	
Chlorobenzene	9.50, 9.66	35.2	
Bromobenzene	11.6, 11.2	35.3	
Iodobenzene	19.3, 18.7	33.0	
Reagent EtI at 80.0°			
Benzene	4.26, 4.48	36.0	15.80
Chlorobenzene	11.8, 12.5	30.8	16.91
Bromobenzene	17.0, 16.6	33.2	15.90
Iodobenzene	26.9, 28.0	33.2	15.90
Reagent EtI at 100.0°			
Benzene	14.5, 14.9	36.3	
Chlorobenzene	45.0, 45.1	31.0	
Bromobenzene	56.8, 57.4	33.4	
Iodobenzene	92.4, 93.5	32.2	

The most interesting observation that can be made from our data was that the solvent effect on the rate constant increases in the order iodobenzene > bromobenzene > chlorobenzene > benzene, but several additional observations may also be made.

(1) The rate constant varies with the polarizability of the substituent group on the benzene ring of the solvent. This is showed by the linear plot in Fig. 2.

(2) The relative rates do not seem to depend upon the temperature. The reaction of ethyl iodide and pyridine is 6.25 times as fast in iodobenzene as in benzene at 80° and 6.31 times as fast at 100°. For ethyl bromide, the numbers are 7.08 and 6.69 at the same temperatures.

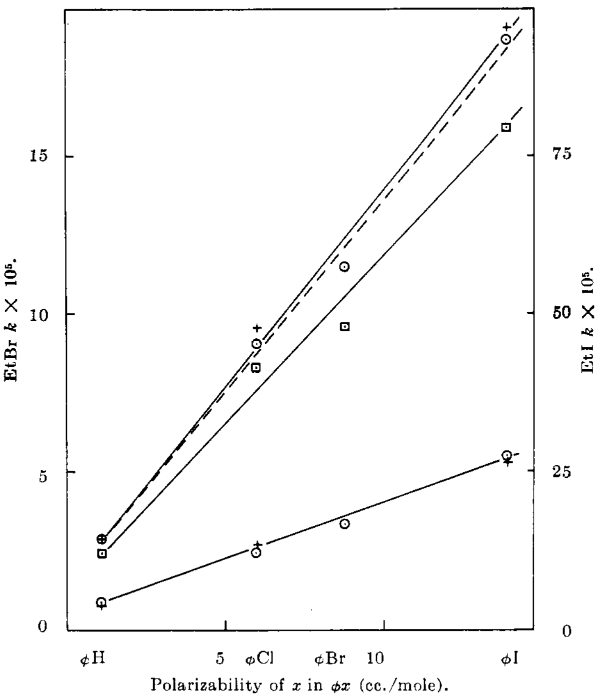

Fig. 2.—Polarizability of the solvent *vs.* rate constant: circles, ethyl iodide + pyridine; crosses, ethyl bromide + pyridine; squares, ethyl iodide + triethyl amine; the scale on the right is exaggerated 5:1 for this reaction. The upper curves are reactions at 100°; the lower curve, 80°.

(3) The nature of the group displaced does not seem to have a great influence on the relative reaction rate constants. This can be seen by comparing the relative rate increases for ethyl iodide and ethyl bromide in the solvents benzene and iodobenzene. With ethyl bromide and pyridine, $k_{\phi I}/k_{\phi H}$ is 7.08, while the same ratio is 6.25 for the reagent ethyl iodide at 80°. At 100°, the ratios are 6.69 and 6.31, respectively.

(4) The nature of the amine does not seem to have a great effect on the relative reaction rate constants. The data of Grim, Ruf, and Wolf[7] for the reaction of triethylamine and ethyl iodide are plotted in Fig. 2. The curve is similar to those for the reaction of pyridine, and the ratio $k_{\phi I}/k_{\phi H}$ is 6.41 at 100°.

What the fundamental causes for the rate increases observed with the change of solvent from benzene to iodobenzene? Some of the possibilities are the effect of electrostatic forces on the activity coefficients of the reagents and the transition state, solvation of the reagents and the transition state by forces other than electrostatic forces, catalysis by salts, and special salt effects in solvents of low dielectric constant.

The salt effects and the effect of electrostatic forces as the major causes for the rate constant increases were rejected for the following reasons.

(1) The only salt present in the reaction mixture is the reaction product, triethylpyridinium halide. If this is to cause the increases by means of surface catalysis or through the effect of its ionic strength, the rate should increase as the concentration of the product increases. The reaction should follow the course of an autocatalytic reaction, and the rate constant would increase during a run. There should be considerable curvature during the run of our plot of $1/C$ *vs.* time. We did not observe such curvature. A second argument is that catalysis depends strongly on the amount

of catalyst present. Changes in initial concentration would cause a different amount of catalyst to be formed when the reaction was proceeding. The data of Norris and Prentiss indicate that the changes in initial concentration do not have a large effect, but one of the order of 10%. These effects are not large enough to account for our factor of 6–7.

(2) Salt effects of considerable magnitude have been observed by Winstein and co-workers.[18] They have suggested that the salt effects can become very large in solvents of low D. Rate increases of factors of more than 10 have been observed for the ionization of alkyl toluenesulfonates. In Winstein's relationship

$$k = k_0\,[1 + b(\mathrm{LiClO_4})]$$

the magnitude of b is a measure of the salt effect. In solvents of comparable D, for example acetone and acetic acid, the nonhydroxyllic solvent has the larger b. Generally, the larger b value is associated with lower D for solvents of the same type. For the special salt effect to apply to our data, the b values would have to be in the order iodobenzene > bromobenzene > chlorobenzene > benzene. This is not the order of D, which is given in Table I. Further, the solvent of lowest D should have the highest rate if the special salt effect applies, but we observe the lowest rate for benzene.

(3) The quantitative relationship between electrostatic forces and the rate constant is given by equation 1. This equation represents the effect of electrostatic forces on the activity coefficients of the species present in the reaction mixture. If the assumption is made that ϕ is small compared to the remainder of the equation, a plot of ln k *vs.* $[(D - 1)/(2D + 1)] = X$ should give a straight line. If $\omega_*{}^2/r_*{}^3 > (\omega_\mathrm{A}{}^2/r_\mathrm{A}{}^3 + [\omega_\mathrm{B}{}^2/r_\mathrm{B}{}^3])$, then the second term of the equation is positive, and the reaction rate constant increases with increasing D. This seems reasonable, for the dipole moment of the transition state, in which ionic bonds are present, should be much greater than the dipole moments of the uncharged reagents. Tommila[13] has observed this relationship with mixed solvent systems in which acetone was one component of the binary solvent system. Fuoss and Wanatabe[14] found the same relationship for the mixed solvent propylene carbonate–diphenyl ether. Fuoss has summarized the objections to the universal application of this equation however. If equation 1 is followed, then all solvents with $D > 30$ should have the same solvent effect on a given reaction. This follows from the observation that X varies from 0 to 0.476 as D varies from 1 to 30; further increase in D to infinity causes only a slight increase in X to 0.50. Fuoss noted exceptions to these deductions in that the rate constant for the reaction of butyl bromide with pyridine in tetramethylenesulfone ($D = 42$) is about twice that in propylene carbonate ($D = 65$). He attributes the unusually high rate in tetramethylenesulfone to "specific short range forces which depend on structure in a way and are superimposed on the longer range electrostatic forces." In the present research, the change in D is small and the observed changes in rate constant do not parallel the changes in the dielectric constant factor X. Electrostatic forces alone cannot explain our rate changes. It is interesting to note in passing that equation 1 seems to hold for mixed solvents. Glasstone, Laidler, and Eyring[19] have suggested that the transition state in the mixed solvent acetone–benzene is solvated by only one of the molecules, acetone. This suggests that the short range nonelectrostatic term which is presumably due to solvation, remains constant, while the D of the bulk of the solution varies. These are the conditions for the linear relationship between ln k and X.

The linear relationship given in Fig. 2 indicates that the polarizability of the solvent is the determining factor in the observed rate increases. Caldin and Peacock have suggested that the high rate constants for the Menschutkin reaction in aromatic solvents is due to the greater polarizability of the benzene ring as compared to aliphatic solvents. We have plotted the polarizability of the substituent group on the ring, rather than that of the entire ring. The solvation of the transition state, as proposed by Fuoss, may be identified as the rate influencing factor and Fuoss "short range forces" are identified as London Forces.

In order to make an estimate of the magnitude of the London force energy of solvation, it is first necessary to know the site of solvation in the reagents and the transition state and the number of molecules of solvation. Gonikberg has provided evidence that the transition state is solvated and that not more than two molecules of solvent are present in the transition state.[20] Since the reagents were pyridine and two different alkyl halides, a reasonable hypothesis was that the common reagent, pyridine, was the site of solvation. As the pyridine molecule approaches the carbon atom of the alkyl halide, it develops a partial positive charge. This charge could attract solvent molecules through an ion-polarizable solvent molecule interaction. A study of the models showed that two solvent molecules could be conveniently placed in the transition state as nitrogen solvating molecules. However, this site does not seem to be tenable for the reaction of triethylamine in the same solvents. In this case, the four ethyl groups completely cover the nitrogen, so that there is no space for the solvent molecules to occupy. Since the relative solvent effect is the same for the two amines, solvation of the nitrogen atom seems to be ruled out. The other likely site is the halogen atom, which also develops charge in the transition state, and which is not sterically hindered. The fact that the solvent effect is the same for both the alkyl iodide and the alkyl bromide seems to be a powerful argument against this site, for the absolute magnitude of the polarizability of the iodine atom and the iodide ion are greater than those for bromine. The surprising observation is that the per cent increase in polarizability in going from the atom to the transition state is the same for iodine and bromine. The figures are $\mathrm{I} \rightarrow \mathrm{I}^{-1/2} = 13.6 \rightarrow 16.4$, or 18.9%, and $\mathrm{Br} \rightarrow \mathrm{Br}^{-1/2} = 8.8 \rightarrow 10.7$, or 21.6%. If the change in rate constant is due to the difference in solvation of the halide ion in the transition state and the halogen atom of the reagent, the per cent increase should be the same for both halogens. Some support for the halogen as the site of solvation is given by spec-

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tral studies. Popovici and Popovici[21] have observed that there is a shift in the center of the ethyl iodide absorption band which is proportional to ln k for the reaction of ethyl iodide and triethylamine in nonhydroxylic solvents. The per cent increase in polarizability for the bromine atom is slightly larger than that of the iodine atom. While this is in the expected order, for the solvent effect on ethyl bromide is slightly greater than for ethyl iodide, no quantitative significance is attached to the per cent increase.

Calculations of the London energy of interaction between the polarizable solvent molecule and the leaving halogen atom were made with the aid of equation 2.[22]

$$U = 2.1 + \frac{3}{2}\frac{\alpha_A\,\alpha_B}{R^6}\left(\frac{I_A\,I_B}{I_A + I_B}\right) \qquad (2)$$

U is the energy of interaction; α_A and α_B are the polarizabilities of the groups involved; I_A and I_B are the ionization potentials; R is the distance between the centers of the groups. The following assumptions were made in the calculations. (a) The dielectric constant was 1. (b) The average values of the radius, ionization potential, and the polarizability could be used for the transition state. The numerical values for the constants were taken from Pauling,[23] Moellar,[24] Rice,[25] and Ingold.[26] (c) One molecule of solvent was in the transition state.

The results of these calculations are given in Table III. The energies given in columns 2 and 3 were obtained with the van der Waal's radii, while those in the 4th column were obtained with an R 0.1 Å. smaller. The ΔH of solvation is obtained by subtracting the values in column 2 from columns 3 or 4. The ΔH for transition state$_1$ has a positive value, while that of the transition state$_2$ with the smaller R has the expected negative value. If the assumption is made that the ΔS^* remains constant, the differences in ΔH give the $\Delta\Delta F^*$. The experimental values for the reaction are given in the last column. The agreement is reasonable, and indicates that the London energies of interaction are of the correct order of magnitude to account for the observed rate changes.

TABLE III

ENERGY OF SOLVATION OF ETHYL BROMIDE IN VARIOUS SOLVENTS

	(−)Energy of solvation[a]					
Solvent	Reagent EtBr	Trans.[b] state$_1$	Trans.[c] state$_2$	ΔH[d]	$\Delta\Delta F$[d] Calcd.	$\Delta\Delta F$[e] Obsd.
Benzene	5.9	5.5	6.7	0.8	0	0
Chlorobenzene	13.4	12.6	14.9	1.5	0.7	0.8
Bromobenzene	15.1	14.4	16.8	1.7	0.9	1.1
Iodobenzene	16.4	15.8	18.2	1.8	1.0	1.3

[a] Energy of solvation for one molecule of solvent. All energies are in kcal./mole. [b] The radius is the sum of the van der Waal's radii. [c] The radius is the sum of the van der Waal's radii minus 0.1 Å. [d] For trans. state$_2$. [e] Temperature, 80°.

The effect of the solvent on the reaction rate constant seems to involve H bonding, electrostatic forces, and London forces. Any one of these may be dominant under a given set of conditions. It does not seem likely that a single analytical expression with one physical property of the solvent as the variable can represent the solvent effects of an entire range of solvents. Vorob'ev and Titova[27] have suggested that the loss of an alcohol of solvation accounts for the different solvent effects in alcoholic solvents. Caldin and Peacock's classification of the reactions into hydroxylic, aliphatic, and aromatic type solvents suggests the importance of H bonding. Kosower's Z correlates the rate constants of alcohols, but he points out that the rate in acetone is too great by a factor of 22. It seems probable that the solvation of the leaving halide has become important rather than the solvation of the amine reagent. Unfortunately, Z values are not available for the aromatic solvents, so that it is not possible to see if acetone is a single exception, or if it represents a general class. Fuoss has pointed out the limits of equation 1 in which ϕ is assumed to be constant. It appears that the effect of nonelectrostatic forces is quite important in nonhydroxylic solvents and these may be the major cause for the lack of correlation of solvent effects in pure solvents. The conclusion that there is no single measure of the solvation capacity is disappointing, but perhaps not unexpected.

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