

different modes of solvation open to the two series of ions used to develop these functions.

Sulfuric acid has often been recognized as a nearly ideal electrolytic solvent. At 20°, its low frequency dielectric constant is 110,³⁴ a good 30 units greater than water. It is naturally an extraordinarily poor hydrogen bond acceptor. Accordingly, the behavior observed by Boyd is exactly what would be expected from the picture we have outlined: large spherical ions have considerable incentive to reduce their energies through transfer from water to sulfuric acid, while small polybasic acidic ions must sacrifice specific solvation to water in order to enjoy the greater non-specific solvation in sulfuric acid.

Boyd's results show clearly that anilinium ions are appreciably solvated and that their solvation differs with the degree of the aniline base. In agreement with this observation, independent measurements³⁵ in the writer's laboratory show clearly that there is a considerably different H_0 acidity function for a series of tertiary amine indicators than that published recently for primary ones³⁶; furthermore, the function for the tertiary ones falls part way between that for the primaries and the H_R function for carbonium ions in conformity with the above discussion. This observation has two other important implications. Firstly, it shows clearly the severe limitations of the activity coefficient postulate^{3,6,20} upon which the exact use of the

(34) J. C. D. Brand, J. C. James, and A. Rutherford, *J. Chem. Soc.*, 2447 (1953).

(35) G. Mach and E. M. Arnett, unpublished results.

(36) M. J. Jorgenson and D. R. Hartter, *J. Am. Chem. Soc.*, **85**, 878 (1963).

H_0 function for Brønsted bases is hinged. Secondly, it indicates that the widely quoted calculation of the H_0 acidity function by Bascombe and Bell³⁷ purely from the concentration of tetrahydrated hydrogen ions and the activity of water is fortuitous. Those authors make clear that their treatment assumes negligible hydration of the indicator and its cation, a requirement which is no longer supportable as Taft has already suggested.³²

Effect of Temperature on the H_R Acidity Scale.—Gelbstein, *et al.*,⁹ found that the H_0 scale does not change much with temperature and that the direction of change depends upon the strength of acid. The H_R scale behaves the same way becoming steadily more negative with increasing temperature for solutions above 65% and behaving erratically in lower concentrations. The H_0 function is determined by three activity terms and the H_R function by four. We feel that an analysis of the effects of temperature on these different components would be an unwarranted and fruitless speculation at this time.³⁸

Acknowledgment.—In the development of this work the authors have had many useful discussions with various colleagues. We are particularly indebted to the help of Professors N. C. Deno, H. Frank, E. Grunwald, L. P. Hammett, and R. W. Taft, Jr.

(37) R. P. Bell and K. N. Bascombe, *Discussions Faraday Soc.*, **24**, 158 (1957).

(38) Professor Hammett suggests that the small temperature coefficients of the H_0 and H_R acidity scales implies that the heat of transfer of a proton from aqueous solution to the medium in question is nearly equal to the difference between the heats of transfer of the ammonium or carbonium ion and its corresponding base to the same solution. This is supported by the fact that ΔH° values in both series are of comparable magnitude over most of the acidity range.

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The Solvation of Polar Groups. III. Conformational and Chemical Effects of the Solvation of Polar Groups¹

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Dissociation constants for the 1:1 complexes of acetonitrile and of *p*-anisonitrile with dimethyl sulfoxide are found to be essentially the same as those previously found for a series of substituted benzonitriles. The importance of this type of specific solvation on the equilibrium of *cis*- and *trans*-4-*t*-butylcyclohexylcarbonitrile and on the relative rates of borohydride reduction of cyclohexanone and dihydroisophorone is illustrated, and the generality of the effects is discussed.

In earlier work,¹ we have shown that the cyano group and the carbonyl group of solutes in dimethyl sulfoxide or dimethylformamide solvents form 1:1 complexes with the solvent in which the solvent attachment is to the polar group rather than to the entire molecule. The implications of this discovery are manifold, and the phenomenon is almost certainly a general one for many polar groups and polar solvents.

In the present paper, we report results which further indicate the insensitivity of stability of the complexes to electronic features of the moiety of the solute not directly involved in the complex formation. In order

to observe the sensitivity of the complex formation to steric effects, and at the same time illustrate the importance of specific solvation on the chemical and physical properties of solutes, we have studied the solvent effects on the equilibrium constant for the conversion of *cis*- to *trans*-4-*t*-butylcyclohexylcarbonitrile, and on the relative rates of borohydride reduction of cyclohexanone and 3,3,5-trimethylcyclohexanone (dihydroisophorone).

Methods and Results

Solvent Effects on the Intensities of Infrared Nitrile Bands.—The solvent effects on the infrared intensities of the nitrile bands of acetonitrile and of *p*-anisonitrile in binary mixtures of carbon tetrachloride and dimethyl sulfoxide were studied by the previously developed methods.¹ The data obtained for acetonitrile

(1) For previous papers in this series, see C. D. Ritchie, B. A. Bierl, and R. J. Honour, *J. Am. Chem. Soc.*, **84**, 4687 (1962); and C. D. Ritchie and A. L. Pratt, *J. Phys. Chem.*, **67**, 2498 (1963). This paper was presented in part at the International Symposium on Solvation Phenomena, Calgary, Alberta, Canada, August, 1963.

(2) National Science Foundation Faculty Fellow, 1962–1963.

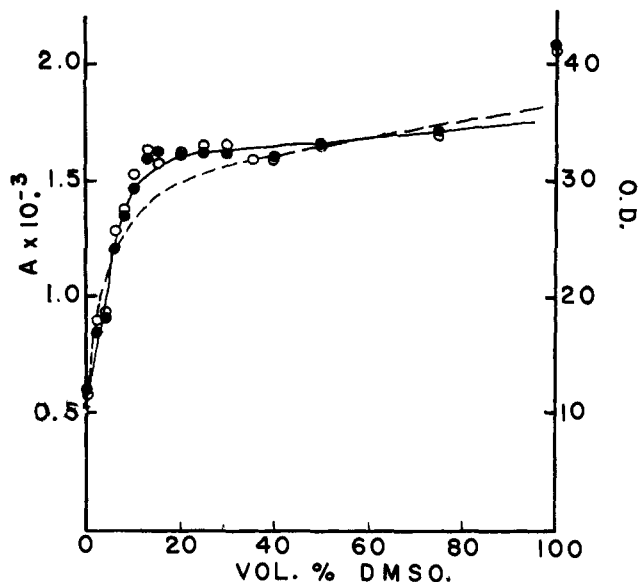


Fig. 1.—Acetonitrile in CCl_4 -DMSO solvents: ●, integrated intensities; ○, optical densities; - - - -, calculated from $K_{\text{diss}} = 0.84 \text{ mole l.}^{-1}$.

at a concentration of 0.0117 g./ml. is shown in Fig. 1, and that for *p*-anisonitrile at a concentration of 0.0100 g./ml. is shown in Fig. 2. The variations of intensity with increasing proportion of dimethyl sulfoxide as solvent are completely analogous to those of the other nitriles which have been studied. Treatment of the data as before shows the formation of 1:1 solute dimethyl sulfoxide complexes with dissociation constants of 0.84 mole l.⁻¹ for both acetonitrile and *p*-anisonitrile. The theoretical curves for these equilibria are shown by the dashed lines in the figures. The agreement could be improved by taking account of self-association of the polar solvent, and this factor is treated in the Discussion section.

The fact that the intensity of the nitrile band of *p*-anisonitrile reaches a maximum value at 30–70% dimethyl sulfoxide is further discussed in the Discussion section. For purposes of calculating the equilibrium constant, we have used the intensity maximum at 60% dimethyl sulfoxide to arrive at the intensity of absorption of the complexed nitrile.

In the case of acetonitrile, in addition to the nitrile band at 2242 cm.^{-1} , there is a lower intensity band at 2283 cm.^{-1} . The intensity of this band does not vary with solvent composition, and we therefore infer that it is not associated with the nitrile group vibrations.

Beer's law plots of the nitrile bands of both nitriles are linear to a concentration of about 0.02 g./ml., but show large deviations at higher concentrations. When the solvent dependence of the intensity of the nitrile band of acetonitrile was measured using a nitrile concentration of 0.047 g./ml., the same qualitative behavior was found as for lower concentrations, but the dissociation constant for the nitrile-dimethyl sulfoxide complex was found to be 2.2 moles l.⁻¹. Both the deviations from Beer's law and this high dissociation constant may be attributed to the self-association of the nitrile in concentrated solutions.

Equilibration of *cis*- and *trans*-4-*t*-Butylcyclohexylcarbonitrile in Dimethyl Sulfoxide Solvent.—The equilibration of *cis*- and *trans*-4-*t*-butylcyclohexylcarbonitrile in dimethyl sulfoxide solution was carried out

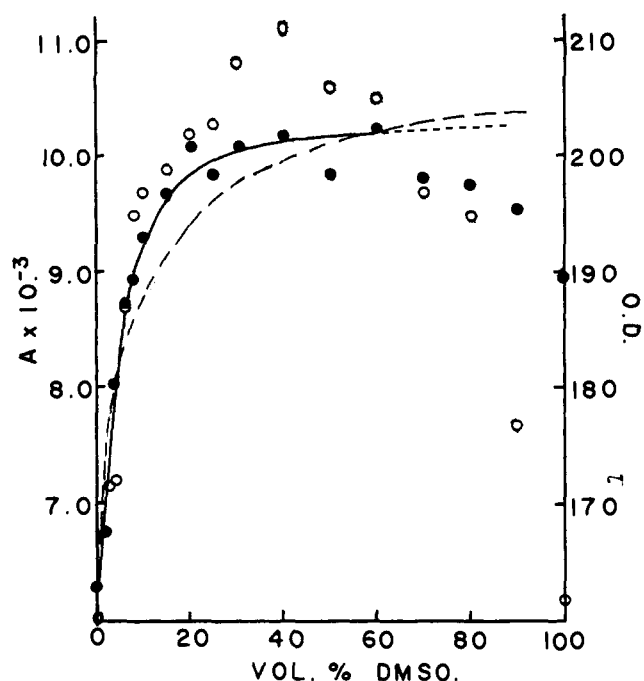


Fig. 2.—Anisonitrile in CCl_4 -DMSO solvents: ●, integrated intensities; ○, optical densities; - - - -, calculated from $K_{\text{diss}} = 0.84 \text{ mole l.}^{-1}$.

using potassium *t*-butoxide as catalyst by the methods described by Allinger.³ Gas chromatographic analyses of the solutions were carried out at various time intervals until no further change in the *cis-trans* ratio occurred. Three independent samples, allowing approach to equilibrium from both sides, were used. The results are reported in Table I. The equilibrium constant, *trans/cis*, calculated for all data obtained after 140 hr. is 2.01 with an average deviation of 0.03.

TABLE I

EQUILIBRATION OF *cis*- AND *trans*-4-*t*-BUTYLCYCLOHEXYLCARBONITRILE IN DMSO

Init. concn. of potassium *t*-butoxide, 0.10 *M*; nitrile concn., 0.08 *M*; $T = 28.0^\circ$

Time, hr.	Sample 1		Sample 2		Sample 3	
	% <i>cis</i>	% <i>trans</i>	% <i>cis</i>	% <i>trans</i>	% <i>cis</i>	% <i>trans</i>
0	36.0	64.0	36.0	64.0	1.0	99.0
30	32.7	67.3	31.7	68.3	12.2	87.8
140	33.5	66.5	33.0	67.0	33.1	66.9
190	33.9	66.1	32.8	67.2	33.3	66.7

The discrepancy between the value obtained here and the value of 1.41 reported by Rickborn and Jensen⁴ may be due to differences in the concentrations of nitrile and base in the two studies, or may have been due to the presence of water in the dimethyl sulfoxide used by the previous investigators. The presence of a small amount of water does slightly shift the equilibrium toward the *cis* isomer. In one of our experiments, a hole was discovered in the serum bottle cap sealing the reaction mixture, thus allowing the entrance of moisture. The equilibrium constant found for this sample was 1.8.

We have also carried out the equilibration of the nitriles in *t*-butyl alcohol at 28° using the same concentrations of nitrile and base as those used in dimethyl sulfoxide solvent. The value obtained for the equi-

(3) N. L. Allinger and W. Szkrybalo, *J. Org. Chem.*, **27**, 4601 (1962).

(4) B. Rickborn and F. R. Jensen, *ibid.*, **27**, 4606 (1962).

librium constant is 1.24, in good agreement with that of 1.27 reported by Rickborn and Jensen for tenfold more concentrated solution. Thus, concentration does not appear to have a large effect in *t*-butyl alcohol solvent.

Borohydride Reductions in Pyridine and Dimethyl Sulfoxide Solvent.—The reactions of cyclohexanone and of dihydroisophorone (3,3,5-trimethylcyclohexanone) with lithium borohydride in pyridine and in dimethyl sulfoxide solvents were studied by infrared spectrophotometry after it was found that the usual quenching techniques are not applicable for reductions in these solvents.⁵

The stoichiometry of the reaction in pyridine solvent was found to correspond to the equation⁵



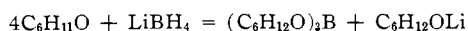
The reaction could be followed by the disappearance of the 1705 cm.⁻¹ carbonyl band or the 2240 cm.⁻¹ borohydride band, or the appearance of the 2380 cm.⁻¹ pyridine-borane band.

The reaction of cyclohexanone followed good second-order kinetics to better than 75% completion. Three independent kinetic runs utilizing both the 1705 and the 2240 cm.⁻¹ bands gave a rate constant of 4.2×10^{-1} l. mole⁻¹ min.⁻¹ with an average deviation of 0.1×10^{-1} .

The reduction of dihydroisophorone also followed second-order kinetics and the same stoichiometry. The rate constant obtained for dihydroisophorone in pyridine is 1.5×10^{-2} l. mole⁻¹ min.⁻¹ with an average deviation of 0.05×10^{-2} .

As previously reported,⁵ the reduction of dihydroisophorone gives 90.9% of the *cis* (equatorial) alcohol and 9.1% of the *trans* alcohol.

In dimethyl sulfoxide solvent, the stoichiometry of the reaction corresponds to the equation



where the alkoxyboron is written for simplicity rather than actually having been observed. If alkoxyborons are formed, they must be very rapidly hydrolyzed in aqueous solution.

The reaction can again be followed by the infrared carbonyl or borohydride bands. The reaction of cyclohexanone followed second-order kinetics to about 50% completion, but then appreciable deviations occurred. Color also became obvious in the solutions, and may have been caused by aldol condensation. The rate constant for the reaction of cyclohexanone was found to be 9.2×10^{-4} l. mole⁻¹ min.⁻¹ with an average deviation of 0.2×10^{-4} .

The reduction of dihydroisophorone with LiBH₄ in dimethyl sulfoxide followed strict second-order kinetics for only about 25% completion. Three independent kinetic runs, using both the carbonyl and borohydride bands, gave a rate constant of 5.0×10^{-5} l. mole⁻¹ min.⁻¹ with an average deviation of 0.1×10^{-5} .

When the reduction of dihydroisophorone in dimethyl sulfoxide was allowed to go to completion and then worked up, the product was found to contain 35.6% of the *cis* alcohol and 64.4% of the *trans* alcohol.

The difficulties which we have previously reported for the quenching of borohydride reductions in pyridine⁵ have also been found for dimethyl sulfoxide.

Solvent Effects on the Carbonyl Infrared Band of Cyclohexanone.—An attempt to measure the complex formation of cyclohexanone with dimethyl sulfoxide by the method previously used for acetone¹ was unsuccessful since the intensity of the band remained constant within experimental error for all binary mixtures of carbon tetrachloride and dimethyl sulfoxide.

The frequency of the carbonyl band, however, shows a shift of 12 cm.⁻¹ in going from pure carbon tetrachloride to 90% dimethyl sulfoxide. The most rapid change in frequency occurs at low concentrations (less than 30%) of dimethyl sulfoxide, and a plot of the data does indicate complex formation. The precision of the spectrophotometer is not good enough to place much confidence in the value for the equilibrium constant calculated, but a value of approximately 1.4 obtained from the data does show fair agreement with that earlier calculated for acetone.¹

Discussion

The equilibrium constants for all the solvent-solute complexes obtained thus far by us are given in Table II. The equilibrium constants for the nitriles with dimethyl sulfoxide are remarkably insensitive to the structure of the nitrile, being equal in all cases to 1.0 ± 0.2 mole l.⁻¹. This lack of sensitivity to the resonance and inductive effects of the solute requires that the complex formation involve the nitrile group specifically.

TABLE II

DISSOCIATION CONSTANTS FOR SOLVENT-SOLUTE COMPLEXES

Solute	Solvent	K_{dissoc} , moles l. ⁻¹
Benzonitrile	DMSO ^a	1.1
<i>p</i> -Chlorobenzonitrile	DMSO	1.1
<i>p</i> -Nitrobenzonitrile	DMSO	1.1
<i>m</i> -Nitrobenzonitrile	DMSO	1.1
<i>p</i> -Anisonitrile	DMSO	0.85
Acetonitrile	DMSO	0.85
Benzonitrile	DMF ^b	1.6
Benzonitrile	Pyridine	6.2
Acetone	DMSO	2.7
Cyclohexanone	DMSO	1.5 (?) ^c

^a Dimethyl sulfoxide. ^b Dimethylformamide. ^c Approximate value; see text.

One of the factors which we have neglected in the calculations of dissociation constants is the possible self-association of the polar solvent component. Actually the quality of the fit of the calculated curve to the experimental data shown in Fig. 1 and 2 could be greatly improved by taking this factor into account. We do not as yet have data as to the degree of such association and have considered it unwise to make an empirical correction until such data are available. It should be noted, however, that the equilibrium constants which we have calculated will need to be corrected for solvent association before detailed comparison of different solvents is considered.

If we assume only solvent dimerization, we may easily obtain the equation

$$K_{dissoc} = \frac{(N)}{(C)} \frac{K_s[(1 + 8S_0/K_s)^{1/2} - 1]}{4} \quad (1)$$

where (N) is the concentration of uncomplexed solute,

(5) C. D. Ritchie, *Tetrahedron Letters*, **30**, 2145 (1963).

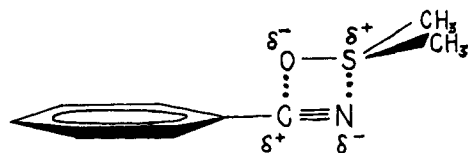


Fig. 3.—The postulated geometry of the benzonitrile–dimethyl sulfoxide complex; see text.

(C) is that of the solvent–solute complex, S_0 is the apparent concentration of polar solvent, and K_s is the dissociation constant for the solvent dimer. The calculated dissociation constants reported in this and the preceding papers are based on the equation

$$K_{\text{dissoc}} = (N)S_0/(C) \quad (2)$$

The curve-fitting technique which we use in the calculations, however, minimizes the differences in the values according to eq. 1 and 2 caused by solvent association, at the expense of the calculated value for the intensity of absorption for the complexed species. The largest discrepancy between the points calculated by eq. 2 and the experimental points, caused by solvent association, would occur near the break in the curve of intensity *vs.* solvent composition as is observed in Fig. 1 and 2.

These factors will be covered in detail in a later paper. For the present time, if we limit comparisons of dissociation constants to those involving the same polar solvent, no difficulty arises.

In our first report of specific solvation,¹ we argued that the results of the study of the solvent dependence of substituent effects on the acidities of 4-X-substituted bicyclo[2.2.2]octane-1-carboxylic acids⁶ seemed to indicate that the dimethyl sulfoxide molecule was so oriented in the complex that its dipole was aligned opposite to that of the nitrile group. Taft's⁷ report of solvent effects on the chemical shifts in the F¹⁹ n.m.r. spectra of *m*-substituted fluorobenzenes confirms this indication in that the cyano group shows an apparent reduced electron withdrawing ability in dimethyl sulfoxide solvent.

On these bases, we visualized the nature of the nitrile–dimethyl sulfoxide complex and, by implication, other solvent–solute complexes of this type to be as shown in Fig. 3. The dotted lines are intended to be noncommittal as to the type of attraction involved. The important feature of this concept is the association of the solvent at the carbon of the nitrile. Although hydroxylic solvents can form relatively strong complexes with solutes by hydrogen bonding, the complex is one in which the bulk of the solvent need not approach closely to the bulk of the solute species. Thus the type of complex formation visualized for dipolar-aprotic solvents with polar groups of solutes might be expected to have more important effects on conformations of solutes, and to be more sensitive to steric effects and therefore more selective than hydrogen bonded complex formation.

The reality of the importance of dipolar complex formation to conformation of solute species is shown by comparison of the results obtained in dimethyl sulfoxide with those obtained in other solvents^{3,4}

for the equilibrium constant for the *cis* to *trans* isomerization of 4-*t*-butylcyclohexylcarbonitrile.

Rickborn and Jensen⁴ have reported an equilibrium constant of 1.28 for equilibration in *t*-butyl alcohol, and of 1.26 for equilibration in methanol solution. The value of 2.01 for dimethyl sulfoxide solution obtained in the present study shows that specific complex formation has shifted the equilibrium toward the *trans* isomer by a factor of 1.6. If we assume that complexing of the *cis* isomer can occur only from the front side of the nitrile, whereas complex formation can occur at either side in the *trans* isomer, we should predict a change by a factor of two.

Allinger and Szkrybalo³ report an equilibrium constant of 1.44 for tetrahydrofuran solution. The difference between this value and those reported for the alcohol solutions may indicate some weak complexing of the cyano group by tetrahydrofuran. This result is not too surprising in view of Taft's indication of considerable complexing of the cyano group by dioxane solvent,⁷ and our previous findings of a very weak solvation of the cyano group by pyridine solvent.¹

Another of the results of steric effects on the ability of solute molecules to form complexes with solvents is expected to be a "solvent leveling" of steric hindrances to reactions taking place in complexing solvents. Thus, if one molecule reacts with some reagent slower than does a second molecule, because of steric hindrance in the first, the differences in reactivity will be made less if a solvent is found which will complex the second molecule more than it does the first. It is even conceivable that in cases where steric hindrance to reaction is small, perhaps because of a small reagent, and steric hindrance to solvation is large, the relative reactivities of two species may be reversed by a change from a noncomplexing to a complexing solvent. In essence, one might look upon a complexing solvent as a very mild form of blocking reagent.⁸

The application of the above ideas, of course, is dependent on finding a reaction which does not show the same specificity of solvation for the transition state as for the reactants.

Since dimethyl sulfoxide is a notoriously poor anion solvator,⁹ it appeared to us that the reduction of ketones with borohydride, in which the transition state must somewhat resemble an alkoxide,⁵ would be a desirable reaction with which to test the above concepts. The obvious application of the concepts to synthetic chemistry involving borohydride were also influential in our choice.

Cyclohexanone and dihydroisophorone came to our attention^{10,11} as examples of unhindered and hindered ketones, respectively, in borohydride reductions. The maximum effect which could be expected would be a factor of two in the relative reactivities in complexing to noncomplexing solvent, since both ketones have one identical side of the carbonyl group.

Using pyridine as an example of a noncomplexing solvent, and dimethyl sulfoxide as the complexing sol-

(8) When the rates of formation and dissociation of solvated species are fast in comparison to the reaction being considered, one does not need to treat the possibility of separate reactivities of the solvated and unsolvated species. An excellent discussion of this point is given by J. E. Lefler and E. Grunwald, "Rates and Equilibria of Organic Reactions," John Wiley and Sons, Inc., New York, N. Y., 1963, Chapter 5.

(9) A. J. Parker, *Quart. Rev. (London)*, **16**, 163 (1962).

(10) H. Haubenstock and E. L. Eliel, *J. Am. Chem. Soc.*, **84**, 2368 (1962).

(11) P. T. Lansbury and R. Macleay, *J. Org. Chem.*, **28**, 1940 (1963).

(6) C. D. Ritchie and E. S. Lewis, *J. Am. Chem. Soc.*, **84**, 591 (1962).

(7) R. W. Taft, E. Price, I. R. Fox, I. C. Lewis, K. K. Andersen, and G. T. Davis, *ibid.*, **85**, 709 (1963).

vent, several difficulties arose. First, we found that neither ketone in these solvents showed measurable reaction with sodium borohydride in 0.1 to 0.5 *M* solution after several days at room temperature.⁵ This result, obtained by following the reaction by infrared spectrophotometry, was discovered after several initial competitive reductions had been carried out by quenching the reactions with aqueous acid and analyzing the products by gas chromatography.

In these early experiments, aliquots of the reaction were removed and quenched by slowly adding dilute aqueous HCl. It is significant that in these experiments, in which reaction occurred only after addition of HCl,¹² we obtained relative rates of reaction of cyclohexanone/dihydroisophorone of 25 in pyridine, 13 in dimethyl sulfoxide, and 15 in dioxane. The ratio of *trans/cis* alcohol obtained from dihydroisophorone was in all cases 69:31. Runs in which the "quenching" was carried out by pouring the reaction mixture into aqueous acid gave erratic results, but uniformly low selectivities.

We also found that the course of the reduction of ketones with lithium borohydride is different in the two solvents. In pyridine, the reaction proceeds with the loss of only one hydride per mole of borohydride and the formation of pyridine borane.⁵ In dimethyl sulfoxide, the reaction follows the stoichiometry and kinetics previously found for reaction in hydroxylic solvents.¹³ In both cases, however, the rate-determining step of the reaction is the attack of borohydride on the ketone, and comparison of the rates obtained in the two solvents is therefore justified.

The relative rate of reduction of cyclohexanone-dihydroisophorone, obtained by infrared spectrophotometric measurements of the individual rate constants, is 28 in pyridine solvent and 18 in dimethyl sulfoxide solvent. Thus, the effect of changing from pyridine to dimethyl sulfoxide is to change the relative rates by a factor of 1.5.

Two facts make it appear improbable that this solvent effect can be ascribed to anything other than specific solvation of the initial states.

First, although the reaction of cyclohexanone with lithium borohydride is slower by a factor of 450 in dimethyl sulfoxide than in pyridine, the selectivity of the lithium borohydride is found to be greater in pyridine solvent. This, of course, is opposite to the usual observation that increased reactivity leads to *decreased* selectivity.

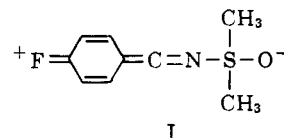
Second, the stereochemistry of the attack of borohydride on dihydroisophorone appears to be nearly the same in both solvents. Eliel¹⁰ has reported that the reduction of dihydroisophorone with triisopropoxyborohydride in diglyme solvent gives 77% *trans* and 23% *cis* alcohol. Assuming that the alkoxyborohydride which is initially formed in dimethyl sulfoxide solution, and which accounts for 75% of the total reduction, gives this same stereochemical result, we can calculate from the over-all stereochemistry of the reaction in dimethyl sulfoxide (64.4% *trans* alcohol) that the attack of borohydride gives approximately 3% *trans* and 97% *cis* alcohol. The agreement be-

tween the result of this naïve calculation and the actual stereochemistry observed for pyridine solvent indicates that the transition states for the borohydride reduction are quite similar in the two solvents.

On the basis of complex formation between the ketone and dimethyl sulfoxide, it would be expected that the reduction would be slower in dimethyl sulfoxide than in pyridine solvent. Using the equilibrium constant of 1.5 for the dissociation of the cyclohexanone-dimethyl sulfoxide complex, we can calculate that the complex formation should lower the rate of reduction by a factor of about ten.¹⁴ The additional factor of 45 (450/10) observed must then be ascribed to the effect of solvent on a reaction in which charge becomes less concentrated in the transition state than in the initial state. The direction and magnitude of the observed effect is reasonable for such a reaction since pyridine and dimethyl sulfoxide have dielectric constants which differ by a factor of nearly four.¹⁵

The only bothersome point observed in the present study concerns the infrared study of the *p*-anisonitrile-dimethyl sulfoxide complex. The points in Fig. 2 follow the theoretical curve to about 70% dimethyl sulfoxide, but then the intensity decreases with further increase of dimethyl sulfoxide concentration. This behavior may be due to an increased contribution of the dipolar resonance form of anisonitrile in more polar solvents,¹⁶ which causes a decreased attraction of the solvent to the nitrile group.

This anomaly is further accentuated by Taft's observation that the shielding of the fluorine in the F¹⁹ n.m.r. spectrum of *p*-cyanofluorobenzene decreases as we go from carbon tetrachloride to dimethyl sulfoxide solvent,¹⁷ whereas the opposite behavior is observed for the *m*-cyanofluorobenzene.⁷ On the basis of these results, Taft¹⁸ has suggested that the *p*-cyanofluorobenzene-dimethyl sulfoxide complex has an appreciable contribution from the resonance form I.



If this were a major contributor to the *p*-anisonitrile complex, however, we would have expected to see an appreciable shift in the nitrile stretching frequency from its normal value. This was not observed. We do not as yet see how these results can be reconciled.

Experimental

Infrared Studies.—The materials used were Eastman Spectrograde acetonitrile and White Label *p*-anisonitrile. Dimethyl sulfoxide was Baker A.R. grade and was purified by fractional freezing prior to use.

Infrared spectra were obtained on a Perkin-Elmer Model 21 spectrophotometer equipped with sodium chloride optics. A

(14) J. E. Leffler and E. Grunwald, "Rates and Equilibria of Organic Reactions," John Wiley and Sons, Inc., New York, N. Y., 1963, Chapter 2, particularly p. 34.

(15) This rationalization does not imply that specific solvent effects other than the one considered above are absent. It is only necessary to suppose that any other specific effects are operable in both reactants and transition state. For a discussion of this point, see R. W. Taft and G. Clarke, *J. Am. Chem. Soc.*, **84**, 2295 (1962).

(16) R. W. Taft, R. E. Glick, I. C. Lewis, I. Fox, and S. Ehrenson, *ibid.*, **82**, 756 (1960).

(17) R. W. Taft, *et al.*, *ibid.*, **85**, 3146 (1963).

(18) R. W. Taft, personal communication, March, 1963.

(12) Compare with the acid-catalyzed reduction of enamines with borohydride reported by J. A. Marshall and W. S. Johnson *J. Org. Chem.*, **28**, 421 (1963).

(13) H. C. Brown and K. Ichikawa, *Tetrahedron*, **1**, 214 (1957).

mechanical slit width of 0.028 mm., corresponding to a spectral width of about 3 cm.⁻¹, was maintained for all readings. The infrared cells had a path length of 0.26 mm.

The experimental details were as reported in the earlier paper.¹ For acetonitrile, two sets of experiments, utilizing a nitrile concentration of 0.0117 and of 0.047 g./ml., were performed. For *p*-anisonitrile, a nitrile concentration of 0.010 g./ml. was used for all measurements. Beer's law plots of the nitrile band absorbance were linear up to approximately 0.020 g./ml. for both nitriles.

For acetonitrile, in addition to the nitrile band at 2246 there appeared a second band at 2286 cm.⁻¹. Since the literature did not reveal an assignment for this band, we tried to establish whether it was related to the nitrile group. Beer's law plots of this band were linear to a concentration of about 0.050 g./ml. in dimethyl sulfoxide, carbon tetrachloride, or pyridine solvent. The intensity of the band was independent of the concentration of dimethyl sulfoxide in binary mixtures with carbon tetrachloride. From these facts, we infer that this band is not related to the nitrile group.

Equilibration of *cis*- and *trans*-4-*t*-Butylcyclohexylcarbonitrile.—Preparation of the nitriles followed the procedures of Rickborn and Jensen.⁴ The transformation of the *trans*-4-*t*-butylcyclohexanecarboxylic acid, obtained by fractional crystallization of the mixed isomers from the reduction of 4-*t*-butylbenzoic acid,¹⁹ gave an over-all yield of 30% of the nitrile which was found to contain 1% of the *cis* isomer by gas chromatography.

We were not able to obtain the *cis*-4-*t*-butylcyclohexanecarboxylic acid in pure form, but instead used the partially separated mixture of isomers to prepare the nitrile. The nitrile obtained from the mixture was found to contain 36% of the *cis* nitrile and 64% of the *trans* nitrile.

Samples were equilibrated by placing 0.138 g. of the nitrile in 10 ml. of solvent and adding 0.11 g. of potassium *t*-butoxide. The reaction flasks were sealed with serum bottle caps and placed in a constant temperature bath at 28.0°. Samples were withdrawn with a hypodermic syringe, quenched with water, and extracted into pentane; the pentane solution dried and evaporated to a volume of about 0.5 ml. The samples were analyzed by gas chromatography on a 20% GE XF 1170 on Chromosorb W column (obtained commercially from the F and M Company), at a temperature of 120° and an inlet pressure of 30 p.s.i.g. The injection port of the chromatograph was maintained at 275°.

The data obtained are reported in Table I.

Lithium Borohydride Reductions.—Commercial lithium borohydride (96.7%, Metal Hydrides, Inc.) was used without further purification. Dimethyl sulfoxide (Baker AR grade) was fractionally frozen and stored over Molecular Sieves 4-A (The Linde Co.). Reagent grade pyridine was distilled from KOH and stored over Molecular Sieves 4-A. Commercial samples of cyclohexanone and of dihydroisophorone were used without further purification after gas chromatographic analysis had indicated the absence of other ketones. All manipulations of lithium borohydride were carried out under a dry nitrogen atmosphere. Reactions were carried out at room temperature of 24 ± 1°.

(19) H. H. Lau and H. Hart, *J. Am. Chem. Soc.*, **81**, 4897 (1959).

A typical kinetic run of the reduction of cyclohexanone in pyridine solvent was carried out as follows. A sample of lithium borohydride was transferred into a tared 10-ml. volumetric flask and weighed 0.0694 g. The flask was filled to volume with pyridine, and 3.2 ml. of the resulting solution (1.0 mmole of LiBH₄) was pipetted into a second 10-ml. volumetric flask and diluted to just below the mark with pyridine. A micropipet was then used to add 0.100 ml. of cyclohexanone to the solution. The reaction mixture was brought to volume exactly and, by means of a hypodermic syringe, an infrared cell was filled with the solution. The well matched reference cell was filled with pyridine beforehand. Infrared readings of the absorbance at 1705, 2240, and 2380 cm.⁻¹ were taken at frequent intervals for the first hour of reaction. The infrared cells used had a path length of 0.26 mm. which gave conveniently high absorbances for the dilute solutions.

For the reduction of cyclohexanone in dimethyl sulfoxide solution, higher concentrations of ketone and lithium borohydride were necessary to give an easily measurable rate. A typical run used 0.40 *M* borohydride and an equal initial concentration of ketone. The reaction mixture was kept in a 10-ml. volumetric flask, and samples were withdrawn and diluted to about one-fifth for infrared analyses. In a typical run, analyses were performed at intervals of 5, 160, 300, 480, and 700 min.

For the reductions in dimethyl sulfoxide, the data were plotted according to the integrated second-order, 4:1 stoichiometry, rate expression, $k_2t = (1/3K_0) \ln (K + 3K_0)/4K$, for the concentration of ketone where K is the concentration of ketone at time t , K_0 is the initial concentration of ketone, which is equal to the initial concentration of borohydride, and k_2 is the second-order rate constant. An analogous expression is obtained for the concentration of borohydride.

The usual second-order, 1:1 stoichiometry, integrated rate expression was used for the reductions in pyridine.

As previously reported, we found that a large amount of reduction occurs on attempted quenching of these reaction mixtures with aqueous acid, aqueous base, or aqueous potassium iodate.⁵

The stereochemistry of the reductions of dihydroisophorone was determined by allowing the reduction to proceed to completion as indicated by infrared analysis. The reaction mixture was then poured into dilute HCl and extracted with ether. After drying, the ether was removed and the products were analyzed by gas chromatography on an 8 ft. UCON (water soluble) on firebrick column at 130°. The *cis* and *trans* alcohols, cyclohexanone, dihydroisophorone, and cyclohexanol were all completely resolved on this column.

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Behavior of Esters in Liquid Hydrogen Fluoride. Walden Inversions and Ring Cleavage in Tetrahydrofuran Derivatives

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The behavior of esters of five polyhydroxytetrahydrofurans (1,4-anhydroglycitols) in liquid hydrogen fluoride has been examined. Deacylation was observed in every case, accompanied by Walden inversion, or ring cleavage, or both. Mechanisms are proposed to rationalize the observed reactions.

Recent investigations have shown that esters of polyhydroxycyclohexanes² and of polyhydroxytetra-

(1) Visiting Associate, 1961-1963.

(2) E. J. Hedgley and H. G. Fletcher, Jr., *J. Am. Chem. Soc.*, **84**, 3726 (1962).

hydropyrans³ readily undergo deacylation, often with concomitant Walden inversion, when treated with liquid hydrogen fluoride. In all cases studied, Walden

(3) E. J. Hedgley and H. G. Fletcher, Jr., *ibid.*, **85**, 1615 (1963).