ORGANIC AND BIOLOGICAL CHEMISTRY

[Contribution from Department of Chemistry, Duke University]

A Study of the Association of Phenol with Several Ketones by Infrared Absorption Measurements

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The equilibrium constants for the dissociation of carbon tetrachloride solutions of hydrogen-bonded complexes between phenol and acetone, methyl ethyl ketone, diethyl ketone, 4-heptanone and acetophenone have been determined quantitatively by means of infrared measurements carried out at 24.6 ± 1°. The constants, corrected for phenol association, were determined from the intensity of the OH absorption band of monomeric phenol at 3610 cm.$^{-1}$ for a number of mixtures of phenol and ketone. The magnitude of the shift of the OH–O complex band from the phenol OH monomer band was measured in each case and comparison of this with dissociation constant for the complex indicates that a steric effect may hinder the formation of the phenol–acetophenone complex. Formation of a six-membered ring by intramolecular hydrogen bonding in the case of 4-heptanone does not appear to take place to an extent sufficient to influence the phenol–ketone intermolecular complex formation.

Introduction

Infrared absorption spectroscopy became a quite useful tool for studying hydrogen bond formation after it was discovered such bonding resulted in a shift of the OH fundamental toward the lower frequencies.[1] A large number of qualitative investigations of association between proton-donor and proton-acceptor molecules through hydrogen bonding have been made using infrared absorption measurements, but very few quantitative data on dissociation constants have been reported. Most of the studies have been directed to evaluating the magnitude of shift of the OH or similar absorption band due to association. Fox and Martin[2] and Badger and Bauer[3] showed that the strength of the hydrogen bond could be estimated by the magnitude of the shift. Later, in several papers, Gordy and co-workers[4] found a direct relationship between the magnitude of the shift and the basic strengths of the proton-acceptor solvents. Errera and Sack,[5] Errera, Gaspart and Sack[6] and Zezyulinskii[7] compared the shifts observed for several proton-donor compounds in binary mixtures with different proton-acceptor solvents, and in tertiary mixtures with an inactive solvent. Prigogine[8] has reported the association constants of the complexes between ethyl alcohol and several active solvents as determined spectroscopically in ternary solutions with carbon tetrachloride as an inert solvent. In Prigogine's work two cases were considered, namely, where the concentration of alcohol was small enough to ignore the formation of alcohol complexes and where the two kinds of complexes were to be found. In the latter case an extension of the Mecke and Kempter[9] relation was used to evaluate the constants.

A large number of studies of association of phenol both with itself and with organic bases have been reported. Mecke and Kempter[9] have determined the association constant of phenol in carbon tetrachloride for higher associated complexes and a number of investigators, including Wulf,[10] Coggeshall,[11] Gordy and Nielsen,[4] Lüttke and Mecke,[12] have made spectrophotometric studies of phenol and a number of substituted phenols in a wide variety of solvents. Zezyulinskii[13] has investigated phenol association with several bases in dilute solutions of carbon tetrachloride. The intensities and shapes of the bands were recorded and the shifts due to hydrogen bonding were measured and related to the strength of the hydrogen bond. In general the results of the above investigations have been reported as to the extent of shift in the OH fundamental when complexing occurs.

In view of the somewhat limited quantitative determinations of dissociation constants of phenol and organic bases, using infrared measurements, it seemed of interest to investigate this problem. The dissociation constants of the hydrogen bonded complexes between phenol and five different ketones, namely, acetone, methyl ethyl ketone, diethyl ketone, 4-heptanone and acetophenone, have been determined using dilute solutions of phenol and the ketones in carbon tetrachloride as an inert solvent.

Experimental

The absorption measurements were made using a Perkin–Elmer model 21 double beam infrared spectrophotometer equipped with a 60° rock-salt prism. During operation, the settings used were those recommended by the manufacturer[14] for quantitative work. Absorption measurements were recorded in the spectral region 5000 to 2860 cm.$^{-1}$ (2

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[12] W. Lüttke and R. Mecke, *Z Elektrochem.*, **53**, 241 (1949).

[13] V. M. Zezyulinskii, *Zhur. Fis. Khim.*, **25**, 702 (1951).

[14] "Instruction Manual—Model 21 Infrared Spectrophotometer Operating and Maintenance Instructions, Vol. 3B, The Perkin–Elmer Corp., Norwalk, Conn., 1952, p. 45.

to 3.5 μ). Close to 3610 cm.$^{-1}$ (2.77 μ), namely, the region of absorption of OH in monomeric phenol, the spectrometer was run manually at a very low speed in order to obtain the best value of the transmittancy at the point of maximum absorption. Two 1-cm. cells made of stainless steel, each equipped with two circular NaCl plates of 25-mm. diameter were used. The cells were cylindrical in shape, 1.00 ± 0.01 cm. long and 2.10 cm. in diameter.

The double beam feature of the instrument allowed satisfactory compensation of absorption bands due to the carbon tetrachloride and the ketones, which occurred in the region of interest. Preliminary recorded spectra of 0.4 *M* acetone in carbon tetrachloride in the region between 5000 and 2500 cm.$^{-1}$ (2 to 4 mμ), with carbon tetrachloride in the reference beam, and with identical solutions of acetone in both beams, showed that the acetone band at 3390 cm.$^{-1}$ (2.95 mμ) was fully compensated. In actual measurements, a solution of carbon tetrachloride, phenol and ketone was placed in the sample beam and a solution of an equal concentration of ketone in carbon tetrachloride in the reference beam of the instrument. By this method, a clear picture was obtained of the changes in the OH intensity produced by varying the ketone concentration while keeping the phenol concentration constant. An example of the spectrum obtained is given for the phenol–diethyl ketone complex in Fig. 1. For each ketone two different concentrations of phenol and generally four or five different ratios of ketone to phenol for each phenol concentration were used.

The spectrophotometer recorded the percentage transmittancy of phenol directly, since the 0 and 100% transmittancy settings were carefully set before each run and rechecked frequently. A small correction for background absorption of the phenol was made to obtain a somewhat more accurate value of the transmittancy. The OH absorption band was quite narrow and the low background absorption at the sides of the band was identical with the general background absorption in other regions. The background absorption varied from 1 to 2 units in percentage transmittancy and was corrected for by the equation

$$T_s = \frac{I_2}{I'_2 - b}$$

where T_s is the transmittancy of the sample, I'_2 the transmitted intensity of the pure solvent and I_2 the transmitted intensity of the solution. The background absorption b was taken as the difference between the transmitted intensity of pure solvent (100%) and that of the solution (about 98 to 99%) at the short wave length shoulder of the OH band. The background absorption was corrected for each solution as the correction varied slightly from one solution to another.

The ketones, phenol and solvent used were purified as follows. Merck and Co. reagent grade acetone was purified by the method of Shipsey and Werner.[15] Immediately before it was used, the acetone was distilled in an all-glass system three times from phosphorus pentoxide. Timmermans and Gillo[16] obtained a sample containing less than 0.0002% of water by this method. The index of refraction of the acetone was $n^{20}\text{D}$ 1.3590; Timmermans[17] gives a value of $n^{20}\text{D}$ 1.35911. Eastman Kodak Co.'s white label methyl ethyl ketone was purified using the same procedure and criteria of purity as for acetone. The record of the physical constants of the particular sample of purified product used in this investigation has been lost but the values obtained indicated, at the time, a state of purity such as to warrant use in the investigation.

Eastman Kodak Co. white label diethyl ketone was purified by distilling five times from phosphorus pentoxide in an all-glass system, the last distillation being made immediately before use. The fraction distilling at 102.1–102.2° was used. The density at 24.6° was 0.8099 g./ml.; Timmermans[17] gives 102.00° as the normal boiling point, and a density, by interpolation, of 0.8099 g./ml. at 24.6°. Carbon and Carbide Co. best grade of 4-heptanone was purified in the same way as was diethyl ketone. The normal boiling point was 143.5° and the density at 24.6° was 0.8143 g./ml. Timmermans[17] gives 143.52 and 143.55° as the normal boiling point and a density, by interpolation, of 0.8145 g./ml. at 24.6°. Eastman Kodak Co. white label acetophenone was purified by alternate fractional fusion and fractional distillation under vacuum from phosphorus pentoxide. The fraction boiling at 87.0–87.3° at 15 mm. was used; Timmermans[17] gives 87.2° as the boiling point at 15 mm. Baker and Adamson Co. reagent grade phenol was purified by alternate fractional fusion and fractional distillation under vacuum. The fraction boiling at 85.5–86.0° at 20 mm. was used; Timmermans[17] gives 85.8° as the boiling point at 20 mm. Eastman Kodak Co. white label carbon tetrachloride was purified and dried using the method reported by Harris and Hobbs.[18]

Results and Discussion

The existence of a complex between phenol and a ketone can be seen qualitatively in Fig. 1. Although the phenol concentration is kept constant, the intensity of the OH band at 3610 cm.$^{-1}$ (2.77 μ) decreases as ketone is added to the system. The new band which appears at about 3333 cm.$^{-1}$ (3.00 μ) and increases with increasing ketone concentration is attributed to the OH–O bond of the complex.

The equilibrium constant *K* for the dissociation of the 1-to-1 complex into phenol and ketone is

$$K = \frac{A \times B}{C}$$

where *A*, *B* and *C* are, respectively, the concentrations at equilibrium of monomeric phenol, of free ketone and of the complex. It is possible to calculate *K* by measuring *A* by infrared absorption of the OH band provided one knows the total concentrations of phenol and ketone. A complicating factor arises from the fact that, even at low concentration, phenol associates with itself, so that a side reaction occurs as

$$\begin{array}{l} \text{A}_1 + \text{B} \rightleftarrows \text{C} \\ + \\ \text{A}_n \rightleftarrows \text{A}_{n+1} \end{array}$$

The equilibrium constant for the dissociation of the complex phenol–ketone thus becomes

$$K = \frac{A_1 \times B}{C}$$

where A_1 is the concentration of monomolecular phenol, the other quantities having the same meaning as above. In Fig. 2, the absorbancy of several solutions of phenol in carbon tetrachloride ranging from 0.0005 mole/liter to about 0.01 mole/liter were plotted *versus* concentration. It is seen that, even at low concentrations, there are deviations from the Bouguer–Beer law, caused by the phenol association. The extrapolated value of the molar absorbancy index $\epsilon = 95 \pm 5$ for infinite dilution of phenol in carbon tetrachloride, and the measured values of the absorbancy allows one to calculate the corresponding concentration of monomolecular phenol A_1 on the basis that the ratio of the observed absorbancy at 2.77 μ to the extrapolated value of ϵ is equal to A_1. Figure 2 permits the evaluation of the several terms of the equilibrium constant as follows: (1) A_1 is read on the linear curve of the graph from the measured absorbancy of the various carbon tetrachloride solutions of phenol and ketones. (2) If A_0 is the total concentration of phenol and $A_1 + nA_n + (n - 1) A_{n+1}$ the concentration of phenol not involved in the complex with the ketone it follows that for 1-to-1 complexes

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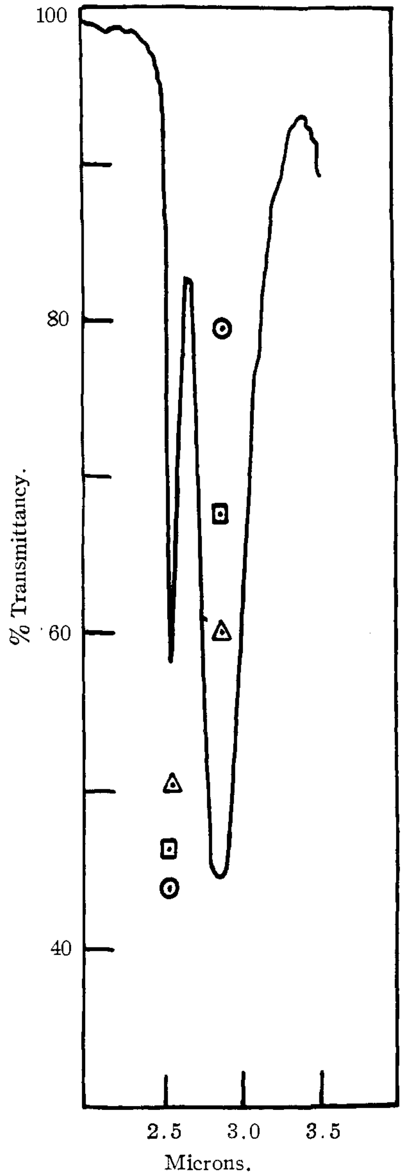


Fig. 1.—Phenol OH absorption band in monomeric phenol (2.77 μ) and the complex phenol-diethyl ketone (2.94 μ). Phenol concentration is 0.005277 mole/liter and ketone concentrations in mole/liter are as follows: curve, 0.1317; △, 0.05645; ◻, 0.03761; ⊙, 0.01881.

of phenol and ketone $C = A_0 - A_1 + nA_n + (n-1)A_{n+1}$. Thus $B = B_0 - C$ where B_0 is the total concentration of ketone.

The concentrations ranges investigated involved solutions of phenol from approximately 0.004 to 0.013 mole per liter with ketone concentrations varying from approximately 0.04 to 0.55 mole per liter at 24.6 ± 1°. Table I gives a summary of the average values of the dissociation constants of the complexes calculated as above along with the standard deviation for the mean value σ_m and of a single observation σ. The number of individual solutions used in deriving the constants is recorded under the column headed by n.

In some cases, the complex band was so broad and intense that there was a possibility of its overlapping the phenol band and increasing its apparent absorption. This effect would be largest in the solutions of greatest phenol and ketone concentrations, and would tend to give a large value for K. The results showed no tendency for K to have higher values for increasing concentrations of phenol and ketones. Thus it appears that error caused by overlap was not serious. The value of σ for the five constants varied from 5 to 10% and σ_m was within 2 to 3%. This precision is about what would be expected for this method of determining K, as a small error in the transmittancy for the OH band would be reflected as a fairly large error in K.

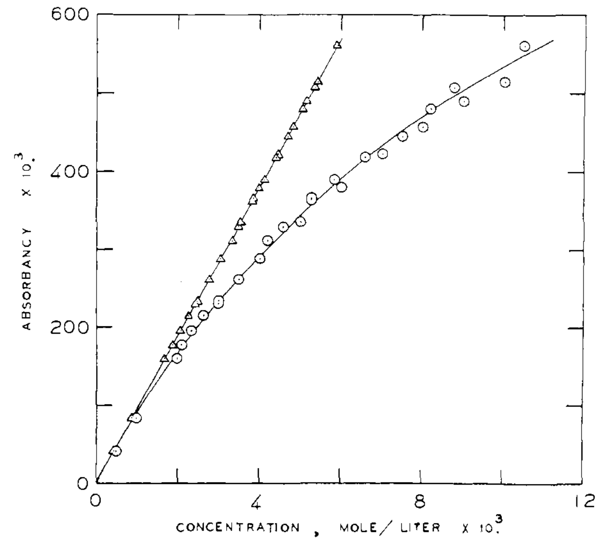


Fig. 2.—Absorbancy at 2.77 μ of phenol in carbon tetrachloride at 24.6 ± 1.0°. Circles represent plot of absorbancy against total phenol concentration. Triangles represent calculated monomeric phenol concentration, plotted against measured absorbancy.

TABLE I

DISSOCIATION CONSTANTS FOR HYDROGEN BONDED COMPLEXES BETWEEN PHENOL AND KETONES AT 24.6°

Complex	K	σ	σ_m	n
Phenol–acetone	0.118	0.011	0.004	10
Phenol–methyl ethyl ketone	.125	.007	.003	8
Phenol–diethyl ketone	.136	.011	.004	8
Phenol–4-heptanone	.139	.007	.003	7
Phenol–acetophenone	.146	.008	.003	7

Fox and Martin[2] and Badger and Bauer[3] state that the magnitude of the shift of the OH band to lower frequency should depend upon the strength of the hydrogen bond: the stronger the bonding, the greater the shift. Therefore, if there are no important entropy differences for the complex formation, the greatest shift should have occurred for the phenol–acetone complex which has the smallest dissociation constant, and the smallest shift for the phenol–acetophenone complex, the other three cases being intermediate. Table II gives, for the different complexes, the values of the dissociation constants K, the magnitude of the shift in cm.$^{-1}$ and the approximate value of the energy obtained from a graph given by Badger and Bauer.[3]

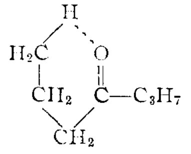
TABLE II

RELATION BETWEEN STRENGTH OF HYDROGEN BOND AND MAGNITUDE OF THE SHIFT

Complex	K	$\Delta\nu$ in cm.$^{-1}$ $\pm$ 10 cm.$^{-1}$	Energy in kcal./mole (approximate)
Phenol–acetone	0.118	266	7.0
Phenol–methyl ethyl ketone	.125	230	6.0
Phenol–diethyl ketone	.136	209	5.4
Phenol–4-heptanone	.139	197	5.2
Phenol–acetophenone	.146	243	6.5

Although there is very little difference between the magnitudes of the shifts, the phenol–acetophenone complex does not follow the apparent trend in shifts. Since the equilibrium constant depends upon the entropy as well as the energy, and the shift of the OH frequency is presumed to depend only on the energy of the OH–O bond, the large dissociation constant of the phenol–acetophenone complex may be associated with some type of steric hindrance, possibly between the two large benzene rings. The fact that the OH–O bond for the phenol–acetophenone complex is broader than that of the other complexes further indicates that there may be a steric factor hindering the formation of a definitely oriented complex structure.

According to the theory of the six-membered ketone ring discussed by Newman,[19] it was expected that the 4-heptanone might show intramolecular hydrogen bonding to form the six-membered ring structure



If there were a strong tendency to form this intramolecular bond, one would expect this reaction to compete with the formation of the phenol–4-heptanone complex by intermolecular hydrogen bonding and in this case the dissociation constant of the intermolecular complex should be larger than that for the phenol–diethyl ketone complex. From the results it appears that this intramolecular bond is not sufficiently strong to compete with the phenol, since there is only a small and possibly insignificant increase in K in going from diethyl ketone to 4-heptanone, the values of K being 0.136 and 0.139, respectively.

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DURHAM, NORTH CAROLINA

[CONTRIBUTION NO. 2135 FROM THE GATES AND CRELLIN LABORATORIES OF CHEMISTRY, CALIFORNIA INSTITUTE OF TECHNOLOGY]

The Behavior of Several Nitrogenous Compounds in Sulfuric Acid

BY JOSEPH L. O'BRIEN[1] AND CARL NIEMANN[2]

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It has been shown that the carboxamide group present in glycinamide cation is more basic than the carboxyl group present in glycine cation, that benzoylglycinamide undergoes normal rather than complex ionization in sulfuric acid, that trichloroacetamide, benzenesulfonamide and phthalimide are completely ionized and *o*-benzoicsulfimide is only partially ionized in this solvent, that DL-phenylalanine undergoes rapid nuclear sulfonation under the experimental conditions encountered in cryoscopic studies and that in sulfuric acid benzhydrazide is converted into a mixture of benzoic acid and dibenzhydrazide at temperatures below 25° and into 2,5-diphenyl-1,3,4-oxadiazole at 100°.

Because the simple carboxamides, such as isobutyramide and benzamide, and the corresponding carboxylic acids undergo complete ionization in sulfuric acid[3–6] it is impossible to determine their relative basicities in this solvent. However, it has been reported[7,8] that glycine in sulfuric acid exhibits an *i*-factor of 2.2 and it may be inferred from this observation that the protonation of the carboxyl group of the glycine cation $\overset{+}{N}H_3CH_2CO_2H$ is limited to about 20% of the theoretical amount by the positively charged α-ammonium group present in this molecule. It therefore appeared desirable to compare the cryoscopic behavior of sulfuric acid solutions of glycine and those of glycinamide in order to arrive at an estimate of the relative basicities of the carboxyl and carboxamide groups present in these particular molecules.

In order to bring our observations into proper perspective with those made earlier[6] the cryoscopic behavior of benzamide in sulfuric acid was reinvestigated and an *i*-factor of 2.0 was obtained. This finding is consistent with the earlier conclusion[6] that benzamide is completely ionized as a mono-acid base in sulfuric acid. The cryoscopic properties of sulfuric acid solutions of glycinamide sulfate were then determined and an *i*-factor of 2.7 was obtained. Thus, in contrast to the protonation of the glycine cation $\overset{+}{N}H_3CH_2CO_2H$ which proceeds only to an extent of about 20% in sulfuric acid it is seen that the protonation of the glycinamide cation $\overset{+}{N}H_3CH_2CONH_2$ proceeds to extent of about 70% in the same solvent and that the carboxamide group is more basic than the carboxyl group.

The cryoscopic behavior of benzoylglycinamide in sulfuric acid was then examined and in contrast to benzoylglycine[9,10] the former compound was found to undergo normal rather than complex ionization in sulfuric acid. The observed *i*-factor of

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