

DETERMINATION OF THE ENERGY OF AN INTRAMOLECULAR HYDROGEN BOND BY  
MEANS OF COMPETING EQUILIBRIA

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In spite of the large number of papers dealing with the investigation of specific molecular interactions, the energetics of the strong intramolecular hydrogen bond remains almost unstudied up to the present time. The direct determination of the difference in the depths of the potential wells corresponding to configurations with an intramolecular hydrogen bond (cis- and gauche-forms) and without an intramolecular hydrogen bond (trans-form), which is normally termed the energy of the intramolecular hydrogen bond, requires the measurement of the absolute or relative populations of the potential wells of the cis- and trans-forms over a certain range of temperature. Such measurements have not been realized for systems in which the energy of the intramolecular hydrogen bond exceeds 3 to 4 kcal/mole. The sensitivity of the measurements which are used for this purpose make it necessary to work at temperatures of 200 to 300°K, that is, under conditions where many organic compounds undergo decomposition.

In the present paper an attempt has been made to determine the energy of an intramolecular hydrogen bond by investigating the equilibria between the forms with intramolecular and intermolecular hydrogen bonds. The method which is used is based on the experimental fact that, when a sufficiently strong proton acceptor is added to a solution of a compound with an intramolecular hydrogen bond, complexes with an intermolecular hydrogen bond are formed. The interaction with the proton acceptor leads to a reduction in the energy of the trans-configuration (an intermolecular hydrogen bond cannot be formed in the cis-form) and the equilibrium between the cis- and trans-forms is displaced in favor of the trans-form such that the concentrations of the two rotamers can become commensurate. This is shown schematically in Fig. 1 using a substituted phenol as the example. The energy level  $E_1$  is shown by a dashed line since the bands corresponding to the trans-form of the free molecules cannot be observed in the IR spectrum over the working range of temperatures. In Fig. 1,  $\Delta H_{13}$  is the enthalpy change accompanying the formation of an intermolecular hydrogen bond in the trans-form (energy of intermolecular hydrogen bond),  $\Delta H_{12}$  is the enthalpy change accompanying the trans-cis transition (energy of intramolecular hydrogen bond). Here  $\Delta H_{23}$  is the enthalpy change accompanying the transition from the cis-form to a complex with an intermolecular hydrogen bond. If  $\Delta H_{13}$  and  $\Delta H_{23}$  are known, the value of  $\Delta H_{12}$  is determined as their difference. Experimentally, it is easy to measure the quantity  $\Delta H_{23}$  for any system for which an intramolecular hydrogen bond  $\nleftrightarrow$  intermolecular hydrogen bond equilibrium is observed, while the magnitude of  $\Delta H_{13}$  cannot be measured directly. In order to estimate this latter quantity, one may use correlations between the energy of an intermolecular hydrogen bond and the spectral characteristics of the complex such as the change in the intensity of the  $\nu_{XH}$  band in the IR spectrum, the frequency shift in the  $\nu_{XH}$  band, or the change in the proton chemical shift of the XH group in the NMR spectrum. The two latter parameters have been used to estimate the contribution of an intermolecular hydrogen bond to the stability of the trans-enol form of  $\beta$ -dicarbonyl compounds relative to the configuration of the cis-enol form with an intramolecular hydrogen bond [1, 2]. The frequency shift of the  $\nu_{XH}$  band is of less potential use, since, in the case of a fairly strong hydrogen bond, the band becomes very asymmetric, acquires a complex structure, and the accuracy to which the frequency can be measured is low. Hence, first of all, the relationship between the enthalpy and the change in the intensity of the  $\nu_{XH}$  band in the IR spectrum, which has been established for a large number of substances [3], merits attention. Of course, the indeterminacy in the accuracy of the parameter  $\Delta H_{13}$ , estimated using correlations, does not permit one to give an objective assessment of the accuracy of the value of  $\Delta H_{12}$ , which is obtained using this quantity. However, by repeating such a procedure using several proton acceptors of different

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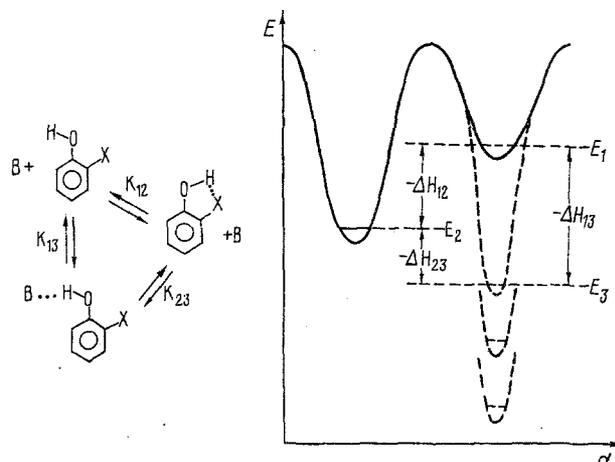


Fig. 1. Diagram of the competing intramolecular hydrogen bond  $\rightleftharpoons$  intermolecular hydrogen bond equilibria in a system consisting of a mono-o-substituted phenol + proton acceptor and the energy levels of the phenol in these equilibria.

strength (Fig. 1), it is possible to gain some idea of the error in the determination of the quantity  $\Delta_{12}$ , which must be independent of the form of the acceptor.

The measurements were carried out for 8-hydroxyquinoline and 2-fluoro-, 2-methoxy, 2-nitro-, and 2-formylphenol in solutions in  $\text{CCl}_4$  or  $\text{C}_2\text{Cl}_4$ . Hexamethylphosphoric triamide, collidine, pyridine, tetraammonium bromide, tetrahydrofuran, and acetonitrile were used as the proton acceptor. Calibration experiments were carried out with diacetone alcohol, for which the  $\nu_{\text{OH}}$  bands of the free hydroxyl groups and of the hydroxyl groups participating in an intramolecular hydrogen bond have a comparable intensity and the magnitude of  $\Delta H_{12}$  can be determined directly. The work was carried out at donor concentrations of 0.004 to 0.35 mole/liter and acceptor concentrations of 0.08 to 2.5 mole/liter over a temperature range from 20 to 110°C. The spectra were recorded on a UR-20 instrument in desmountable cells with fluoride window and a thickness of 0.003 to 4 cm. The cells were put into a cylindrical electrical oven with a length of 10 cm which ensured that the temperature was sufficiently uniform along the length of the cell. The temperatures was measured with an accuracy of 0.5°C by means of a thermocouple. In treating the results, account was taken of the dependence of the density of the solution on temperature. The values of  $\Delta H_{23}$  were found from the temperature dependence of the equilibrium constant  $K_{23}$ :

$$K_{23} = \frac{C^{ab}}{C^a C^b} = \frac{C_0^a - C^a}{C^a [C_0^b - (C_0^a - C^a)]}$$

where  $C_0^a$ ,  $C_0^b$  are the initial concentrations of the proton donor and proton acceptor;  $C^a$  is the concentration of proton-donor molecules in the cis-form. In order to determine  $K_{23}$ , it suffices to measure  $C^a$ . In the case of 8-hydroxyquinoline, 2-fluoro-, and 2-methoxyphenol,  $C^a$  was measured using the  $\nu_{\text{OH}}$  band of the cis-forms of these compounds at 3411, 3591, and 3557  $\text{cm}^{-1}$ , respectively. The half-width of this band barely changed as the temperature was changed and, hence,  $C^a$  could be determined from the peak intensity. When  $C^a$  was determined at different temperatures using this band, allowance was made for the dependence of the absorption coefficient on temperature. The qualitative pictures of the changes in the IR spectra of the compounds in the presence of a proton acceptor were identical and this is illustrated in Fig. 2, taking the system consisting of 2-methoxyphenol + pyridine in  $\text{CCl}_4$  as the example. As the temperature was increased, the intensity of the  $\nu_{\text{OH}}$  band of the complex with an intermolecular OH...N hydrogen bond at 3050  $\text{cm}^{-1}$  decreased while the intensity of the band due to the cis-form with an intramolecular hydrogen bond at 3557  $\text{cm}^{-1}$  increased. This means that the energy level of the complex with an intermolecular hydrogen bond lies below the level corresponding to the cis-form with an intramolecular hydrogen bond; i. e., the formation of the complex with a intermolecular hydrogen bond is accompanied by the evolu-

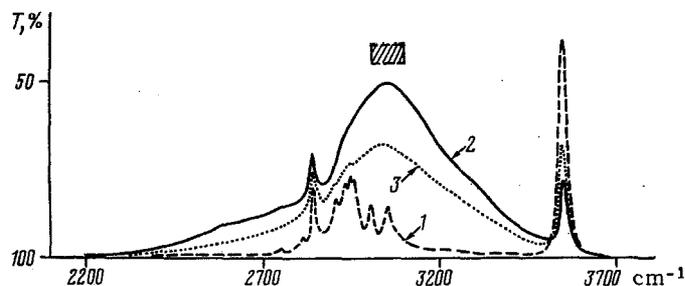


Fig. 2. 2-Methoxyphenol in  $\text{CCl}_4$  (1) and 2-methoxyphenol + pyridine in  $\text{CCl}_4$  (2, 3):  $C_0^a = 0.007$  (1) and 0.0065 mole/liter (2, 3);  $C_0^b = 1.506$  mole/liter (2, 3);  $T = 20$  (2) and  $72^\circ\text{C}$  (3);  $d = 3$  mm (1-3). The total-absorption region of the system solvent-proton acceptor is shown by the cross hatching.

TABLE 1. Spectroscopic and Thermodynamic Characteristics of Proton-Donor-Proton-Acceptor Systems

Donor	Acceptor	$\Gamma \cdot 10^{-4}$ , $\text{cm}^2 \cdot \text{mole}^{-1}$	$\text{kcal/mole}$		
			$-\Delta H_{13}$	$-\Delta H_{23}$	$-\Delta H_{12}$
$\text{CH}_3\text{COCH}_2\text{COH}$ ( $\text{CH}_3$ ) <sub>2</sub>	[( $\text{CH}_3$ ) <sub>2</sub> N] <sub>3</sub> PO	2,61	7,0 (7,1*)	4,6	2,5
$\text{CH}_3\text{COCH}_2\text{COH}$ ( $\text{CH}_3$ ) <sub>2</sub>					2,4
2-F — $\text{C}_6\text{H}_4\text{OH}$	$\text{CH}_3\text{CN}$	2,10	4,1 (4,7†)	4,0	0,7
2-F — $\text{C}_6\text{H}_4\text{OH}$	( $\text{CH}_2$ ) <sub>4</sub> O	3,35	6,0 (5,9†)	5,3	0,6
2-F — $\text{C}_6\text{H}_4\text{OH}$	$\text{C}_6\text{H}_5\text{N}$	4,55	7,5 (8,2†)	7,0	1,2
2-F — $\text{C}_6\text{H}_4\text{OH}$	[( $\text{CH}_3$ ) <sub>2</sub> N] <sub>3</sub> PO	6,62	9,7 (8,5†)	7,4	1,1
2-OCH <sub>3</sub> — $\text{C}_6\text{H}_4\text{OH}$	( $\text{C}_4\text{H}_9$ ) <sub>4</sub> NBr	4,51	7,6	3,5	4,1
2-OCH <sub>3</sub> — $\text{C}_6\text{H}_4\text{OH}$	$\text{C}_6\text{H}_5\text{N}$	5,04	8,3	4,0	4,3
2-OCH <sub>3</sub> — $\text{C}_6\text{H}_4\text{OH}$	[( $\text{CH}_3$ ) <sub>2</sub> N] <sub>3</sub> PO	5,91	9,2	5,2	4,0
8- $\text{C}_6\text{H}_6\text{NOH}$	$\text{C}_6\text{H}_5\text{N}$	4,58	7,5	2,7	4,8
8- $\text{C}_6\text{H}_6\text{NOH}$	[( $\text{CH}_3$ ) <sub>2</sub> N] <sub>3</sub> PO	5,61	8,7	3,5	5,2
2- $\text{NO}_2$ — $\text{C}_6\text{H}_4\text{OH}$	( $\text{CH}_3$ ) <sub>3</sub> $\text{C}_5\text{H}_2\text{N}$	5,52	8,1	2,0	6,1
2- $\text{NO}_2$ — $\text{C}_6\text{H}_4\text{OH}$	[( $\text{CH}_3$ ) <sub>2</sub> N] <sub>3</sub> PO	7,19	9,7	3,4	6,3
2-CHO — $\text{C}_6\text{H}_4\text{OH}$	$\text{C}_6\text{H}_5\text{N}$	6,11	8,9	1,5	7,4
2-CHO — $\text{C}_6\text{H}_4\text{OH}$	[( $\text{CH}_3$ ) <sub>2</sub> N] <sub>3</sub> PO	10,30	12,6	3,9	8,7

\*Measured from the temperature dependence of the equilibrium constant  $K_{13}$ .

†Obtained from the correlation between  $\Delta H$  and  $\nu_{\text{OH}}$ .

tion of energy. The opposite situation, when the energy of the complex with an intermolecular hydrogen bond would be less than the energy of the cis-trans-transition was not observed experimentally. This is also quite natural since such a process is not only unfavorable from the energetic point of view but is also accompanied by a decrease in the entropy. The following data is presented in Table 1: the magnitudes of  $\Delta H_{23}$ , measured using the temperature dependence of the  $\nu_{\text{OH}}$  band intensity of the cis-form; the magnitudes of  $\Delta H_{13}$ , which were estimated using (from [3]) the empirical formula  $-\Delta H = 5.0 (\Gamma^{1/2} - \Gamma_0^{1/2})$ , where  $\Gamma \equiv \frac{1}{cd} \int \ln \frac{i_0}{i} d(\ln \nu)$ .

The integral absorption coefficients of the  $\nu_{\text{OH}}$  band of the trans-form which are required for this calculation but which cannot be determined under our experimental conditions were taken from the spectra of the corresponding phenols which were substituted in the 3- and 4-positions (see [4]). They were very similar to one another. It can be seen from Table 1 that, in the case of 2-methoxyphenol and 8-hydroxyquinoline, the values which were obtained for  $\Delta H_{12}$  are identical for the different proton acceptors. In the case of 2-methoxyphenol, a similar value of 4.27 kcal/mole has been obtained [5] chromatographically for the intramolecular hydrogen bond increment which it was assumed characterizes the energy of the intramolecular hydrogen bond but is noticeably larger than the value of 2.00 kcal/mole which was found from the  $\nu_{\text{OH}}$  torsional frequencies in [6] for a solution in  $\text{C}_6\text{H}_{12}$ . In the case of the 2-fluorophenol however, the scatter in the value of  $\Delta H_{12}$  found in such a manner is fairly large. In this case it is also meaningful to use the correlation between the enthalpy and the frequency shift [7] in order to estimate the values of  $\Delta H_{13}$  since the  $\nu_{\text{OH}}$  band of the

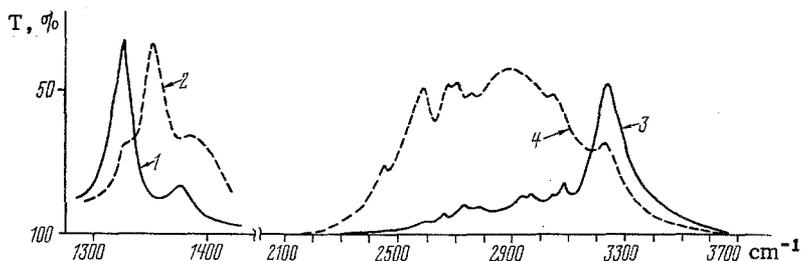


Fig. 3. 2-Nitrophenol in  $\text{CCl}_4$  (1, 3) and 2-nitrophenol + hexamethylphosphoric triamide in  $\text{CCl}_4$  (2, 4);  $C^a = 0.292$  (1, 3),  $0.321$  (2), and  $0.395$  mole/liter (4);  $C^b = 2.380$  (2) and  $0.699$  mole/liter (4);  $d = 40$  (1),  $50$  (2),  $177$  (3) and  $107$   $\mu$  (4);  $T = 20^\circ\text{C}$ .

complexes with an intramolecular hydrogen bond has a fairly simple contour. The measured values of  $\Delta\nu_{\text{OH}}$  were equal to  $245$ ,  $355$ ,  $650$ , and  $685$   $\text{cm}^{-1}$ , respectively, for the acceptors enumerated in Table 1. The values of  $\Delta H_{12}$  obtained by this method were in somewhat better agreement with one another. The mean value of  $\Delta H_{12}$  for 2-fluorophenol of  $0.9$  kcal/mole is comparable with the value of  $1.44$  kcal/mole which was obtained in [8] from the frequencies of the torsional  $\nu_{\text{OH}}$  vibrations for a solution in  $\text{C}_6\text{H}_{12}$ .

In 2-nitro- and 2-formylphenol the strength of the intramolecular hydrogen bond is already fairly large and the  $\nu_{\text{OH}}$  band has a large width and a distinct structure so that it is not possible to separate the bands due to the complex with an intermolecular hydrogen bond and the cis-form with an intramolecular hydrogen bond with sufficient accuracy. In the case of these compounds it is advisable to determine  $\Delta H_{23}$  from the  $\nu_{\text{SNO}_2}$  and  $\nu_{\text{C=O}}$  bands of the acceptor groups participating in the formation of the intramolecular hydrogen bond. In the case of these bands, the changes in the IR spectra when a proton acceptor is added to the solution are qualitatively identical and have the form shown in Fig. 3, which uses the 2-nitrophenol + hexamethylphosphoric triamide in  $\text{CCl}_4$  as the example. The band at  $1327$   $\text{cm}^{-1}$  belongs to a vibration of the  $\text{NO}_2$  group which is involved in the intramolecular hydrogen bond with the hydroxyl group. The band at  $1343$   $\text{cm}^{-1}$  belongs to a free  $\text{NO}_2$  group of 2-nitrophenol in the complex with an intermolecular hydrogen bond. The concentration  $C^a$  was measured using the  $1327$   $\text{cm}^{-1}$  band. In doing this, an allowance was also made for the dependence of the absorption coefficient at the maximum of this band and the density of the solution on temperature. In the case of 2-formylphenol  $C^a$  was measured using the  $\nu_{\text{C=O}}$  band at  $1654$   $\text{cm}^{-1}$  which is also shifted to higher frequencies when an intermolecular hydrogen bond is formed. The quantity  $\Delta H_{13}$  was estimated, as described above, from the integral intensity of the  $\nu_{\text{OH}}$  band of the complex. In estimating this quantity allowance was made for that part of the phenol which remained in the form with an intramolecular hydrogen bond. The data which were obtained are shown in Table 1. In the case of 2-nitrophenol the values of  $\Delta H_{12}$  which were obtained using two different acceptors were in good agreement with one another (the value  $8 \pm 1$  kcal/mole is given in [5]). In the case of 2-formylphenol the divergence is quite significant. This is probably due to the ambiguity associated with the separation of the overlapping  $\nu_{\text{C=O}}$  bands and the error in the determination of the integral intensity of the  $\nu_{\text{OH}}$  band.

In conclusion, we will deal with the results of an investigation on the diacetone alcohol + hexamethylphosphoric triamide system for which all three quantities  $\Delta H_{12}$ ,  $\Delta H_{23}$ , and  $\Delta H_{13}$  can be measured independently. The IR spectra of diacetone alcohol in  $\text{C}_2\text{Cl}_4$  were investigated over a range of temperature from  $20$  to  $110^\circ\text{C}$  and the integral absorption coefficients of the bands due to free OH groups at  $3618$   $\text{cm}^{-1}$  and of the  $\text{OH}\dots\text{O}=\text{C}$  groups participating in the intramolecular hydrogen bond at  $3540$   $\text{cm}^{-1}$  were measured as in [9]. With the help of these values, the concentrations of the forms with an intramolecular hydrogen bond and without one were found and the quantity  $\Delta H_{12}$  was measured from the temperature dependence of their ratio, that is, the equilibrium constant for the rupture of the intramolecular hydrogen bond. The value of  $2.5$  kcal/mole which was found was practically identical to the value of  $2.6$  kcal/mole obtained from the temperature dependence of the ratio of the integral intensities of the two bands and is not very different from the value of  $2.93$  kcal/mole cited in [10].

In the presence of hexamethylphosphoric triamide an intense band appears in the spectrum at  $3330\text{ cm}^{-1}$  which does not strongly overlap with the  $\nu_{\text{CH}}$  and  $\nu_{\text{OH}}$  bands of the two forms of diacetone alcohol so that its integral intensity can be measured fairly accurately. The value of  $\Delta H_{1,3}$ , estimated using the correlation [3] from the integral intensity of this band as  $7.0\text{ kcal/mole}$  agrees with the value of  $7.1\text{ kcal/mole}$  obtained from the temperature dependence of the equilibrium constant as described above and from which a value of  $2.4\text{ kcal/mole}$  can be found for  $\Delta H_{1,2}$  using the method of competing equilibria which agrees with the directly measured magnitude of  $2.5\text{ kcal/mole}$ .

Thus, the method which has been described may be useful for estimating the energy of intramolecular hydrogen bonds of medium strength (2 to 7 kcal/mole) in compounds for which it is possible to select several proton acceptors of sufficient strength in order that the competing equilibrium between intramolecular and intermolecular hydrogen bonds may be observed. The accuracy of the method is apparently 1 to 2 kcal/mole.

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