

Studies of Hydrogen Bonding

Part V*. The Intermolecular Hydrogen Bond Association of Amides with Phenol and Pentachlorophenol

THOR GRAMSTAD and WILLY JOHANNES FUGLEVIK

Norwegian Defence Research Establishment, Division for Toxicology, Kjeller, Norway

The intermolecular hydrogen bond association constants of twenty-six N,N-disubstituted amides with phenol and pentachlorophenol respectively, have been determined at 20 and 50°C. It has been found that for each system the ΔH , ΔF , ΔS , $\nu_{\frac{1}{2}}$ and $\epsilon_{\max} \times \nu_{\frac{1}{2}}$ values form linear relationships with the hydrogen bond frequency shift.

The influence of various substituents in the amides on the hydrogen bond association constants is discussed. The effect of solvent interaction on the hydrogen bond association is also considered.

It has been shown in two previous publications^{1,2} that organophosphorus compounds (OPC) containing the P=O group form very strong intermolecular hydrogen bonds with various hydroxy-compounds. Furthermore, it was shown that the association constants, K_{ass} , form a linear relationship with the frequency shift, $\nu_{\text{O-H}}$, of the O—H band, which accompanies the formation of the hydrogen bond. Linear relationships between frequency shift and ΔH , ΔF , ΔS , $\nu_{\frac{1}{2}}$ and $\epsilon_{\max} \times \nu_{\frac{1}{2}}$ respectively, were found to be valid only when kept to one system, *e.g.*, OPC-phenol, OPC-pentachlorophenol *etc.* It was also shown that the curves ΔH and ΔS *vs.* the frequency shift flatten with increasing acidity of the proton donor. With regard to the effect of solvent interaction on hydrogen bond association, it was observed that when carbon tetrachloride was replaced by carbon disulphide as the solvent, the association constant and the enthalpy of association increased, particularly for the system OPC-pentachlorophenol. It was also observed that for each system an increase in the enthalpy was compensated by an increase in the entropy of association, except for OPC-pentachlorophenol where an increase in $-\Delta H$ was accompanied by an decrease in $-\Delta S$. A study of the hydrogen bond association between a number of nitrogen compounds and various hydroxy-compounds revealed

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that pentachlorophenol forms 1:1, 2:1 and 3:1 hydrogen bonded complexes with tertiary amines, whereas phenol forms only 1:1 complexes³. In addition it was shown that there exists for the system pyridines-phenol a linear relationship between the logarithms of the association constants and the pK_a values of the proton acceptors, and that this relationship was not applicable to tertiary aliphatic amines. In a fourth paper⁴ it was shown that the ability of organophosphorus compounds to form addition compounds with iodine and hydrogen bonds with hydroxy-compounds was related by a linear relationship. To our knowledge no systematic study has hitherto been reported concerning the equilibrium reaction of amides with phenol and pentachlorophenol. We therefore found it of interest to extend our research to this field to see if the same fundamental relationships found for organophosphorus compounds containing the P=O group, are valid for N,N-disubstituted amides.

The ability of amides to form intermolecular hydrogen bonds has long been recognised⁵⁻⁸. Flett⁵ has shown that N,N-dimethylformamide forms hydrogen bonded complexes with phenol, diphenylamine, *p*-benzotoluidide, and benzyl alcohol. He also evaluated the thermodynamic data for these complexes using infrared spectroscopy. Lundgren and Beakley⁶ have determined, among others, the equilibrium constant for the association of phenol with N,N-dimethylformamide by using rhodamine-B as indicator. The method involves measurement of the change from colourless rhodamine to the coloured zwitter-ionic form produced by the hydrogen donor. The results obtained were in accordance with those found by Flett⁵. Tsuboi *et al.*⁷ have evaluated the thermodynamic data for the system phenol-N,N-dimethylacetamide in various solvents while Becker⁸ has studied the interaction between N,N-dimethylformamide and methanol, ethanol, and *t*-butanol.

EXPERIMENTAL

Materials. Phenol, pentachlorophenol, carbon tetrachloride and carbon disulphide were the same as described elsewhere². The amides studied were synthesised from the corresponding acid chlorides and secondary amines. They were purified, either by fractional distillation or by recrystallisation, just before use, and their purity was checked by infrared spectroscopy. Their melting and boiling points are listed in Table 1.

Infrared and near-infrared measurements. The instruments, the instrumental conditions and the methods of running the spectra and the method of calculation of the association constant were the same as described elsewhere³. For the determination of the frequency shift of the ground state stretching vibration of the O—H band which accompanies the formation of the hydrogen bond the concentration of the proton donors was kept at 0.06 M, and that of the amides at 0.03 M. For the calculation of association constant in near-infrared region the concentration of the proton donors was kept at 0.006 M to prevent self-association. The concentrations of the proton acceptors for the system amides-phenol, were 0.012, 0.024, 0.036 and 0.06 M, and for the system amides-pentachlorophenol, were 0.003, 0.006, 0.012 and 0.06 M.

RESULTS

Association constant and free energy. It has been shown^{1,2} that the logarithms of the association constants, K_{ass} , between organophosphorus compounds and methanol, phenol, α -naphthol and pentachlorophenol respectively, form a linear relationship with the frequency shift $\nu_{\text{O-H}}$. This relationship was only

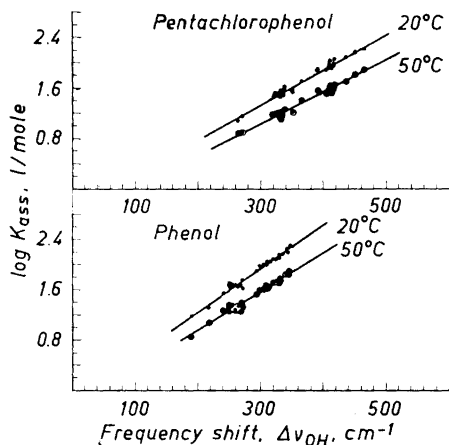


Fig. 1. The relation between the logarithms of the association constants and the frequency shifts for the association of di-substituted amides with phenol and pentachlorophenol. Solvent, carbon tetrachloride.

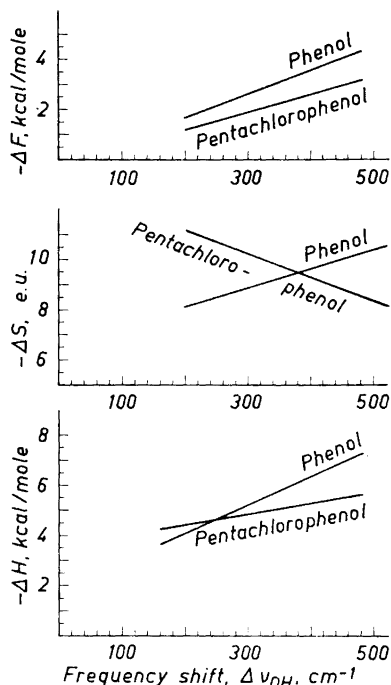


Fig. 2. Free energy $-\Delta F$, entropy $-\Delta S$, and enthalpy $-\Delta H$, vs. the frequency shift, $\Delta\nu_{\text{O-H}}$ of the O-H bond in hydrogen bonded systems.

valid when kept to one system, *e.g.*, OPC-phenol, OPC-pentachlorophenol, *etc.* As can be seen from Fig. 1 the same relation has now been found to be valid for the association of N,N-disubstituted amides with phenol and pentachlorophenol. A least-squares fit to the calculated $\log K_{\text{ass}}$ values (see Table 1) at 20 and 50°C, give the straight lines shown in Fig. 1. For each system the lines at 20 and 50°C have different slopes. The sequence is, in order of decreasing divergence, amides-phenol > amides-pentachlorophenol. The difference in slope between the K_{ass} vs. $\Delta\nu_{\text{O-H}}$ plots for 20 and 50°C for each system, is strongly reflected in the ΔH vs. $\Delta\nu_{\text{O-H}}$ and ΔS vs. $\Delta\nu_{\text{O-H}}$ plots (see Fig. 2). Furthermore, we have found smaller association constants for the system amides-pentachlorophenol than for the system amides-phenol. These observations are all in accordance with those found for the association of organophosphorus compounds with the corresponding proton donors². The anomalies found in the latter study were believed to be due, at least partly, to hydrogen bond formation between the proton donor and the solvent.

Enthalpy and entropy. Fig. 2 shows the relationship ΔH vs. $\Delta\nu_{\text{O-H}}$ and ΔS vs. $\Delta\nu_{\text{O-H}}$. The values used are calculated from the smoothed values of

Table 1. Data on the hydrogen bonding of amides to phenol and pentachlorophenol. Solvent, carbon tetrachloride.

Proton acceptor	M.p. °C	ν_{CO} cm ⁻¹	Phenol				Pentachlorophenol			
			$\Delta\nu_{\text{O-H}}$ cm ⁻¹	K_{ass} l/mole 20°C	K_{ass} l/mole 50°C	$\Delta\nu_{\text{CO}}$ cm ⁻¹	$\Delta\nu_{\text{OH}}$ cm ⁻¹	K_{ass} l/mole 20°C	K_{ass} l/mole 50°C	$\Delta\nu_{\text{CO}}$ cm ⁻¹
CH ₃ C(O)N(C ₆ H ₁₁) ₂	104.5	1652	342	176.7	71.7	22	464	173.7	78.5	39
CH ₃ CH ₂ CH ₂ C(O)N(C ₆ H ₁₁) ₂	39.0	1650	313	112.2	44.6	21	—	—	—	—
CH ₃ CH ₂ C(O)N(C ₆ H ₁₁) ₂	63.5	1650	307	104.8	45.6	20	415	101.0	41.8	33
C ₆ H ₅ C(O)N(C ₆ H ₁₁) ₂	98.0	1638	311	106.0	41.5	25	410	109.0	44.0	31
CH ₂ CCl(O)N(C ₆ H ₁₁) ₂	116.0	1656	250	42.5	18.7	15	327	31.3	16.1	23
<i>p</i> -NO ₂ C ₆ H ₄ C(O)N(C ₆ H ₁₁) ₂	175.0	1648	272	41.0	21.0	21	350	34.9	16.7	32
CH ₃ C(O)N(C ₂ H ₅) ₂	Bp. 59/6	1657	340	157.2	70.1	17	435	126.5	51.5	32
CH ₃ CH ₂ CH ₂ C(O)N(C ₂ H ₅) ₂	Bp. 2/0.5	1650	325	123.8	52.3	18	408	80.4	35.2	33
CH ₃ CH ₂ C(O)N(C ₂ H ₅) ₂	Bp. 55/2	1657	329	134.5	55.1	20	415	93.6	38.9	28
C ₆ H ₅ C(O)N(C ₂ H ₅) ₂	Bp. 100/2	1646	298	97.1	40.2	23	390	81.8	37.5	37
CH ₂ ClC(O)N(C ₂ H ₅) ₂	Bp. 55/0.2	1667	263	45.7	21.8	18	330	31.8	14.4	25
<i>p</i> -NO ₂ C ₆ H ₄ C(O)N(C ₂ H ₅) ₂	66.0	1650	267	47.0	18.3	20	330	31.8	13.6	22
CH ₃ C(O)N(CH ₂) ₅	Bp. 60/0.4	1657	330	135.0	60.1	22	415	112.7	43.7	36
CH ₃ CH ₂ CH ₂ C(O)N(CH ₂) ₅	Bp. 70/1	1651	328	129.1	50.7	22	409	81.9	35.4	30
CH ₃ CH ₂ C(O)N(CH ₂) ₅	Bp. 50/4	1652	320	122.1	52.6	19	404	79.4	33.0	34
C ₆ H ₅ C(O)N(CH ₂) ₅	45	1648	306	102.6	40.8	26	408	84.6	34.8	36
CH ₂ ClC(O)N(CH ₂) ₅	Bp. 80/0.5	1664	252	47.7	22.1	16	323	32.3	15.8	21
<i>p</i> -NO ₂ C ₆ H ₄ C(O)N(CH ₂) ₅	122	1650	260	45.3	19.1	19	325	30.3	13.4	22
CH ₃ C(O)N(C ₆ H ₅) ₂	102.5	1684	270	59.0	25.9	19	337	41.8	18.5	25
CH ₃ CH ₂ CH ₂ C(O)N(C ₆ H ₅) ₂	68.0	1685	250	45.5	22.3	24	330	35.1	16.7	30
CH ₃ CH ₂ C(O)N(C ₆ H ₅) ₂	65.0	1687	250	44.0	20.2	22	328	33.3	15.4	29
C ₆ H ₅ C(O)N(C ₆ H ₅) ₂	181.0	1674	240	34.8	18.6	24	318	30.2	15.4	24
CH ₂ ClC(O)N(C ₆ H ₅) ₂	121.0	1694	217	21.0	12.0	5	270	14.8	8.0	22
<i>p</i> -NO ₂ C ₆ H ₄ C(O)N(C ₆ H ₅) ₂	158.5	1673	190	15.3	7.5	14	262	12.2	7.6	21
HC(O)N(CH ₃) ₂	Bp. 94/10	1692	292	78.6	33.0	17	364	54.1	25.9	20
CH ₃ NCH=CHCH=O	Bp. 63/0.5	1676	345	202.4	77.5	19	448	149.7	65.5	16

log K_{ass} taken from the straight lines in Fig. 1. As can be seen the ΔH and ΔS curves flatten on passing from phenol to pentachlorophenol and this also is in accordance with previously reported observations on organophosphorus compounds². In Table 2 are shown the range of ΔH and ΔS values, and the slope for each system. In the case of the system amides-phenol an increase in

Table 2. Maximum and minimum values of enthalpy and entropy changes on hydrogen bond formation together with the slopes for different systems. Solvent, carbon tetrachloride.

System	ΔH kcal/mole		ΔS e.u.		Slope **	
	from	to	from	to	ΔH -curve	ΔS -curve
OPC *-phenol	-4.3	-7.8	-6.2	-10.5	0.55	0.70
OPC *-pentachlorophenol	-4.1	-6.4	-7.3	-6.5	0.26	-0.0086
Amides-phenol	-4.0	-5.7	-8.1	-9.2	0.45	0.30
Amides-pentachlorophenol	-4.7	-5.6	-10.6	-8.7	0.17	-0.38

* OPC means a series of organophosphorus compounds (see Ref.²).

** See Fig. 2 and Ref.²

the enthalpy of association is compensated by an increase in the entropy of association, whereas the reverse is the case with the system amides-pentachlorophenol.

Half band width and intensity. Fig. 3 shows the observed half band widths, $\nu_{\frac{1}{2}}$, of the hydrogen bonded O—H band plotted as a function of the frequency shift, $\Delta\nu_{\text{O-H}}$. The straight lines drawn through the observed values cut the $\nu_{\frac{1}{2}}$ -axis at 45 and 50 cm^{-1} which correspond approximately to the half band widths of the hydroxyl groups, in carbon tetrachloride, of phenol and pentachlorophenol, respectively. As can be seen, a fairly good linear relationship is found between $\Delta\nu_{\text{O-H}}$ and $\nu_{\frac{1}{2}}$ for each system. Furthermore, we see that for each proton donor there is a systematic increase in $\Delta\nu_{\text{O-H}}$ and $\nu_{\frac{1}{2}}$ as the base strength increases. These results are in agreement with those reported elsewhere for organophosphorus compounds and the same proton donors². The correlation between the intensity expressed in terms of $\epsilon_{\text{max}} \times \nu_{\frac{1}{2}}$ and the frequency shift shown in Fig. 4 is close to a linear relation. The straight lines drawn cut the ordinate at 2.43 and 4.0 which correspond to the $\epsilon_{\text{max}} \times \nu_{\frac{1}{2}} \times 10^{-3}$ values of phenol and pentachlorophenol, respectively. ϵ_{max} is the molecular extinction coefficient at the absorption maximum and is calculated as shown elsewhere².

DISCUSSION OF RESULTS

The present study on ternary solutions of N,N-disubstituted amides and phenol or pentachlorophenol in carbon tetrachloride has established the following facts, which also are in accordance with previously reported results on interaction of OPC with various hydroxy-compounds^{1,2}: Firstly, in each system, the hydrogen bonded O—H band is enhanced in integrated intensity ($\epsilon_{\text{max}} \times \nu_{\frac{1}{2}}$), broadened in contour, and progressively lowered in frequency as the base strength of the proton acceptor increases. Secondly, phenol forms hydrogen bonds more readily with amides than does pentachlorophenol (see

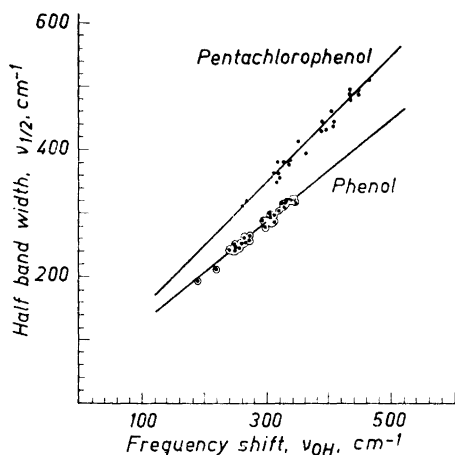


Fig. 3. Half band width $\nu_{1/2}$, vs. frequency shift, $\Delta\nu_{O-H}$, of the O—H bond in hydrogen bonded systems.

Table 1). Thirdly, the slopes of the ΔF vs. $\Delta\nu_{O-H}$, ΔH vs. $\Delta\nu_{O-H}$ and ΔS vs. $\Delta\nu_{O-H}$ curves are greater for the system amides-phenol than for the system amides-pentachlorophenol. Fourthly, the association constants for the system OPC-phenol are, in relation to the frequency shift, larger than those for the system amides-phenol, whereas when phenol is replaced by pentachlorophenol the reverse tends to be the case. Some examples are given below:

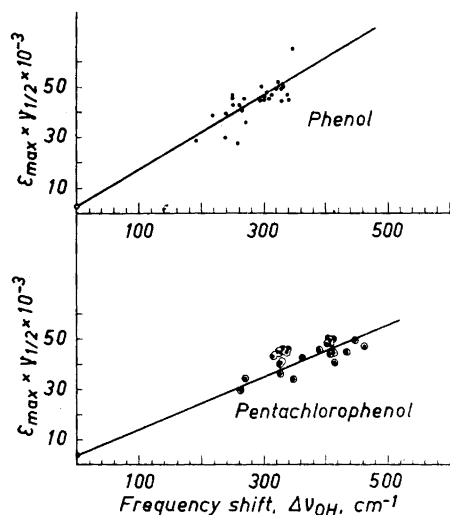


Fig. 4. The frequency shift, $\Delta\nu_{O-H}$, vs. intensity, $\epsilon_{\max} \times \nu_{1/2}$, of the O—H bond in hydrogen bonded systems.

	Phenol		Pentachlorophenol	
	$\Delta\nu_{\text{O-H}}$	$K_{\text{ass}}^{20^\circ\text{C}}$	$\Delta\nu_{\text{O-H}}$	$K_{\text{ass}}^{20^\circ\text{C}}$
	cm^{-1}	l/mole	cm^{-1}	l/mole
$p\text{-NO}_2\text{C}_6\text{H}_4\text{C(O)N(C}_2\text{H}_5)_2$	260	45.3	325	30.3
$\text{CCl}_3\text{P(O)(OC}_2\text{H}_5)_2$ (Ref. ²)	260	73.2	330	29.7
$\text{CH}_3\text{NCH=CHCH=CHCO}$	345	202.4	448	149.7
$\text{C}_2\text{H}_5\text{OP(O)(OC}_2\text{H}_5)_2$ (Ref. ²)	345	350.5	481	153.1

These results indicate that we have to take into account not only the strong solvent interaction with pentachlorophenol but also the effect of solvent interaction with the amides in comparison with that with the phosphorus compounds, and also with the hydrogen bonded complexes. As shown earlier^{2,3}, the thermodynamic data of hydrogen bonds are very much affected by solvent interaction. It was suggested that the fall in the values of the association constants for the system OPC-pentachlorophenol when compared with OPC-phenol was due, at least partly, to hydrogen bond formation between the proton and the solvent. In contrast, no such fall was found for the corresponding association constants of pyridine and collidine. As can be seen in Table 1, the results obtained with the amides are consistent with those found with the organophosphorus compounds studied, *i.e.*, the association constant for an amide-pentachlorophenol system is lower than that of the corresponding amide-phenol system. Furthermore, we found (see Table 3) a marked increase in the association constants and enthalpies of association for the systems amides-phenol and amides-pentachlorophenol when carbon tetrachloride was replaced by carbon disulphide as the solvent. These results are also in accordance with those found for organophosphorus compounds^{2,3}. The difference in frequency shift should also be noticed, *e.g.*, 448 and 481 cm^{-1} , respectively, for N-methylpyridone and triethylphosphate with pentachlorophenol, although with phenol the frequency shift is the same, namely 345 cm^{-1} (see the examples above).

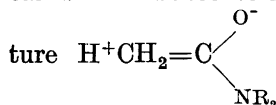
It has been shown earlier¹, that the thermodynamic properties of hydrogen bonds between OPC's and phenols are very much affected by the nature of the substituents in the phosphorus compounds, probably because of the easy deformation of the electronic atmosphere around the phosphorus atom. The same effect, although to a smaller extent, has now been found in amides. The influence of different substituents on the stretching vibration of the carbonyl group is recorded in Table 1. The general tendency is that electron withdrawing substituents, *e.g.*, $\text{R}' = \text{CH}_2\text{Cl}$ (see structures below) reduce the polarity of the C=O bond and so raise the C=O bond frequency. A phenyl or *p*-nitrophenyl group in the R' position, however, reduces its frequency due to direct conjugation of the carbonyl group with the benzene ring, while N-phenyl substitution has the opposite effect. This suggests that in N-phenyl compounds the phenyl group withdraws the unshared electron pair on the nitrogen from conjugation with the carbonyl group. There does, however, seem to be a correlation between the C=O frequency and the ability of the amide to form a hydrogen bond if amides containing the phenyl or *p*-nitrophenyl group in R' position are excluded. The sequence, as can be seen from Table 1, is with few exceptions, in order of decreasing ability to form hydrogen bond,

Table 3. A comparison of thermodynamic data for hydrogen bonds in different solvents.

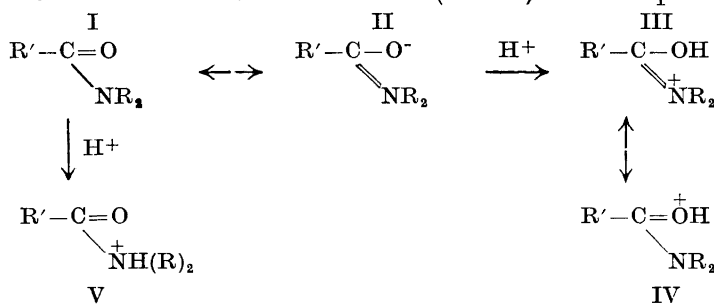
Compound	$\Delta\nu_{\text{OH}}$ cm^{-1}	K_{ass} l/mole 20°C	K_{ass} l/mole 50°C	ΔH kcal/mole	ΔF kcal/mole	ΔS e.u.	ν_{CO} cm^{-1}	$\Delta\nu_{\text{CO}}$ cm^{-1}	$\nu_{\frac{1}{2}}$ cm^{-1}	Solvent
$\text{C}_6\text{H}_5\text{OH}\cdots\text{OC}(\text{H})\text{N}(\text{CH}_3)_2$	292	78.6	33.0	-5.4	-2.5	-9.9	1692	17	286	CCl_4
	277	116.7	60.5*	-6.0	-2.8	-11.0	1690	20	282	CS_2
	364	54.1	25.9	-4.6	-2.3	-7.8	1688	20	394	CCl_4
	398	74.3	39.1*	-5.8	-2.5	-11.4	1691	22	462	CS_2
$\text{C}_6\text{H}_5\text{OH}\cdots\text{OC}(\text{CH}_3)\text{N}(\text{C}_2\text{H}_5)_2$	340	157.2	70.1	-5.1	-2.9	-7.2	1657	17	340	CCl_4
	331	259.1	122.4*	-6.8	-3.2	-12.3	1654	34	354	CS_2
$\text{C}_6\text{Cl}_5\text{OH}\cdots\text{OC}(\text{CH}_3)\text{N}(\text{C}_2\text{H}_5)_2$	435	126.5	51.5	-5.6	-2.1	-9.6	1654	32	478	CCl_4
	440	172.6	92.3*	-5.7	-3.0	-9.2	1653	30	450	CS_2
$\text{C}_6\text{H}_5\text{OH}\cdots\text{OC}(\text{CH}_3)\text{N}(\text{C}_6\text{H}_{11})_2$	342	167.1	62.7	-6.1	-3.0	-10.8	1652	22	336	CCl_4
	394	257.4	119.1*	-7.0	-3.2	-12.9	1646	33	452	CS_2
$\text{C}_6\text{Cl}_5\text{OH}\cdots\text{OC}(\text{CH}_3)\text{N}(\text{C}_6\text{H}_{11})_2$	464	151.2	57	-6.1	-2.9	-10.9	1647	39	510	CCl_4
	457	243.0	120.3*	-6.4	-3.2	-10.9	1648	26	460	CS_2

* Measured at 40°C .

$\text{CH}_3 > \text{CH}_3\text{CH}_2\text{CH}_2 > \text{CH}_3\text{CH}_2 > \text{C}_6\text{H}_5 > \text{CH}_2\text{Cl} > p\text{-NO}_2\text{C}_6\text{H}_4$. The enhanced ability of compounds containing the CH_3 group to form a hydrogen bond can be attributed to hyperconjugation through the contribution of the structure



The question as to whether amides protonate on the oxygen or nitrogen atom has remained open for many years. The usual argument for assuming O-protonation is that amides are mesomeric ($\text{I} \leftrightarrow \text{II}$) and that proton addition



should occur at the atom with highest electron density and hence give the structure III. This O-protonated form is again stabilised by mesomerism ($\text{III} \leftrightarrow \text{IV}$), unlike the N-protonated form V. Infrared spectroscopy has shown that the carbonyl oxygen in all the amides studied by us participates in hydrogen bonding both with phenol and pentachlorophenol. Recently, Katritzky *et al.*⁹ reviewed the protonation of amides and their heterocyclic analogues, and concluded that the evidence as a whole strongly indicates that amides are predominantly protonated at the oxygen atom. The most positive evidence for O-protonation is that from nuclear magnetic resonance spectra which appears to be well-founded. There is, however, also feasible evidence for N-protonation especially from infrared spectroscopy and from application of the Hammett equation¹⁰ to the basicities of *m*- and *p*-substituted benzamides. With regard to hydrogen bonding it may be questionable whether there is any difference in principle between hydrogen bonding and proton-transfer since it is generally accepted that proton-transfer reactions are initiated by the formation of a hydrogen bond.

REFERENCES

1. Aksnes, G. and Gramstad, T. *Acta Chem. Scand.* **14** (1960) 1485.
2. Gramstad, T. *Acta Chem. Scand.* **15** (1961) 1337.
3. Gramstad, T. *Acta Chem. Scand.* **16** (1962) 807.
4. Gramstad, T. and Snaprud, S. I. *Acta Chem. Scand.* **16** (1962) 999.
5. Flett, M. St. C. *J. Soc. Dyers Colourists* **68** (1952) 59.
6. Lundgren, H. P. and Binkley, C. H. *J. Polymer Sci.* **14** (1954) 139.
7. Mizushima, S., Tsuboi, M., Shimanouchi, T. and Tsuda, Y. *Spectrochim. Acta* **7** (1955) 100.
8. Becker, E. D. *Spectrochim. Acta* **17** (1961) 436.
9. Katritzky, A. R., Richard, A. Y. and Jones, B. A. *Chem. & Ind. (London)* **1961** 722.
10. Edward, J. T., Chang, H. S., Yates, K. and Stewart, R. *Can. J. Chem.* **38** (1960) 1518.

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