

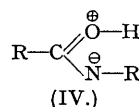
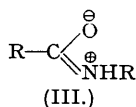
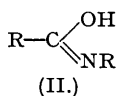
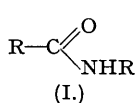
237. Spectroscopic Studies of the Amide Linkage.

By R. E. RICHARDS and H. W. THOMPSON.

The infra-red absorption spectra of a number of simple and substituted amides have been measured between 2 and 15 μ . The regions of particular interest are 5–7 μ and 3 μ , where absorption bands characteristic of the amide grouping occur. There are significant alterations in the spectra according to the state of aggregation in which the substance is measured, and these have an important bearing upon the interpretation of the results. A satisfactory explanation of the positions and shifts of the bands has been given. It is concluded that the amides exist predominantly in the ketonic form, which associates in the solid state through N–H···O bridges. The results provide a basis for more detailed studies on complex amides, amino-acids, and peptides.

THE correlation of the infra-red absorption spectra of simple molecules with the presence of particular structural groups has recently made it possible to apply the method successfully in studying polymers and macro-molecules. It is natural to enquire whether information can be obtained in this way about the structure of proteins, and other compounds in which the amide linkage forms an essential part. We have already obtained some promising results with nylon 66 and its derivatives, and new experimental methods suggest fresh possibilities for the infra-red examination of proteins. Other workers have also explored the subject (Wright, *J. Biol. Chem.*, 1939, 127, 137; Buswell and Gore, *J. Physical Chem.*, 1942, 46, 575). It remains certain, however, that before any detailed understanding of these more complicated molecules is achieved, much must first be explained about the spectra of simple amides and amino-acids.

The conventional plausible structures for an amide are the keto- (I; R = H) and the enol (II; R = H) form. Each of these structures would probably be stabilized by resonance with



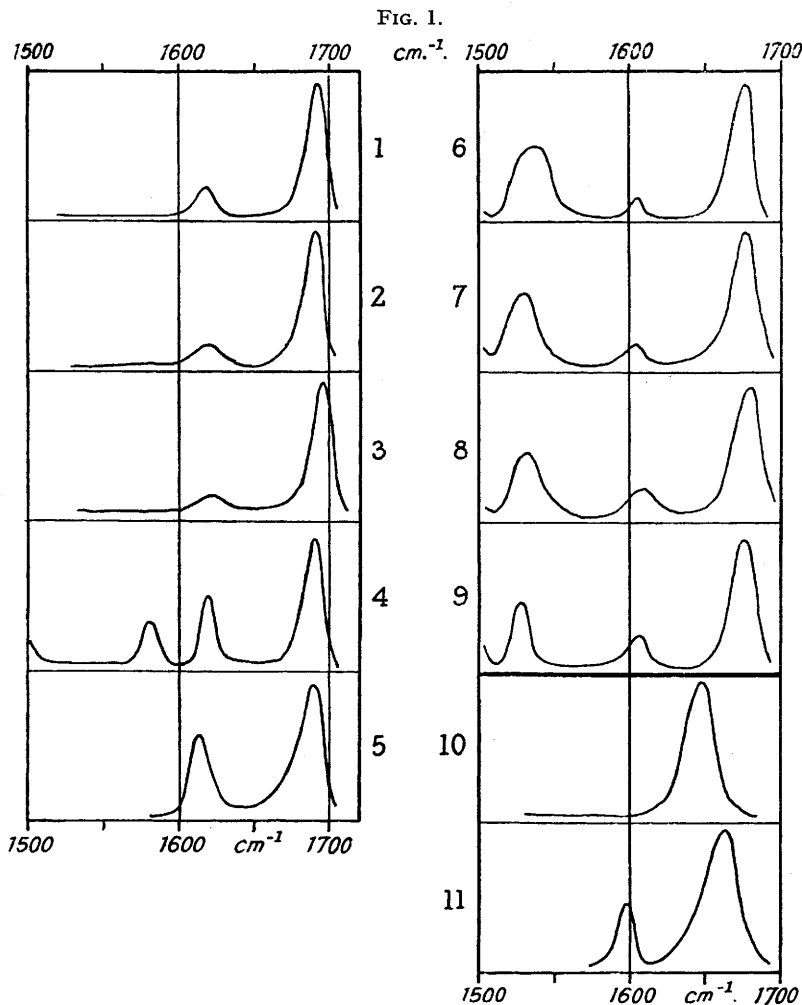
a dipolar form, such as (III; R = H) or (IV; R = H). Hantzsch (*Ber.*, 1931, 64, 661) measured the ultra-violet absorption spectra of amides in various solvents, and concluded that in the cases studied—trichloroacetamide and benzamide—the enolic form predominates. On the other hand, more recent X-ray measurements by Senti and Harker (*J. Amer. Chem. Soc.*, 1940, 62, 2008) show that in the solid state these molecules are associated into ring polymers, and that the occurrence of the enolic form is very unlikely. Some infra-red measurements by Buswell, Rodebush, and Roy (*ibid.*, 1938, 60, 2444), by Buswell, Downing, and Rodebush (*ibid.*, 1940, 62, 2759), and by Buswell and Gore (*J. Physical Chem.*, 1942, 46, 575) have been described, but the results are not conclusive.

The amide grouping may be expected to have vibrational frequencies corresponding to the stretching of C:O, N–H, C:N, or O–H bonds, and also the associated bending oscillations. These several frequencies will be expected to give rise to absorption bands in the regions 5–7 μ and near 3 μ . Absorption bands due to less localized vibrations of the molecular skeleton as a whole will for the most part lie at wave-lengths longer than 7 μ , and between 7 and 14 μ at least are not usually very significant for our present purpose. Results are summarised below of measurements on the spectra of a number of amides in the solid state and in solution, and interpretations are suggested in terms of the possible molecular structure.

EXPERIMENTAL.

Between 7 and 15 μ the spectra were measured with a single-beam recording spectrometer using a rock-salt prism (Whiffen and Thompson, *J.*, 1945, 268). Most of the measurements considered here,

however, are for the regions $5-7\ \mu$ and $3\ \mu$, for which a large double-beam recording spectrometer with calcium fluoride prism was used (Sutherland and Thompson, *Trans. Faraday Soc.*, 1945, **41**, 174; Thompson, Whiffen, Richards, and Temple, to be published shortly). This instrument not only has the marked advantage that there is no disturbance in the region $5-7\ \mu$ from the atmospheric water vapour band, but also use is made of the greater dispersion of fluorite compared with rock-salt. Calibration of wave-lengths was obtained with the absorption lines of water, ammonia, carbon dioxide (Oetjen, Kao, and Randall, *Rev. Sci. Instr.*, 1942, **13**, 515), nitrous oxide, and other substances. At about $1700\ \text{cm}^{-1}$ the position of bands could be measured to within $\pm 3\ \text{cm}^{-1}$, and at $3000\ \text{cm}^{-1}$ to within $\pm 8\ \text{cm}^{-1}$,



Solutions in dioxan.

- | | |
|-----------------------------------|---|
| 1. <i>Butyramide.</i> | 7. <i>Phenylaceto-tert.-butylamide.</i> |
| 2. <i>Hexoamide.</i> | 8. <i>Phenylaceto-tert.-amylamide.</i> |
| 3. <i>Phenylacetamide.</i> | 9. <i>Phenylacetocyclohexylamide.</i> |
| 4. <i>Benzamide.</i> | 10. <i>Acetodiethylamide.</i> |
| 5. <i>Furoamide.</i> | 11. <i>Acetophenylmethylamide.</i> |
| 6. <i>Phenylacetomethylamide.</i> | |

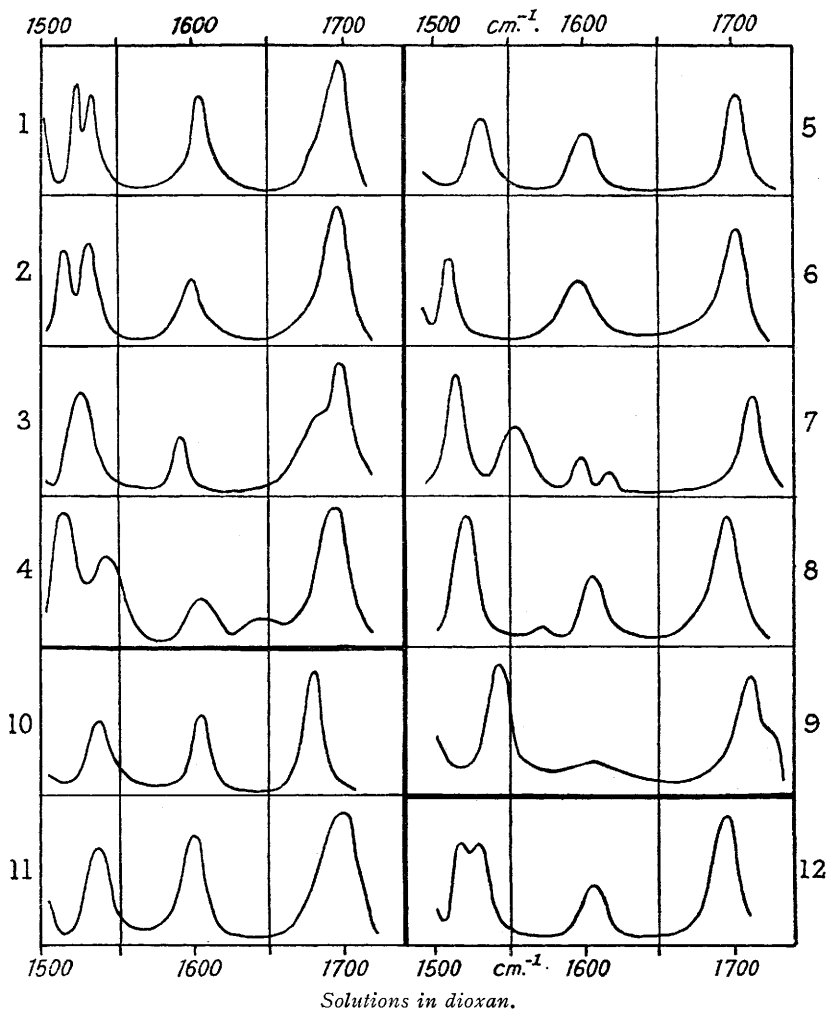
depending upon the breadth of the bands concerned. In many cases where comparisons were being made to discover a general trend, the relative positions of bands of different substances were probably more accurately determined than their absolute values, since several spectra could be measured on the same chart. As indication of the resolving power of the instrument, it was possible when using it as a single-beam spectrometer to resolve clearly lines $2-3\ \text{cm}^{-1}$ apart at $1700\ \text{cm}^{-1}$, and about $15\ \text{cm}^{-1}$ apart at $3000\ \text{cm}^{-1}$; with the double-beam arrangement, which necessitated somewhat wider slits, the corresponding figures were about $5\ \text{cm}^{-1}$ and $20\ \text{cm}^{-1}$.

Solutions were measured in cells 0.01 and $0.2\ \text{cm}$. in thickness, according to the dilution used. The choice of solvent is limited by the solubilities of these compounds, and by the absorption of the solvent.

Dioxan, chloroform, methyl cyanide, and methanol were normally used, being purified in the standard manner. Amides were measured in the solid state by grinding to a fine paste with medicinal paraffin and pressing between a pair of rock-salt plates. By suitable adjustment of the size of the particles, specimens prepared in this way produce little scattering and a satisfactory spectrum can be obtained with only a few mg. of the solid.

The compounds examined were either prepared in this laboratory or obtained commercially. In all cases they were purified by recrystallisation or other appropriate methods.

FIG. 2.



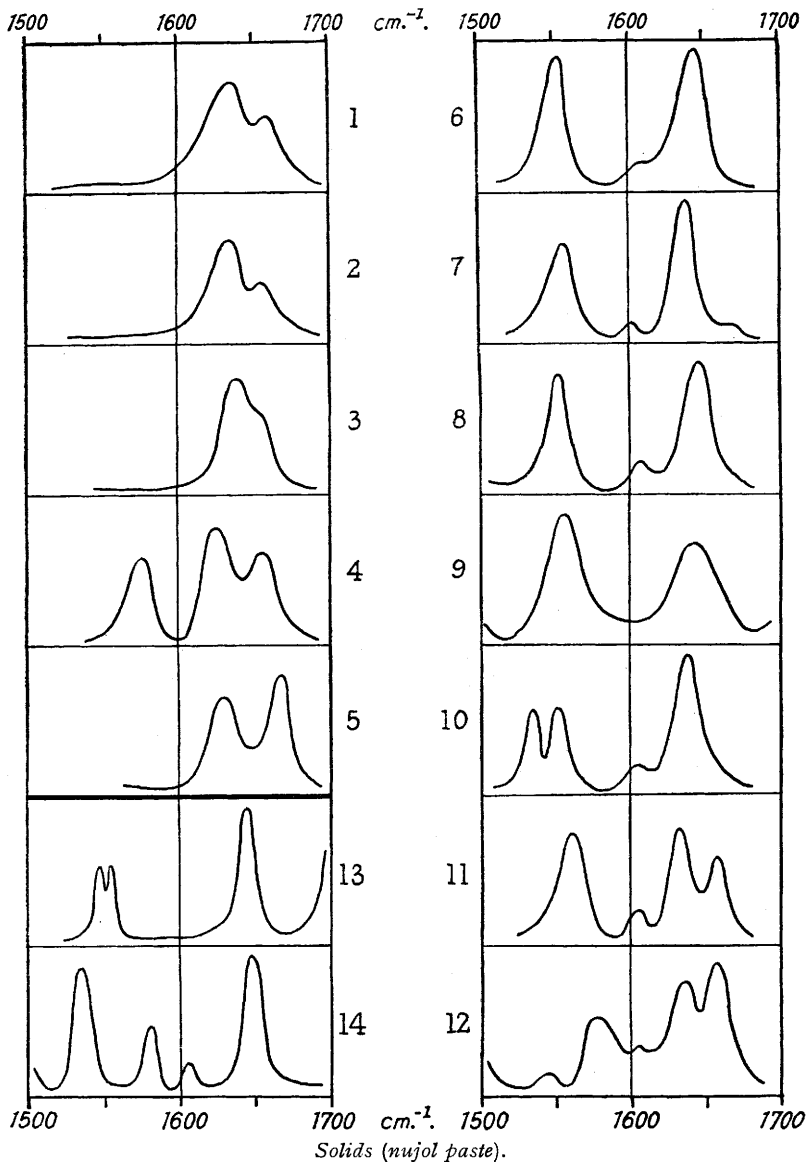
- Solutions in dioxan.
- | | |
|-------------------------------------|---|
| 1. Acetanilide. | 7. <i>p</i> -Nitroacetanilide. |
| 2. Aceto- <i>p</i> -toluidide. | 8. 3-Bromoaceto- <i>p</i> -toluidide. |
| 3. Aceto- <i>o</i> -toluidide. | 9. 3-Bromo-5-nitroaceto- <i>p</i> -toluidide. |
| 4. Aceto- <i>p</i> -methoxyanilide. | 10. Benzanilide. |
| 5. <i>p</i> -Chloroacetanilide. | 11. Phenylacetanilide. |
| 6. <i>p</i> -Bromoacetanilide. | 12. Phenylaceto- <i>p</i> -toluidide. |

Results.—Solutions in dioxan. Fig. 1 shows the spectra (1—5) of five simple unsubstituted amides in dioxan near $6\ \mu$. Any effect of this solvent on C=O or C=N groups by association or similar interactions must be negligibly small. Two bands occur in this region, a strong one near $1690\ \text{cm}^{-1}$ and a weaker one of somewhat variable intensity at $1615\text{--}1620\ \text{cm}^{-1}$. Fig. 1 also shows (6—9) some *N*-alkyl mono-substituted amides, which exhibit two bands at $1675\text{--}1680\ \text{cm}^{-1}$ and $1530\text{--}1540\ \text{cm}^{-1}$. In these cases the latter band is more marked in intensity than the band of the unsubstituted amides at $1615\text{--}1620$. With the two *NN*-disubstituted amides there is only one band, near $1650\ \text{cm}^{-1}$ unless a phenyl group is one of the substituents, in which case the band lies at slightly higher frequencies. All the compounds containing a phenyl group show the well-known sharp, even if weak, bands near 1500 and $1600\ \text{cm}^{-1}$. These results are summarised broadly in Table I. The band at the higher frequencies will be called the A band, and that at the lower frequency the B band.

TABLE I.
Solutions in dioxan.

	Band A.	Band B.
R·CO·NH ₂	1690	1620
R·CO·NHAlk	1680	1530
R·CO·NR ₁ R ₂	1650	—

FIG. 3.



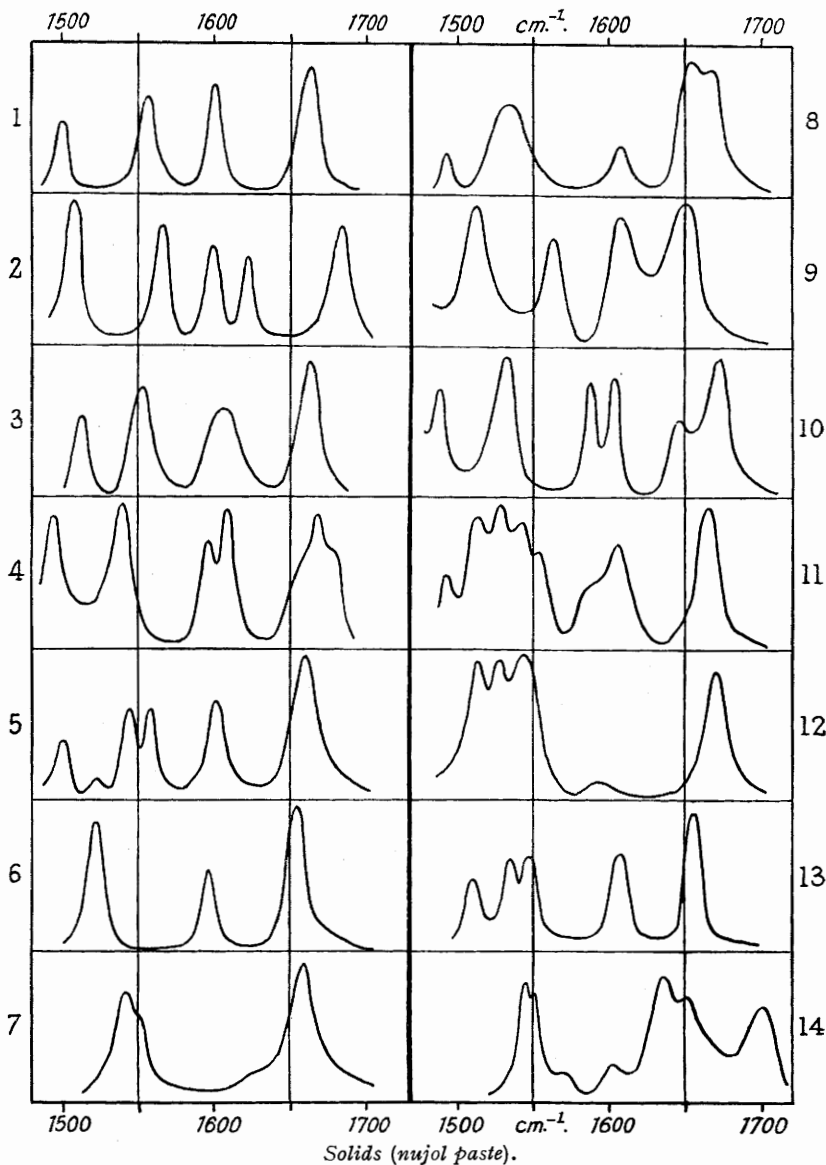
1. Butyramide.
2. Hexoamide.
3. Phenylacetamide.
4. Benzamide.
5. Furoamide.
6. Phenylaceto-tert.-amylamide.
7. Phenylacetocyclohexylamide.

8. Phenylaceto-tert.-butylamide.
9. Methyl phenylacetamidoacetate.
10. Phenylacetobenzylamide.
11. Phenylaceto-n-propylamide.
12. Phenylacetomeihylamide.
13. N-Hexoylglycine.
14. Ethyl hippurate.

The results suggest that the band B only appears when there is at least one hydrogen atom in the amide group, and that both the bands A and B are lowered in frequency by substitution of alkyl groups on the nitrogen atom.

Fig. 2 shows the spectra of some derivatives of acetanilide in dioxan. The main feature with these compounds is that the band A lies at about 1700 cm.^{-1} , distinctly higher than with the *N*-alkyl-substituted amides. It should be noted that when the group attached to the nitrogen atom is strongly electrophilic, the frequency of this band is further raised, and although such increases of $10\text{--}15\text{ cm.}^{-1}$

FIG. 4.



- | | |
|--------------------------------------|--|
| 1. Acetanilide. | 8. Aceto- <i>o</i> -toluidide. |
| 2. <i>p</i> -Nitroacetanilide. | 9. Aceto- <i>p</i> -methoxyanilide. |
| 3. Aceto- <i>p</i> -toluidide. | 10. <i>p</i> -Bromoacetanilide. |
| 4. <i>p</i> -Chloroacetanilide. | 11. 3-Bromoaceto- <i>p</i> -toluidide. |
| 5. Phenylacetanilide. | 12. 3-Bromo-5-nitroaceto- <i>p</i> -toluidide. |
| 6. Phenylaceto- <i>o</i> -toluidide. | 13. Phenylaceto- <i>p</i> -toluidide. |
| 7. Phenylacetamidomethyl cyanide. | 14. Hippuramide. |

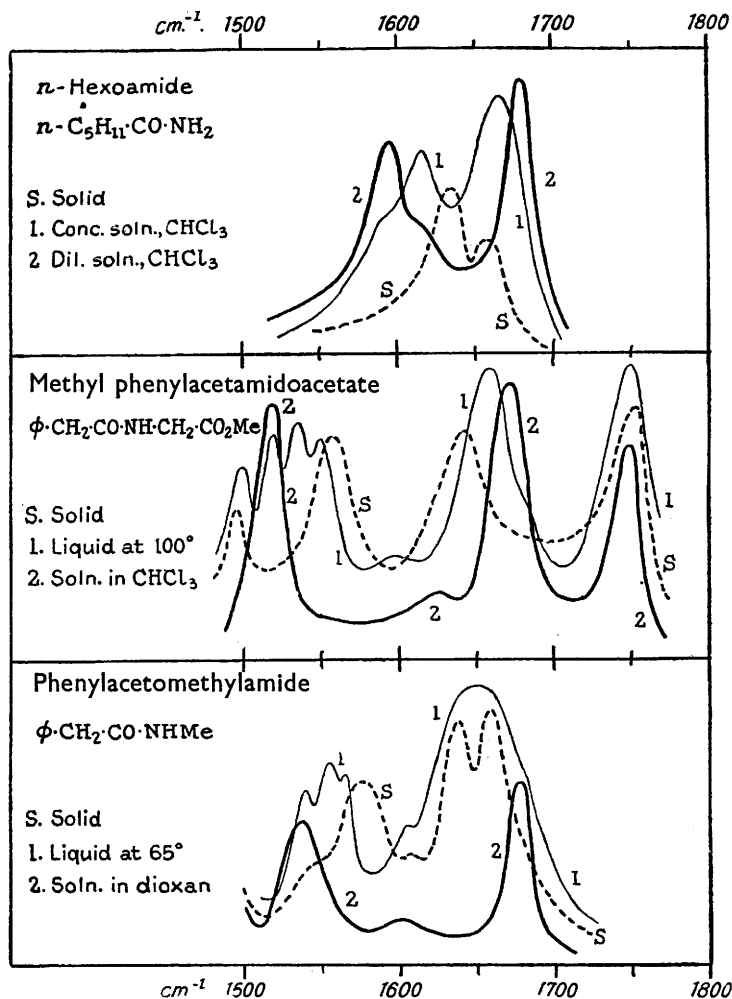
may be regarded as small, they are nevertheless real and regular. Conversely, we should expect electrophobic substituents to lower the frequency, and this seems to occur. As regards the band B of the acetanilides, although there is some interference in the region $1500\text{--}1550\text{ cm.}^{-1}$ from bands due to the aromatic ring and other substituent groupings, there seems to be a less definite influence of the *N*-substituents upon its position.

Solutions in other solvents. Many of the amides have also been measured in chloroform and methanol, with particular reference to the position of the band A. The general behaviour found with all amides is that the frequency of this band falls in passing along the series dioxan, chloroform, methanol, and is illustrated by the examples listed in Table II.

TABLE II.

	Frequency (cm. ⁻¹) of band A in :		
	Dioxan.	Chloroform.	Methanol.
Hexoamide	1692	1682	1672
Phenylaceto- <i>tert.</i> -amylamide	1682	1668	1657
Aceto- <i>NN</i> -diethylamide	1647	1629	1615 (broad)

FIG. 5.



- (1) *Hexoamide* : s. Solid. 1. Conc. soln. in CHCl₃. 2. Dil. soln. in CHCl₃.
 (2) *Methyl phenylacetamidoacetate* : s. Solid. 1. Liquid at 100°. 2. Solution in CHCl₃.
 (3) *Phenylacetomethylamide* : s. Solid. 1. Liquid at 65°. 2. Solution in dioxan.

Solids. The spectra of a number of solid amides measured as a paste in "Nujol" in the region of 6 μ are shown in Fig. 3. In Fig. 4, further examples are given of *N*-monosubstituted amides in which the substituent group has either electron-attracting or electron-repelling character. The simple unsubstituted amides show two fairly close bands in the region 1620—1670 cm.⁻¹. The *N*-alkylamides show bands at about 1560 and 1640 cm.⁻¹, whereas the amides with electrophilic *N*-substituents have the second band—the band A mentioned above—at higher frequencies than 1640 cm.⁻¹. The position of the band B is variable, as found with the solutions in dioxan. One solid *NN*-disubstituted amide, namely aceto-*N*-methylanilide, was examined and the position of the band A was hardly affected in

passing from solution in dioxan to the solid state. The above results are summarised broadly in Table III.

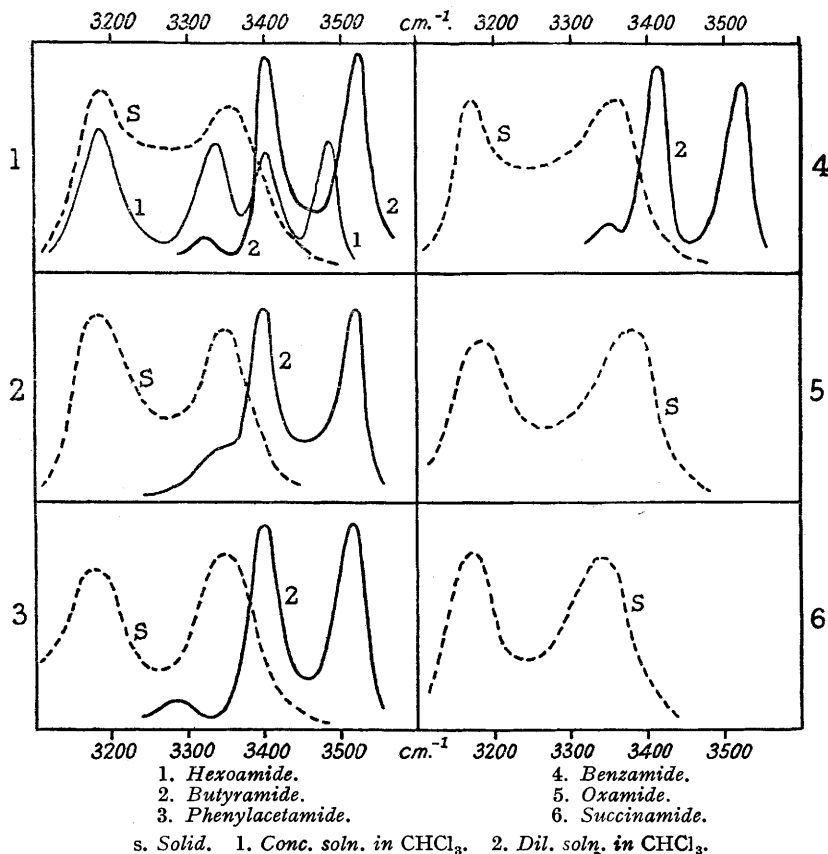
TABLE III.

Solids (R = alkyl, R_e = electrophilic group).

Approximate position (cm.⁻¹) of bands:

	A.	B.
R'·CO·NH ₂	1655	1630
R'·CO·NHR	1640	1560
R'·CO·NHR _e	1660—1680	1530—1570

FIG. 6.

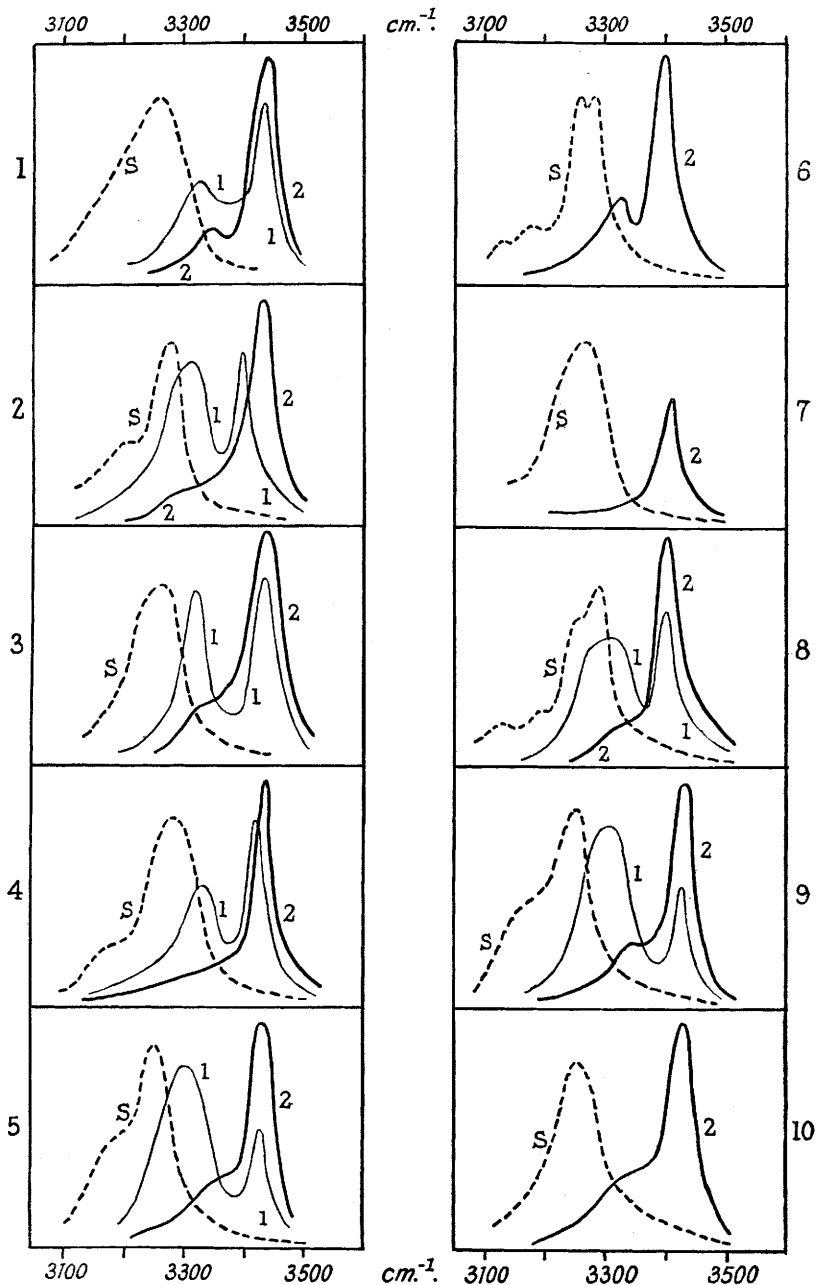


It can be seen that in the solid state the unsubstituted amides show the A band at about 1655 cm.⁻¹, and the *N*-alkyl-substituted amides at about 1640 cm.⁻¹, in both cases a noticeable decrease from the values found (Table I) for the solutions in dioxan. With the *NN*-disubstituted amides, either liquid or solid, there is little change in the frequency of this band on passing from the liquid or solid to the solution, although the band may broaden. With the solid *N*-alkylamides a fairly strong band appears at about 1560 cm.⁻¹, corresponding to that at 1530 cm.⁻¹ with solutions in dioxan.

The increase in frequency of the A band of the solids when the *N*-substituent is electrophilic is parallel to the change found with the solutions. It may also be noted that when this band is raised in frequency by the electrophilic substituent, the band normally at 1560 cm.⁻¹ is generally lowered. Finally, the relative intensity of the bands A and B appears to alter with the change of state, the latter usually becoming stronger with the solid.

Gradual Transitions from Solid or Liquid to Dilute Solution.—Several examples have been examined of the changes associated with the transition from the solid or liquid amide to a very dilute solution, through intermediate concentrations of the solute. Some of the results are shown in Fig. 5 for *n*-hexoamide, phenylacetomethylamide, and methyl phenylacetamidoacetate in chloroform. Some of bands shown are connected with groups with which we are not immediately concerned; for example, that at 1750 cm.⁻¹ due to the carbonyl group of the ester. The main point to notice is that in every case the passage from the solid (or liquid) to the dilute solution brings about an increase in the frequency of the band A and a simultaneous decrease in the frequency of the band B. Thus with hexoamide, the

FIG. 7.



1. Phenylacetomethylamide.
2. Phenylaceto-*tert*-butylamide.
3. Phenylaceto-*n*-propylamide.
4. Phenylaceto-*tert*-amylamide.
5. Phenylacetocyclohexylamide.

6. Phenylacetanilide.
7. Phenylaceto-*o*-toluidide.
8. Phenylaceto-*p*-toluidide.
9. Phenylacetamidomethyl cyanide.
10. Methyl phenylacetamidoacetate.

s. Solid. 1. Conc. soln. in CHCl_3 . 2. Dil. soln. in CHCl_3 .

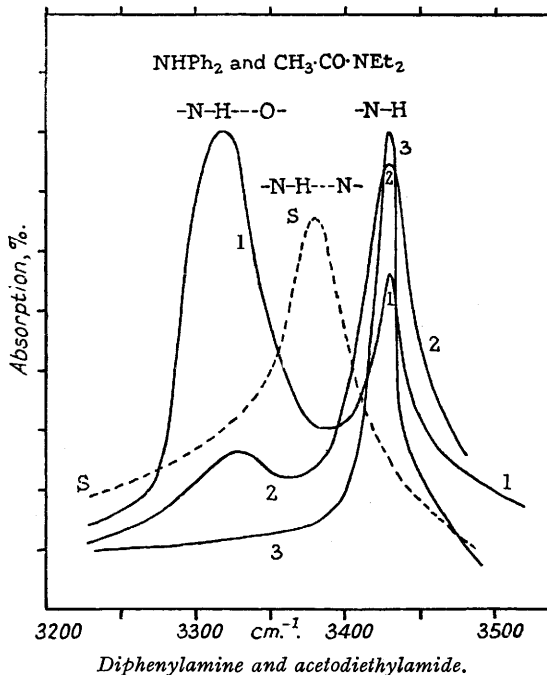
solid has the bands at 1655 and 1635 cm^{-1} , in concentrated solution they lie at 1668 and 1615 cm^{-1} , and in dilute solution at 1680 and 1595 cm^{-1} . With methyl phenylacetamidoacetate the solid has bands at 1642 and 1557 cm^{-1} , the liquid (at 100°) at 1660 and 1535 cm^{-1} , and the solution in chloroform at 1672 and 1517 cm^{-1} . (The band at about 1750 is due to the carbonyl link in the ester group.)

The region of 3μ . The spectra of many unsubstituted and *N*-substituted amides have been measured between 3000 and 3600 cm^{-1} , as solids and also as solutions in chloroform. The curves are shown in Figs. 6 and 7. With substances containing phenyl radicals, there is usually a band near 3070 cm^{-1} connected with a vibration of the aromatic C-H linkages, but this is not significant for our present purpose. Dilute solutions of the unsubstituted amides appear to have two sharp bands at about 3400 and 3520 cm^{-1} , which give place in the solids to two others at about 3180 and 3350 cm^{-1} . In concentrated solutions all four bands may appear simultaneously.

In dilute solutions, the *N*-monosubstituted amides have one sharp band at about 3430 cm^{-1} which gives place in the solid to a broader band at about 3270 cm^{-1} . In concentrated solutions the latter band seems to appear at frequencies rather higher than 3270 cm^{-1} , and can be found concurrently with the sharp band near 3430 cm^{-1} .

In connexion with the possible interpretation of these bands and shifts, we have examined the spectra of diphenylamine in dilute solution in carbon tetrachloride and as a solid, and also of solutions of diphenylamine to which acetodiethylamide had been added. This experiment is a variant on that

FIG. 8.



- s. Solid diphenylamine.
1. 2 G. diphenylamine + 1 c.c. acetodiethylamide : 25 c.c. CCl_4 , 0.1 mm. thick.
 2. 2 G. diphenylamine + 1 c.c. acetodiethylamide : 500 c.c. CCl_4 , 2.0 mm. thick.
 3. 2 G. diphenylamine + 1 c.c. acetodiethylamide : 5000 c.c. CCl_4 , 2 cm. thick.

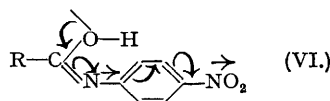
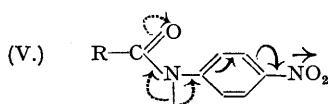
previously described by Buswell, Downing, and Rodebush (*loc. cit.*). The results are depicted in Fig. 8. It can be seen that the dilute solution of diphenylamine has the N-H stretching vibration band at 3430 cm^{-1} , but in the solid state this is replaced by the broader association band at 3320 cm^{-1} . Similar N-H---N association has been recorded with ethyleneimine (Thompson and Harris, *J.*, 1944, 301). When the acetodiethylamide is added to the solution of diphenylamine, the band at 3430 cm^{-1} is diminished in intensity and a new band appears at 3320 cm^{-1} . This change corresponds to the formation of N-H---O bridges. As the mixture of diphenylamine and acetodiethylamide is diluted, the association band at 3320 cm^{-1} is much diminished whilst the normal N-H frequency at 3430 cm^{-1} is strengthened. This phenomenon is markedly parallel to that seen in Fig. 7 for the *N*-substituted amides.

DISCUSSION.

The results described above show that the vibration frequencies exhibited by amides are much affected by the change of state from solid to solution. It will be convenient first to consider the spectra of solutions before discussing the shifts which occur on passing to the solids.

As already stated, a simple *N*-monosubstituted amide could exist as either the ketonic (I) or the enolic (II) form, each of these being capable of hybridisation with its corresponding dipolar structure, (III) and (IV), respectively. The band A of *NN*-disubstituted amides which occurs at about 1650 cm^{-1} must be attributed to the stretching vibration of the C=O bond, since

no enolisation of the conventional type can occur. The lower value as compared with that in ketones—about 1710 cm.^{-1} —will result from the resonance with the ionic form. In the case of the simple or *N*-monosubstituted amides the band A could be interpreted in the same way. In this case, however, enolisation would lead to some form of $\text{C}=\text{N}$ link, and it is well known from the Raman spectra of ketoximes that this can give rise to a band in the region $1650\text{--}1660\text{ cm.}^{-1}$ (Hibben, "The Raman Effect," p. 280). Now the above measurements with the amides having a strongly electrophilic *N*-substituent provide an argument against this correlation of the band A with the vibration of a $\text{C}=\text{N}$ bond, as follows. If the amide has the ketonic form, the presence of strongly electrophilic groups on the nitrogen atom should cause the dipolar form (III) to be less stable relative to the non-polar form (I). Alternatively, the electron-attracting groups can be regarded as opposing the conjugation from the nitrogen atom to the carbonyl group, as in



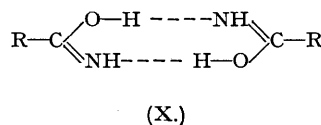
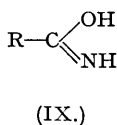
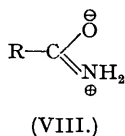
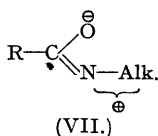
(V). In these circumstances the carbonyl group will be expected to have greater double-bond character, and a rather higher stretching-vibration frequency, which is in fact found. If the molecule existed in the enolic form, however, the converse would apply. An electrophilic substituent on the nitrogen atom would then favour the dipolar form, shown by (VI), and the double-bond character of the $\text{C}=\text{N}$ bond would be lowered.

It therefore seems satisfactory to attribute the band A in the amides as a whole to the stretching vibration of the essentially ketonic carbonyl group. In connexion with these arguments it is interesting to consider the effect of *N*-alkyl substituents upon the frequency of the band A. The results of Table I and Fig. 1 suggest that these groups have an opposite effect to those groups which are known to be electron-attracting. Now, alkyl groups are known to be readily polarisable (Ingold, *Chem. Reviews*, 1934, 15, 238), that is, they can provide or accept electrons according to the particular group to which they are attached. This is well illustrated by the values for the dipole moments of some simple compounds quoted by Watson ("Modern Theories of Organic Chemistry," 2nd edition, p. 93), and listed in Table IV. It is possible,

TABLE IV.
Dipole moments of compounds RX.

R/X =	Cl.	Br.	I.	CN.	NO_2 .	OH.
H	1.03	0.78	0.38	2.93	—	1.84
CH_3	1.87	1.80	1.64	3.94	3.54	1.69
C_2H_5	2.05	2.01	1.87	4.04	3.58	1.69

therefore, that in the alkyl-substituted amides the fractional positive charge on the nitrogen atom is shared by the alkyl group. In other words, the energy of the charge separation in (VII)



is lower than in (VIII). In that case, the relative contribution of (VII) to the hybrid will be greater than that of (VIII), so that the carbonyl group will have less double-bond character and a lower vibration frequency in the alkyl derivatives.

The interpretation of the band B found between 1520 and 1630 cm.^{-1} with the unsubstituted and *N*-monosubstituted amides is more difficult. It might be explained in four ways, namely, (i) as the stretching vibration of the $\text{C}-\text{N}$ link in a ketonic form, if this bond has acquired considerable double-bond character due to resonance with the dipolar form; (ii) as the stretching vibration of the $\text{C}=\text{N}$ link in an enolic form, reduced in frequency by resonance with its dipolar structure; (iii) as a bending frequency of the $\text{N}-\text{H}$ link; or (iv) as an overtone or combination band. As already explained, the band is not observed with disubstituted amides where there will certainly be contributions from the dipolar form. Also, the degree of double-bond character required to produce such a high frequency seems much greater than is plausible from the molecular bond lengths found in some solid amides such as acetamide (Senti and Harker, *loc. cit.*). These arguments make the first interpretation improbable.

The assignment of the band B to the $\text{C}=\text{N}$ link of an enolic form would imply the simultaneous existence of both ketonic and enolic forms both in solution and in the solid state. The X-ray measurements have shown, however, that in the solid state only the ketonic form is present. Further, in no case is the shift produced by the substitution of an electron-attracting group by an alkyl group consistent with this interpretation. Also, the band B increases in frequency on passing from the solution to the solid. This is contrary to what would be expected if this change were accompanied by the formation of bridged links in passing from (IX) to (X).

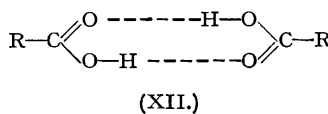
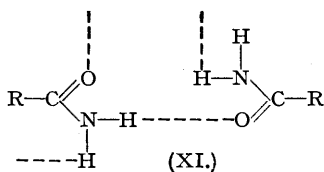
Finally, if an amide were to exist as a mixture of the ketonic and the enolic form, samples from different sources and recrystallised from different solvents would be expected to show different proportions of the two forms. In no case have such variations been detected.

The possibility that the band B is due to an overtone cannot be ruled out, but it is improbable. The band varies in intensity in different compounds, but with the *N*-monosubstituted derivatives it is usually stronger than might be expected for anything but a fundamental. Experiments with deuterated compounds might help to settle this question.

The third possibility seems to us the most reasonable. It explains the absence of the band in the disubstituted amides, and the shift of the band B in passing from the solid to solution—namely, a decrease in frequency—agrees with that expected of a bending mode of the *N*-H link if the latter takes part in hydrogen bridges in the solid state. The difference between the band B in unsubstituted amides on the one hand, and *N*-monosubstituted amides on the other, can be explained by interaction between the two *N*-H bonds in the former case. Hence, it seems that in dilute solution in dioxan, the amides exist predominantly in the ketonic form.

The results of Table II illustrate the effect of solvent on the stretching frequency of the carbonyl group. This may be due to two causes, namely, the difference in dielectric constant of the medium, or the effect of hydrogen bonding from the solvent to the carbonyl group of the amide. The energy of the charge separation in (VII) or (VIII) might be lowered by an increase in the dielectric constant of the medium, and the stretching frequency of the carbonyl group would then be expected to lie at lower values than in a medium of low dielectric constant. In methyl cyanide, however ($\epsilon = 37.5$), the frequency of the carbonyl group is substantially the same as in dioxan ($\epsilon = 2.2$), so this influence of dielectric constant cannot be very significant. On the other hand, solvation by hydrogen bonding to a carbonyl group lowers the frequency of the latter. With acetone in carbon tetrachloride solution, it lies at 1710 cm.^{-1} , but in methyl alcohol at 1701 cm.^{-1} . It is therefore possible that the changes shown in Table II are caused by a change in hydrogen bonding from the solvent to the carbonyl group.

In the solid state, the stretching frequency of the carbonyl group in an unsubstituted or *N*-monosubstituted amide lies at a much lower value than in dilute solution in dioxan, whilst the band B lies at higher values. Our own measurements, and those of Gordy (*J. Chem. Physics*, 1939, 7, 163) show, as just outlined, that the frequency of the carbonyl group is reduced by hydrogen bonding. Since the X-ray measurements indicate that acetamide exists in a



polymeric form (XI), it is evident that the bonding will lower the frequency of the carbonyl group. Moreover, in such polymers, the strength of the hydrogen bridges will be increased by the presence of a greater positive charge on the nitrogen atom, or a greater negative charge on the oxygen atom, and therefore by an increase in the contribution of the dipolar structure to the hybrid. It follows that in the associated form of the amides the carbonyl link will have a smaller double-bond character than in the unassociated form, and hence a lower frequency of vibration. The *NN*-disubstituted amides, which cannot undergo such association, show no such shifts of the frequency with change of state.

That this association has a powerful effect on the stretching vibration frequency of the carbonyl group is further borne out by our measurements on acetic acid and phenylacetic acid in the liquid and in the solid state, where the substances are known to exist as dimers of the type (XII). With liquid acetic acid the band lies at 1712 cm.^{-1} , and with solid phenylacetic acid there is a double band at $1704\text{--}1692 \text{ cm.}^{-1}$. A dilute solution of acetic acid in dioxan, however, shows bands at 1730 and 1753 cm.^{-1} , which may correspond to the dimeric and the monomeric

form. Herman and Hofstadter (*J. Chem. Physics*, 1939, 7, 460) have similarly shown that in the vapour state the frequencies of the carbonyl group in dimeric and monomeric aliphatic acids lie at about 1740 and 1770 cm^{-1} , so the shift is about 30 cm^{-1} . In dioxan, phenylacetic acid shows one sharp band at 1735 cm^{-1} , and the shift in passing from the dimer to the monomer is therefore closely parallel to that found with amides in passing from solutions in dioxan to the solid state.

If this interpretation of the shift is correct, we might expect that in concentrated solutions of the amides, the co-existence of both unassociated and associated forms might give rise to two frequencies of the carbonyl group, and there is some evidence to support this. The curves of Fig. 5 show that the band due to the carbonyl group is broad with concentrated solutions of hexoamide and phenylaceto-*tert.*-butylamide, and there are signs of a double band. Dilute solutions of hexoamide in chloroform show three bands at 1595 (strong), 1615 (weak), and 1678 (strong and sharp), whereas with concentrated solutions the bands are at 1595 (weak), 1615 (strong), and 1668 (strong and broad). This suggests that in concentrated solutions the dimers giving rise to 1615, 1668 predominate, whilst in dilute solutions the monomer (1595, 1678) is in excess. Two amides were examined as liquids at temperatures above their melting point, and the bands A and B were displaced to positions intermediate between those found for the solids and for the solutions, and were also broad suggesting the presence of more than one species.

To sum up, therefore, the bands in the region 5—7 μ suggest that amides have the ketonic structure, resonating with its corresponding bipolar form. In dilute solution in dioxan and chloroform the amides appear to be monomeric, but in more concentrated solutions in chloroform, and in the liquid state, association occurs. In the solid state this association is complete.

In the region of 3 μ we should expect to find absorption bands due to the stretching vibration of N-H links, and of O-H links if present. In dilute solutions, the unsubstituted amides show sharp bands at about 3400 cm^{-1} and 3520 cm^{-1} , which might at once be correlated with the symmetrical and antisymmetrical vibrations of the NH_2 group in an unassociated form. On the other hand, the band at 3520 cm^{-1} might be assigned to the O-H link of an enolic form. However, the frequency due to the unassociated hydroxyl link in a large number of alcohols and phenols lies between 3610 and 3680 cm^{-1} , and with fatty acids at about 3550 cm^{-1} . We might therefore expect the unassociated hydroxyl band in an enolized amide to lie at about 3600 cm^{-1} . Only in the case of trichloroacetic acid (Buswell, Rodebush, and Roy, *J. Amer. Chem. Soc.*, 1938, 60, 2239) does this band lie at a frequency as low as 3520 cm^{-1} , and in this case the O-H link must certainly be weaker than in the amide. Hence it is unlikely that the amide band at 3520 cm^{-1} could be due to the hydroxyl group, and the explanation given at the start is to be preferred.

In very dilute solution, the *N*-monosubstituted amides show one band at 3420—3440 cm^{-1} . This low value cannot possibly be due to an enolic O-H group, and lies as expected between the two frequencies of the unsubstituted amides. *NN*-Disubstituted amides show no absorption in this region.

In the solid state, the unsubstituted amides have strong bands at about 3180 and 3350 cm^{-1} , which are plausibly interpreted as being due to two bonded N-H groups of a polymeric complex such as was indicated above. In the concentrated solutions, illustrated for hexoamide in Fig. 6, both the association bands at 3180, 3350 cm^{-1} , and the unassociated N-H bands at 3400, 3520 cm^{-1} appear simultaneously.

N-Monosubstituted amides have one band only in the solid state, at 3270 cm^{-1} , which again corresponds to a bonded N-H group. Here too, in concentrated solutions, both the association band and the "normal" band at 3430 cm^{-1} are simultaneously present. In these cases the association band appears to shift gradually towards higher frequencies and has a diminishing intensity as the dilution is increased, which would imply some gradual weakening of the bonding strength.

This interpretation of the bands of *N*-monosubstituted amides near 3 μ is supported by the measurements already described with diphenylamine and acetodiethylamide. These showed that the unbonded N-H link in diphenylamine has a frequency of 3430 cm^{-1} , and the strongly bonded N-H -- O group has a frequency of 3320 cm^{-1} . These values fall exactly into line with those for the unsubstituted amides.

It seems, therefore, that the spectroscopic data in both the regions, 3 μ and 6 μ , indicate the existence of the amides in the ketonic form, which associates through N-H -- O bonds in concentrated solutions, in the liquids and in the solids. This preliminary survey will be useful in our later consideration of the more complex amides, amino-acids, and peptides.

We thank the Government Grant Committee of the Royal Society for a grant in aid of equipment, and the Department of Scientific and Industrial Research for a Maintenance Grant to one of us. We are also pleased to record appreciation of some valuable discussions which one of us had with workers at the University of Michigan, and at the Shell Development Company, Emeryville, during 1945, on the above and related problems.

THE PHYSICAL CHEMISTRY LABORATORY,
OXFORD UNIVERSITY.

[Received, November 6th, 1946.]
