

By observing the following precautions, hydrolytic decompositions have been prevented: avoid excess base; keep solutions cool during mixing; avoid long contact of salt with mother liquor; recrystallize from dioxane.

The melting points of twenty-two of the salts prepared lie between 140 and 170°. There is not sufficient diversity to make these salts satisfactory derivatives of general application. Mixtures of salts with identical or nearly identical melting points produce depressions of 5 to 9°. They do offer advantages over S-benzylthiuronium salts in making certain distinctions; formate from butyrate, for example.

Analyses of the salts by the Kjeldahl method show good agreement with the calculated values.

#### I. ALIPHATIC SALTS

	M. p. cor., °C.		M. p. cor., °C.
Acetate	140	Oxalate	194
Butyrate	139	Palmitate	146
Caproate	143	Propionate	143
Formate	148	Succinate	167
Monochloroacetate	158	Trichloroacetate	148
Oleate	131	Valerate	142

#### II. AROMATIC SALTS

Benzene sulfonate	184	<i>m</i> -Iodobenzoate	154
Benzoate	155	<i>p</i> -Iodobenzoate	177
<i>o</i> -Bromobenzoate	165	Phthalate	166
<i>m</i> -Bromobenzoate	161	Salicylate	162
<i>p</i> -Bromobenzoate	172	Sulfosalicylate	181
<i>o</i> -Chlorobenzoate	159	<i>o</i> -Toluate	150
<i>m</i> -Chlorobenzoate	157	<i>m</i> -Toluate	151
<i>p</i> -Chlorobenzoate	173	<i>p</i> -Toluate	161
Cinnamate	167	<i>p</i> -Toluenesulfonate	193
<i>o</i> -Iodobenzoate	162		

#### Summary

*p*-Chlorobenzyl pseudothiuronium chloride has been prepared and used as the reagent in the preparation of *p*-chlorobenzyl pseudothiuronium salts of organic acids.

The melting points of the salts of thirty-one organic acids have been recorded.

Dioxane has been found to be a satisfactory solvent for the recrystallization of these salts.

PORTLAND, OREGON

RECEIVED AUGUST 7, 1939

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## Infrared Absorption Studies. IX. Bonding of Hydrogen in Nitrogen Compounds

BY A. M. BUSWELL, J. R. DOWNING AND W. H. RODEBUSH

The behavior of hydroxyl hydrogen has been treated at length in previous publications by ourselves and by other authors. In organic molecules the hydrogen of hydroxyl is usually sufficiently active to show bonding (association, chelation or perturbation) with oxygen, hydroxyl or other basic groups. The hydroxyl group is active in the infrared, showing a strong absorption usually in the neighborhood of 2.75  $\mu$ . When association or chelation takes place, this absorption is increased markedly and shifted to the neighborhood of 3.0  $\mu$ , the extent of the shift and the breadth of the resulting band depending to a considerable extent upon the particular molecules involved. Enolization, for example, is nearly always the result, rather than the cause, of such bonding. With a few exceptions, therefore, the behavior of hydroxyl hydrogen is easily followed by the infrared absorption and definite statements can be made as to whether the hydrogen is bonded or not.

As a matter of fact, little doubt need usually be felt as to the exceptions mentioned above. Certain alcohols show a somewhat lower hydroxyl

frequency (longer wave length) than is customary. Examples are given in Figs. 1 and 2. The hydroxyl in benzoin shows an absorption at 2.87  $\mu$  under circumstances where there seems to be no question of association or chelation. This displacement must be due to the phenyl group but other factors may be involved.

One peculiar case has been discussed elsewhere. Wulf<sup>1</sup> and his collaborators investigated the *cis* monoxime of benzil and found the second harmonic present contrary to the predictions from the assigned structure. So far as the infrared is concerned the two compounds might be identical and both molecules show evidence of association with increasing concentration. As might have been expected, we have verified the results of Wulf that no chelation occurs.

In a previous publication<sup>2</sup> we have presented results of our investigation of association in the acid amides and oximes. Those compounds in which the hydrogen attached to nitrogen is acidic,

(1) G. E. Hilbert, O. R. Wulf, S. B. Hendricks and U. Liddell, *THIS JOURNAL*, **58**, 548 (1936).

(2) A. M. Buswell, W. H. Rodebush and M. F. Roy, *ibid.*, **60**, 2444 (1938).

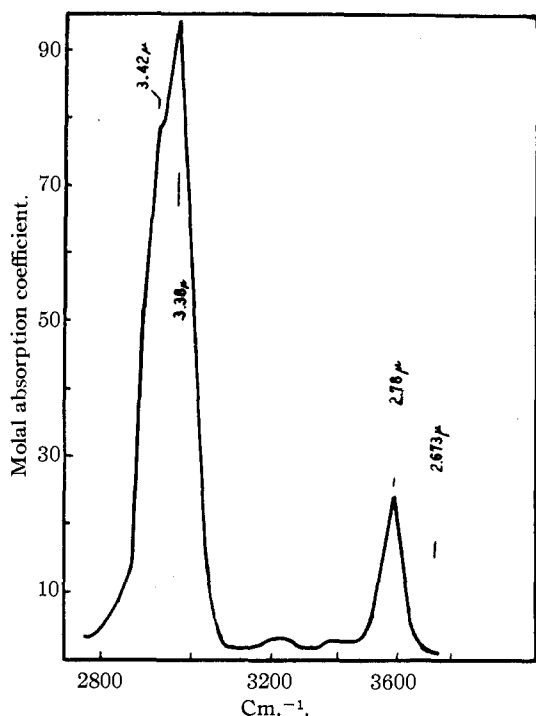


Fig. 1.—Pivaloin in carbon tetrachloride: 0.016 *M* in 1.262-cm. cell.

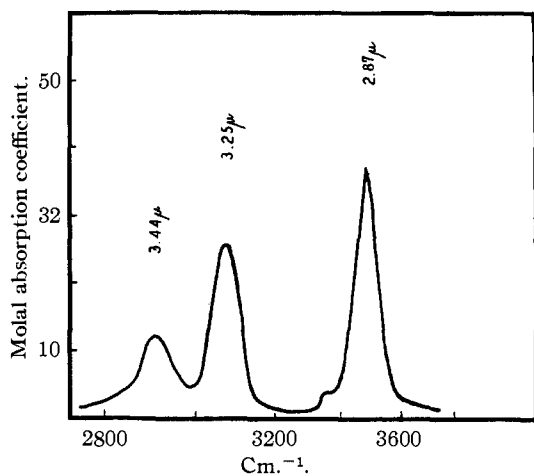


Fig. 2.—Benzoin in  $\text{CCl}_4$ : 0.016 *M* in 1.262-cm. cell.

as for example the acid amides, show a very strong tendency toward association, greater perhaps even than the alcohols. It was not possible to deduce with certainty in the case of these substances whether the intermolecular association was the result of  $\text{N-H} \rightarrow \text{N}$  or  $\text{N-H} \rightarrow \text{O}$  bonding and in some cases at least there was strong reason to believe that the hydrogen might have shifted to the oxygen in the process of association.

In order to settle the questions suggested above,

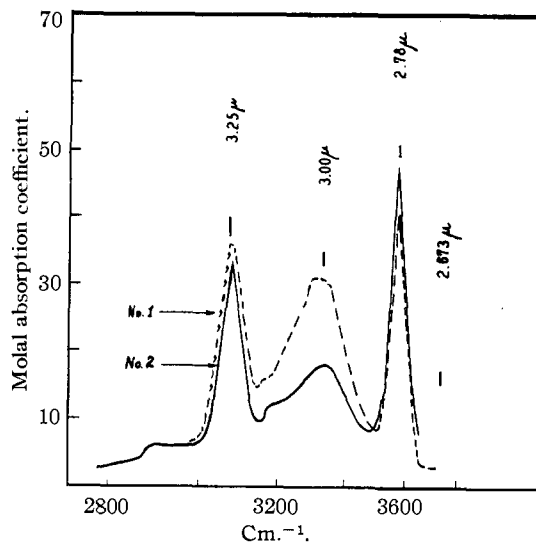


Fig. 3.—*trans* Benzil monoxime in  $\text{CCl}_4$ : (1) 0.008 *M* in 2.532-cm. cell; (2) 0.002 *M* in 10.180-cm. cell. Identical curves are obtained for the *cis* isomer.

it would be desirable to study nitrogen compounds which do not contain oxygen. Naturally the amines would be the first to be considered. These compounds, however, have proved to be very disappointing as material for infrared study. In the first place the more basic amines show very little absorption due to hydrogen. This low absorption coefficient appears to characterize the N-H bond in the more basic nitrogen compounds. One may assume therefore that the dipole moment of the N-H bond in these molecules is small. The small dipole moment may be taken as an indication that the linkage of hydrogen to nitrogen is largely covalent rather than ionic in character. Since we have assumed elsewhere<sup>3</sup> that the formation of a hydrogen bond involves a transformation of the bond character toward the ionic type, we may therefore anticipate little tendency toward hydrogen bond formation in the more basic types of nitrogen compounds. Even aniline shows no evidence of bonding in the pure liquid (Fig. 4). The absorption at 3.09  $\mu$  is apparently present at all concentrations. Liquid aniline has a dielectric constant about the same as liquid acetic acid. The latter substances exist largely in the form of dimers of zero dipole moment but there is no reason to suppose that aniline can form a closed dimer. There is some evidence from other sources<sup>4</sup> of a slight association in aniline but there

(3) W. H. Rodebush and A. M. Buswell, *J. Phys. Chem.*, **43**, 219 (1939).

(4) M. J. Copley, G. T. Zellhoefer and C. S. Marvel, *THIS JOURNAL*, **60**, 2666 (1938).

is certainly no strong tendency as exists for example in the alcohols.

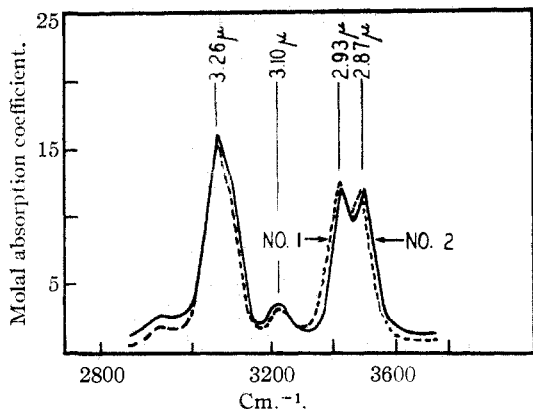


Fig. 4.—Aniline (in  $\text{CCl}_4$ ): (1) 0.64  $M$  in 0.158-cm. cell; (2) 0.01  $M$  in 10.180-cm. cell.

One must assume that in the case of N-H the tendency toward bonding is small; the shift in frequency when a bond is found likewise small according to the rule of Venkateswaran and the increase in absorption is not comparable to that observed with O-H. Hence for all these reasons we do not expect to find a strong absorption characteristic of  $\text{N-H} \rightarrow \text{N}$  or  $\text{N-H} \rightarrow \text{O}$  bonding. The foregoing postulates will constitute the basis for some of our significant conclusions later on in this paper.

Since the tendency of aniline toward association appears non-existent it seemed desirable to investigate the tendency of *o*-nitroaniline toward chelation and in particular the acetanilide derivatives where an activation of the hydrogen sufficient to produce bonding might be expected. Acetanilide is itself only slightly soluble in carbon tetrachloride, as might be expected from its similarity to acetamide. *o*-Nitroacetanilide, on the other hand, is fairly soluble and shows no change in absorption with concentration. One must believe, therefore, that its tendency toward association is slight and that this is due perhaps to chelation since the N-H absorption is fairly strong and occurs at  $2.96 \mu$  (Fig. 5). One must, of course, consider the question as to whether this is N-H absorption at all. The molecule in question may enolize in two ways. Only one of these could lead to chelation but the  $2.96 \mu$  frequency is more nearly what we would expect from an  $\text{OH} \rightarrow \text{N}$  bond. On the other hand, we must recognize that the rule of Venkateswaran predicts a small shift and a narrow absorption band for an inactive

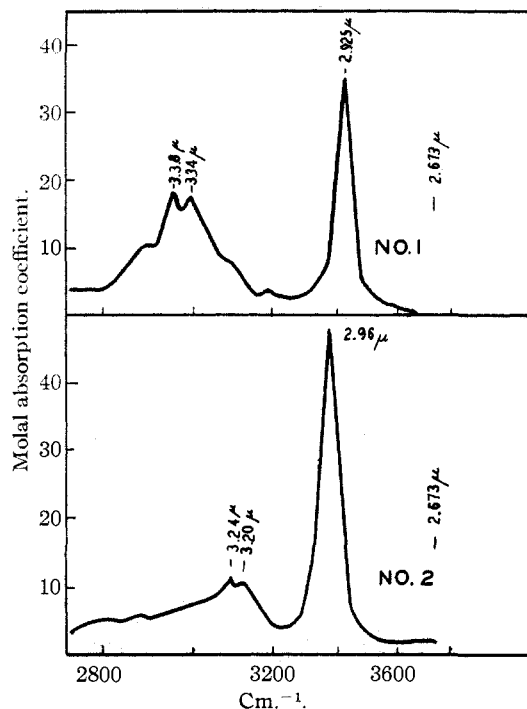


Fig. 5.—(1) 6-Methyl-2-nitroacetanilide (in  $\text{CCl}_4$ ): 0.004  $M$  in 5.070-cm. cell; (2) 2-nitroacetanilide (in  $\text{CCl}_4$ ): 0.128  $M$  in 0.158-cm. cell.

hydrogen. When the hydrogen of chloroform<sup>5</sup> is bonded, for example, the shift is scarcely observable but a considerable increase in absorption is noted. So here the N-H absorption of acetanilide is about  $2.89 \mu$  and the shift to  $2.96 \mu$  with increased absorption may well be taken as evidence for chelation. This conclusion seems more necessary when we consider the case of 2-nitro-6-

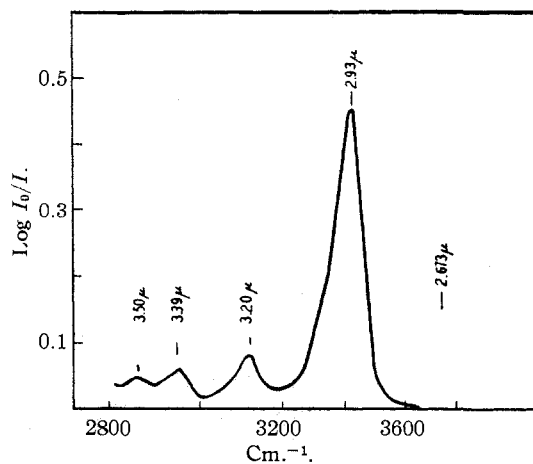


Fig. 6.

(5) A. M. Buswell, W. H. Rodebush and M. F. Roy, *THIS JOURNAL*, **60**, 2528 (1938).

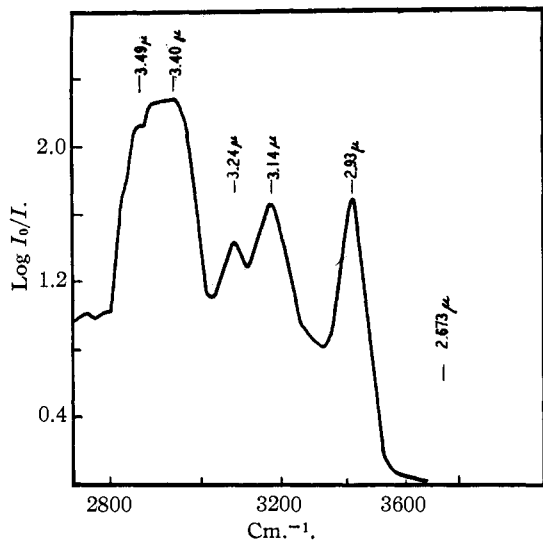


Fig. 7.—50% pyrrole-50% di-*n*-butylamine in  $\sim 0.005$ -cm. cell.

methyl-acetanilide. Chaplin and Hunter<sup>6</sup> have collected a great deal of evidence to show that the methyl derivative is not chelated, presumably because of steric effects between the methyl group and the acetyl group. Certainly the high melting point and low solubility of the methyl derivative argue for association in the solid state into large polymers. The N-H frequency is shifted only a little from that of acetanilide and its absorption is not much stronger so that we assume there is only a slight tendency toward chelation. On the other hand, the obvious absence of association both in the solid state and in solution in the case of *o*-nitroacetanilide seems to have no other explanation than chelation. Acetanilide itself must be strongly associated in the crystalline phase since it is slightly soluble. N-Methylacetanilide shows considerable increase in solubility and in its basic properties presumably because of the disappearance of this association.

Two nitrogen compounds which contain a hydrogen of sufficient activity to form bonds are hydrogen azide and pyrrole.<sup>7</sup> The first of these will be discussed in detail elsewhere. Neither compound shows much tendency toward association. Liquid pyrrole has an absorption at  $2.93 \mu$  whereas in dilute solution the absorption is at  $2.85 \mu$ . With basic substances such as pyridine or dibutylamine, however, an absorption at  $3.11 \mu$  and  $3.14 \mu$ , respectively, can be attributed definitely to N-H  $\rightarrow$  N bonding between molecules.

(6) H. O. Chaplin and L. Hunter, *J. Chem. Soc.*, 375 (1938).

(7) O. R. Wulf and U. Liddell, *THIS JOURNAL*, **57**, 1464 (1935).

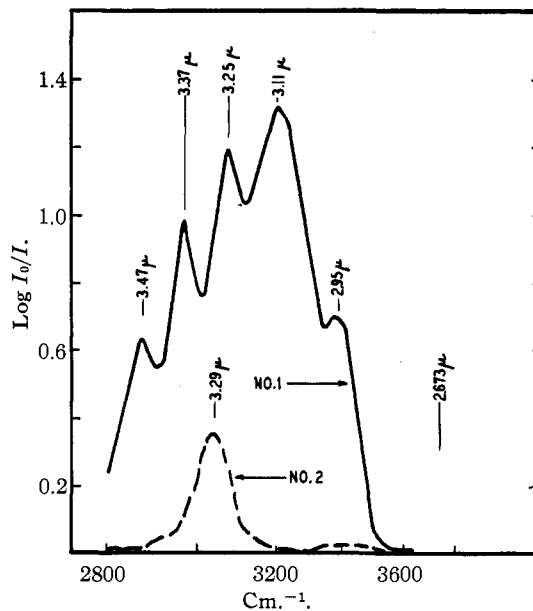


Fig. 8.—(1) 50% pyrrole-50% pyridine in  $\sim 0.005$ -cm. cell; (2) pyridine in  $\sim 0.005$ -cm. cell (half size).

This is characteristic of pyrrole only, however. Hydrogen azide has its fundamental frequency at  $3.03$  instead of  $2.85 \mu$  and the bonded frequency is shifted by a correspondingly greater amount. Each nitrogen compound therefore appears to be a law unto itself. Bonding takes place only when the hydrogen has somewhat of an acidic character and the shift in frequency is itself a variable quantity.

**The Protein Problem.**—In a previous publication we showed<sup>2</sup> that certain of the amides on association show an absorption similar to gelatine and that this absorption is characteristic of the linkage  $R-C-N-R$ . If this linkage is continued it



becomes identical with the peptide linkage. We suspect that the peculiar absorption noted in this type of molecule will be found characteristic of many of the proteins and will give information as to the cross linkage of the proteins through hydrogen bonding.<sup>8</sup> As a preliminary to this we have worked with various polypeptides, diketopiperazines, etc. The difficulties of solubility make it clear that this problem can be continued only by working with the crystalline material and we are developing the technique of measuring the absorption of thin crystalline films. Meanwhile we have prepared one or two dipeptides of sufficient solubility to obtain absorption curves. In

(8) L. Pauling and C. Niemann, *ibid.*, **61**, 1860 (1939).

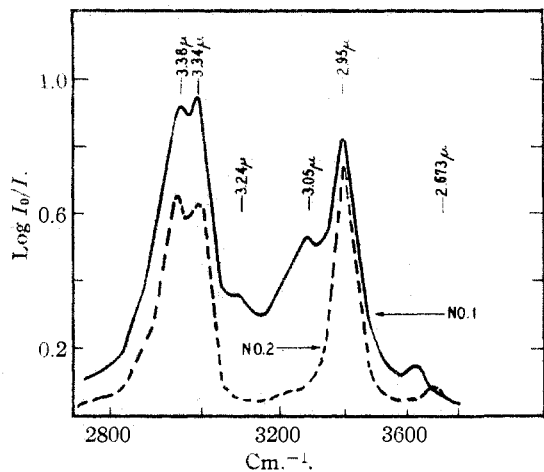
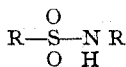
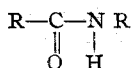


Fig. 9.—Glycyglycine ethyl ester (in  $\text{CCl}_4$ ): (1) satd. soln. ( $\sim 0.05 M$  in 0.640-cm. cell); (2) 0.008  $M$  in 2.532-cm. cell.

Fig. 9 the curves for glycyglycine ethyl ester show, as might of course be expected, a behavior very similar to the monosubstituted amides. The most characteristic thing about this absorption is the appearance at higher concentrations of a strong absorption a little beyond  $3.0 \mu$  which by its location and intensity suggests a bonded O-H rather than N-H. Since the possibility of enolization exists in all the compounds studied so far, we were anxious to investigate a compound where enolization could not occur. A promising compound in this respect is a sulfonamide and in Fig. 10 are shown curves obtained upon the benzenesulfonamide of cyclohexylamine. It is obvious at once that this molecule shows the striking behavior on association that is characteristic of the monosubstituted amides. Organic chemists believe that there is no possibility of enolization in the group



and there is of course no indication from infrared data that such enolization occurs in the single molecule. When association occurs, however, there is the same possibility of intermolecular enolization that exists with the group



At first thought it would appear strange that the hydrogen should be transferred to the oxygen but it must be remembered that the nitrogen in this molecule is almost exactly like the nitrogen of sulfamic acid. Sulfamic acid is a strong mono-

basic acid and in liquid ammonia becomes a dibasic acid. One must therefore assume that the NHR group is very acidic and that the possibility of intermolecular enolization has not been eliminated. It is hoped by further study to determine the exact mechanics of association which produces this type of absorption.

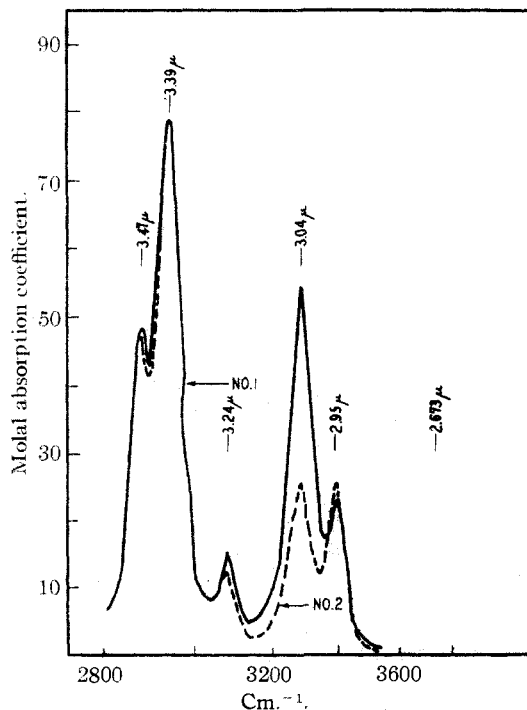


Fig. 10.—Benzenesulfonamide of cyclohexylamine (in  $\text{CCl}_4$ ): (1) 0.008  $M$  in 2.532-cm. cell; (2) 0.002  $M$  in 10.180-cm. cell.

### Summary

An extensive study of nitrogen compounds has been made in the region of the fundamental absorption of the N-H group. It is found that the absorption due to the N-H group is distinctly weaker than for the O-H group and there is a much greater variability in the characteristic frequency. Infrared absorption is a less reliable criterion for bonding of hydrogen attached to nitrogen than for hydrogen attached to oxygen. There is no positive proof of association involving the formation of  $\text{N}-\text{H} \rightarrow \text{N}$  bonds but there is a strong tendency toward association if the hydrogen is somewhat acidic. The characteristic absorption produced by association of molecules containing the peptide linkage may be due to an enolized hydrogen.