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Evidence for Intramolecular Hydrogen Bonding in Aryl Allophanates and Alkyl or Aryl–Alkyl Biurets

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The near infrared absorption spectra of 1-ethyl-3-phenylurea, 1-methyl-1,3-diphenylurea, 1,1,3-triethylurea, ethyl carbanilate, *p*-chlorophenyl and *p*-methoxyphenyl carbamate show a strong absorption band in the region of 6750 cm.$^{-1}$. The band is not exhibited by ethyl α,γ-diphenylallophanate, ethyl α,p-chlorophenyl-γ-phenylallophanate, ethyl α,p-methoxyphenyl-γ-phenylallophanate, 1,3,5,5-tetraethylbiuret and 1-phenyl-3,5,5-triethylbiuret. It is proposed that the absence of this band is due to the presence of an intramolecular hydrogen bond.

Although examples of intramolecular hydrogen bonding in compounds containing an OH group have been demonstrated by means of near infrared spectra studies,[1] no use has been made of this method of investigation for determining intramolecular hydrogen bonding in molecules containing the NH group.

The hydroxyl group has an absorption band in the region of 7000 cm.$^{-1}$ when no intramolecular hydrogen bonding is expected.[2] This represents the first overtone of the fundamental stretching vibration of the OH group. Hilbert, Wulf, Hendricks and Liddel[3,4] found that absorption in this region is absent for a large number of compounds which have configurations that favor the formation of the intramolecular hydrogen bond. They found absorption was present in related compounds, the configuration of which excluded possible formation of such a bond; *e.g.*, in *o*-nitrophenol, absorption in the 7000 cm.$^{-1}$ region is absent, but it is present in *m*- and *p*-nitrophenol.

Correspondingly, the NH group has an absorption band in the region of 6700–6800 cm.$^{-1}$ which has been correlated with the first harmonic of the fundamental NH stretching vibration at 3500 cm.$^{-1}$.[5] We now have found that intramolecular hydrogen bonding can be detected by means of near infrared absorption spectra in α,γ-diaryl allophanates and in *unsym*-aryltrialkyl and *sym*-tetraalkyl biurets.

The aryl and alkyl ureas and aryl carbamates that we have examined exhibited strong absorption bands in the region of 6750, 5000, 4900 and 4850 cm.$^{-1}$ (Table I). The absence of the absorption band at 6750 cm.$^{-1}$ in the spectra of the allophanates (no. 1–7, Table II) and of the biurets (no. 8 and 9, Table II) strongly suggests that these compounds are intramolecularly hydrogen bonded. The molecular weight of the allophanates and biurets (no. 1–9, Table II) indicated these compounds to be in the monomeric state. In the region of 4831–4877 cm.$^{-1}$, a broad absorption band was found for those compounds suspected of having hydrogen bonding. Kaye,[6] in his study of methanol, showed that a broadening of the absorption bands in this region took place when hydrogen bonding increased.

TABLE I

RNHCOR'

No.	R	R'	Concn.[a] moles/liter	Absorption band, cm.$^{-1}$			
1	C_6H_5	OC_2H_5	2.425	6756	5045	4970	4880
2	p-$CH_3OC_6H_5$	OC_2H_5	0.5020	6743	5083	4940	4850
3	p-ClC_6H_5	OC_2H_5	.5150	6748	5038	4945	4855
4	C_6H_5	$N(CH_3)C_6H_5$	.1500	6710	5022	4946	4867
5	C_2H_5	NHC_6H_5	.0500	6725	4915	(broad band)	
6	C_2H_5	$N(C_2H_5)_2$	.7500	6780	4974	4915	4865

[a] All spectra were determined at 26 ± 0.5° and were carried out in 10.00-mm. and 25.00-mm. quartz cells using carbon tetrachloride as the solvent.

Interestingly, *sym*-triethyl and triphenyl biuret exhibited a weak absorption band in the region of 6750 cm.$^{-1}$ (no. 10 and 11, Table II) and showed three distinct absorption bands at 5000–5276, 4920–4943, 4825–4870 cm.$^{-1}$ instead of one broad band. An examination of Fisher–Hirschfelder–Taylor molecular models indicated that only one NH group can be intramolecularly hydrogen bonded at any one time to an oxygen atom, and therefore an absorption band should appear in the region of 6750 cm.$^{-1}$. Thus the three absorption bands are probably due to the unassociated NH of the biuret which completely masks the broad band due to associated NH.

Additional evidence lending support to the theory that the allophanate molecule is intramolecularly hydrogen bonded is found in the reactions of phenyl isocyanate with ethyl carbanilate[7] and cyanic acid with alcohol.[8] The products of the reactions are always the carbanilate and allophanate. No polyallophanate is isolated as might be expected if no intramolecular hydrogen bonding were present to tie up the NH group.

Experimental[9]

Materials.—Ethyl carbanilate, m.p. 48–49°, ethyl *p*-chlorophenylcarbamate, m.p. 66–67°, and ethyl *p*-methoxyphenylcarbamate, m.p. 65°, were prepared by the procedure of Vittenet.[10] Ethyl-α,γ-diphenylallophanate, m.p. 94°, ethyl α,p-chlorophenyl-γ-phenylallophanate, m.p. 89–90°, and ethyl α,p-methoxyphenyl-γ-phenylallophanate were

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TABLE II

H.....O
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R—N—CON(R')C—R''

No.	R	R'	R''	Concn.[a] moles/liter	Absorption band, cm.$^{-1}$			
1	C_6H_5	C_6H_5	OC_2H_5	1.056[b]	4843			
2	C_6H_5	C_6H_5	OC_2H_5	0.3520[c]	4843			
3	C_6H_5	C_6H_5	OC_2H_5	.278[b]	4843			
4	C_6H_5	C_6H_5	OC_2H_5	.1408[c]	4843			
5	C_6H_5	C_6H_5	OC_2H_5	.0704[c]	4843			
6	C_6H_5	p-$CH_3OC_6H_5$	OC_2H_5	.1592[c]	4831			
7	C_6H_5	p-ClC_6H_5	OC_2H_5	.3140[c]	4836			
8	C_6H_5	C_2H_5	$N(C_2H_5)_2$	.3800[c]	4877			
9	C_2H_5	C_2H_5	$N(C_2H_5)_2$	.0807[c]	4877			
10	C_6H_5	C_6H_5	NHC_6H_5	.1620[b]	6711	5276	4943	4870
11	C_2H_5	C_2H_5	NHC_2H_5	.1605[c]	6725	5000	4920	4825

[a] All spectra were determined at 26 ± 0.5° and carried out in 10.00- and 25.00-mm. quartz cells. [b] Carbon tetrachloride was used as the solvent. [c] Benzene was used as the solvent.

prepared according to the procedure of Kogon.[11] 1-Ethyl-3-phenylurea was prepared according to the procedure of Thiele and Pickard,[12] m.p. 96–97°. 1-Methyl-1,3-diphenylurea was prepared according to the procedure of Gebhardt[13] m.p. 104°. 1,1,3-Triethylurea was prepared according to the procedure of Hofmann,[14] m.p. 62°. 1,3,5-Triphenylbiuret, m.p. 150–151°, and 1,1,3-triethyl-5-phenylbiuret, m.p. 113–113.5°, were kindly supplied by E. J. Goldberg.[15] 1,3,5-Triethylbiuret[16] (*Anal.* Calcd. for $C_8H_{17}N_3O_2$: N, 22.4. Found: N, 22.6) and 1,1,3,5-tetraethylbiuret (*Anal.* Calcd. for $C_{10}H_{21}N_3O_2$: N, 19.4. Found: N, 19.6) were prepared according to the procedure of Baker and Holdsworth.[17] A boiling point for these compounds was not obtained due to their ease of decomposition.

Preparation of Solutions.—The solutions were carefully made up by weighing the compound directly into a 50-ml. or 100-ml. volumetric flask and diluting with sufficient carbon tetrachloride or benzene to give 50 or 100 ml. of solution. The solution was then added directly to a 100.0- or 25.0-mm. quartz cell. Prior to each run the cells were washed once with acetone, followed by three to five washings with reagent grade carbon tetrachloride, then dried *in vacuo*. The cells were rinsed twice with 2 ml. of the solution to be examined and then filled.

Spectrophotometric Method.—Measurements were made in a 100.0- or 25.0-mm. quartz cell using the Cary spectrophotometer model No. 14. The cell holder was held at a temperature of 26 ± 0.5°. The samples were run at a scan speed of 50 Å./sec., chart speed of 5″/min., and a slit control of 0.15 mm.

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Paper Chromatography of Flavins and Flavin Nucleotides[1,2]

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Methods and solvent systems are described for the paper chromatographic separation and identification of flavins and flavin nucleotides.

Numerous investigations concerned with flavins and flavin nucleotides have been facilitated greatly by the application of chromatographic methods to these problems. Following the work of Crammer,[4] who first separated Rb,[5] FMN and FAD by paper chromatography, this technique has been utilized further in such studies as: the isolation[6–8] and chemical synthesis[9–11] of FAD and FMN, the identification of riboflavinyl glucoside,[12] the identification of Rb analogs,[13] the failure of P^{32}-labeled orthophosphate to be incorporated into FAD by respiring tissue homogenates[14] and the identifica-

(1) Paper IV in the series "Flavin Nucleotides and Flavoproteins"; for paper III, see THIS JOURNAL, **77**, 6716 (1955).
(2) Supported by research grants from Eli Lilly and Co. and Initiative 171, State of Washington.
(3) A portion of this material is taken from the Dissertation of Gordon L. Kilgour offered in partial fulfillment of the requirements for the degree of Doctor of Philosophy.
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(5) The following abbreviations will be used: Rb, riboflavin; Lx, lyxoflavin; RbG, riboflavinyl glucoside; GalF, galactoflavin; IsoRb, isoriboflavin; LF, lumiflavin; LC, lumichrome; FMN, riboflavin 5′-phosphate (flavin mononucleotide); cyc-FMN, riboflavin-4′,5′-phosphate (cyclic); RbPP, riboflavin 5′-pyrophosphate; Rb-diP, riboflavin 4′,5′-diphosphate; FAD, flavin-adenine dinucleotide; FAD-X, cyclic analog of FAD.
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