14. Studies in Hydrogen-bond Formation. Part III.* The Reactivity of Amines, Amides, and Azo-compounds in Aqueous and Non-aqueous Solutions.

By F. M. Arshid, C. H. Giles, S. K. Jain, and A. S. A. Hassan.

The method of detecting complex-formation in solution by refractometry and dilectric-constant measurement has been applied to binary systems containing basic and other nitrogen-containing compounds, in aqueous and in non-aqueous solution.

The reactions of some substituted and unsubstituted simple aliphatic amides with a variety of second solutes are tentatively interpreted as indicating that the enol-tautomer of the unsubstituted or *N*-monosubstituted compounds predominates in most non-aqueous solutions, and the keto-form in aqueous solutions.

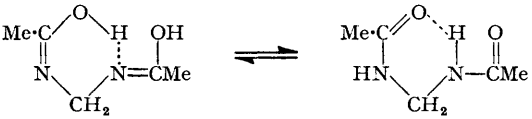
The behaviour of some sulphonated *o*-hydroxyazo-dyes indicates that their azo-groups do not interact in water with alcoholic groups in a second solute.

Experiments with use of the refractive index method to detect intermolecular and chelate complexes involving a variety of nitrogen-containing compounds are described. As one of our aims was the elucidation of the mechanism by which certain polymers, especially proteins, adsorb organic solutes, including dyes, various amido- and amino-compounds have been used as models of these polymers.

The method and general significance of the results have been fully described in Part II (*J.*, 1955, 67). The specific results of the present tests are shown in the Table and the Figure, and their interpretation is discussed below. Some of the present results, as indicated, have also been obtained by the dielectric-constant method.

Reactivity of the Amides.—In view of the importance of the reactivity of the amide group in adsorption by proteins and certain synthetic materials, *e.g.*, nylon, we have examined a number of binary systems containing amides and diamides, in various solvents.

One of the diamides, *viz.*, diacetamidomethane, probably exists in chelated forms :



and thus behaves as a monoamide, whereas in anilidoacetylglycine ($Ph{\cdot}NH{\cdot}CO{\cdot}CH_2{\cdot}NHAc$) and diacetamidohexamine no such stable ring can exist and the pairs of amide groups appear to react independently.

If the complexes detected (see Table) are assumed to result from hydrogen-bonding, the results appear to indicate that: (*a*) the tautomeric equilibrium in solutions of unsubstituted and monosubstituted amides is in favour of the enol form in benzene, carbon tetrachloride, or toluene † (as suggested in Part I, *J.*, 1952, 3799), and the keto-form in water. This tentative hypothesis is supported by adsorption on Nylon and wool of a variety of solutes in aqueous and non-aqueous solutions (Chipalkatti, Giles, and Vallance, *J.*, 1954, 4375); (*b*) The reactivity of the carbonyl group in the keto-form is similar to its reactivity in aldehydes (see Part IV, in the press); (*c*) The reactivity of the nitrogen atom in the primary, secondary, and tertiary amides is similar to its reactivity in the corresponding amines.

The tertiary amides, dimethyl- and diethyl-acetamide react with proton acceptors,

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* Parts I and II, *J.*, 1952, 3799; 1955, 67.

† Buswell, Rodebusch, and Roy (*J. Amer. Chem. Soc.*, 1938, **60**, 2444) observed, in infrared spectroscopic studies, that monosubstituted amides, *e.g.*, *N*-ethylacetamide, enolise (and associate) in carbon tetrachloride.

Solute b	Solution Solvent *	Solution Total concn. (moles)	Method † (temp.)	Mol. ratio of complex (a : b) ‡
Amides.—Solute a : *Acetamide.*				
Benzoquinone	T, El	0·04	n 20°	1 : 1
,,	W	0·1	n 20	2 : 1
Ethanol	D	0·2	n 21	(1 : 1)
Hæmatoxylin	Ac	0·3	ε —	(2 : 1)
Phenol	W	0·25	n 22	1 : 1
,,	D	0·2	n 21	1 : 1
Pyridine	W	0·2	n 19	1 : 1
Quinol	W	0·25	n 20	2 : 1
Triethylamine	W	0·2	n 19	(1 : 1)
Solute a : N-n-*Butylpropionamide.*				
Diethylamine	T	0·2	ε, n 20	(1 : 2)
Ethanol	T	0·2	ε, n 20	1 : 1*y*
Urea	El	0·1	n 20	1 : 1
Solute a : *Diethylacetamide.*				
Azobenzene	T	0·1	n 20	4 : 1
Solute a : *Dimethylacetamide.*				
Azobenzene	T	0·1	n 14	4 : 1
Benzoquinone	T	0·1	n 14	4 : 1
Solute a : *Dimethylformamide.*				
Acetone	B	0·25	ε —	*x*
Aniline	B	0·25	ε, n 20	2 : 1
Diethylamine	B	0·25	ε —	1 : 1
Diphenylamine	C	0·05	n 17	*x*
Hæmatoxylin	W	0·05	n 20	4 : 1
Phenol	B	0·25	ε —	1 : 1
,,	W	0·25	n 19, 35	1 : 1
,,	C	0·1	n 22	1 : 1, 1 : 2 §
Diamides.—Solute a : *Diacetamidomethane.*				
Diethylamine	W	0·1	n 17	*x*
,,	El	0·1	n 17	1 : 1
Phenol	El	0·1	n 21	1 : 1
,,	W	0·1	n 17	1 : 1
Pyridine	W	0·2	n 22	*x*
Triethylamine	W	0·1	*n* 17	*x*
,,	El	0·1	*n* 16·5	1 : 1
Solute a : *Anilidoacetylglycine.*				
Phenol	El	0·1	n 17	1 : 2
Triethylamine	An	0·05	n 17	*x*
,,	El	0·05	n 21	(1 : 2)
Solute a : *Diacetamidohexane.*				
n-Pentanol	W	0·1	n 19	(1 : 2)
Phenol	El	0·1	n 21	1 : 2
Triethylamine	El	0·1	n 21	*x*
Amines.—Solute a : *Aniline.*				
Anisole	B	0·25	ε —	*x*
Diethylamine	W	0·25	n 18	1 : 1
Triethylamine	W	0·25	n 19	(1 : 1)
Solute a : *Diethylamine.*				
Azobenzene	B	0·25	n 19	1 : 1 *z*
o-Nitrophenol	B	0·25	n 18	1 : 1
Phenol	B	0·25	n 19	1 : 1 *z*
,,	D	0·1	n 20	1 : 1, (1 : 2)
,,	T	0·05	n 17	1 : 1, (1 : 2)
,,	W	0·25	n 18, 20	1 : 1 *y*
Triethylamine	D	0·2	n 22	*x*
,,	W	0·1	n 17	(*x*)
,,	El	0·1	n 17	*x*

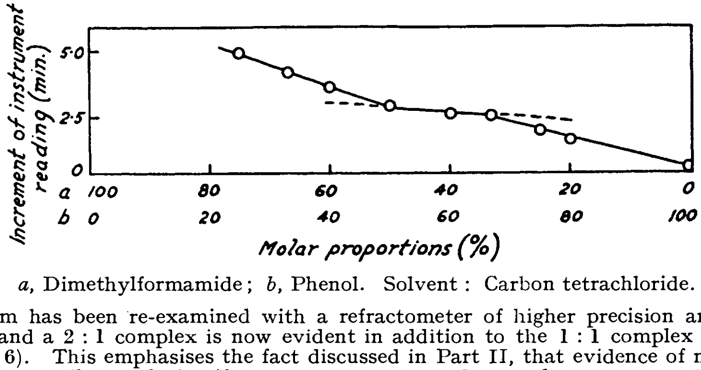
TABLE. (*Continued.*)

Solute b	Solvent *	Solution Total concn. (moles)	Method † (temp.)	Mol. ratio of complex (a : b) ‡
		Solute a : *Triethylamine.*		
Ethanol	W	0·25	n 21	*x*
Resorcinol	T	0·25	ε, n 20	2 : 1
Azo-compounds.—Solute a :		$PhNH_2 \to 2:3:6\text{-}C_{10}H_5(OH)(SO_3Na)_2$		
Diethylamine	W	0·05	n 20	1 : 2
Ethanol	W	0·05	n 20	*x*
Glycol	W	0·05	n 20	*x*
Phenol	W	0·05	n 20	1 : 1
		Solute a : $PhNH_2 \to 1\text{-}C_{10}H_7{\cdot}NH_2$		
Phenol	T	0·1	ε, n 20	(1 : 3, 1 : 4)
		Solute a : $PhNH_2 \to 3\text{-}C_{10}H_7{\cdot}NH_2$		
Phenol	T	0·1	ε, n 20	1 : 2
		Solute a : $PhNH_2 \to 2\text{-}C_{10}H_7{\cdot}OH$		
Aniline	B	0·25	ε —	2 : 1
Phenol	B	0·25	ε —	1 : 1, (1 : 2)
Quinol	D	0·1	n 20	1 : 1, (2 : 1)
Resorcinol	E	0·25	ε —	2 : 1, 1 : 1
$CCl_2{:}CHCl$	T	0·1	ε, n 20	1 : 2
		Solute a : *Azobenzene.*		
Aniline	B	0·25	n 19	2 : 1 *z*
Benzoquinone	T	0·1	*n* 19	*x*
$PhCH_2{\cdot}OH$	C	0·1	n 20	1 : 1
Diethylamine	B	0·25	n 19	1 : 1 *z*
Phenol	B	0·25	n 19	1 : 1, 1 : 2 *z*
Triethylamine	D	0·1	n 18	*x*
		Solute a : *Sodium sulphanilate acid→2-naphthol.*		
Glycol	W	0·1	n 20	*x*
Quinol	W	0·1	n 20	2 : 1

* Ac = acetone; An = aniline; B = benzene; C = carbon tetrachloride; D = dioxan; E = diethyl ether; El = ethanol; T = toluene. † ε = dielectric constant; n = refractive index. ‡ Data in parentheses denote uncertain indications. § See Fig.

x No evidence of complex formation. *y* Curves show particularly pronounced change of slope. *z* Results by dielectric constant method reported in Part I.

Relation between refractive index [as instrument reading] and component ratio in (0·1M) *binary phenol–dimethylformamide solutions in carbon tetrachloride.*



a, Dimethylformamide; *b*, Phenol. Solvent: Carbon tetrachloride.

This system has been re-examined with a refractometer of higher precision and at a different temperature, and a 2 : 1 complex is now evident in addition to the 1 : 1 complex already detected (Part II, Fig. 6). This emphasises the fact discussed in Part II, that evidence of no complex formation is not necessarily conclusive if measurements are made at only one temperature or with only one second solute.

Direct instrument readings are plotted here, since over very small ranges these vary linearly with concentration, as do the n^2 values normally used.

presumably through the hydrogen on the α-carbon atom, which is activated by the adjacent carbonyl group.*

Azo-compounds.—The free nitrogen atom in sulphonated *o*-hydroxyazo-compounds forms complexes with phenol in aqueous solution (cf. Part II), but not apparently with alcohols. Diethylamine appears to react by salt-formation with the sulphonic acid groups. Trichloroethylene in organic solvents evidently forms a complex by a C–H • • • N bond with the azo-group. This may explain its good solvent power for unsulphonated azo-dyes. The presence of a chelate ring in aniline→2-naphthylamine is revealed by its complex ratio with phenol, when compared with those of aniline→1-naphthylamine and phenol.

Note on Previous Work.—The present methods bear a close relation to the " method of continuous variations " for the spectrophotometric determination of the molar ratio of organic complexes in solution, apparently first studied by Ostromisslensky (*Ber.*, 1911, **44**, 268), although more fully discussed, both as to principles and implications, independently by Denison (*Trans. Faraday Soc.*, 1912, **8**, 20, 35), and later used for inorganic–inorganic and inorganic–organic complexes by Job and his collaborators [Job, *Compt. rend.*, 1925, **180**, 928, 1108, 1932; 1926, **182**, 1621; 1927, **184**, 204, 1066; 1928, **186**, 1546; 1933, **196**, 181; 1934, **198**, 827; 1935, **200**, 831; *Ann. Chim.* (*France*), 1928, **9**, 113; 1936, **6**, 97; Bernard and Job, *Compt. rend.*, 1930, **190**, 186; Job and Brigando, *ibid.*, 1940, **210**, 438] and by Vosburgh and Cooper (*J. Amer. Chem. Soc.*, 1941, **63**, 437). Spacu and Popper (*Z. phys. Chem.*, 1934, *B*, **25**, 460) also determined refractive index values for binary aqueous solutions of certain inorganic salts by a similar method, and detected complex formation.

EXPERIMENTAL

The technique has been fully described in Parts I and II (*locc. cit.*). For the present refractive-index measurements the apparatus mainly used was the new high-precision Bellingham and Stanley Pulfrich instrument.

Anilidoacetylglycine.—Glycine was acetylated and the product condensed with aniline (Granacher, Schelling, and Schlatter, *Helv. Chim. Acta*, 1925, **8**, 873). It formed colourless flakes (from hot water), m. p. 189°.

Diacetamidohexane, prepared by reaction between hexamethylenediamine and acetic anhydride in the cold, formed colourless needles (from water), m. p. 125°.

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DEPARTMENT OF TECHNICAL CHEMISTRY
ROYAL TECHNICAL COLLEGE,
GLASGOW, C.1.

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* Kandar (*Bull. Chem. Soc. Japan*, 1950, **23**, 4, 137; through *J. Text. Inst.*, 1951, **42**, *A*, 575; *Chem. Researches, Japan*, 1951, **9**, 133; through *Chem. Abs.*, 1951, **45**, 7610) has proposed an α-keratin model embodying this type of C–H • • • N bond between peptide groups. Anslow (*Discuss. Farady Soc.*, 1950, **9**, 299) has observed C–H • • • N and C–H • • • O absorption components in the ultraviolet spectra of some protein solutions.