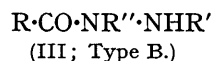
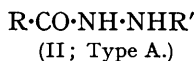
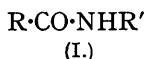


68. *The Associating Effect of the Hydrogen Atom. Part VI.
The Acid Hydrazides.*

By HERBERT T. HAYES and LOUIS HUNTER.

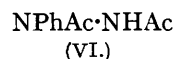
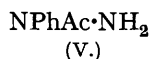
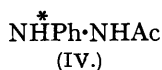
By molecular-weight determinations in naphthalene solution, and by observations of solubility, it is shown that the acid hydrazides are associated. The association is due to the formation of hydrogen bonds between the oxygen of the acyl group and, primarily, the hydrogen of the adjacent imino-group; to a much less extent bonding can occur with the hydrogen of the second imino-group. The bearing of these facts on the tautomerism of the hydrazides is discussed.

THE similarity between amides (I) and hydrazides (II) indicated by their formal constitution was the subject of thorough investigation by Curtius, Stollé, and their co-workers some 40 years ago. In view of this resemblance it appeared likely that the state of molecular association shown by the amides (for references see Part I, J., 1937, 1114) might also prevail in the hydrazides, and a series of molecular-weight determinations of substances of this class has been undertaken. From the results obtained it would appear that, provided the imino-group adjacent to the acyl group remains unsubstituted, association is general, but that replacement of the imino-hydrogen atom by alkyl, aryl, or acyl groups considerably reduces, or even entirely prevents, association. The association is therefore attributed to hydrogen-bond formation between the $-\text{CO}\cdot\text{NH}-$ groups in separate molecules, of a type similar to that suggested for the amides and sulphonamides (*loc. cit.*, p. 1116).



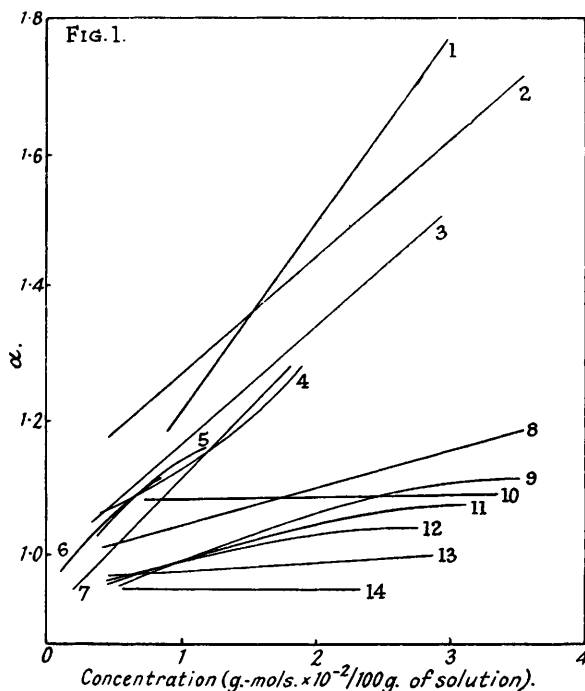
The apparent molecular weights were measured cryoscopically in naphthalene solution over a range of concentration, and deduced according to the ideal-solution laws, the association factor (α) being calculated as the ratio of the apparent molecular weight to the formula weight. Comparison of the behaviour of hydrazides possessing the grouping $-\text{CO}\cdot\text{NH}-$ (Type A, *e.g.*, II) and those in which the imino-hydrogen atom is replaced (Type B, *e.g.*, III), is expressed graphically in Fig. 1, showing the variation of the association factor with concentration. The curves fall sharply into two groups, those due to compounds of type A being steeply sloped, and those due to compounds of type B being flat or gently sloped. Although, owing to deviations from the ideal laws, no quantitative significance can be attached to the values of α , a steep curve is taken to indicate considerable association, and a flat curve little or no association.

The difference in behaviour of the two types of hydrazide is made remarkably evident in a comparison of the two isomeric acetophenylhydrazides (Fig. 2). The β -phenyl compound (IV), which belongs to type A, is highly associated, whilst the α -phenyl compound (V, type B) is practically non-associated. The $\alpha\beta$ -diacetyl compound (VI), as would be expected, is also highly associated.

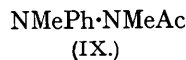
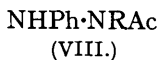
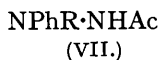


The possibility of the participation of the second imino-group in hydrogen-bond formation [*i.e.*, through the hydrogen atom marked with an asterisk in (IV)] is not

entirely excluded by the results obtained, for some of the substances of type B in Fig. 1 give curves of marked slope, though this may be no more than a result of departures from the ideal-solution laws. Nevertheless, the results expressed in Fig. 3, showing the effect on the association factor of the progressive substitution of aceto- β -phenylhydrazide (IV), lend support to the view that the marked hydrogen atom may participate in hydrogen-bond formation. Although replacement of the β -hydrogen atom by methyl

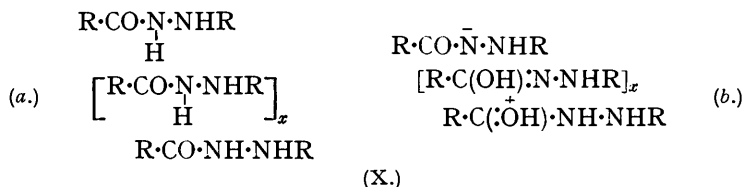


(VII; R = Me) or by phenyl (VII; R = Ph) diminishes the slope of the association-concentration curve, yet a more marked diminution is produced in the α -substituted



isomers (VIII; R = Me or Ph), but the greatest effect of all is observed when both α - and β -positions are substituted, as in aceto- β -phenyl- $\alpha\beta$ -dimethylhydrazide (IX).

The results illustrated in Fig. 1, however, make it clear that the main contribution to the molecular association of hydrazides of type A is made by chain polymers of the type depicted in (X), where a and b are the two resonance forms of which the substance R·CO·NH·NHR is a hybrid. The possibility of cyclic dimers (see Part I) is not excluded, although the steepness of the association-concentration curves renders it unlikely that



such dimers, if they do exist, are present in conspicuous proportion. A formulation similar to (X) may be ascribed for the much less prevalent hydrogen-bond association involving the imino-group adjacent to the -CO·NH- group.

Although no exact solubility measurements have been made, the solubilities of the hydrazides run roughly parallel to the results of molecular-weight determinations. For instance, there is a sharp distinction in solubility between hydrazides of the two types; those of type A are readily soluble in water and in other electron-donor solvents (and indeed are best recrystallised from dilute aqueous alcohol), but only sparingly in hydrocarbon solvents, whilst those of type B are insoluble in water but readily soluble in hydrocarbon solvents.

Formula (X) provides a possible explanation of the known tautomeric behaviour of the hydrazides, $R \cdot CO \cdot NH \cdot NHR \rightleftharpoons R \cdot C(OH) : N \cdot NHR$, for it makes possible two alternative modes of dissociation of the hybrid (X), *viz.*, the unreal form (Xa) into monomolecules of the former component of the tautomeric equilibrium, and (Xb) into monomolecules of the latter component. The presence of the hydroxyl component of this equilibrium in all hydrazides of type A would provide an added reason for their marked tendency to dissolve in water and other hydroxylic solvents.

In the following tables concentrations are expressed as g.-mols. $\times 10^{-2}/100$ g. of solution, the formula weights appearing in parentheses; *M* is the apparent molecular weight, and α the association factor. The key to Figs. 1—3 is included in the tables.

FIG. 1.

Compounds of type A.				Compounds of type B.				
	Concn.	<i>M</i> .	α .		Concn.	<i>M</i> .	α .	
Aceto- β -phenylhydrazide (150) (Curve 1)	0.91	180	1.19	Aceto- $\alpha\beta$ -diphenylhydr- azide (226) (Curve 8)	0.44	228	1.01	
	1.83	211.5	1.41		1.69	238	1.05	
	2.42	244	1.63		2.62	259	1.145	
	2.95	263	1.75		3.50	267	1.18	
Aceto- β -1-naphthyl- hydrazide (200) (Curve 2)	0.39	238.5	1.19	Aceto- β -phenyl- α - <i>p</i> - tolylhydrazide (240) (Curve 9)	0.58	226	0.95	
	0.82	243	1.215		1.35	243	1.02	
	1.53	267.5	1.34		2.105	257	1.08	
	2.25	298	1.49		2.89	264	1.10	
	2.95	319	1.60		3.52	266	1.11	
Aceto- β - <i>p</i> -tolylhydrazide (164) (Curve 3)	0.41	170	1.035	Aceto- β -phenyl- α - benzylhydrazide (240) (Curve 10)	0.57	259	1.08	
	0.91	189	1.15		1.15	270	1.12	
	1.37	201	1.23		1.97	267	1.11	
	1.79	211	1.29		2.76	260	1.08	
	2.21	222.5	1.36		3.35	257	1.07	
Benzo- β -phenylhydrazide (210) (Curve 4)	2.89 *	246	1.50	Aceto- $\alpha\beta$ - <i>di-p</i> -tolyl- hydrazide (254) (Curve 11)	0.45	225	0.96	
	0.43	226	1.07		1.01	251	0.99	
	0.81	231.5	1.10		1.46	260	1.02	
	1.20	240	1.14		2.07	266	1.05	
	1.52	251	1.19		2.54	267	1.05	
Propiono- β - <i>p</i> -tolyl- hydrazide (178) (Curve 5)	1.84 *	269	1.28	Aceto- $\alpha\beta$ - <i>di-p</i> -chloro- phenylhydrazide (295) (Curve 12)	3.09	274	1.08	
	0.38	182	1.025		0.45	283	0.96	
	0.77	197	1.11		0.88	296	1.00	
	1.18 *	207	1.16		1.51	300	1.015	
Aceto- β -2-naphthyl- hydrazide (200) (Curve 6)	Propiono- β -phenyl- hydrazide (164) (Curve 7)	0.18	191	0.96	$\alpha\beta$ -Diacetylphenyl- <i>o</i> -tolyl- hydrazine (282) (Curve 13)	2.11	301	1.02
		0.37	211	1.05		2.70	308	1.04
		0.57	213	1.07		0.46	273	0.97
		0.75 *	220	1.10		1.14	275	0.97
Aceto- $\alpha\beta$ - <i>di-o</i> -tolyl- hydrazide (254) (Curve 14)	0.20	150	0.95	Aceto- α -phenylhydrazide (150) (Curve 3)	1.79	276	0.98	
	0.99	175	1.07		2.415	277	0.98	
	1.38	195	1.19		2.85	282	1.00	
	1.76 *	208	1.27		0.58	242	0.95	
					1.11	241	0.95	
			1.63	241	0.95			
			2.31	242	0.95			

* Solute separates at higher concentrations.

FIG. 2.

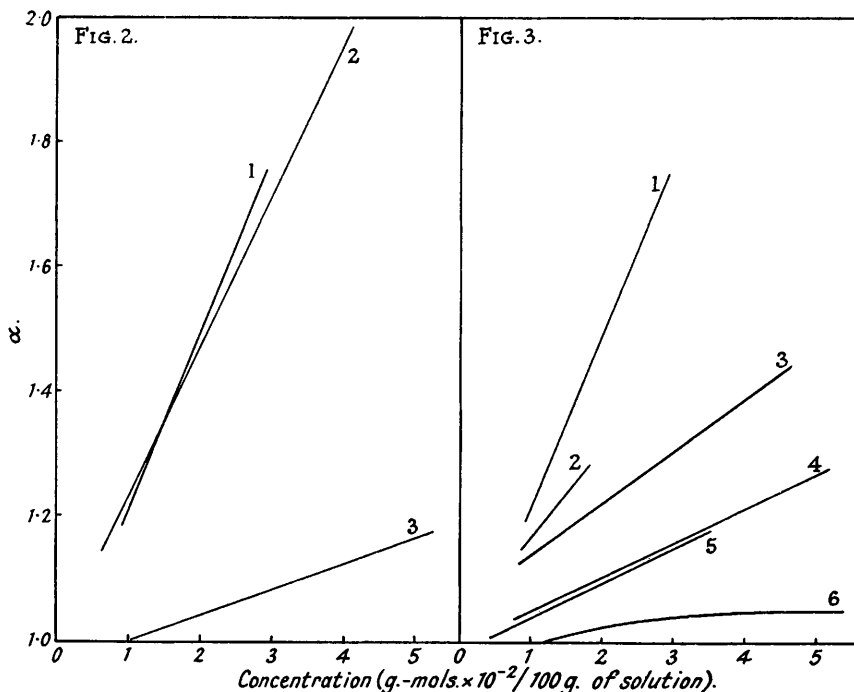
Aceto- β -phenylhydrazide (for data see Fig. 1) (Curve 1)

$\alpha\beta$ -Diacetylphenyl- hydrazine (192) (Curve 2)	0.65	221	1.15	Aceto- α -phenylhydrazide (150) (Curve 3)	1.01	150	1.00
	1.59	263	1.37		1.98	152	1.02
	2.50	311	1.62		2.93	164	1.09
	3.37	352	1.835		3.85	168	1.12
	4.22	404	2.10		5.29	177	1.18

FIG. 3.

Aceto- β -phenylhydrazide (for data see Fig. 1) (Curve 1)

Aceto- $\beta\beta$ -diphenyl- hydrazide (226) (Curve 2)	{	0.88	261	1.15	Aceto- β -phenyl- α - methylhydrazide (164) (Curve 4)	{	0.80	169	1.03		
		1.16	270	1.19			1.97	177	1.08		
		1.44	271	1.225			3.10	191	1.165		
Aceto- β -phenyl- β - methylhydrazide (164) (Curve 3)	{	1.85	291	1.29	Aceto- $\alpha\beta$ -diphenylhydrazide (for data see Fig. 1) (Curve 5)	{	4.175	200	1.22		
		0.81	185	1.13			5.22	210	1.28		
		1.96	200	1.22			Aceto- β -phenyl- $\alpha\beta$ -di- methylhydrazide (178) (Curve 6)	{	1.12	178	1.00
		2.90	215	1.31					2.17	183	1.03
3.77	226	1.38	3.16	186	1.04						
		4.63	234	1.43			4.29	182	1.025		
							5.385	185	1.04		



EXPERIMENTAL.

The solvent naphthalene was the specially purified product for cryoscopic use, obtained from the British Drug Houses. The following new compounds were prepared in the course of the investigation. Nitrogen analyses were carried out by Drs. Weiler and Strauss, Oxford.

*Aceto- $\alpha\beta$ -di-*o*-tolylhydrazide.*—*oo'*-Hydrazotoluene, prepared by the alkaline reduction of *o*-nitrotoluene, was only incompletely acetylated even by boiling with acetic anhydride for $\frac{1}{2}$ hour. After repeated decolorisation with charcoal, the *product* formed large white rhombs from aqueous alcohol, m. p. 107° (Found: N, 11.0. $C_{16}H_{18}ON_2$ requires N, 11.0%).

*Aceto- $\alpha\beta$ -di-*p*-tolylhydrazide,* prepared similarly from *pp'*-hydrazotoluene, formed small white prisms from alcohol, m. p. 120° (Found: N, 11.2%).

*Aceto- $\alpha\beta$ -di-*p*-chlorophenylhydrazide* formed small, very pale yellow tetrahedra from aqueous alcohol, m. p. 145° (Found: N, 9.1; Cl, 24.1. $C_{14}H_{12}ON_2Cl_2$ requires N, 9.5; Cl, 24.0%).

*$\alpha\beta$ -Diacetylphenyl-*o*-tolylhydrazine.*—Ordinary methods of acetylation of *p*-methylhydrazobenzene proved unsuccessful, but Smith and Orton's method (J., 1908, **93**, 1249) led to the *diacetyl* compound, which formed white triangular prisms from alcohol, m. p. 91° (Found: N, 10.2. $C_{17}H_{18}O_2N_2$ requires N, 9.9%). The acetophenyl-*p*-tolylhydrazide, m. p. 140° , prepared by Jacobson and Lischke (*Annalen*, 1898, **303**, 370), is now shown to be *aceto- β -phenyl- α -*p*-tolylhydrazide* by the following proof. The substance, whose m. p. was unaltered by repeated crystallisation from alcohol, was reduced by boiling with iron filings

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and acetic acid; the resulting mixture was cooled, made alkaline with ammonia, and steam-distilled. The steam-distillate contained only aniline, precipitated as and recognised by its tribromo-derivative, m. p. 118°. The filtered residue from the steam distillation deposited aceto-*p*-toluidide (m. p. and mixed m. p. 147°) on cooling.

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