

234. *The Associating Effect of the Hydrogen Atom. Part I.*  
*Amides and Sulphonamides.*

By HUBERT O. CHAPLIN and LOUIS HUNTER.

THE classical molecular-weight measurements of v. Auwers and his co-workers (for references see *Ber.*, 1937, **70**, 966) and of Meldrum and Turner (J., 1908, **93**, 876; 1910, **97**, 1605, 1805) provide ample evidence that amides and anilides are associated in solution. Replacement of both amide-hydrogen atoms, however, in the few cases in which measurements have been made (Meldrum and Turner, J., 1910, **97**, 1605; Mascarelli and Benati, *Gazzetta*, 1909, **39B**, 642), appears to prevent association. It appeared of interest to find whether this is a general tendency, and if so, whether it is extended to the sulphonamides, which are themselves associated (v. Auwers, *Z. physikal. Chem.*, 1897, **23**, 449). The molecular weights of a series of *N*-substituted amides and sulphonamides have therefore been measured cryoscopically over a range of concentration, usually in benzene solution. The results clearly show that molecular association (as indicated by a steep association-concentration curve) is general in amides and sulphonamides possessing a free amide-hydrogen atom, but that replacement of both amide-hydrogen atoms effectively checks association (as indicated by a flat or gently sloped curve).

This dependence of association upon the presence of the amide-hydrogen atom clearly points to hydrogen-bond formation as the cause of association in the amides. The most probable type of hydrogen bond is that in which the hydrogen atom is shared between the nitrogen atom of one amide group and the oxygen atom of another. Whether this sharing is confined to two molecules or continues further, the molecular-weight evidence is insufficient to decide; but it appears probable that this mechanism of association has an intimate bearing on the tautomeric behaviour of amides and sulphonamides. In this connection it appeared vital to examine the case of the imino-ethers, which display no such tautomerism. It would seem from their superior volatility (see table) that these

	B. p.		B. p.
Ethylacetimino-ether .....	90—91°	<i>N</i> -Ethylacetamide ...	205°
Methylbenzimidino-ether .....	96/13 mm.	<i>N</i> -Methylbenzamide ...	167/11 mm.; 291/765 mm.
Ethylbenzimidino-ether .....	102/15 mm.	<i>N</i> -Ethylbenzamide ...	285/745 mm.

substances are molecularly simpler than the corresponding isomeric *N*-alkylamides. Determinations of the molecular weight of ethylacetimino-ether do indeed show that this substance is completely non-associated, though the isomeric *N*-ethylacetamide shows considerable association in benzene solution (see Fig. 1). This absence of association can only be due to the fact that the imino-ether, although it still possesses an imino-hydrogen atom, cannot utilise it to form a hydrogen bond because the oxygen atom, being ethereal and not ketonic, is available as a hydrogen acceptor only by becoming an oxonium ion. Such an alternative appears to be improbable in view of the small dipole moment of ethylacetimino-ether as compared with those of acetamide and its *N*-alkyl derivatives (Kumler and Porter, *J. Amer. Chem. Soc.*, 1934, **56**, 2549).

This evidence strongly favours the view that association of amides (and presumably also of sulphonamides) and their tautomeric behaviour are due to one and the same cause, *viz.*, the intermolecular sharing of hydrogen by resonance. The case is, indeed, similar to that already proposed for the diazoamino-compounds by one of us (this vol., p. 320). The attached formulæ represent typical resonance open-chain (I) and cyclic (II) polymers, in which the number of individual molecules is purely arbitrary. It is suggested that the amides are resonance hybrids of extremes such as (Ia) and (Ib), or (IIa) and (IIb), or some variant of these. Dissociation of these polymers into the unimolecular form can thus follow two routes, giving either the amide or the isomeric imino-alcohol or both, according to the conditions imposed by the interacting reagent. The results of an X-ray analysis of fatty amides obtained by Henderson (*Proc. Roy. Soc. Edin.*, 1928, **48**, 20) and of isatin by Cox, Goodwin, and Wagstaff (*Proc. Roy. Soc.*, 1936, *A*, **157**, 399) would seem

FIG. 1.

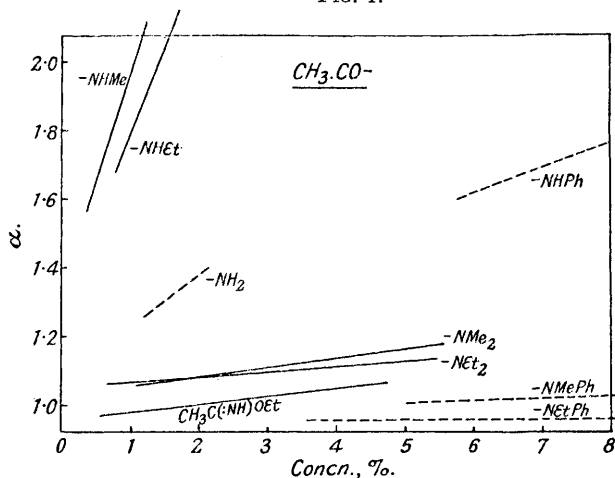


FIG. 2.

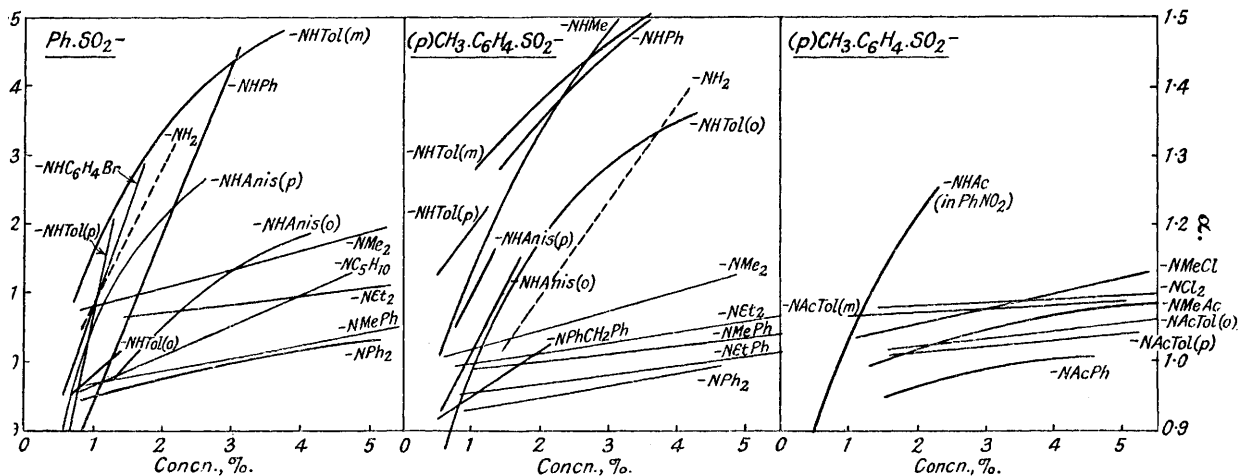
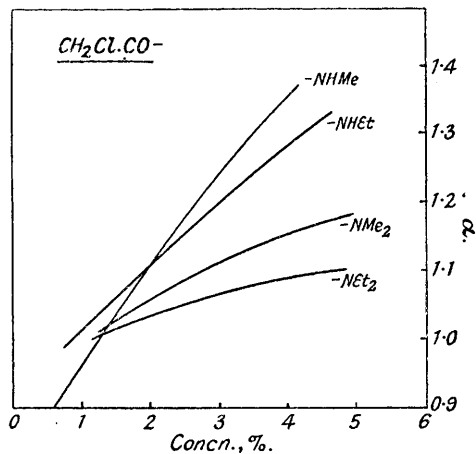


FIG. 3.

FIG. 4.

FIG. 5.

Data for  $\text{CH}_3\cdot\text{CO}\cdot\text{NH}_2$  ebullioscopically in  $\text{CHCl}_3$  } Meldrum and Turner, J., 1908, **93**, 882.  
 "  $\text{CH}_3\cdot\text{CO}\cdot\text{NHPh}$  " "  $\text{C}_6\text{H}_6$  }  
 "  $\text{CH}_3\cdot\text{CO}\cdot\text{NMePh}$  " " " } *Idem*, J., 1910, **97**, 1612.  
 "  $\text{CH}_3\cdot\text{CO}\cdot\text{NEtPh}$  " " " }  
 "  $\text{Ph}\cdot\text{SO}_2\cdot\text{NH}_2$  cryoscopically in  $\text{C}_{10}\text{H}_8$  } v. Auwers, *Z. physikal. Chem.*, 1897, **23**, 449.  
 " *p*- $\text{Tol}\cdot\text{SO}_2\cdot\text{NH}_2$  " " " }

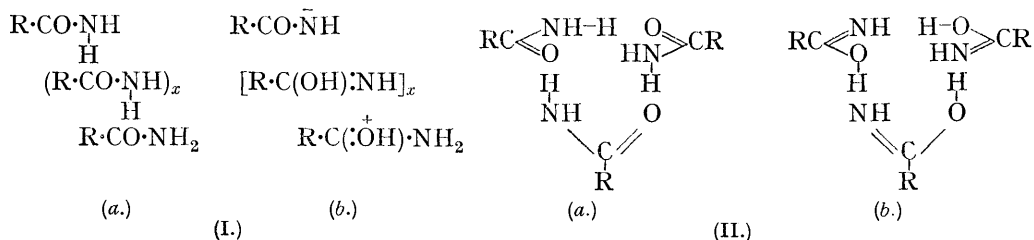
Broken lines.

$\text{CH}_3\cdot\text{CO}\cdot\text{NH}_2$  ebullioscopically in chloroform } Meldrum and Turner, J., 1908, **93**, 882.  
 $\text{CH}_3\cdot\text{CO}\cdot\text{NHPh}$  " " benzene }  
 $\text{CH}_3\cdot\text{CO}\cdot\text{NMePh}$  } ebullioscopically in benzene, Meldrum and Turner, J., 1910, **97**, 1612.  
 $\text{CH}_3\cdot\text{CO}\cdot\text{NEtPh}$  }  
 $\text{Ph}\cdot\text{SO}_2\cdot\text{NH}_2$  } cryoscopically in naphthalene, v. Auwers, *Z. physikal. Chem.*, 1897, **23**, 449.  
*p*- $\text{Tol}\cdot\text{SO}_2\cdot\text{NH}_2$  }

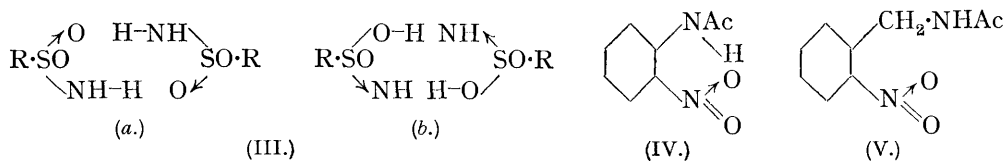
to favour a cyclic dimeride of type (II), at least for amides in the undissolved condition, and a recent investigation of the molecular weight of  $\alpha$ -piperidone in benzene solution (Jenkins and Taylor, this vol., p. 495) indicates that with increasing concentration this substance approaches a dimeric state.

Reference to the tables given later will show that, in dilute solutions of amides and sulphonamides, the proportion of associated molecules is usually small. Resonance of the types suggested above, therefore, does not exclude other types, and it is evident that

the main contribution to the substantial dipole moments of acetamide and its alkyl derivatives (Kumler and Porter, *loc. cit.*) is due to resonance between  $R\cdot C \begin{smallmatrix} \text{O} \\ \text{<} \\ \text{NH}_2 \end{smallmatrix}$  and  $R\cdot C \begin{smallmatrix} \text{O} \\ \text{+} \\ \text{NH}_2 \end{smallmatrix}$  (Pauling and Sherman, *J. Chem. Physics*, 1933, **1**, 606; Clow and Thompson, *Nature*, 1936, **138**, 802), a process which is necessarily confined to the unimolecular condition.



Formulae similar to (I) and (II) may be adopted for the sulphonamides; *e.g.*, a cyclic dimeric polymer is depicted in (III).



In a recent review of physical measurements on the amides, v. Auwers (*loc. cit.*) decides in favour of a tautomeric equilibrium between the normal and the hydroxy-imino forms, at least for amides in the dissolved or liquid state. Most of the facts which he reviews can, in our opinion, be more satisfactorily interpreted in the light of a resonance phenomenon. In particular, reference may be made to the "cryoscopically normal" behaviour of numerous anilides possessing an ortho-substituent. Evidently in these compounds the tendency of the  $-CO\cdot NH-$  group to accept and to donate hydrogen is checked by some intramolecular cause, and it is significant that in the majority the *o*-substituents are hydrogen-acceptors so constituted that six-membered chelation involving hydrogen is easily achieved. For example, whilst *o*-nitroacetanilide (IV) is not associated, its *m*-isomer is strongly associated; similarly, *o*-nitrobenzanilide is associated, but benzo-*o*-nitroanilide is not. In contrast to this, acet-*o*-nitrobenzylamide (V), where chelate ring-formation would not be anticipated, is as strongly associated as its *p*-isomer and as the parent acetobenzylamide (v. Auwers, *Z. physikal. Chem.*, 1897, **23**, 449).

In the following tables and curves, the association factors are calculated according to the ideal-solution laws, and are to be regarded merely as a qualitative indication of association. This probably accounts for some instances of apparent dissociation among the results. The abnormally high apparent molecular weights of *N*-methyl- and *N*-ethyl-acetamide (see Fig. 1) are probably attributable to the fact that under the prevailing experimental conditions the benzene solution is approaching the point at which separation into two layers occurs. Although no quantitative interpretation of the association factor is justified (Sidwick, "The Electronic Theory of Valency," 1927, p. 149), some degree of association is reasonably certain.

A few results of other authors have been included in the figures (shown as broken lines, Figs. 1, 3, and 4), especially when, for reasons of solubility, the cryoscopic method in benzene proved unsuitable. Figures in parentheses indicate the normal molecular weight;  $M$  is the apparent molecular weight. Concentrations are given as g./100 g. of benzene;  $\alpha$  is the association factor.

			Derivatives of acetamide (Fig. 1).					
	Concn.	M.	a.		Concn.	M.	a.	
N-Methylacetamide (73)	0.38	115.1	1.58	N-Diethylacetamide (115)	0.66	121.8	1.06	
	0.795	133.6	1.83		1.41	121.9	1.06	
	1.23	153.6	2.10		2.66	125.1	1.09	
N-Ethylacetamide (87)	0.83	146.4	1.68	Ethylacetimino-ether (87)	4.39	127.2	1.11	
	1.81	189.8	2.18		5.27	129.7	1.13	
	1.02	92.8	1.06		0.63	84.1	0.97	
N-Dimethylacetamide (87)	2.27	95.6	1.10		1.28	85.8	0.99	
	3.16	99.0	1.14		2.58	89.2	1.03	
	4.03	99.9	1.15		3.46	90.4	1.04	
	5.50	103.8	1.19		4.68	92.5	1.06	
			Derivatives of chloroacetamide (Fig. 2).					
N-Methylchloroacetamide (107.5)	0.57	96.3	0.90	N-Ethylchloroacetamide (121.5)	0.74	117.3	0.97	
	1.02	105.9	0.985		1.49	128.4	1.06	
	1.46	112.9	1.05		2.40	139.7	1.15	
	1.89	118.2	1.10		3.40	148.7	1.22	
	3.10	133.2	1.24		4.58	160.2	1.32	
N-Dimethylchloroacetamide (121.5)	4.02	146.2	1.36	N-Diethylchloroacetamide (149.5)	1.15	147.8	0.99	
	1.28	123.7	1.02		2.47	156.7	1.05	
	2.89	135.0	1.11		4.87	165.7	1.11	
	4.89	143.1	1.18					
			Derivatives of benzenesulphonamide (Fig. 3).					
Benzenesulphonanilide (233)	0.68	199.3	0.86	Benzenesulphondimethylamide (185)	0.95	199.6	1.08	
	1.66	257.3	1.11		1.89	198.9	1.075	
	2.59	307.0	1.32		3.15	208.3	1.13	
	3.04	336.8	1.45		4.23	213.5	1.15	
Benzenesulphon- <i>p</i> -bromoanilide (312)	0.64	298.0	0.96	Benzenesulphon-diethylamide (213)	5.24	219.4	1.19	
	1.18	348.1	1.12		1.51	228.1	1.07	
	1.75	398.1	1.28		2.55	230.5	1.08	
Benzenesulphon- <i>o</i> -toluidide (247)	0.86	237.2	0.96	Benzenesulphon-piperidide (225)	4.21	233.6	1.10	
	1.28	250.4	1.01		5.19	236.2	1.11	
	0.73	268.4	1.09		0.78	214.9	0.96	
Benzenesulphon- <i>m</i> -toluidide (247)	1.61	316.4	1.28	Benzenesulphonphenylmethylamide (247)	1.93	226.8	1.01	
	2.58	341.3	1.38		3.15	236.7	1.05	
	3.76	365.4	1.48		4.76	255.0	1.13	
Benzenesulphon- <i>p</i> -toluidide (247)	0.46	179.3	0.73	Benzenesulphonphenylamide (309)	0.95	239.3	0.97	
	0.87	247.6	1.00		2.10	250.2	1.01	
	1.30	294.5	1.19		4.01	251.2	1.02	
	1.34	258.2	0.98		5.25	260.8	1.06	
Benzenesulphon- <i>o</i> -anisidide (263)	2.16	284.7	1.08		6.32	268.0	1.08	
	3.05	299.8	1.14		0.44	277.2	0.90	
	4.11	309.0	1.18		1.10	300.7	0.97	
Benzenesulphon- <i>p</i> -anisidide (263)	0.64	235.4	0.90		1.83	309.6	1.00	
	1.60	320.8	1.22		3.52	320.2	1.04	
	2.46	331.3	1.26		4.74	316.1	1.02	
			Derivatives of <i>p</i> -toluenesulphonamide (Fig. 4).					
<i>p</i> -Toluenesulphonmethylamide (185)	0.56	188.7	1.02	<i>p</i> -Toluenesulphondimethylamide (197)	0.67	199.1	1.01	
	1.38	231.6	1.25		1.44	205.6	1.04	
	2.22	255.7	1.38		2.07	204.9	1.04	
	3.26	280.8	1.52		3.39	214.3	1.09	
	3.97	295.3	1.60		4.87	221.8	1.13	
<i>p</i> -Toluenesulphonanilide (247)	1.43	317.6	1.29	<i>p</i> -Toluenesulphon-diethylamide (227)	0.90	217.0	0.96	
	2.59	350.5	1.42		2.56	230.0	1.01	
	3.79	374.0	1.51		4.42	237.7	1.05	
	4.64	387.3	1.57		5.97	242.4	1.07	
<i>p</i> -Toluenesulphon- <i>o</i> -toluidide (261)	0.58	227.3	0.87	<i>p</i> -Toluenesulphonphenylmethylamide (261)	1.10	251.6	0.96	
	1.23	293.5	1.13		2.02	257.9	0.99	
	1.92	311.6	1.19		4.81	269.8	1.03	
	2.57	327.8	1.26		6.23	277.1	1.06	
	3.31	343.5	1.32		0.91	261.5	0.95	
<i>p</i> -Toluenesulphon- <i>m</i> -toluidide (261)	4.23	353.6	1.36	<i>p</i> -Toluenesulphonphenylethylamide (275)	1.67	267.3	0.97	
	1.08	334.8	1.28		2.98	270.3	0.98	
	1.82	358.3	1.37		3.98	277.1	1.01	
	2.61	373.0	1.43		5.80	281.3	1.02	
<i>p</i> -Toluenesulphon- <i>p</i> -toluidide (261)	3.59	390.0	1.49	<i>p</i> -Toluenesulphonphenylamide (323)	0.93	291.0	0.90	
	0.56	295.0	1.13		1.47	307.5	0.95	
	1.21	320.0	1.23		2.50	315.6	0.98	
<i>p</i> -Toluenesulphon- <i>o</i> -anisidide (277)	0.65	257.3	0.93	<i>p</i> -Toluenesulphonphenylbenzylamide (337)	3.54	315.9	0.98	
	1.09	295.8	1.07		4.55	321.1	0.99	
	1.82	320.8	1.16		0.54	310.3	0.92	
<i>p</i> -Toluenesulphon- <i>p</i> -anisidide (277)	0.83	291.4	1.05		1.37	325.8	0.97	
	1.30	322.7	1.17		2.05	344.7	1.02	

N-Chloro- and N-acetyl derivatives of *p*-toluenesulphonamide (Fig. 5).

	Concn.	M.	<i>a</i> .		Concn.	M.	<i>a</i> .
<i>p</i> -Toluenesulphon- methylchloroamide (219·5)	1·16	227·1	1·04	<i>N</i> -Acetyl- <i>p</i> -toluene- sulphonanilide (289)	1·59	274·5	0·95
	2·97	238·7	1·09		2·86	284·6	0·99
	4·42	244·4	1·11		4·48	292·7	1·01
	6·19	252·4	1·15		1·77	308·1	1·02
<i>p</i> -Toluenesulphondi- chloroamide (240)	1·50	258·4	1·08	<i>N</i> -Acetyl- <i>p</i> -toluene- sulphon- <i>o</i> -toluidide (303)	3·30	319·3	1·05
	2·85	260·6	1·09		6·01	323·2	1·07
	3·83	260·6	1·09		1·06	324·2	1·07
	6·14	264·9	1·10		2·09	328·7	1·085
<i>N</i> -Acetyl- <i>p</i> -toluene- sulphonamide (213)	0·41*	187·2	0·88	<i>N</i> -Acetyl- <i>p</i> -toluene- sulphon- <i>m</i> -toluidide (303)	3·57	323·5	1·07
	1·41*	240·7	1·13		4·97	327·2	1·08
	2·17*	262·8	1·23		1·75	311·7	1·03
<i>N</i> -Acetyl- <i>p</i> -toluene- sulphonmethylamide (227)	1·42	223·1	0·98	<i>N</i> -Acetyl- <i>p</i> -toluene- sulphon- <i>p</i> -toluidide (303)	2·97	306·9	1·01
	2·62	237·5	1·05		4·04	314·0	1·04
	4·10	242·1	1·07		5·10	319·3	1·05
	5·48	245·1	1·08				

\* Concentrations in nitrobenzene.

## EXPERIMENTAL.

Molecular weights were measured cryoscopically in benzene, except that for *N*-acetyl-*p*-toluenesulphonamide nitrobenzene was used. Materials were prepared and purified by usual methods, and the constants of known compounds are reported only when they differ from those recorded in the literature. They are as follows: ethylacetimino-ether, b. p. 90—91° (lit., 92—95°); *N*-diethylchloroacetamide, b. p. 105—107°/11 mm. (lit., 126·5—128·5°/21 mm.); benzenesulphon-*m*-toluidide, m. p. 97—98° (lit., 80°, 95°); benzenesulphondimethylamide, m. p. 51—52° (lit., 47—48°); *p*-toluenesulphon-*p*-toluidide, m. p. 119—120° (lit., 117—118°); *p*-toluenesulphondimethylamide, m. p. 80—81° (lit., 78—79°, 86—87°).

The following new compounds were prepared in the course of the investigation.

*p*-Toluenesulphonphenylbenzylamide, prepared by the action of *p*-toluenesulphonyl chloride on *N*-benzylaniline, formed white needles from alcohol, m. p. 139—140° (Found: N, 4·1; S, 9·7. C<sub>20</sub>H<sub>19</sub>O<sub>2</sub>NS requires N, 4·2; S, 9·5%).

*N*-Acetyl-*p*-toluenesulphonamide.—Equimolecular proportions of *p*-toluenesulphonamide and acetic anhydride were heated under reflux for 3 hours on an oil-bath at 140°. When the product was poured into cold water, the acetyl compound separated as a white crystalline powder, which was crystallised from alcohol. The substance is dimorphous, being obtained as stout rhombs from alcohol, but as needles from aqueous alcohol. Each form can be obtained from an alcoholic solution of the other by seeding with an appropriate crystal; both forms melt at 136—137°, and neither depresses the m. p. of the other. The substance is very sparingly soluble in water giving an acid reaction, decomposes carbonates, and behaves towards alkali as a monobasic acid with phenolphthalein as indicator (Found: N, 6·6; S, 15·0; equiv., 211·4. C<sub>9</sub>H<sub>11</sub>O<sub>3</sub>NS requires N, 6·6; S, 15·0%; equiv., 213). The molecular weight (see Fig. 5) of this substance was determined in nitrobenzene, as it was not sufficiently soluble in benzene.

The acetylation of the secondary sulphonamides is not so easily effected as that described above, and requires a higher temperature (180—200°) and the presence of freshly fused sodium acetate. The resulting compounds, having no tautomeric hydrogen, are neutral in reaction.

*N*-Acetyl-*p*-toluenesulphonmethylamide crystallises from alcohol in white prisms, m. p. 58—59° (Found: N, 6·1; S, 14·1. C<sub>10</sub>H<sub>13</sub>O<sub>3</sub>NS requires N, 6·2; S, 14·1%). *N*-Acetyl-*p*-toluenesulphonanilide crystallises from alcohol in white rhombs, m. p. 149—150° (Found: N, 4·8\*; S, 11·2. C<sub>15</sub>H<sub>15</sub>O<sub>3</sub>NS requires N, 4·8; S, 11·1%). *N*-Acetyl-*p*-toluenesulphon-*o*-toluidide crystallises from alcohol in large clusters of white prisms, m. p. 100° (Found: N, 4·3; S, 10·9. C<sub>16</sub>H<sub>17</sub>O<sub>3</sub>NS requires N, 4·6; S, 10·6%). *N*-Acetyl-*p*-toluenesulphon-*m*-toluidide crystallises from alcohol in small white plates, m. p. 120° (Found: N, 4·5\*; S, 10·6%). *N*-Acetyl-*p*-toluenesulphon-*p*-toluidide forms small white plates from alcohol, m. p. 135° (Found: N, 4·5\*; S, 10·6%).

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\* The analyses denoted by an asterisk were carried out by Dr. G. Weiler.