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insoluble in water and only slowly hydrolyzed. Hydrolysis is rapid, however, in the presence of alkali. They are uniformly soluble in organic solvents. They are readily converted by ammonia, primary amines, and secondary amines to compounds of the types $R_2NSO_2NH_2$, R_2NSO_2NHR' , and $R_2NSO_2NR_2$, respectively (synthesis 28).

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28. N- AND N,N'-SUBSTITUTED SULFAMIDES

 $\begin{array}{l} R_2 NSO_2 Cl + 2NH_3 \rightarrow R_2 NSO_2 NH_2 + NH_4 Cl \\ R_2 NSO_2 Cl + 2RNH_2 \rightarrow R_2 NSO_2 NHR + RNH_3 Cl \\ R_2 NSO_2 Cl + 2R_2 NH \rightarrow R_2 NSO_2 NR_2 + R_2 NH_2 Cl \end{array}$

SUBMITTED BY ANTONIO VANDI* AND THERALD MOELLER* CHECKED BY ELMER SCHLEMPER† AND DOYLE BRITTON†

Dialkylsulfamoyl chlorides, R_2NSO_2Cl , have been prepared by the reaction of sulfuryl chloride with the appropriate amine hydrochloride^{1,2} (synthesis 27), by the treatment of dialkylaminosulfinic (dialkylamidosulfurous) acids with

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chlorine in carbon tetrachloride,³ and by the careful addition of amines to an excess of sulfuryl chloride followed by refluxing.^{4,5} The dialkylsulfamoyl chlorides are particularly useful in the synthesis of N- and N,N'-substituted sulfamides since, contrary perhaps to expectation, the direct formation of the latter by the aminolysis of sulfuryl chloride is difficult to control and leads to polymeric products.⁶ Reactions of the dialkylsulfamoyl chlorides with ammonia, primary amines, or secondary amines are the bases of the most convenient of the known procedures for preparing, respectively, substances of the types $R_2NSO_2NH_2$, R_2NSO_2 -NHR, and $R_2NSO_2NR_2$.⁷

These products are obtained in good yields either by treating the sulfamoyl chloride with liquid ammonia or by refluxing it with the appropriate amine in an inert solvent such as chloroform, benzene, or diethyl ether. Reactions with aliphatic amines are usually complete in 12 hours; those with aromatic amines require up to 24 hours. Two typical procedures are given.

The method of synthesis described herein is the best procedure for preparing unsymmetrically substituted sulfamides, but it can be applied also to the symmetrically substituted ones. However, it may be a longer procedure for the latter, although the yields obtained will be consistently higher than those obtained by either direct aminolysis of sulfuryl chloride or deamination of sulfamide. The direct aminolysis of sulfuryl chloride does not work well with aromatic amines, for which ring chlorination is a complication.

Procedure

A. N,N-Di-n-PROPYLSULFAMIDE

A 500-ml. three-necked flask, equipped with a mechanical stirrer, a dropping funnel, and a reflux condenser with a drying tube filled with potassium hydroxide, is cooled to about -70° in a Dry Ice-acetone bath. Some 300 ml. of

liquid ammonia is then condensed into the flask at -70° . and 60 g. (0.33 mol) of di-n-propylsulfamovl chloride^{4,5} (synthesis 27) is added from the dropping funnel in small portions and with vigorous stirring.* Stirring is continued at -70° for 6 hours after addition of the chloride is complete. The flask is then allowed to warm to room temperature to remove unreacted ammonia and recooled to -70° . An additional 200 ml. of ammonia is condensed into the flask to complete the reaction, and the flask is rewarmed to room temperature.[†] The residue in the flask is extracted with three 50-ml. portions of diethyl ether to separate the product from ammonium chloride.[‡] The solid obtained upon evaporation of the ether is recrystallized from n-heptane (petroleum ether C, b.p. 90 to 100°, is an acceptable substitute) to a white crystalline solid melting at 69°. The yield is 44.0 g. (85%).

B. N,N-PENTAMETHYLENE-4-MORPHOLINESULFONAMIDE

[4-(Piperidinosulfonyl)morpholine]

Eight and seventy-one hundredths grams of morpholine (0.1 mol), dissolved in 50 ml. of anhydrous benzene, is placed in a 250-ml. three-necked flask equipped with a mechanical stirrer, a dropping funnel, and a reflux condenser fitted with a drying tube containing calcium chloride. N,N-Pentamethylenesulfamoyl chloride (9.18 g.;0.05 mol) (synthesis 27) dissolved in 50 ml. of anhydrous benzene is added at room temperature in small portions and with stirring. The reaction mixture is then heated for 12 hours with gentle refluxing. The amine hydrochloride formed is

* Ammonolysis proceeds only when the pure compounds are mixed, and not in the presence of a diluent.

† The second treatment with ammonia improves the yield but is otherwise not necessary. It can be omitted if time is more important than yield.

t The di-n-propyl, diethyl, dimethyl, and di-n-butyl derivatives are all very soluble in cold water. The less soluble morpholine and piperidine derivatives can be freed from ammonium chloride by washing with water.

	Yield,	M.P.,*	B.P. *	ادر ۲	Car	nod	Hydı	ogen	Nitro	ogen
575504TP00	8	ບູ່	°C./mm. Hg	n	Caled.	Found	Calcd.	Found	Caled.	Found
N.NDimethyls ulfamide	8	86			19.36	19.38	6.49	6.47	22.58	22.63
N,N-Diethylsulfsmide	82	46			31.57	31.49	7.95	7.72	18.41	18.49
N,N-Di-n-propylsulfamide	85	69			39.99	40.10	8.95	8.95	15.55	15.50
N,N-Di-n-butylsulfamide	87	20			46.15	45.91	9.68	9.83	13.46	13.71
N,N-Pentamethylenesulfamide	73	120			36.57	36.82	7.36	7.31	17.06	16.88
4-Morpholinesulfonsmide	60	160-162			28.92	29.05	6.0 6	5.80	16.86	17.06
N,N-Diethyl-N'-cyclohexylsulfamide	60	49			51.28	51.00	9.47	9.40	11.95	11.85
N,N-Diethyl-N',N'-di-n-butylsulfamide	65		88/0.15	1.450016	54.53	54.35	10.68	10.65	10.60	10.75
N,N-Diethyl-N'-phenylsulfamide	61	31	171/2.51	1.5260**	52.64	52.48	7.06	7.11	12.28	11.95
N, N-Pentamethylene-N'-cyclohexylsulfamide	65	75			53.64	53.62	9.00	8.99	11.37	11.26
N, N-Pentamethylene-N'-m-tolylaulfamide	70	123-124			56.67	56.83	7.13	7.15	11.02	10.74
N,N-Pentamethylene-N'-o-tolylsulfamide	62	94	-		56.67	56.87	7.13	7.11	11.02	10.74
N,N-Pentamethylene-N'-p-tolylsulfamide	55	97–98			56.67	56.91	7.13	7.20	11.02	10.94
N,N-Pentamethylene-4-morpholinesulfonamide	81	71-72			46.14	46.27	7.74	7.70	11.96	11.93
N,N,N',N'-Dipentamethylenesulfamide (N,N'-sul-										
fonyidipiperidine)	77	92–93			51.69	51.60	8.68	8.75	12.06	11.27

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TABLE I. PROPERTIES AND ANALYSES OF N-SUBSTITUTED SULFAMIDES

• Melting points and boiling points are uncorrected. † The checkers recommend distillation at the lowest possible pressure.

removed by filtration and washed several times with benzene. The combined filtrate and washings are freed of solvent by distillation under vacuum. The resulting brown residue is purified by recrystallization from 100 ml. of *n*-heptane (or 150 ml. of petroleum ether C) to a white crystalline product melting at 71 to 72°. The yield is 9.5 g. (81%).

Properties

Analytical, melting point, boiling point, and refractive index data, together with yields, for a series of compounds prepared by procedures of these types are given in Table I. The N,N-disubstituted sulfamides are white crystalline compounds that dissolve readily in water and many organic solvents. The tri- and tetrasubstituted compounds are either white crystalline solids or colorless oils that dissolve in the common organic solvents but not in cold water. They are only slightly soluble in boiling water.

Recrystallization is best effected from n-heptane, carbon tetrachloride, or diethyl ether. The fact that many amines yield sharply melting derivatives with the sulfamoyl chlorides suggests that the latter may be useful in characterizing the former.

The crystal structure of tetramethylsulfamide is consistent with participation of d orbitals in sulfur-nitrogen bonding.⁸ Data on bond angles and bond lengths significant to this structure are \angle SNC, 119° (av.); \angle CNC, 112.9° (av.); \angle OSO, 119.7°; S-O, 1.445 A. (av.); S-N, 1.623 A.; N-C, 1.476. A. (av.)

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29. DIALKYLAMIDES OF (TRICHLORO-PHOSPHORANYLIDENE)SULFAMIC ACID [N,N-Dialkyl-N'-(trichlorophosphoranylidene)sulfamides; Dialkylamino Trichlorophosphazo Sulfones]

 $R_2NSO_2NH_2 + PCl_5 \rightarrow R_2NSO_2N = PCl_3 + 2HCl$

SUBMITTED BY ANTONIO VANDI* AND THERALD MOELLER* CHECKED BY SHERMAN THOMAS† AND DOYLE BRITTON†

N,N-Dialkylsulfamides, like sulfamide (synthesis 30), react with phosphorus(V) chloride to give the corresponding N-trichlorophosphoranylidene derivatives (phosphazo chlorides).^{1,2} The reactions are carried out by mixing the reactants in an inert solvent. If the reactants are pure and moisture is excluded, the products are obtained pure and in almost quantitative yields. The synthesis of N-(trichlorophosphoranylidene)-4-morpholinesulfonamide is described as typical. The same general procedure is applicable to the preparation of corresponding dialkyl compounds.

Procedure

Eight and three-tenths grams (0.05 mol) of 4-morpholinesulfonamide, $\ddagger 10.4 \text{ g}$. (0.05 mol) of dry pulverized phosphorus(V) chloride, and 50 ml. of dry carbon tetrachloride are placed in a 250-ml. round-bottomed flask fitted with a

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^{‡ 4-}Morpholinesulfonamide is obtained by ammonolysis of the corresponding sulfamoyl chloride (synthesis 28).