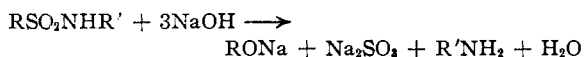


[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE UNIVERSITY OF ILLINOIS]

The Hydrolysis of Substituted Sulfonanilides. II

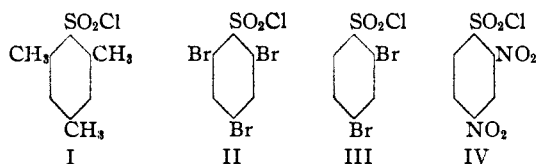
BY MARGARET PEZOLD, R. S. SCHREIBER AND R. L. SHRINER

The marked activating effect of ortho and para nitro groups in accelerating the alkaline cleavage of sulfonanilides¹ according to the equation



suggested that a study of the hydrolysis of sulfonanilides substituted by groups other than the nitro group would determine whether the activating effect observed in the above reaction was similar to the activation of a halogen or amino group by the nitro group. Also, by correlating the activating effect with some definite property of the groups it might be possible to obtain a more precise description of an activating group.

The substituted sulfonanilides were prepared by treating the sulfonyl chlorides (Formulas I, II, III, IV) with aniline and methylaniline. The



hydrolysis of each of the resulting compounds was studied and the results have been collected in Table I.

TABLE I
HYDROLYSIS OF SUBSTITUTED SULFONANILIDES BY MEANS
OF 80% SODIUM HYDROXIDE

Compound	Temp., °C.	Yield of amine, %
$\text{C}_6\text{H}_5\text{SO}_2\text{NHC}_6\text{H}_5$	250	0
$2,4,6\text{-(CH}_3)_3\text{C}_6\text{H}_2\text{SO}_2\text{NHC}_6\text{H}_5$	170-225	0
$2,4,6\text{-(CH}_3)_3\text{C}_6\text{H}_2\text{SO}_2\text{N(CH}_3)_2\text{C}_6\text{H}_5$	185-225	0
$2,4\text{-Br}_2\text{C}_6\text{H}_3\text{SO}_2\text{NHC}_6\text{H}_5$	210-215	0.8
$2,4\text{-Br}_2\text{C}_6\text{H}_3\text{SO}_2\text{N(CH}_3)_2\text{C}_6\text{H}_5$	210-215	.56
$2,4,6\text{-Br}_3\text{C}_6\text{H}_2\text{SO}_2\text{NHC}_6\text{H}_5$	210-215	5.3
$2,4,6\text{-Br}_3\text{C}_6\text{H}_2\text{SO}_2\text{N(CH}_3)_2\text{C}_6\text{H}_5$	210-215	3.4
$2,4\text{-(NO}_2)_2\text{C}_6\text{H}_3\text{SO}_2\text{NHC}_6\text{H}_5$	155	79.0
$2,4\text{-(NO}_2)_2\text{C}_6\text{H}_3\text{SO}_2\text{N(CH}_3)_2\text{C}_6\text{H}_5$	155	71.0

The above hydrolytic data show clearly that the nitro group is the most potent group for accelerating the cleavage between the ring-carbon atom and the sulfur atom. The ortho bromine atom had a slight effect and the methyl group none at all. The yields of amine from the alkali soluble sulfonanilides were slightly greater than those from the alkali insoluble N-methyl sulfonanilides.

(1) Schreiber and Shriner, *THIS JOURNAL*, **56**, 114 (1934).

These results parallel other studies which have shown the superiority of the nitro group in causing activation. These particular substituted sulfonanilides were chosen since they show that the weight and size of the ortho-para groups are not factors in causing activation as may be observed from Table II.

Property	TABLE II		
	-CH ₃	-Br	-NO ₂
Weight	15	79.9	46
Radius Å.	1.73	2.11	1.92
Activating effect	None	Slight	Great

Steric hindrance is not a factor in this cleavage since the tribromo derivatives hydrolyze to a greater extent than the trimethyl or dibromo compounds.

Another difference in the effects which the three groups, methyl, bromo and nitro exert on the ring is to be found in the differences in the experimental procedures used in the preparation of the sulfonyl chlorides. It is worthy of note that mesitylene is converted smoothly to the sulfonyl chloride (I) by chlorosulfonic acid at 0° whereas *sym*-tribromobenzene required sulfonyl chloride in addition to chlorosulfonic acid and four hours heating at a temperature of 100° in order to produce the sulfonyl chloride (II). *sym*-Trinitrobenzene could not be sulfonated at all and all attempts to obtain 2,4,6-trinitrobenzenesulfonyl chloride have failed.

Experimental

2,4,6-Trimethylbenzenesulfonyl chloride.—The procedure described by Demény² was followed except that five moles of chlorosulfonic acid to one of mesitylene were used. This change raised the yield from 46 to 74%, m. p. 56°.

2,4-Dibromobenzenesulfonyl chloride.—A mixture of 100 g. of *m*-dibromobenzene, 100 cc. of chlorosulfonic acid and 100 cc. of sulfonyl chloride was heated at 100° for one hour. The excess sulfonyl chloride was removed by vacuum distillation and the residue, after cooling, was slowly poured into ice water. The crude 2,4-dibromobenzenesulfonyl chloride separated as an oil which solidified after cooling and stirring. The mixture was filtered and the crude product purified by two recrystallizations from petroleum ether. The yield was 105 g. (73.5%) of colorless crystals which melted at 82°. Bässmann³ found a m. p. of 79-79.5°.

(2) Demény, *Rec. trav. chim.*, **50**, 51 (1931).

(3) Bässmann, *Ann.*, **191**, 206 (1878).

Anal. Calcd. for $C_6H_3Br_2SO_2Cl$, Cl: 1.06. Found: 1.04.

2,4,6-Tribromobenzenesulfonylchloride.—A mixture of 20 g. of 2,4,6-tribromobenzene, 30 cc. of chlorosulfonic acid and 30 cc. of sulfonyl chloride was heated at 100° for four hours. The reaction mixture was worked up by the same procedure as above. The yield was 15–19 g. (57–72%) of a buff colored product which melted at 63.5–64°.

2,4-Dinitrobenzenesulfonylchloride.—Oxidative cleavage of 2,4,2',4'-tetranitrodiphenyl disulfide by aqua regia according to the procedure previously described¹ yielded this sulfonylchloride in 72% yields, m. p. 100–101°.

Attempted Preparation of 2,4,6-Trinitrobenzenesulfonylchloride.—Attempts to prepare this compound by the action of phosphorus pentachloride alone, in a solution of xylene, and mixtures of it with phosphorus trichloride and oxychloride on the sodium salt of 2,4,6-trinitrobenzene sulfonate, prepared by the method of Willgerodt,⁴ at various temperatures from 80–180°, were unsuccessful. The only product isolated was picryl chloride.

This sulfonylchloride could not be prepared by the method used above for the 2,4-dinitrobenzenesulfonylchloride because the reaction between picryl chloride and sodium disulfide gave only the hexanitrodiphenylsulfide. Variations in conditions failed to produce any disulfide. The action of potassium hydrogen sulfide on picryl chloride also gave the monosulfide and no disulfide or thiopicric acid.

The 2,4,6,2',4',6'-hexanitrodiphenylsulfide was produced in almost quantitative yields by the first reaction. It decomposed at 227–228°.

Anal. Calcd. for $C_{12}H_4O_{12}N_6S$; S, 7.01; Found: S, 7.03.

(4) Willgerodt, *J. prakt. Chem.*, **32**, 117 (1885).

Preparation of Sulfonanilides and N-Methyl Sulfonanilides.—The general method followed consisted in adding the powdered sulfonylchloride to an excess of the amine at a temperature below 10° with vigorous stirring. The sulfonanilides were washed with water, dilute acid and again with water. The solids were recrystallized from alcohol or glacial acetic acid and the liquids vacuum distilled. Table III summarizes the data on new compounds; the 2,4-dinitrosulfonanilide and methylsulfonylchloride have been previously described.¹

TABLE III

Compound	M. p., °C.	Solvent for crys.	Analyses, %	
			Calcd.	Found
2,4-Br ₂ C ₆ H ₃ SO ₂ NHC ₆ H ₅	145.4–6.5	Alc.	N 3.59	3.63
2,4-Br ₂ C ₆ H ₃ SO ₂ N(CH ₃)C ₆ H ₅	Oil B. p.			
	210–214° (4 mm.)		N 3.46	3.47
2,4,6-Br ₃ C ₆ H ₂ SO ₂ NHC ₆ H ₅	118	Alc.	N 2.99	3.20
2,4,6-Br ₃ C ₆ H ₂ SO ₂ N(CH ₃)C ₆ H ₅	148–8.5	HOAc	N 2.90	3.10
2,4,6-(CH ₃) ₂ C ₆ H ₃ SO ₂ NHC ₆ H ₅	108–9	Alc.	S 11.64	11.68
2,4,6-(CH ₃) ₂ C ₆ H ₃ SO ₂ N(CH ₃)C ₆ H ₅	95–6	Alc.	S 11.07	10.92

Alkaline Hydrolysis.—The general procedure followed the same lines as previously described.¹ The yields of amines and temperatures of heating have been given in Table I. The time of heating varies from thirty minutes for the nitro compounds to four hours for the others.

Summary

A study of the alkaline cleavage of substituted benzene-sulfonanilides indicates that nitro groups are more effective in promoting the cleavage than bromo- or methyl groups. The results indicate that weight, size or steric hindrance effects are not factors in this cleavage.

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[CONTRIBUTION FROM THE LABORATORY OF ORGANIC CHEMISTRY OF THE UNIVERSITY OF WISCONSIN]

The Reaction of Organic Halides with Piperidine. IV. Bromo Esters

BY W. V. DRAKE AND S. M. McELVAIN

The previous papers¹ of this series have shown (1) that the rate of reaction of various alkyl bromides with piperidine is in the order primary > secondary > tertiary, and (2) that primary bromides, in general, react with 2 moles of piperidine to give one mole of a tertiary amine and one mole of piperidine hydrobromide; tertiary bromides react with one mole of piperidine with the elimination of hydrogen bromide and the formation of unsaturated compounds; secondary bromides follow both of these reaction courses but, with the exception of cyclohexyl bromide, give considerably more of the tertiary amine than unsaturated compound.

(1) (a) Semb and McElvain, *THIS JOURNAL*, **53**, 690 (1931); (b) Howk and McElvain, *ibid.*, **54**, 282 (1932); (c) Drake and McElvain, *ibid.*, **55**, 1155 (1933).

It seemed desirable to extend this study to the bromo esters in order to ascertain what effect the presence of a carboxy group in the molecule would have on the rate and course of reaction of these three types of bromides. The present paper reports the results obtained from thirteen different bromo esters.

Experimental

Bromo Esters.—The α -bromo esters used were made by the reaction of ethyl alcohol with the α -bromo acid bromides which were obtained by the direct bromination of the acid bromides. Ethyl β -bromopropionate was prepared from ethylene cyanohydrin.² Ethyl γ -bromobutyrate and ethyl δ -bromovalerate were prepared by

(2) "Organic Syntheses," Coll., Vol. I, 1932, p. 241.