

Sulfonamides of Hydroxylamine Derivatives<sup>1a</sup>

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We report the synthesis of N-alkoxy-O-arylsulfonylacylimines (I,  $\text{ArSO}_2(\text{R})\text{C}=\text{NOR}$ ) (Table I) the isomeric N-acyl-N-arylsulfonyl-O-alkylhydroxylamines (II,  $\text{RCON}(\text{OR})\text{SO}_2\text{Ar}$ ), and arylsulfonyl-O-alkylhydroxylamines (III,  $\text{ArSO}_2\text{NHOR}'$ ) (Table II) as potential bacteriostatic agents.

Several representatives of I and III showed no significant antibacterial or antifungal activity.<sup>2</sup>

## Experimental Section

Melting points are corrected. Microanalyses were performed by Drs. Weiler and Strauss (Oxford, England) and Dr. A. Bern-

of the two peaks  $\tau$  4.92 and 4.86 was 0.7:1.0 and was due to *syn* and *anti* structures I.<sup>4</sup> In  $\text{CF}_3\text{CO}_2\text{H}$ , singlet 3 H at  $\tau$  8.1, singlet 2 H at  $\tau$  5.2, multiplet 14 H  $\tau$  2.5. *Anal.* ( $\text{C}_{21}\text{H}_{19}\text{NO}_4\text{S}$ ) C, H, N, S.

**Benzyl Benzenesulfonylbenzimidino Ether.** **Method II.**—A mixture of 4.54 g (0.02 mole) of N-benzo-O-benzylhydroxylamine 3.76 g (0.0212 mole) of  $\text{C}_6\text{H}_5\text{SO}_2\text{Cl}$ , and 20 ml of 20% NaOH was shaken until the odor of benzenesulfonyl chloride had disappeared. The mixture was extracted ( $\text{Et}_2\text{O}$ ), and the ether was dried and distilled. The residue (1.2 g) was recrystallized from petroleum ether to give 0.90 g (12%) of product: mp 72.2–73.2°; ir (Nujol),  $\text{SO}_2$  at 1380 and 1180, C–O at 1310, and C–O–C at 1255  $\text{cm}^{-1}$ . *Anal.* ( $\text{C}_{20}\text{H}_{17}\text{NO}_4\text{S}$ ) C, H, N, S.

**N-Acetyl-O-propylhydroxylamine with p-Acetylamino benzenesulfonyl Chloride in Pyridine.** **Method III.**—Following the method of Robin and Winnek,<sup>5</sup> 5.85 g (0.050 mole) of N-acetyl-O-propylhydroxylamine<sup>4</sup> and 23 g (0.10 mole) of p-acetylamino benzenesulfonyl chloride were dissolved in 100 ml of dry pyridine. The mixture was warmed on a steam bath overnight. When the pyridine was removed under reduced pressure, a solid formed. Part of the solid dissolved ( $\text{H}_2\text{O}$ ) and the remainder was recrystallized ( $\text{AcOH}$ ,  $\text{EtOH}$ ), yield 6.0 g (28%), mp 126–126°. *Anal.* ( $\text{C}_{13}\text{H}_{18}\text{N}_2\text{O}_5\text{S}$ ) C, H, N, S. The ir spectrum was as expected for I.

TABLE I  
COMPOUNDS I

R	R'	Ar	Method of prepn	% yield	Mp, °C	Formula
$\text{C}_6\text{H}_5$	$\text{C}_3\text{H}_5$	<i>p</i> - $\text{CH}_3\text{C}_6\text{H}_4$	I	54	95–96	$\text{C}_{17}\text{H}_{17}\text{NSO}_4$
<i>p</i> - $\text{CH}_3\text{C}_6\text{H}_4$	$\text{C}_3\text{H}_7$	<i>p</i> - $\text{CH}_3\text{C}_6\text{H}_4$	II	35	98.5–99.5	$\text{C}_{18}\text{H}_{21}\text{NO}_4\text{S}$
<i>p</i> - $\text{CH}_3\text{C}_6\text{H}_4$	$\text{C}_6\text{H}_5\text{CH}_2$	<i>p</i> - $\text{CH}_3\text{C}_6\text{H}_4$	II	8	109.5–110.5	$\text{C}_{22}\text{H}_{21}\text{NO}_4\text{S}$
<i>p</i> - $\text{CH}_3\text{C}_6\text{H}_4$	$\text{CH}=\text{CCH}_3$	<i>p</i> - $\text{CH}_3\text{C}_6\text{H}_4$	II	9	95.5–96.5	$\text{C}_{18}\text{H}_{17}\text{NO}_4\text{S}$
<i>p</i> - $\text{CH}_3\text{OC}_6\text{H}_4$	$\text{C}_6\text{H}_5\text{CH}_2$	$\text{C}_6\text{H}_5$	II	11	103.5–104	$\text{C}_{21}\text{H}_{19}\text{NO}_5\text{S}$

TABLE II  
COMPOUNDS III

R'	Ar	Method of prepn <sup>a</sup>	% yield	Mp, °C	Formula
$\text{C}_3\text{H}_5$	<i>p</i> - $\text{CH}_3\text{C}_6\text{H}_4$	I <sup>b</sup>	26	92–93	$\text{C}_{10}\text{H}_{15}\text{NSO}_3$
$\text{C}_3\text{H}_7$	<i>p</i> - $\text{CH}_3\text{CONHC}_6\text{H}_4$	I <sup>c</sup>	24	139–140	$\text{C}_{11}\text{H}_{16}\text{N}_2\text{O}_4\text{S}$
$\text{C}_6\text{H}_4\text{CH}_2$	<i>p</i> - $\text{CH}_3\text{C}_6\text{H}_4$	II <sup>d</sup>	81	94–95	$\text{C}_{14}\text{H}_{18}\text{NO}_4\text{S}$

<sup>a</sup> Isolation by acidification and extraction ( $\text{Et}_2\text{O}$ ). <sup>b</sup> Starting material, N-aceto-O-allylhydroxylamine; the N-acetyl group was lost. <sup>c</sup> N-Propano-O-propylhydroxylamine was the starting material. <sup>d</sup> Benzylhydroxylamine was the starting compound; purified by M. W. Mosher.

hardt (Mühlheim, Germany). The infrared spectra were determined with a Perkin-Elmer 137, and the nmr spectra with a Varian A-60 spectrometer. Where analyses are indicated only by the symbols of the elements, the analytical results obtained for those elements were within  $\pm 0.4\%$  of the theoretical values.

**Benzyl p-Toluenesulfonylbenzimidino Ether.** **Method I.**—When 5.0 g of 23% NaH (in mineral oil) was added to 11.35 g (0.050 mole) of N-benzoyl-O-benzylhydroxylamine<sup>3</sup> in 100 ml of dry  $\text{C}_6\text{H}_6$ ,  $\text{H}_2$  was evolved and a white precipitate formed. *p*-Toluenesulfonyl chloride (9.52 g, 0.050 mole) in 50 ml of  $\text{C}_6\text{H}_6$  was added, and the mixture was refluxed for 3 days. Water was added and the benzene solution was separated and concentrated, and the residue was chromatographed on alumina. The mineral oil was eluted with petroleum ether (bp 60–90°) and 14.01 g (73%) of product was eluted with benzene, mp 95–96° after recrystallization from  $\text{C}_6\text{H}_6$ ; ir (Nujol),  $\text{C}=\text{N}$ , 1580,  $\text{SO}_2$ , 1365 and a doublet at 1170–1180  $\text{cm}^{-1}$ ; nmr ( $\text{CDCl}_2$ ), singlets at  $\tau$  8.1 (3 H), 4.92 and 4.86 (2 H), multiplet at  $\tau$  2.6 (14 H). The ratio

**N-Benzoyl-N-p-toluenesulfonyl-O-benzylhydroxylamine.**—A mixture of 2.77 g (0.01 mole) of N-p-toluenesulfonyl-O-benzylhydroxylamine in 20 ml of anhydrous pyridine and 1.40 g (0.01 mole) of  $\text{C}_6\text{H}_5\text{COCl}$  was stirred for 6 hr. A precipitate was obtained on addition of water and 3.3 g (86%) of product, mp 112–113°, was obtained (from  $\text{EtOH}$ ). *Anal.* ( $\text{C}_{21}\text{H}_{19}\text{NO}_4\text{S}$ ) C, H, N, S. Ir (Nujol) was expected for II,  $\text{C}=\text{O}$  at 1650  $\text{cm}^{-1}$ .

(4) G. J. Karabatsos, R. A. Taller, and F. M. Vane, *J. Am. Chem. Soc.*, **85**, 2326, 2327 (1963).

(5) R. O. Robin, Jr., and P. S. Winnek, *ibid.*, **62**, 1999 (1940).

N<sup>4</sup>-Substituted N<sup>1</sup>-Toluenesulfonylpiperazines

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In our continuing search for potential hypoglycemic agents, we have altered a series of sulfonyleureas by replacing the toluenesulfonamido moiety by a toluenesulfonylpiperazino moiety. We wish to report the synthesis of some new 1-(*p*-toluenesulfonyl)-4-carbamoylpiperazines and 1-(*p*-toluenesulfonyl)-4-thiocarbamoylpiperazines. The compounds showed no hypoglycemic, hypotensive, or anticonvulsant activity.

Experimental Section<sup>1</sup>

**1-(p-Toluenesulfonyl)-4-n-butylcarbamoylpiperazine.**—To a solution of 4.0 g (0.016 mole) of 1-(*p*-toluenesulfonyl)piperazine<sup>2</sup> in 25 ml of acetonitrile was added 2.6 g (0.25 mole) of *n*-butyl isocyanate all at once. The reaction was exothermic and, on stirring vigorously, 6.4 g of the product crystallized out. It was filtered and washed with cold acetonitrile. Recrystallization from acetonitrile yielded 3.8 g. The other compounds listed in Table I were prepared similarly.

(1) Melting points were taken on a Fisher-Johns block and are corrected. Analyses are by Midwest Microlab, Inc., Indianapolis, Ind.

(2) T. S. Moore, M. Boyle, and V. M. Thorn, *J. Chem. Soc.*, 39 (1929).

(1) (a) We are indebted to the National Science Foundation for Grant NSF G 13289 and to the National Institutes of Health for Grant E-4173 in support of this work. A portion of the results was presented at the Northwest Regional Meeting of the American Chemical Society, Spokane, Wash., June 1964. (b) Taken in part from the Ph.D. thesis of B. N. Misra, Feb 1967, the M.S. thesis of W. D. Bills, June 1960, and the M.S. thesis of J. R. Throckmorton, June 1960.

(2) We thank Dr. R. E. Kent of the Chas. Pfizer Co. for the tests on I and Dr. Glen R. Gale of the Medical College of South Carolina for the tests on III.

(3) J. H. Cooley, W. D. Bills, and J. R. Throckmorton, *J. Org. Chem.*, **25**, 1734 (1960).