Sulfonamides of Hydroxylamine Derivatives[1a]

JAMES H. COOLEY, BHUPENDRA N. MISRA,[1b] JAMES R. THROCKMORTON,[1b] and WILLIAM D. BILLS[1b]

Department of Chemistry, University of Idaho, Moscow, Idaho 83843

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We report the synthesis of N-alkoxy-O-arylsulfonylacylimines (I, $ArSO_3(R)C{=}NOR$) (Table I) the isomeric N-acyl-N-arylsulfonyl-O-alkylhydroxylamines (II, $RCON(OR)SO_2Ar$), and arylsulfonyl-O-alkylhydroxylamines (III, $ArSO_2NHOR'$) (Table II) as potential bacteriostatic agents.

Several representatives of I and III showed no significant antibacterial or antifungal activity.[2]

Experimental Section

Melting points are corrected. Microanalyses were performed by Drs. Weiler and Strauss (Oxford, England) and Dr. A. Bernhardt (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 ±0.4% of the theoretical values.

Benzyl *p*-Toluenesulfonylbenzimino 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[3] in 100 ml of dry C_6H_6, H_2 was evolved and a white precipitate formed. *p*-Toluenesulfonyl chloride (9.52 g, 0.050 mole) in 50 ml of C_6H_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 C_6H_6; ir (Nujol), C=N, 1580, SO_2, 1365 and a doublet at 1170–1180 cm^{-1}; nmr ($CDCl_2$), singlets at τ 8.1 (3 H), 4.92 and 4.86 (2 H), multiplet at τ 2.6 (14 H). The ratio of the two peaks τ 4.92 and 4.86 was 0.7:1.0 and was due to *syn* and *anti* structures I.[4] In CF_3CO_2H, singlet 3 H at τ 8.1, singlet 2 H at τ 5.2, multiplet 14 H τ 2.5. *Anal.* ($C_{21}H_{19}NO_4S$) C, H, N, S.

Benzyl Benzenesulfonylbenzimino Ether. Method II.—A mixture of 4.54 g (0.02 mole) of N-benzo-O-benzylhydroxylamine, 3.76 g (0.0212 mole) of $C_6H_5SO_2Cl$, and 20 ml of 20% NaOH was shaken until the odor of benzenesulfonyl chloride had disappeared. The mixture was extracted (Et_2O), 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), SO_2 at 1380 and 1180, C–O at 1310, and C–O–C at 1255 cm^{-1}. *Anal.* ($C_{20}H_{17}NO_4S$) C, H, N, S.

N-Acetyl-O-propylhydroxylamine with *p*-Acetylaminobenzenesulfonyl Chloride in Pyridine. Method III.—Following the method of Robin and Winnek,[5] 5.85 g (0.050 mole) of N-acetyl-O-propylhydroxylamine[4] and 23 g (0.10 mole) of *p*-acetylaminobenzenesulfonyl 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 (H_2O) and the remainder was recrystallized (AcOH, EtOH), yield 6.0 g (28%), mp 126–126°. *Anal.* ($C_{13}H_{18}N_2O_5S$) 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
C_6H_5	C_3H_5	*p*-$CH_3C_6H_4$	I	54	95–96	$C_{17}H_{17}NSO_4$
p-$CH_3C_6H_4$	C_3H_7	*p*-$CH_3C_6H_4$	II	35	98.5–99.5	$C_{18}H_{21}NO_4S$
p-$CH_3C_6H_4$	$C_6H_5CH_2$	*p*-$CH_3C_6H_4$	II	8	109.5–110.5	$C_{22}H_{21}NO_4S$
p-$CH_3C_6H_4$	$CH{\equiv}CCH_2$	*p*-$CH_3C_6H_4$	II	9	95.5–96.5	$C_{18}H_{15}NO_4S$
p-$CH_3OC_6H_4$	$C_6H_5CH_2$	C_6H_5	II	11	103.5–104	$C_{21}H_{19}NO_5S$

TABLE II
COMPOUNDS III

R'	Ar	Method of prepn[a]	% yield	Mp, °C	Formula
C_4H_5	*p*-$CH_3C_6H_4$	I[b]	26	92–93	$C_{10}H_{13}NSO_3$
C_3H_7	*p*-$CH_3CONHC_6H_4$	I[c]	24	139–140	$C_{11}H_{16}N_2O_4S$
$C_6H_5CH_2$	*p*-$CH_3C_6H_4$	II[d]	81	94–95	$C_{14}H_{15}NO_3S$

[a] Isolation by acidification and extraction (Et_2O). [b] Starting material, N-aceto-O-allylhydroxylamine; the N-acetyl group was lost. [c] N-Propano-O-propylhydroxylamine was the starting material. [d] Benzyloxyamine was the starting compound; purified by M. W. Mosher.

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 C_6H_5COCl 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 EtOH). *Anal.* ($C_{21}H_{19}NO_4S$) C, H, N, S. Ir (Nujol) was expected for II, C=O at 1650 cm^{-1}.

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(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).

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N⁴-Substituted N¹-Toluenesulfonylpiperazines

J. R. SHROFF

USV Pharmaceutical Corporation, Yonkers, New York 10701

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In our continuing search for potential hypoglycemic agents, we have altered a series of sulfonylureas 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[1]

1-(*p*-Toluenesulfonyl)-4-*n*-butylcarbamoylpiperazine.—To a solution of 4.0 g (0.016 mole) of 1-(*p*-toluenesulfonyl)piperazine[2] 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).