an aqueous acetic acid solution of the material to pH 5 with NH_4OH.

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Some N-Substituted Derivatives of Bis(4-amino-3-nitrophenyl) Sulfone[1]

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As part of a systematic study of the chemistry of bis(4-chloro-3-nitrophenyl) sulfone[2] several N-substituted derivatives of bis(4-amino-3-nitrophenyl) sulfone[3] of potential physiological interest have been prepared.

N-Substituted derivatives of bis(4-amino-3-nitrophenyl) sulfone, listed in Table I, were prepared by two variations of the same procedure.

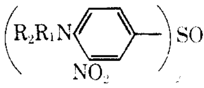
Procedure A.—To bis(4-chloro-3-nitrophenyl) sulfone (3.77 g, 0.01 mole) and 5.5 g (0.04 mole) of anhydrous K_2CO_3, 0.025 mole of freshly distilled amine dissolved in 60 ml of absolute ethanol was added and the reaction mixture was refluxed for 3 hr with stirring. In some cases, after 2 hr of refluxing 6 ml of water was added and the refluxing was continued for an additional 1 hr. The cooled reaction mixture was poured into 200 ml of water. The precipitate was filtered, washed with water, and air dried. The crude product was treated with decolorizing carbon in the appropriate solvent, frequently glacial acetic acid or ethanol, and was recrystallized several times.

Procedure B was the same as procedure A except that 0.045 mole of amine dissolved in 200 ml of absolute ethanol was used in the absence of K_2CO_3. If on slow cooling an oil separated, the reaction mixture was refluxed an additional 20 min and then cooled slowly. The precipitate was filtered, washed with water, air dried, treated with decolorizing carbon in alcohol solution, and finally recrystallized several times from the appropriate solvent. In a few cases where the product failed to separate, the reaction mixture was poured into 400 ml of water and worked up as in procedure A.

In some cases where products were obtained only as oils using procedure A, the use of procedure B resulted in crystalline products. In general better yields were obtained by the use of procedure B.

TABLE I

N-SUBSTITUTED DERIVATIVES OF BIS(4-AMINO-3-NITROPHENYL) SULFONE[a]



No.	R_1	R_2	Procedure	Yield,[b] %	Mp, °C	Recrystn solvent[c]	Formula	Calcd, % C	Calcd, % H	Calcd, % N	Calcd, % S	Found, % C	Found, % H	Found, % N	Found, % S
1	CH_3	H	A	70	249–250	AcOH	$C_{14}H_{14}N_4O_6S$	45.89	3.85	15.29	8.75	45.93	3.77	15.18	8.64
2	CH_3	CH_3	A	74	169–171	AcOH	$C_{16}H_{18}N_4O_6S$	48.72	4.60	14.21	8.12	49.21	4.72	14.98	8.08
3	n-C_4H_9	H	A	88	150–151	AcOH	$C_{20}H_{26}N_4O_6S$	53.32	5.32	12.43	7.11	53.53	5.26	12.44	7.11
4	i-C_4H_9	H	A	85	122–124	Et	$C_{20}H_{26}N_4O_6S$	53.32	5.32	12.43	7.11	53.62	5.20	12.33	7.06
5	n-C_6H_{13}	H	B	43	104–105	Et	$C_{24}H_{34}N_4O_6S$	56.91	6.78	11.06	6.33	56.98	6.92	11.29	6.54
6	n-C_7H_{15}	H	A	45	74–75	AcOH	$C_{26}H_{38}N_4O_6S$	58.40	7.16	10.48	5.99	58.61	7.23	10.37	6.04
7	n-C_8H_{17}	H	B	34	76–78	E–H	$C_{28}H_{42}N_4O_6S$	59.76	7.52	9.96	5.69	60.02	7.52	10.12	5.69
8	n-$C_{10}H_{21}$	H	B	56	87–88	Et	$C_{32}H_{50}N_4O_6S$	62.10	8.14	9.05	5.18	62.12	8.22	9.07	5.12
9	n-$C_{12}H_{25}$	H	B	36	84–85	Et	$C_{36}H_{58}N_4O_6S$	64.06	8.66	8.30	4.75	64.42	8.72	8.48	4.88
10	n-$C_{14}H_{29}$	H	A	29	82–83	A	$C_{40}H_{66}N_4O_6S$	65.71	9.10	7.66	4.38	65.67	8.98	7.74	4.46
11	n-$C_{16}H_{33}$	H	A	36	83–85	A	$C_{44}H_{74}N_4O_6S$	67.13	9.47	7.12	4.07	66.98	9.89	7.22	4.01
12	n-$C_{18}H_{37}$	H	A	17	91–92	A	$C_{48}H_{82}N_4O_6S$	68.36	9.80	6.64	3.80	68.36	9.49	6.76	3.87
13	n-$C_{18}H_{37}$	CH_3	B	75	81–83	Et	$C_{50}H_{86}N_4O_6S$	68.92	9.95	6.43	3.68	68.86	9.90	6.20	3.50
14	m-$CH_3C_6H_4$	H	B	23	196–198	An	$C_{26}H_{22}N_4O_6S$	60.22	4.28	10.81	6.18	60.08	4.38	10.82	6.12
15	p-$CH_3C_6H_4$	H	A	44	221–223	B–P	$C_{26}H_{22}N_4O_6S$	60.22	4.28	10.81	6.18	60.25	4.35	10.73	6.09
16	p-$CH_3OC_6H_4$	H	A	58	238–239	T	$C_{26}H_{22}N_4O_8S$	56.72	4.03	10.18	5.82	56.94	4.17	10.25	6.02
17	p-$C_2H_5OC_6H_4$	H	A	65	216–217	T–P	$C_{28}H_{26}N_4O_8S$	58.12	4.53	9.68	5.54	58.34	4.59	9.54	5.46
18	$-CH_2CH_2OCH_2CH_2-$		A	94	204–206	AcOH	$C_{20}H_{22}N_4O_8S$	50.20	4.63	11.71	6.70	50.03	4.85	11.83	6.75
19	$-CH_2(CH_2)_2CH_2-$		A	44	227–229	A	$C_{20}H_{22}N_4O_6S$	53.80	4.97	12.55	7.18	53.54	4.80	12.62	7.21

[a] All compounds are yellow. [b] Yield calculated after one recrystallization. [c] A = acetone, An = acetonitrile, B = benzene, E = ether, Et = ethanol, H = heptane, AcOH = glacial acetic acid, P = petroleum ether, T = toluene.

Experimental Section[4]

Bis(4-chloro-3-nitrophenyl) sulfone was prepared in 97% yield by the nitration of bis(4-chlorophenyl) sulfone by the method of Buehler and Masters.[5,2]

The derivatives of methylamine and dimethylamine (**1** and **2**, Table I) were prepared by procedure A, using a large excess of the amine hydrochloride and anhydrous K_2CO_3. The yields were not improved by procedure B employing pressure at 150° for 4 hr[3a] but the products were more readily purified.

Several attempts to N-alkylate the products which were secondary amines using methyl iodide or dimethyl sulfate under various conditions were unsuccessful. Similarly, all attempts to quaternize the products which were tertiary amines using methyl iodide, dimethyl sulfate, benzyl chloride, or methyl p-toluenesulfonate were unsuccessful.

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[1] Abstracted in part from the theses of R. T. Enright and R. V. Mark, presented to the Graduate School of St. John's University in partial fulfillment of the requirements for the degree of Master of Science, June 1964 and June 1966, respectively.

[2] W. F. Hart and M. E. McGreal, *J. Med. Chem.*, **8**, 141 (1965).

[3] For previous literature see (a) F. Ullmann and J. Korselt, *Ber.*, **40**, 643 (1907); (b) R. J. LeFevre and E. E. Turner, *J. Chem. Soc.*, 1113 (1927).

[4] Melting points were taken in capillary tubes and are corrected. Elemental analyses were determined by Drs. Weiler and Strauss, Oxford, England.

[5] C. A. Buehler and J. E. Masters, *J. Org. Chem.*, **4**, 262 (1939).