days. At that time the solution was filtered and evaporated to dryness. The residue was partitioned between water and chloroform. The aqueous layer was evaporated to dryness *in vacuo* and the residue was crystallized from 2 ml. of water–3 ml. of absolute ethanol–20 ml. of ether yielding 70 mg. of product, as needles, m.p. 247–249° dec.; $\lambda_{max}^{0.1\,N\ HCl}$ 289 mμ (log ϵ 4.00), λ_{min} 244 mμ; $\lambda_{max}^{pH\ 7\ buffer}$ 274 mμ (log ϵ 3.93), λ_{min} 250 mμ; $\lambda_{max}^{0.1\,N\ NaOH}$ 278 mμ (log ϵ 3.84), λ_{min} 256 mμ; $[\alpha]^{27}$D +30.6° (*c* 0.49, water).

Anal. Calcd. for $C_{10}H_{14}FN_3O_5$: C, 43.64; H, 5.13; N, 15.27; F, 6.91. Found: C, 43.44, 43.68; H, 5.15, 5.13; N, 15.01, 15.35; F, 7.13.

Some Bis(3-nitro- and 3-amino-4-alkoxy- and -4-aryloxyphenyl) Sulfones

WILLIAM F. HART

Department of Chemistry, Lafayette College,
Easton, Pennsylvania 18042

AND MARTIN E. MCGREAL

Department of Chemistry, St. Johns University,
Jamaica, New York 11432

Received September 11, 1964

As part of a systematic study of the chemistry of bis(4-chloro-3-nitrophenyl) sulfone a group of bis(4-alkoxy- and 4-aryloxy-3-nitrophenyl) sulfones (Table I) and some corresponding 3-amino compounds (Table II) which have potential physiological interest have been synthesized.

Experimental

Bis(4-chlorophenyl) Sulfone.—This compound, m.p. 148–149°, was kindly contributed by the Stauffer Chemical Company. It was used for nitration without further purification.

Bis(4-chloro-3-nitrophenyl) Sulfone.—The above sulfone was nitrated in 97% yield by the method of Buehler and Masters.[1] After recrystallization from glacial acetic acid or dioxane it melted at 201–202° which agrees with the literature.[2]

Bis(4-alkoxy-3-nitrophenyl) Sulfones.—The first two members of this series have been described by Annaheim[3] and by Ullman and Korselt.[2] Annaheim prepared bis(4-methoxy-3-nitrophenyl) sulfone (I) and bis(4-ethoxy-3-nitrophenyl) sulfone (II) by nitration of the corresponding bis(4-alkoxyphenyl) sulfones. He reported the melting points of these compounds to be 214–215° and 192°, respectively. Ullman and Korselt prepared these compounds by treating bis(4-chloro-3-nitrophenyl) sulfone with the sodium alkoxides in the presence of the respective alcohol under pressure at 160° for 5 hr. They reported for I, m.p. 240°, and for II, m.p. 192°. Our preparation of I by the method described below melted at 216–217°.

We have found that the strenuous conditions used by Ullman and Korselt are not necessary to give satisfactory yields. The reaction is essentially complete at 65° in 15–60 min., except in the case of I which required 40 hr. at the temperature of refluxing methanol.

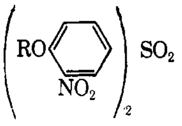
To a stirred solution of 1.6 g. (0.07 g.-atom) of sodium in 80 ml. of the anhydrous alcohol cooled to 40° was added 10 g. (0.026 mole) of bis(4-chloro-3-nitrophenyl) sulfone in portions. On warming, a mildly exothermic reaction occurred; the temperature was maintained at 65° for periods of 15–60 min. It was found that higher temperatures produced tarry products from which no crystalline product could be isolated. In the case of water-soluble alcohols, the reaction mixture was poured into 400 ml. of water, and the product was removed by vacuum filtration. In the case of the higher alcohols, the excess alcohol was removed by steam distillation, and the solid product was separated by filtration. The crude product was washed with water until the filtrates were colorless and free of chloride ion. The product after air drying was recrystallized two or more times from glacial acetic acid with the use of decolorizing carbon.

Bis[4-(2,3-dibromo)-3-nitropropoxyphenyl] Sulfone.—Compound VIIa was prepared by bromination of bis(4-allyloxy-3-nitrophenyl) sulfone (VII) in chloroform solution containing 3% by volume of glacial acetic acid. The stoppered flask was kept in the dark for 3 days at room temperature. The excess bromine was removed by addition of 10% NaOH solution and the chloroform was removed by steam distillation. The product which solidified on chilling was washed free of alkali, air-dried, and recrystallized from glacial acetic acid, m.p. 130–132°.

Bis(4-aryloxy-3-nitrophenyl) Sulfones.—The 4-phenoxy VIII and 4-*p*-toloxy IX compounds were prepared by the method of Brewster and Groenig.[4] A spontaneous reaction occurred at 120° when the bis(4-chloro-3-nitrophenyl) sulfone was added in two portions to the potassium phenolate, and the reaction was maintained at this temperature for 30 min. The reaction mixture was taken up in cold NaOH solution, and the product separated by filtration. The crude products were washed with water

TABLE I

BIS(4-ALKOXY- AND 4-ARYLOXY-3-NITROPHENYL) SULFONES



Compd.	R	Yield,[a] %	M.p., °C.[b]	Formula	—% carbon— Calcd.	Found	—% hydrogen— Calcd.	Found	—% nitrogen— Calcd.	Found
I	CH_3	79	216–217	$C_{14}H_{12}N_2O_8S$	45.65	45.76	3.28	3.20	7.60	7.49
II	C_2H_5	62	195–196	$C_{16}H_{16}N_2O_8S$	48.48	48.50	4.06	4.21	7.06	6.98
III	n-C_3H_7	72	197–198	$C_{18}H_{20}N_2O_8S$	50.93	50.58	4.74	4.89	6.60	6.70
IV	n-C_4H_9	78	160–161	$C_{20}H_{24}N_2O_8S$	53.08	53.27	5.34	5.50	6.19	6.15
V	n-C_5H_{11}	34	120–121	$C_{22}H_{28}N_2O_8S$	54.98	55.31	5.87	5.97	5.83	5.65
VI	n-$C_{12}H_{25}$[c]	17	104–105	$C_{36}H_{56}N_2O_8S$	63.87	63.99	8.33	8.45	4.13	4.24
VII	$CH_2{=}CHCH_2$	74	189–190	$C_{18}H_{16}N_2O_8S$	51.42	51.42	3.83	3.86	6.66	6.50
VIIa	$CH_2(Br)CH(Br)CH_2$		130–132	$C_{18}H_{16}Br_4N_2O_8S$	29.21	29.31	2.18	2.16	3.78	3.72
VIII	C_6H_5	71	173–176	$C_{24}H_{16}N_2O_8S$	58.53	58.21	3.27	3.25	5.68	5.35
IX	p-$CH_3C_6H_4$	74	173–175	$C_{26}H_{20}N_2O_5S$	59.99	59.44	3.87	3.96	5.38	5.67
X	p-$NO_2C_6H_4$	79	218	$C_{24}H_{14}N_4O_{12}S$[d]	49.48	49.60	2.42	2.45	9.62	9.76

[a] Yields calculated after one recrystallization. [b] Melting points were determined on a Fisher-Johns block and are uncorrected. [c] Reaction carried out using 140 ml. of alcohol. [d] Calcd.: S, 5.50. Found: S, 5.68.

---

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

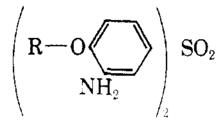
[2] F. Ullman and J. Korselt, *Ber.*, **40**, 643 (1907).

[3] J. Annaheim, *Ann.*, **172**, 49 (1874).

[4] R. Q. Brewster and T. Groenig, "Organic Synthesis," Coll. Vol. II, John Wiley and Sons, Inc., New York, N. Y., 1943, p. 445.

TABLE II

BIS(3-AMINO-4-ALKOXY- AND -4-ARYLOXYPHENYL) SULFONES



Compd.	R	Yield,[a] %	M.p., °C.[b]	Formula	—% carbon— Calcd.	Found	—% hydrogen— Calcd.	Found	—% nitrogen— Calcd.	Found
XI	CH_3	85	234–237	$C_{14}H_{16}N_2O_4S$	54.55	54.97	5.23	5.39	9.09	8.98
XII	C_2H_5	30	171–174	$C_{16}H_{20}N_2O_4S$	57.12	57.17	5.99	5.92	8.33	8.39
XIII	n-C_3H_7		134–137	$C_{18}H_{24}N_2O_4S$	59.31	59.11	6.64	6.30	7.69	7.75
XIV	C_6H_5	30	147–149	$C_{24}H_{20}N_2O_4S$	66.64	66.56	4.66	4.77	6.48	6.48
XV	p-$CH_3C_6H_4$		190–192	$C_{26}H_{24}N_2O_4S$	67.80	67.90	5.25	5.13	6.08	6.13

[a] Yield calculated after one recrystallization. [b] Melting points were determined on a Fisher-Johns block and are uncorrected.

until the filtrates were colorless, air-dried, and recrystallized three times from glacial acetic acid with the use of decolorizing carbon.

Bis[3-nitro-4-(4-nitrophenoxy)phenyl] Sulfone.—Sodium p-nitrophenoxide was prepared by dissolving 10 g. (0.25 mole) of NaOH in 10 ml. of water and 75 ml. of alcohol. The solvent was removed using reduced pressure, two portions of benzene were added and similarly distilled to free the salt of alcohol and water. The residual salt was suspended in 250 ml. of acetone, 47.2 g. (0.125 mole) of bis(4-chloro-3-nitrophenyl) sulfone was added, and the mixture was refluxed for 8 hr. The reaction mixture was filtered on sintered glass and washed with acetone and then with water until the washings were free of Cl^-. The air-dried product was taken up twice in 350-ml. portions of boiling glacial acetic acid in which it is only slightly soluble, cooled, and filtered. The air-dried slightly yellow product melted at 216–218°; yield, 63 g. (86.5%). An attempted preparation in boiling 40% sodium xylenesulfonate solution gave a smaller yield of a product having a lower melting point.

Bis(3-amino-4-alkoxy- and -4-aryloxyphenyl) Sulfones.—The nitrophenyl sulfones were reduced to the corresponding aminophenyl sulfones using alcoholic stannous chloride and HCl.[5-8] To a suspension of 0.01 mole of the bis(3-nitrophenyl) sulfone in 25 ml. of methanol was added in portions 0.06 mole of stannous chloride dihydrate dissolved in 80 ml. of warm methanol. The reduction of the two diaryl ethers was carried out in ethanol solution. Refluxing for 30 min. resulted in dissolution of the sulfone. After addition of 0.12 mole of 12 N HCl, the refluxing was continued an additional 2 hr. The alcohol was removed by evaporation on a steam bath and to the concentrate was added 1.2 moles of NaOH in 120 ml. of solution which had been chilled to 10°. The product separated upon standing in a refrigerator and was separated by filtration on sintered glass or by centrifugation. The precipitate was washed repeatedly until free of alkali, filtering or centrifuging each wash to separate the precipitate.

Bis(3-amino-4-methoxyphenyl) Sulfone (XI).—This compound is soluble in warm 3 N HCl and was purified by treating this solution with decolorizing carbon. It was precipitated by addition of 3 N NaOH solution, filtered, washed till free of alkali, air-dried, and recrystallized from 50% alcohol.

The other bis(3-aminophenyl) sulfones were not sufficiently soluble in 3 N HCl to use this procedure. The bis(3-amino-4-alkoxyphenyl) sulfones were recrystallized from 50% alcohol and the bis(3-amino-4-aryloxyphenyl) sulfones from 95% alcohol, using decolorizing carbon in each case.

The bis(3-amino-4-n-butoxy-, -n-pentoxy-, -alloxy-, and -n-dodecoxyphenyl) sulfones were obtained as gummy solids which resisted crystallization and which could not be obtained in analytically pure form. The bis[3-amino-4-(4-aminophenoxy)phenyl] sulfone was somewhat unexpectedly found to be an oil, which was readily oxidized in either acidic or alkaline media, so that pure derivatives could not be prepared readily.

---

(5) F. Ullman and G. Pasdermadjian, *Ber.*, **34**, 1150 (1901).

(6) G. W. Raiziss, L. W. Clemence, M. Severac, and J. C. Moetsch, *J. Am. Chem. Soc.*, **61**, 2764 (1939).

(7) H. Bradbury and F. J. Smith, *J. Chem. Soc.*, 793 (1956).

(8) G. W. Stacey, E. R. Bresson, R. E. Harmon, and R. C. Thanum, *J. Org. Chem.*, **22**, 298 (1957).

A Convenient Synthesis of Aminotryptamines Analogous to Serotonin

S. P. HIREMATH AND S. SIDDAPPA

Department of Chemistry, Karnatak University, Dharwar, India

Received July 16, 1964

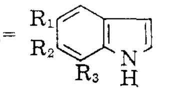
5-[1] and 6-aminotryptamines[2] and 5-amino-2-ethyltryptamine[1] are known structural analogs of serotonin of known or potential interest as antagonists of this factor. We are now reporting the synthesis of 5-, 6-, and 7-aminotryptamines by an alternate route, and that of nuclear methyl and methoxy derivatives of these amines.

Experimental[3]

4-, 5-, 6- and 7-Nitroindoles, required as starting materials, were prepared from the corresponding nitrophenylhydrazones of ethyl pyruvate[4] according to Parmerter, *et al.*[5] 4-Nitro-7-methylindole, 5-nitro-7-methylindole, 5-methyl-7-nitroindole, and 5-methoxy-7-nitroindole were prepared by the Fischer method as described in a previous communication.[6]

$$\underset{\text{I}}{R} \longrightarrow \underset{\text{II}}{RCH_2N(C_2H_5)_2} \longrightarrow \underset{\text{III}}{RCH_2N^{-}CH_3(C_2H_5)_2{\cdot}I^-} \longrightarrow$$

$$\underset{\text{IV}}{RCH_2CN} \longrightarrow \underset{\text{V}}{RCH_2CH_2NH_2} \qquad R=$$



I–IVa, $R_1 = NO_2$
b, $R_2 = NO_2$
c, $R_3 = NO_2$
d, $R_1 = NO_2$; $R_3 = CH_3$
e, $R_1 = CH_3$; $R_3 = NO_2$
f, $R_1 = OCH_3$; $R_3 = NO_2$

Va, $R_1 = NH_2$
b, $R_2 = NH_2$
c, $R_3 = NH_2$
d, $R_1 = NH_2$; $R_3 = CH_3$
e, $R_1 = CH_3$; $R_3 = NH_2$
f, $R_1 = OCH_3$; $R_3 = NH_2$

Undesignated R groups refer to hydrogen

3-Diethylaminomethylnitroindoles (II).—To a solution of diethylamine (25%, 2.4 ml.) cooled in ice, formaldehyde (33%, 1.6 ml.) was added followed by glacial acetic acid (2 ml.). To the resulting mixture a solution of the appropriate nitroindole (2 g.) in glacial acetic acid (6 ml.) was added, and the entire mixture was heated to 50° and maintained at that temperature for 2 hr. The mixture was then cooled and rendered alkaline with dilute ammonia with ice cooling, when 3-diethylaminomethylnitroindole separated out as a resinous solid. This was dissolved in dilute HCl, decolorized with Norit and reprecipitated with ammonia to obtain a yellow crystalline mass. This

---

(1) E. Shaw and D. W. Woolley, *J. Am. Chem. Soc.*, **75**, 1877 (1953).

(2) J. B. McKay, R. M. Parkhurst, R. M. Silverstein, and W. A. Silverstein, *Can. J. Chem.*, **41**, 2585 (1963).

(3) Melting points are corrected and were determined by the capillary tube method.

(4) H. N. Rydon and S. Siddappa, *J. Chem. Soc.*, 2462 (1951).

(5) S. M. Parmerter, A. G. Cook, and W. B. Dixon, *J. Am. Chem. Soc.*, **80**, 4621 (1958).

(6) S. P. Hiremath and S. Siddappa, *J. Indian Chem. Soc.*, in press.