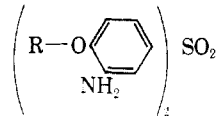
TABLE II

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.

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A Convenient Synthesis of Aminotryptamines Analogous to Serotonin

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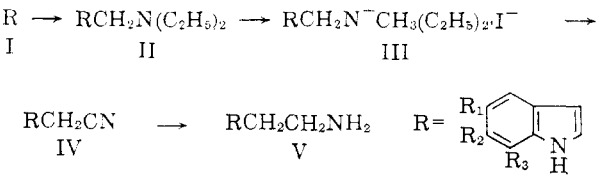
5-[1] and 6-aminotryptamines[2] and 5-amino-2-ethyltryptamine[1] are known structural analogs of serotonin of known or potential interest as antagonists of this factor. We are now reporting the synthesis of 5-, 6-, and 7-aminotryptamines by an alternate route, and that of nuclear methyl and methoxy derivatives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



I–IVa, $R_1 = NO_2$; b, $R_2 = NO_2$; c, $R_3 = NO_2$; d, $R_1 = NO_2$; $R_2 = CH_3$; 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, $R_1 = NH_2$; $R_2 = CH_3$; e, $R_2 = CH_3$; $R_3 = NH_2$; 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

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TABLE I

3-DIETHYLAMINOMETHYLNITROINDOLES (II) AND THEIR METHIODIDES

Compd.	R_1	R_2	R_3	M.p., °C.	Yield, %	Formula	%C Calcd.	%C Found	%H Calcd.	%H Found	%N Calcd.	%N Found	Methiodide, m.p., °C.
IIa	NO_2	H	H	141	70	$C_{13}H_{17}N_3O_2$	63.16	63.25	6.88	6.97	17.00	17.20	166–167
IIb	H	NO_2	H	186–187	73	$C_{13}H_{17}N_3O_2$	63.16	63.42	6.88	7.05	17.00	17.25	198–199
IId	NO_2	H	CH_3	151–152	74	$C_{14}H_{19}N_3O_2$	64.37	64.20	7.28	7.50	16.09	16.25	205–206
IIe	CH_3	H	NO_2	92–93	81	$C_{14}H_{19}N_3O_2$	64.37	64.00	7.28	7.42	16.09	16.07	193–194
IIf	OCH_3	H	NO_2	93	78	$C_{14}H_{19}N_3O_3$	60.64	61.02	6.86	7.25	15.16	15.25	200

TABLE II

NITROINDOLE-3-ACETONITRILES (IV)

Compd.	R_1	R_2	R_3	M.p., °C.	Yield, %	Formula	%C Calcd.	%C Found	%H Calcd.	%H Found	%N Calcd.	%N Found
IVa[a]	NO_2	H	H	180–181	67	...	...	...	...	...	...	...
IVb[b]	H	NO_2	H	154–155	65	...	...	...	...	..	...	...
IVd	NO_2	H	CH_3	222–223	68	$C_{11}H_9N_3O_2$	61.41	61.62	4.19	4.45	19.54	19.95
IVe	CH_3	H	NO_2	216–217	70	$C_{11}H_9N_3O_2$	61.41	61.37	4.19	4.63	19.54	19.23
IVf	OCH_3	H	NO_2	189	69	$C_{11}H_9N_3O_3$	57.15	57.62	3.89	4.35	18.18	18.50

[a] *Cf.* ref. 1. [b] *Cf.* R. K. Brown and R. A. Garrison, *J. Am. Chem. Soc.*, **77**, 3839 (1955).

TABLE III

AMINOTRYPTAMINES (V) AND THEIR DERIVATIVES

Compd.[a]	R_1	R_2	R_3	Yield, %	M.p., °C.	Dibenzoyl Derivative Formula	%C Calcd.	%C Found	%H Calcd.	%H Found	%N Calcd.	%N Found
Va	NH_2	H	H	51	165–166	$C_{24}H_{21}N_3O_2$	75.19	74.76	5.48	5.74	10.96	10.74
Vb[b]	H	NH_2	H	46	158–159	$C_{24}H_{21}N_3O_2$	75.19	75.26	5.48	5.65	10.96	11.05
Vc	H	H	NH_2	69	186–187	$C_{24}H_{21}N_3O_2$	75.19	75.50	5.48	6.06	10.96	10.62
Vd	NH_2	H	CH_3	68	198–199	$C_{25}H_{23}N_3O_2$	75.56	75.85	5.79	6.14	10.58	10.72
Ve	CH_3	H	NH_2	57	215–216	$C_{25}H_{23}N_3O_2$	75.56	76.02	5.79	6.21	10.58	10.81
Vf	OCH_3	H	NH_2	68	165–166	$C_{25}H_{23}N_3O_3$	72.63	72.95	5.57	6.02	10.16	10.55

[a] Va, c–f were obtained as semisolid and did not crystallize. [b] M.p. 106–107°.

was collected, washed with water, dried, and crystallized from alcohol.

All the 3-diethylaminomethylnitroindoles (IIa–f) were prepared by this procedure; the compounds with their physical properties and their analytical data are presented in Table I.

Nitroindole-3-acetonitriles (IV).—Methyl iodide (4 ml.) was added to II in absolute ethanol (50 ml.) with external cooling. The mixture was left in the refrigerator for 24 hr., when the methiodide (III) separated as yellow flakes, which were collected, washed with cold ethanol, and dried (melting point of all the methiodides are given in Table I).

The above methiodide (2 g.) was mixed with *n*-amyl alcohol (60 ml.) and sodium acetate–acetic acid buffer solution (60 ml.) (6 g. of acetic acid and 8.2 g. of sodium acetate/l.). Sodium cyanide (2 g.) was then added, and the mixture was heated to 70° for 2 hr. with occasional shaking. The alcohol was removed by steam distillation and the residual liquid was cooled and left for sometime when the nitrile IV separated out. It was collected, washed several times with water, and dried. All the nitroindole-3-acetonitriles (IVa, b, d–f) were purified by crystallization from methanol and are described in Table II. 7-Nitroindole-3-acetonitrile (IVc) was prepared as reported previously.[7]

Aminotryptamines (V).—Nitroindole-3-acetonitrile (1 g.) was reduced in methanol (50 ml.) with freshly prepared Raney nickel (0.5 g.) and hydrogen 4.2 kg./cm.^{2} (60 p.s.i.) in a Parr low-pressure hydrogenation apparatus for 4 hr. The Raney nickel was removed by filtration and washed with hot methanol. The combined filtrate was decolorized with Norit but the yellow color still persisted. So it was again reduced for another 4 hr. with fresh Raney nickel (0.5 g.) when a colorless solution was obtained. The catalyst was filtered off, and the solvent was removed completely under reduced pressure, whereby the aminotryptamine was obtained as a colorless substance. This was found to change color after keeping for sometime. Hence, it was immediately converted into the dibenzoyl derivative and crystallized from aqueous alcohol.

All the aminotryptamines (Va–f), along with their dibenzyol derivatives, are described in Table III.

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New Derivatives of 9-Amino-1,2,3,4-tetrahydroacridine

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This note describes the preparation of a series of physiologically active 9-alkylamino and substituted-alkylamino derivatives of 1,2,3,4-tetrahydroacridine (Table I). The literature has been reviewed by Sargent and Small.[1] Most compounds of this series have been made at high temperatures in sealed tubes. Contrary to the conclusion of the prior literature, we have found that such compounds can be made more conveniently by heating 9-chloro-1,2,3,4-tetrahydroacridine and the appropriate amine in phenol[2] at atmospheric pressure. The yields varied from about 45 to nearly 60%.

Experimental

9-Butylamino-1,2,3,4-tetrahydroacridine Hydrochloride.—A mixture of 15.0 g. (0.069 mole) of 9-chloro-1,2,3,4-tetrahydroacridine and 45.0 g. of phenol was heated and stirred at 85° in a flask fitted with a condenser, Drierite tube, and magnetic stirring bar until a homogeneous solution was formed. Butylamine (12.8 g., 0.152 mole) was added, the temperature of the mixture was raised to 125–130°, and the reaction thus con-

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