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.

(7) S. P. Hiremath and S. Siddappa, *J. Karnataku Univ.*, **6**, 1 (1961).

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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-

(1) L. J. Sargent and L. Small, *J. Org. Chem.*, **11**, 359 (1946).

(2) A. Albert, R. Goldacre, and E. Heymann, *J. Chem. Soc.*, 654 (1943).

TABLE I
9-ALKYLAMINO AND SUBSTITUTED-ALKYLAMINO 1,2,3,4-TETRAHYDROACRIDINE HYDROCHLORIDES

Substituent	% yield	M.p., °C.[a]	Formula	C, % Calcd.	C, % Found	H, % Calcd.	H, % Found	Cl, % Calcd.	Cl, % Found	N, % Calcd.	N, % Found
9-Methylamino	47.5	297–300	$C_{14}H_{17}ClN_2$	67.6	67.7	6.9	6.8	14.3	14.6	11.3	11.6
9-Butylamino	57.5	200–203	$C_{17}H_{23}ClN_2$	70.2	70.4	7.9	8.2	12.2	12.2	9.6	9.6
9-Allylamino	53.3	228–231	$C_{16}H_{19}ClN_2$	69.9	69.7	7.0	7.0	12.9	12.7	10.2	10.5
9-Benzylamino[c]	47.5	252–254	$C_{20}H_{21}ClN_2$	73.9	73.7	6.5	6.7	10.9	10.8	8.6	8.6
9-(2-Phenethyl)amino	52.2	216–218	$C_{21}H_{23}ClN_2$	74.4	74.2	6.8	6.8	10.5	10.4	8.3	8.4

[a] Considerable product precipitated out with the benzylamine hydrochloride in the original reaction. [b] All melting points are uncorrected and determined in a Fisher-Johns melting point apparatus.

tinued for 3 hr. The reaction mixture was cooled, and 700 ml. of ether was added. The butylamine hydrochloride which precipitated was filtered and the filtrate was extracted with three 100-ml. portions of 20% NaOH solution. The ether solution, which contained the product, was dried ($MgSO_4$) and filtered. The ether was then distilled, and the residue was washed with hexane to give 14.0 g. of crude 9-butylamino-1,2,3,4-tetrahydroacridine which melted at 60–62°. Recrystallization of a small portion of the crude product from hexane gave crystals, m.p. 63–65°. The 9-butylamino-1,2,3,4-tetrahydroacridine was dissolved in dilute aqueous HCl. The resulting clear solution was evaporated to dryness at 50° under reduced pressure and the residue was recrystallized from isopropyl alcohol to give 11.5 g. of hydrochloride, m.p. 200–203°.

The other compounds were made with appropriate modifications of the general method described above and recrystallized from isopropyl or absolute ethyl alcohol.

7- and 12-(*o*-Halophenyl)benz[*a*]anthracenes[1a]

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The title compounds were prepared as part of a program to make substituted benz[*a*]anthracenes available for antitumor screening. The synthetic routes to these compounds involve extensions to useful reactions previously recorded.[2]

Experimental[3-5]

Two typical experiments are described.

2-(1-Naphthylmethyl)-2'-chlorobenzophenone.—The Grignard reagent prepared from 11.8 g. (0.04 mole) of 2-(1-naphthylmethyl)bromobenzene and 1.22 g. (0.05 g.-atom) of magnesium in dry ether was added slowly to a boiling solution of 6.61 g. (0.04 mole) of 2-chlorobenzoyl chloride in toluene. Ether was allowed to distil until the boiling point of the solution reached 105°, and the solution was heated an additional 3 hr. The solution was cooled, decomposed with cold 25% sulfuric acid, and worked up in the usual way. The low-boiling fractions were removed under reduced pressure and the residue[6] was triturated with ethyl ether giving 0.3 g. of 7-(2-chlorophenyl)benz[*a*]anthracene which was removed. The dark oil was chromatographed on a 30.5-cm. column of Florisil, then on a column of basic alumina, and again on Florisil yielding 3.55 g. (25%) of light, yellow oil which crystallized[7] on standing 3 days (see Table I).

7-(2-Chlorophenyl)benz[*a*]anthracene (I).—A mixture of 1 g. (0.003 mole) of 2-(1-naphthylmethyl)-2'-chlorobenzophenone, 60 ml. of glacial acetic acid, and 15 ml. of 48% HBr was sealed in a Carius tube and heated for 7 hr. at 180°.[8] The usual work-up plus elution chromatography on basic alumina using 30–60° petroleum ether as the eluent finally gave a crystalline material which on recrystallization from 95% ethanol had a constant m.p. of 165–166°[9] (see Table II).

TABLE I
NEW KETONES

Compd.	% yield	M.p., °C.	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found	Halogen, % Calcd.	Halogen, % Found
2-(1-Naphthylmethyl)-2'-chlorobenzophenone*	25	90–91	80.78	80.53	4.80	4.77	9.94	9.50
2-(1-Naphthylmethyl)-2'-fluorobenzophenone*	20	54–55	84.69	84.46	5.03	4.96	5.58	5.47
2-(2-Naphthylmethyl)-2'-chlorobenzophenone	38	104–107	80.78	80.41	4.80	4.91	9.94	10.16
2-(2-Naphthylmethyl)-2'-fluorobenzophenone	37	73–74	84.69	84.54	5.03	5.18	5.58	5.72

TABLE II
NEW BENZ[*a*]ANTHRACENES

Compd.	% yield	M.p., °C.	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found	Halogen, % Calcd.	Halogen, % Found
7-(2-Chlorophenyl)benz[*a*]anthracene (I)*	42	165–166	85.07	85.16	4.47	4.47	10.46	10.42
7-(2-Fluorophenyl)benz[*a*]anthracene (II)*	87	154–155	89.42	89.43	4.69	4.67	5.89	5.80
12-(2-Chlorophenyl)benz[*a*]anthracene (III)	91	144–145	85.07	84.74	4.47	4.29	10.46	10.62
12-(2-Fluorophenyl)benz[*a*]anthracene (IV)	79	127–128	89.42	88.93	4.69	4.75	5.89	5.90

(1) (a) This investigation was supported by Public Health Service Research Grant No. CA-04412-06 from the National Cancer Institute. (b) Taken in part from the M.S. Thesis of L. Ojakaar presented to the Virginia Polytechnic Institute, 1961. Allied Chemical Co. Fellow 1963–1964. (c) National Science Foundation Undergraduate Research Participant, summer 1962, from Randolph-Macon Woman's College.

(2) F. A. Vingiello, M. O. L. Spangler, and J. Bondurant, *J. Org. Chem.*, **25**, 2091 (1960).

(3) Analyses were performed by Geller Laboratories, Bardonia, N. Y., except those marked with an asterisk which were performed by Galbraith Laboratories, Knoxville, Tenn.

(4) Melting points are corrected, boiling points are not.

(5) All g.p.c. analyses were performed on a Micro-Tek Model 1600 gas chromatograph equipped with a 152.4 × 3.02 cm. (5 ft. × 1/8 in.) column packed with 5% SE-30 on Chromosorb W (60–80 mesh) operated at a column temperature of 280°, inlet temperature of 330°, and using a hydrogen flame detector.

(6) The product decomposed when an attempt was made to distil it under reduced pressure. The experiment had to be repeated.

(7) This material showed only one peak on g.p.c. analysis, whereas the crude material showed three peaks.

(8) Attempted cyclization employing the usual reflux procedure resulted in recovery of starting material.

(9) The ultraviolet and visible spectra of I and II were taken on a Model 3000 Spectracord and the spectra of III and IV were taken with a Beckman DK-2A ratio recording spectrophotometer at 10 mg./l. in 95% ethanol. The wave-length maxima in mμ are for I: 221, 230, 254, 258, 270, 280, 292, 300, 320, 335, and 345; for II: 221, 230, 254, 258, 270, 280, 292, 300, 320, 334, 345; for III: 226, 260, 269, 277, 289, 320, 335, 345; for IV: 225, 258, 268, 278, 289, 320, 335, and 345.