TABLE I

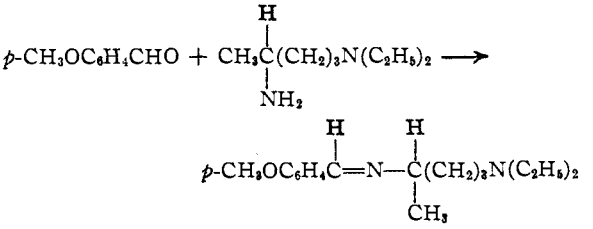
ANILS FROM 1,1-DIETHYLAMINO-4-AMINOPENTANE

Benzal group	B. p., °C.	Mm.	Yield, %	$n^{20}D$	Sp. g.$^{20}_{20}$	Formula	Analyses, % N Calcd.	Found
(1) Benzal	148–150	2.5	67	1.5134	0.9087	$C_{16}H_{26}N_2$	11.38	11.36
(2) *o*-Chlorobenzal	150–151	3.0	72	1.5225	.9989	$C_{16}H_{25}N_2Cl$	10.00	10.17
(3) *o*-Methoxybenzal	154–155	3.0	80	1.5210	.9558	$C_{17}H_{26}ON_2$	10.14	10.38
(4) *p*-Methoxybenzal	153–154	3.0	76	1.5250	.9584	$C_{17}H_{26}ON_2$	10.14	10.32
(5) *p*-Dimethylaminobenzal	193–194	3.0	64	1.558	.9450	$C_{18}H_{31}N_3$	14.53	14.54

This compound has a chlorophenyl group in place of the fuzed chlorobenzo group in atebrin. Later[2] it was shown that another related model, 2-(3′-chlorophenyl)-4-[(α-methyl-ϑ-diethylaminobutyl)-amino]-6-methylquinoline, was also active.

The principle involved was then extended so that the simple central pyridine nucleus of atebrin was used as a fundamental grouping.[3] Among the compounds examined was 2-(*p*-γ-diethylaminopropylaminophenyl)-pyridine which was shown to be active in experimental avian malaria.

A logical extension from the fuzed trinuclear system of atebrin, to the fuzed dinuclear system of quinoline, to the simple pyridine nucleus was to some appropriately substituted anils having the azomethine grouping which is present in the aforementioned nitrogen heterocycles. Several anils were prepared in accordance with the typical reaction



None of these compounds was found active.

Experimental

Anils Derived from 1,1-Diethylamino-4-aminopentane.—Equimolecular quantities of the amine and the aldehyde were dissolved and mixed in benzene. The reaction was usually instantaneous, the mixture becoming warm and turbid, but in the case of the *p*-methoxy- and the *p*-dimethylamino- derivatives it was desirable to apply heat to start the reaction. The mixture was allowed to stand for ten to fourteen hours, the water was separated, and the benzene layer dried over anhydrous sodium sulfate. The solvent was removed by distillation and the product distilled under reduced pressure. The benzaldehyde derivative was a colorless liquid, and the other compounds were yellow liquids.

5-(*p*-Anisalamino)-8-methylquinoline.—(By Fred J. Marshall). A mixture of 4.7 g. (0.03 mole) of 5-amino-8-methylquinoline and 4 g. (0.03 mole) of *p*-anisaldehyde in 35 cc. of benzene was refluxed for three and one-half hours. After removal of the benzene under reduced pressure, the product was crystallized from methanol. The yield was 5.7 g. (68%) of compound melting at 102–104°.

Anal. Calcd. for $C_{18}H_{16}ON_2$: N, 10.14. Found: N, 10.37.

In addition to the compounds described, the following were also examined and found to be inactive in experimental avian malaria: benzal-*m*-bromoaniline, benzal-*p*-bromoaniline, *m*-bromobenzal-aniline, benzal-*o*-hydroxyaniline, benzal-*p*-dimethylaminoaniline, *p*-dimethylaminobenzalaniline and *p*-dimethylaminobenzal-*o*-methoxyaniline.[4]

Acknowledgment.—The authors are grateful to Drs. R. J. Porter and L. T. Coggeshall, of the University of Michigan, for the antimalarial tests, the results of which will be published elsewhere.

(2) Gilman, Christian and Spatz, *ibid.*, **68**, in press (1946).

(3) Gilman and Edward, *ibid.*, **68**, in press (1946).

(4) The last three compounds were supplied by Merrill Speeter. See, Gilman, Tolman, Yeoman, Woods, Shirley and Avakian, THIS JOURNAL, **68**, 426 (1946), on N-(*m*-trifluoromethylbenzal)-*m*-trifluoromethylaniline and 4-(*m*-trifluoromethylbenzalamino)-dibenzofuran which were also found to be inactive.

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The Methylation of Carvacrylamine

BY JOHN F. R. KUCK AND J. V. KARABINOS

The preparation and physical constants of carvacrylamine as well as its N-methylated derivatives are reported in this communication.

Carvacrylamine was obtained by the nitration of *p*-cymene according to the method of Kobe and Doumani,[1] and catalytic reduction of the 2-nitro-*p*-cymene.[2] Purification was accomplished by recrystallization of the formyl derivative from hot water and regeneration of the free base.

An attempt to make the N-methyl derivative by reductive alkylation[3] gave a mixture of amines. Careful vacuum fractionation gave a 15% yield of the pure tertiary amine which boils slightly lower than the other two.

Other methods for monomethylation were tried. Methylation of N-formyl-N-carvacryl sodamide in dry toluene with dimethyl sulfate gave a low yield of fairly pure secondary amine, and autoclaving 2-bromo-*p*-cymene with aqueous methylamine in the presence of cuprous chloride at 600 lb./sq. in. max. and 150 to 175° gave the N-methyl derivative in 25% yield. All methods attempted in this Laboratory for alkylating the amine directly gave a mixture of amines from which the pure secondary amine could be separated by a nitrosation procedure.[4]

(1) K. A. Kobe and T. F. Doumani, "Organic Syntheses," Vol. 21, John Wiley and Sons, Inc., New York, N. Y., 1941, p. 96.

(2) C. F. H. Allen and J. Van Allan, "Organic Syntheses," Vol. 22, 1942, p. 9.

(3) W. S. Emerson and H. W. Mohrman, THIS JOURNAL, **62**, 69 (1940).

(4) J. S. Buck and C. S. Ferry, "Organic Syntheses," Coll. Vol. 2, John Wiley and Sons, Inc., New York, N. Y., 1943, p. 290.

The physical constants of the three amines as well as some derivatives are listed below.

TABLE I

PHYSICAL CONSTANTS OF THE CARVACRYLAMINES AND THEIR DERIVATIVES

	Carvacryl-amine	N-Methyl-	N,N-Dimethyl-
B. p., °C.	242	236	84 (5 mm.)
$n^{22}D$	1.5402	1.5363	1.5131
d^{22}_4	0.9463[a]	0.9325	0.9028
Oxalate			
M. p., °C.	149–150[b]	114–115[c]	132–133
Phenylthiourea			
M. p., °C.	117	95–96	.....

[a] F. W. Semmler, *Ber.*, **25**, 3352 (1892), reported 0.9442 but this was recorded in Beilstein as 0.9942. [b] R. G. Cooke and A. K. Macbeth, *J. Chem. Soc.*, 1593 (1937) reported m. p. of 150°. [c] Apparently an acid salt, unstable on standing. May also be dehydrated.

Anal. Calcd. for N-methyl carvacrylamine acid oxalate hydrate, $C_{10}H_{13}NHCH_3 \cdot C_2H_2O_4 \cdot H_2O$: C, 57.53; H, 7.80; N, 517. Found: C, 57.72; H, 7.55; N, 5.12, 5.38.

Anal. Calcd. for N,N-dimethyl carvacrylamine oxalate, $(C_{10}H_{13}NC_2H_6)_2 \cdot C_2H_2O_4 \cdot H_2O$: subs. 0.2652 g., 0.1340 g.; 0.09661 *N* KOH, 20.35 ml., 10.34 ml. Found: 20.48 ml., 10.34 ml.

Anal. Calcd. for carvacrylamine, $C_{10}N_{15}N$: N, 9.39. Found: N, 9.16.

Anal. Calcd. for N-methylcarvacrylamine, $C_{11}H_{17}N$: N, 8.59. Found: N, 8.65, 8.70.

Anal. Calcd. for N,N-dimethylcarvacrylamine, $C_{12}H_{19}N$: N, 7.91. Found: N, 7.78, 7.82.

Anal. Calcd. for carvacrylamine phenylthiourea, $C_{17}H_{20}N_2S$: C, 71.78; H, 7.09. Found: C, 71.75; H, 7.00.

Anal. Calcd. for N-methylcarvacrylamine phenylthiourea, $C_{16}H_{22}N_2S$: C, 72.45; H, 7.43. Found: C, 72.36; H, 7.04.

AIRCRAFT ENGINE RESEARCH LABORATORY
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Carbalkoxythiophanones

BY EDMOND E. MOORE AND MARJORIE B. MOORE

Several reports on the direction of the ring closure of dialkyl esters of β-carboxyethylthioglycolic acid have appeared in the recent literature.[1,2,3,4]

Using sodium in benzene Karrer and Schmid[1] and Buchman and Cohen[2] reported that the main product formed was 4-carbalkoxythiophan-3-one. Woodward and Eastman[3] using sodium methoxide in ether reported that at low temperatures the main product was 2-carbalkoxythiophan-3-one while at high temperatures (110°) sodium methoxide in toluene gave mostly 4-carbalkoxythiophan-3-one. Avison, *et al.*,[4] reported that sodium in benzene gave 2-carbalkoxythiophan-3-one.

During the course of some work on ring closures of this type, we investigated the use of methyl and ethyl alcohols as solvents in order to eliminate the necessity of preparing powdered sodium, sodamide or alcohol-free sodium ethylate. We found that reactions could be carried out more quickly, the yields were good, and the direction of ring closure not affected.

Ethyl-β-carbomethoxyethylthioglycolate was cyclized at 0° in four ways, the ureides prepared and their melting points compared with those of known ureides.[4]

(A) Sodium methylate in ether: The major product was 2-carbomethoxythiophan-3-one (oil, b. p. −102.5–105° [5–6 mm.]). *Anal.* calcd. for $C_6H_8O_3S$; C, 44.99; H, 5.03. Found: C, 45.76; H, 5.15. Ureide, m. p. 221–222°.

(B) Sodium methylate in methyl alcohol gave the same product as (A). *Anal.* Found: C, 45.08; H, 5.16. Ureide, m. p. 222°.

(C) Sodium ethylate in ether gave 2-carbethoxythiophan-3-one (oil, b. p. 98–101° [3–4 mm.]). *Anal.* calcd. for $C_7H_{10}O_3S$; C, 48.26; H, 5.79; Found: C, 48.09; H, 5.68. Ureide, m. p. 171–172°.

(D) Sodium ethylate in ethyl alcohol gave the same product as (C). Found: C, 48.00; H, 5.80. Ureide, m. p. 172°.

In all cases the 2-carbalkoxythiophan-3-one was the main product formed.

Methyl and ethyl alcohols are suitable solvents for this ring closure if one keeps in mind the possibility of ester exchange such as occurred to a large extent in (A) and completely in (B).

ABBOTT LABORATORIES
NORTH CHICAGO, ILLINOIS RECEIVED APRIL 4, 1946

(1) Karrer and Schmid, *Helv. Chim. Acta*, **27**, 124 (1944).
(2) Buchman and Cohen, THIS JOURNAL, **66**, 847 (1944).
(3) Woodward and Eastman, *ibid.*, **66**, 849 (1944).
(4) Avison, Bergel, Cohen and Haworth, *Nature*, **154**, 459 (1944).

6-Methoxy-8-amino-1,2,3,4-tetrahydroquinoline[1]

BY CHARLES C. PRICE[2] AND HARRY F. HERBRANDSON

Although Balaban[3] has reported the successful reduction of 5-amino-6-methoxyquinoline and 5-amino-8-methoxyquinoline to the tetrahydro analogs by the action of tin and hydrochloric acid, 6-methoxy-8-aminoquinoline was reported to form an intensely purple solution from which the tetrahydroquinoline was not isolated.

We have experienced no difficulty in isolating the product in good yield, either from tin and hydrochloric acid reduction or catalytic hydrogenation. The product is easily oxidizable and discolors on exposure to air. It was characterized as the picrate and by conversion to the imidazole.

8-Amino-6-methoxy-1,2,3,4-tetrahydroquinoline Hydrochloride.—To 3.5 g. (0.02 mole) of distilled 8-amino-6-

(1) The work reported in this note was carried out under a contract, recommended by the Committee on Medical Research, between the Office of Scientific Research and Development and the University of Illinois.
(2) Present address: Department of Chemistry, University of Notre Dame, Notre Dame, Indiana.
(3) Balaban, *J. Chem. Soc.*, 2624 (1932).