which represented 7, 30, 32, and 31% of the product as determined by the weight of paper cuts of the peaks. Isolation of the four components was accomplished by fractionation through the vapor fractometer.

The 20.8-min. component, n_D^{23} 1.4083 (lit.[9] n_D^{20} 1.40909), was identical with an authentic sample of methyl vinylacetate (II) (prepared by the method of Corey[10]) as shown by their infrared spectra.

The 25.2-min. component, n_D^{23} 1.4223 (lit.[11] n_D^{20} 1.4225), was methyl *cis*-crotonate (III).

The 32.4-min. component, n_D^{23} 1.4182 (lit.[12] n_D^{20} 1.41866), was identical with an authentic sample of methyl cyclopropanecarboxylate V [prepared by the methylation of cyclopropanecarboxylic acid (Aldrich)] as shown by their infrared and NMR spectra.

The 36-min. component, n_D^{22} 1.4248 (lit.[9] n_D^{20} 1.42466), was identical with an authentic sample of methyl *trans*-crotonate (IV) (K and K Laboratories) as shown by their infrared and NMR spectra.

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(9) G. H. Jeffery and A. J. Vogel, *J. Chem. Soc.*, 658 (1948).

(10) E. J. Corey, *J. Am. Chem. Soc.*, **75**, 2251 (1953).

(11) J. L. H. Allan, E. R. H. Jones, and M. C. Whiting, *J. Chem. Soc.*, 1862 (1955).

(12) G. H. Jeffery and A. J. Vogel, *J. Chem. Soc.*, 1804 (1948).

Preparation of Quinazolo[2,3-c]benzo[1,4]thiazine-12-(6H)one

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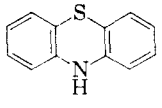
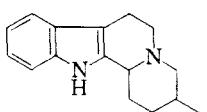
During the course of an investigation of compounds with potential psychotherapeutic activity it appeared that derivatives of a ring system containing some of the features of phenothiazine (I)

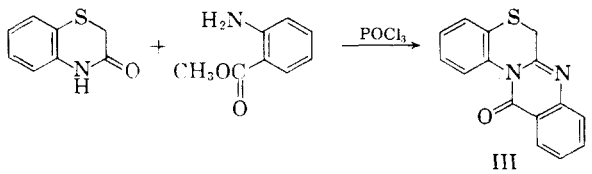


I



II

and benz[g]indole[2,3-a]quinolizine (II) (the reserpine nucleus) would be of interest. The quinazolo[2,3-c]benzo[1,4]thiazine system was selected and quinazolo[2,3-c]benzo[1,4]thiazine-12-(6H)one (III) was prepared by the method outlined below.



III

Preliminary pharmacological testing, however, indicates that this compound has negligible psychotherapeutic activity and the investigation in this area has been discontinued.

EXPERIMENTAL

Condensation of benzo[1,4]thiazine-3-one with methyl anthranilate. To a solution of 16.6 g. of benzo[1,4]thiazine-3-one dissolved in hot, anhydrous toluene, a solution of 30.4 g. of freshly distilled phosphorus oxychloride in 25 ml. of dry toluene was added slowly. After heating under reflux with rapid, mechanical stirring for 10 min., 30.2 g. of methyl anthranilate was added slowly and the resulting mixture heated under reflux for 8 hr. At the end of this time a yellow mass began to separate. The toluene was evaporated under reduced pressure, and the residue was dissolved in chloroform. The chloroform solution was dried over magnesium sulfate, filtered, and the chloroform evaporated on a steam bath. The residue was crystallized from 200 ml. of an 80% ethanol-water mixture.

The product was recrystallized twice from ethanol to give 12.5 g. (45%) of quinazolo[2,3-c]benzo[1,4]thiazine-12-(6H)one, yellow prisms, m.p. 154.5–156°.

Anal. Calcd. for $C_{15}H_{10}N_2OS$: C, 67.7; H, 3.8; N, 10.5; S, 12.0. Found: C, 67.8; H, 3.9; N, 10.4; S, 11.8.

Acknowledgment. We are grateful for the financial support by the Smith Kline and French Laboratories for a postdoctoral fellowship under which the work of one of us (J. E. M.) was performed.

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Amebicidal 8-Quinolinol Compounds

KONOMU MATSUMURA AND MOTOKO ITO

Received March 30, 1959

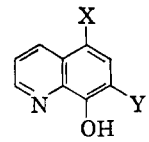
This note describes the preparation of several halogenated 8-quinolinol compounds which were made in the hope that they may be of therapeutic value.

The Results of Biological Study.[1] A number of 8-quinolinol compounds, including those reported in the present paper, has been tested against *Endamoeba histolytica in vitro*, and when indicated, against experimental amebiasis in guinea pigs. II was a hundred times as active as 5,7-diiodo-8-quinolinol in Balamuth media. Others (V and VIII) were somewhat more active than, or equal in activity to this standard. In animal assay, V and VIII possessed good antiamebic activity while II had no activity. It is noteworthy that V was of remarkably low toxicity when administered orally ($L.D._{50}$: 80 mg. per 20 g. body weight of a mouse).

(1) We are indebted to Dr. Akira Hirabayashi of our Institute who has kindly performed the biological testing and reported the results. Details of these test results will be published by A. Hirabayashi in a separate communication.

TABLE I

HALOGEN DERIVATIVES OF 8-QUINOLINOL COMPOUNDS



No.	X (5 position)	Y (7 position)	Yield, %	Solvent	Form[a]	M.p., °C.	Formula	Anal. N, % Calcd.	Found
I[b]	CH_3—CO—	I	90	EtOH	Needles	183 (dec.)	$C_{11}H_8INO_2$	4.47	4.44
II[b]	 -CO-	I	90	EtOH	Plates	209–210	$C_{16}H_{10}INO_2$	3.73	3.60
III[c]	Cl—CH_2—CO—	I	95	Glacial AcOH	Needles	227 (dec.)	$C_{11}H_7ClINO_2$	4.03	3.97
IV[d]	I—CH_2—CO—	H	96	C_6H_6	Plates	135 (dec.)	$C_{11}H_8INO_2$	4.47	4.56
V[e]	CCl_3—CH(OH)—	I	96	50% AcOH	Prisms	192 (dec.)	$C_{11}H_7Cl_3INO_2$	3.35	3.26
VI[f]	EtOOC—	I	98	EtOH	Needles	199–200	$C_{12}H_{10}INO_3$	4.08	4.21
VII[f]	BuOOC—	I	98	EtOH	Plates	155	$C_{14}H_{14}INO_3$	3.77	3.78
VIII[g]	HOOC—	I	70	EtOH	Prisms	228–229 (dec.)	$C_{10}H_6INO_3$	4.44	4.43
IX[h]	Cl	NO_2	80	EtOH	Needles	197 (dec.)	$C_9H_5ClN_2O_3$	12.47	12.90
X[i]	Cl	NH_2	86	Et_2O	Slightly brown prisms	162–163	$C_9H_7ClN_2O$	14.40	14.20
XI[j]	Cl	$NHCOCH_3$	76	C_6H_6	Colorless needles	201–202 (dec.)	$C_{11}H_9ClN_2O_2$	11.84	11.36

[a] Unless otherwise stated all crystal colors are orange. [b] Iodinated by method A-A1. [c] Iodinated by method B. [d] Prepared by method E. [e] Prepared by method C. [f] Iodinated by method A-A2. [g] Iodinated by method D. [h] Prepared by the addition of concentrated nitric acid (63%, 1 ml.) to a mixture of 5-chloro-8-quinolinol (1.8 g.) and glacial acetic acid (25 ml.) below 25°. [i] Made by stirring a mixture of IX (0.6 g.) pyridine (5 ml.) sodium hydrosulfite (4 g.) and water (20 ml.) at room temperature. [j] Made by allowing a mixture of X (0.4 g.) acetic anhydride (0.22 g.) freshly fused sodium acetate (0.4 g.) and ether (20 ml.) to stand at room temperature for 2 days.

EXPERIMENTAL

Method of Iodination. (A) 0.1 *N* Iodine–potassium iodide solution (20 ml.) was added dropwise into a solution of 5-substituted-8-quinolinol (0.001 mol.) and sodium acetate (0.25 g.) in methanol (40 ml.) at about 10° during 0.5 hr. After standing, excess iodine was destroyed by sulphur dioxide.

A1. The reaction mixture was evaporated on water bath to one-half volume and then made up to the original volume by addition of water. The resulting solid was crystallized from solvent.

A2. The product separated upon adding water (100 ml.) to the reaction mixture.

B. 0.1 *N* Methanolic iodine solution (20 ml.) was used and other conditions similar to that of A-A2.

C. One-half normal methanolic iodine solution (80 ml.) was added to a solution of 5-(α-hydroxy-β-trichloroethyl)-8-quinolinol (0.02 mol.) and sodium acetate (10 g.) in methanol (800 ml.) at about 10° during 1 hr.

Sulphur dioxide was added, if necessary, after the reaction mixture had stood overnight.

Most of the methanol was evaporated in vacuo below 50°. The product separated upon adding water (250 ml.) to the residual paste.

D. 0.1 *N* Iodine-iodide solution (20 ml.) was added dropwise with stirring to a solution of 5-carboxy-8-quinolinol (0.001 mol.) and sodium hydroxide (0.001 mol.) in water (50 ml.) at about 15° during 0.5 hr. The reaction mixture was acidified with acetic acid, the resulting solid filtered and dissolved in dilute sodium carbonate. The undissolved diiodo-8-quinolinol (0.05 g., m.p. 192–200°) which was formed as a byproduct was filtered off. The product separated upon adding acetic acid to the filtrate. It can be recrystallized from ethanol or glacial acetic acid.

E. A normal solution (4 ml.) of sodium iodide in acetone was added a little at a time to a mixture of 5-chloroacetyl-8-quinolinol (0.004 mol.) and acetone (30 ml.) with stirring at room temperature. After standing for a few hours, most of acetone was removed in vacuo. The product separated upon adding water to the residue.

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Chalcone-Type 8-Quinolinol Compounds

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The compounds were prepared by condensation of 5-acetyl-8-quinolinol with aromatic aldehydes in the presence of potassium hydroxide or hydrochloric acid. None of them possessed any notable antituberculous or antiamebicidal activity.

EXPERIMENTAL

Method of condensation. A. In methanolic potassium hydroxide. To a solution of 5-acetyl-8-quinolinol (0.38 g., 0.002 mol.) and aromatic aldehyde (0.002 mol.) in methanol (6 ml.) was added a solution of potassium hydroxide (1 g.) in water (2 ml.) with stirring. The resulting solution was allowed to stand at room temperature or gently refluxed on a water bath. Then the reaction mixture was diluted with water, acidified with acetic acid, the separated solid filtered on standing and recrystallized.