vigorous stirring and the mixture was brought to a volume of 2 l. by the addition of water. During the dilution white crystals of product separated. Filtration yielded 9.6 g. (84%) of almost colorless product, m.p. 161–163° dec. The colorless analytical sample, m.p. 167–168° dec., was prepared by recrystallization from aqueous ethanol with the use of charcoal.

Anal. Calcd. for $C_{13}H_{10}NO$: C, 67.4; H, 4.35; N, 6.05. Found: C, 67.7; H, 4.7; N, 5.9.

4-Mercapto-3-styrylpyridine-1-oxide. A mixture of 2.0 g. of 4-chloro-3-styrylpyridine-1-oxide, 0.6 g. of thiourea, and 20 ml. of ethanol was heated under reflux for 1.5 hr. The mixture was then chilled and filtered to give 1.71 g. (68%) of the thiouronium hydrochloride salt, m.p. 162° dec. This salt was suspended in 10 ml. of water and 5 ml. of cold 10% sodium hydroxide added with shaking. The mixture was filtered (yellow residue, 0.3 g., m.p. 200° dec.), the filtrate acidified with acetic acid and the precipitated solid collected by filtration to give 0.83 g. (62%, based on the thiouronium salt) of 4-mercapto-3-styrylpyridine-1-oxide, m.p. 145–146°.

Anal. Calcd. for $C_{13}H_{11}NOS$: C, 68.1; H, 4.8; N, 6.1. Found: C, 68.3; H, 4.6; N, 6.0.

Bis(1-oxy-3-styryl-4-pyridyl)sulfide. The yellow residue obtained above was purified by dissolution in boiling aqueous acetic acid and reprecipitation with ammonium hydroxide. The analytical sample m.p. 198–200° dec. was prepared by recrystallization from dimethylformamide.

Anal. Calcd. for $C_{26}H_{20}N_2O_2S$: C, 73.6; H, 4.8; N, 6.6. Found: C, 73.2; H, 4.7; N, 6.8.

Acknowledgment. We are indebted to Parke, Davis and Company for carrying out the pharmacological screening of these compounds.

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Pyrazolines[1]

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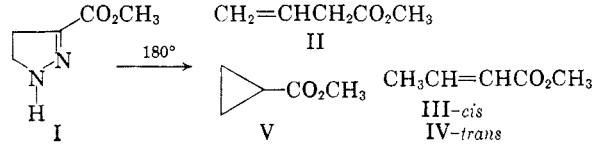
The pyrolysis of pyrazolines has long been regarded as a synthetic method for the preparation of derivatives of cyclopropane.[2] Particular use has been made of this method in the preparation of cyclopropanecarboxylic esters[3] and related compounds[4] where the pyrazoline is readily prepared by the addition of a diazoalkane to an α,β-unsaturated ester.

Of the methyl substituted 3-carbomethoxypyrazolines studied by von Auwers and Konig[3] only those which contained a methyl at the 3- position were found to give a cyclopropane product. A reinvestigation of this work which is now under way has shown that the products of pyrolysis of 3-carbomethoxypyrazolines are mixtures which contain in general α,β- and β,γ-unsaturated esters as well as the expected cyclopropanecarboxylic ester. A recent observation of the formation of a β,γ-unsaturated ketone from the pyrolysis of a pyrazoline in the steroid series has been reported.[5]

3-Carbomethoxypyrazoline (I), which was reported[3] to give in 81% yield methyl vinylacetate (II), has been shown to give a mixture in 80% yield of II, methyl *cis*-crotonate (III), methyl *trans*-crotonate (IV), and methyl cyclopropanecarboxylate in the ratio of 7:30:31:32, respectively.



Similarly methyl 2-methylcyclopropanecarboxylate has been isolated from the pyrolysis product from 4-methyl-3-carbomethoxypyrazoline and 5-methyl-3-carbomethoxypyrazoline in yields of 4 and 34%, respectively.[6]

That II, III, IV, and V were thermally stable under the reaction conditions was determined by heating each in a sealed tube for two hours at 195°. Not more than 2% rearrangement was observed. In the presence of iodine at 195° for five days, both II and IV gave an equilibrium mixture of the three olefins which contained 84% of IV, 12% of III, and 4% of II. These results would indicate that II and III are formed in the pyrolysis reaction by a kinetically controlled step and that although some isomerization may occur under the reaction conditions, it does not occur at a fast enough rate to give an equilibrium mixture.

It is hoped that by an extensive study of pyrazoline pyrolyses it will be possible to learn more about the mechanism[7] and the scope of the reaction as a synthetic method for the preparation of olefins and substituted cyclopropanes.

EXPERIMENTAL[8]

Pyrolysis of 3-carbomethoxypyrazoline (I). Thirteen g. of I (m.p. 65°, lit.[3] m.p. 66–68°) was placed in a 50-ml. round bottom flask fitted with a distilling head and heated in an oil bath. Pyrolysis began at 150° and was vigorous at 180°. The product distilled during pyrolysis and after 1 hr. 8 g. (80%) of a colorless liquid was collected.

Vapor chromatography of the product through a 10-ft. dinonyl phthalate column at 80° with a helium flow rate of 67 cc./min. gave four peaks at 20.8, 25.2, 32.4, and 36 min.

(1) Support for this work was received from the National Research Council of Canada and from the President's Committee on Research of the University of British Columbia.

(2) R. Huisgen, *Angew. Chem.*, **67**, 439 (1955).

(3) K. von Auwers and F. Konig, *Ann.*, **496**, 252 (1932).

(4) D. Gotkis and J. B. Cloke, *J. Am. Chem. Soc.*, **56**, 2710 (1934).

(5) H. L. Slates and N. L. Wender, *J. Am. Chem. Soc.*, **81**, 5472 (1959).

(6) Unpublished results from this laboratory.

(7) For proposals on the mechanism of this reaction see W. G. Young, L. J. Andrews, S. L. Lindenbaum, and S. J. Cristol, *J. Am. Chem. Soc.*, **66**, 810 (1944) and W. M. Jones, *J. Am. Chem. Soc.*, **81**, 3776 (1959).

(8) The instrument and columns for the vapor chromatograms were those available commercially under the trade name Aerograph.

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).

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

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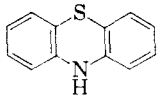
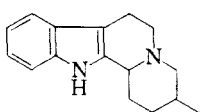
During the course of an investigation of compounds with potential psychotherapeutic activity it appeared that derivatives of a ring system containing some of the features of phenothiazine (I)

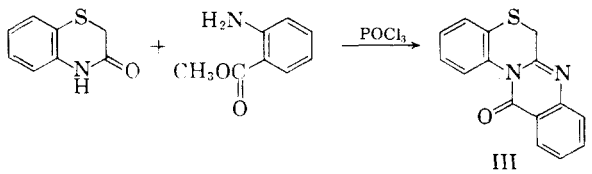


I



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.

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Amebicidal 8-Quinolinol Compounds

KONOMU MATSUMURA AND MOTOKO ITO

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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.