

*Anal.* Calcd. for  $C_{12}H_{20}Br_2N_2O_2$ : C, 37.52; H, 5.25; N, 7.29. Found: C, 37.46; H, 5.05; N, 7.01.

Anhydrous 2-pyridylacetylcholine bromide hydrobromide was kept for long periods over anhydrous calcium chloride but it rapidly absorbed water in a moist atmosphere.

*Acknowledgment.* The authors are thankful to Dr. I. I. A. Tabachnick of the Pharmacology Department of Schering Corporation for his interest and kind advice with regard to the pharmacological aspects of this work, to Dr. H. Tabor of the National Institute of Arthritis and Metabolic Diseases, National Institutes of Health, Bethesda, Md., for a copy of his manuscript<sup>14</sup> in advance of publication, and to Mr. Edwin Conner and his associates of the Microanalytical Laboratories of Schering Corporation for the microanalyses reported herein.

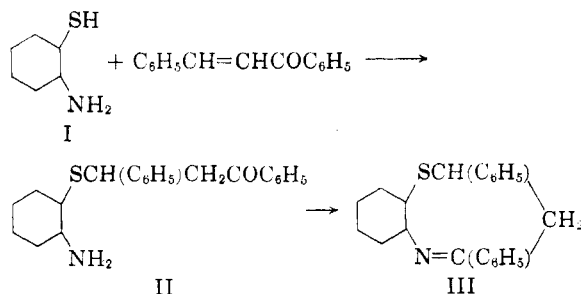
MEDICINAL CHEMICAL RESEARCH DEPARTMENT  
SCHERING CORPORATION  
BLOOMFIELD, N. J.

### A Seven-Membered Heterocycle from *o*-Aminobenzenethiol and Chalcone<sup>1</sup>

WILLIAM D. STEPHENS AND LAMAR FIELD

Received April 6, 1959

Herz and Tarbell found that the thiol group of a thiophenol could be blocked to permit operations elsewhere in the molecule by addition of the thiophenol to 3-nitrobenzalacetophenone, which subsequently could be removed.<sup>2</sup> When chalcone (benzalacetophenone) itself was used in essentially this procedure to protect the thiol group of *o*-aminobenzenethiol (I), prior to reactions of the amino group, two products were obtained. These proved to be the desired ketone (II) and a cyclized product (III).



Preparation of II (58% yield) could be achieved, however, by omitting acetic acid and using only piperidine in the procedure of Herz and Tarbell.

(1) Research supported by the Office of Ordnance Research, U. S. Army.

(2) A. H. Herz and D. S. Tarbell, *J. Am. Chem. Soc.*, **75**, 4657 (1953).

Addition of acetic acid to the reaction mixture resulted in the isolation of the cyclized product (III) in 62% yield. Treatment of the isolated ketone II in methanol with acetic acid also converted it to III (78%).

The structures of II and III are supported by the elementary analyses and by the fact that II has a strong infrared-absorption band in the region expected for a carbonyl group, unlike III which lacks this band but has another in the region reasonably attributable to a C=N linkage. Further evidence is provided by the fact that since our work was completed Ried and Marx have demonstrated the same reactions with thiophene counterparts of chalcone; they reported the independent synthesis of a typical heterocyclic product.<sup>3</sup> It is interesting that the heterocyclic ring of III withstands the action of alkali, at least in water.

#### EXPERIMENTAL<sup>4</sup>

*$\beta$ -Phenyl- $\beta$ -(*o*-aminophenylmercapto)propiofenone* (II). Chalcone (5.00 g.) and *o*-aminobenzenethiol<sup>5</sup> (I, 3.00 g.) were dissolved in 50 ml. of boiling methanol. The heat was removed and piperidine (25 drops) was added. White needles of II precipitated upon cooling; yield, 4.64 g. (58%), m.p. 127–134°. Repeated recrystallization from hexane gave II with a constant m.p. of 134–135°. Strong infrared absorption at  $1670\text{ cm.}^{-1}$  is consistent with the presence of an aryl ketone linkage.

*Anal.* Calcd. for  $C_{21}H_{19}NOS$ : C, 75.64; H, 5.74. Found: C, 75.42; H, 5.59.

*2,4-Diphenyl-6,7-benzo-1-thia-5-aza-4,6-cycloheptadiene* (III). Chalcone (5.00 g.) and I (3.00 g.) were dissolved in 25 ml. of boiling methanol. The heat was removed and piperidine (25 drops) was added. After the mixture had cooled to room temperature, an additional 25-ml. portion of methanol was added and the slurry heated until all material dissolved. Glacial acetic acid (10 ml.) then was added and the mixture allowed to stand overnight at 25°. Yellow crystalline III separated which amounted to 4.70 g. (62%), m.p. 111.5–115°. This material was repeatedly recrystallized from *t*-butyl alcohol to a constant m.p. of 114–115°. Strong infrared absorption occurred at about  $1613\text{ cm.}^{-1}$  (C=N), which was absent in the spectrum of II, with no other appreciable absorption from  $1613\text{--}2940\text{ cm.}^{-1}$

*Anal.* Calcd. for  $C_{21}H_{17}NS$ : C, 79.95; H, 5.43. Found: C, 79.64; H, 5.31.

When 1.00 g. of the III was heated at 70° for 2 days with 50 ml. of 10% aqueous sodium hydroxide, 0.98 g. of III was recovered, m.p. and mixture m.p. 111–114.5°.

*Conversion of II to III.* A mixture of 0.50 g. of II and 25 drops of glacial acetic acid was heated in 10 ml. of methanol on a steam bath for 20 min. After standing overnight, the mixture was concentrated to about one-half volume; yield of III, 0.28 g. (59%), m.p. and mixture m.p. (with III as prepared above), 114–115°. A second crop of 0.09 g. (19%), m.p. and mixture m.p. 112–115°, brought the total yield to 78%.

DEPARTMENT OF CHEMISTRY  
VANDERBILT UNIVERSITY  
NASHVILLE 5, TENN.

(3) W. Ried and W. Marx, *Chem. Ber.*, **90**, 2683 (1957).

(4) Melting points are corrected. Analyses are by Galbraith Laboratories, Knoxville, Tenn.

(5) Kindly provided by the American Cyanamid Company, New York, N. Y.