Ferguson and Barnes[11] reported that ultraviolet absorption in conjugated systems involving α,β-unsaturated carbonyl compounds ranges above 319 mμ, whereas these isoximes absorb at 260 and 270 mμ. This does not lend support to the isoxime structures.

EXPERIMENTAL

Preparation of isoxazolines IX *and* X. 3-phenyl-5-anisylisoxazoline (IX) and 3-anisyl-5-phenylisoxazoline (X) were prepared according to Blatt[12] and Barnes[13] by treating *p*-methoxybenzalacetophenone and benzal-*p*-methoxyacetophenone, respectively, with excess hydroxylamine in alcoholic potassium hydroxide.

	M.P., ° C.	Color	Analysis
IX	101–102°	White	Calcd. for $C_{16}H_{15}NO_2$: C, 75.88; H, 5.92. Found: C, 75.85; H, 6.00.
X	96°	White	Calcd. for $C_{16}H_{15}NO_2$: C, 75.88; H, 5.92. Found: C, 75.83; H, 6.02

Preparation of isoxazoles V *and* VI. Chromic acid oxidation[12,13] of isoxazolines IX and X yielded isoxazoles VI and V, respectively, identified by mixture melting points with samples obtained by acidification of isoximes IV and III.

Treatment of isoximes with ozone. Prolonged treatment of alcoholic solutions of isoximes III and IV gave no cleavage products. The isoximes were recovered unchanged.

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Thiol Addition of Thiourea in Heterocyclic Ring Formation: Preparation of 5-Ethyl-6-phenyl-*meta*-thiazane-2,4-dione

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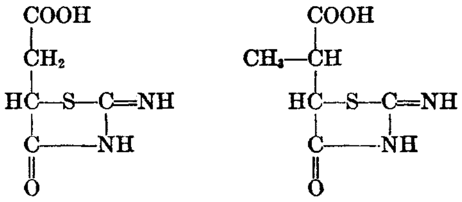
Thiourea has been made to undergo a thiol-type addition to a monobasic, α,β-unsaturated acid and to its ethyl ester. A simultaneous condensation between the carboxyl group of the acid and the amine group of thiourea has resulted in the formation of a derivative of the six-membered, sulfur containing heterocycles the *meta*-thiazanes.

Several reactions of thiourea that have been previously observed by other workers indicate that in some instances the thiol tautomer is the predominant reacting species. Thus, upon alkylating thiourea with hydrocarbon halides or with alkyl sulfates, *S*-alkyl- and *S*-arylthiouronium salts are formed.[1] Oxidation of thiourea in acid solution leads to the formation of dithiodiformamidine.[2] Andreasch[3] has reacted thiourea with maleic or fumaric acid to give I and with citraconic to give II (Fig. 1). These reactions were carried out by heating a fused mixture of the reactants either dry or with a small amount of water. The products obtained indicate that both a thiol addition of the thiourea to the unsaturated acid and a condensation, involving the elimination of water from the carboxyl group and from the amine group of the thiourea, occur. Attempts to repeat this reaction with such monobasic, unsaturated acids as oleic, crotonic, cinnamic, 2-phenyl-3-methylacrylic, and methacrylic were not successful. Either polymeric products were obtained or else amine addition by the thiourea occurred forming thiopyrimidines.[3,4] Thus with cinnamic acid, 4-phenyl-2-thio-6-ketopyrimidine was obtained.[4] However, a thiol addition reaction between thiourea and acrylic acid has been accomplished by hydrogen chloride catalysis in alcohol to give *S*-(β-carboxyethyl)-isothiouronium hydrochloride[5] without accompanying cyclization.


I Figure 1 II

In the present work, a sulfuric acid solution of thiourea was treated with the α,β-unsaturated acid *trans*-α-ethylcinnamic acid, and with its ethyl ester, and in both cases the same *meta*-thiazane derivative was obtained. This product which no longer contains unsaturation can only arise from a reaction where the thiol tautomer of thiourea adds to the unsaturated system, since the sulfur is part of the heterocyclic ring. The possible sequences of reactions which would result in such a product are shown in Fig. 2. Both the addition and the condensation reaction occur under the same conditions. Upon running the above reaction for shorter times and using the same

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[2] J. Boeseken, *Rec. trav. chim.*, **55**, 1040 (1936).

[3] R. Andreasch, *Monatsh.* **16**, 789 (1895); **18**, 56 (1897).

[4] H. Erlenmeyer and F. Heitz, *Helv. Chim. Acta*, **25**, 832 (1942).

[5] (a) E. H. Behringer and P. Zillikens, German Patent-Anm. B. **16741** (1951); (b) O. Bayer, *Angew. Chem.*, **61**, 236 (1949); (c) J. Houben, *Methoden der Organischen Chemie*, vol. IX, G. Thiele, Leipzig, Germany, 1955, p. 902.

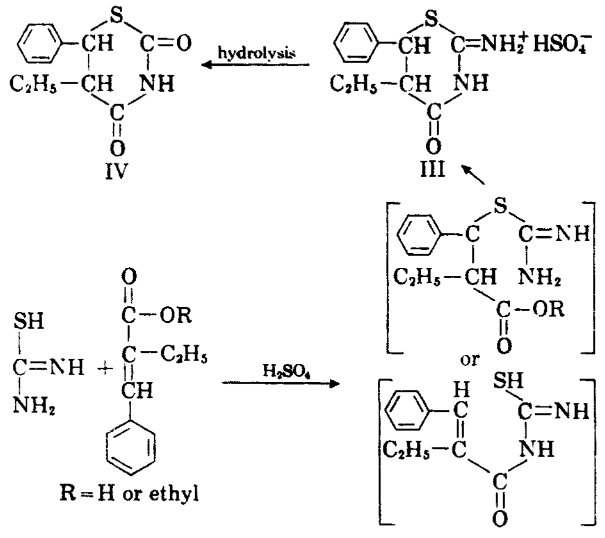

Figure 2

isolation procedures used throughout in this work, no other compounds than the *meta*-thiazane derivative have been isolated. Therefore, no information is available on the comparative rates of the condensation and addition reactions. III, an imine sulfate could not be isolated because of its solubility in concentrated and dilute sulfuric acid. Therefore, it was converted to the *meta*-thiazane-2,4-dione (IV), by acid hydrolysis which was then readily isolated in a 51.5 % yield.

5-Ethyl-6-phenyl-*meta*-thiazane-2,4-dione (IV) had been previously prepared from thiourea and 2-ethyl-3-bromo-3-phenylpropionic acid.[6] That reaction was repeated in the present work to obtain a 35% yield of the dione. In that reaction, the imine salt analogous to III was obtained and also converted to IV by acid hydrolysis. The methods of preparation of a number of other substituted *meta*-thiazane-2,4-diones are given in the above reference. Langlet,[7] in considerably older literature, describes the preparation of a number of 2-imino-4-oxo-*meta*-thiazanes by the reaction of thiourea and *N*-substituted thioureas with β-iodopropionic acid. This same worker also prepared a number of substituted *meta*-thiazane-2,4-diones by reaction of *N*-substituted thiocarbamates with β-iodopropionic acid.[7]

EXPERIMENTAL

trans-α-Ethylcinnamic acid was prepared by the Perkin reaction; however earlier methods of preparation were modified by using potassium carbonate as catalyst and by simplification of the isolation and purification procedures. A mixture of 272.0 g. (2.55 mole) of benzaldehyde, 508 g. (3.2 mole) of butyric anhydride, and 178.0 g. (1.3 mole) of anhydrous potassium carbonate was stirred and gradually heated to 140°. At this temperature an exothermic reaction occurred, causing considerable foam formation accompanied by a rapid temperature rise. The foaming was controlled by occasionally cooling the reaction flask in cold water. After reheating and cooling the reaction mixture three times, it was heated to 180°. After heating at this temperature for 20 hr., the mixture was poured with stirring into 1900 ml. of water containing 454.0 g. of sodium carbonate. After allowing this mixture to stand for 30 min., the dark oil that separated from the aqueous phase was discarded. The product was precipitated from the aqueous phase by the addition of 110.0 ml. of concentrated sulfuric acid with vigorous stirring, bringing the *p*H to 5.0. The mixture was stirred for 30 min. and the precipitate was removed by vacuum filtration. The filter cake was washed three times with water and then dried at 70° for 16 hr. to give 225.3 g. (50.2%) of *trans*-α-ethylcinnamic acid, m.p. 103–104° (lit.[8b] m.p. 104°).

Ethyl trans-α-ethylcinnamate was prepared by the Claisen reaction from benzaldehyde and ethyl butyrate.[8c]

Authentic 5-ethyl-6-phenyl-meta-thiazane-2,4-dione was prepared according to the method of Wheeler and Gash[6] from thiourea and 2-ethyl-3-bromo-3-phenylpropionic acid. Upon recrystallization from alcohol this material melted at 160–162° [lit.[6] m.p. (of unrecrystallized material) 153–155°] and was obtained in a 35% yield.

Reaction of thiourea with trans-α-ethylcinnamic acid. Two hundred and sixteen g. (2.8 mole) of thiourea was dissolved, with stirring and cooling, into one liter of 100% technical sulfuric acid, keeping the temperature below 55°. To the mixture, with mechanical stirring, was added 250.0 g. (1.4 mole) of *trans*-α-ethylcinnamic acid, then heating and stirring the mixture at 52–55° for 16 hr. The mixture was poured into 6.0 liters of water and the water solution refluxed for 16 hr. The solution was then cooled to 70° and 750 ml. of benzene was added. The mixture was then vigorously stirred for 5 min. and allowed to separate into two phases. The benzene layer was separated and filtered and its volume reduced to one-half on a steam bath. Upon cooling the residual benzene solution at room temperature, 170 g. (51.5% yield) of 5-ethyl-6-phenyl-*meta*-thiazane-2,4-dione, m.p. 155–158° (lit.[6] m.p. 153–155°) was obtained after vacuum filtering and drying the crystals for 4 hr. at 100°. The solid obtained above was dissolved into 800 ml. of boiling ethanol, the solution filtered and the volume reduced to one half. On cooling at room temperature for 16 hr., 155 g. of the dione, m.p. 162–163° was obtained.

Anal. Calcd. for $C_{12}H_{13}O_2NS$: C, 61.25; H, 5.57. Found: C, 61.33; H, 5.50.

Admixture of this product with an authentic sample of 5-ethyl-6-phenyl-*meta*-thiazane-2,4-dione caused no depression of its melting point.

Reaction of thiourea with ethyl trans-α-ethylcinnamate. Ten and seven tenths g. (0.14 mole) of thiourea was dissolved into 75 ml. of concentrated sulfuric acid, with stirring and cooling, keeping the temperature below 55°. To this solution, with stirring, was added 14.3 g. (0.07 mole) of ethyl *trans*-α-ethylcinnamate. The mixture was heated at 52° for 7 hr. and then poured into 300 ml. of water. The water mixture was refluxed for 16 hr. and then cooled for 16 hr. at 5°. An amorphous lump which settled out of solution was dissolved into 35 ml. of boiling alcohol. The resultant solution was filtered and cooled at 5° for 16 hr. From two crops, there was obtained 5.1 g. (31.0% yield) of 5-ethyl-6-phenyl-*meta*-thiazane-2,4-dione, m.p. 157–159° (lit.[6] m.p. 153–155°). Admixture of this material with an authentic sample of the dione and with the dione prepared from thiourea and trans-α-ethylcinnamic acid (above) caused no depression of its melting point.

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(6) K. W. Wheeler and V. W. Gash, U. S. Patent 2,585,-064, Example II (1952).

(7) N. A. Langlet, *Ber.* **24**, 3851 (1891); *Over. Svenska Vetenskaps-Akad. Forh.*, **166**, 306 (1892); 376 (1894); 37 (1895), *Beilstein*, **XXVII**, 246.

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