207–208°. Admixture with the product obtained by method A did not depress the melting point.

The yield of pure products as obtained by the three methods was 55%, 60%, and 95% respectively.

1-(2'-Carboxyphenyl)-2-mercapto-4,4,6-trimethyl-1,4-dihydropyrimidine. 4-Isothiocyano-4-methyl-2-pentanone (5 g.) was added to a mixture of anthranilic acid (4.5 g.) in sodium bicarbonate solution. The mixture was warmed to 50° for 3 hr. when disappearance of the oily layer indicated completion of the reaction. The sodium salt (8.5 g.) was salted out with the help of saturated sodium chloride solution and crystallized from brine. A sample of 1-(2'-carboxyphenyl)-2-mercapto-4,4,6-trimethyl-1,4-dihydropyrimidine was obtained by acidification of the pure sodium salt solution, washed with water, and after drying in vacuum at 20° had the following analysis.

Anal. Calcd. for $C_{14}H_{16}N_2O_2S$: C, 60.87; H, 5.79. Found: C, 61.13; H, 5.98.

1,3,3-Trimethyl-6-imino-3H,6H,-pyrimido[1,2-a][3,1]-benzothiazine. A mixture of 4-isothiocyano-4-methyl-2-pentanone (1.02 g.) and *o*-aminobenzonitrile hydrochloride (1 g.) was placed in a hard glass test tube and heated in an oil bath, the temperature being maintained at 110° for 45 min. The reaction mixture turned into a liquid which solidified in about 25 min. into a hard solid. The resulting hydrochloride on crystallization from glacial acetic acid furnished a crystalline solid, m.p. 295°; yield 1.2 g. (63.3%).

Department of Chemistry
Panjab University
Hoshiarpur, India

Studies in Thiazolopyrimidines. I. A Case of Michael Retrogression

(Miss) N. Gill, N. K. Ralhan, H. S. Sachdev, and K. S. Narang

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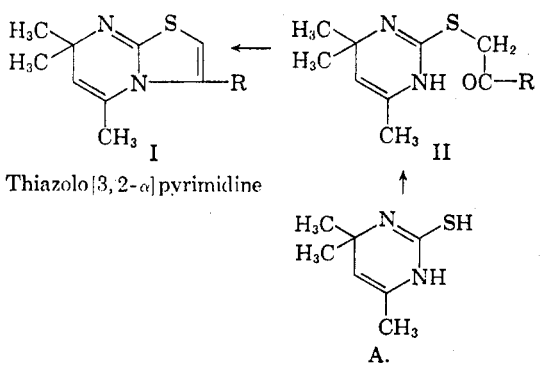
Several thiazole and pyrimidine derivatives are physiologically important. To obtain the compounds for antibacterial evaluation, the synthesis of thiazolopyrimidines (I) by ring closure of II was undertaken.



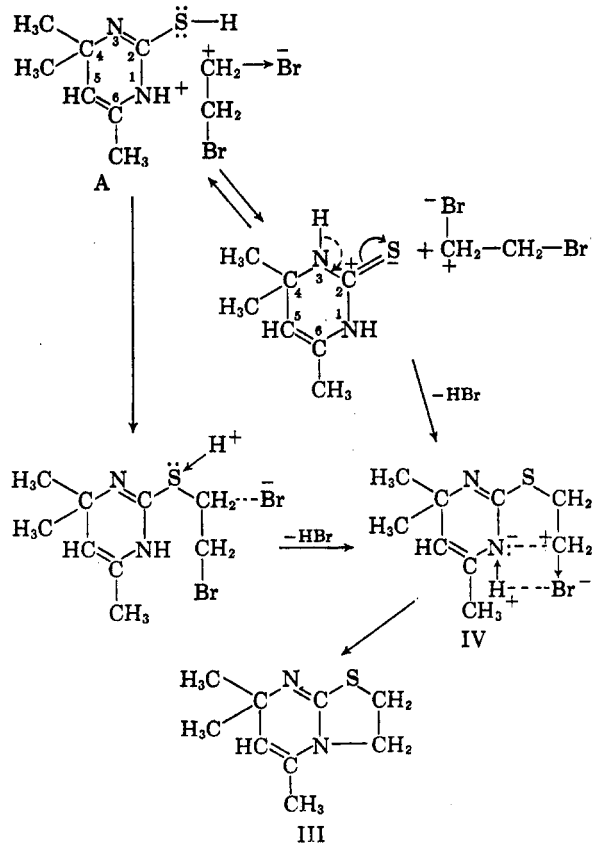
I — Thiazolo[3,2-*a*]pyrimidine

II

A.

However, the condensation of 2-mercapto-4,4,6-trimethyl-1,4-dihydropyrimidine[1] (A) with ω-bromoacetophenone and with *p*-methoxy-ω-bromoacetophenone in boiling ethanol furnished solids which on treatment with base and crystallization gave 2-amino-4-phenylthiazole and 2-amino-4-(*p*-methoxyphenyl)thiazole respectively. These were identified through analyses as well as by undepressed mixed melting points with authentic samples. The enthanolic filtrates after separation of the solids, referred to above, were treated in each case with 2,4-dinitrophenylhydrazine, and the 2,4-dinitrophenylhydrazone of mesityl oxide was isolated from each filtrate and its structure confirmed by comparison with an authentic sample.

On the other hand 2-mercaptopyrimidine (A) readily condensed with ethylenedibromide to give III, the structure being confirmed through undepressed mixed melting point with the product obtained by cyclization of 1-(β-hydroxyethyl)-2-mercapto-4,4,6-trimethyl-1,4-dihydropyrimidine.[2] The formation of III by the condensation of ethylene dibromide and 2-mercaptopyrimidine (A) shows that H attached to N at 3 is more mobile; the formation of intermediate products could be visualized to take place as follows:



A — III — IV

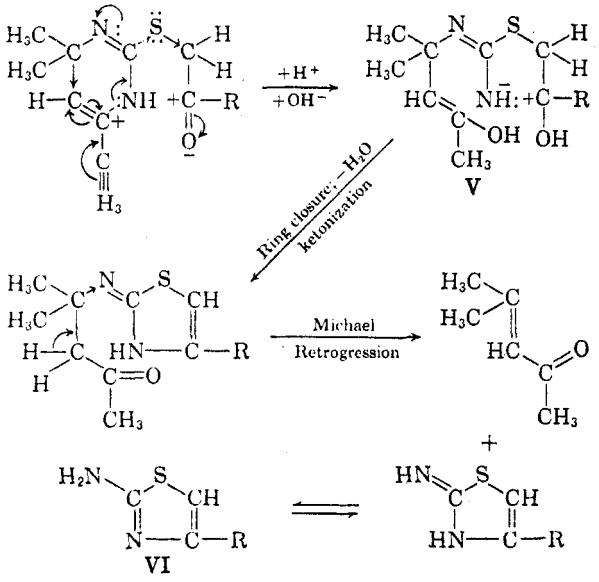
The essential difference between the intermediate in the case of the two ω-haloacetophenones (II. R = C_6H_5, *p*-$CH_3OC_6H_4$) and the intermediate in the case of ethylene dibromide (IV) is that the former contains a C = O group which plays a central part in the Michael Retrogression. The mech-

(1) Roger A. Mathes, Floyd D. Stewart, and Frank Swedish, Jr., *J. Am. Chem. Soc.*, 70, 1452 (1948).

(2) Roger A. Mathes, *J. Am. Chem. Soc.*, 75, 1747 (1953).

anism leading to the formation of 2-aminothiazoles (VI) could be shown below:

Hyperconjugation by CH_3 is opposed by the electron release by $(CH_3)_2C$; the former being stronger would leave a slight positive charge at the C-atom. It would appear that addition of a H at O and consequent demand at N of NH weakens the bond between it and the adjoining carbon and the breakage of this bond is followed by addition of OH resulting in the structure (V)



EXPERIMENTAL

Condensation of 2-mercapto-4,4,6-trimethyl-1,4-dihydropyrimidine with ω-bromoacetophenone: isolation of 2-amino-4-phenylthiazole and mesityl oxide. A mixture of 2-mercaptopyrimidine (A)(5.0 g.) and ω-bromoacetophenone (5.6 g.) was refluxed in ethanol (30 ml.) on a steam bath. After refluxing for about 1.5 hr., both components went into solution, whereafter a crystalline solid began to separate. After heating for 6 hr. the mixture was allowed to cool and the solid filtered and made basic with sodium bicarbonate. The base was collected by suction, washed with water, and crystallized from dilute ethanol, giving compound melting at 146°; the yield was 2.8 g. (50.2%).

Anal. Calcd. for $C_9H_8N_2S$: C, 61.3; H, 4.5. Found: C, 61.2; H, 4.6.

The analysis agrees with 2-amino-4-phenylthiazole. Moreover, the product did not depress the melting point on admixture with an authentic sample. The filtrate obtained after the separation of the solid was treated with 2,4-dinitrophenylhydrazine. The hydrazone so obtained melted at 199–200° and was identical with an authentic sample.

2-Mercaptopyrimidine (A) was similarly condensed with *p*-methoxy-ω-bromoacetophenone; the product on treatment with base of the solid crystallized from dilute ethanol; m.p. 205°. The yield was 36.8%.

Anal. Calcd. for $C_{10}H_{10}ON_2S$: C, 58.2; H, 4.8. Found: C, 58.5; H, 4.8%.

The product did not show a depression in melting point on admixture with an authentic sample of 2-amino-4(*p*-methoxyphenyl)thiazole.

Preparation of (III). A mixture of 2-mercaptopyrimidine (A) (5.0 g.) and ethylene dibromide (5.4 g.) was heated in an oil bath at 150° for 45 min. The orange yellow sirupy mass was cooled and treated with sodium bicarbonate. The solid so obtained was collected by suction, washed with water, and crystallized from dilute ethanol, giving a product melting at 180°; the yield being 4 g. (76%).

Anal. Calcd. for $C_9H_{14}N_2S$: C, 59.3; H, 7.6. Found: C, 58.9; H, 7.5.

Cyclization of 1-(β-hydroxyethyl)-2-mercapto-4,4,6-trimethylpyrimidine to (III). A 2.0-g. sample of 1-(β-hydroxyethyl)-2-mercapto-4,4,6-trimethylpyrimidine was treated in oil bath at 150° for 1.5 hr. The solid so obtained was crystallized from dilute ethanol, m.p. 180° and was confirmed to be III through its undepressed mixed melting point with the product obtained from the preceding experiment.

DEPARTMENT OF CHEMISTRY
PANJAB UNIVERSITY
HOSHIARPUR, INDIA

Preparation of Substituted Thiamorpholine 1,1-Dioxides

V. BALIAH AND T. RANGARAJAN

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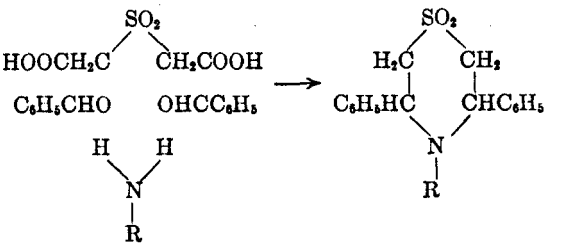
The work reported in this communication is a continuation of what has been published earlier by us.[1] Sulfonyldiacetic acid condensed with benzaldehyde and several aliphatic amines to give substituted thiamorpholine 1,1-dioxides.



The condensation proceeded as in the case of ammonia[1] but the yields are very much poorer with amines than with ammonia. The amines used were methylamine, ethylamine, allylamine, and benzylamine.

Diphenacyl sulfone also underwent condensations similar to diethyl sulfonyldiacetate[1] giving 2,6-dibenzoyl-3,5-diarylthiamorpholine 1,1-dioxides.

EXPERIMENTAL

3,5-Diphenyl-4-methylthiamorpholine 1,1-dioxide. A mixture of 2.73 g. (0.015 mole) of sulfonyldiacetic acid, 1.74 g. (0.015 mole) of a 25% aqueous solution of methylamine, 3.2 g. (0.03 mole) of benzaldehyde and 5 ml. of acetic acid was heated under reflux for 1.5 hr. After cooling, 50 ml. of ether was added to the product. The clear ethereal layer was separated, saturated with dry hydrogen chloride, and left overnight. The *hydrochloride* that separated was removed by filtration, washed with dry ether, and recrystallized from ethanol-ether, m.p. 255–257°. The yield was 0.7 g. (14%).

Anal. Calcd. for $C_{17}H_{20}ClNO_2S$: C, 60.42; H, 5.97. Found: C, 60.21; H, 5.93.

(1) V. Baliah and T. Rangarajan, *J. Chem. Soc.*, 3068 (1954).