7-Methyl-Thiocinchoninamide*

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The preparation of 7-methyl-thiocinchoninamide is described. Evidence is given for the stability of this compound in inert solvents; however, decomposition occurred at 85° in the presence of dialkylaminoalkylamines.

THE 4-thioamide of 7-methylquinoline was prepared in relation to the testing program sponsored by the Chemotherapy Center of Tropical Medicine. It was hoped that 7-methyl-thiocinchoninamide would serve as an intermediate in the synthesis of substituted amidines; however, under the conditions employed, this thioamide was converted back to 4-cyano-7-methylquinoline when heated with alkyl amines of high molecular weight. Schlatter (1) has commented on similar reactions of certain thioamides.

The preparation of quinoline derivatives from 2- and 4-cyanoquinolines has been described by Coates, *et al.* (2). In the present work the procedure of Olin and Johnson (3) provided a very simple synthetic method.

7-METHYL-THIOCINCHONINAMIDE (CC1029)[1]

Coates, *et al.* (2), described the formation of thiocinchoninamide by the addition of hydrogen sulfide to the cyano group of 4-cyanoquinoline. In preparing the corresponding derivative of 7-methylquinoline, an adaptation of the method of Olin and Johnson (3) was used. A chilled solution of 10 cc. of triethanolamine in 75 cc. of methanol was saturated with hydrogen sulfide. After addition of a solution of 18 Gm. of 4-cyano-7-methylquinoline (4) in 150 cc. of dry benzene, the stream of hydrogen sulfide was continued for an hour. After a further eighteen hours at room temperature, 11 Gm. of a crystalline product was collected on a filter. The mother liquor plus 3 cc. of triethanolamine was again saturated with hydrogen sulfide; after thirty-six hours a second crop of 6.7 Gm. was collected. The crude yield was 80% of the theoretical.

7-Methyl-thiocinchoninamide was crystallized from 95% ethanol; about 70 cc. of solvent per gram of crude thioamide was used for extraction and the alcoholic mother liquor was recirculated. After several subsequent recrystallizations, the product melted at 209° with decomposition.

Anal.—Calcd. for $C_{11}H_{10}N_2S$: N = 13.86; S = 15.84. Found: N = 13.67; S = 15.76.

Reaction of 7-Methyl-thiocinchoninamide with High Molecular Weight Amines.—This thioamide had been prepared as a possible intermediate in the synthesis of quinoline amidines. Although the thioamide was stable when heated in a liquid medium at fairly high temperatures, it decomposed when heated with several typical organic amines.

(*a*) After refluxing a suspension in toluene for one hour it was possible to recover 7-methyl-thiocinchoninamide unchanged.

(*b*) However, when the thioamide was heated at 85° in diethylaminoethylamine, a strong evolution of hydrogen sulfide occurred and 4-cyano-7-methylquinoline was recovered.

(*c*) With novol diamine[2] no reaction occurred on very mild heating; decomposition to 4-cyano-7-methylquinoline occurred with more vigorous heating. The 4-cyano-7-methylquinoline was identified by mixed melting point determination and by solubility properties.

SUMMARY

7-Methyl-thiocinchoninamide was prepared from 4-cyano-7-methylquinoline by the addition of hydrogen sulfide in the presence of triethanol amine. Simple attempts to convert this to an amidine were not successful.

REFERENCES

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(4) Ramsey, V. G., Baldwin, W. E., and Tipson, R. S., *J. Am. Chem. Soc.*, **69**, 67(1947).

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[1] The number assigned the compound by the testing program of the Chemotherapy Center for Tropical Diseases under the National Research Council.

[2] 1-Methyl-4-diethylaminobutylamine.