Attempted condensations with potassium N^1-chloro-N^4-acetylsulfanilamide in aqueous alcohol or aqueous dioxane were unsuccessful, N^4-acetylsulfanilamide being recovered pure in 80% yield.

2-Methylmercapto-5-carbethoxy-6-chloropyrimidine.—2-Methylmercapto-5-carbethoxy-6-oxypyrimidine (11.5 g.) was dissolved in 50 cc. of thionyl chloride and the mixture refluxed for three hours. Excess thionyl chloride was removed by distillation and the residue decomposed cautiously with ice. Water was added to make the volume 50 cc., and the mixture warmed and stirred on the steam-bath. The yellow solid which separated on cooling (10.5 g., 84%) was washed with water and dried in vacuo over calcium chloride, m. p. 54–58°. Recrystallization from aqueous alcohol gave white crystals, m. p. 58–59.5°.

Anal. Calcd. for $C_8H_9ClN_2O_2S$: C, 41.3; H, 3.9. Found: C, 41.5; H, 4.1.

Sulfilimine from 2-Methylmercaptoquinoline and Chloramine-T.—2-Methylmercaptoquinoline[10] when treated with potassium N^1-chloro-N^4-acetylsulfanilamide in aqueous alcohol yielded only N^4-acetylsulfanilamide (43% of purified material).

To a solution of 4.6 g. of chloramine-T in 25 cc. of water and 15 cc. of alcohol was added a solution of 1.8 g. of 2-methylmercaptoquinoline in 10 cc. of warm alcohol and the mixture was heated on the steam-bath for ninety minutes. The yellow oil which separated on cooling slowly solidified, yielding 1.1 g. of product, m. p. 124–127°. Recrystallization from alcohol yielded 0.9 g. of pure material, m. p. 128–129°.

Anal. Calcd. for $C_{17}H_{16}N_2O_2S_2$: C, 59.3; H, 4.7. Found: C, 59.6; H, 4.9.

(10) Beilenson and Hamer, *J. Chem. Soc.*, 143 (1939).

Summary

1. Sodium and potassium salts of N^1-chloro (and bromo)-N^4-acetylsulfanilamide have been prepared.

2. The salts have been condensed with alkyl and aryl sulfides to yield a series of sulfilimines derived from N^4-acetylsulfanilamide; the reaction is affected by the *p*H. The sulfilimine from diphenyl sulfide has been hydrolyzed stepwise to yield sulfanilyldiphenylsulfilimine, which on further hydrolysis yields sulfanilamide and diphenyl sulfoxide.

3. 2-Acetaminothiazoline, 2-methylmercapto-5-carbethoxy-6-oxypyrimidine and 2-methyl-mercaptoquinoline do not yield sulfilimines when treated with salts of N^1-chloro-N^4-acetylsulfanilamide; 2-methylmercaptoquinoline, however, gives a sulfilimine with chloramine-T.

4. Three new sulfilimines derived from *p*-toluenesulfonamide are reported.

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[CONTRIBUTION FROM THE RESEARCH LABORATORIES OF THE WINTHROP CHEMICAL CO., INC.]

A New Synthesis of Sulfanilylamidines

BY CHARLES E. KWARTLER AND PHILIP LUCAS

The preparation of some sulfanilylamidines has recently been announced by several investigators.[1,2] The synthesis of compounds of this class has been accomplished independently in this Laboratory. In the work already reported, these amidine derivatives were prepared by reduction of the corresponding nitrosulfanilylamidines which in turn were made by the action of *p*-nitrobenzenesulfonyl chloride on amidines or by a series of reactions starting with N′-acyl-*p*-nitrobenzenesulfonamides. It is the purpose of this paper to describe the preparation of a series of N^4-acetylsulfanilylamidines and the specific conditions required for the hydrolysis of these acetyl compounds to the corresponding sulfanilylamidines. This method of synthesis avoids the use of the comparatively expensive *p*-nitrobenzenesulfonyl chloride.

(1) S. R. Geigy A.-G., British Patent No. 538,822; see *Chem. Abst.*, **36**, 3511 (1942).

(2) Northey, Pierce and Kertesz, THIS JOURNAL, **64**, 2763 (1942).

The N^4-acetylsulfanilylamidines were readily obtained through the addition of an acetone solution of *p*-acetaminobenzenesulfonyl chloride to a cold aqueous solution or suspension of an amidine salt (hydrochloride, nitrate or carbonate). The reaction mixture was kept neutral or slightly alkaline by the addition of sodium hydroxide. The N^4-acetylsulfanilylamidines prepared by this method are listed in Table I.

The hydrolytic removal of the acetyl group without disturbing the amidine part of the molecule required special conditions. For example, if an N^4-acetylsulfanilylamidine is boiled for only fifty minutes with dilute hydrochloric acid or alkali, complete hydrolysis to sulfanilamide occurs. After many attempts at hydrolysis under a variety of conditions, the action of 15–25% alcoholic hydrogen chloride over periods of twelve to thirty-six hours at room temperature was investigated. Under these conditions, the

desired sulfanilylamidines were obtained in yields ranging from 52 to 75%. The detailed conditions for the hydrolysis are given in the experimental part of this paper. The sulfanilylamidines prepared by this method are listed in Table II. Pharmacological tests are being carried out on these compounds and the results will be presented elsewhere. To test the generality of this method, hydrolyses of other amides by this method are in progress. The results of these experiments will subsequently be reported.

In the course of this work it was necessary to prepare tridecaniminoethyl ether hydrochloride and tridecanamidine hydrochloride. These preparations being new, details are furnished in the experimental part of the paper.

Experimental

The general method of synthesis employed is conveniently illustrated by detailed directions for the preparation of sulfanilylacetamidine.

Preparation of N^4-Acetylsulfanilylacetamidine.—A solution of 35 g. (0.15 mole) of *p*-acetaminobenzenesulfonyl chloride in 100 ml. of acetone was added dropwise to a mechanically stirred solution, at 0–5°, of 9.45 g. (0.1 mole) of acetamidine hydrochloride in 40 ml. of water, and the reaction mixture was kept neutral or slightly alkaline with dilute alkali. After stirring at room temperature overnight, the precipitated acetyl compound was filtered from the neutralized reaction mixture, and recrystallized from aqueous acetic acid; yield, 13 g., 51%; m. p., 241–243°.

Anal. Calcd. for $C_{10}H_{13}N_3O_3S$: N, 16.47. Found: N, 16.47.

Preparation of Sulfanilylacetamidine.—A suspension of 47 g. of the acetyl compound in a mixture of 500 ml. of 20% alcoholic hydrogen chloride and 4 ml. of concentrated hydrochloric acid was shaken at room temperature for thirty-six hours. The sulfanilylacetamidine hydrochloride (m. p. 191–195° dec.) was collected by filtration, dissolved in water, and its aqueous solution was neutralized in the cold to precipitate sulfanilylacetamidine; this was cooled and filtered. The solid was redissolved in hot water and the solution clarified by filtration; on cooling, the sulfanilylacetamidine crystallized. After another recrystallization from water, the yield was 23 g. (58.6%) of a product of melting point 150–152°.

Anal. Calcd. for $C_8H_{11}N_3O_2S$: N, 19.71. Found: N, 19.88.

Preparation of Tridecaniminoethyl Ether Hydrochloride.—A solution of 78 g. (0.4 mole) of tridecanonitrile and 18.5 g. (0.4 mole) of absolute alcohol in 150 ml. of anhydrous ether was saturated with dry hydrogen chloride with cooling in an ice-salt bath; the reaction product was kept at 5°. After nine days, 51 g. of the hygroscopic product had separated. This was filtered and dried. It melted at 99–102° (dec.). The mother liquor, on concentration, yielded another 26 g. of product; the total yield was 77 g. (69.5%).

Anal. Calcd. for $C_{15}H_{32}ClNO$: N, 5.04. Found: N, 5.31.

Preparation of Tridecanamidine Hydrochloride.—A solution of 50 g. of the imino ester hydrochloride in 200 ml. of 9.5% alcoholic ammonia was allowed to stand at room temperature for twenty hours and, on concentration and treatment with ether, yielded 37 g. (82.6%) of tridecanamidine hydrochloride, m. p. 135–136°.

Anal. Calcd. for $C_{13}H_{29}ClN_2$: N, 11.27. Found: N, 11.63.

TABLE I

ACETYLSULFANILYLAMIDINES

Acetylsulfanilyl	M. p., °C.	Formula	N Analyses, %[3] Calcd.	Found
Acetamidine	241–243	$C_{10}H_{13}N_3O_3S$	16.47	16.47
Propionamidine	192–195	$C_{11}H_{15}N_3O_3S$	15.60	15.91
Butyramidine	149–151	$C_{12}H_{17}N_3O_3S$	14.83	14.60
Tridecanamidine	114–116	$C_{21}H_{35}N_3O_3S$	10.27	10.20
Benzamidine	211–212	$C_{15}H_{15}N_3O_3S$	13.25	13.24
Phenylacetamidine	193–195	$C_{16}H_{17}N_3O_3S$	12.69	12.25

TABLE II

SULFANILYLAMIDINES

Sulfanilyl	M. p., °C.	Formula	N Analyses, %[3] Calcd.	Found
Acetamidine	150–152	$C_8H_{11}N_3O_2S$	19.71	19.88
Propionamidine	149–151	$C_9H_{13}N_3O_2S$	18.50	18.68
Butyramidine	79– 82	$C_{10}H_{15}N_3O_2S$	17.42	17.48
Tridecanamidine	94– 95	$C_{19}H_{33}N_3O_2S$	11.44	11.19
Benzamidine	207–209	$C_{13}H_{13}N_3O_2S$	15.29	15.00
Phenylacetamidine	173–175	$C_{14}H_{15}N_3O_2S$	14.52	14.62

Summary

The preparation of a series of N^4-acetylsulfanilylamidines and sulfanilylamidines has been described. Particular note is made of the conditions found to be essential for the hydrolysis of the acetyl compounds to the desired sulfanilylamidines.

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(3) The authors are indebted to Miss E. A. Bass for the microanalyses.