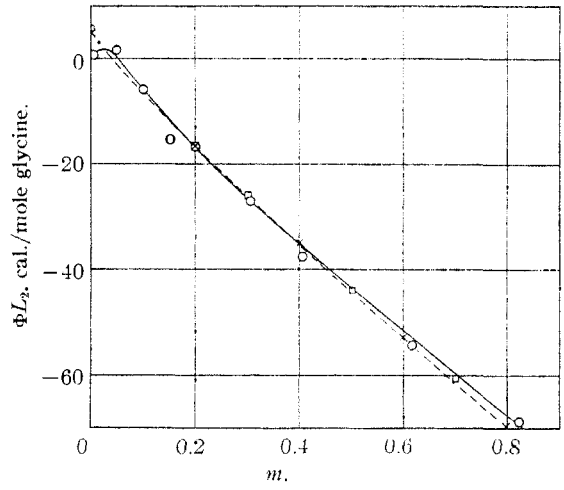


Fig. 2.—Plot showing the variation of ΦL_2 with molality: O, this research; ×, Gucker, Pickard and Ford; □, Sturtevant; full curve computed from equation (6); dashed curve from Equation 2 of Gucker, Pickard and Ford.[6]

made coincident at 0.2 *m* so as to eliminate discrepancies arising from different methods of extrapolation. Only in the dilute range (<0.05 *m*) are there significant deviations of the several curves. For the 32 experiments performed in this study with concentrations less than 0.2 *m*, the average deviation of measured from calculated (see equation 6) heat effects is 0.0023 cal. In the same concentration range the data of Gucker, Pickard and Ford show an average deviation from their equation (2) of 0.0040 cal. for 36 experiments. For the 14 runs above 0.2 *m* the average deviation of measured from calculated is 0.0044 cal. for our data, and 13 runs by Gucker, Pickard and Ford show an average deviation of 0.0043 cal. from their equation above 0.2 *m*. Sturtevant's results are mostly for concentrated solutions and are reported to deviate approximately 0.04 cal. on the average from his equation.

The results of this study for $m < 0.05$ reveal that the slope $\partial\Phi L_2/\partial m$ is changing rapidly with concentration, apparently becoming positive at very great dilutions. However, the heat effects below 0.05 molal are extremely small and are not as reproducible as could be desired. These difficulties are evidenced by a large uncertainty in the computed limiting slope. The S^0 value (see equation 3) of +167 has associated with it a probable error of ±233,[16] which, of course, is too large to allow the sign of the initial slope to be definitely established. If, however, correction is made for ionization effects, after the calculations of Sturtevant, these measurements indicate the existence of a positive limiting slope. In any case, the measurements at high dilutions strongly suggest that the true limiting slope is appreciably less negative than previously has been reported.[6,7]

Summary

The heats of dilution of aqueous glycine solutions have been measured from 0.8 to 0.0003 molal at 25°. The partial molal heat contents have been calculated for the components over the concentration range studied.

The behavior in very dilute solutions appears to conform more closely to the theory of Fuoss than do the results of previous studies.

(16) Estimated from the uncertainties in the data from which it was obtained (see ref. 14).

PITTSBURGH, PA. RECEIVED MAY 25, 1942

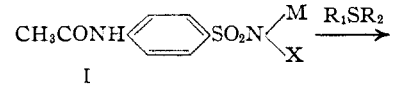
[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF THE UNIVERSITY OF ROCHESTER]

Sulfilimines Derived from Sulfanilamide

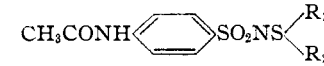
BY C. W. TODD, JOHN H. FLETCHER AND D. S. TARBELL

In view of the possible importance of new types of sulfanilamide derivatives, we have extended previous work on sulfilimines[1] to the preparation of a series of sulfilimines derived from sulfanilamide.

When the method of preparing sulfilimines which was successful with *p*-toluenesulfonamide[1]—heating the sulfoxide and sulfonamide together with an acid dehydrating agent—was tried with sulfanilamide and diethyl or diphenyl sulfoxide, no product was obtained. It was found possible, however, to prepare compounds of type I from N^4-acetylsulfanilamide, by treatment



I



II

with the appropriate hypohalite, where M is sodium or potassium, and X is chlorine or bromine. Condensation of the type I compounds with sul-

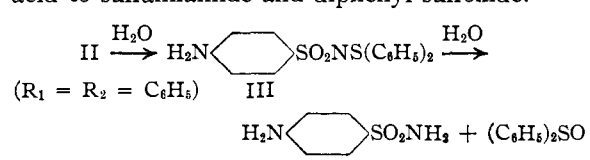
(1) Tarbell and Weaver, THIS JOURNAL, 63, 2939 (1941).

fides led to the formation of the sulfilimines II. Potassium N^1-chloro-N^4-acetylsulfanilamide (I, M = K, X = Cl) was employed in most of the work because it is more readily prepared with good yields in a high state of purity than the other three analogous compounds. Type I compounds could not be obtained from sulfanilamide itself, due no doubt to the sensitivity of the free amino group to oxidation.

The reaction of type I compounds with sulfides is affected markedly by the *p*H; in early work using the sodiochloro compound it was observed that the ease of sulfilimine formation with a given sulfide varied greatly with different samples of sodiochloro compound. This was found to be due to the presence of varying amounts of alkali in the samples; when sufficient acid was added to bring the *p*H to 7, samples of I which were otherwise unreactive toward a sulfide reacted promptly.

The sulfilimines prepared are listed in the table, which also includes three prepared from chloramine-T for purposes of comparison.

The hydrolysis of N^4-acetylsulfanilyldiphenylsulfilimine (II, $R_1 = R_2 = C_6H_5$) was studied to obtain, if possible, a sulfilimine with a free amino group for pharmacological tests. The compound was hydrolyzed by hydrochloric acid in aqueous dioxane to sulfanilyldiphenylsulfilimine III, which could be hydrolyzed further using concentrated acid to sulfanilamide and diphenyl sulfoxide.



Compound III has almost exactly the same percentage composition for carbon and hydrogen as II, but there was a depression in mixed m. p.'s. The presence of the free amino group in III was shown by diazotization and coupling with β-naphthol to yield a red dye. This series of reactions incidentally constitutes a structure proof for the sulfilimines.

The alkaline hydrolysis of acetylsulfanilyldi-*n*-butylsulfilimine (II, $R_1 = R_2 = C_4H_9$) yielded sulfanilamide and a mixture apparently composed of dibutyl sulfoxide and dibutyl sulfide. The latter was isolated and characterized by condensing with chloramine-T to yield a crystalline sulfilimine; since this sulfilimine had not been reported previously, it was prepared from a known sample of dibutyl sulfide for purposes of comparison.

Because of the effect of certain nitrogen heterocycles in increasing the activity of sulfanilamide, several nitrogen compounds containing sulfur were prepared, including 2-acetaminothiazoline (this compound may have been derived from the tautomer of 2-aminothiazoline), 2-methylmercapto-5-carbethoxy-6-oxypyrimidine, and 2-methylmercaptoquinoline. None of these compounds gave a sulfilimine derived from N^4-acetylsulfanilamide, but 2-methylmercaptoquinoline did give a sulfilimine when treated with chloramine-T. Apparently the presence of the basic nitrogen does not preclude sulfilimine formation with derivatives of the proper sulfonamide, but the compounds of type I seem to be much less reactive than chloramine-T.

Experiments on the condensation of triphenylarsine and tributylarsine with sulfanilamide to form arsinimines[2] of the type p-$H_2NC_6H_4SO_2$-$NAsR_3$ have been so far unsuccessful, but work is being continued along these lines.

Several of the sulfilimines were tested for activity against *Streptococcus hemolyticus*, through the courtesy of Dr. E. H. Volwiler of the Abbott Laboratories. The tests indicated activity in only one compound, N^4-acetylsulfanilylmethyl-*p*-tolylsulfilimine (II, $R_1 = CH_3$, $R_2 = p$-CH_3-C_6H_4) and here the activity was much less than that of sulfanilamide. Sulfanilyldiphenylsulfilimine (III) which contains the free amino group was inactive, as was N^4-acetylsulfanilyldi-(*p*-acetaminophenyl)-sulfilimine (II, $R_1 = R_2 = p$-$CH_3CONHC_6H_4$). This compound was of interest because it has been found that 4,4′-diaminodiphenyl sulfoxide and the corresponding sulfone have activity.[3] This sulfoxide might be formed by hydrolysis of the sulfilimine in the organism. Both the sodium and potassium salts of N^1-chloro-N^4-acetylsulfanilamide (I, M = Na or K, X = Cl) were tested for antiseptic properties. Both possessed some activity, but were inferior to chloramine-T.

Experimental

Sodium N^1-Chloro-N^4-acetylsulfanilamide.[4]—To 100 g of N^4-acetylsulfanilamide dissolved in 200 cc. of water containing 18.8 g. of sodium hydroxide, the mixture being

(2) Mann, *J. Chem. Soc.*, 958 (1932).

(3) Fourneau, *et al.*, *Compt. rend. soc. biol.*, **127**, 393 (1938).

(4) This is essentially the procedure of Inglis, *J. Soc. Chem. Ind.*, **37**, 289 T (1918) for the preparation of Chloramine-T. The yield and quality of product is greatly influenced by small changes in the reaction conditions. We are indebted to Dr. F. D. Smith of the Monsanto Chemical Company, St. Louis, Missouri, for a supply of N^4-acetylsulfanilamide.

TABLE I

SULFILIMINES DERIVED FROM N^4-ACETYLSULFANILAMIDE CH_3CONH–C$_6$H$_4$–$SO_2NS(R_1)(R_2)$

R_1	R_2	Melting point, °C.	Formula	Analyses, % Calcd. C	Calcd. H	Found C	Found H
CH_3	CH_3	141–142 dec.	$C_{10}H_{14}N_2O_3S_2$	43.8	5.1	43.9	5.3
C_2H_5	C_2H_5	181–182 dec.	$C_{12}H_{18}N_2O_3S_2$	47.7	6.0	47.9	6.1
n-C_3H_7	n-C_3H_7	166–167 dec.	$C_{14}H_{22}N_2O_3S_2$	50.9	6.7	51.0	6.8
n-C_4H_9	n-C_4H_9	160–160.5 dec.	$C_{16}H_{26}N_2O_3S_2$	53.6	7.3	53.6	7.3
n-C_5H_{11}	n-C_5H_{11}	158.5–160 dec.	$C_{18}H_{30}N_2O_3S_2$	55.9	7.9	56.1	7.8
C_6H_5	C_6H_5	204–204.5	$C_{20}H_{18}N_2O_3S_2$	60.3	4.6	60.6	4.6
$C_6H_5CH_2$	$C_6H_5CH_2$	192.5–193	$C_{22}H_{22}N_2O_3S_2$	62.0	5.2	62.2	5.4
CH_3	p-$C_6H_4CH_3$	180–180.5	$C_{16}H_{18}N_2O_3S_2$	54.8	5.2	55.2	5.3
p-$CH_3CONHC_6H_4$	p-$CH_3CONHC_6H_4$	163.5–164.5 dec.	$C_{24}H_{24}N_4O_5S_2 \cdot H_2O$	54.3	4.9	54.3	5.1
SULFILIMINES FROM p-TOLUENESULFONAMIDE							
p-$CH_3C_6H_4SO_2NS(CH_3)_2$		154–155	$C_9H_{13}NO_2S_2$	46.7	5.7	47.1	5.6
p-$CH_3C_6H_4SO_2NS(n$-$C_3H_7)_2$		110–111.5	$C_{13}H_{21}NO_2S_2$	54.3	7.4	54.7	7.4
p-$CH_3C_6H_4SO_2NS(n$-$C_4H_9)_2$		77.5–78.5[a]	$C_{15}H_{25}NO_2S_2$	57.1	7.9	57.2	7.8

[a] This material melting at 77.5–78.5° does not give the calculated analytical values, and appears to contain p-toluenesulfonamide as an impurity. The product was purified by dissolving in benzene and extracting with 5% aqueous sodium hydroxide; on the addition of petroleum ether (90–100°) to the benzene solution the sulfilimine separates as an oil which crystallizes on standing. These crystals were once more taken up in benzene and precipitated by petroleum ether. This gave crystals melting at 64–65°, which gave the proper analytical values. The melting point of this material was not depressed by p-toluenesulfonamide. Recrystallization by heating appeared to cause some decomposition. Analyses were done by R. W. King and R. Baumann.

kept in an ice-bath, was added with stirring a solution prepared by the addition of 40 g. of chlorine to 48 g. of sodium hydroxide in 100 cc. of water and 200 g. of ice. After the addition was complete the mixture was stirred for an additional five hours with continued cooling in the ice-bath. The reaction mixture was a pasty mass and could best be stirred with a powerful motor and a Hershberg stirrer. The reaction mixture was then filtered and the paste spread out to dry, which caused the surface of the originally yellowish material to turn dark on standing. The dry product weighed 133 g., decomposed at 210° and was found to have 80% of the theoretical oxidizing power when titrated with acidified potassium iodide solution and standard thiosulfate. This corresponds to an 84% yield of 100% pure material.

Alternative Procedure.—N^4-Acetylsulfanilamide (43 g., 0.2 mole) was dissolved in 275 cc. of water containing 8.0 g. (0.2 mole) of sodium hydroxide, and the solution was filtered. A solution of sodium hypochlorite was prepared by passing 14.2 g. of chlorine into a mixture of 16 g. (0.4 mole) of sodium hydroxide, 30 cc. of water and 100 g. of ice. The N^4-acetylsulfanilamide solution was cooled to 10° and the hypochlorite solution was added with stirring; the mixture soon thickened to a paste. The solid which tended to clog the filter during isolation was dried at 75° after being washed once with alcohol.

Three other analogous compounds were obtained by this general procedure, with the results shown in the table. The purity of these salts was determined in each case by an iodometric titration with standard thiosulfate using starch as an indicator.

Compound	Yield, %	Purity, %	Decomposition, °C.
Sodio-chloro	36	97	195–205
Sodio-bromo	61	95	250–260
Potassio-chloro	83	97	190–200
Potassio-bromo	79	94	210–220

Preparation of the Sulfilimines. N^4-Acetylsulfanilyldi-n-butylsulfilimine (II, $R_1 = R_2 = n$-C_4H_9) **Method A.**—To a solution of 5.9 g. (0.02 mole) of potassium N^1-chloro-N^4-acetylsulfanilamide (I, M = K, X = Cl) in 40 cc. of water and 60 cc. of alcohol was added 2.9 g. (0.02 mole) of di-n-butyl sulfide (Eastman Kodak Co., redistilled). The mixture was stirred and refluxed for two hours. After 50 cc. of solvent had been removed by distillation, an oil separated in the aqueous residue, which, when cooled, readily crystallized. The solid was collected, washed with water and dried at 75°. After recrystallization from dioxane the white crystals melted with dec. at 160–160.5°, yield 4.0 g. (56%).

Method B.—To filtered solution of 5.9 g. (0.02 mole) of I (M = K, X = Cl) in 60 cc. of water was added 2.9 g. of the sulfide. The mixture was stirred well for two and one-half hours; the solid which separated was collected, washed with water and dried at 75°; yield, 3.8 g. (53%); m. p. 161–162° dec.

The sulfilimines from the sulfides of lower molecular weight were prepared by method A and the others by method B. The yields ranged from 55 to 85%.

N^4-Acetylsulfanilyl-di-(p-acetaminophenyl)-sulfilimine (II, $R_1 = R_2 = p$-$CH_3CONHC_6H_4$).—Thirteen grams (0.043 mole) of 4,4′-diacetaminodiphenyl sulfide[5] was dissolved in 650 cc. of alcohol by heating, and the hot solution was filtered. To a solution of 17.3 g. (0.043 mole) of 68% sodium N^1-chloro-N^4-acetylsulfanilamide (I, M = Na, X = Cl) in 175 cc. of water was added a few drops of concentrated hydrochloric acid, after which the solution was filtered into the alcoholic solution of the sulfide. The

(5) Prepared by the excellent procedure of Raiziss, Clemence, Severac and Moetsch, THIS JOURNAL, **61**, 2763 (1939).

clear mixture was heated and stirred under reflux for twenty-two hours. The alcohol was removed by distillation and the solid which separated in the residue on the addition of water was collected and dried at 75°. The yield was 14.2 g. (65%) of material with m. p. 161–163° dec. A sample recrystallized from alcohol melted with dec. at 163.5–164.5°. The carbon and hydrogen analysis of the compound indicated a monohydrate; attempts to dehydrate the compound by heating with acetyl chloride, toluene or xylene were unsuccessful.

Sulfanilyldiphenylsulfilimine (III).—To a mixture of 11 cc. of water, 11 cc. of concentrated hydrochloric acid and 53 cc. of dioxane was added 27.6 g. of the sulfilimine (II, $R_1 = R_2 = C_6H_5$). The mixture was heated on the steam-bath for forty-five minutes, then was cooled and made alkaline, causing the separation of an oily layer which soon solidified. This material, when collected, and washed with water and dried in a vacuum desiccator, had the m. p. 165–170° and gave a depression on mixed m. p. with either the starting material or with N^4-acetylsulfanilamide. The product was dried further by refluxing with benzene, which yielded 9.6 g.; after recrystallization from dry dioxane, the compound melted at 183–184°.

Anal. Calcd. for $C_{18}H_{16}N_2O_2S_2$: C, 60.6; H, 4.5. Found: C, 60.7; H, 4.6.

One gram of this product was heated with 4 cc. of concentrated hydrochloric acid on the steam-bath for one-half hour. On cooling, 0.35 g. of diphenyl sulfoxide separated, which, after recrystallization from benzene–petroleum ether, melted at 66–68° and gave no depression on mixed m. p. with an authentic sample. Neutralization of the filtrate yielded 0.30 g. of sulfanilamide, m. p. 161–162°, not depressed on mixing with a known sample.

Diazotization and Coupling of Sulfanilyldiphenylsulfilimine (III).[6]—Sodium nitrite (0.5 g.) was added to a solution of 7 cc. of concentrated sulfuric acid and 3 cc. of water at 10°. To this solution was added a solution of 1.0 g. of III in 7 cc. of quinoline, keeping the temperature below 10°, and continuing the stirring for one-half hour after the addition was complete. Crushed ice (35 cc.) and urea (0.3 g.) were added and the mixture filtered. To the clear solution was added 0.26 g. of β-naphthol in 1.5 cc. of quinoline. The solution, which immediately became deep red, was diluted with 30 cc. of water and, after standing two days, deposited a dark red product, m. p. 170–175°. After refluxing with 20% aqueous ethanol for thirty minutes, the product was recrystallized twice from hot toluene, m. p. 210–211°.

One gram of N^4-acetylsulfanilyldiphenylsulfilimine was carried through the same procedure; although a red solution was formed, no crystals were obtained on standing for two days. This indicates that the III actually possessed a free amino group and that the acetyl compound did not hydrolyze and diazotize under the conditions of the experiment.

Alkaline Hydrolysis of N^4-Acetylsulfanilyldi-*n*-butylsulfilimine.—Ten grams of II ($R_1 = R_2 = n\text{-}C_4H_9$) was heated under reflux with 250 cc. of 1% sodium hydroxide and 25 cc. of toluene; the layers were separated while still hot. The aqueous layer on acidification and concentration yielded 2.7 g. (56%) of sulfanilamide, proved by a mixed m. p. The toluene layer was distilled, yielding 1.65 g. of liquid, b. p. 175–200°, probably a mixture of di-*n*-butyl sulfide and sulfoxide. Upon treatment of this crude product with aqueous chloramine-T, a solid sulfilimine slowly formed, m. p. 75–77°, giving no depression in mixed m. p. with *p*-toluenesulfonyl-di-*n*-butylsulfilimine.

Acetylsulfanilyldi-*n*-propylsulfilimine behaved similarly; the presence of dipropyl sulfide was shown by preparation of the sulfilimine with chloramine-T and comparison with an authentic sample, m. p. 107–110°.

2-Acetaminothiazoline.—Crude 2-aminothiazoline[7] (56.1 g.) was dissolved in 350 cc. of boiling benzene, some yellow gummy material being removed by filtration. To the filtrate was added 56 g. of acetic anhydride in 50 cc. of benzene and the mixture distilled until the boiling temperature reached 82°. The solid which separated on addition of petroleum ether (b. p. 60–70°) was removed and washed with dilute alkali to remove acetic acid. White crystals (34.0 g.) were obtained, and 12.2 g. additional on evaporation of the mother liquors (60% yield). The product when recrystallized from water formed white needles, melting to a red liquid at 194.5–195°. The position of the acetyl group was not rigorously proved.

Anal. Calcd. for $C_5H_8N_2OS$: C, 41.6; H, 5.6. Found: C, 41.6; H, 5.7.

2-Acetaminothiazoline Sulfoxide.—To a solution of 1.44 g. (0.01 mole) of 2-acetaminothiazoline in 50 cc. of dioxane and 10 cc. of water was added a filtered solution of 4.3 g. (0.011 mole) of 70% sodium N^1-chloro-N^4-acetylsulfanilamide in 40 cc. of water. The mixture was refluxed for one hour, concentrated to one-half its original volume, and then allowed to stand overnight. The solid product was washed with dilute alkali to remove N^4-acetylsulfanilamide, after which it was recrystallized from dioxane containing a small amount of alcohol. The product melted at 199–200°, and its melting point was depressed by the addition of either N^4-acetylsulfanilamide or 2-acetaminothiazoline.

Anal. Calcd. for $C_5H_6N_2O_2S$ (the sulfoxide): C, 37.5; H, 5.0. Found: C, 37.3; H, 5.9

2-Methylmercapto-5-carbethoxy-6-oxypyrimidine.—Methyl iso-thiourea sulfate (22.3 g.) was dissolved in 250 cc. of water, and 34.5 g. of redistilled ethoxymethylenemalonic ester[8] was added. A solution of 26.4 g. of 85% potassium hydroxide pellets in 50 cc. of water was added dropwise with rapid stirring, keeping the mixture at 10°; a thick paste formed soon after the addition of the alkali was complete. The mixture was heated on the steam-bath to dissolve the solid, and the solution was extracted twice with hot benzene to remove unreacted ester. The aqueous solution was made weakly acid to litmus with hydrochloric acid and allowed to cool; the product separated as a white solid; yield 11.5 g. (34%, m. p., after recrystallization from benzene–petroleum ether, 132–133°.

Anal.[9] Calcd. for $C_8H_{10}N_2O_3S$: C, 44.9; H, 4.7. Found: C, 45.2; H, 4.9.

(6) *Cf.* de Milt and van Zandt, THIS JOURNAL, **58**, 2044 (1936).

(7) Prepared according to Raiziss and Clemence, *ibid.*, **63**, 3125 (1941).

(8) Wheeler and Johns, *Am. Chem. J.*, **40**, 233 (1908).

(9) Wheeler, Johnson and Johns, *ibid.*, **37**, 405 (1907), prepared the basic hydroiodide of this compound by condensing methylisothiourea hydroiodide with ethoxymethylenemalonic ester, but did not obtain the compound itself.

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.

ROCHESTER, NEW YORK RECEIVED NOVEMBER 30, 1942

[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