10.07. Found: C, 60.3; H, 9.99), and a bis-*p*-bromophenacyl ester, m. p. 125–126° (*Anal.* Calcd. for $C_{36}H_{38}O_6Br_2$: C, 52.38; H, 4.73. Found: C, 52.38; H, 4.71).

2,7-Dimethyloctane-1,8-diol, VIII.—Thirteen grams of α,α-dimethylsuberic acid, m. p. 133.5–134°, was esterified with methanol and concentrated sulfuric acid in the usual manner and yielded 12.5 g. of the dimethyl ester, b. p. 128° (3–5 mm.). *Anal.* Calcd. for $C_{12}H_{22}O_4$: sapon. equiv., 115.2. Found: sapon. equiv., 117.3. This ester was dissolved in alcohol and hydrogenated in a high pressure bomb over 2.5 g. of copper chromite catalyst at 200–250°.[11] Removal of the catalyst and solvent left 7.98 g. of a colorless, viscous oil, which could not be crystallized. It was characterized by preparation of the bis-3,5-dinitrobenzoate, which was recrystallized from benzene, m. p. 175–176°. *Anal.* Calcd. for $C_{24}H_{26}O_{12}N_4$: C, 51.24; H, 4.66. Found: C, 52.19; H, 4.62.

A sample of VI, 0.0528 g., m. p. 108.5–109.5°, was hydrogenated in alcohol solution with platinum oxide catalyst. The theoretical amount of hydrogen was absorbed. Removal of the catalyst and solvent left 0.0506 g. of a colorless, viscous oil. Several such preparations were converted to the bis-3,5-dinitrobenzoate. The products were oily and resisted all attempts at crystallization.

(11) The assistance of Prof. Homer Adkins in carrying out this hydrogenation is gratefully acknowledged.

Summary

Acetylene and α-methylacrolein have been condensed to yield 2,7-dimethylocta-1,7-diene-4-yn-3,6-diol, which was rearranged to 2,7-dimethyl-octa-2,6-diene-4-yn-1,8-diol.

MADISON, WIS. RECEIVED JULY 25, 1947

[CONTRIBUTION FROM THE CHEMOTHERAPY DIVISION, STAMFORD RESEARCH LABORATORIES, AMERICAN CYANAMID COMPANY]

The Iodination of Certain Phenylsulfonamido- and Amino-heterocycles[1]

BY ROBERT G. SHEPHERD AND CATHERINE E. FELLOWS

Introduction

In a study of variously substituted sulfanilamido- and metanilamido-pyrimidines, the unique antimalarial effect of halogen substitution in the 5-position of the pyrimidine ring was discovered.[2] The preparation of iodinated pyrimidines was investigated in this connection and also because of their particular suitability for the preparation of cyano analogs.[2b] A satisfactory preparative method has now been found in the use of iodine and mercuric acetate. Using pyrimidines and other aromatic nuclei, this method was compared with the usual procedures involving iodine chloride and iodine in alkaline solution with the results set forth in the experimental section and Table II. Certain relationships of reactivity to structure were also investigated.

Experimental

The properties and analyses of the new compounds prepared in the subsequent procedures are listed in Table I by the Roman numerals accompanying them in the text.

Iodination of Aminoheterocycles. 2-Aminopyrimidine.—A solution of 23 g. (0.24 mole) of this amine in 200 cc. of water was treated with 32 g. (0.1 mole) of mercuric acetate and the mixture stirred for two minutes on the steam-bath. The initial yellow precipitate quickly turned to a thin white slurry which was treated at 70° with a solution of 50.8 g. (0.2 mole) of iodine in 200 cc. of hot dioxane. All of the iodine reacted during a half hour of stirring during which time considerable evaporation occurred. The thick slurry was poured into several volumes of 15% potassium iodide solution and washed on the filter with fresh iodide solution until white. Recrystallization from absolute alcohol (25 cc./g.) gave mercury-free **2-amino-5-iodopyrimidine** (I). Methanol and acetic acid are equally satisfactory purification solvents.

Iodination in hot acetic acid, as used for the sulfonamides, gave an orange-colored product in only 30% yield along with a large amount of mercury-containing tar.

The structure of the product was determined by conversion into 2-phenylsulfonamido-5-iodopyrimidine, the constitution of which had been previously demonstrated.[2b]

2-Aminopyridine.—The first method applied to this amine gave a 60% yield of product which was separated from the tarry by-product by ethylene dichloride extraction after the potassium iodide treatment. 5-Iodination was established by comparison (mixed m. p.) with **2-amino-5-iodopyridine** prepared according to the literature.[3]

Using two moles of iodine and one of mercuric acetate, **2-amino-3,5-diiodopyridine** (VIII) was obtained by hot ethylene dichloride extraction. After recrystallization from 95% alcohol (10 cc./g.) and ethylene dichloride (*ca.* 3 cc./g.), the melting point was 12° higher than that reported by Caldwell, *et al.*[4] Its identity was confirmed by nitrogen and iodine analyses and by conversion[4] to 2-hydroxy-3,5-diiodopyridine identical (mixed m. p.) with that prepared[4] by iodination of 2-hydroxypyridine. This amine differs from the mono-iodo derivative in being relatively insoluble in dilute acid and less soluble in ether.

Sulfonamides from Aminoheterocycles (Compounds VI, IX, X and XIII).—In this and other reactions of various benzenesulfonyl chlorides with amines in pyridine, the purification of the products has been aided materially by the addition of hot glacial acetic acid to the reaction mixture and isolation by cooling. The colored and alkali-insoluble materials which are thrown down by the usual addition of water remain in solution in this procedure which seems to have general application. The procedure for XIII given below illustrates the method.

A boiling solution of 3.5 g. (0.02 mole) of benzenesulfonyl chloride and 4.4 g. (0.02 mole) of 2-amino-5-iodopyrimidine in 3.2 cc. (0.04 mole) of dry pyridine was heated for fifteen minutes, allowing evaporation of the pyridine, to a final reaction temperature of about 150°. The temperature was then reduced to 105° for forty-five minutes and the crystalline mass was treated with 10 cc. of boiling glacial acetic acid and filtered at 30°; The 2-

(1) Presented before the Division of Organic Chemistry at the Chicago meeting of the American Chemical Society, September 12, 1946.

(2) (a) English, Clark, Clapp, Seeger and Ebel, THIS JOURNAL, **68**, 453 (1946); (b) English, Clark, Shepherd, Marson, Krapcho and Roblin, *ibid.*, **68**, 1039 (1946).

(3) v. Schickh, German Patent 473,213 (1929).

(4) Caldwell, Tyson and Lauer, THIS JOURNAL, **66**, 1479 (1944).

TABLE I

IODO DERIVATIVES AND RELATED INTERMEDIATES

	Name	M. p.,[a] °C.	Empirical formula	Analyses,[b] % Calcd. N	Found N
I	2-Amino-5-iodo-Pm[c]	224–225	$C_4H_4IN_3$	19.0	19.0[d]
II	2-(4-Nitrophenylsulfonamido)-5-iodo-Pm	290	$C_{10}H_7IN_4O_4S$	13.8	13.8
III	2-Sulfanilamido-5-iodo-Pm	269	$C_{10}H_9IN_4O_2S$	14.9	14.9
IV	2-(N^4-Acetylsulfanilamido)-5-iodo-Pm	284–285	$C_{12}H_{11}IN_4O_3S$	13.4	13.2
V	2-(N^3-Acetylmetanilamido)-5-iodo-Pm	270–271	$C_{12}H_{11}IN_4O_3S$		[e]
VI	2-(4-Nitrophenylsulfonamido)-Pm	273	$C_{10}H_8N_4O_4S$		[f]
VII	N^1-Methyl 2-(N^3-acetylmetanilamido)-Pm	189–190	$C_{13}H_{14}N_4O_3S$	18.3	18.1
VIII	2-Amino-3,5-diiodo-Py[g]	147–148[h]	$C_5H_4I_2N_2$	8.1	7.8[i]
IX	2-(4-Nitrophenylsulfonamido)-5-iodo-Py	220	$C_{11}H_8IN_3O_4S$	10.4	10.2
X	2-(N^4-Acetylsulfanilamido)-5-iodo-Py[k]	247	$C_{13}H_{12}IN_3O_3S$	10.1	10.2
XI	4'-Iodobenzenesulfonanilide	159–160	$C_{12}H_{10}INO_2S$	3.9	3.9
XII	Mercury bis-(2-phenylsulfonamido-Pm)	260	$C_{20}H_{16}HgN_6O_4S_2$		[m]
XIII	2-Phenylsulfonamido-5-iodo-Pm	255–256	$C_{10}H_8IN_3O_2S$		[n]
XIV	2-(3-Nitrophenylsulfonamido)-5-iodo-Pm	256–257	$C_{10}H_7IN_4O_4S$		[n]

[a] Corrected values obtained by rapid heating. The m. p.'s above 200° were accompanied by decomposition with the exception of the first compound. [b] The values given are the average of two results differing by less than 0.3. Performed in this Laboratory under the direction of Dr. J. A. Kuck. [c] Pm = pyrimidine. [d] Calcd.: C, 21.7; H, 1.8. Found: C, 21.6 by Van Slyke wet combustion; H, 2.1. [e] Calcd.: C, 34.5; H, 2.7. Found: C, 34.7; H, 3.0. [f] Calcd.: C, 42.9; H, 2.9. Found: C, 42.8; H, 2.7. [g] Py = pyridine. [h] Caldwell, *et al.* (ref. 4), reported a m. p. of 135–137°. [i] Calcd.: I, 73.4. Found: I, 73.2. [k] This compound has been reported in French Patent 846,191 (1939) (through *C. A.*, **35**, 1185 (1941)) to melt at 234°. [m] Calcd.: Hg, 30.0. Found: Hg, 30.1. [n] Ref. 2b.

phenylsulfonamido-5-iodopyrimidine (XIII) was washed with acetic acid, 5 *N* hydrochloric acid (to remove the unreacted amine) and water. Yield was 78%; m. p. 255–256° unchanged by mixture with material prepared by iodination of 2-phenylsulfonamidopyrimidine.[5]

By this method, compounds IX and X were obtained in 80% yield from 2-amino-5-iodopyridine[3] which reacted rapidly at 70–80°. The products were identical with those prepared from the corresponding sulfonamides by the iodination method described below.

Iodination of Phenylsulfonamidoheterocycles (Compounds II, IV, V, IX, X, XIII and XIV).—With the sulfonamides, it was necessary for rapid reaction to use two equivalents (1 mole) of mercuric acetate. The reaction proceeded to completion rapidly at 120° but only slowly at 60°. It was generally preferable to add this salt to the refluxing iodine–acetic acid solution of sulfonamide. The effect of the mercuric acetate could not be duplicated by the use of sodium acetate or pyridine in the acetic acid medium or by the use of a pyridine or aqueous alkaline medium.

A. Method.—One mole of the phenylsulfonamidoheterocycle was almost completely dissolved in boiling glacial acetic acid (0.6–4 liters) and treated with 1.15 moles of iodine. The heating was stopped and one mole of powdered mercuric acetate was added with vigorous shaking. In some cases, an immediate precipitation of the mercury salt of the product occurred and in all cases, silky yellow leaves of mercuric iodide formed after a few minutes. The reaction mixture was kept almost at the boiling point by intermittent heating during twenty to thirty minutes. The excess iodine was removed only by long heating and neither this nor use of more iodine with brief heating produced any significant increase in yield. The product was precipitated by addition to 1–2 volumes of 15% potassium iodide solution. The solid was filtered and thoroughly washed on the filter with fresh potassium iodide solution and water. The material at this point contained too little mercury to be detected with ammonium sulfide solution. However, precipitation from alkaline solution and hydrogen sulfide treatment changed the white suspension to gray. This test was negative after recrystallization from glacial acetic acid (10–80 cc./g.) or purification through the sodium salt. The latter was carried out by solution in ammonia followed by addition of excess sodium hydroxide or by treatment of a slurry in several volumes of water with 1.5 moles of 5 *N* alkali.

B. Proof of Structure.—To show that the position of iodination was the same in nitro- and acetaminophenylsulfonamido heterocycles, compounds IV, V and X were also prepared by acetylation (as for the preparation of compound VII) of the corresponding amines obtained from the reductions described below. In each case, the product was identical by mixed melting point with the material obtained by iodination of the acetaminophenylsulfonamide. Also, the amine III obtained from this reduction was shown to be identical with the amine prepared by acid hydrolysis of 2-(N^4-acetaminophenylsulfonamido)-pyrimidine after iodination.

Compounds IV and V were shown to be 5-iodopyrimidines by hydrolysis to 2-amino-5-iodopyrimidine (I) in 80% yield by the action of 65% sulfuric acid for one-half hour at the boiling point.

The proof of structure of the mono-iodo phenylsulfonamidopyridines (IX and X) is described in the preceding section. Attempted reaction of these products with more iodine failed to produce any di-iodination even under more drastic conditions.

Qualitative Test for Iodine.—Earlier work[6] on certain iodoacetyl compounds had disclosed a useful qualitative test for iodine. The test employs concentrated sulfuric acid and is based primarily on the observation of the characteristic purple vapor of iodine which is evolved from the brown iodine solution. The brown color of the solution is often masked or duplicated by organic decomposition products but the color of the vapor and the subsequent formation of a characteristic crystalline sublimate make the test specific for iodine. The sensitivity is limited only by the minute amount of iodine required to produce a visible color. Since most substances dissolve in concentrated sulfuric acid at room temperature, it is possible to take advantage of the fact that iodine is formed from a sample test at a temperature characteristic of its chemical combination. Thus, iodine, inorganic iodides and various addition complexes[7] give the test at 20–30° while iodoacetyl compounds

(5) English, Chappell, Bell and Roblin, THIS JOURNAL, **64**, 2516 (1942).

(6) Shepherd, Ph.D. Dissertation, The Johns Hopkins University, 1940.

(7) *E. g.*, the addition compound formed from 2-aminopyridine and iodine chloride: German Patent 503,920 (1930) and English Patents 264,508 and 283,576 (1927).

require moderate heating. Only at or near the boiling point is the iodine liberated from *unactivated* aromatic combination. These facts make it possible in many cases to distinguish between reagent, by-product (such as mercuric iodide) and desired product.

Reduction of Nitro Compounds II, IX and XIV.—When the nitrosulfonamide was boiled with one mole of commercial ammonium sulfide solution for two minutes, a heavy precipitate formed. A second precipitation occurred after addition of another mole of sulfide solution and six minutes of boiling. The red-brown mixture was added to excess 60% acetic acid and the solid purified by solution in dilute (1:3) ammonia (10 cc./g.) with charcoal treatment. The colorless filtrate was mixed with one volume of 5 *N* sodium hydroxide and after cooling, the sodium salt was separated and washed with alkali. After solution in warm 20% alcohol (10 cc./g.), the product was precipitated by addition to excess 60% acetic acid. Yields were 75–85% of amine III, 2-sulfanilamido-5-iodopyridine and 2-metanilamido-5-iodopyrimidine.

Comparatively brief heating with ammonium sulfide was used to avoid possible removal of the iodine.

N¹-Methyl-2-(N⁴-acetylmetanilamido)-pyrimidine (VII).—The corresponding metanilamide[2b] (1 g.) was boiled with 2 cc. of glacial acetic acid and treated with 2 cc. (5 equivalents) of acetic anhydride. The product obtained on cooling was purified by recrystallization from 10 cc. of absolute alcohol.

2-Sulfanilamido-5-iodopyrimidine (III).—The insolubility of the alkali salts of IV and III and of the acid salts of III made the usual hydrolytic methods unsatisfactory for the preparation of this sulfanilamide. This difficulty was overcome by utilizing the high solvent power of 60% sulfuric acid (8.5 cc./g.) and a reaction time of three minutes at the boiling point. A 25% yield of 2-amino-5-iodopyrimidine was obtained in addition to 65% of the desired product.

In general, the iodine substitution produces a marked change in solubility of the salts of the phenyl, pyridine and pyrimidine sulfonamides. The parent compounds form very water-soluble sodium salts and less soluble ammonium salts while the corresponding iodo derivatives form very insoluble sodium salts which are precipitated from the solution of the highly soluble ammonium salts. These characteristics formed the basis for very sharp separation methods in several instances. Introduction of the iodine also causes the hydrochlorides of the metanilamido- and sulfanilamido-pyrimidines to lose their water solubility.

4-Iodoacetanilide.—Reaction of acetanilide with one mole of iodine and mercuric acetate occurred rapidly in glacial acetic acid at 90° and the iodo derivative was precipitated by addition of potassium iodide solution. This product, melting at 184°, was identical with that obtained by iodination with iodine chloride[8] or by acetylation of 4-iodoaniline.

In connection with the benzene *versus* heterocyclic specificity of the reagents, an equimolar mixture of acetanilide and 2-phenylsulfonamidopyrimidine was iodinated in two ways. Iodination with iodine and mercuric acetate in boiling acetic acid gave roughly equal yields of the iodo derivatives of each. However, iodine chloride reacted only with the acetanilide present in the mixture.

4'-Iodobenzenesulfonanilide (XI).—Benzenesulfonanilide slowly reacted with iodine chloride in acetic acid with the result shown in Table II. The reaction was rapid when iodination was carried out with six equivalents of iodine in 8 *N* potassium hydroxide solution. Neither of these products was further iodinated by treatment with an excess of either reagent. The iodinated sulfonamide was isolated only in low yield from the mercuric acetate iodination in acetic acid owing to the formation of mercury-containing tar and the consumption of several moles of iodine.

The products precipitated from the reaction mixtures above were purified by solution in 1.5 *N* sodium hydroxide (7 cc./g.) to obtain the crystalline sodium salts. The iodo derivatives obtained by acidification of the aqueous salts all gave no depression of the melting point of the sulfonamide prepared in 69% yield from 4-iodo-aniline and benzenesulfonyl chloride by the glacial acetic acid method.[9]

Comparative Iodinations of Various Aromatic Nuclei.—The iodination results with different nuclei are summarized in Table II for purposes of comparison. The alkaline iodine procedure of v. Schickh[3] was used except for aniline in which case sodium bicarbonate is more suitable. Iodine chloride experiments were carried out in boiling glacial acetic acid for three hours employing a 10–20% excess of reagent. The mercuric acetate iodinations were conducted in boiling glacial acetic acid for the sulfonamides and in aqueous dioxane at 70° for the amines. The reactivity of acetanilide toward all three reagents was destroyed by the para-sulfonamido substitution in N⁴-acetylsulfanilamide.

TABLE II

IODINATION OF VARIOUS NUCLEI BY IODINATING AGENTS

Compound	Per cent. yield and product from I_2–KOH	ICl	I_2–$Hg(OAc)_2$
Aniline	80, 4-I[a]	[b]	Tar
Acetanilide	0, SM[c]	80, 4-I	92, 4-I
Benzenesulfonanilide	60, 4'-I	70, 4'-I	[d], 4'-I
2-Aminopyridine	90, 5-I	0, [e]	20, 3,5-I_2[f]
2-(N⁴-Acetylsulfanilamido)-Py[g]	0, SM	0, SM	77, 5-I
2-Aminopyrimidine	Trace[h]	15, 5-I	70, 5-I
2-Phenylsulfonamido-Pm[k]	0, SM	0[m]	69, 5-I
N¹-Methyl-2-(N⁴-acetylsulfanilamido)-Pm	0, SM	0, SM	0, SM
2-Aminothiazole	[n]		Tar
2-(N⁴-Acetylsulfanilamido)-pyrazine			0, dec.[o]

[a] "Organic Syntheses," Coll. Vol. II, 347 (1943). [b] Some control of substitution up to tri-iodoaniline can be obtained by using one, two or three moles; *cf.* ref. 8. [c] SM = starting material recovered after attempted reaction. [d] Very low due to side-reactions. [e] An addition complex is formed which iodinates only on heating with alkali; *cf.* ref. 7. [f] With one mole of iodine, a 60% yield of mono-substituted product was obtained. [g] Py = Pyridine. [h] About 0.3% of 2-amino-5-iodopyrimidine was isolated and identified. [k] Pm = Pyrimidine. [m] The lack of reaction here contrasts with the ready halogenation by chlorine and bromine; see ref. 2b. [n] Some non-ionic iodination product was formed but has not yet been characterized. [o] No evidence of iodination even when heating was carried to the decomposition point with partial recovery of starting material.

The results with 2-(4-nitrophenylsulfonamido)-pyridine were similar to those tabulated for the acetamino analog, the third reagent giving an 88% yield of mono-iodo derivative. The phenyl-substituted derivatives of 2-phenylsulfonamidopyrimidine were unreactive except to iodine–mercuric acetate which gave the following yields of 5-iodopyrimidines: 3-nitro, 67%; 4-nitro, 74%; 3-acetamino, 63%, and 4-acetamino, 80%. The ring N-methylated pyridine, 1-methyl-2-(N⁴-acetylsulfanilimido)-1,2-dihydropyridine,[9a] reacted with iodine–mercuric acetate at 60–70° but the reaction appeared to take another course since very water-soluble products were formed. With 2-(N⁴-acetylsulfanilamido)-thiazole, alkaline iodine gave a non-ionic iodination product and iodine–mercuric acetate caused a rapid reaction at 90° yielding water-soluble products.

Mercury bis-(Phenylsulfonamidopyrimidine) (XII).—A solution of 6.4 g. (0.02 mole) of mercuric acetate in 50 cc. of boiling glacial acetic acid was added to 4.7 g. (0.02 mole) of 2-phenylsulfonamidopyrimidine in 75 cc. of boil-

(8) Michael and Norton, *Ber.*, **11**, 107 (1878).

(9) Shepherd, *J. Org. Chem.*, **12**, 275 (1947).

(9a) Shepherd, *et al.*, THIS JOURNAL, **64**, 2532 (1942).

ing acetic acid and the clear mixture evaporated to about 50 cc. Slight cooling gave a heavy white precipitate which was washed with acetic acid and recrystallized from 90 cc. of acetic acid; yield was 85%.

Material, identical by mixed melting point, resulted from treatment of a cold solution of 2-phenylsulfonamidopyrimidine in 2.5% ammonia (8 cc./g.) with excess 16% mercuric acetate solution in water.

Both materials gave an immediate test for mercury on treatment with ammonium sulfide solution. The same result was obtained with the mercury derivative (m. p. 300°) of 2-phenylsulfonamido-5-chloropyrimidine[3b] which was prepared in hot acetic acid.

Discussion

The absence of iodination in those cases (SM) of Table II where the starting material was recovered was confirmed by the delicate qualitative test for iodine described above. This table illustrates the greater reactivity of iodine–mercuric acetate compared to the other reagents. The direct di-iodination of 2-aminopyridine is to be preferred from the standpoint of yield and time required to the four-step synthesis previously employed.[4] Preparation of iodo derivatives from the phenylsulfonamidopyrimidines themselves by the method described is more satisfactory than from sulfonylation of the iodoamine.[10] It is of interest to point out the retention of the high reactivity of the heterocyclic nucleus toward iodine–mercuric acetate after substitution with the deactivating sulfonamido group (Table II) and the heterocyclic specificity of this reagent in the presence of a benzene-activating acetamino group (IV, V and X). The undiminished reactivity of the nitrophenylsulfonamides (intermediate to II, IX and XIV) is in contrast to the results of chlorination of analogous sulfonamides where nitro substitution has been reported to reduce either the rate[11] or extent[12] of halogenation of the N-substituent. A further contrast with chlorination results is found in the case of benzenesulfonanilide (Table II) which has been observed to undergo *ortho* chlorination in an alkaline medium[13] and *para* chlorination under acidic conditions.[14] The most striking effect of simple structural variation on reactivity toward mercury-induced iodination is the lack of reaction caused by N^1-methylation of 2-(N^3-acetylmetanilamido)-pyrimidine (Table II).

Since the effect of mercuric acetate on pyrimidine iodinations could not be duplicated by other substances, the possibility of intermediate mercuration was investigated. This was shown to be unlikely and, instead, the intermediate appears to be the mercury salt of the sulfonamide. This salt might facilitate iodination by making possible the formation of N-iodine intermediates but the importance of the rearrangement of such compounds in halogenations is made questionable by the work of Orton, *et al.*[15] The high reactivity of the phenylsulfonamido- heterocycles to iodine–mercuric acetate in contrast to their lack of reactivity with other iodinating agents suggests the possibility that a covalent structure peculiar to the mercury salt is responsible for the high reactivity observed.

Acknowledgment.—We are indebted to Dr. Jackson P. English for his interest and counsel during the course of this investigation.

Summary

Iodine and mercuric acetate has been found particularly suitable for iodination of certain heterocyclic nuclei.

2-Aminopyrimidine, 2-aminopyridine and various phenylsulfonamido derivatives of both amines could be iodinated in the 5-position of the heterocyclic ring exclusively.

The hitherto unreported di-iodination of 2-aminopyridine has been accomplished by this method.

4′-Iodobenzenesulfonanilide was prepared by three iodination procedures as well as by coupling 4-iodoaniline in glacial acetic acid.

A mercury bis-sulfonamide salt was prepared and is discussed in relation to the iodination of the phenylsulfonamido-heterocycles.

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(10) 2-Amino-5-iodopyrimidine is less reactive toward sulfonyl chlorides than the parent amine, a property shared by the corresponding chloro and bromo compounds (ref. 2).

(11) Jones, *J. Chem. Soc.*, 1231 (1936).

(12) Schuloff, Pollak and Riesz, *Ber.*, **62B**, 1846 (1929).

(13) Raper, Cohen and Thompson, *J. Chem. Soc.*, **85**, 372 (1904).

(14) Wallach and Huth, *Ber.*, **9**, 426 (1876).

(15) Orton, *et al.*, *J. Chem. Soc.*, **95**, 1456 (1909); *ibid.*, 998 (1928).