lucent tan mixture resulted. The cooled mixture was filtered and the xylene filtrate was evaporated *in vacuo* to dryness. The residue was dissolved in 100 ml. of chloroform. The original xylene-insoluble material was extracted with boiling chloroform (three 100-ml. portions). All the chloroform solutions were combined and washed with 30% potassium iodide (two 200-ml. portions), then water (200 ml.), dried over magnesium sulfate, and evaporated *in vacuo* to dryness.

The orange syrup thus obtained was dissolved in 60 ml. of absolute methanol and 3 ml. of 1 *N* sodium methoxide in methanol was added. The dark red solution that resulted was refluxed for 30 min., evaporated *in vacuo* to about 25 ml., and then poured quickly into 25 ml. of cold water. Amberlite IR-120 (H) ion-exchange resin was added in small batches to the stirred mixture until pH 7 was obtained. The resin was removed by filtration and washed first with water and then with methanol until the methanol removed no more color. The filtrate and washings were combined and evaporated to dryness *in vacuo*. The residue was dissolved in 30 ml. of warm water and the aqueous solution was washed with 30-ml. portions of chloroform until the chloroform layer remained colorless (four 30-ml. portions). The aqueous layer was evaporated to dryness *in vacuo*. The residue, dried thoroughly by evaporating it twice with 25 ml. of absolute ethanol, was crystallized from 15 ml. of hot ethanol with charcoal treatment; yield, 1.19 g. (37%).

The analytical sample was obtained by recrystallization from absolute ethanol. It was dried at 78° (0.07 mm.) over phosphorus pentoxide for 16 hr.; m.p. 208–210°; R_f 0.49; λ_{max} mμ ($\epsilon \times 10^{-3}$): pH 1—255 (7.05), pH 7—266 (12.1), pH 13—266 (11.4).

Anal. Calcd. for $C_{17}H_{18}N_4O_5$: C, 56.98; H, 5.06; N, 15.64. Found: C, 56.93; H, 5.12; N, 15.51.

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The Direct Conversion of Chloropurines to Fluoropurines[1]

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A general method is described for the direct conversion of various 7- or 9-alkylated 2-, 6-, and 8-chloropurines to the corresponding fluoropurines. This procedure utilizes silver fluoride in the presence of toluene or xylene. Several of the requisite methylated chloropurine intermediates have been prepared for the first time.

Although new general methods for the preparation of chloropurines[2,3] and bromopurines[4] have been described recently, only a few fluoropurines have been prepared. The conversion of 2-aminopurines to the corresponding 2-fluoropurines[5] by the modified Schieman reaction appears to be limited to the synthesis of 2-fluoropurines.[6]

The synthesis of 9-substituted 6-fluoropurines has been reported recently[7] by the ring closure of the appropriate 5-amino-4-substituted-amino-6-fluoropyrimidine. This method, however, is obviously inapplicable to the preparation of 8-fluoropurines.

The synthesis of various fluorinated nitrogen heterocyclic compounds has been reported from the corresponding chloro derivatives in the *s*-triazines,[8-11] pyrimidines,[7,12,13] and thiadiazoles.[14] In all instances reported, the halogen exchange was accomplished by repeated distillation of the chloro heterocycle over antimony trifluoride dichloride,[9,10] potassium fluorosulfinate,[8] or silver fluoride[7,11-14] to yield the final product.

This general method of synthesis of fluoro derivatives of nitrogen heterocycles, however, is limited to compounds which are relatively volatile and which do not decompose during the distillation processes. In the application of this procedure to the synthesis of more complex fluoroheterocycles, *i.e.*, those possessing a condensed ring system such as purine, considerable difficulty was encountered. In an effort to accomplish halogen exchange successfully in purine derivatives, a variety of reaction conditions were tried in the hope that the required fluoropurines would be isolated without decomposition.

Finger and Starr[15] report the use of potassium fluoride in dimethylformamide for the conversion of various chloropyridines to fluoropyridines. This method, however, when applied to 6-chloropurine, gave only decomposition and polymeric products. It has now been discovered that treatment of the appropriate 7- or 9-methylchloropurines with silver fluoride in refluxing toluene or xylene provides a facile and general route for the preparation of the corresponding methylated 2-, 6-, and 8-fluoropurines. This method has the advantage that the product need not be distilled to be recovered. The cooled reaction mixture need only to be filtered to remove the silver fluoride and silver chloride, and the solid product is recovered from the hydrocarbon filtrate. In this manner, treatment of

(1) Supported by research grants CY-4008(C3) and (C4) from the National Cancer Institute of the National Institutes of Health, Public Health Service.

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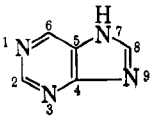
TABLE I

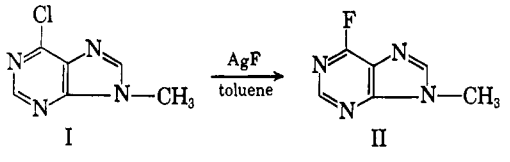
ULTRAVIOLET ABSORPTION OF SOME CHLORO- AND FLUOROPURINES



2	6	8	7	9	MeOH λ_{max}, mμ	ε	pH 1 λ_{max}, mμ	ε	pH 11 λ_{max}, mμ	ε
Cl	H	H	CH_3	...	275	6,600	273	7,400	275	6,800
Cl	H	H	...	CH_3	271.5	7,800	271	8,300	271.5	8,000
H	H	Cl	CH_3	...	287	11,200	282.5	11,800	225	4,400
									286	11,500
H	H	Cl	...	CH_3	267	11,300	269	8,300	267	11,000
Cl	Cl	H	CH_3	...	278–283	7,400	277–282	7,700	277	7,500
Cl	Cl	H	...	CH_3	274	10,100	276	10,600	275	11,200
H	Cl	O	CH_3	CH_3	283.5	14,200	282.5	15,100	283	15,100
F	H	H	...	CH_3	266	8,300	265	8,700	266.5	8,600
H	H	F	...	CH_3	260	6,700	261	6,400	280	9,300
									285–290[a]	8,800
F	F	H	CH_3	...	255	6,800	254	7,700	267	10,200
									270–275[a]	9,400
F	F	H	...	CH_3	255	7,100	255	7,200	267.5	15,000
									272–275[a]	13,600
F	F	OH	CH_3	...	275	7,500	275	7,500	285	11,000
H	F	H	...	$CH_2C_6H_5$	248	8,000	249	8,400	262	12,800
									265–268[a]	12,300

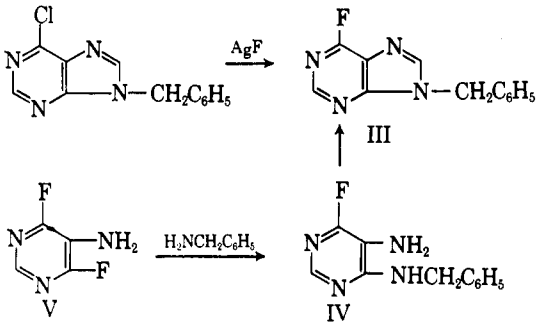
[a] Shoulder.

6-chloro-9-methylpurine (I)[16] with silver fluoride in refluxing toluene gave 6-fluoro-9-methylpurine (II)[7] in good yield. Similarly, 6-chloro-9-benzylpurine[17] gave



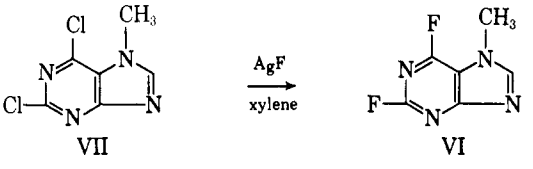
I II

6-fluoro-9-benzylpurine (III). In order to verify the structure, III also was synthesized by an unambiguous route by ring closure of 5-amino-4-benzylamino-6-fluoropyrimidine (IV) with ethyl orthoformate and acetic anhydride. The synthesis of IV was accomplished in turn from 5-amino-4,6-difluoropyrimidine (V)[7] which has been utilized in a similar synthesis of 9-methyl-6-fluoropurine.[7] When 8-chloro-9-methylpurine was refluxed in the presence of silver fluoride in toluene, 8-fluoro-9-methylpurine was formed. The formation of this compound is particularly significant in that it is the first example of the synthesis of an 8-fluoropurine. Conversion of 2-chloro-9-methylpurine to 2-fluoro-9-methylpurine required the use of the higher boiling solvent, xylene. This is in accord with the lessened reactivity of chlorine in the 2-position toward nucleophilic displacement as compared with positions 6 and 8.



III

V IV



VII VI

2,6-Difluoro-7-methylpurine (VI) was formed from 2,6-dichloro-7-methylpurine (VII). However, when 7-methyl-2,6,8-trichloropurine[18,19] was treated with silver fluoride in refluxing xylene, a difluorohydroxy-7-methylpurine (probably 2,6-difluoro-7-methyl-8-hydroxypurine) was obtained. Commercial preparations of silver fluoride frequently have been observed to be contaminated with acid which (with a trace of water in the solvent) may have given rise to the hydrolysis of one of the fluorine atoms. It is considered probable that the hydroxyl group is at position 8 by analogy to the formation of the 8-hydroxy derivative from 7-methyl-2,6,8-trichloropurine under acidic conditions.[19] The ultraviolet absorption spectral data also support this assignment

Attempts to convert 2-chloropurine, 8-chloropurine, and 2-amino-6-chloropurine directly to the corresponding fluoropurines were unsuccessful; starting material was recovered in each instance. In all cases studied, where halogen exchange was accomplished, it was necessary to replace the imidazole hydrogen with a substituent group at either position 7 or 9.

A number of previously unknown 7- and 9-methylchloropurines were required for the present study. Thus, 2-chloropurine[3] was methylated by the general

(16) R. K. Robins and H. H. Lin, *J. Am. Chem. Soc.*, **79**, 490 (1957).
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method employed by Montgomery and Temple[17] for the alkylation of 6-chloropurine. The isomeric 2-chloro-7-methylpurine and 2-chloro-9-methylpurine obtained were separated by fractional crystallization. The structural assignment of these isomers was made possible by conversion to the known 7- and 9-methylpurines[20,21] by dehalogenation with palladium on carbon in the presence of hydrogen. Similarly, 8-chloro-9-methylpurine was obtained from 8-chloropurine[3] and its structure determined by hydrogenation to 9-methylpurine. The rather inaccessible 2,6-dichloro-9-methylpurine[22,23] was readily obtained from a similar methylation of 2,6-dichloropurine.[3] Methylation of 6,8-dichloropurine[3] by this general procedure, however, unexpectedly gave 6-chloro-7,8-dihydro-7,9-dimethylpurinone-8. The structure of this latter compound was established by catalytic dehalogenation to 7,8-dihydro-7,9-dimethylpurinone-8.[24,25]

The ultraviolet absorption spectra of several chloro- and fluoropurines are given in Table I.

Experimental[16]

Methylation of 2-Chloropurine.—Thirty-five grams of 2-chloropurine[3] was dissolved in 245 ml. of dimethyl sulfoxide at 18°. With stirring 35 g. of anhydrous potassium carbonate was added followed by 29.2 ml. of methyl iodide. The temperature rose to 39° in 10 min. and then fell. The mixture was stirred for 1.5 hr.; 380 g. of crushed ice was added and the aqueous dimethyl sulfoxide solution was extracted with seven 600-ml. portions of ethyl acetate. Evaporation of the ethyl acetate gave 36.2 g. (95%) of methylated products. The first two extracts (29.6 g.) consisted largely of 2-chloro-9-methylpurine, which was obtained pure by crystallization from water to give fine needles, m.p. 135–136°.

Anal. Calcd. for $C_6H_5ClN_4$: C, 42.7; H, 3.0; N, 33.2. Found: C, 42.3; H, 3.2; N, 33.3.

The third extract (3.8 g.) was a mixture of 2-chloro-7-methylpurine and 2-chloro-9-methylpurine. The fourth extract (1.2 g.) was about 70% 2-chloro-7-methylpurine. The final three extracts gave 1.6 g. of 2-chloro-7-methylpurine, which was recrystallized from water to give heavy needles, m.p. 199–201°.

Anal. Calcd. for $C_6H_5ClN_4$: C, 42.7; H, 3.0; N, 33.2. Found: C, 42.8; H, 3.2; N, 33.4.

The structure of the product, m.p. 135–136°, was established as 2-chloro-9-methylpurine by hydrogenation (5% Pd/C, 30 lb. of H_2) in 3% aqueous ammonia solution. The solution was evaporated and the residue recrystallized from benzene and finally sublimed to give 9-methylpurine, m.p. 161–162° (reported[20,21] m.p. 162–163°). The product possessed the same ultraviolet absorption spectrum as reported by Bendich[21] for 9-methylpurine. The structure of the product, m.p. 199–201° was established as 2-chloro-7-methylpurine by hydrogenation (5% Pd/C, 30 lb. H_2) in 3% aqueous ammonia to give 7-methylpurine, which was recrystallized from ethyl acetate to give crystals, m.p. 182.5–183° (reported[20,21] m.p. 184 and 183–184°). The product possessed the same ultraviolet absorption spectrum as reported by Bendich[21] for 7-methylpurine.

Methylation of 8-Chloropurine.—To a solution of 15 g. of 8-chloropurine,[3] in 120 ml. of dimethyl sulfoxide at room temperature, was added 15 g. of anhydrous potassium carbonate followed by 13 ml. of methyl iodide. The mixture was stirred at 24–44° (heat of reaction) for 1.5 hr. and 250 g. of crushed ice was added. The solution was filtered, if not clear, and the filtrate extracted with three 250-ml. portions of ethyl acetate. The solid obtained upon evaporation of the ethyl acetate was recrystallized from benzene to give spheres, m.p. about 120–130° dec. The filtrate was evaporated to a small volume to yield broad needles, m.p. 103–106°. The broad needles were recrystallized from *n*-heptane to give 8-chloro-9-methylpurine as needles, m.p. 106–108° (1.25 g.).

Anal. Calcd. for $C_6H_5ClN_4$: C, 42.7; H, 3.0; N, 33.2. Found: C, 42.4; H, 2.8; N, 33.0.

The pellets (first crop) were recrystallized from benzene, then ethyl acetate, and finally ethyl acetate-*n*-heptane to give 8-chloro-7-methylpurine as needles (0.7 g.). When a small sample of these needles was placed on a block at 140° and heated rapidly, melting with decomposition took place at about 150°.

Anal. Calcd. for $C_6H_5ClN_4$: C, 42.7; H, 3.0. Found: C, 43.2; H, 3.1.

The structure of the product, m.p. 106–108°, was proved to be 8-chloro-9-methylpurine by hydrogenation (5% Pd/C, 30 lb. of H_2) in 0.4% aqueous ammonia solution to give 9-methylpurine (purified by recrystallization from benzene and then *n*-heptane followed by sublimation), m.p. 161–162°, which possessed the ultraviolet spectrum reported by Bendich.[21]

Methylation of 2,6-Dichloropurine.—To a solution of 50.6 g. of 2,6-dichloropurine,[3] in 500 ml. of dimethyl sulfoxide at room temperature, was added 41 g. of anhydrous potassium carbonate followed by 35 ml. of methyl iodide. The mixture was stirred at 26–41° (heat of reaction) for 3.5 hr. About 1 kg. of crushed ice was added and the resulting clear solution was extracted with three 700-ml. portions of ethyl acetate. Evaporation of the ethyl acetate gave a quantitative yield of crude methylated product. The crude solid was stirred with fifteen parts of ethyl acetate at room temperature and most of the more soluble 2,6-dichloro-9-methylpurine dissolved. This material, obtained by evaporation of the ethyl acetate, was recrystallized from five parts of boiling ethyl acetate to give 20.3 g. of 2,6-dichloro-9-methylpurine, m.p. 152–153° (reported[22,23] m.p. 153 and 151.5–152.5°). The solid remaining undissolved upon trituration of the crude material with ethyl acetate at room temperature was recrystallized from ninety parts of boiling water to give 10.8 g. of crude 2,6-dichloro-7-methylpurine, m.p. 175–192°. Recrystallization of the crude 2,6-dichloro-7-methylpurine from water gave fine needles, m.p. 195° (reported[27,28] m.p. 196–197 and 195.5–196°). This compound possessed the same ultraviolet absorption spectra as an authentic sample.[28]

Methylation of 6,8-Dichloropurine.—Twenty-three grams of 6,8-dichloropurine[3] was dissolved in 230 ml. of dimethyl sulfoxide at 27°. With stirring 18.6 g. of anhydrous potassium carbonate was added, followed by 15 ml. of methyl iodide. The temperature rose to 37° in 10 min. The mixture was stirred for 2 hr., 500 g. of crushed ice was added, and the solution was extracted with three 400-ml. portions of ethyl acetate. The solid obtained upon evaporation of the ethyl acetate was slurried in 50 ml. of water at room temperature, filtered, and dried to give 3.5 g. of crude product. This product was purified by recrystallization from boiling water (75 ml.) and sublimation to give 6-chloro-7,8-dihydro-7,9-dimethylpurinone-8 as needles, m.p. 175–178°.

Anal. Calcd. for $C_7H_7ClN_4O$: C, 42.3; H, 3.7; N, 28.2. Found: C, 42.3; H, 4.0; N, 28.3.

The structure of 6-chloro-7,8-dihydro-7,9-dimethylpurinone-8 was established by hydrogenation (5% Pd/C, 30 lb. of H_2) in 2% aqueous ammonia solution to give 7,8-dihydro-7,9-dimethylpurinone-8 (purified by recrystallization from benzene-*n*-heptane), m.p. 110° (reported[24] m.p. 112°), which possessed the same ultraviolet absorption spectrum as reported by Brown.[25]

5-Amino-4-benzylamino-6-fluoropyrimidine (IV).—A solution of 1 g. of 5-amino-4,6-difluoropyrimidine (V),[7] 50 ml. of absolute ethanol, and 4.3 ml. of benzylamine was refluxed for 2 hr. The solid obtained upon evaporation was triturated with water and dried to give 1.7 g. (quantitative yield) of crude product. Recrystallization from boiling water gave crystals, m.p. 148–152°.

Anal. Calcd. for $C_{11}H_{11}FN_4$: F, 8.7; N, 25.7. Found: 8.3; N, 25.6.

9-Benzyl-6-fluoropurine (III). Method A.—A solution of 1.23 g. of 5-amino-4-benzylamino-6-fluoropyrimidine (IV), in 12 ml. of 2:1 (v./v.) ethyl orthoformate–acetic anhydride, was boiled in

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(24) E. Fischer, *Ber.*, **17**, 32 (1884).

(25) D. J. Brown and S. F. Mason, *J. Chem. Soc.*, 682 (1957).

(26) All melting points were taken on a Fisher-Johns melting point apparatus.

(27) E. Fischer, *Ber.*, **30**, 2400 (1897).

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an open flask for 15 min. The excess solvent was removed *in vacuo* and the resulting oil was recrystallized from hot *n*-heptane to give needles, m.p. 127–131°.

Anal. Calcd. for $C_{12}H_9FN_4$: C, 63.1; H, 4.0; F, 8.3; N, 24.6. Found: C, 62.7; H, 4.0; F, 8.1; N, 24.6.

Method B.—A solution of 5 g. of 9-benzyl-6-chloropurine[17] in 100 ml. of reagent toluene was refluxed and stirred with 25 g. of silver fluoride (AgF, Harshaw Chemical Company) for 1.5 hr. The silver salts were filtered. Evaporation of the toluene filtrate gave 3.5 g. of solid which was recrystallized from benzene–*n*-heptane to give 3.0 g. of needles, m.p. 124–126°. This product was identical to 9-benzyl-6-fluoropurine prepared by method A.

2-Fluoro-9-methylpurine.—To a solution of 2 g. of 2-chloro-9-methylpurine in 80 ml. of reagent xylene (b.p. 137–140°) was added 20 g. of silver fluoride, and the mixture was refluxed with stirring for 0.75 hr. The silver salts were filtered. The filtrate was returned to the reaction flask; 20 g. of fresh silver fluoride was added; and the mixture refluxed with stirring for 0.5 hr. The silver salts were removed by filtration and the xylene allowed to evaporate to give 0.6 g. of crude product which was purified by crystallization from boiling benzene to give crystals, m.p. 151–151.5°.

Anal. Calcd. for $C_6H_5FN_4$: C, 47.4; H, 3.3; F, 12.5; N, 36.8. Found: C, 47.6; H, 3.6; F, 12.3; N, 36.6.

6-Fluoro-9-methylpurine (II).—To a solution of 3 g. of 6-chloro-9-methylpurine (I)[16] in 75 ml. of reagent toluene was added 21 g. of silver fluoride, and the mixture was stirred and refluxed for 1.5 hr. The silver salts were filtered and the toluene evaporated to give 1.55 g. of crystalline solid. This was recrystallized from 1:1 (v./v.) benzene–*n*-heptane to give 1.40 g. of needles, m.p. 125–127°. The product was identical to the 6-fluoro-9-methylpurine prepared from 5-amino-6-fluoro-4-methylaminopyrimidine.[7]

8-Fluoro-9-methylpurine.—To a solution of 0.55 g. of 8-chloro-9-methylpurine in 75 ml. of reagent toluene was added 6 g. of finely divided silver fluoride, and the mixture was stirred and refluxed for 1.5 hr. The silver salts were removed by filtration and the toluene filtrate allowed to evaporate slowly to a small volume to give 0.3 g. of prisms, m.p. 111–112°.

Anal. Calcd. for $C_6H_5FN_4$: C, 47.4; H, 3.3; F, 12.5; N, 36.8. Found: C, 47.2; H, 3.7; F, 12.7; N, 36.9.

2,6-Difluoro-7-methylpurine (VI).—To a solution of 3.0 g. of 2,6-dichloro-7-methylpurine (VII)[28] in 100 ml. of reagent xylene (b.p. 137–140°) was added 30 g. of silver fluoride. The mixture was refluxed and stirred for 1 hr. and the silver salts were removed by filtration. The filtrate was returned to the reaction flask; 30 g. of fresh silver fluoride was added; and the mixture refluxed and stirred for 1.5 hr. The silver salts were filtered and the filtrate allowed to evaporate to give 0.34 g. of crystalline solid, which was recrystallized from benzene to give needles, m.p. 154–161°.

Anal. Calcd. for $C_6H_4F_2N_4$: C, 42.4; H, 2.4; F, 22.3; N, 32.9. Found: C, 41.9; H, 2.7; F, 22.3; N, 32.4.

Reaction of 7-Methyl-2,6,8-trichloropurine and Silver Fluoride.—To a solution of 4 g. of 7-methyl-2,6,8-trichloropurine[18,19] in 100 ml. of reagent xylene was added 40 g. of silver fluoride. The mixture was refluxed and stirred for 0.75 hr. and the silver salts were removed by filtration. The filtrate was returned to the reaction flask; 30 g. of fresh silver fluoride was added; and the mixture refluxed and stirred for 0.75 hr. The silver salts were filtered and the filtrate allowed to evaporate. The crude product was washed with three 3-ml. portions of benzene to give 1.5 g. of crystalline solid, which was recrystallized first from benzene and then from ethyl acetate to give crystals, m.p. 228–233°. The analyses showed the product to be a difluorohydroxy-7-methylpurine; presumably the hydroxy group is at position 8.

Anal. Calcd. for $C_6H_4F_2N_4O$: C, 38.7; H, 2.2; F, 20.4; N, 30.1. Found: C, 38.4; H, 2.0; F, 20.0; N, 29.7.

3,4-Dihydro-3-imino-2*H*-1,2,4-benzothiadiazine 1,1-Dioxides

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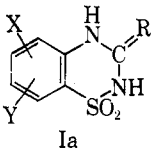
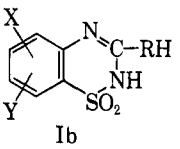
A number of 3,4-dihydro-3-imino-2*H*-1,2,4-benzothiadiazine 1,1-dioxides have been prepared by fusion of substituted *o*-aminobenzenesulfonamides with guanidine carbonate. The properties and reactions of these compounds have been investigated and certain comparisons made with the corresponding 3-oxo compounds. Possible distinction between the alternate tautomeric forms of certain compounds is discussed in the light of spectral evidence.

3,4-Dihydro-3-oxo-2*H*-1,2,4-benzothiadiazine 1,1-dioxide (I, R = O, X = Y = H) was first synthesized by Schräder[1] in 1917. Parke and Williams[2] prepared this compound and others of the same type bearing substituents in the phenyl ring by utilizing the reaction of a substituted *o*-aminobenzenesulfonamide with urea at high temperatures. The properties and reactions of the ring system were examined briefly by Parke and Williams[2] and more extensively in a number of papers by Raffa.[3] Other publications[4] have also recently appeared which describe the synthesis of sulfamoyl substituted 3,4-dihydro-3-oxo-2*H*-1,2,4-benzothiadiazine 1,1-dioxides.

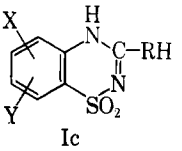
We became interested in the possible synthesis of compounds of the ring system (I) where R = NH[5] and



Ia



Ib



Ic

investigated the condensation of guanidine with orthanilamide. The fusion of orthanilamide with guanidine carbonate at 180–200° gave *ca.* a 50% yield of 3,4-dihydro-3-imino-2*H*-1,2,4-benzothiadiazine 1,1-dioxide (I, R = NH, X = Y = H). The same compound was obtained when cyanamide was substituted for guanidine carbonate, but in much lower yield. With aminoguanidine bicarbonate under similar reaction conditions, I (R = NH, X = Y = H) was isolated in very poor yield. A number of other 3,4-dihydro-3-imino-2*H*-1,2,4-benzothiadiazine 1,1-dioxides containing halogen and alkyl substituents in the phenyl por-

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(2) D. O. Parke and R. T. Williams, *J. Chem. Soc.*, 1760 (1950).

(3) (a) L. Raffa, *Farmaco* (Pavia) *Ed. sci.*, **12**, 293 (1957); (b) p. 400; (c) p. 495; (d) p. 502; (e) L. Raffa, M. DiBella, and A. Monzani, *ibid.*, **15**, 716 (1960); (f) L. Raffa, M. DiBella, M. Melegari, and G. Vampa, *ibid.*, **16**, 3 (1961). (g) L. Raffa and A. Monzani, *ibid.*, **16**, 14 (1961); (h) L. Raffa, A. Monzani, and M. DiBella, *ibid.*, **17**, 234 (1962).

(4) W. J. Close, L. R. Swett, L. E. Brady, J. H. Short, and M. Vernsten, *J. Am. Chem. Soc.*, **82**, 1132 (1960); F. C. Novello, S. C. Bell, E. L. A. Abrams, C. Ziegler, and J. Sprague, *J. Org. Chem.*, **25**, 970 (1960).

(5) At the outset of our investigations no mention of these compounds had appeared in the literature. Since then reports of their synthesis have been published: ref. 3a; ref. 3g. (a) E. Angeletti, *Gazzetta*, **90**, 841 (1960); (b) U. M. Testino and G. Maffii, British Patent 847,176 (1960); (c) L. Raffa, M. DiBella, M. Melegari, and G. Vampa, *Farmaco* (Pavia) *Ed sci.*, **17**, 331 (1962).