warm water and just neutralized with 5% sodium hydroxide. The white solid which precipitated was filtered and washed with a small amount of ice–water and recrystallized from 95% ethanol, m.p. 208–210°, white, 0.10 g.

Anal. Calcd. for $C_{13}H_{10}N_2O_4$: C, 60.46; H, 3.90; N, 10.85. Found: C, 60.26; H, 3.91; N, 10.98.

3,3′-Dinitro-4,4′-di(2-pyridylmethyl)azoxybenzene (V).—In a 125-ml. erlenmeyer flask 5 g. of 2-(2-nitro-4-aminobenzyl)pyridine (m.p. 118.5°, prepared according to the procedure of Nunn and Schofield[4]), 40 ml. of glacial acetic acid, 10 ml. of 30% hydrogen peroxide, and 2 drops of concentrated sulfuric acid were combined. The mixture was kept at room temperature for 48 hr., and 50 ml. of water was added followed by treatment with 20% sodium hydroxide. An oil which separated was extracted with toluene, the toluene extract washed with water and dried over anhydrous magnesium sulfate. After removal of the drying agent, the toluene was removed in a current of warm air. The solid yellow residue was recrystallized with a charcoal treatment from aqueous ethanol. The pure compound was yellow and melted at 135–136° (70% yield). The infrared spectrum showed no NH absorption bands.

Anal. Calcd. for $C_{24}H_{18}N_6O_5$: C, 61.27; H, 3.86; N, 17.87; mol. wt., 470.43. Found: C, 61.36; H, 3.97; N, 18.01; mol. wt., 464.0 (vapor pressure method).

2-(2,4-Dinitrobenzoyl)pyridine.—This material was prepared from 2-(2,4-dinitrobenzyl)pyridine by a procedure utilized by Nunn and Schofield[4] to oxidize analogous benzylpyridines. The 2-(2,4-dinitrobenzoyl)pyridine was obtained as white crystals melting at 149.5–151° (lit.[5] m.p. 148°).

2-(2,4-Dinitro-α-hydroxybenzyl)pyridine (VI).—In a 500-ml. round-bottom flask fitted with a condenser, stirrer, and addition funnel, a suspension of 2.75 g. (0.010 mole) of 2-(2,4-dinitrobenzoyl)pyridine in 150 ml. of commercial absolute methanol was cooled to 0° and an ice-cold solution of 1.04 g. (0.028 mole) of sodium borohydride in 15 ml. of methanol was quickly added. The reddish purple mixture was stirred at 0° for 1 hr. and then the temperature allowed to rise. After 1.5 hr. at room temperature the reaction mixture was heated at 50° for 1 hr. Dilute sulfuric acid was added and the inorganic material filtered. The filtrate was evaporated to one-fifth its original volume, an equal volume of water added, and the solution made basic with 2% sodium hydroxide. This mixture was extracted with ether, the ether extracts dried over anhydrous magnesium sulfate, and the drying agent removed. Evaporation of the ether afforded a yellow solid. Recrystallization from ethanol furnished pale yellow crystals melting at 134.5–135° dec. The infrared spectrum showed absence of C=O band and presence of OH band.

Anal. Calcd. for $C_{12}H_9N_3O_5$: C, 52.37; H, 3.30; N, 15.27. Found: C, 52.62; H, 3.36; N, 15.13.

4-(2-Nitro-4-cyanobenzyl)pyridine (VII).—A magnetically stirred solution of 1.5 g. (0.0065 mole) of 4-(2-nitro-4-aminobenzyl)pyridine (m.p. 129–130°, lit.[4] m.p. 130–131°) and 1.68 ml. (0.020 mole) of concentrated hydrochloric acid in 5 ml. of water was cooled to 0° and the amine diazotized by gradual addition of 0.45 g. (0.0065 mole) of sodium nitrite in 4 ml. of water. The diazonium solution was then added to a magnetically stirred mixture of 0.58 g. (0.0065 mole) of cuprous cyanide, 0.85 g. (0.013 mole) of potassium cyanide, 5 ml. of water, and 75 ml. of toluene at 5–10°. The reaction mixture was heated at 80° for 2.5 hr., cooled, and made basic with 5% sodium hydroxide. Solids were collected on a filter. They and the water layer of the filtrate were extracted several times with toluene. The combined extracts were washed with 3% sodium hydroxide, water, and then dried over anhydrous magnesium sulfate. Evaporation of the toluene afforded 0.63 g. of amber residue which rapidly crystallized. Several crystallizations from toluene–ligroin (charcoal treatment) furnished pale yellow crystals melting at 73–74°. The infrared spectrum showed the presence of C≡N group.

Anal. Calcd. for $C_{13}H_9N_3O_2$: C, 65.27; H, 3.79. Found: C, 64.89; H, 3.95.

Acknowledgment.—The authors wish to thank Mr. C. DiPietro for the chemical analyses.

Michael-Type Addition Reactions of 4-Chloropyrrolo[2,3-*d*]pyrimidines

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Received October 11, 1962

4-Chloropyrrolo[2,3-*d*]pyrimidines react with acrylonitrile and ethyl acrylate under strong base catalysis giving N-7 adducts. These addition compounds are shown to be valuable synthetic intermediates.

It previously has been reported that 4-chloropyrrolo[2,3-*d*]pyrimidine and its 2-methyl relative were readily alkylated on the pyrrole nitrogen (N-7) using alkyl halides under alkaline conditions at room temperatures.[1]

The present investigation deals with the addition of these chloropyrrolopyrimidines, presumably as their anions, to acrylonitrile and to ethyl acrylate. These additions proceeded in excellent yields in refluxing ethanol with a catalytic amount of sodium ethoxide using excesses of the acrylic reagents (Table I). Paper chromatographic studies revealed that, with three moles of either ethyl acrylate or acrylonitrile to each mole of the pyrimidine, the additions were essentially complete after two hours. However, with four or five reactant molar ratios, much troublesome polymeric material resulted. With one or two reactant molar ratios of the acrylic reagents, unchanged materials were detected chromatographically even after four hours at reflux temperatures.[2]

Paper chromatographic studies failed to detect any di- or tri- addition products even after twenty-four hours at reflux. Further paper chromatographic studies revealed that strong base and moderately elevated temperatures were absolute requirements for these addition reactions to proceed within a reasonable length of time (twenty-four hours). The additions did not proceed in glacial acetic acid as shown by chromatography and by quantitative recovery of unchanged pyrrolopyrimidine.

Reaction of these adducts in alkaline media showed them to be reasonably stable. No retrogression was evident when they were heated in aqueous potassium hydroxide solutions (see experimental data and Reaction Scheme II) or when refluxed with an equimolar amount of sodium ethoxide for several hours. The chloro ester compounds under the former conditions yielded the chlorocarboxylic acids, however, as expected. The chloronitrile derivatives did not react under these

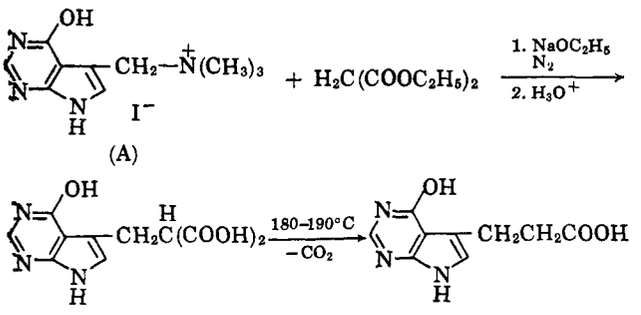
(1) R. A. West and L. Beauchamp, *J. Org. Chem.*, **26**, 3809 (1961).

(2) The solvent system employed in these chromatographic studies was a mixture of 5 ml. of isopropyl alcohol and 95 ml. of a 5% aqueous ammonium sulfate solution using 1.5-in.-wide Whatman no. 1 paper strips using the ascending technique. The spots were detected on the dried papers, in a darkroom, using a Fisher Mineralite ultraviolet lamp (2537 Å.).

conditions; there was no evidence of nitrile hydrolysis, chlorine displacement, or retrogression. Retrogression does occur, however, if 2 *M* sodium ethoxide is used at reflux temperatures for short periods; however, even after five to six hours at reflux, retrogression is not complete.

Although simple alkylations of 4-chloropyrrolo[2,3-*d*]-pyrimidines yielded N-7 derivatives, it could not be assumed that such would be the case with these addition reactions. The heat requirement for the addition reactions as well as the excessive molar proportions of the acrylic reagents required as optimum reaction conditions evoked speculation that the modes of attack differed. The reaction mechanisms differ somewhat. The simple alkylations are SN2 reactions, whereas these additions are, presumably, the addition of the pyrrolopyrimidine anion to the electron-deficient β-carbon of the α,β-unsaturated acceptor moleculer. By resonance considerations, the pyrrolopyrimidine anion hybrid should receive contributions from a β-carbanion structure through which C-5 addition might occur.[3] To prove that such C-5 addition did not occur, a C-5 derivative was prepared by the Reaction Scheme I. The

REACTION SCHEME I

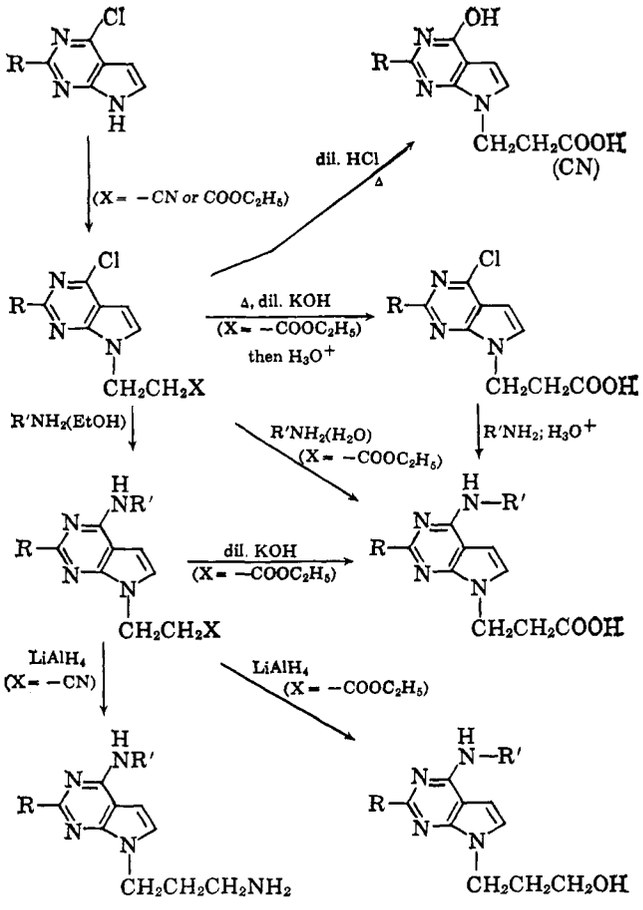


structure of the Mannich base methiodide (A) has been established previously.[4]

The 4-hydroxy-5-(β-carboxyethyl)pyrrolo[2,3-*d*]pyrimidine (B) arising from this reaction sequence proved to be isomeric (analyses) with that product obtained by the aqueous acid hydrolysis of the 4-chloropyrrolopyrimidine–ethyl acrylate adduct (see Reaction Scheme II and Experimental). The isomers proved to be distinctly different by ultraviolet absorption spectra, paper chromatography, and by melting point properties as described later. The adducts, therefore, were assigned the structures as indicated in Table I and in Reaction Scheme II.

These addition compounds proved to be valuable synthetic intermediates. Being bifunctional, by virtue of a displaceable chlorine and an aliphatic-type of nitrile or ester group, they give rise to a variety of interesting derivatives which would be difficultly accessible by other routes. Reaction Scheme II indicates the facile transformations which may be effected thereby. Benzylamine was chosen as a model amine (being of intermediate nucleophilicity) in these chlorine displacement reactions. These reactions proceed readily in water using a sllght excess of the amine with potassium carbonate as the proton acceptor. With the chloronitrile adducts only the halogen was displaced, the nitrile group being unaffected. However, the chloro esters yielded the 4-benzylamino-7-carboxylic acid derivatives. These latter derivatives also are obtained by similar treatment of the corresponding 4-chloro-7-carboxylic acid compounds with benzylamine in water. The 4-benzylamine-7-carboxylic esters could be obtained, however, by the reaction of the chloro ester adduct in ethanol with three molar equivalents of the amine at elevated temperatures in sealed containers. These esters are readily saponified to the corresponding carboxylic acids without affecting the benzylamino moiety as described in the Experimental. Despite the elevated temperatures and excess of amine employed, there was no evidence of amide formation in these reactions.

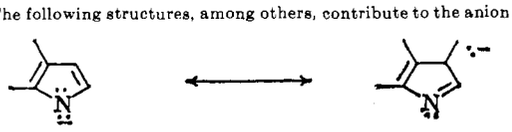
REACTION SCHEME II
(R = H or CH_3 throughout, R′ = benzyl throughout)



Excesses of lithium aluminum hydride were used to reduce the 4-benzylamino esters and nitriles to their 7-γ-hydroxypropyl and 7-γ-aminopropyl derivatives, respectively. There was no evidence of ring reduction or reductive debenzylation in these reactions. These derivatives were best isolated and purified as their anhydrous monohydrochlorides as noted in Table II.

All of these 4-benzylamino compounds have quite characteristic ultraviolet absorption spectra. The peaks of maximum absorption are between 274–282 mμ with molar absorptivity coefficients on the order of

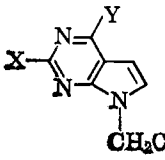
(3) The following structures, among others, contribute to the anion hybrid.



(4) R. A. West, *J. Org. Chem.*, **26**, 4959 (1961).

TABLE I

ADDITION COMPOUNDS AND DERIVATIVES



X	Y	Z	M.p.,[a] °C.	Yield, %	Formula	—Carbon, %— Calcd.	Found	—Hydrogen, %— Calcd.	Found	—Nitrogen, %— Calcd.	Found
H	Cl	CN	110–111[c]	90	$C_9H_7N_4Cl$	52.1	52.0	3.4	3.5	27.1	26.9
H	Cl	$COOC_2H_5$	[b]	92	$C_{11}H_{12}N_3O_2Cl$	52.3	52.1	4.7	4.7	..	..
CH_3	Cl	CN	99–100[c]	84	$C_{10}H_9N_4Cl$	54.4	54.3	4.1	3.8	25.3	25.1
CH_3	Cl	$COOC_2H_5$	27[c]	84	$C_{12}H_{14}N_3O_2Cl$	53.8	54.0	5.3	5.2	15.7	15.7
H	Cl	COOH	169–171	92	$C_9H_8N_3O_2Cl$	47.8	47.9	3.6	3.7	18.6	18.2
CH_3	Cl	COOH	155–157	98	$C_{10}H_{10}N_3O_2Cl$	50.1	50.3	4.2	4.4	17.5	17.8
H	OH	COOH	250–253	86	$C_9H_9N_3O_3$	52.2	52.3	4.4	4.5	20.2	19.9
CH_3	OH	COOH	265–267	72	$C_{10}H_{11}N_3O_3$	54.3	53.9	5.0	5.0	19.0	18.8
H	$C_6H_5CH_2N$(H)—	COOH	189–190	81	$C_{16}H_{16}N_4O_2$	64.9	64.6	5.4	5.4	18.9	19.1
CH_3	$C_6H_5CH_2N$(H)—	COOH	233–234	83	$C_{17}H_{18}N_4O_2$	65.7	65.4	5.8	5.6	18.1	17.9
H	$C_6H_5CH_2N$(H)—	CN	110–111[c]	82	$C_{16}H_{15}N_5$	69.3	69.3	5.5	5.6	25.2	24.8
CH_3	$C_6H_5CH_2N$(H)—	CN	114[c]	82	$C_{17}H_{17}N_5$	70.2	70.0	5.8	5.8	24.0	23.7
H	$C_6H_5CH_2N$(H)—	$—CH_2NH_2$	149–150	76	$C_{16}H_{19}N_5$	68.3	68.2	6.8	7.0	24.9	24.8
CH_3	$C_6H_5CH_2N$(H)—	$—CH_2NH_2$	193–194[d]	80[d]	$C_{17}H_{21}H_5 \cdot HCl$	61.5	61.5	6.7	6.8	21.1	21.0
H	$C_6H_5CH_2N$(H)—	$—CH_2OH$	180–181[d]	73[d]	$C_{16}H_{18}N_4O \cdot HCl$	60.2	60.3	5.9	5.7	17.6	17.5
CH_3	$C_6H_5CH_2N$(H)—	$—CH_2OH$	163–164[d]	84[d]	$C_{17}H_{24}N_4O \cdot HCl$	61.2	60.9	6.3	6.7	16.8	16.8

[a] Uncorrected. Köfler hot plate. From aqueous ethanol unless noted otherwise. [b] Oil at room temperatures. [c] From ether–pentane. [d] Isolated and purified as these salts.

1.5×10^4 and 1.8×10^4 in acid and base buffers, respectively (pH 1.0 and 13.0).

Experimental[5]

4-Hydroxy-5-(β,β-dicarboxyethyl)pyrrolo[2,3-*d*]pyrimidine.—To 70 ml. of absolute ethanol containing 0.042 mole of sodium ethoxide were added 0.036 mole (11.5 g.) of 4-hydroxy-5-dimethylaminomethylpyrrolo[2,3-*d*]pyrimidine methiodide and 0.039 mole (6.2 g.) of diethyl malonate. The reaction mixture was refluxed under a stream of nitrogen until amine was no longer liberated (16 hr.). The solvent was removed *in vacuo*, and the residue was taken up in 75 ml. of water containing 3.5 g. of potassium hydroxide and heated on low steam for 1 hr. After chilling and acidifying to pH 2.0 a flocculent precipitate formed. It was refrigerated overnight, filtered, and dried *in vacuo* giving 6.0 g. (67% yield) of the expected dicarboxylic acid which required no further purification. It decomposed slowly above 220° and became a black tar between 290–300°.

Anal. Calcd. for $C_{10}H_9N_3O_6$: C, 47.8; H, 3.6; N, 16.7. Found: C, 47.7; H, 3.7; N, 16.7.

4-Hydroxy-5-(β-carboxyethyl)pyrrolo[2,3-*d*]pyrimidine (Compound B, Reaction Scheme I).—The dicarboxylic acid was best decarboxylated in a dry state as described later. Earlier attempts at aqueous alkali decarboxylations were only partially successful.

Two grams of this preparation was heated in an open flask at 185–190° for 2 hr. Most of the carbon dioxide was evolved during the first hour of heating. The remaining residue was recrystallized from water using a small amount of Darco yielding 1.5 g. (91%) of the desired product. It turned tan at 270°, black at 285°, and decomposed further to a dark oil at 310°.

Anal. Calcd. for $C_9H_9N_3O_3$: C, 52.1; H, 4.4; N, 20.1. Found: C, 52.4; H, 4.7; N, 20.1.

(5) All melting points were taken on a Köfler hot plate and are uncorrected.

Compound B was compared chromatographically and spectrophotometrically with its isomer, compound C, which is described in Table II and later in these experimental details. The data (Table II) serve to differentiate between the two isomers. The isomers were chromatographed in duplicate in two different solvent systems. They were applied along opposite sides of the same paper strip in each case and detected as previously described. The solvent systems employed were *n*-butyl alcohol saturated with 0.1 *N* acetic acid at room temperature (solvent A) and the same alcohol saturated with 0.1 *N* hydrochloric acid at room temperature (solvent B).

TABLE II

	R_f solvents A	B	Ultraviolet spectral data: pH 1.0 λ_{max} (mμ)	pH 1.0 ε (10^3)	pH 13.0 λ_{max} (mμ)	pH 13.0 ε (10^3)
Isomer C	0.33	0.43	263	8.7	267	7.3
Isomer B	.21	.56	270	7.9	272	8.9

Preparation of the Adducts (Table I).—A small piece of sodium metal (25–35 mg.) was allowed to react with 100 ml. of absolute ethanol. To this were added 0.03 mole of the appropriate 4-chloropyrrolopyrimidine and 0.09 mole of either ethyl acrylate or acrylonitrile. After 3 hr. at reflux under anhydrous conditions, the solvent was driven off and the thick oils remaining were extracted with 200 ml. of ether leaving a small amount of tarry residue. The ether solution was dried over anhydrous sodium sulfate overnight, filtered, and two volumes of pentane were added. After chilling overnight, the pure adducts were filtered off and air dried.

4-Chloro-7-(β-carboxyethyl)pyrrolo[2,3-*d*]pyrimidines.—One gram of the appropriate chloro ester addition compound in 25 ml. of a 70% aqueous ethanol solution containing 1.5 g. of potassium hydroxide was warmed for 0.5 hr. on low steam. After the addition of two volumes of cold water and acidifying to pH 2.0, the carboxylic acids were obtained quantitatively almost in a pure

4-Hydroxy-7-(β-carboxyethyl)pyrrolo[2,3-*d*]pyrimidines.—One and one-half grams of the appropriate 4-chloropyrrolopyrimidine ethyl acrylate adduct was refluxed for 3 hr. in 60 ml. of 3.0 *N* hydrochloric acid. The solution was taken to dryness with water pump vacuum in a 60° water bath. The residues were triturated with 5 ml. of water, filtered, and recrystallized from ethanol yielding 0.7–0.8 g. of the desired products. The 4-hydroxy-7-carboxylic compound (referred to as compound C) was compared to its isomer, compound B, for structural proof.

4-Benzylamino-7-(β-cyanoethyl)pyrrolo[2,3-*d*]pyrimidines.—To 0.0113 mole of the appropriate 4-chloro-7-cyanoethyl derivative in 75 ml. of water containing 0.0115 mole (1.6 g.) of anhydrous potassium carbonate was added 0.0123 mole of benzylamine. After heating at slow reflux for 3 hr., the suspension was chilled and the solid was taken up in 200 ml. of ether and dried overnight over anhydrous sodium sulfate. Addition of an equal volume of pentane to the filtered ethereal solutions yielded the pure desired compounds.

4-Benzylamino-7-(β-carbethoxyethyl)pyrrolo[2,3-*d*]pyrimidines.—To 0.0113 mole of the appropriate chloro ester adduct in 100 ml. of absolute ethanol was added 0.034 mole of benzylamine and then heated at 130° for 3 hr. in sealed containers. The solvent was driven off and the thick oils were taken up in ether and dried over anhydrous sodium sulfate. (Paper chromatography on these solutions revealed only one component present.) Addition of pentane to the filtered ethereal solutions gave gums which resisted all attempts to crystallize. They were used as such in the reductions described later. They also were hydrolyzed to the carboxylic acids by the method described earlier for the alkaline hydrolysis of the 4-chloro adducts except that the pH was adjusted carefully to 3.5 for maximum recovery. These 4-benzylamino-7-carboxylic acids also may be prepared as described subsequently.

4-Benzylamino-7-(β-carboxyethyl)pyrrolo[2,3-*d*]pyrimidines.—These may be prepared likewise by the reaction of the 4-chloropyrrolopyrimidine–ethyl acrylate adducts using water as solvent and potassium carbonate with benzylamine as described before for the 4-benzylamino-7-(β-cyanoethyl)-compounds. They may be prepared also by similarly treating the 4-chloro-7-carboxylic acids with aqueous benzylamine and potassium carbonate. These compounds precipitate maximally at pH 3.5–3.8.

4-Benzylamino-7-(γ-hydroxypropyl and γ-aminopropyl)pyrrolo-[2,3-*d*]pyrimidines.—To rapidly stirred suspensions of 0.01 mole (0.38 g.) of lithium aluminum hydride in 300 ml. of anhydrous ether was added, dropwise over 20 min., 0.009 mole of the appropriate 4-benzylamino-7-β-carbethoxy or -β-cyanoethyl compound in 70 ml. of anhydrous ether. After stirring at room temperature for 0.5 hr. longer, 1.0 ml. of water was added dropwise to the vigorously stirred mixtures, followed by 2 ml. of a 25% aqueous sodium hydroxide solution, and finally 2 ml. more of water. After 30 min. of vigorous stirring, the inorganic materials were filtered off and extracted twice with 100 ml. of anhydrous sodium sulfate. The products were best obtained pure as monohydrochlorides by the addition of a slight excess (5–10%) of an ethanolic solution of hydrogen chloride to the previously filtered ethereal solutions and allowing them to stand overnight at room temperature.

Acknowledgment.—The author thanks Miss Lilia Beauchamp for her technical assistance and Dr. S. Blackman and Mrs. R. Purdey for their microanalytical contributions.

Synthesis and Reactions of Some 1,2,4-Pyrimido[4,5-*e*]thiadiazine 1,1-Dioxides[1]

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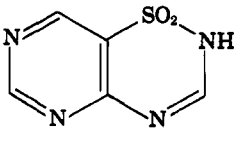
Synthesis of 5,7-dimethyl-1,2,4-pyrimido[4,5-*e*]thiadiazine-6,8-dione 1,1-dioxide and 8-amino-6-methylthio-1,2,4-pyrimido[4,5-*e*]thiadiazine 1,1-dioxide was effected by the cyclization of the corresponding 4-amino-5-pyrimidinesulfonamides with ethyl orthoformate. N-Alkylation of 5,7-dimethyl-1,2,4-pyrimido[4,5-*e*]thiadiazine-6,8-dione 1,1-dioxide was observed giving evidence that the double bond is localized in the 3,4-position. Various reactions of the 1,2,4-pyrimido[4,5-*e*]thiadiazine 1,1-dioxides are reported together with the preparation and reactions of some 5-pyrimidinesulfonic acids and their derivatives.

As a part of the intensive current effort to find more effective anticancer agents, considerable attention has been given to the fields of pyrimidine and purine chemistry in a search for potential antimetabolites of the naturally occurring pyrimidines and purines involved in biosyntheses. A large number of pyrimidine and purine derivatives containing sulfur have been reported and also tested for anticancer properties. 6-Mercaptopurine is one of the more effective of this group.[3] It is felt that pyrimidine and purine derivatives containing sulfur in some of its higher oxidation states have been neglected. The first synthesis of a purinesulfonamide was described recently by Beaman and Robins.[4] Kromov-Borisov and Karlinskaya[5] have shown that derivatives of pyrimidine-5-sulfonic acids display antileukemic activity. This prompted us to prepare various purine and pyrimidine derivatives containing sulfonic acid and sulfonamide groups so that their anticancer properties could be evaluated.

Two examples of a 1,2,4-thiadiazine 1,1-dioxide ring system fused to a heterocyclic system have been reported. Blicke and Lee[6] reported the fusion of this system to an imidazole ring while Yale, Losee, and Bernstein[7] have fused it to a pyridine ring. If the 1,2,4-thiadiazine 1,1-dioxide ring system also could be fused to a pyrimidine ring, two general types of derivatives could be formed (**1** and **2**).[8]



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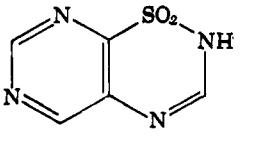

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(1) This investigation was supported by the National Cancer Institute, National Institutes of Health, contract no. CY-5252.

(2) Undergraduate Research Participant supported by a grant, NSF G-12070, from the National Science Foundation.

(3) H. E. Skipper, J. A. Montgomery, J. R. Thomson, and F. M. Schabel Jr., *Cancer Res.*, **19**, No. 4, 425 (1959).

(4) A. G. Beaman and R. K. Robins, *J. Am. Chem. Soc.*, **83**, 4038 (1961).

(5) N. V. Khromov-Borisov and R. L. Karlinskaya, *Zh. Obschch. Khim.*, **24**, 2212 (1954); *Chem. Abstr.*, **50**, 355 (1956).

(6) F. F. Blicke and C.-M. Lee, *J. Org. Chem.*, **26**, 1861 (1961).

(7) H. L. Yale, K. Losee, and J. Bernstein, *J. Am. Chem. Soc.*, **82**, 2044 (1960).

(8) It has been shown by F. C. Novello, *et al.*, (ref. 15), Ekbom [*Bih. Svensk Velenskakad Handl.*, **27**, II, 3 (1902)], and H. L. Yale and J. T. Sheehan (ref. 14) that the 1,2,4-thiadiazine 1,1-dioxide system exists as a tautomeric equilibrium in which the hydrogen resides on either the 2- or 4-position. This would indicate that I and II also might exist as a tautomeric equilibrium; however, for simplicity only one of the tautomers is shown in each case.