6-Amino-2-hydrazinopurine (X).—A solution of 2-chloroadenine[17] (440 mg.) in 15 ml. of anhydrous hydrazine was heated at 80° for 12 hours. The excess hydrazine was removed under reduced pressure and the resultant gray solid triturated with warm water, removed by filtration, and dried *in vacuo* over P_2O_5; yield 200 mg. (47%), m.p. >300°; γ_{max} 3300 cm.$^{-1}$ (secondary NH), 3100 cm.$^{-1}$ (NH_2), 2980 cm.$^{-1}$ (CH), 2800–2500 cm.$^{-1}$ (acidic NH), 1655 cm.$^{-1}$ (NH), 1600 and 1545 cm.$^{-1}$ (C=C, C=N), 1450 cm.$^{-1}$ (CH), 1331 cm.$^{-1}$ (C–N), 934 cm.$^{-1}$ (CH).

A small sample was recrystallized from water for analysis.

Anal. Calcd. for $C_5H_7N_7$: C, 36.40; H, 4.25; N, 59.5. Found: C, 36.2; H, 4.55; N, 60.34.

2-Chloro-6-hydrazinopurine (VII).—2,6-Dichloropurine (2.5 g.) was added to 15 ml. of anhydrous hydrazine with stirring and intermittent cooling. After standing overnight at room temperature the mixture was evaporated under reduced pressure and the solid residue boiled with 25 ml. of distilled water. The suspension was then cooled and the solid removed by filtration and dried *in vacuo* over P_2O_5; yield 1.98 g. (81%), m.p. >300°; γ_{max} 3340 cm.$^{-1}$ (secondary NH), 3250, 3100 cm.$^{-1}$ (NH), 2800–2400 cm.$^{-1}$ (acidic NH), 1665 and 1655 (sh) cm.$^{-1}$ (NH), 1605 cm.$^{-1}$ (C=C, C=N), 1450 cm.$^{-1}$ (CH), 1305 cm.$^{-1}$ (CN), 925 cm.$^{-1}$ (CH).

The ultraviolet and infrared spectra of a small sample recrystallized from water for analysis were practically unchanged.

Anal. Calcd. for $C_5H_5ClN_6$: C, 32.50; H, 2.75; Cl, 19.25. Found: C, 32.6; H, 2.87; Cl, 19.4.

2-Chloro-6-hydroxypurine (XIII).—A solution of 2,6-dichloropurine (500 mg.) in 25 ml. of 1 *N* sodium hydroxide was refluxed for one hour, cooled, neutralized with acetic acid, and allowed to stand in a refrigerator overnight. The light yellow crystals were removed by filtration, washed with ice water, and dried *in vacuo* over P_2O_5; yield of almost pure material, 300 mg. (66%), m.p. >300°.

A small sample was recrystallized from water for analysis; λ_{max}^{pH1} 250 mμ ($a_M \times 10^{-3}$ 11.2), λ_{max}^{pH7} 259 mμ ($a_M \times 10^{-3}$ 10.1), λ_{max}^{pH13} 265 mμ ($a_M \times 10^{-3}$ 11.6); γ_{max} 3020 cm.$^{-1}$ (NH), 2900 cm.$^{-1}$ (CH), 2800–2300 cm.$^{-1}$ (acidic H), 1680 cm.$^{-1}$ (C=O), 1562, 1530 (sh) cm.$^{-1}$ (C=C, C=N), 950 cm.$^{-1}$ (CH).

Anal. Calcd. for $C_6H_3ClN_4O$: C, 35.20; H, 1.76; N, 32.82. Found: C, 35.4; H, 1.93; N, 32.65.

2-Hydrazino-6-hydroxypurine (XIV) (A).—A solution of 6-hydroxy-2-methylmercaptopurine[18] (720 mg.) in 10 ml. of anhydrous hydrazine was refluxed for 20 hours, cooled, and the excess hydrazine removed at reduced pressure. The gray residue was triturated with water, removed by filtration, and dried *in vacuo* over P_2O_5; yield of almost pure material, 200 mg. (30%). A small sample of this material was recrystallized from water for analysis, m.p. >300°; γ_{max} 3305 cm.$^{-1}$ (secondary NH), 3160 cm.$^{-1}$ (NH), 3000 cm.$^{-1}$ (CH), 2800–2300 cm.$^{-1}$ (acidic NH), 1665 cm.$^{-1}$ (NH and C=O), 1600, 1590 (sh), 1537 (sh) cm.$^{-1}$ (C=C, C=N), 1455 cm.$^{-1}$ (CH), 1308 cm.$^{-1}$ (CN), 942 cm.$^{-1}$ (CH).

Anal. Calcd. for $C_5H_6N_6O$: C, 36.2; H, 3.62. Found: C, 36.4; H, 4.17.

(B).—A solution of 2-chloro-6-hydroxypurine (3.5 g.) in 25 ml. of anhydrous hydrazine was heated at 80° for 14 hours, cooled, and the product isolated as described in Method A above; yield of almost pure material, 3.1 g. (91%); the ultraviolet and infrared spectra were identical with that of the material obtained by Method A above.

A 100-mg. sample was recrystallized from 200 ml. of water and dried over P_2O_5 *in vacuo* at 110°; yield 65 mg.

Anal. Calcd. for $C_5H_6N_6O$: C, 36.2; H, 3.62; N, 50.60. Found: C, 36.25; H, 4.13; N, 50.05.

2-Amino-6-methylmercaptopurine (XI).—Thioguanine[19] (5 g., 30 m*M*) was dissolved with heating in 253 ml. of 0.115 *N* sodium hydroxide (30 m*M*). This solution was cooled to 30–40° and dimethyl sulfate (3.79 g., 2.8 ml., 30 m*M*) added dropwise with stirring. After stirring the mixture for another hour, the material which had precipitated was removed by filtration and dried. The yield of almost pure material was 3.5 g., m.p. 239–239.5°; λ_{max}^{pH1} 241, 272, 318 mμ ($a_M \times 10^{-3}$ 6.72, 9.6, 12.4), λ_{max}^{pH7} 242, 310 mμ ($a_M \times 10^{-3}$ 12.1, 10.6), λ_{max}^{pH13} 227, 314 mμ ($a_M \times 10^{-3}$ 19.9, 10.3). An additional gram of material, m.p. 239–240°, was obtained by concentration of the mother liquor.

A small sample of the material was recrystallized from water and dried *in vacuo* at 80–100° for about 6 hours, m.p. 239.5–240°; λ_{max}^{pH1} 241, 273, 317 mμ ($a_M \times 10^{-3}$ 7.0, 10, 13), λ_{max}^{pH7} 242, 309 mμ ($a_M \times 10^{-3}$ 12.7, 11.0), λ_{max}^{pH13} 228, 313 mμ ($a_M \times 10^{-3}$ 20.2, 10.6); γ_{max} 3350–3050 cm.$^{-1}$ (NH), 2960 cm.$^{-1}$ (CH_3), 2800–2400 cm.$^{-1}$ (acidic NH), 1635 (sh) cm.$^{-1}$ (NH), 1600 and 1556 cm.$^{-1}$ (C=C, C=N), 1450 cm.$^{-1}$ (CH), 1308 cm.$^{-1}$ (C–N), 911 cm.$^{-1}$ (CH).

Anal. Calcd. for $C_6H_7N_5S$: C, 39.8; H, 3.86. Found: C, 39.8; H, 3.91.

2-Amino-6-hydrazinopurine (X).—A solution of 2-amino-6-methylmercaptopurine (505 mg.) in 10 ml. of anhydrous hydrazine was refluxed for 12 hours. Most of the excess hydrazine was removed under reduced pressure and 10 ml. of *n*-propanol added to the residue. The resultant gray solid was removed by filtration, triturated with boiling water, again collected by filtration and dried *in vacuo* over P_2O_5 at 100° for 3 hours; yield of almost pure material, 310 mg. (67%). A small amount of this material was recrystallized from water for analysis and dried *in vacuo* over P_2O_5 for 3 hours at 100°, m.p. >300°; γ_{max} 3345 cm.$^{-1}$ (secondary NH), 3250 and 3140 cm.$^{-1}$ (NH), 2930 cm.$^{-1}$ (CH), 2800–2500 cm.$^{-1}$ (acidic NH), 1645 (sh) and 1625 (sh) cm.$^{-1}$ (NH and C=C, C=N), 1590 cm.$^{-1}$ (C=C, C=N), 1436 cm.$^{-1}$ (CH), 1332 cm.$^{-1}$ (C–N), 930 cm.$^{-1}$ (CH).

Anal. Calcd. for $C_5H_7N_7$: C, 36.38; H, 4.23; N, 59.5. Found: C, 36.05; H, 4.29; N, 59.2.

(19) Francis Earle Laboratories.

BIRMINGHAM 5, ALABAMA

[CONTRIBUTION FROM THE KETTERING-MEYER LABORATORY,[1] SOUTHERN RESEARCH INSTITUTE]

Synthesis of Potential Anticancer Agents. IV. 4-Nitro- and 4-Amino-5-imidazole Sulfones

BY L. L. BENNETT, JR., AND HARRY T. BAKER

RECEIVED NOVEMBER 19, 1956

A number of 4-nitro- and 4-amino-5-imidazole sulfones have been prepared as potential antagonists of 4-amino-5-imidazolecarboxamide. Attempts to prepare 4-amino-5-imidazolesulfonamide by several methods were unsuccessful. A convenient preparation of 4-acetamidoimidazole is described.

The synthesis of compounds designed to interfere with purine metabolism has been the subject of considerable recent literature.[2] Most of the com-

(1) Affiliated with Sloan-Kettering Institute. This work was supported by grants from the C. F. Kettering Foundation and the Alfred P. Sloan Foundation, Inc. For the preceding paper in this series, see J. A. Montgomery and L. B. Holum, THIS JOURNAL, **79**, 2185 (1957).

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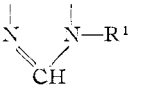
TABLE I

4-NITRO-5-IMIDAZOLE SULFIDES AND 4-AMINO-5-IMIDAZOLE SULFIDES



R	R^2	R^3	Yield, %	M.p., °C.	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found	Nitrogen, % Calcd.	Nitrogen, % Found	Sulfur, % Calcd.	Sulfur, % Found
H	NO_2	CH_3	70	187–189	30.19	30.54	3.17	3.33	26.41	26.00	20.12	20.00
H	NO_2	C_2H_5	60	196–198	34.68	34.99	4.08	4.12	24.27	24.19		
H	NO_2	*n*-C_3H_7	55	159–161	38.50	38.52	4.85	4.62	22.45	23.18		
H	NO_2	*n*-C_4H_9	75	215–216	41.79	42.07	5.51	5.94	20.89	20.95		
H	NO_2	$C_6H_5CH_2$	90	212–213	51.06	51.43	3.86	3.97	17.87	18.42	13.61	13.30
CH_3	NO_2	CH_3	90	119–120	34.68	34.53	4.08	4.13	24.27	25.64	18.44	18.25
CH_3	NO_2	C_2H_5	98	68–70	38.50	38.54	4.85	4.62	22.45	22.94		
CH_3	NO_2	*n*-C_3H_7	80	43–44	41.79	42.56	5.51	5.60	20.89	20.85		
CH_3	NO_2	*n*-C_4H_9	92	45–46	44.64	44.98	6.09	6.09	19.53	19.46		
CH_3	NO_2	C_6H_5	95	77–78	51.06	51.43	3.86	3.87	17.87	17.48	13.61	13.42
CH_3	NO_2	*o*-$NH_2C_6H_4$	95	129–132	48.00	48.05	4.02	3.97	22.39	22.31		
CH_3	NO_2	*o*-$(CH_3CONH)C_6H_4$	65	162–163	49.31	49.39	4.14	4.15	19.17	19.09	10.94	10.90
CH_3	NO_2	$C_6H_5CH_2$	90	113–115	53.01	52.94	4.45	4.47	16.86	16.77		
CH_3	$NH_2 \cdot HCl$	C_6H_5	70	210–211	49.68	49.50	4.97	4.84	17.38	17.11		
CH_3	$NH_2 \cdot HCl$	$C_6H_5CH_2$	60	181–182	51.65	51.04	5.52	5.48	16.43	16.20		

pounds prepared for this purpose have been analogs or derivatives of purines and their ribosides. Although imidazole ribotides have been implicated for some time as intermediates in the biosynthesis of purines,[3–5] there have been no reports of attempts to prepare imidazoles as antagonists of 4-aminoimidazole or 4-amino-5-imidazolecarboxamide which, as their ribotides, occur as intermediates in *de novo* synthesis of purines.[3–5] This paper is concerned with the synthesis of certain 4-amino-5-imidazole sulfones and related compounds as potential antagonists of 4-amino-5-imidazolecarboxamide.

A number of 2-mercaptoimidazoles are known, but only a few 4-mercaptoimidazoles are recorded in the literature.[6] A series of sulfones derived from 2-mercaptoimidazole has been reported recently,[7] but there have been no reports of sulfones derived from 4-mercaptoimidazoles.

In the present work, two series of imidazole sulfides and sulfones were prepared: one derived from 4-nitro-5-mercaptoimidazole and one from 1-methyl-4-nitro-5-mercaptoimidazole. 1-Methyl-4-nitro-5-chloroimidazole[8] and 4-nitro-5-bromoimidazole[9] were converted to the ammonium salts of 1-methyl-4-nitro-5-mercaptoimidazole and 4-nitro-5-mercaptoimidazole, respectively, by reaction with hydrogen sulfide in ammoniacal methanol, a method used by Bhagwat and Pyman[10] for the synthesis of 2-methyl-4-nitro-5-mercaptoimidazole. The nitroimidazole mercaptans were then alkylated in methanolic sodium methoxide, and the resulting sulfides were oxidized to the sulfones with hydrogen peroxide in glacial acetic acid. The nitroimidazole sulfones finally were reduced to 4-amino-5-imidazole sulfones by Raney nickel in absolute ethanol. In the 1-methyl series the sulfides also were prepared easily from the reaction of 1-methyl-4-nitro-5-chloroimidazole with mercaptans in ammoniacal ethanol, but 4-nitro-5-bromoimidazole failed to react with a variety of mercaptans under these conditions. 1-Methyl-4-nitro-5-(*p*-acetamidophenylsulfonyl)-imidazole was prepared by reaction of 1-methyl-4-nitro-5-chloroimidazole with *p*-acetamidobenzenesulfinic acid[11] under the conditions used by Baker, *et al.*,[12] for the preparation of 2,4-dinitro-4′-acetamidodiphenyl sulfone. The sulfides and sulfones prepared are listed in Tables I and II.

In the course of this work, a number of attempts were made to prepare 4-amino-5-imidazolesulfonamides. 1-Methyl-4-nitro-5-imidazolesulfonic acid[13] failed to react with phosphorus pentachloride, phosphorus pentachloride–phosphorus oxychloride mixtures, thionyl chloride, or chlorosulfonic acid under a variety of conditions; this failure was anticipated from the unsuccessful attempts of Pyman and co-workers[14,15] to prepare sulfonyl chlorides from other imidazolesulfonic acids. Chlorosulfonic acid at 190–200° converted 4-bromoimidazole[9] to 4-bromo-5-imidazolesulfonyl chloride which was converted readily to the corresponding sulfonamide. However, the bromine atom in this sulfonamide and in its derivative, 4-bromoimidazole-5-N,N-dibenzylsulfonamide, was inert toward ammonia and amines under a variety of conditions. Considerable inertness to replacement by hydroxyl groups has been observed by Eliel and Nelson[16] in studies with *p*-chlorobenzenesulfonamides.

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TABLE II

4-NITRO-5-IMIDAZOLE SULFONES AND 4-AMINO-5-IMIDAZOLE SULFONES R^2—C=C—SO_2R^3 (N—R^1, CH)

R^1	R^2	R^3	Yield, %	M.p., °C.	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found	Nitrogen, % Calcd.	Nitrogen, % Found	Sulfur, % Calcd.	Sulfur, % Found
H	NO_2	CH_3	80	276–277	25.17	25.24	2.64	2.94	21.99	22.33	16.75	16.85
H	NO_2	C_2H_5	90	246.5–247	29.27	29.51	3.44	3.61	20.49	20.53		
H	NO_2	n-C_3H_7	60	215–217	32.88	32.58	4.14	3.98	19.18	19.25		
H	NO_2	$C_6H_5CH_2$	85	252–256	44.95	45.22	3.40	3.67	15.73	15.96	11.98	11.56
CH_3	NO_2	CH_3	25	160–161	29.27	29.55	3.44	3.68	20.49	20.47		
CH_3	NO_2	C_2H_5	85	158–160	32.88	32.37	4.14	4.17	19.18	18.22		
CH_3	NO_2	n-C_3H_7	90	165–166	36.05	35.83	4.76	4.78	18.02	17.93		
CH_3	NO_2	n-C_4H_9	60	82–84	38.87	38.99	5.30	5.33	17.00	16.15	12.94	12.79
CH_3	NO_2	C_6H_5	80	130–133	44.95	45.08	3.40	3.42	15.73	15.53	11.98	11.48
CH_3	$NO_2 \cdot H_2O$	p-$(CH_3CONH)C_6H_4$	55	125–127	42.11	42.49	4.12	3.91	16.37	16.35		
CH_3	NO_2	$C_6H_5CH_2$	70	161–162.5	46.98	46.78	3.94	3.97	14.94	15.10	11.38	11.84
H	$NH_2 \cdot HCl$	CH_3	65	193–195	24.31	24.03	4.08	3.92	21.26	20.98	16.23	16.12
H	$NH_2 \cdot HCl$	$C_6H_5CH_2$	25	208–210	43.87	43.82	4.42	4.94	15.35	15.79		
CH_3	$NH_2 \cdot HCl \cdot H_2O$	CH_3	80	207–208	26.14	26.37	5.27	4.97	18.29	18.44	13.96	13.90
CH_3	$NH_2 \cdot HCl \cdot H_2O$	n-C_4H_9	70	165–167	35.35	35.12	6.67	6.46	13.46	16.21		
CH_3	NH_2	p-$(CH_3CONH)C_6H_4$	60	220–222	48.96	48.71	4.79	4.81	18.36	18.66		
CH_3	$NH_2 \cdot HCl$	$C_6H_5CH_2$	60	221–222	45.90	45.44	4.90	4.94	14.60	14.75	(Cl) 12.38	(Cl) 12.19

Attempted chlorosulfonation of 4-acetamidoimidazole[17] led only to decomposition products from which no sulfonyl chloride could be isolated. Unsuccessful attempts were also made to convert 1-methyl-4-nitro-5-mercaptoimidazole to the sulfonamide *via* the sulfenamide, a method recently used with success by Greenbaum[18] for the conversion of 6-mercaptouracil to uracil-6-sulfonamide.

4-Acetamidoimidazole, used for the attempted chlorosulfonation mentioned above, was prepared by reduction of 4-nitroimidazole[19] with Raney nickel in a mixture of acetic anhydride and acetic acid, a method considerably more convenient for the preparation of this compound in quantity than the stannous chloride reduction method of Hunter and Nelson.[17] Under the conditions of the Raney nickel reduction, 4-aminoimidazole was isolated as a diacetyl derivative, which on the basis of a comparison of its infrared spectrum with that of an authentic sample of 1-acetylimidazole,[20] was assigned the structure of 1(or 3)-acetyl-4-acetamidoimidazole. Boiling water readily removed the ring acetyl group, giving 4-acetamidoimidazole in 88% yield from the diacetyl compound.

Acknowledgments.—The authors are indebted to Dr. B. R. Baker, Dr. J. A. Montgomery and Miss K. Hewson for helpful discussions; to Mr. J. P. Holmquist for elemental analyses; and to Dr. W. C. Coburn and Mr. J. W. Murphy for infrared spectra determinations.

Experimental

All melting points are uncorrected. The infrared spectra were run in pressed potassium bromide pellets with a Perkin-Elmer model 21 spectrophotometer.

4-Nitro-5-mercaptoimidazole.—This compound was prepared by the same method used by Bhagwat and Pyman[10] for 2-methyl-4-nitro-5-mercaptoimidazole.

4-Nitro-5-bromoimidazole[9] (2.0 g.) was dissolved in 20 ml. of warm 5 *N* ammonium hydroxide and hydrogen sulfide was bubbled through the solution for 15 min. The ammonium salt of the mercaptoimidazole separated as bright orange needles, m.p. >300°, yield 1.9 g. (82%). The crude product was crystallized from methanol.

Anal. Calcd. for $C_3H_6N_4O_2S$: C, 22.20; H, 3.73; N, 34.52; S, 19.75. Found: C, 22.11; H, 3.54; N, 34.37; S, 19.58.

The ammonium salt of 1-methyl-4-nitro-5-mercaptoimidazole, m.p. 197–198°, was prepared similarly in 58% yield and purified by crystallization from methanol by the addition of ether.

Anal. Calcd. for $C_4H_8N_4O_2S$: C, 27.27; H, 4.58; N, 31.78; S, 18.19. Found: C, 27.70; H, 4.46; N, 31.79; S, 18.14.

4-Nitro-5-imidazole Sulfides.—The imidazole sulfides were prepared either by alkylation of the mercaptoimidazole or by reaction between the 4-nitro-5-haloimidazole and mercaptans.

Alkylation of Mercaptoimidazoles.—The ammonium salt (2.0 g.) of the 4-nitro-5-mercaptoimidazole was dissolved in 50 ml. of methanol containing about 1 g. of sodium methoxide. The alkyl halide (5–10% excess) was added and the mixture was refluxed for two hours. After the solvent had been removed by evaporation in a stream of nitrogen, the residue was crystallized from water or aqueous ethanol.

Reaction of 4-Nitro-5-haloimidazoles with Mercaptans.—This reaction, which was used only in the 1-methyl series, was carried out under the conditions reported by Overberger, *et al.*,[21] for the synthesis of *p*-nitrobenzyl sulfide.

To a solution of 1-methyl-4-nitro-5-chloroimidazole[8] (10.0 g.) in 200 ml. of warm ethanol there was added an equimolar amount of the mercaptan, and ammonia was bubbled through the solution for two hours. The reaction mixture was allowed to stand overnight after which the solution was evaporated to dryness and the residue was crystallized from aqueous ethanol.

4-Nitro-5-imidazole Sulfones.—The imidazole sulfide was dissolved in a small volume (about 10 ml./g. sulfide) of glacial acetic acid at 60°, and oxidized by the dropwise addition of 30% hydrogen peroxide[21] (10 ml./g. sulfide). After the yellow color of the original solution had disappeared, the solution was warmed at 80° for 30 min. The sulfone usually crystallized at this point or upon standing overnight; in some cases it was necessary to concentrate the solution or to add water or ethanol to cause precipitation. The sulfones were purified by crystallization from water or ethanol.

1-Methyl-4-nitro-5-(*p*-acetamidophenylsulfonyl)-imidazole.—A solution of 1-methyl-4-nitro-5-chloroimidazole (5.0 g.) and 6.2 g. of *p*-acetamidobenzenesulfinic acid in 25 ml. of ethanol and 5 ml. of 6 *N* NaOH was refluxed for 30 min. After the mixture had been cooled to room temperature, 200 ml. of water was added. The precipitated yellow solid was washed with water and alcohol and dried; wt. 5.4 g., m.p. 120–125°. Recrystallization of the sulfone

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from alcohol with charcoal treatment gave white needles, m.p. 125–127°, which analyzed as a monohydrate (Table II).

4-Amino-5-imidazole Sulfones.—The 4-nitroimidazole sulfone was suspended in dry ethanol (100 ml./g. sulfone) containing Raney nickel which had been washed repeatedly with dry ethanol. The suspension was reduced in a Parr hydrogenation apparatus at atmospheric pressure until the theoretical amount of hydrogen was taken up (about 15 min. required). While air was excluded by a nitrogen atmosphere, the catalyst was removed, four volumes of anhydrous ether were added, and dry hydrogen chloride was bubbled through the solution for 30 min. After the solvents had been removed by evaporation at 40–60° in a stream of nitrogen, the residue was taken up in 2–3 ml. of dry ethanol, decolorized with charcoal, and the amine hydrochloride was precipitated by addition of a large volume of dry ether. When 1-methyl-4-nitro-5-(*p*-acetamidophenylsulfonyl)-imidazole was reduced, the free base began to precipitate from the reaction mixture, and was obtained in a pure state by removing the catalyst and evaporating the ethanol *in vacuo*.

The 4-amino-5-imidazole sulfides reported (Table I) were prepared similarly by reduction of the nitro compounds.

Infrared Spectra.—All of the reaction products described above were characterized by infrared spectra which were compared with the spectra of known imidazoles. Reduction of 4-nitro-5-imidazole sulfones caused the disappearance of bands in the ranges 1460–1550 and 1360–1380 cm.$^{-1}$; these ranges correspond fairly well to those in which the aromatic nitro group is known to absorb.[22] Concurrent with the disappearance of the nitro group there appeared a strong amino band at 1630–1650 cm.$^{-1}$ and increased NH absorption in the range 3100–3400 cm.$^{-1}$. Oxidation of 4-nitro-5-imidazole sulfides to sulfones caused the appearance of new bands in the ranges 1120–1170 cm.$^{-1}$ and 1300–1330 cm.$^{-1}$, regions in which sulfones are known to absorb.[22] When these compounds were reduced, strong bands were retained in the ranges 1120–1170 and 1300–1330 cm.$^{-1}$. It was difficult, however, to make a definite assignment of the sulfone absorption, since the 4-nitro-5-imidazole sulfides showed some absorption in the same regions, and since there was apparently some interaction between the sulfone and nitro groups.

4-Bromo-5-imidazolesulfonamide.—To 10 ml. of chlorosulfonic acid in a small flask was added 2.0 g. of 4-bromoimidazole.[9] With exclusion of moisture, the mixture was heated slowly to 190–200° and kept at this temperature for 2 hr. The mixture was then poured onto 50 g. of crushed ice, and the colorless sulfonyl chloride, which precipitated, was removed and dried in air; m.p. 186–188° (dec.), wt. 1.7 g. (51%). For preparation of the amide, the crude acid chloride was dissolved in 20 ml. of concd. NH_4OH at room temperature. After 10 min., excess ammonium was removed by gentle warming in a stream of nitrogen and the solution was acidified with HCl. The precipitate weighed 0.76 g. (55%), m.p. 243–244°. After crystallization from water, the m.p. was 246–247°.

Anal. Calcd. for $C_3H_4BrN_3O_2S$: C, 15.92; H, 1.77; N, 18.60; Br, 35.40; S, 14.18. Found: C, 15.99; H, 1.79; N, 18.47; Br, 35.34; S, 14.25.

(22) L. J. Bellamy, "The Infrared Spectra of Complex Molecules," Methuen and Company Ltd., London, 1954.

The anilide and the N,N-dibenzylamide were prepared by the Schotten–Baumann method. *Anal.* Calcd. for anilide: $C_9H_8BrN_3O_2S$: C, 35.79; H, 2.65; N, 13.90; Br, 26.94; S, 10.60. Found: C, 35.37; H, 2.62; N, 13.99; Br, 26.37; S, 10.69. Calcd. for dibenzylamide: $C_{17}H_{16}BrN_3O_2S$: C, 50.20; H, 3.94. Found: C, 50.14; H, 4.12.

Treatment of the amide with nitrous acid[23] gave the sulfonic acid, m.p. 265–267°. *Anal.* Calcd. for $C_3H_3BrN_2O_3S$: C, 15.88; H, 1.32; N, 12.32. Found: C, 15.72; H, 1.40; N, 12.40.

A sample of 4-bromo-5-imidazolesulfonic acid, prepared by sulfonation of 4-bromoimidazole according to Balaban and Pyman,[9] melted at 270–271°; a mixed melting point of this sample with that prepared above was 265–267°. The infrared spectra of the two samples were identical in the fingerprint region.

1(or 3)-Acetyl-4-acetamidoimidazole and 4-Acetamidoimidazole.—4-Nitroimidazole[19] (2.3 g.) was suspended in 50 ml. of acetic anhydride to which was added 20 ml. of glacial acetic acid and 1 teaspoonful of Raney nickel slurry. The mixture was shaken in a Parr hydrogenation apparatus at 31 p.s.i. initial pressure until the theoretical pressure drop occurred (about 2 hr. required). Raney nickel was removed and, while air was excluded by blowing dry nitrogen on the surface, the clear solution was evaporated to dryness on a steam-bath. The black residue was treated with cold water; a gray insoluble residue, which was removed by filtration, weighed 1.2 g. and melted at 225–227°. After crystallization from dioxane with charcoal treatment, the product was obtained colorless and melted at 227.5–228.5°. The infrared spectrum showed a strong band at 1680 cm.$^{-1}$, characteristic of the amide carbonyl group, and an additional band at 1720 cm.$^{-1}$. Since 1-acetylimidazole[20] was found to have a strong band at 1725 cm.$^{-1}$, the compound was assigned the structure of 1(or 3)-acetyl-4-acetamidoimidazole. The infrared spectrum of N-acetylimidazole has also been determined recently by Otting[24] who reported a peak at 1747 cm.$^{-1}$ for the N-acetyl group.

Anal. Calcd. for $C_7H_9N_3O_2$: C, 50.30; H, 5.38; N, 25.12. Found: C, 50.37; H, 5.36; N, 25.06.

When the above compound was treated with a solution of picric acid in aqueous ethanol, a picrate was formed which analyzed as the picrate of 4-acetamidoimidazole, m.p. 202°, reported[17] 208°.

Anal. Calcd. for $C_{11}H_{10}N_6O_8$: C, 37.29; H, 2.82; N, 23.73. Found: C, 37.12; H, 3.08; N, 23.25.

For conversion to 4-acetamidoimidazole, a sample of the diacetyl compound was boiled in water for 30 min., after which the solution was evaporated to dryness *in vacuo* on a steam-bath. The residue was crystallized from dioxane to yield white crystals which were dried *in vacuo* at 140° and 1 mm. pressure; m.p. 220°, reported m.p. 226°[17]; yield 88% from the diacetyl derivative.

Anal. Calcd. for $C_5H_7N_3O$: C, 48.00; H, 5.60; N, 33.59. Found: C, 47.77; H, 5.36; N, 33.28.

(23) F. Muth, in "Methoden der Organischen Chemie," IV Auflage, Vol. IX, edited by E. Müller, Georg Thieme, Stuttgart, 1955, p. 531.

(24) W. Otting, *Chem. Ber.*, **89**, 1940 (1956).

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