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The Synthesis of Imidazo[4,5-*c*]- and *v*-Triazolo[4,5-*c*]pyridazines

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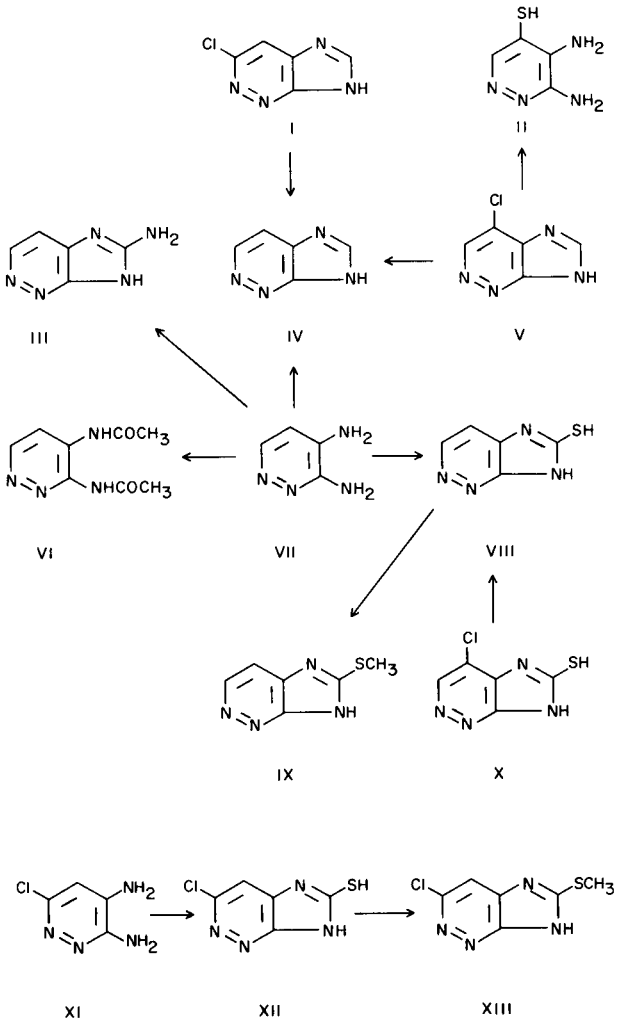
The parent imidazo[4,5-*c*]pyridazine (IV) has been prepared for the first time by three different routes. 1-Methylimidazo[4,5-*c*]pyridazine (XX) and 3-methylimidazo[4,5-*c*]pyridazine (XXVII) have been prepared by unequivocal syntheses. The constitution of the methylation product of imidazo[4,5-*c*]pyridazine-2-thiol (VIII) has been shown to be 2-methylthioimidazo[4,5-*c*]-pyridazine (IX) by the unequivocal syntheses of 1-methylimidazo[4,5-*c*]pyridazine-2-thiol (XXIII) and 3-methylimidazo[4,5-*c*]pyridazine-2-thiol (XXXIII). Likewise, the structure of the methylation product (XIII) was shown to be *S*-methylation by the unequivocal syntheses of 1-methyl-2-methylthio-6-chloroimidazo[4,5-*c*]pyridazine (XXIV) and 3-methyl-2-methylthio-6-chloroimidazo[4,5-*c*]pyridazine (XXXI), respectively. Several 7-substituted amino-*v*-triazolo-[4,5-*c*]pyridazines (XXXVIII) have been prepared from 7-chloro-*v*-triazolo[4,5-*c*]pyridazine (XXXVII).

The synthesis of members of the imidazo[4,5-*c*]pyridazine ring system was first reported by Kuraishi and Castle (2). In a second paper by these authors (3) two additional imidazo[4,5-*c*]pyridazines were reported. In this communication the preparative chemistry of this relatively unknown ring system has been extended.

The unsubstituted imidazo[4,5-*c*]pyridazine (IV) has been prepared by three routes. When 3,4-diaminopyridazine (VII) (4) was treated with formic acid, IV was obtained in 68% yield. Compound IV was also obtained by catalytic dechlorination of both 7-chloroimidazo[4,5-*c*]-pyridazine (V) (2) (36% yield) and 6-chloroimidazo-[4,5-*c*]pyridazine (I) (3) (68% yield) with palladium on charcoal in ethanolic alkali. Attempts to prepare imidazo-[4,5-*c*]pyridazine-7-thiol from 7-chloroimidazo[4,5-*c*]-pyridazine (V) by the novel phosphorus pentasulfide-pyridine thiation procedure (2,5,6,7,8,9) did not give the bicyclic thiol, rather the halogen atom was replaced by a mercapto group and the imidazole ring was opened to give 3,4-diaminopyridazine-5-thiol (II). 3,4-Diamino-pyridazine (VII) was readily converted into 3,4-bis-acetylaminopyridazine (VI) with acetic anhydride. Compound VII was treated with cyanogen bromide following the general procedure of Leonard, Curtin and Beck (10). The product was 2-aminoimidazo[4,5-*c*]pyridazine hydrochloride (III) in 69% yield. With carbon disulfide in alkali, 3,4-diaminopyridazine (VII) was converted into imidazo[4,5-*c*]pyridazine-2-thiol (VIII) in 53% yield. Compound VIII was also obtained from 7-chloroimidazo-[4,5-*c*]pyridazine-2-thiol (X) (2) by catalytic dechlorination with palladium on charcoal in ethanolic alkali in 65% yield. Imidazo[4,5-*c*]pyridazine-2-thiol (VIII) was treated



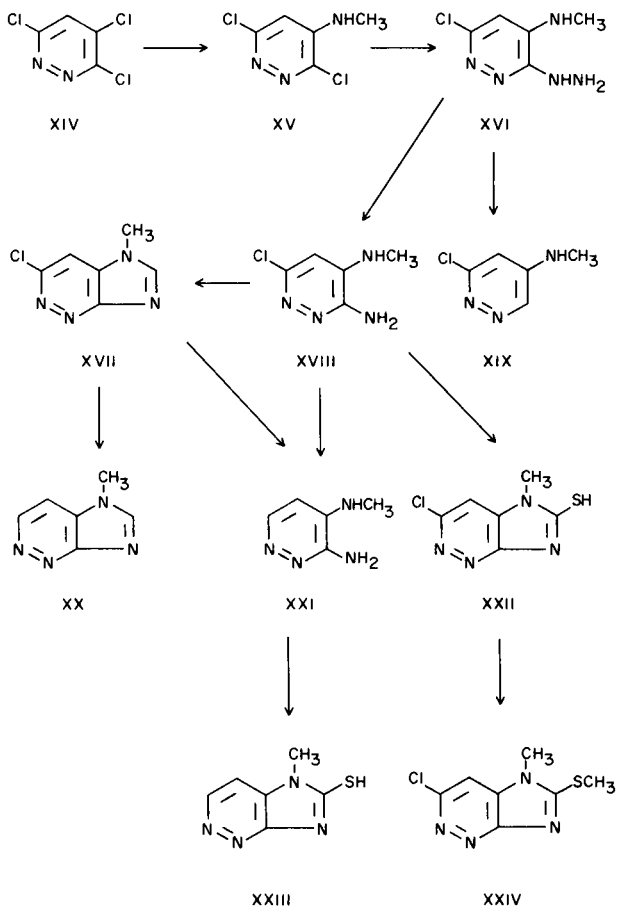
with methyl iodide in alkaline solution. The product was obtained in 41% yield and assigned the structure based upon *S*-methylation, namely 2-methylthioimidazo[4,5-*c*]-pyridazine (IX). Likewise, 3,4-diamino-6-chloropyridazine (XI) (11) was allowed to react with carbon disulfide in alkali. 6-Chloroimidazo[4,5-*c*]pyridazine-2-thiol (XII) was obtained in 30% yield. When compound XII was treated with methyl iodide in alkaline solution, a product was obtained in 40% yield which was assigned the structure XIII based upon the expected *S*-methylation.

Since in the case of methylation of VIII as well as XII, neither N^1- or N^3-methylation is precluded, the unequivocal syntheses of 1-methylimidazo[4,5-*c*]pyridazine-2-thiol (XXIII) and 3-methylimidazo[4,5-*c*]pyridazine-2-thiol (XXXIII) were undertaken to definitely establish IX as the proper methylation product. Likewise, the unequivocal syntheses of 1-methyl-6-chloroimidazo-[4,5-*c*]pyridazine-2-thiol (XXII) and 3-methyl-6-chloroimidazo[4,5-*c*]pyridazine-2-thiol (XXVIII) were undertaken to definitely establish the structure of XIII. The synthetic routes to these and related compounds are described below.

3,4,6-Trichloropyridazine (XIV) (12) was treated with methylamine following the amination procedure of Gerhardt and Castle (11). 3,6-Dichloro-4-methylaminopyridazine (XV) was obtained in 43% yield. With hydrazine, XV gave 6-chloro-4-methylamino-3-hydrazinopyridazine (XVI) in 65% yield. When XVI was allowed to react with aqueous copper sulfate solution, the hydrazino group was smoothly removed to give 3-chloro-5-methylaminopyridazine (XIX) in 69% yield. Raney nickel cleavage of the hydrazino group of XVI gave 4-methylamino-6-chloro-3-aminopyridazine (XVIII) in 67% yield. Compound XVIII was treated with ethyl orthoformate and 1-methyl-6-chloroimidazo[4,5-*c*]pyridazine (XVII) was obtained in 82% yield. Compound XVII was catalytically dechlorinated in the presence of palladium on charcoal in ethanolic alkali. The product, 1-methylimidazo[4,5-*c*]-pyridazine (XX) was obtained in 60% yield.

4-Methylamino-3-aminopyridazine (XXI) was obtained by two routes. 4-Methylamino-6-chloro-3-aminopyridazine (XVIII) was catalytically dechlorinated in the presence of palladium on charcoal in ethanolic alkali to give 4-methylamino-3-aminopyridazine (XXI) in 42% yield. Compound XXI was also obtained by reductive ring opening of 1-methyl-6-chloroimidazo[4,5-*c*]pyridazine (XVII) in the presence of palladium on charcoal. 1-Methylimidazo-[4,5-*c*]pyridazine-2-thiol (XXIII) was prepared by cyclization of XXI with carbon disulfide in alkali in 38% yield. 4-Methylamino-6-chloro-3-aminopyridazine (XVIII) was treated with carbon disulfide in alkali. The product was 1-methyl-6-chloroimidazo[4,5-*c*]pyridazine-2-thiol (XXII) in 70% yield. The treatment of XXII with methyl iodide in alkaline solution gave 1-methyl-2-methylthio-6-chloroimidazo[4,5-*c*]pyridazine (XXIV) in 43% yield.

4-Amino-3,6-dichloropyridazine (XXVI) (11) was treated with methylhydrazine and the product was 4-amino-6-chloro-3-(1′-methyl)hydrazinopyridazine (XXV) in 40% yield. The structure proof that methylhydrazine had attacked position 3 and not position 6 was established by the cyclization of XXIX into two different imidazo[4,5-*c*]-pyridazines (XXVIII and XXX). Compound XXIX was obtained from XXV. 4-Amino-6-chloro-3-methylaminopyridazine (XXIX) was prepared by two routes. The simplest route was from 4-amino-3,6-dichloropyridazine (XXVI). When XXVI was treated with methylamine, 4-amino-6-chloro-3-methylaminopyridazine (XXIX) was obtained in 55% yield. Compound XXIX was also obtained by Raney nickel cleavage of the methylhydrazino group of XXV in 33% yield. Compound XXIX was cyclized with ethyl orthoformate to give 6-chloro-3-methylimidazo-[4,5-*c*]pyridazine (XXX) in 75% yield. Compound XXX was catalytically dechlorinated with palladium on charcoal in alkaline solution. The product was 3-methylimidazo-[4,5-*c*]pyridazine (XXVII) in 43% yield. 4-Amino-3-methylaminopyridazine (XXXII) has been prepared by two routes. The best of these methods was the catalytic dechlorination with palladium on charcoal in alkaline solution of 4-amino-6-chloro-3-methylaminopyridazine



(XXIX). Compound XXXII was obtained in 72% yield. However, XXXII was obtained in only 42% yield by the dechlorinative ring opening of 3-methyl-6-chloroimidazo-[4,5-*c*]pyridazine (XXX). Hydrogenation with palladium on charcoal in alkaline solution was used to accomplish this dechlorinative ring opening reaction. 4-Amino-3-methylaminopyridazine (XXXII) was treated with carbon disulfide in alkali and the cyclization product, 3-methyl-imidazo[4,5-*c*]pyridazine-2-thiol (XXXIII) was obtained in 50% yield. 4-Amino-6-chloro-3-methylaminopyridazine (XXIX) was allowed to react with carbon disulfide in alkali and the product was 3-methyl-6-chloroimidazo-[4,5-*c*]pyridazine-2-thiol (XXVIII) in 60% yield. When XXVIII was treated with methyl iodide in alkaline solution, 3-methyl-2-methylthio-6-chloroimidazo[4,5-*c*]-pyridazine (XXXI) was the product in 60% yield.

3,4,5-Triaminopyridazine (XXXIV) (4) was treated with carbon disulfide in alkali and only one cyclization product was obtained. Since XXXIV could cyclize to give either an imidazo[4,5-*c*]pyridazine or an imidazo[4,5-*d*]-pyridazine, it was necessary to establish the structure of the product. The product was dethiated by heating with Raney nickel in absolute ethanol and the product was shown to be identical with the known 7-aminoimidazo-[4,5-*c*]pyridazine (XXXV) (2) by comparison of the melting points and the infrared spectrum, therefore, the product XXXV was assigned the structure 7-aminoimidazo-[4,5-*c*]pyridazine-2-thiol.

4-Chloro-*v*-triazolo[4,5-*c*]pyridazine (XXXVII) (11) was treated with methylamine, dimethylamine, morpholine, piperidine and benzylamine, respectively. The products were the substituted amines (XXXVIIIa-e) in yields ranging from 34-65%.

EXPERIMENTAL (13)

3,4-Diaminopyridazine (VII).

This compound was prepared by the method of Guither, Clark and Castle (4).

7-Chloroimidazo[4,5-*c*]pyridazine (V).

This compound was prepared by the method of Kuraishi and Castle (2), m.p. 191° dec.

6-Chloroimidazo[4,5-*c*]pyridazine (I).

This compound was prepared by the method of Kuraishi and Castle (3), m.p. 254-255° dec.

Imidazo[4,5-*c*]pyridazine (IV).

Method 1.

A mixture containing 0.8 g. (0.005 mole) of 7-chloroimidazo-[4,5-*c*]pyridazine (V), 0.3 g. (0.075 mole) of sodium hydroxide and approximately 2 g. of palladium on charcoal in 200 ml. of ethanol was hydrogenated at atmospheric pressure. After removal of the catalyst and evaporation of the solvent under reduced pressure, the residue was extracted with absolute ethanol to yield after recrystallization from absolute ethanol, 0.2 g. (36%) of the product, m.p. 225-226° dec.; U.V. λ max (absolute ethanol); 225 (ε, 12,000); 255 (ε, 2,170); 270 mμ (ε, 2,220), infrared, cm^{-1}; 3075 (w), 2950 (w), 2700 (w), 2525 (w), 1825 (m), 1625 (s), 1550 (s), 1450 (m), 1425 (m), 1390 (s), 1325 (s), 1275 (s), 1140 (w), 1040 (s), 915 (s), 840 (s), 795 (m), 640 (s), 600 (m), 450 (m).

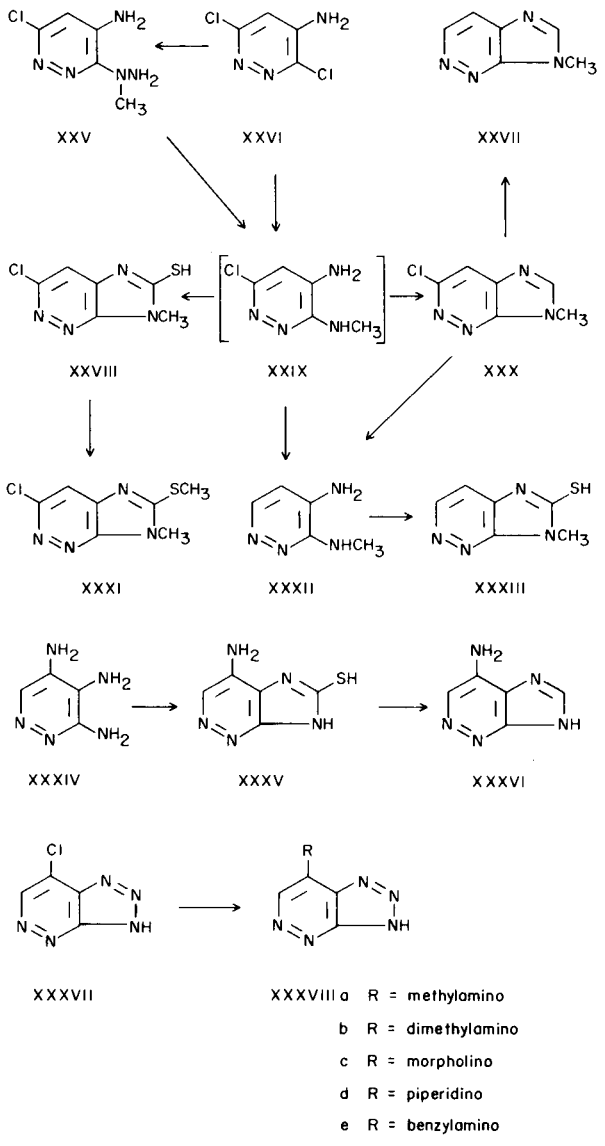
Anal. Calcd. for $C_5H_4N_4$: C, 50.0; H, 3.4; N, 46.6. Found: C, 50.1; H, 3.6; N, 46.4.

Method 2.

3,4-Diaminopyridazine (VII) (0.6 g., 0.005 mole) was suspended in 4.6 g. (0.1 mole) of formic acid and heated under reflux for 3 hours. After removal of the solvent under reduced pressure, the residue was recrystallized from absolute ethanol, yielding 0.4 g. (68%) of product, m.p. 225-226°. The infrared spectrum was identical with that from the sample prepared as described in Method 1.

Method 3.

A mixture containing 0.8 g. (0.005 mole) of 6-chloroimidazo-[4,5-*c*]pyridazine (I) and approximately 2 g. of 5% palladium on



charcoal in 200 ml. of 95% ethanol was hydrogenated at atmospheric pressure and room temperature. After the theoretical amount of hydrogen was absorbed, the solution was filtered and the solvent was evaporated under reduced pressure. The residue was extracted with hot absolute ethanol giving after recrystallization from absolute ethanol, 0.4 g. (68%), m.p. 225-226°. The infrared spectrum was identical with that obtained from the sample prepared as described in Method 1.

3,4-Diaminopyridazine-5-thiol (II).

A solution containing 0.7 g. (0.005 mole) of 7-chloroimidazo[4,5-*c*]pyridazine (V) and 4.4 g. (0.02 mole) of phosphorus pentasulfide in 20 ml. of dry pyridine was protected from moisture and heated under reflux for 8 hours. After removal of the pyridine under reduced pressure, the residue was poured on ice and stirred. The mixture was heated on the steam bath for 2 hours, filtered while still warm and acidified with glacial acetic acid to about *p*H 4 and chilled. The crystals were collected and recrystallized from water giving 0.1 g. (17%), m.p. 300° dec.; U.V. λ max (95% ethanol); 210 (ε, 14,580); 236 (sh) (ε, 10,690); 350 mμ (ε, 4,150); infrared cm^{-1}; 3420 (w), 3340 (w), 3200 (w), 1640 (s), 1540 (s), 1460 (s), 1320 (s), 1280 (s), 1250 (s), 1160 (w), 1040 (m), 910 (s), 840 (m), 810 (w), 760 (m), 660 (w), 610 (m), 560 (m), 520 (m).

Anal. Calcd. for $C_4H_6N_4S$: C, 33.8; H, 4.3; N, 39.4. Found: C, 33.7; H, 3.8; N, 39.5.

2-Aminoimidazo[4,5-*c*]pyridazine Hydrochloride (III).

The method of Leonard, Curtin and Beck (10) was modified to some extent. Cyanogen bromide (0.5 g., 0.005 mole) was added in small portions with shaking to a suspension of 0.6 g. (0.005 mole) of 3,4-diaminopyridazine (VII) in 4 ml. of water. The suspension was filtered after standing overnight at room temperature. Sodium hydroxide (0.2 g., 0.005 mole) in 5 ml. of water was then added and the solution was evaporated on a steam bath. A dark oil separated on cooling. The oil was dissolved in 95% ethanol and yellow prisms separated (0.5 g., 69%), m.p. 173-174°; U.V. λ max (95% ethanol); 207 (ε, 14,500); 221 (sh) (ε, 9,300); 260 (ε, 3,600); 302 mμ (ε, 6,250); infrared cm^{-1}; 3375 (m), 3300 (m), 2350 (w), 1660 (s), 1625 (s), 1570 (s), 1500 (s), 1350 (m), 1290 (w), 1200 (w), 1165 (m), 1120 (w), 1035 (m), 930 (s), 825 (s), 770 (s), 700 (m), 630 (m), 540 (w), 520 (m).

Anal. Calcd. for $C_5H_5N_5 \cdot H_2O \cdot HCl$: C, 31.7; H, 4.3; N, 36.9. Found: C, 32.2; H, 4.5; N, 36.9.

3,4-Diacetylaminopyridazine (VI).

3,4-Diaminopyridazine (VII) (0.6 g., 0.005 mole) was added to 1 ml. of acetic anhydride and the mixture was allowed to stand at room temperature for one hour. After removal of the solvent, the residue was washed with acetone, collected and recrystallized from acetone, yielding 0.4 g. (42%), m.p. 228-229°; U.V. λ max (absolute ethanol); 218 (ε, 17,370); 254 (ε, 9,160); 273 (sh) mμ (ε, 5,050); infrared cm^{-1}; 3440 (w), 3250 (w), 3150 (w), 3075 (w), 2990 (m), 1720 (m), 1690 (m), 1590 (m), 1575 (m), 1540 (m), 1425 (s), 1370 (s), 1320 (s), 1275 (m), 1250 (m), 1210 (w), 1115 (s), 1060 (w), 1030 (w), 1010 (w), 960 (m), 900 (w), 850 (s), 830 (w), 770 (w), 720 (m), 680 (w), 665 (w), 610 (w), 600 (s), 580 (w), 570 (m), 540 (m), 480 (w), 450 (w).

Anal. Calcd. for $C_8H_{10}N_4O_2$: C, 49.5; H, 5.2; N, 28.9. Found: C, 49.7; H, 5.2; N, 29.0.

7-Chloroimidazo[4,5-*c*]pyridazine-2-thiol (X).

This compound was prepared by the method of Kuraishi and Castle (2).

Imidazo[4,5-*c*]pyridazine-2-thiol (VIII).

Method 1.

A mixture containing 1.3 g. (0.005 mole) of 7-chloroimidazo[4,5-*c*]pyridazine-2-thiol (X), 0.3 g. (0.0075 mole) of sodium hydroxide and approximately 2 g. of 5% palladium-charcoal in 200 ml. of ethanol was hydrogenated. After removal of the catalyst and evaporation of the solvent under reduced pressure, the residue was extracted with hot absolute ethanol giving after recrystallization 0.4 g. (65%) of the product, m.p. 360°. The analytical sample was further recrystallized from ethanol; U.V. λ max (95% ethanol); 203 (ε, 5,250); 230 (sh) (ε, 4,460); 244 (ε, 6,790); 326 mμ (ε, 15,970); infrared, cm^{-1}; 3025 (w), 2825 (w), 2775 (w), 1625 (s), 1575 (s), 1500 (m), 1475 (w), 1425 (m), 1380 (w), 1295 (m), 1245 (s), 1195 (s), 1085 (m), 1025 (s), 950 (m), 925 (m), 880 (w), 845 (s), 825 (m), 715 (m), 650 (s), 640 (m), 625 (s), 615 (m), 510 (s), 505 (w), 430 (s).

Anal. Calcd. for $C_5H_4N_4S$: C, 39.5; H, 2.6; N, 36.8. Found: C, 39.3; H, 2.9; N, 36.7.

Method 2.

A mixture of 0.6 g. (0.005 mole) of 3,4-diaminopyridazine, 5.7 g. (0.075 mole) of carbon disulfide, 7.9 g. (0.1 mole) of dry pyridine and 0.4 g. (0.1 mole) of crushed sodium hydroxide was heated for 2.5 hours. After removal of the solvent under reduced pressure, the residue was dissolved in water and acidified with concentrated hydrochloric acid. The precipitated crystals were collected and washed with water giving 0.32 g. (53%) of the product, m.p. 360°. The analytical sample was purified by recrystallization from about 350 ml. of ethanol.

2-Methylthioimidazo[4,5-*c*]pyridazine (IX).

To a solution containing 0.8 g. (0.005 mole) of imidazo[4,5-*c*]pyridazine-2-thiol (VIII) dissolved in 10 ml. of 1*N* potassium hydroxide solution was added 0.8 g. (0.005 mole) of methyl iodide. The mixture was stirred at room temperature for 3 hours. Some crystals of unknown structure separated during the reaction. These were removed and the filtrate was acidified with acetic acid. The solid was collected and recrystallized from water giving 0.4 g. (41%) of the product, m.p. 212-213°; U.V. λ max (absolute ethanol); 211 (ε, 15,770), 233 (sh) (ε, 11,900); 299 (ε, 11,650); 324 (sh) mμ (ε, 9,130); infrared cm^{-1}; 2925 (w), 2550 (w), 1625 (s), 1575 (m), 1550 (m), 1475 (m), 1425 (m), 1400 (s), 1350 (m), 1325 (s), 1260 (m), 1250 (w), 1225 (w), 1195 (s), 1105 (s), 1030 (s), 930 (w), 840 (w), 700 (m), 650 (s), 625 (s), 540 (m), 500 (s), 430 (m), 410 (m).

Anal. Calcd. for $C_6H_6N_4S$: C, 43.4; H, 3.6; N, 33.7. Found: C, 42.9; H, 3.8; N, 33.8.

6-Chloro-3,4-diaminopyridazine (XI).

This compound was prepared by the method of Gerhardt and Castle (11).

6-Chloroimidazo[4,5-*c*]pyridazine-2-thiol (XII).

A mixture of 2.8 g. (0.02 mole) of 6-chloro-3,4-diaminopyridazine (XI), 18 ml. (0.3 mole) of carbon disulfide, 32 ml. (0.04 mole) of dry pyridine and 1.6 g. (0.04 mole) of crushed sodium hydroxide was heated for 2.5 hours. After removal of the solvent under reduced pressure, the residue was dissolved in water and acidified with concentrated hydrochloric acid. The precipitated crystals were collected and washed with water giving 1.1 g. (30%) of the product, m.p. 245-246° dec. The analytical sample was purified by recrystallization from a large amount of 80-85% ethanol; U.V. λ max (95% ethanol); 204 (ε, 18,640), 232 (sh) (ε, 9,160), 250 (ε, 14,020); 336 mμ (ε, 22,630); infrared cm^{-1}; 3450 (m), 3050 (m), 1640 (s), 1590 (s), 1460 (s), 1400 (s), 1340 (s), 1300 (s), 1190 (s), 1140 (s), 1060 (s), 1020 (w), 980 (m),

970 (m), 950 (s), 890 (m), 860 (w), 840 (w), 740 (w), 730 (s), 670 (m), 640 (s), 520 (s), 500 (s).

Anal. Calcd. for $C_5H_3ClN_4S$: C, 32.2; H, 1.6; N, 30.0. Found: C, 32.6; H, 1.7; N, 29.7.

6-Chloro-2-methylthioimidazo[4,5-c]pyridazine (XIII).

To a solution containing 0.1 g. (0.001 mole) of 6-chloroimidazo[4,5-c]pyridazine-2-thiol (XII), dissolved in 10 ml. of 1*N* potassium hydroxide solution was added 0.1 g. (0.001 mole) of methyl iodide. The mixture was stirred at room temperature for 4 hours. The solution was acidified with acetic acid. The solid was collected and recrystallized from absolute ethanol giving 0.08 g. (40%) of product, m.p. 262° dec.; U.V. λ max (absolute ethanol); 205 (ε, 6,200); 226 (ε, 15,600); 302 mμ (ε, 15,150); infrared cm^{-1}; 3080 (s), 2940 (w), 2800 (w), 1640 (m), 1550 (m), 1450 (w), 1390 (s), 1350 (w), 1310 (s), 1255 (m), 1221 (w), 1195 (w), 1154 (m), 1067 (s), 965 (s), 945 (m), 887 (w), 843 (w), 783 (w), 725 (m), 675 (m), 628 (m), 524 (w), 475 (w).

Anal. Calcd. for $C_6H_5ClN_4S$: C, 35.9; H, 2.5; N, 27.9. Found: C, 35.7; H, 2.4; N, 27.7.

4-Methylamino-3,6-dichloropyridazine (XV).

The procedure of Kuraishi (2) was modified and scaled up. A stainless steel reaction vessel was charged with 9.2 g. (0.05 mole) of 3,4,6-trichloropyridazine (XIV) (12) and 50 ml. of about 13% absolute ethanolic methylamine. The reaction mixture was heated at 85-95° in a rocking autoclave for 12 hours. The crude reaction product was recrystallized from water, yield 3.8 g. (43%), m.p. 146-147°; U.V. λ max (absolute ethanol); 208 (ε, 15,400); 222 (sh) (ε, 9,200); 262 (ε, 13,400); 300 mμ (ε, 4,150); infrared cm^{-1}; 3320 (s), 3070 (m), 2920 (w), 1570 (s), 1520 (s), 1440 (s), 1375 (s), 1350 (s), 1300 (s), 1257 (w), 1175 (s), 1135 (s), 1090 (w), 1062 (s), 1049 (s), 935 (s), 838 (s), 725 (m), 640 (m), 620 (m), 590 (m), 520 (m), 503 (m), 455 (m).

Anal. Calcd. for $C_5H_5Cl_2N_3$: C, 33.7; H, 2.8; N, 23.6. Found: C, 33.7; H, 2.8; N, 23.4.

4-Methylamino-6-chloro-3-hydrazinopyridazine (XVI).

A solution containing 1.8 g. (0.01 mole) of 4-methylamino-3,6-dichloropyridazine (XV) dissolved in 8 ml. of 95% hydrazine was heated on the steam bath for 2.5 hours. After cooling and the addition of water, the crystals were collected and recrystallized from water. There was obtained 1.1 g. (65%) of XVI, m.p. 217-218°; U.V. λ max (absolute ethanol); 217 (ε, 15,300); 270 (ε, 8,550); 298 mμ (sh) (ε, 5,550); infrared cm^{-1}; 3320 (m), 3150 (w), 3080 (w), 3020 (w), 2950 (w), 1600 (s), 1470 (m), 1430 (s), 1350 (s), 1265 (m), 1180 (s), 1145 (m), 1105 (s), 1075 (m), 993 (m), 940 (s), 830 (s), 759 (w), 640 (m), 520 (m), 460 (m).

Anal. Calcd. for $C_5H_8ClN_5$: C, 34.6; H, 4.6; N, 40.3. Found: C, 34.8; H, 4.7; N, 40.4.

3-Chloro-5-methylaminopyridazine (XIX).

In 100 ml. of hot water was suspended 3.5 g. (0.02 mole) of 6-chloro-4-methylamino-3-hydrazinopyridazine (XVI) and to this suspension was added 100 ml. of an aqueous solution containing 19.9 g. (0.05 mole) of copper sulfate pentahydrate. The mixture was heated for 1.5 hours. The solution was made basic with 10% sodium hydroxide solution and it was heated again for 5 minutes. The precipitated copper oxide was removed by filtration, the filtrate was acidified with acetic acid and evaporated to dryness under reduced pressure. The residue was extracted with acetone, the acetone extract evaporated and the residue recrystallized from water, yield 2.0 g. (69%), m.p. 172-173° dec; U.V. λ max (absolute ethanol); 207 (ε, 9,200); 214 (ε, 8,850); 261 (ε, 15,450), 300 mμ (sh) (ε, 3,100); infrared cm^{-1}; 3250 (s), 3075 (m), 2940 (m), 1600 (s), 1440 (m), 1425 (w), 1375 (m), 1340 (s), 1281 (m), 1168 (m), 1120 (s), 1085 (m), 1070 (w), 1055 (m), 1042 (m), 1000 (s), 984 (s), 915 (s), 827 (s), 721(m), 705 (w), 451 (w), 420 (w).

Anal. Calcd. for $C_5H_6ClN_3$: C, 41.8; H, 4.2; N, 29.3. Found: C, 41.4; H, 4.4; N, 28.9.

4-Methylamino-6-chloro-3-aminopyridazine (XVIII).

A mixture of 0.9 g. (0.005 mole) of 6-chloro-4-methylamino-3-hydrazinopyridazine (XVI) and 0.3 g. of freshly prepared Raney nickel catalyst in 100 ml. of absolute ethanol was hydrogenated at atmospheric pressure and room temperature. After removal of the catalyst, the filtrate was evaporated at room temperature under a stream of compressed air. The residue was recrystallized from water, yield 0.5 g. (67%), m.p. 201-202°; U.V. λ max (absolute ethanol); 213 (ε, 19,000); 230 (sh) (ε, 11,900); 268 (ε, 7,850); 302 mμ (ε, 6,300); infrared cm^{-1}; 3360 (m), 3250 (w), 2940 (w), 1650 (m), 1580 (s), 1470 (s), 1425 (s), 1400 (w), 1350 (s), 1285 (m), 1195 (s), 1160 (w), 1123 (m), 1078 (m), 940 (s), 825 (m), 800 (w), 760 (w), 675 (m), 538 (w).

Anal. Calcd. for $C_5H_7ClN_4$: C, 37.9; H, 4.5; N, 35.3. Found: C, 37.6; H, 4.4; N, 35.0.

1-Methyl-6-chloroimidazo[4,5-c]pyridazine (XVII).

A solution containing 1.6 g. (0.01 mole) of 4-methylamino-6-chloro-3-aminopyridazine (XVIII) was suspended in 30 ml. (0.2 mole) of freshly distilled ethyl orthoformate and heated under reflux for 1 hour. After cooling, the crystals were collected, washed with ether and recrystallized from water, yield 1.4 g. (82%), m.p. 182-183°; U.V. λ max (absolute ethanol); 212.5 (ε, 34,400); 281.5 mμ (ε, 4,000); infrared cm^{-1}; 3440 (m), 3070 (m), 1620 (s), 1550 (m), 1490 (s), 1440 (w), 1400 (s), 1340 (s), 1300 (m), 1274 (s), 1180 (s), 1110 (w), 1071 (s), 1057 (w), 933 (m), 892 (m), 816 (m), 791 (m), 770 (w), 662 (s), 652 (w), 620 (s), 575 (w), 511 (w).

Anal. Calcd. for $C_6H_5ClN_4$: C, 42.7; H, 3.0; N, 33.2. Found: C, 43.0; H, 3.1; N, 33.1.

1-Methylimidazo[4,5-c]pyridazine Hydrochloride (XX).

A mixture containing 0.8 g. (0.005 mole) of 1-methyl-6-chloroimidazo[4,5-c]pyridazine (XVII) and approximately 0.5 g. of 5% palladium-charcoal in 50 ml. of absolute ethanol was hydrogenated. After removal of the catalyst and evaporation of the solvent under reduced pressure, the residue was dissolved in chloroform and acidified with hydrogen chloride gas. The precipitated crystals were collected and washed with chloroform giving 0.51 g. (60%) of the product, m.p. 252-253°. The analytical sample was purified by recrystallization from absolute ethanol; U.V. λ max (absolute ethanol); 209 (ε, 21,150); 270 mμ (ε, 5,150); infrared cm^{-1}; 3430 (m), 3020 (m), 2950 (w), 2060 (m), 2010 (m); 1840 (w), 1750 (w), 1640 (s), 1590 (w), 1550 (m), 1490 (s), 1470 (w), 1440 (m), 1420 (s), 1350 (s), 1293 (m), 1260 (m), 1227 (m), 1167 (m), 1103 (m), 1050 (s), 985 (w), 930 (w), 906 (w), 887 (s), 794 (m), 730 (s), 631 (s), 594 (s), 551 (s), 512 (s).

Anal. Calcd. for $C_6H_6N_4 \cdot HCl$: C, 42.2; H, 4.1; N, 32.8. Found: C, 42.4; H, 4.2; N, 33.1.

4-Methylamino-3-aminopyridazine (XXI).

Method I.

A mixture containing 1.6 g. (0.01 mole) of 4-methylamino-6-chloro-3-aminopyridazine (XVIII), 0.6 g. (0.15 mole) of sodium hydroxide and approximately 2 g. of 10% palladium-charcoal in 200 ml. of 95% ethanol was hydrogenated. After removal of the catalyst and evaporation of the solvent under reduced pressure,

the residue was extracted with hot absolute ethanol giving after recrystallization from water, yield 0.5 g. (42%), m.p. 277-278° dec.; U.V. λ max (absolute ethanol); 275 (ε, 14,900); 263 (ε, 7,650); 297 mμ (ε, 7,250); infrared cm^{-1}; 3380 (w), 3320 (w), 3250 (w), 3100 (w), 2990 (w), 2830 (m), 2710 (m), 2550 (m), 2450 (w), 1850 (m), 1670 (s), 1580 (s), 1480 (s), 1440 (m), 1430 (w), 1350 (s), 1298 (s), 1180 (s), 1130 (w), 1083 (s), 892 (s), 820 (s), 780 (m), 768 (w), 645 (w), 623 (m), 554 (m), 531 (s), 460 (m).

Anal. Calcd. for $C_5H_8N_4$: C, 48.4; H, 6.5; N, 45.1. Found: C, 48.3; H, 6.6; N, 44.9.

Method 2.

A mixture containing 1.7 g. (0.01 mole) of 1-methyl-6-chloroimidazo[4,5-c]pyridazine (XVII), 0.6 g. (0.15 mole) of sodium hydroxide and approximately 1 g. of 10% palladium-charcoal in 150 ml. of ethanol was hydrogenated. After removal of the catalyst and evaporation of the solvent under reduced pressure, the residue was extracted with hot absolute ethanol giving after recrystallization from water, 0.7 g. (58%). The infrared spectrum was identical with that from the sample prepared as described in Method 1.

1-Methylimidazo[4,5-c]pyridazine-2-thiol (XXIII).

A mixture of 0.6 g. (0.005 mole) of 4-methylamino-3-aminopyridazine (XXI), 5 ml. (0.08 mole) of carbon disulfide, 8 ml. (0.1 mole) of dry pyridine and 0.4 g. (0.01 mole) of crushed sodium hydroxide was heated for 1.5 hours. After removal of the solvent under reduced pressure, the residue was dissolved in water and acidified with concentrated hydrochloric acid. The precipitated crystals were collected and washed with water giving 0.3 g. (38%) of the product, m.p. 308° dec. The analytical sample was purified by recrystallization from about 300 ml. of absolute ethanol; U.V. λ max (absolute ethanol); 209 (ε, 6,800); 235 (sh) (ε, 9,750); 245 (ε, 12,800); 326 mμ (ε, 22,550); infrared cm^{-1}; 3440 (w), 3020 (w), 2925 (w), 2650 (w), 1800 (m), 1625 (s), 1590 (w), 1480 (m), 1425 (m), 1370 (w), 1340 (m), 1261 (m), 1232 (w), 1150 (m), 1124 (w), 1085 (s), 1025 (s), 950 (w), 928 (s), 834 (s), 771 (w), 747 (m), 724 (w), 667 (m), 648 (m), 614 (w), 588 (m), 545 (s), 434 (s).

Anal. Calcd. for $C_6H_6N_4S$: C, 43.4; H, 3.6; N, 33.7. Found: C, 43.3; H, 3.7; N, 33.5.

1-Methyl-6-chloroimidazo[4,5-c]pyridazine-2-thiol (XXII).

A mixture of 0.6 g. (0.01 mole) of 4-methylamino-6-chloro-3-aminopyridazine (XVIII), 9 ml. (0.15 mole) of carbon disulfide, 16 ml. (0.2 mole) of dry pyridine and 0.8 g. (0.02 mole) of crushed sodium hydroxide was heated for 1.5 hours. After removal of the solvent under reduced pressure, the residue was dissolved in water and acidified with concentrated hydrochloric acid. The precipitated crystals were collected and washed with water giving 1.4 g. (70%) of the product m.p. 245-246° dec. The analytical sample was purified by recrystallization from a large amount of absolute ethanol; U.V. λ max (absolute ethanol); 205 (ε, 16,300); 251.5 (ε, 15,600); 334.5 mμ (ε, 21,300); infrared cm^{-1}; 3350 (w), 3050 (s), 1750 (w), 1620 (s), 1470 (m), 1440 (m), 1360 (s), 1310 (m), 1264 (s), 1230 (s), 1183 (m), 1125 (m), 1102 (s), 1060 (s), 989 (w), 950 (s), 855 (m), 805 (w), 772 (m), 700 (m), 661 (w), 637 (w), 593 (s), 570 (s), 498 (s).

Anal. Calcd. for $C_6H_5ClN_4S$: C, 35.9; H, 2.5; N, 27.9. Found: C, 36.4; H, 2.8; N, 27.6.

6-Chloro-1-methyl-2-methylthioimidazo[4,5-c]pyridazine (XXIV).

To a solution containing 2 g. (0.01 mole) of 1-methyl-6-chloroimidazo[4,5-c]pyridazine-2-thiol (XXII) dissolved in 20 ml. of 1*N* potassium hydroxide solution was added 1.4 g. (0.01 mole) of methyl iodide. The mixture was stirred at room temperature for 3 hours. The crystals were collected and recrystallized from ethanol, yield 0.9 g. (43%), m.p. 217-218°; U.V. λ max (95% ethanol); 207 (ε, 15,950); 228 (ε, 14,900); 237 (ε, 15,900); 266 (ε, 9,050); 306 mμ (ε, 10,600); infrared cm^{-1}; 3425 (w), 3250 (m), 3180 (m), 3090 (m), 2925 (m), 1620 (s), 1540 (m), 1510 (m), 1470 (s), 1450 (m), 1430 (s), 1425 (s), 1410 (s), 1375 (m), 1360 (m), 1330 (s), 1300 (w), 1250 (m), 1215 (w), 1190 (s), 1155 (m), 1128 (s), 1078 (s), 1061 (s), 1028 (m), 980 (m), 940 (m), 875 (m), 781 (s), 771 (s), 712 (w), 690 (m), 672 (m), 615 (w), 590 (w), 566 (w), 527 (w), 490 (w), 476 (w).

Anal. Calcd. for $C_7H_7ClN_4S$: C, 39.2; H, 3.3; N, 26.1. Found: C, 39.0; H, 3.5; N, 26.4.

4-Amino-3,6-dichloropyridazine (XXVI).

This compound was prepared by the improved procedure of Gerhardt and Castle (11).

4-Amino-6-chloro-3-(1′-methyl)hydrazinopyridazine (XXV).

A solution containing 3.3 g. (0.02 mole) of 4-amino-3,6-dichloropyridazine (XXVI), dissolved in 13 ml. of 95% methylhydrazine was heated on the steam bath for 2.5 hours. After cooling and the addition of water, the crystals were collected and recrystallized from water. There was obtained 1.4 g. (40%) of XXV, m.p. 163-164°; U.V. λ max (absolute ethanol); 222 (ε, 15,700); 271 (ε, 7,350); 308 mμ (ε, 4,800); infrared cm^{-1}; 3340 (s), 3150 (m), 2970 (w), 2710 (w), 1630 (s), 1560 (s), 1470 (m), 1440 (m), 1400 (s), 1325 (s), 1232 (m), 1165 (s), 1130 (s), 1105 (w), 1079 (w), 1035 (m), 961 (s), 900 (m), 881 (m), 765 (w), 480 (w), 460 (w).

Anal. Calcd. for $C_5H_8ClN_5$: C, 34.6; H, 4.6; N, 40.3. Found: C, 34.9; H, 4.7; N, 40.2.

4-Amino-6-chloro-3-methylaminopyridazine (XXIX).

Method 1.

A stainless steel reaction vessel was charged with 8.2 g. (0.05 mole) of 4-amino-3,6-dichloropyridazine (XXVI) and 30 ml. of 40% aqueous methylamine. The reaction mixture was heated at 110-120° in a rocking autoclave for 8 hours. After cooling the crystals were collected and recrystallized from water, yield 4.3 g. (55%) m.p. 241-242°; U.V. λ max (absolute ethanol); 213 (ε, 17,000); 228 (ε, 15,600); 265 (ε, 7,250); 307 mμ (ε, 5,550); infrared cm^{-1}; 3350 (m), 3200 (m), 2950 (w), 1660 (s), 1590 (m), 1560 (s), 1500 (s), 1475 (w), 1410 (s), 1340 (m), 1294 (s), 1190 (m), 1142 (s), 1098 (m), 1060 (s), 965 (s), 865 (w), 847 (s), 785 (m), 761 (m), 675 (m), 633 (w), 525 (w), 470 (w).

Anal. Calcd. for $C_5H_7ClN_4$: C, 37.9; H, 4.5; N, 34.3. Found: C, 37.1; H, 4.4; N, 34.0.

A satisfactory carbon analysis was never obtained but the structure is certain by virtue of its conversion into several other compounds *e.g.* XXVIII, XXX and XXXII.

Method 2.

A suspension containing 0.3 g. (0.002 mole) of 4-amino-6-chloro-3-(1′-methyl)hydrazinopyridazine (XXV) and approximately 1 g. of freshly prepared Raney nickel in 50 ml. of absolute ethanol was hydrogenated at atmospheric pressure and at room temperature. After removal of the catalyst, the filtrate was evaporated at room temperature under a stream of compressed air. The residue was recrystallized from water, yield 0.1 g. (33%), m.p. 241-242°. The infrared spectrum was identical with that from the sample prepared as described in Method 1.

3-Methyl-6-chloroimidazo[4,5-c]pyridazine-2-thiol (XXVIII).

A mixture of 1.2 g. (0.0075 mole) of 4-amino-6-chloro-3-

methylaminopyridazine (XXIX), 7.5 ml. (0.11 mole) of carbon disulfide, 12 ml. (0.15 mole) of dry pyridine and 0.6 g. (0.075 mole) of crushed sodium hydroxide was heated for 1.5 hours. After removal of the solvent under reduced pressure, the residue was dissolved in water and acidified with concentrated hydrochloric acid. The precipitated crystals were collected and washed with water giving 0.9 g. (60%) of the product, m.p. 295° dec. The analytical sample was purified by recrystallization from about 900 ml. of water; U.V. λ max (absolute ethanol); 205 (ε, 18,050); 250 (ε, 16,000); 335 mμ (ε, 21,350); infrared cm^{-1}; 3450 (m), 3100 (m), 3000 (w), 2830 (w), 2720 (w), 1640 (s), 1570 (m), 1460 (s), 1410 (s), 1320 (s), 1288 (w), 1231 (s), 1158 (s), 1117 (s), 1060 (s), 1004 (w), 976 (s), 881 (s), 768 (s), 660 (m), 637 (s), 565 (m), 501 (s), 426 (w).

Anal. Calcd. for $C_6H_5ClN_4S$: C, 35.9; H, 2.5; N, 27.9. Found: C, 35.8; H, 2.6; N, 28.0.

6-Chloro-2-methylthio-3-methylimidazo[4,5-c]pyridazine (XXXI).

To a solution containing 1 g. (0.005 mole) of 3-methyl-6-chloroimidazo[4,5-c]pyridazine-2-thiol (XXVIII) dissolved in 10 ml. of 1*N* potassium hydroxide solution was added 0.7 g. (0.005 mole) of methyl iodide. The mixture was stirred at room temperature for 2 hours. The crystals were collected and recrystallized from ethanol, yield 0.6 g. (60%), m.p. 175-176°; U.V. λ max (95% ethanol); 224 (ε, 17,200); 287 (sh) (ε, 15,250); 300 (ε, 18,550); 309 mμ (sh) (ε, 15,150); infrared cm^{-1}; 3060 (w), 3010 (w), 2925 (w), 1590 (m), 1510 (w), 1480 (s), 1460 (s), 1425 (m), 1420 (s), 1380 (m), 1370 (s), 1360 (s), 1330 (s), 1325 (m), 1248 (m), 1213 (w), 1180 (w), 1152 (s), 1130 (s), 1116 (m), 1085 (w), 1058 (s), 989 (m), 978 (m), 952 (s), 888 (s), 869 (m), 855 (m), 778 (m), 758 (s), 713 (m), 682 (s), 649 (s), 640 (w), 635 (m), 570 (w), 470 (s).

Anal. Calcd. for $C_7H_7ClN_4S$: C, 39.2; H, 3.3; N, 26.1. Found: C, 39.5; H, 3.5; N, 25.9.

6-Chloro-3-methylimidazo[4,5-c]pyridazine (XXX).

A solution containing 0.8 g. (0.005 mole) of 4-amino-6-chloro-3-methylaminopyridazine (XXIX) was suspended in 15 ml. (0.1 mole) of freshly distilled ethyl orthoformate and heated under reflux for 2.5 hours. After cooling, the crystals were collected, washed with ether and recrystallized from water, 0.6 g. (75%), m.p. 193-194°; U.V. λ max (absolute ethanol); 210 (ε, 27,950); 260 (ε, 5,350); 299 mμ (ε, 3,750); infrared cm^{-1}; 3450 (w), 3090 (m), 3060 (m), 2925 (w), 1890 (w), 1600 (m), 1560 (m), 1510 (s), 1470 (w), 1430 (s), 1340 (s), 1300 (s), 1255 (m), 1239 (m), 1130 (s), 1069 (s), 950 (s), 922 (m), 817 (s), 788 (w), 761 (s), 661 (m), 637 (w), 608 (s), 510 (w).

Anal. Calcd. for $C_6H_5ClN_4$: C, 42.7; H, 3.0; N, 33.2. Found: C, 42.5; H, 3.0; N, 33.1.

3-Methylimidazo[4,5-c]pyridazine (XXVII).

A mixture containing 0.8 g. (0.005 mole) of 6-chloro-3-methylimidazo[4,5-c]pyridazine (XXX), 0.3 g. (0.075 mole) of sodium hydroxide and approximately 0.08 g. of 5% palladium-charcoal in 100 ml. of 95% ethanol was hydrogenated at room temperature and atmospheric pressure. After removal of the catalyst and evaporation of the solvent under reduced pressure, the residue was dissolved in water and neutralized to *p*H 6-7 with dilute hydrochloric acid. The solution was evaporated to dryness leaving a yellow-colored residue. This residue was extracted with absolute ethanol, the absolute ethanol extract evaporated and the residue recrystallized from 2-propanol, yield 0.3 g. (43%), m.p. 170-176°; U.V. λ max (absolute ethanol); 207 (ε, 19,800); 254 (ε, 6,800); 286 mμ (ε, 4,350); infrared cm^{-1}; 3450 (m), 3060 (m), 3030 (w), 2925 (w), 1950 (w), 1870 (w), 1600 (s), 1510 (s), 1475 (m), 1450 (w), 1425 (m), 1400 (s), 1350 (s), 1320 (m), 1300 (s), 1248 (m), 1204 (s), 1158 (w), 1140 (m), 1113 (s), 1063 (m), 1023 (m), 945 (m), 918 (m), 872 (s), 795 (m), 765 (w), 737 (s), 640 (m), 611 (s), 592 (m), 561 (m), 502 (w).

Anal. Calcd. for $C_6H_6N_4$: C, 53.7; H, 4.5; N, 41.8. Found: C, 53.4; H, 4.6; N, 41.8.

3-Methylamino-4-aminopyridazine (XXXII).

Method 1.

A mixture containing 3.2 g. (0.002 mole) of 4-amino-6-chloro-3-methylaminopyridazine (XXIX), 1.3 g. (0.32 mole) of crushed sodium hydroxide, approximately 0.3 g. of 5% palladium on charcoal and 100 ml. of 95% ethanol was hydrogenated at atmospheric pressure and room temperature. After the theoretical amount of hydrogen was absorbed, the solution was filtered, neutralized to *p*H 6-7 with dilute hydrochloric acid and evaporated to dryness leaving a yellow-colored residue. This residue was extracted with absolute ethanol, the absolute ethanol extract evaporated and the residue recrystallized from water, yield 1.8 g. (72%), m.p. 222-223° dec.; U.V. λ max (absolute ethanol); 208.5 (ε, 12,750); 233 (ε, 11,400); 278 (ε, 4,350); 313 mμ (ε, 6,900); infrared cm^{-1}; 3380 (w), 3300 (w), 3120 (w), 2960 (w), 1670 (m), 1630 (w), 1575 (s), 1550 (s), 1500 (s), 1440 (m), 1410 (s), 1360 (m), 1325 (s), 1297 (w), 1172 (m), 1135 (m), 1080 (w), 1058 (m), 990 (w), 920 (w), 895 (w), 832 (s), 780 (w), 760 (w), 620 (s), 564 (m), 545 (s), 512 (w), 472 (w).

Anal. Calcd. for $C_5H_8N_4 \cdot 2H_2O$: C, 37.5; H, 7.6; N, 35.0. Found: C, 37.9; H, 7.3; N, 35.0.

Method 2.

A mixture containing 1.7 g. (0.01 mole) of 6-chloro-3-methylimidazo[4,5-c]pyridazine (XXX), 0.6 g. (0.15 mole) of sodium hydroxide and approximately 1 g. of 10% palladium-charcoal in 150 ml. of ethanol was hydrogenated at room temperature and atmospheric pressure. After removal of the catalyst and evaporation of the solvent under reduced pressure, the residue was extracted with hot absolute ethanol giving after recrystallization from water, 0.5 g. (42%), m.p. 222-223° dec. The infrared spectrum was identical with that from the sample prepared as described in Method 1.

3-Methylimidazo[4,5-c]pyridazine-2-thiol (XXXIII).

A mixture 0.6 g. (0.005 mole) of 3-methylamino-4-aminopyridazine (XXXII), 5 ml. (0.08 mole) of carbon disulfide, 8 ml. (0.1 mole) of dry pyridine and 0.4 g. (0.01 mole) of crushed sodium hydroxide was heated for 1.5 hours. After removal of the solvent under reduced pressure, the residue was dissolved in water and acidified with concentrated hydrochloric acid. The precipitated crystals were collected and washed with water giving 0.4 g. (50%) of the product, m.p. 319° dec. The analytical sample was purified by recrystallization from about 400 ml. of absolute ethanol; U.V. λ max (absolute ethanol); 207 (ε, 7,150); 231 (sh) (ε, 9,650); 245 (ε, 12,750); 327 mμ (ε, 22,100); infrared cm^{-1}; 3450 (w), 3080 (w), 2940 (w), 2820 (w), 2650 (w), 1800 (m), 1680 (m), 1570 (m), 1480 (s), 1400 (s), 1360 (s), 1325 (s), 1295 (m), 1254 (s), 1230 (m), 1147 (s), 1120 (s), 1084 (w), 1060 (w), 1028 (s), 1000 (w), 970 (w), 931 (w), 911 (m), 880 (w), 852 (s), 775 (w), 757 (w), 747 (s), 665 (w), 639 (s), 630 (w), 614 (w), 593 (m), 555 (m), 545 (w), 504 (w), 435 (m).

Anal. Calcd. for $C_6H_6N_4S$: C, 43.4; H, 3.6; N, 33.7. Found: C, 43.7; H, 3.7; N, 33.6.

3,4,5-Triaminopyridazine (XXXIV).

This compound was prepared by the method of Guither, Clark and Castle (4).

7-Aminoimidazo[4,5-*c*]pyridazine-2-thiol Hydrochloride (XXXV).

A mixture of 0.9 g. (0.007 mole) of 3,4,5-triaminopyridazine, 6 ml. (0.1 mole) of carbon disulfide, 11 ml. (0.14 mole) of dry pyridine and 0.6 g. (0.014 mole) of crushed sodium hydroxide was heated for 3 hours. After removal of the solvent under reduced pressure, the residue was dissolved in water and acidified with concentrated hydrochloric acid. The precipitated crystals were collected and washed with water giving 0.7 g. (62%) of the product, m.p. 310-311° dec. The analytical sample was purified by recrystallization from a large amount of water; U.V. λ max (water); 200.5 (ε, 13,820); 218 (sh) (ε, 11,810); 243 (ε, 14,670); 312 mμ (ε, 13,770); infrared cm^{-1}; 3400 (m), 3300 (m), 3100 (w), 1900 (w), 1670 (s), 1610 (w), 1590 (m), 1540 (s), 1490 (m), 1440 (m), 1370 (s), 1330 (w), 1290 (s), 1240 (s), 1210 (m), 1190 (m), 1170 (m), 1080 (w), 960 (m), 910 (m), 845 (s), 780 (m), 760 (m), 715 (m), 680 (s).

Anal. Calcd. for $C_5H_5N_5S \cdot 1 \cdot 5HCl$: C, 27.1; H, 3.0; N, 31.6. Found: C, 27.1; H, 2.9; N, 31.4.

7-Aminoimidazo[4,5-*c*]pyridazine (XXXVI).

A mixture of 0.8 g. (0.005 mole) of 7-aminoimidazo[4,5-*c*]-pyridazine-2-thiol (XXXV) and approximately 0.6 g. of Raney nickel in 50 ml. of absolute ethanol was heated on the steam bath for 4 hours. After removal of the catalyst, the filtrate was evaporated on the steam bath under reduced pressure. The residue was recrystallized from acetone giving 0.2 g. (29%) of a solid, m.p. 336-338° dec. The infrared spectrum was identical with that from the sample prepared as described by Kuraishi and Castle (2).

4-Chloro-*v*-triazolo[4,5-*c*]pyridazine (XXXVII).

This compound was prepared by the method of Gerhardt and Castle (11).

7-Methylamino-*v*-triazolo[4,5-*c*]pyridazine (XXXVIIIa).

A mixture of 0.8 g. (0.005 mole) of 7-chloro-*v*-triazolo[4,5-*c*]-pyridazine (XXXVII) in 100 ml. of absolute ethanol containing about 12% methylamine was heated in a stainless steel reaction vessel in a rocking autoclave at 140-150° for 12 hours. After removal of the solvent, the residue was recrystallized from water (Norite) and then chromatographed on activated alumina with ethanol. The yield was 0.4 g. (51%) of product, m.p. 310-311° dec.; U.V. λ max (95% ethanol); 208 (ε, 9,100); 274 (ε, 2,500); 355 mμ (ε, 10,100); infrared cm^{-1}; 3230 (w), 1820 (w), 1620 (s), 1500 (m), 1430 (m), 1370 (s), 1350 (s), 1280 (m), 1250 (w), 1220 (w), 1195 (w), 1145 (m), 1050 (s), 900 (s), 780 (w), 755 (w), 695 (w), 660 (w), 620 (s), 560 (w), 525 (m), 495 (w), 470 (w).

Anal. Calcd. for $C_5H_6N_6$: C, 40.0; H, 4.0; H, 56.0. Found: C, 40.0; H, 4.2; N, 56.1.

7-Dimethylamino-*v*-triazolo[4,5-*c*]pyridazine (XXXVIIIb).

Compound XXXVII (0.7 g., 0.005 mole) was treated with about 12% of dimethylamine in 100 ml. of ethanol as described for XXXVIIIa. The yield was 0.4 g. (42%), m.p. 321-322° dec; U.V. λ max (95% ethanol); 212 (ε, 11,700); 282 (ε, 4,700); 346 (ε, 15,200); 358 (sh) mμ (ε, 10,600); infrared cm^{-1}; 3450 (w), 3200 (w), 3100 (w), 3000 (w), 2800 (w), 1620 (s), 1500 (m), 1420 (m), 1350 (s), 1260 (m), 1205 (m), 1170 (w), 1125 (m), 1100 (w), 1045 (s), 980 (m), 930 (m), 880 (w), 865 (s), 755 (w), 670 (w), 630 (s), 555 (w), 505 (s).

Anal. Calcd. for $C_6H_8N_6$: C, 43.9; H, 4.9; N, 51.2. Found: C, 43.5; H, 5.2; N, 51.7.

7-Morpholino-*v*-triazolo[4,5-*c*]pyridazine (XXXVIIIc).

A mixture of 0.8 g. (0.005 mole) of XXXVII and 2.2 g. (0.025 mole) of morpholine was allowed to react as described for XXXVIIIa. The residue was recrystallized from water (Norite) before chromatography on alumina (ethanol), yield 0.43 g. (33%), m.p. 342-343° dec; U.V. λ max (95% ethanol); 205 (ε, 10,300); 288 (ε, 4,250); 346 (ε, 10,600); 360 mμ (ε, 11,500); infrared cm^{-1}; 3450 (w), 3100 (w), 3000 (w), 2970 (w), 2850 (w), 1600 (s), 1500 (m), 1450 (m), 1370 (m), 1320 (m), 1305 (m), 1285 (m), 1270 (m), 1250 (s), 1230 (s), 1205 (s), 1150 (w), 1110 (s), 1040 (w), 1030 (s), 980 (w), 920 (m), 870 (s), 820 (w), 760 (w), 670 (w), 650 (w), 630 (w), 590 (s), 550 (w), 510 (m), 500 (w), 470 (w).

Anal. Calcd. for $C_8H_{10}N_6O$: C, 46.6; H, 4.9; N, 40.8. Found: C, 46.8; H, 5.1; N, 40.4.

7-Piperidino-*v*-triazolo[4,5-*c*]pyridazine (XXXVIIId).

A mixture of 0.8 g. (0.005 mole) of XXXVII and 2.1 g. (0.025 mole) of piperidine in 50 ml. of absolute ethanol was heated in a stainless steel reaction vessel in a rocking autoclave at 125-135° for 3 hours. After removal of the solvent, the residue was crystallized from water. The yield was 0.4 g. (34%) of product, m.p. 324-325° dec.; U.V. λ max (95% ethanol); 204 (ε, 8,000); 280 (ε, 1,800); 346 mμ (ε, 13,300); infrared cm^{-1}; 3025 (w), 2950 (w), 2850 (w), 2270 (w), 1600 (s), 1480 (m), 1450 (m), 1380 (m), 1295 (s), 1250 (m), 1230 (m), 1180 (w), 1160 (w), 1130 (m), 1075 (w), 1045 (s), 1025 (w), 1010 (w), 980 (w), 915 (w), 865 (w), 855 (w), 810 (w), 760 (w), 670 (w), 630 (w), 575 (m), 550 (w), 510 (m), 490 (w).

Anal. Calcd. for $C_9H_{12}N_6$: C, 52.9; H, 5.9; N, 41.2. Found: C, 53.0; H, 6.0; N, 41.4.

7-Benzylamino-*v*-triazolo[4,5-*c*]pyridazine (XXXVIIIe).

A mixture of 0.66 g. (0.005 mole) of XXXVII and 2.7 g. (0.0025 mole) of benzylamine was allowed to react as described for XXXVIIIa except the reaction temperature was 115-125° for 10 hours. After removal of the solvent, the residue was recrystallized from water. The yield was 0.72 g. (65%), m.p. 274-275°; U.V. λ max (absolute ethanol); 207.5 (ε, 23,500); 277 (ε, 6,800); 338 (ε, 14,550); 348 mμ (ε, 10,300); infrared cm^{-1}; 3400 (m), 3200 (w), 3100 (w), 1850 (w), 1650 (s), 1500 (s), 1450 (s), 1400 (m), 1350 (s), 1300 (s), 1280 (m), 1260 (w), 1200 (w), 1140 (w), 1120 (m), 1060 (s), 1040 (m), 990 (s), 915 (s), 880 (w), 860 (w), 800 (w), 740 (s), 700 (s), 670 (s), 610 (s), 530 (s), 510 (s), 450 (m).

Anal. Calcd. for $C_{11}H_{10}N_6$: C, 58.4; H, 4.5; N, 37.2. Found: C, 58.1; H, 4.5; N, 36.9.

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