Reactivity of Methyl (3,6-Dichloropyridazin-4-yl)acetate Towards Nucleophiles

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Methyl (3,6-dichloropyridazin-4-yl)acetate (II), prepared from methyl (3,6-dihydroxypyridazin-4-yl)acetate (I) by chlorination with phosphorus oxychloride, was used for studies of nucleophilic displacement reactions and it has been found that only the chlorine atom at position 6 was displaced with hydrazine. With diluted hydrochloric acid both chlorine atoms were displaced with the 6-oxo isomer predominating. By turning the aromatic ring of pyridazine into an *o*-quinoid system, the chlorine atom at position 3 became mobile. Cyclization of (6-hydrazino-*s*-triazolo[4,3-*b*]pyridazin-7-yl)acetic acid hydrazide (XIX) gave 6-aminopyrrolo[3,2-*e*]*s*-triazolo[4,3-*b*]-pyridazin-7(8*H*)one (XXI).

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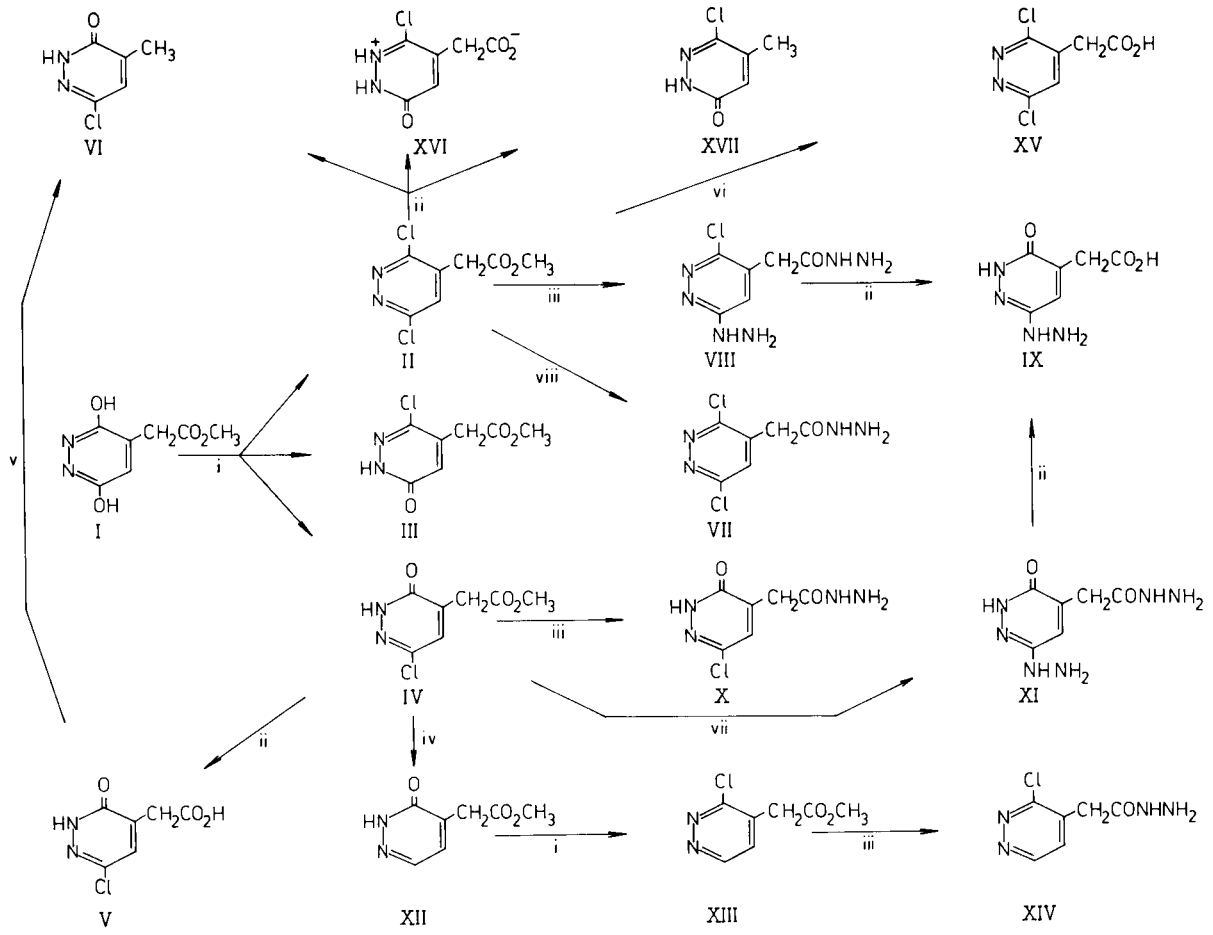
The mobility of halogen atoms of halopyridazines is known to be affected by the nature and the position of other groups on the ring (1). The presence of a methyl group at the 4 (or 5) position in 3,6-dichloropyridazine allows the selective displacement of the chlorine atoms. The reaction with methoxide (2-4) gave both monosubstituted isomers with a slight predominance of the 3-methoxy derivative; with alkoxides of increasing size (2) and with ammonia (2) the substiutiton occurs preferentially at position 6. With dimethylamine (2,5) only one isomer was obtained, which was assigned the structure of 6-dimethylamino derivative. In addition, both acids and alkalis (2,6,7) displace preferentially the chlorine atom at position 3.

Scanty attention was devoted to the study of the influence of electron-withdrawing groups on the mobility of halogen atoms at the 3 and 6 positions, possibly because of the difficulty of preparing such compounds.

Our interest in studying the effect of carboethoxy groups on the reactivity of the pyridazine nucleus (8-10) led us to undertake a research on the mobility of the halogen atoms of methyl (3,6-dichloropyridazin-4-yl)-acetate (II), which was prepared by chlorination of the dihydroxy derivative (I) with phosphorus oxychloride. From this reaction we also isolated the monochloro derivatives III and IV, whose structures were assigned by hydrolysis and decarboxylation of the latter to the known 6-chloro-4-methylpyridazin-3(2*H*)one (VI) (2). Treatment of compound II with hydrazine hydrate at room temperature yielded only the hydrazide VII; but the halogen atom at position 6 was selectively displaced to give the hydrazino derivative VIII, when the same mixture was refluxed for 10 minutes. The structure of compound VIII was determined by its conversion into the acid IX, which was also obtained from the ester IV through compounds X and XI.

Several attempts to replace the chlorine atom at position 3 with an hydrazino group were unsuccessful; increasing the reaction time or raising the temperature yielded only tars. The poor reactivity of the halogen atom at position 3 of compound VIII towards hydrazine is not exclusively due to the presence of an electron-donating group at position 6, since also (3-chloropyridazin-4-yl)acetate (XIII) reacted with the same reagent to give only the hydrazide XIV. The ester XIII was obtained by catalytic dehalogenation of compound IV to XII followed by chlorination of the latter with phosphorus oxychloride.

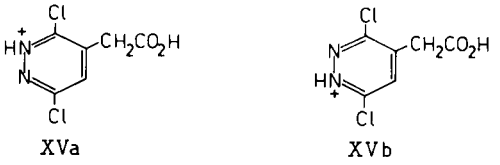
When the dichloro derivative II was heated at 50° with diluted hydrochloric acid, only the carbomethoxy group was hydrolysed and the acid XV was obtained in high yield. At higher temperatures (~ 90°), the halogen atoms were also displaced with the chlorine atom at position 6 being the more mobile. Under these conditions we could not avoid the decarboxylation of the haloacids which, in the case of (6-chloro-3(2*H*)oxopyridazin-4-yl)acetic acid was complete. From the reaction we isolated a mixture of



Reagents: i, phosphorus oxychloride; ii, hydrochloric acid at 90°; iii, refluxing 85% hydrazine hydrate; iv, hydrogen, palladium/charcoal; v, Δ; vi, hydrochloric acid at 50°; vii, refluxing 98% hydrazine hydrate; viii, 85% hydrazine hydrate.

Scheme 1

(3-chloro-6(1*H*)oxopyridazin-4-yl)acetic acid (XVI) (47%), the decarboxylated compound XVII (15%) and 6-chloro-4-methylpyridazin-6(2*H*)one (VI) (30%). The mobility of the halogen atoms in acidic media could be rationalized by the protonation of the intermediate XV (forms XVa and XVb) which largely favoured a nucleophilic attack at positions 3 and 6, respectively.

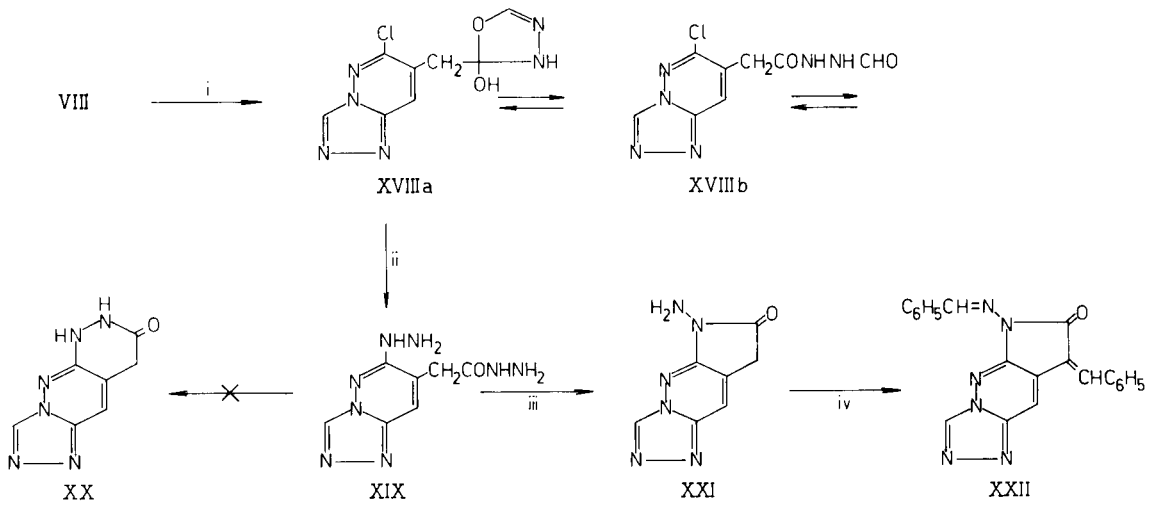


Scheme 2

Unlike the isomer V, the acid XVI exists as a dipolar ion in the solid state. In fact the infrared spectrum shows a sharp band at 3200 (NH stretching), a very broad pattern between 3100 and 1800 (maxima at 2460 and 1940) and a broad complex and symmetrical pattern between 1700 and 1520 (maxima at 1700, 1630, 1540 and 1520) and a broad band at 1200 cm^{-1}.

The mobility of the halogen atom at position 3 increases remarkably when the aromatic pyridazine system was turned into an *ortho*-quinoid form. Thus, the *s*-triazolo-[4,3-*b*]pyridazine (XVIII) reacted with hydrazine hydrate, at room temperature, to give the hydrazino derivative XIX. For compound XVIII, obtained from the hydrazino derivative VIII with formic acid, several tautomeric structures must be taken into account:

The spectral data (see Experimental) suggest that the oxadiazole form (XVIIIa) predominated both in the solid



Reagents: i, formic acid; ii, 85% hydrazine hydrate; iii, Δ; iv, benzaldehyde.

Scheme 3

state and in solution.

Compound XIX could represent an intermediate suitable for synthesising the hitherto unknown pyridazino[3,4-*c*]-pyridazine system. However, when (6-hydrazino-*s*-triazolo-[4,3-*b*]pyridazin-7-yl)acetic acid hydrazide (XIX) was refluxed in toluene for several hours, cyclisation to compound XX did not occur and 6-aminopyrrolo[3,2-*e*]*s*-triazolo[4,3-*b*]pyridazin-7(8*H*)one (XXI) was obtained instead. The structure of the latter was determined on the basis of spectral data and confirmed by its conversion into the bis-benzylidene derivative XXII. Attempts to enlarge the *N*-aminopyrrolone system have been unsuccessful.

Several of the compounds described were tested for pharmacological and microbiological activity, but only the chloro derivative IV proved to be active as a hypotensive agent.

EXPERIMENTAL

All melting points are uncorrected. Unless otherwise stated, ir spectra were measured on potassium bromide discs with a Perkin-Elmer 457 spectrometer and ^{1}H nmr spectra were recorded for solutions in DMSO-d_6 with a Varian A-56/60 instrument; chemical shifts are reported in ppm downfield from internal tetramethylsilane. Uv spectra were determined for solutions in methanol with a Cary 14 spectrophotometer. Silica gel (0.2-0.5 mm) was used for column chromatography. Light petroleum refers to the fraction b.p. 30-50°.

Chlorination of Methyl (3,6-Dihydroxypyridazin-4-yl)acetate.

A mixture of methyl (3,6-dihydroxypyridazin-4-yl)acetate (I) (II) (10 g.) and phosphorus oxychloride (25 ml.) was heated at 60° for 10 minutes. Removal of the phosphorus oxychloride under reduced pressure left a residue which was poured on crushed ice and extracted with chloroform; the extracts were dried (sodium sulfate) and evaporated to give a viscous residue which was treated with ether. The white solid which separated, was filtered off and the ethereal solution was evaporated to dryness; the residual product was then crystallized from light petroleum to yield methyl (3,6-dichloropyridazin-4-yl)acetate (II) (4.5 g., 37.5%) as white needles, m.p. 32-33°; uv λ max: 272.5 (log ε 3.16) and 295s (log ε 2.63) nm; ir: 3060(w), 1735(s), 1440(m), 1370(s), 1320(s), 1150(s) cm^{-1}.

Anal. Calcd. for $C_7H_6Cl_2N_2O_2$: C, 38.01; H, 2.74; N, 12.68; O, 14.48. Found: C, 38.20; H, 2.90; N, 12.80; O, 14.90.

The aqueous solution was made weakly acidic (*p*H 4-5) with aqueous ammonium hydroxide and extracted again with chloroform. The solid left after removal of the solvent was combined with the white residue previously isolated and the mixture was resolved into three components by column chromatography. Elution with chloroform gave, in order of mobility, a small amount of compound II, methyl (6-chloro-3(2*H*)oxopyridazin-4-yl)acetate (IV) (2.15 g., 19.5%), and methyl (3-chloro-6(1*H*)oxopyridazin-4-yl)acetate (III) (0.35 g., 3.2%).

Compound IV was crystallized from benzene, m.p. 150-152°; uv λ max: 209 (log ε 4.31), 225s (log ε 3.67) and 297 (log ε 3.46) nm; ir: 3160-2700 (broad) 1730(s), 1660(s), 1600(s), 1345(m), 1270(m), 1180(m), 890(m), 640(m), (in chloroform: 3480, 1740, 1670, 1605) cm^{-1}; nmr: δ = 3.58 (s, 2, CH_2), 3.62 (s, 3, CH_3), 7.54 (s, 1, C_5-H), 13.16 (broad, 1, NH).

Anal. Calcd. for $C_7H_7ClN_2O_3$: C, 41.58; H, 3.44; N, 13.87; Cl, 17.51. Found: C, 41.61; H, 3.60; N, 14.08; Cl, 17.34.

Compound III was crystallized from benzene, m.p. 145-147°; uv λ max: 210 (log ε 4.38), 225s (log ε 3.69), and 295 (log ε 3.32) nm; ir: 3200-2700 (broad), 1730(s), 1670(s), 1600(m), 1350(m), 1210(m), 1150(m), 670(m) cm^{-1}; nmr: δ = 3.70 (s, 3, CH_3), 3.78 (s, 2, CH_2), 7.07 (s, 1, C_5-H), 13.2 (broad, 1, NH).

Anal. Calcd. for $C_7H_7ClN_2O_3$: C, 41.58; H, 3.44; N, 13.87; Cl, 17.51. Found: C, 41.49; H, 3.33; N, 13.86; Cl, 17.57.

(6-Chloro-3(2*H*)oxopyridazin-4-yl)acetic Acid (V).

The ester IV (1 g.) was heated in aqueous hydrochloric acid (18%, 10 ml.) at 90° for 3 hours; the resulting solution was cooled

and neutralized with aqueous sodium hydroxide. The white solid which precipitated was collected and recrystallized from diluted hydrochloric acid to give the acid V (0.6 g., 64.5%), m.p. 160-162°; uv λ max: 297 (log ε 3.39) nm; ir: 3250-2300 (broad), 1700(s), 1640(m), 1600(s), 1290(s), 950(m), 670(m) cm^{-1}.

Anal. Calcd. for $C_6H_5ClN_2O_3$: C, 38.22; H, 2.67; N, 14.86; Cl, 18.81. Found: C, 38.48; H, 2.65; N, 14.64; Cl, 18.85.

6-Chloro-4-methylpyridazin-3(2*H*)one (VI).

The acid V (0.55 g.) was heated with copper powder (0.3 g.) at 150° for 20 minutes. The mixture was cooled and extracted with chloroform; crystallization from water of the residue left after removal of the solvent gave the chloro derivative VI (0.3 g., 71.2%), m.p. 164-166° [lit. (2) m.p. 170°]; ir: 3200-2700 (broad), 1680(s), 1600(s), 1290(m), 1110(m), 935(m), 670(s) cm^{-1}; nmr: δ = 2.07 (d, 3, J = 1 Hz, CH_3), 7.37 (q, 1, J = 1 Hz, C_5-H).

Dechlorination of Compound IV.

A solution of the ester IV (1 g.) in methanol (60 ml.) containing palladium/carbon (10%, 0.25 g.) and magnesium oxide (0.1 g.) was hydrogenated at room temperature and pressure. Removal of the catalyst and solvent left a residue, which, crystallized from ethyl acetate, yielded compound XII, m.p. 121-123° (0.8 g., 96.3%); uv λ max: 202 (log ε 4.14), 224 (log ε 3.47), and 288 (log ε 3.55) nm; ir: 3160(m), 1720(s), 1660(s), 1610(s), 1340(s), 1260(m), 1215(m), 1170(m), (in chloroform: 3480, 1740, 1665, 1610) cm^{-1}; nmr (in deuteriochloroform): δ = 3.63 (d, 2, J = 0.9 Hz, CH_2), 3.73 (s, 3, CH_3), 7.25 (dt, 1, J = 4 and 0.9 Hz, C_5-H), 7.8 (d, 1, J = 4 Hz, C_6-H), 12.8 (broad, 1, NH).

Anal. Calcd. for $C_7H_8N_2O_3$: C, 50.00; H, 4.80; N, 16.66. Found: C, 50.26; H, 4.83; N, 16.90.

When hydrogenation was carried out without magnesium oxide, (3-oxopyridazin-4-yl)acetic acid was obtained, m.p. 168-170° dec. from water, yield 60%; ir: 3200-2500 (broad), 1720(s), 1640(s), 1600(m), 1560(m), 1230(m), 850(m) cm^{-1}.

Anal. Calcd. for $C_6H_6N_2O_3$: C, 46.76; H, 3.92; N, 18.18. Found: C, 46.55; H, 3.96; N, 18.28.

Methyl (3-Chloropyridazin-4-yl)acetate (XIII),

A mixture of the ester XII (0.5 g.) and phosphorus oxychloride (5 ml.) was heated at 60° for 30 minutes. The oxychloride was evaporated under reduced pressure, the residue was poured onto ice and extracted with chloroform. The chloroform extracts were dried and evaporated. Attempts to distil the crude product led to extensive decomposition; an analytical sample of compound XIII, which darkened on standing at room temperature, was obtained by column chromatography with chloroform as the developer (0.1 g., 18%); ir: 1735(s), 1330(s), 1250(m), 1200(s), 1170(s), 1120(m) cm^{-1}; nmr (in deuteriochloroform): δ = 3.73 (s, 3, CH_3), 3.78 (s, 2, CH_2), 7.49 (d, 1, J = 5 Hz, C_5-H), 9.07 (d, 1, J = 5 Hz, C_6-H).

Anal. Calcd. for $C_7H_7ClN_2O_2$: C, 45.04; H, 3.75; N, 15.01. Found: C, 44.99; H, 3.70; N, 15.32.

(3-Chloropyridazin-4-yl)acetic Acid Hydrazide (XIV).

A solution of the ester XIII (0.1 g.) and hydrazine hydrate (85%, 0.1 ml.) in methanol (1 ml.) was heated on a steam-bath for 1 hour. The solution evaporated to dryness under reduced pressure left a residue which, washed with water and crystallized from benzene, gave compound XIV (0.05 g., 50%), as yellow needles, m.p. 125-126°; ir: 3300(broad), 1650(s), 1605(s), 1350(s), 1120(m), 995(m) cm^{-1}.

Anal. Calcd. for $C_6H_7ClN_4O$: C, 38.64; H, 3.75; N, 30.04; Cl, 19.01. Found: C, 38.42; H, 3.89; N, 30.20; Cl, 18.81.

Hydrolysis of Methyl (3,6-Dichloropyridazin-4-yl)acetate.

A.

A mixture of the ester II (2 g.) and hydrochloric acid (18%, 70 ml.) was heated at 90° for 1 hour. The solution was evaporated to dryness under reduced pressure and the residue was extracted several times with hot benzene. Crystallization from water of the insoluble material afforded 3-chloro-6(1*H*)oxopyridazin-4-yl)acetic acid (XVI) (0.8 g., 47%), m.p. 169-171°; uv λ max: 295 (log ε 3.32) nm; ir: 3200(m), 3100-1800(broad), 1700(m), 1630(s), 1570(s), 1520(m), 1420(m), 1270(s), 1150(m), 850(m), 670(m) cm^{-1}.

Anal. Calcd. for $C_6H_5ClN_2O_3$: C, 38.22; H, 2.67; N, 14.86; Cl, 18.81. Found: C, 38.19; H, 2.69; N, 15.09; Cl, 18.40.

The benzene extracts were combined and evaporated to dryness to give a solid which was extracted with carbon tetrachloride; the insoluble fraction (0.2 g., 15.3%) was 3-chloro-4-methylpyridazin-6(1*H*)one (XVII), m.p. 219-221° (from ethanol) (lit. (2), m.p. 222°); ir: 3200-2600 (broad), 1700(s), 1600(m), 1160(m) 1110(m), 900(m), 740(m), 670(m), 530(m) cm^{-1}; nmr: δ = 2.17 (d, 3, J = 1.25 Hz, CH_3), 6.83 (q, 1, J = 1.25 Hz, C_5-H), 13 (broad, 1, NH).

Evaporation of the carbon tetrachloride solution afforded 6-chloro-4-methylpyridazin-3(2*H*)one (VI) (0.4 g., 30.6%), m.p. 164-166° (from water) (lit. (2), m.p. 170°).

B.

When the hydrolysis was carried out under the same conditions but at 50°, (3,6-dichloropyridazin-4-yl)acetic acid (XV) was obtained in 85% yield, m.p. 109-111° (from benzene); ir: 3060(w), 3100-2400 (broad), 1725(s), 1365(s), 1310(s), 1190(s), 1155(s) cm^{-1}; nmr: δ = 3.85 (s, 2, CH_2), 8.05 (s, 1, C_5-H).

Anal. Calcd. for $C_6H_4Cl_2N_2O_2$: C, 34.81; H, 1.95; N, 13.53; Cl, 34.26. Found: C, 34.99; H, 1.97; N, 13.55; Cl, 33.95.

(3-Chloro-6(1*H*)oxopyridazin-4-yl)acetic Acid Hydrazide.

The ester III (0.1 g.) and hydrazine hydrate (85%, 0.03 ml.) in ethanol (1 ml.) was heated on a steam-bath until a solution was obtained. The hydrazide separated from the cooled mixture, m.p. 242-245° (from ethanol), yield 0.05 g. (50%); ir: 3290(m), 3080-2500(broad), 1680(s), 1650(s), 1590(m), 1150(m), 1110(m), 970(m), 940(m), 920(m), 750(m), 630(m) cm^{-1}.

Anal. Calcd. for $C_6H_7ClN_4O_2$: C, 35.58; H, 3.46; N, 27.67; Cl, 17.51. Found: C, 35.82; H, 3.57; N, 27.52; Cl, 17.60.

Reactions of Compound IV with Hydrazine.

A.

A mixture of compound IV (0.3 g.) and hydrazine hydrate (85%, 1 ml.) was heated at 90° for 30 minutes. The cooled solution was evaporated to dryness. The residue was crystallized from water and gave the hydrazide X (0.22 g., 73%), m.p. 194-196°; uv λ max: 206 (log ε 4.36), 225s (log ε 3.68), and 298 (log ε 3.45) nm; ir: 3320(m), 3260(m), 3160-2750(broad), 1660(s), 1600(s), 1550(m), 1450(m), 1110(m), 1035(m), 1010(m), 670(m) cm^{-1}.

Anal. Calcd. for $C_6H_7ClN_4O_2$: C, 35.58; H, 3.46; N, 27.67; Cl, 17.51. Found: C, 35.42; H, 3.51; N, 27.79; Cl, 17.42.

B.

A mixture of compound IV (0.3 g.) and hydrazine hydrate (98%, 30 ml.) was refluxed for 1 hour. The solid, which separated from the cooled solution, was crystallized from water to give compound XI (0.06 g., 19%), m.p. 249-251°; uv λ max: 232 (log ε 4.22) and 330 (log ε 3.27) nm; ir: 3300(s), 3200(m),

3100-2600(broad), 1670(s), 1645(s), 1600(s), 1420(m), 1160(m), 930(m) cm^{-1}.

Anal. Calcd. for $C_6H_{10}N_6O_2$: C, 36.36; H, 5.09; N, 42.40. Found: C, 36.35; H, 5.20; N, 42.50.

(6-Hydrazino-3(2*H*)oxopyridazin-4-yl)acetic Acid (IX).

A.

Compound XI (0.45 g.) was refluxed with hydrochloric acid (18%, 6 ml.) for 3 hours. On cooling, compound IX, as its hydrochloride, separated, m.p. 223-226° dec. (from diluted hydrochloric acid), yield 0.35 g. (70%); ir: 3280(s), 3250-2500(broad), 1720(s), 1600(s), 1550(s), 1310(m), 1150(m), 860(m), 730(m) cm^{-1}.

Anal. Calcd. for $C_6H_8N_4O_3 \cdot HCl$: C, 32.66; H, 4.11; N, 25.40; Cl, 16.07. Found: C, 32.87; H, 4.11; N, 25.68; Cl, 16.44.

B.

Compound VIII (0.3 g.) was refluxed with hydrochloric acid (18%, 4 ml.) for 3 hours. From the cooled solution separated a solid (0.23 g., 75%) identical (m.p. and ir spectrum) to material prepared as above.

Reactions of Compound II with Hydrazine.

A.

To compound II (0.25 g.) was added hydrazine hydrate (85%, 0.8 ml.); the solution was stirred until the hydrazide VII (0.2 g., 80%) separated, m.p. 137-140° dec. (from water); ir: 3300(broad), 3060(w), 1650(s), 1610(s), 1550(s), 1370(s), 1140(s), 1050(s), 920(m), 570(m) cm^{-1}.

Anal. Calcd. for $C_6H_6Cl_2N_4O$: C, 32.61; H, 2.74; N, 25.35; Cl, 32.09. Found: C, 32.74; H, 2.57; N, 25.06; Cl, 32.14.

B.

When the same mixture was heated at 70-80° for 10 minutes, compound VIII separated from the cooled solution (82%), m.p. 194-196° dec. (from water); ir: 3300(s), 3200(m), 1650(s), 1630(m), 1150(m) cm^{-1}.

Anal. Calcd. for $C_6H_9ClN_6O$: C, 33.25; H, 4.19; N, 38.80; Cl, 16.37. Found: C, 33.18; H, 4.21; N, 38.83; Cl, 16.30.

Bis-benzylidene Derivative.

A solution of compound VIII (0.25 g.) and benzaldehyde (0.3 ml.) in methanol (2 ml.) was refluxed for 1.5 hours. The bis-benzylidene derivative (0.4 g., *ca.* quantitative yield) as white crystals was filtered from the cooled mixture, m.p. 284-285° dec. (from DMF); ir: 3200(w), 3100-2700(broad), 1680(s), 1610(s), 1595(m), 1430(m), 1380(m), 1260(m), 760(m), 695(m) cm^{-1}.

Anal. Calcd. for $C_{20}H_{17}ClN_6O$: C, 61.15; H, 4.36; N, 21.41; Cl, 9.03. Found: C, 61.15; H, 4.45; N, 21.30; Cl, 9.35.

Reaction of Compound VIII with Formic Acid.

Compound VIII (0.25 g.) was refluxed with formic acid (99%, 2 ml.) for 1 hour. The solution evaporated to dryness under reduced pressure left a residue which, crystallized from water, gave compound XVIII (0.12 g., 41%), as colourless needles, m.p. 219-220° dec.; uv λ max: 217 (log ε 4.52), 275 (log ε 3.29), and 301 (log ε 3.38) nm; ir: 3200(m), 3110(w), 1600(s), 1480(m), 1170(m), 825(m), 635(m) cm^{-1}; nmr: δ = 3.77 (s, 2, CH_2), 7.97 (s, 1, C-H oxad.), 8.4 (s, 1, C_8-H), 9.97 (broad, 1) and 10.18 (broad, 1) (OH and NH).

Anal. Calcd. for $C_8H_7ClN_6O_2$: C, 37.73; H, 2.77; N, 33.06; Cl, 13.92. Found: C, 37.69; H, 2.60; N, 33.23; Cl, 14.05.

(6-Hydrazino-*s*-triazolo[4,3-*b*]pyridazin-7-yl)acetic Acid Hydrazide (XIX).

Compound XVIII (0.14 g.) and hydrazine hydrate (85%, 1 ml.) were stirred at room temperature for 1 hour. The precipitate was collected and crystallized from ethanol to give compound XIX (0.11 g., 90%), as yellow crystals, m.p. 183-184°; uv λ max: 221 (log ε 4.36) and 283 (log ε 3.78) nm; ir: 3250(broad), 1660(s), 1620(s), 1550(s), 1490(s), 1350(m), 980(m), 720(m) cm^{-1}.

Anal. Calcd. for $C_7H_{10}N_8O$: C, 37.81; H, 4.54; N, 50.43. Found: C, 38.07; H, 4.52; N, 50.54.

6-Aminopyrrolo[3,2-*e*]-*s*-triazolo[4,3-*b*]pyridazin-7(8*H*)one (XXI).

Compound XIX (0.2 g.) was refluxed in toluene (3 ml.) for 48 hours. Compound XXI was filtered from the cooled mixture (0.12 g., 70%), m.p. > 300° (from water); uv λ max: 230 (log ε 4.35) and 285 (log ε 3.84) nm; ir: 3300-2900(broad), 1735(s), 1660(m), 1570(m), 1525(m), 1310(s), 1200(s), 1020(m), 960(m), 730(m), 660(s) cm^{-1}; nmr: δ = 3.70 (d, 2, J = 1.5 Hz, CH_2), 5.25 (broad, 2, exchangeable with deuterium oxide, NH_2), 8.01 (t, 1, J = 1.5 Hz, C_9-H), 9.33 (s, 1, C_3-H).

Anal. Calcd. for $C_7H_6N_6O \cdot H_2O$: C, 40.39; H, 3.87; N, 40.37. Found: C, 40.24; H, 3.88; N, 40.60.

The same compound was obtained by sublimation of compound XIX at 170°/0.03 mm Hg.

Bis-benzylidene Derivative (XXII).

Compound XXI (0.15 g.) and benzaldehyde (0.2 ml.) in methanol (2 ml.) were refluxed for 2 hours. The bis-benzylidene derivative (0.16 g., 80%), as yellow crystals, was filtered from the cooled solution, m.p. 255-257° dec. (first from DMF, then from ethanol); ir: 1710(s), 1610(s), 1590(s), 1570(s), 1520(s), 1330(s), 1160(s), 1020(m), 950(s), 770(m), 760(m), 710(s), 690(m) cm^{-1}; nmr: δ = 7.8 (m, 12, 2 x C_6H_5-CH=), 9.26 (s, 1) and 9.45 (s, 1) (C_3-H and C_9-H).

Anal. Calcd. for $C_{21}H_{14}N_6O$: C, 68.84; H, 3.85; N, 22.94. Found: C, 68.40; H, 4.04; N, 22.68.

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