

Transformations of N-Heteroarylformamidines and N-Heteroarylformamide Oximes New Syntheses and Transformations of Oxazolo[4,5-*d*]pyridazines

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New syntheses of oxazolo[4,5-*d*]pyridazine derivatives **7** and **11** were achieved by the cyclization of substituted N-pyridazin-5-ylformamide oximes **6** and **10**. Under mild reaction conditions the transformations of the substituted amino group at position 2 of the oxazolo[4,5-*d*]pyridazine system **7** occurred to produce the compounds **11**, **14**, and **15**, while under more drastic reaction conditions the nucleophilic attack at carbon at position 2 followed by the ring opening of the oxazole part of the molecule was observed to give the compounds **13**, **16**, **17** and **18**.

*(Keywords: Cyclization with C—O bond formation; Substituted N-pyridazin-5-ylformamidines and -formamide oximes; Oxazolo[4,5-*d*]pyridazines; Ring opening of oxazolo[4,5-*d*]pyridazines)*

*Transformationen von N-Heteroarylformamidinen und N-Heteroarylformamidinoximen. Neue Synthesen und Transformationen von Oxazolo[4,5-*d*]pyridazinen*

Mittels Cyclisierung substituierter N-Pyridazin-5-ylformamidoxime **6** und **10** wurden neue Synthesemöglichkeiten von Oxazolo[4,5-*d*]pyridazinderivaten erschlossen. Bei milden Reaktionsbedingungen trat Transformation der substituierten Aminogruppe an Position 2 des Oxazolo[4,5-*d*]pyridazin-Systems unter Bildung der Verbindungen **11**, **14** und **15** ein, währenddessen unter drastischeren Reaktionsbedingungen ein nucleophiler Angriff am Kohlenstoff-2, gefolgt von einer Ringöffnung unter Bildung der Verbindungen **13**, **16**, **17** und **18** eintrat.

Introduction

N-Heteroarylformamidines and N-heteroarylformamide oximes are versatile intermediates in the syntheses of various heterocyclic systems,

such as *s*-triazolo[1,5-*x*]azines^{1,2}, isothiazolo[4,5-*d*]pyrazines³, and other systems including purines and pteridines⁴⁻⁸. Recently, we have described a new simple method for the preparation of 2-aminooxazolo[4,5-*c*]quinoline⁹, oxazolo[4,5-*b*]pyridine derivatives¹⁰, and oxazolo[5,4-*d*]pyrimidines¹¹ by cyclization of the corresponding *o*-hydroxy substituted N-heteroarylformamide oximes with N,N-dimethylformamide dimethyl acetal (*DMFDMA*)¹².

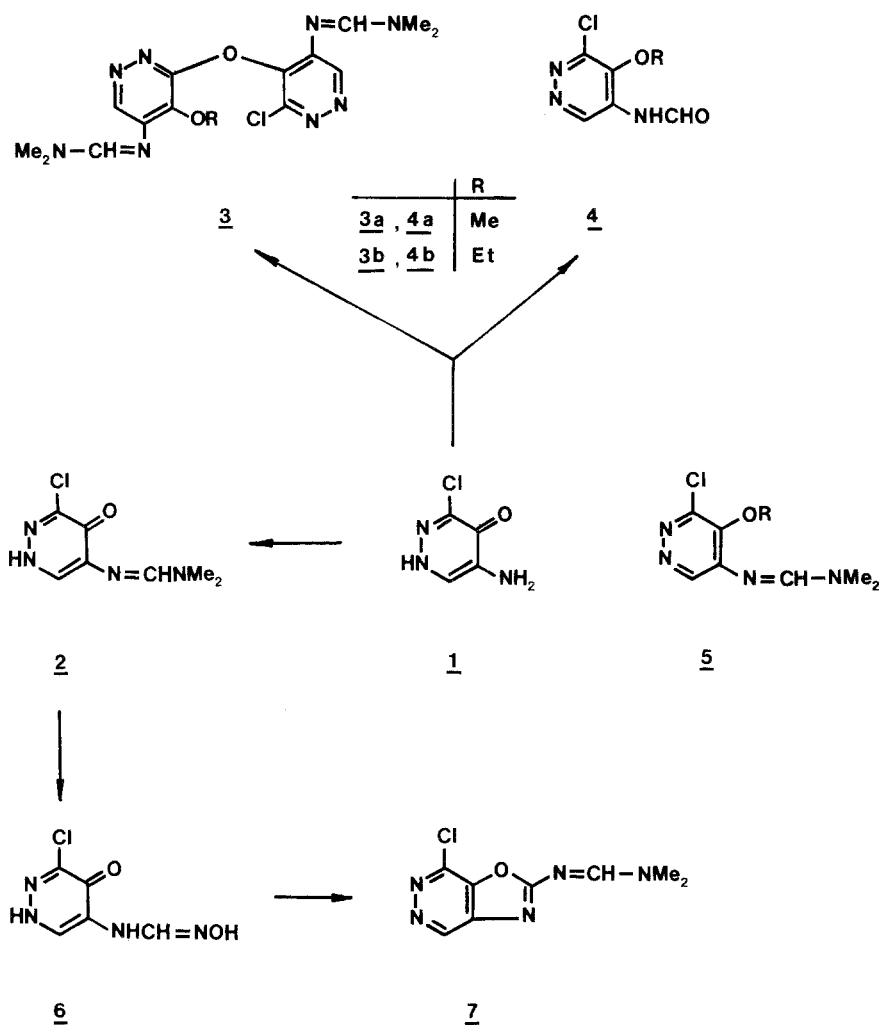
In this communication we report a new approach to the synthesis of a little known oxazolo[4,5-*d*]pyridazine system, as an extension of our previous studies, since the only representative of this bicyclic system was reported in 1958 by condensation of either 5-amino-3,4-dichloropyridazine or 5-amino-3-chloropyridazin-4(1*H*)-one with benzoyl chloride^{13,14}.

Results and Discussion

5-Amino-3-chloropyridazin-4(1*H*)-one (**1**) was used as the starting compound. It was transformed with one mole of N,N-dimethylformamide dimethyl acetal (*DMFDMA*) in toluene at room temperature into 3-chloro-5-(N,N-dimethylaminomethyleneamino)-pyridazin-4(1*H*)-one (**2**) in 73% yield. On the other hand, with an excess of *DMFDMA* two products were isolated [5-(N,N-dimethylaminomethyleneamino)-4-methoxypyridazin-3-yl][3-chloro-5-(N,N-dimethylaminomethyleneamino)-pyridazin-4-yl]ether (**3a**) in 35% yield and 3-chloro-5-formylamino-4-methoxypyridazine (**4a**) in 27% yield. Compound **3a** was the result of an intramolecular nucleophilic substitution of the chlorine at position 3 with a potential hydroxy group or its anion at position 4 of another molecule and O-methylation of the remaining hydroxy group, while compound **4a** was formed by hydrolysis of the corresponding 3-chloro-5-(N,N-dimethylaminomethylaminomethyleneamino)-4-methoxypyridazine (**5**), an intermediate which could not be isolated from the reaction mixture. Similarly, with N,N-dimethyl formamide diethyl acetal (*DMFDEA*), under essentially the same reaction conditions, the corresponding [5-(N,N-dimethylaminomethyleneamino)-4-ethoxypyridazin-yl][3-chloro-5-(N,N-dimethylaminomethyleneamino)-pyridazin-yl]ether (**3b**) and 3-chloro-4-ethoxy-5-formylaminopyridazine (**4b**) were obtained.

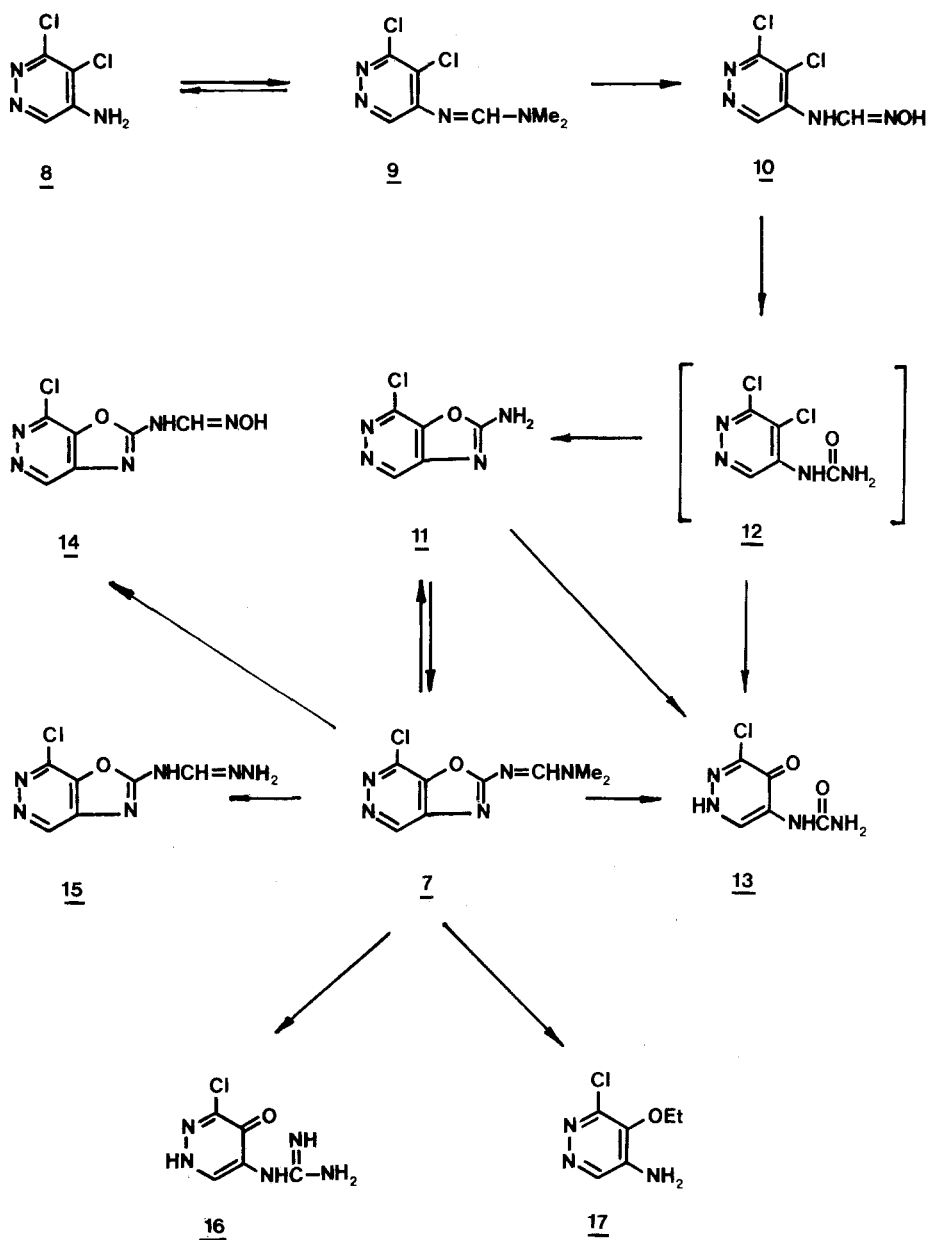
In further transformations the compound **2** was treated with hydroxylamine hydrochloride to give 3-chloro-5-hydroxyiminomethyleneaminopyridazin-4(1*H*)-one (**6**) in 64% yield. This compound was further converted with *DMFDMA* as cycloadehydrating agent into 7-chloro-2-(N,N-dimethylaminomethyleneamino)-oxazolo[4,5-*d*]pyridazine (**7**). The mechanism for the formation of the latter compounds is the same as already proposed for the formation of 2-

Scheme 1



aminooxazolo[4,5-*c*]quinoline derivatives⁹, and heteroaryl substituted 1,2,4- Δ^2 -oxadiazolines¹⁵, in which the corresponding N-heteroaryl substituted cyanoamino intermediates are formed first followed by cyclization into the corresponding aminooxazoloazines and further transformation into the corresponding amidines with an excess of *DMFDMA* (Scheme 1). The same compound was obtained also from 2-amino-7-chlorooxazolo[4,5-*d*]pyridazine (**11**) with *DMFDMA* (Scheme 2).

Scheme 2

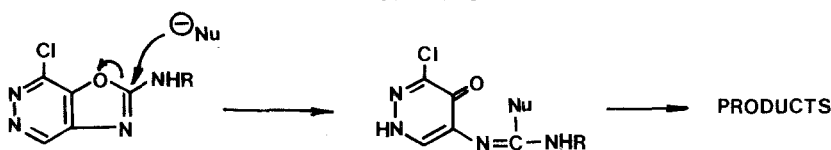


On the other hand, the oxazolo[4,5-*d*]pyridazine system could be formed also in the following way. 5-Amino-3,4-dichloropyridazine (8) was converted with *DMFDMA* into the corresponding 3,4-dichloro-5-(*N,N*-dimethylaminomethyleneamino)-pyridazine (9). When this compound was left with hydroxylamine hydrochloride at room temperature for one hour, the corresponding 3,4-dichloro-5-hydroxyiminomethyleneaminopyridazine (10) was isolated in 75% yield, while after 24 hours at room temperature 2-amino-7-chlorooxazolo[4,5-*d*]pyridazine (11) was formed in 54% yield. Under more drastic reaction conditions, when the compound 9 was heated with hydroxylamine hydrochloride in ethanol for four hours, the corresponding 3-chloro-5-ureidopyridazin-4(1*H*)-one (13) was obtained in 70% yield, as the result of either the *Beckmann* rearrangement of the formamide oxime group in the compound 10 and nucleophilic substitution of chlorine at position 4 with a hydroxy group, or hydrolysis of 2-amino-7-chlorooxazolo[4,5-*d*]pyridazine (11). The formation of 2-amino-7-chlorooxazolopyridazine (11) could thus proceed most probably through 3,4-dichloro-5-ureidopyridazine (12). However, all attempts to isolate this intermediate were not successful (Scheme 2).

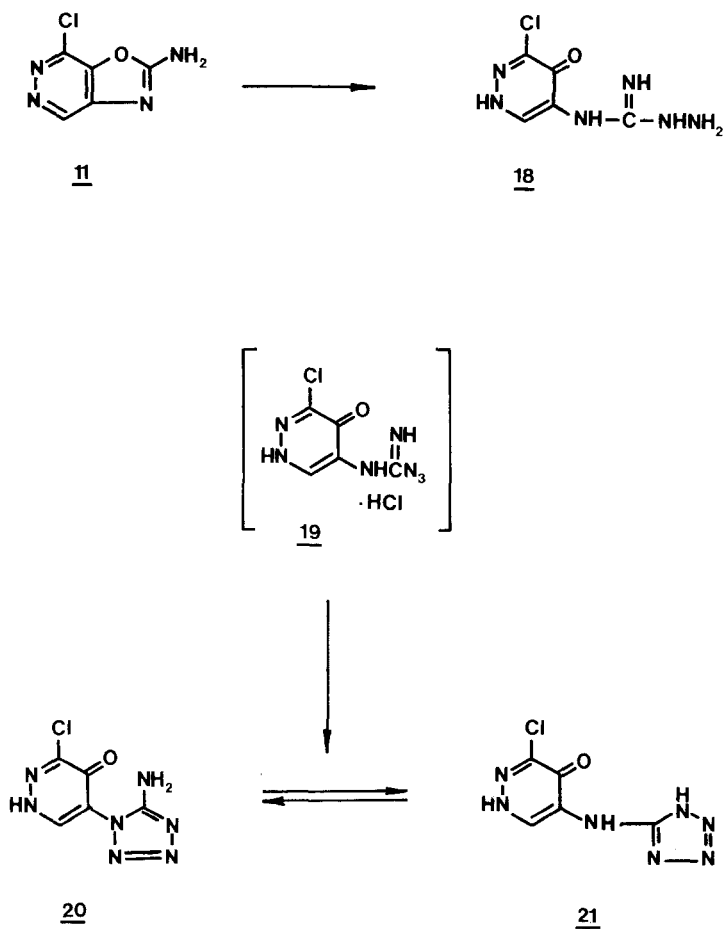
For further studies on the reactivity of this bicyclic system the following transformations were carried out. Under mild conditions—for example anhydrous ammonia in ethanol at room temperature with sodium ethoxide or with sodium hydrogen sulphide—compound 7 was converted into 2-amino-7-chlorooxazolo[4,5-*b*]pyridazine (11), with hydroxylamine hydrochloride into the corresponding hydroxyiminomethyleneamino derivative 14 and with hydrazine hydrate into the corresponding hydrazinomethyleneamino derivative 15.

Under more drastic reaction conditions the oxazolo[4,5-*d*]pyridazine system is not stable. Nucleophilic addition of nucleophiles to position 2 was taking place, followed by ring opening of the oxazole part of the molecule¹⁶. In this respect the following transformations were carried out. Heating of compound 7 with 10% aqueous hydrochloric acid produced 3-chloro-5-ureidopyridazin-4(1*H*)-one (13), with ethanol saturated with gaseous ammonia 3-chloro-5-guanidinopyridazin-4(1*H*)-one (16) or 5-amino-3-chloro-4-ethoxypyridazine (17) (Scheme 2).

Scheme 3



Scheme 4



Further evidence for a nucleophilic attack at position 2 is the reaction with hydrazine (see Scheme 3). When compound **11** was treated with hydrazine hydrate in ethanol under reflux for four hours, the corresponding 5-aminoguanidino-3-chloropyridazin-4(1H)-one (**18**) was formed in 49% yield. This was further transformed with nitrous acid into 5-carboxamideazido-3-chloropyridazin-4(1H)-one (**19**), which showed a characteristic azide band in the IR spectrum ($\nu_{\text{N}_3} = 2180 \text{ cm}^{-1}$) and could be isolated only at room temperature in the form of the hydrochloride salt **19**. By neutralization of an aqueous suspension of this intermediate with solid sodium hydrogen carbonate cyclization was observed producing

compound **20**. The structure of it was supported by the ^1H NMR spectrum which showed a broad singlet (2 H) for the NH_2 group, excluding thus the alternative structure **21** (Scheme 4).

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Experimental

Melting points were determined on a *Kofler* hot plate m.p. apparatus. ^1H NMR spectra were recorded on a JEOL C 60 HL spectrometer (*TMS* as internal standard, δ -values in ppm), mass spectra on a Hitachi-Perkin-Elmer RMU-6 L mass spectrometer and IR spectra on a Perkin-Elmer 727 B spectrometer. Elemental analysis (C, H, N) were obtained with a Perkin-Elmer Analyser 240 C.

3-Chloro-5-(*N,N*-dimethylaminomethyleneamino)-pyridazin-4(1*H*)-one (**2**)

A mixture of 200 mg 5-amino-3-chloropyridazin-4(1*H*)-one (**1**)¹³, 0.2 ml of *N,N*-dimethylformamide dimethyl acetal (*DMFDMA*) and 10 ml of anhydrous toluene was stirred at room temperature for 20 h. The precipitate was collected by filtration to give 200 mg (73%) of the product, m. p. 225–228 °C (from ethanol). MS (*m/e*): 200 (M^+). NMR (*DMSO-d*₆): 2.90 (br, s, NMe_2), 7.93 (s, $\text{CH}=\text{N}$), 9.04 (s, H_6).

$\text{C}_7\text{H}_9\text{N}_4\text{ClO}$ (200.63). Calcd. C 41.90 H 4.52 N 27.93.
Found. C 41.89 H 4.62 N 28.19.

[5-(*N,N*-Dimethylaminomethyleneamino)-4-methoxy-pyridazin-3-yl] [3-chloro-5-(*N,N*-dimethylaminomethyleneamino)pyridazin-4-yl]ether (**3a**) and 3-Chloro-5-formylamino-4-methoxy-pyridazine (**4a**)

A solution of 445 mg **1**, 1.2 ml of *DMFDMA* and 20 ml of anhydrous toluene was heated under reflux for 8 h. After cooling the precipitate was collected by filtration to give 140 mg (35%) of the compound **3a**, m. p. 265–268 °C (dec.) (from ethanol). MS (*m/e*): 378 (M^+). NMR (*DMSO-d*₆): 2.85 (s), 2.90 (s) (NMe_2), 3.93 (s, *OMe*), 7.80 (s, $\text{CH}=\text{N}$), 8.73 (s, H_6), 9.52 (s, H_6).

$\text{C}_{15}\text{H}_{19}\text{N}_8\text{ClO}_2$ (378.83). Calcd. C 47.56 H 5.06 N 29.88.
Found. C 47.72 H 5.21 N 29.60.

The filtrate obtained above was evaporated in vacuo, the dry residue dissolved in 5 ml of chloroform and the mixture separated by preparative thin layer chromatography (PSC-Fertigplatten Kieselgel 60 F 254, Merck, with a mixture of chloroform and ethanol, 9: 1). The band with $R_f = 0.4$ was eluted with chloroform to give, after evaporation of the solvent in vacuo, 50 mg (27%) of **4a**, m. p. 250–253 °C (from ethanol), MS (*m/e*): 187 (M^+). NMR (*DMSO-d*₆): 3.93 (s, *OMe*), 8.27 (s, CHO), 9.22 (s, H_6), 9.91 (br, s, NH).

$\text{C}_6\text{H}_6\text{N}_3\text{ClO}_2$ (187.59). Calcd. C 38.41 H 3.23 N 22.34.
Found. C 38.14 H 3.15 N 22.15.

[4-Ethoxy-5-(*N,N*-dimethylaminomethyleneamino)-pyridazin-3-yl] [3-chloro-5-(*N,N*-dimethylaminomethyleneamino)-pyridazin-4-yl]ether (**3b**) and 4-Ethoxy-5-formylamino-3-chloropyridazine (**4b**)

A solution of 400 mg **1**, 1 ml of *DMFDEA* and 20 ml of anhydrous toluene was heated under reflux for 8 h. The precipitate was collected after cooling to give 100 mg (37%) of **3b**, m. p. 250–253 °C (dec.) (from ethanol). MS (*m/e*): 392 (M^+). NMR (*DMSO-d*₆): 1.38 (t, *Me*), 2.92 (s), 2.97 (s), (*NMe*₂), 4.10 (q, *CH*₂), 7.92 (s), 7.95 (s) (*CH=N*), 8.78 (s), 9.40 (s) (*H*₆, *H*₈), *J*_{*CH*₂*Me*} = 7.0 Hz.

$C_{16}H_{21}N_8ClO_2$ (392.85). Calcd. C 48.92 H 5.38 N 28.52.
Found. C 48.39 H 5.28 N 28.68.

The filtrate obtained above was evaporated in vacuo, the dry residue was dissolved in chloroform and separated by preparative thin layer chromatography (PSC Fertigplatten Kieselgel 60 F 254, Merck, with a mixture of chloroform and ethanol, 9:1). The elution of the band with *R*_f = 0.6 with chloroform gave 35 mg (25%) of **4b**, m. p. 240–241 °C (from ethanol). MS (*m/e*): 201 (M^+). NMR (*DMSO-d*₆): 1.35 (t, *Me*), 4.17 (q, *CH*₂), 8.27 (s, *CHO*), 9.26 (s, *H*₆), 9.95 (br. s, *NH*), *J*_{*CH*₂*Me*} = 7.0 Hz.

$C_7H_8N_3ClO_2$ (201.62). Calcd. C 41.70 H 4.00 N 20.84.
Found. C 41.95 H 4.02 N 21.07.

3-Chloro-5-hydroxyiminomethyleneaminopyridazin-4(1*H*)-one (**6**)

A solution of 500 mg **2**, 200 mg of hydroxylamine hydrochloride and 10 ml of methanol was heated under reflux for 2 h. After cooling the precipitate was collected by filtration to give 300 mg (64%) of the product, m. p. 180–182 °C (from ethanol). MS (*m/e*): 188 (M^+). NMR (*DMSO-d*₆): 7.72 (br. s, *NHCH*), 8.55 (s, *H*₆), 9.52 (br. s, *NOH*).

$C_5H_5N_4ClO_2$ (188.66). Calcd. C 30.40 H 3.06 N 28.34.
Found. C 29.98 H 3.47 N 28.02.

7-Chloro-2-(*N,N*-dimethylaminomethyleneamino)-oxazolo[4,5-*d*]pyridazine (**7**)

A mixture of 200 mg **6**, 0.7 ml of *DMFDMA* and 5 ml of anhydrous toluene was stirred at room temperature for 8 h. The precipitate was collected by filtration to give 170 mg of the product, m. p. 190–193 °C (from water). MS (*m/e*): 225 (M^+). NMR (*DMSO-d*₆): 3.21 (s), 3.27 (s) (*NMe*₂), 8.56 (s, *CH=N*), 9.21 (s, *H*₄).

$C_8H_8N_5ClO$ (225.64). Calcd. C 42.58 H 3.57 N 31.04.
Found. C 42.83 H 3.63 N 31.08.

5-Amino-3,4-dichloropyridazine (**8**)

a) A mixture of 30 mg **9** and 10 ml of 0.5 *N* aqueous sodium hydroxide was heated under reflux for 3 h. After cooling the precipitate was collected and washed with water to give 20 mg (74%) of the product, m. p. 183–185 °C (from water) (Lit.¹³ m. p. 178 °C).

b) A mixture of 110 mg **9** and 5 ml of 10% aqueous hydrochloric acid was heated under reflux for 1 h. After cooling, the solution was neutralized with 2 *N* aqueous potassium hydroxide and the precipitate collected to give 70 mg (85%) of

the product. The IR spectrum of the compound was identical with that of the compound obtained under a).

c) A mixture of 45 mg **9**, 0.1 ml of 80% hydrazine hydrate and 10 ml of ethanol was heated under reflux for 5 h. The solvent was evaporated in vacuo and the residue recrystallized from water to give 25 mg (74%) of the product. The IR spectrum of the compound was identical with that of the compound obtained under a).

3,4-Dichloro-5-(N,N-dimethylaminomethyleneamino)-pyridazine (9)

A mixture of 1.7 g **8**, 1.7 ml of *DMFDMA* and 20 ml of anhydrous toluene was heated under reflux for 2 h. Volatile components were evaporated in vacuo and the residue recrystallized from benzene to give 1.4 g (64%) of the product, m. p. 103–105 °C. MS (*m/e*): 218 (*M*⁺). NMR (*DMSO-d*₆): 3.03 (s), 3.15 (s) (*NMe*₂), 8.18 (s, CH=N), 8.83 (s, H₆).

$C_7H_8N_4Cl_2$ (219.08). Calcd. C 38.37 H 3.67 N 25.58.
Found. C 38.35 H 3.75 N 25.83.

3,4-Dichloro-5-hydroxyiminomethyleneaminopyridazine (10)

A suspension of 300 mg **9** and 150 mg of hydroxylamine hydrochloride in 10 ml of ethanol was stirred at room temperature for 1 h. The new precipitate, which was formed during this time, was collected by filtration to give 200 mg (75%) of the product, m. p. 170 °C (dec.) (from a mixture of tetrahydrofuran and petroleum ether). MS (*m/e*): 206 (*M*⁺). NMR (*DMSO-d*₆): 8.37 (br. s, CHNH), 9.0 (br. s, CHNH), 9.3 (s, H₆).

$C_5H_4N_4Cl_2O$ (207.03). Calcd. C 29.01 H 1.95 N 27.07.
Found. C 29.22 H 1.92 N 27.25.

*2-Amino-7-chlorooxazolo[4,5-*d*]pyridazine (11)*

A mixture of 160 mg **7** and 10 ml of 25% aqueous ammonia was heated under reflux for 2 h. The volatile components were evaporated in vacuo to give 90 mg (75%) of the product, m. p. 300 °C (from water). MS (*m/e*): 170 (*M*⁺). NMR (*DMSO-d*₆): 8.68 (br. s, NH₂), 9.30 (s, H₄).

$C_5H_3N_4ClO$ (170.56). Calcd. C 35.21 H 1.77 N 32.85.
Found. C 35.20 H 1.73 N 32.53.

b) A solution of 225 mg **7** and 100 mg of sodium ethoxide in 10 ml of ethanol was heated under reflux for 5 h. The precipitate, collected after cooling, was dissolved in 10 ml of water and neutralized with 2*N* hydrochloric acid. The precipitate was collected to give 50 mg (29%) of the product. The IR spectrum of it was identical with that of the compound obtained under a).

c) A solution of 225 mg **7** and 100 mg of sodium hydrogen sulphide in 10 ml of water was heated under reflux for 3 h. After cooling the precipitate was collected to give 50 mg (29%) of the product. The IR spectrum of it was identical with that of the compound obtained under a).

d) A solution of 110 mg **7**, 10 ml of ethanol and 5 ml of liquid ammonia was left in a sealed vessel at room temperature for 12 h. The residue obtained after evaporation of volatile components in vacuo was suspended in 10 ml of water and the precipitate was collected to give 30 mg (35%) of the product. The IR spectrum of it was identical with that of the compound obtained under a).

e) A solution of 220 mg **9**, 80 mg of hydroxylamine hydrochloride and 10 ml of

ethanol was stirred at room temperature for 18 h. The solvent was evaporated in vacuo, 10 ml of water was added to the residue and the precipitate collected to give 90 mg (54%) of the product. The IR spectrum of it was identical with that of the compound obtained under a).

3-Chloro-5-ureidopyridazin-4(1H)-one (13)

a) A mixture of 150 mg **7** and 10 ml of conc. hydrochloric acid was heated under reflux for 2 h. After cooling the precipitate was collected to give 80 mg (70%) of the product, m. p. 270 °C (dec.) (from ethanol). MS (*m/e*): 171 (M^+ -17). NMR ($DMSO-d_6$): 6.53 (br. s, NH_2), 8.53 (s, NH), 9.10 (s, H_6).

$C_5H_5N_4ClO_2$ (188.58). Calcd. C 31.83 H 2.67 N 29.71.

Found. C 31.69 H 2.76 N 29.56.

b) A solution of 230 mg **9**, 120 mg of hydroxylamine hydrochloride and 10 ml of ethanol was heated under reflux for 4 h. After cooling the precipitate was collected to give 110 mg (59%) of the product. The IR spectrum of the compound was identical with that of the compound obtained under a).

7-Chloro-2-hydroxyiminomethyleneaminooxazolo[4,5-d]pyridazine (14)

A solution of 150 mg **7**, 100 mg of hydroxylamine hydrochloride in 10 ml of methanol was heated under reflux for 3 h. The crystals were, after cooling, collected to give 50 mg (36%) of the product, m. p. 270 °C (dec.) (from ethanol). MS (*m/e*): 213 (M^+). NMR ($DMSO-d_6$, 130 °C): 8.70 (s, CHNH), 9.20 (s, H_4).

$C_6H_4N_5ClO_2$ (213.59). Calcd. C 33.74 H 1.88 N 32.79.

Found. C 33.49 H 1.83 N 32.20.

7-Chloro-2-hydrazinomethyleneaminooxazolo[4,5-d]pyridazine (15)

A solution of 225 mg **7**, 0.1 ml of 80% hydrazine hydrate and 10 ml of ethanol was heated under reflux for 2 h. The crystals were—after cooling—collected to give 160 mg (75%) of the product, m. p. > 305 °C (from water). MS (*m/e*): 212 (M^+). NMR ($DMSO-d_6$): 7.97 (s, CH=N), 8.95 (s, H_4).

$C_6H_5N_6ClO$ (212.61). Calcd. C 33.89 H 2.37 N 39.53.

Found. C 34.16 H 2.36 N 39.21.

3-Chloro-5-guanidinopyridazin-4(1H)-one (16)

A solution of 300 mg **7** in 10 ml of ethanol was saturated with gaseous ammonia and the mixture was heated in an autoclave at 100 °C for 24 h. After cooling, ethanol and ammonia were evaporated in vacuo to give 160 mg (64%) of the product, m. p. 230 °C (dec.) (from water). MS (*m/e*): 170 (M^+ -17). NMR ($DMSO-d_6$, 150 °C): 6.35 [br. s, $(NH_2)_2$], 7.97 (s, H_6).

$C_5H_6N_5ClO$ (187.60). Calcd. C 32.01 H 3.22 N 37.33.

Found. C 32.00 H 3.19 N 37.44.

5-Amino-3-chloro-4-ethoxypyridazine (17)

A solution of 300 mg **7** in 10 ml of ethanol was saturated with gaseous ammonia. The mixture was heated in an autoclave at 80 °C for 24 h. After cooling, the volatile components were evaporated in vacuo, the residue was suspended in 10 ml of water and the precipitate collected by filtration to give 125 mg (54%) of the product, m. p. 129–130 °C (from ethanol). MS (*m/e*): 173 (M^+). NMR

(*DMSO-d*₆): 1.33 (t, Me), 4.07 (q, CH₂), 5.58 (br. s, NH), 7.83 (s, H₆), $J_{\text{CH}_2\text{Me}} = 7.0$ Hz.

C₆H₈N₃ClO (173.61). Calcd. C 41.50 H 4.61 N 24.20.

Found. C 41.65 H 4.72 N 24.07

5-Aminoguanidino-3-chloropyridazin-4(1H)-one (18)

A solution of 340 mg **11**, 0.2 ml of 80% hydrazine hydrate in 10 ml of ethanol was heated under reflux for 4 h. The precipitate was (after cooling) collected by filtration to give 200 mg (49%) of the product, m.p. 205 °C (dec.) (from water). NMR (*DMSO-d*₆, 50 °C): 8.05 (s, H₆).

C₅H₇N₆ClO (202.61). Calcd. C 29.65 H 3.49 N 41.50.

Found C 29.68 H 3.50 N 41.96.

3-Chloro-5-carboxamideazidopyridazin-4(1H)-one (19) and 5-(5-Aminotetrazol-4-yl)-3-chloropyridazin-4(1H)-one (20)

To a solution of 350 mg **18** in 40 ml of 10% hydrochloric acid a solution of 300 mg of sodium nitrite in 5 ml of water was added dropwise at 0 °C and the resulting suspension was stirred at this temperature for additional 3 h. The precipitate was collected to give **19**. IR (KBr): $\nu_{\text{N}_3} = 2180 \text{ cm}^{-1}$. **19** was suspended in water, neutralized with sodium hydrogen carbonate and the precipitate collected to give 210 mg (75%) of compound **20**, m.p. 220 °C (dec.) (from water). MS (*m/e*): 213 (*M*⁺). NMR (*DMSO-d*₆): 6.70 (s, NH₂), 8.87 (s, H₆).

C₅H₄N₇ClO (213.60). Calcd. C 28.11 H 1.89 N 45.91.

Found. C 28.28 H 1.80 N 45.90.

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- ¹⁶ An analogous ring opening of the oxazole ring has been observed also in benzoxazole series¹⁷.
- ¹⁷ *Cornforth J. W.*, Benzoxazoles and Related Systems. In: Heterocyclic Compounds (*Elderfield R. C.*, ed.), Vol. 5, pp. 418–451. New York: J. Wiley. 1957.