Monatshefte für Chemie 127, 1263–1272 (1996)

Monatshefte für Chemie
Chemical Monthly

Synthesis of New Triazoloquinoxalines, Pyrroloquinoxalines, and Pyrimidopyrroloquinoxalines

A. A. Geies*, A. M. K. El-Dean, and **O. S. Moustafa**

Chemistry Department, Faculty of Science, Assiut University, Assiut 71516, Egypt

Summary. When 2-hydroxyquinoxaline-3-carboxamide (**1**) was reacted with $POCl_3$ in *DMF*, 2-chloro-3-dimethylaminomethylenecarboxamide(**2**) was obtained. The chloro compound **2** was reacted with thiourea and hydrazine hydrate to give the corresponding mercapto and hydrazino derivatives **3** and **8**, respectively. On the other hand, 2-chloroquinoxaline-3-carbonitrile (**13**) reacted with ethyl glycinate to the glycinate derivative **14** which was cyclized to pyrroloquinoxaline **15** by heating with sodium ethoxide. Pyrimidopyrroloquinoxaline derivatives **16** and **17** were obtained *via* the reaction of **15** with formamide and phenyl isothiocyanate, respectively.

Keywords. Quinoxaline; Triazoloquinoxalines; Pyrroloquinoxalines; Pyrimidopyrroloquinoxalines.

Synthese neuer Triazolochinoxaline, Pyrrolochinoxaline und Pyrimidopyrrolochinoxaline

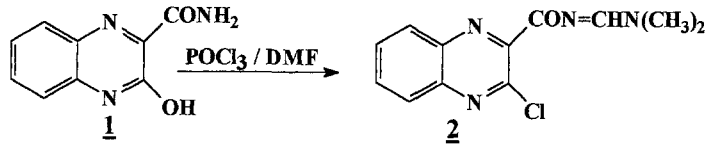
Zusammenfassung. Wenn man 2-Hydroxychinoxalin-3-carboxamid (**1**) mit $POCl_3$ in *DMF* reagieren läßt, erhält man 2-Chlor-3-dimethylaminomethylencarboxamid (**2**). Die Chlorverbindung **2** wurde mit Thioharnstoff und Hydrazinhydrat zu den entsprechenden Mercapto- und Hydrazinderivaten **3** und **8** umgesetzt. Aus 2-Chlorchinoxalin-3-carbonsäurenitril (**13**) und Ethylglycinat erhält man **14**, das durch Erhitzen mit Natriumethylat zum Pyrrolochinoxalin **15** cyclisiert wurde. Die Pyrimidopyrrolochinoxalinderivate **16** und **17** wurden durch Reaktion von **15** mit Formamid bzw. Phenylisothiocyanat erhalten.

Introduction

Numerous quinoxaline derivatives have been synthesized and still attract the attention of many research groups due to their biological importance [1–5]. For example, quinoxaline-2-one has been shown to exhibit anti-inflammatory [6], tranqulizing, and antidepressant properties [7]. Also, triazolo[4,3-*a*]quinoxaline and pyrroloquinoxaline derivatives shown excellent bactericidal [8] and fungicidal [9] activity. In this context and in continuation of our investigations upon the synthesis of polyheterocyclic systems containing a quinoxaline moiety [10, 11], we report herein the synthesis of some new triazoloquinoxalines, pyrroloquinoxalines, and pyrimidopyrroloquinoxalines of potential biological activity.

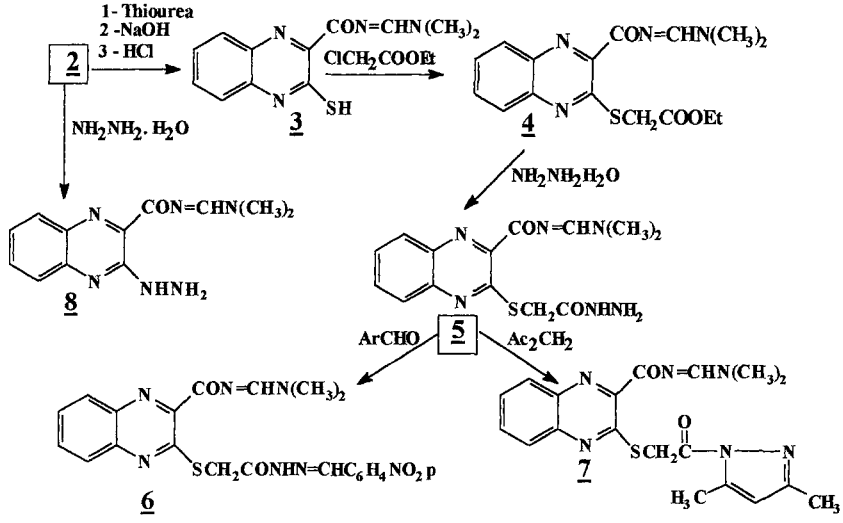
Results and Discussion

Earlier, 2-chloroquinoxaline-3-carbonitrile-4-oxide has been synthesized from 1,2-dihydro-2-oxoquinoxaline-3-carbonitrile-4-oxide and a $POCL_3/DMF$ mixture [12]. Application of this reaction to 2-hydroxyquinoxaline-3-carboxamide (**1**) resulted in a compound with a m.p. of 192 °C obviously differing from that of 2-chloroquinoxaline-3-carbonitrile (160 °C). The ^1H NMR spectrum of this compound in $CDCl_3$ gives signals at $\delta = 2.85$ (s), 7.0–7.3 (m), and 8.1–8.25 (m) ppm. The IR spectrum shows no absorption characteristic for the CN group, and the absorption for C=O is shifted to longer wavelength. These evidences pointed at 2-chloroquinoxaline-3-N-dimethylaminomethylenecarboxamide (**2**), the $POCl_3/DMF$ mixture acting as a *Vilsmeyer* reagent (cf. Scheme 1).



Scheme 1

Compound **2** was reacted with thiourea to give the corresponding 2-mercapto derivative **3** which in turn could easily be S-alkylated by ethyl chloroacetate in the presence of sodium acetate, affording the mercaptoacetate derivative **4**. Upon refluxing with hydrazine hydrate in ethanol, **4** underwent hydrazinolysis to the corresponding carbohydrazide derivative **5**. Reaction of **5** with *p*-nitrobenzaldehyde and acetylacetone yielded the carbohydrazone and pyrazolyl derivatives **6** and **7**, respectively. The 2-hydrazino derivative **8** was obtained by the reaction of **2** with hydrazine hydrate in ethanol (Scheme 2).



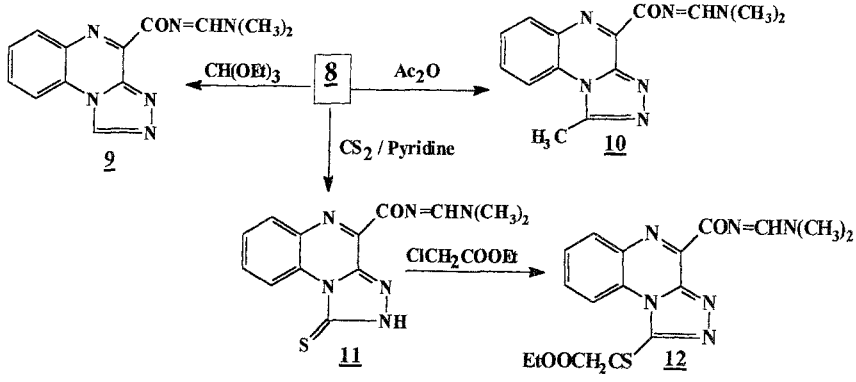
Scheme 2

The hydrazino compound **8** was condensed with triethyl orthoformate and with acetic anhydride to give the triazoloquinoxalines 9 and 10, respectively. **8** was also reacted with CS_2 in pyridine to afford the mercapto triazoloquinoxaline **11** which was alkylated by refluxing with ethyl chloroacetate in ethanol containing anhydrous sodium acetate to give the ester derivative **12** (Scheme 3).

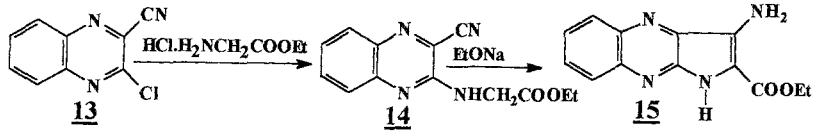
On the other hand, we employed 2-chloroquinoxaline-3-carbonitrile (**13**) as starting material to synthesize other heterocyclic systems. Reaction with ethyl glycinate hydrochloride in DMF/K_2CO_3 resulted in ethyl (3-cyano-quinoxaline-2-yl) glycinate (**14**). Upon treatment with ethanolic sodium ethoxide solution, **14** undergoes cyclization to ethyl 3-amino-1*H*-pyrrolo[2,3-*b*]quinoxaline-2-carboxylate (**15**). (Scheme 4).

Pyrimido[4′,5′:4,5]-5*H*-pyrrolo[2,3-*b*]quinoxaline-4(3*H*)-one (**16**) was produced from the reaction of compound **15** with formamide. Pyrimidopyrroloquinoxaline **17** was obtained from compound **15** by refluxing it with phenyl isothiocyanate in pyridine. **17** was converted into the corresponding hydrazino derivative **18** with hydrazine hydrate in pyridine. Other derivatives of *o*-amino ester **15** were produced *via* hydrazinolysis to give the corresponding carbohydrazide **19** (Scheme 5).

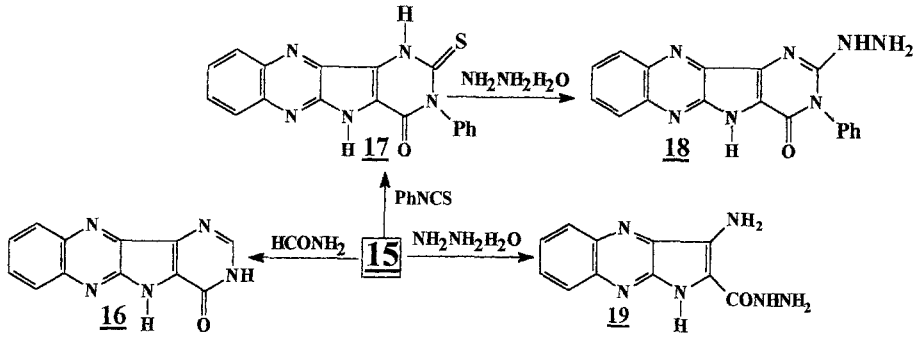
The carbohydrazide **19** was reacted with aromatic aldehydes in ethanol to give the corresponding carbohydrazones **20**. Reaction of **19** with nitrous acid gave the corresponding carboazide **21** which underwent a *Curtius* rearrangement upon boiling in dry xylene to give imidazopyrroloquinoxaline **22**. Other pyrimidopyrroloquinoxalines were synthesized using *o*-aminocarbohydrazide as starting material; thus, when compound **19** was refluxed with formic acid or acetic anhydride, it gave N-formylpyrimidopyrroloquinoxaline (**23**) or N-diacetyl- aminopyrimidopyrroloquinoxaline (**24**), respectively (Scheme 6).



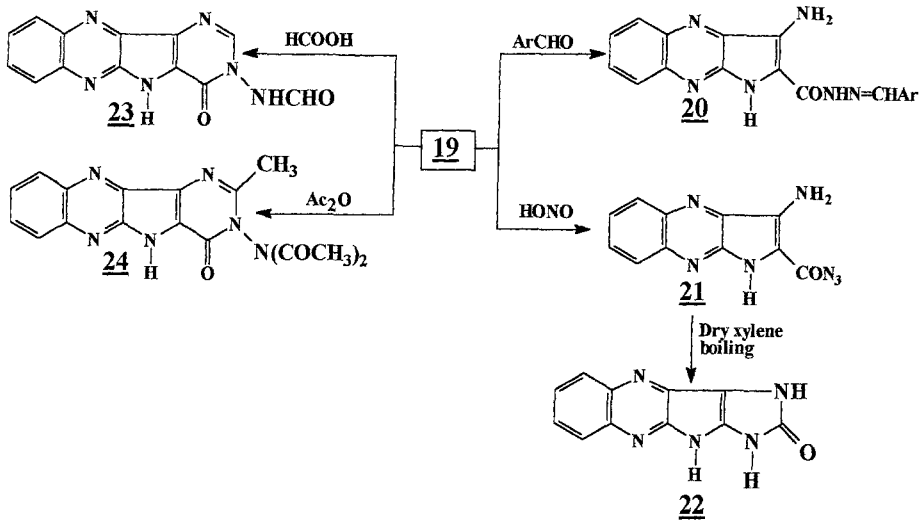
Scheme 3



Scheme 4



Scheme 5

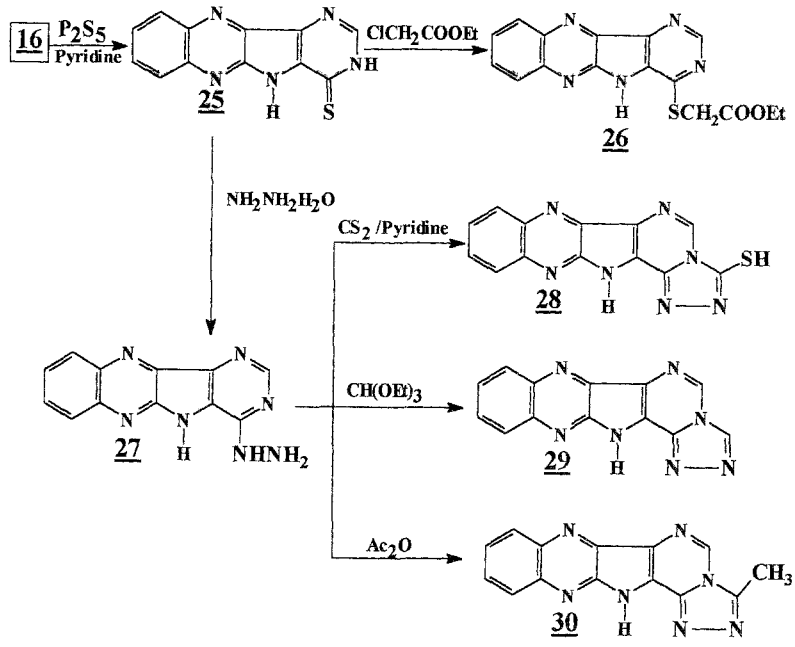


Scheme 6

The pyrimidinone derivative **16** was converted into the corresponding pyrimido[4′,5′:4,5]-5*H*-pyrrolo[2,3-*b*]quinoxaline-4(3H) thione (**25**) by refluxing with P_2S_5 in dry pyridine. The pyrimidinethione **25** could easily be S-alkylated with ethyl chloroacetate in ethanol containing anhydrous sodium acetate to give derivative **26**. On the other hand, compound **25** was converted into the hydrazino compound **27** when reacted with hydrazine hydrate in pyridine. **27** was reacted with carbon disulfide in pyridine to give mercaptotriazolopyrimidopyrroloquinoxaline **28**. With triethyl orthoformate in ethanol containing few drops of acetic acid or with acetic anhydride it afforded the triazolopyrimidopyrroloquinoxaline derivatives **29** and **30**, respectively (Scheme 7).

Experimental

Melting points were determined on a Mel-Temp 11 melting point apparatus and are uncorrected. IR spectra were recorded on a Pye-Unicam SP3-100 spectrophotometer using KBr pellets. ^{1}H NMR spectra were measured on a Varian 390 90 MHz NMR spectrometer in the suitable deutrated solvent, using *TMS* as internal standard. Elemental analyses were performed on a Perkin-Elmer 240C microanalyzer; all compounds gave results in acceptable ranges. Spectroscopic data are listed in Table 1.



Scheme 7

Table 1. Spectroscopic data of compounds **2–31**

	IR (ν, cm^{-1})	^1H NMR δ (ppm)
2	2900 (CH aliphatic), 1680 (C=O), 1600 (C=N)	$CDCl_3$; 2.85 (s, 6H, $2CH_3$), 7.0–7.3, 8.1–8.25 (2m, 5H, ArH and N=CH-)
3	3250 (NH), 1660 (C=O)	$CDCl_3$; 2.95 (s, 6H, $2CH_3$), 7.0–7.30, 8.15–8.30 (2m, 5H, ArH and N=CH-), 12.85 (s, 1H, NH)
4	1730, 1680 (2C=O), 1600 (C=N)	*DMSO*-d_6; 1.35 (t, 3H, CH_3 ester), 3.00 (s, 6H, $2CH_3$), 4.15 (q, 2H, CH_2 ester), 4.3 (s, 2H, SCH_2), 7.3–7.55, 8.2–8.9 (2m, 5H, ArH and N=CH-)
5	3350–3100 ($NHNH_2$), 1680, 1660 (2 C=O)	*DMSO*-d_6; 3.00 (s, 6H, $2CH_3$), 4.15 (s, 2H, CH_2), 4.30 (s, 2H, NH_2), 7.5–8.2 (m, 5H, ArH and N=CH-), 9.34 (s, 1H, NH)
6	3400 (NH), 1700, 1680 (2 C=O)	*DMSO*-d_6; 2.95 (s, 6H, $2CH_3$), 4.15 (s, 2H, CH_2), 7.0–8.8 (m, 9H, ArH and N=CH-), 9.10 (s, 1H, CH), 12.9 (s, 1H, NH)
7	2950–2850 (CH aliphatic), 1720, 1690 (2C=O)	$CDCl_3$; 2.20, 2.35, 2.95 (3s, 12H, $4CH_3$), 4.15 (s, 2H, CH_2), 6.45 (s, 1H, CH), 7.0–8.25 (m, 5H, ArH and N=CH-)
8	3350–3150 ($NHNH_2$), 1660 (C=O)	*DMSO*-d_6; 2.95 (s, 6H, $2CH_3$), 4.95 (s, 2H, NH_2), 7.15–7.65, 8.35–8.60 (2m, 5H, ArH and N=CH-), 9.2 (s, 1H, NH)
9	1690 (C=O), 1600 (C=N)	*DMSO*-d_6; 2.95 (s, 6H, $2CH_3$), 7.0–8.8 (m, 5H, ArH and N=CH-), 8.90 (s, 1H, CH)
10	2950–2850 (CH aliphatic), 1680 (C=O)	

(*Continued*)

Table 1. (*Continued*)

11	3100 (NH), 1660 (C=O)	CF_3COOD; 3.00 (s, 6H, $2CH_3$), 7.0–8.8 (m, 5H, ArH and N=CH-)
12	1730, 1660 (2 C=O)	$CDCl_3$; 1.35 (t, 3H, CH_3 ester), 3.00 (s, 6H, $2CH_3$), 4.25 (q, 2H, CH_2 ester), 4.4 (s, 2H, SCH_2), 7.15–7.65, 8.35–8.60 (2m, 5H, Ar-H and N=CH-)
14	3390 (NH), 2220 (CN), 1680 (C=O)	$CDCl_3$; 1.35 (t, 3H, CH_3 ester), 4.25 (q, 2H, CH_2 ester), 4.4 (d, 2H, N–CH_2), 6.1 (s, 1H, NH), 7.3–8.25 (m, 4H, Ar-H)
15	3480, 3380, 3210 (NH_2, NH), 1690 (C=O)	*DMSO*-d_6; 1.4 (t, 3H, CH_3 ester), 4.4 (q, 2H, CH_2 ester), 6.00 (s, 2H, NH_2), 7.5–8.2 (m, 4H, ArH), 11.2 (s, 1H, NH)
16	3200, 3100 (2NH), 1680 (C=O)	CF_3COOD; 8.1–8.6 (m, 4H, ArH), 9.1 (s, 1H, CH pyrimidine)
17	3400, 3100 (2NH), 1700 (C=O), 1200 (C=S)	CF_3COOD; 7.2–8.9 (m, 9H, ArH)
18	3400–3100 (2NH, NH_2), 1690 (C=O)	
19	3400–3150 (NH, $2NH_2$), 1660 (C=O)	*DMSO*-d_6; 4.3 (s, 2H, NH_2), 5.35 (s, 2H, NH_2), 7.3–7.95 (m, 4H, ArH), 9.3, 11.3 (2s, 2H, 2NH)
20	3500 (NH), 3200–3100 (NH_2), 1690 (C=O)	
21	3400, 3300 (NH_2), 2150 (N_3), 1680 (C=O)	$CDCl_3$; 6.00 (s, 2H, NH_2), 7.5–8.2 (m, 4H, ArH), 12.85 (s, 1H, NH)
22	3380, 3140 (2NH), 1710, 1690 (2C=O)	CF_3COOD; 7.3–8.1 (m, 4H, ArH)
23	3400, 3200 (2NH), 1710, 1680 (2C=O)	*DMSO*-d_6; 7.6–8.2 (m, 4H, ArH), 8.3, 8.5 (2s, 2H, CHO, CH pyrimidine), 11.0, 12.15 (2s, 2H, 2NH)
24	3210 (NH), 2950 (CH aliphatic), 1710–1680 (3C=O)	*DMSO*-d_6; 2.00 (s, 6H, $2COCH_3$), 2.25 (s, 3H, CH_3), 7.3–8.1 (m, 4H, ArH) and 12.2 (s, 1H, NH)
25	3190 (NH), 1200 (C=S)	*DMSO*-d_6; 7.6–8.2 (m, 4H, ArH), 8.3 (s, 1H, CH pyrimidine), 12.1, 12.5 (2s, 2H, 2NH)
26	3100 (NH), 1720 (C=O), 1610 (C=N)	*DMSO*-d_6; 1.2 (t, 3H, CH_3 ester), 4.1 (q, 2H, CH_2 ester), 4.3 (s, H, SCH_2), 7.5–8.5 (m, 4H, ArH), 12.8 (s, 1H, NH)
27	3300, 3200, 3150 (2NH, NH_2)	CF_3COOD; 7.2–8.30 (m, 4H, ArH), 9.3 (s, 1H, CH)
28	3150 (NH), 2800–2600 (SH)	CF_3COOD; 7.2–8.35 (m, 4H, ArH), 9.40 (s, 1H, CH)
29	3100 (NH), 1610 (C=N)	
30	3200 (NH), 2960 (CH aliphatic)	CF_3COOD; 2.6 (s, 3H, CH_3), 7.3–8.5 (m, 4H, ArH), 9.40 (s, 1H, CH)

2-Hydroxyquinoxaline-3-carboxamide (**1**)

Prepared according to the literature; m.p.: 264 °C: (Ref. [12]: m.p.: 264 °C).

2-Chlorquinoxaline-3-N-dimethylaminomethylenecarboxamide (**2**, $C_{12}H_{11}ClN_4O$, 262.70)

To ice cooled *DMF* (0.04 mol), $POCl_3$ (0.02 mol) was added dropwise. After the addition was finished, the mixture was added to a sample of compound **1** (1.89 g, 0.01 mol). The mixture was heated on a steam bath at 70 °C for 8 h, allowed to cool, and poured into an ice/water mixture. The solid product was collected and recrystallized from benzene as yellow crystals in 65% yield; m.p.: 192 °C.

2-Mercaptoquinoxaline-3-N-dimethylaminomethylenecarboxamide (**3**, $C_{12}H_{12}N_4OS$, 260.31)

A mixture of compound **2** (0.01 mol) and thiourea (0.02 mol) in ethanol (30 ml) was refluxed for 3 h and then allowed to cool. The solid product was collected and dissolved in NaOH (20 ml, 10%). Then the mixture was acidified with HCl (0.1 *N*). The solid product was collected and recrystallized from ethanol as yellow needles in 88% yield; m.p.: 280 °C.

2-Ethoxycarbonylmethylthioquinoxaline-3-N-dimethylaminomethylenecarboxamide
(**4**, $C_{16}H_{18}N_4O_3S$, 346.40)

A mixture of compound **3** (0.01 mol), ethyl chloroacetate (0.01 mol), and sodium acetate (0.012 mol) in ethanol (20 ml) was refluxed for 2 h and then allowed to cool. The solid product was filtered off, washed several times with water, and recrystallized from ethanol as white crystals in 86% yield; m.p.: 155 °C.

(3-N-Dimethylaminomethylenecarboxamidoquinoxalin-2-yl)thioacetic hydrazide
(**5**, $C_{14}H_{16}N_6O_2S$, 332.38)

A mixture of compound **4** (0.005 mol) and hydrazine hydrate (99%, 0.01 mol) in ethanol (30 ml) was refluxed for 3 h and then allowed to cool. The solid product was collected and recrystallized from dioxane as white crystals in 78% yield; m.p.: 223 °C.

p-Nitrobenzylidene(3-N-dimethylaminomethylenecarboxamidoquinoxalin-2-yl)thioacetic hydrazone
(**6**, $C_{21}H_{19}N_7O_4S$, 465.49)

A mixture of compound **5** (0.005 mol) and *p*-nitrobenzaldehyde (0.005 mol) in ethanol (20 ml) was heated under reflux for 1 h and then allowed to cool. The solid product was collected and recrystallized from acetic acid as pale yellow crystals in 84% yield; m.p.: 250 °C.

2-(3,5-Dimethylpyrazol-1-yl)carbonylmethylthioquinoxalin(3-N-dimethylaminomethylenecarboxamide)
(**7**, $C_{19}H_{20}N_6O_2S$, 396.47)

A mixture of compound **5** (0.005 mol) and acetylacetone (0.005 mol) in ethanol (20 ml) was refluxed for 6 h and then allowed to cool. The solid product was collected and recrystallized from ethanol as yellowish white crystals in 72% yield; m.p.: 135 °C.

2-Hydrazinoquinoxalin-3-N-dimethylaminomethylenecarboxamide
(**8**, $C_{12}H_{14}N_6O$, 258.28)

A mixture of compound **3** (0.01 mol) and hydrazine hydrate (0.012 mol) in ethanol (20 ml) was refluxed for 6 h and then allowed to cool. The solid product was collected and recrystallized from ethanol as yellow needles in 80% yield; m.p.: 215 °C.

2-N-Dimethylaminomethylenecarboxamido-1,2,4-triazolo[4,3-a]quinoxaline (**9**, $C_{13}H_{12}N_6O$, 268.28)

To a mixture of compound **8** (0.005 mol) and triethyl orthoformate (0.01 mol) in methanol (20 ml), a few drops of acetic acid were added. The mixture was refluxed for 3 h and then allowed to cool. The solid product was collected and recrystallized from ethanol as white crystals in 88% yield; m.p.: 235 °C.

5-Methyl-2-N-dimethylaminomethylenecarboxamido-1,2,4-triazolo[4,3-a]quinoxaline
(**10**, $C_{14}H_{14}N_6O$, 282.30)

A sample of compound **8** (0.5 g) in acetic anhydride (10 ml) was heated under reflux for 2 h, allowed to cool, and poured into an ice/H_2O mixture. The solid product was collected and recrystallized from ethanol as pale yellow crystals in 74% yield; m.p.: 310 °C.

2-N-Dimethylaminomethylenecarboxamido-1,2,4-triazolo[4,3-a]quinoxalin-5(4H)-thione

(**11**, $C_{13}H_{12}N_6OS$, 300.34)

A mixture of compound **8** (0.5 g) and CS_2 (1 ml) in pyridine (10 ml) was heated on steam bath for 12 h and then allowed to cool. The solid product was collected and recrystallized from *DMF* as yellow crystals in 83% yield; m.p.: > 300 °C.

5-Ethoxycarbonylmethylthio-2-N-dimethylaminomethylenecarboxamido-1,2,4-triazolo[4,3-a]quinoxaline (**12**, $C_{17}H_{18}N_6O_3S$, 386.43)

A mixture of compound **11** (0.005 mol), ethyl chloroacetate (0.005 mol), and anhydrous sodium acetate (0.006 mol) in ethanol (20 ml) was refluxed for 2 h and then allowed to cool. The solid product was collected, washed with H_2O, and recrystallized from ethanol as yellowish white crystals in 82% yield; m.p.: 193 °C.

2-Chloroquinoxaline-3-carbonitrile (**13**)

13 was prepared according to the literature; m.p.: 160 °C (Ref. [12]: m.p.: 160 °C).

Ethyl (3-cyanoquinoxaline-2-yl)glycinate (**14**, $C_{13}H_{12}N_4O_2$, 256.26)

A mixture of compound **13** (0.01 mol), ethyl glycinate hydrochloride (0.01 mol) and anhydrous K_2CO_3 (0.2 g) in *DMF* (20 ml) was heated at 70 °C with stirring for 8 h, allowed to cool, and poured into cold water. The solid product was collected and recrystallized from ethanol as yellow crystals in 70% yield; m.p.: 135 °C.

Ethyl 3-amino-1H-pyrrolo[2,3-b]quinoxaline-2-carboxylate (**15**, $C_{13}H_{12}N_4O_2$, 256.26)

To a sample of compound **14** (1 g) in absolute ethanol (20 ml), ethanolic sodium ethoxide (0.1 g in 10 ml ethanol) was added. The mixture was refluxed for 0.5 h, allowed to cool, and poured into cold water. The solid product was collected and recrystallized from ethanol as wine red crystals in 74% yield; m.p.: 245 °C

Pyrimido[4',5':4,5]-5H-pyrrolo[2,3-b]quinoxaline-4(3H)-one (**16**, $C_{12}H_7N_5O$, 237.22)

A sample of compound 15 (1 g) in formamide (10 ml) was refluxed for 3 h. The solid product which separated from the hot mixture was filtered off and recrystallized from pyridine as yellow crystals in 79% yield; m.p.: > 360 °C.

3-Phenyl-4-oxo-pyrimido[4',5':4,5]-5H-pyrrolo[2,3-b]quinoxaline-3(2H)-thione
(**17**, $C_{18}H_{11}N_5OS$, 345.38)

A mixture of quinoxaline derivative **15** (0.01 mol) and phenyl isothiocyanate (0.01 mol) in pyridine (30 ml) was refluxed for 8 h and then allowed to cool. The solid product was collected and recrystallized from *DMF* as yellow crystals in 55% yield; m.p.: > 360 °C.

2-Hydrazino-3-phenyl-4-oxo-pyrimido[4',5':4,5]-5H-pyrrolo[2,3-b]quinoxaline
(**18**, $C_{18}H_{13}N_7O$, 343.35)

A mixture of compound **17** (0.01 mol) and hydrazine hydrate (2 ml, 99%) in pyridine (10 ml) was refluxed for 8 h or until the evolution of H_2S ceased and then allowed to cool. The solid product was collected and recrystallized from dioxane as yellow crystals of **18** in 73% yield; m.p.: > 360 °C.

3-Amino-1H-pyrrolo[2,3-b]quinoxaline-2-carbohydrazide (**19**, $C_{11}H_{10}N_6O$, 242.24)

A mixture of compound **15** (0.01 mol) and hydrazine hydrate (2 ml) was refluxed in ethanol (20 ml) for 4 h. The solid product thus formed was filtered off and recrystallized from dioxane as orange crystals in 86% yield; m.p.: 340 °C.

3-Amino-1H-pyrrolo[2,3-b]quinoxaline-2-arylcarbohydrazones (**20a,b**)

A mixture of the hydrazide derivative **19** (0.01 mol) and aromatic aldehyde (0.01 mol) in ethanol (20 ml) was refluxed for 4 h and then allowed to cool. The solid product was collected and recrystallized from dioxane.

20a $Ar = p\text{-}C_6H_4OCH_3$, $C_{19}H_{16}N_6O_2$, 360.38, yellow crystals in 86% yield; m.p.: 295 °C
20b $Ar = p\text{-}C_6H_4NO_2$, $C_{18}H_{13}N_7O_3$, 375.35 deep red crystals in 88% yield; m.p.: 305 °C.

3-Amino-1H-pyrrolo[2,3-b]quinoxaline-2-carboazide (**21**, $C_{11}H_7N_7O$, 253.22)

To a cooled solution of compound **19** (0.01 mol) in acetic acid (20 ml), sodium nitrite solution (0.69 g in 2 ml H_2O) was added dropwise with stirring. After addition was finished, the stirring was continued for another hour, and the mixture was allowed to stand for 3 h. The solid product was filtered off to give yellow crystals of **21** in 84% yield; m.p.: 160 °C (decomp.) **21** was subjected to the next step without further purification.

1,2,3,4-Tetrahydroimidazo[4',5':4,5]pyrrolo[2,3-b]quinoxalin-2-one (**22**, $C_{11}H_7N_5O$, 225.21)

A sample of compound **21** (0.5 g) in xylene (10 ml) was refluxed for 2 h. The solid product which separated from the hot mixture was filtered off and recrystallized from dioxane as yellow crystals in 78% yield; m.p.: 245 °C.

3-N-formylamino-pyrimido[4',5':4,5]-5H-pyrrolo[2,3-b]quinoxalin-4-one (**23**, $C_{13}H_8N_6O_2$, 280.25)

A sample of compound **19** (0.5 g) in formic acid (5 ml) was refluxed for 5 h and then allowed to cool. The solid product was collected and recrystallized from dioxane as yellow crystals in 79% yield; m.p.: > 360 °C.

3-N-diacetylamino-pyrimido[4',5':4,5]-5H-pyrrolo[2,3-b]quinoxalin-4-one
(**24**, $C_{17}H_{14}N_6O_3$, 350.34)

A sample of compound **19** (1 g) in acetic anhydride (10 ml) was refluxed for 5 h, allowed to cool, and poured into an ice/water mixture. The solid product was collected and recrystallized from dioxane as yellow crystals in 76% yield; m.p.: > 360 °C.

Pyrimido[4',5':4,5]-5H-pyrrolo[2,3-b]quinoxaline-4(3H)-thione (**25**, $C_{12}H_7N_5S$, 253.28)

A mixture of compound **16** (0.01 mol) and P_2S_5 (0.01 mol) in pyridine (30 ml) was refluxed for 6 h, allowed to cool, and poured into an acetic acid/water mixture. The solid product was collected and recrystallized from pyridine as orange crystals in 84% yield; m.p.: > 360 °C.

4-Ethoxycarbonylmethylthiopyrimido[4',5':4,5]-5H-pyrrolo[2,3-b]quinoxaline
(**26**, $C_{16}H_{13}N_5O_2S$, 339.37)

A mixture of compound **25** (0.005 mol), ethyl chloroacetate (0.005 mol), and sodium acetate (0.006 mol) was refluxed in ethanol (30 ml) for 3 h and then allowed to cool. The solid product was collected, washed with water, and recrystallized from ethanol as yellow crystals in 82% yield; m.p.: 225 °C.

4-Hydrazinopyrimido[4',5':4,5]-5H-pyrrolo[2,3-b]quinoxaline (**27**, $C_{12}H_9N_7$, 251.25)

A mixture of compound **25** (0.01 mol) and hydrazine hydrate (1 ml, 99%) was refluxed in pyridine for 5 h or until the evolution of H_2S ceased and then allowed to cool. The solid product was collected and recrystallized from pyridine as orange crystals in 74% yield; m.p.: > 360 °C.

4-Mercapto-1,2,4-triazolo[3'',4'',6',1']pyrimido[4',5':4,5]-7H-pyrrolo[2,3-b]quinoxaline
(**28**, $C_{13}H_7N_7S$, 293.31)

A mixture of the hydrazino derivative **27** (0.005 mol) and CS_2 (2 ml) in pyridine (10 ml) was refluxed on a steam bath for 5 h and then allowed to cool. The solid product was collected and recrystallized from *DMF* as deep red crystals in 78% yield; m.p.: 340 °C.

1,2,4-triazolo[3'',4'':6',1']pyrimido[4',5':4,5]-7H-pyrrolo[2,3-b]quinoxaline
(**29**, $C_{13}H_7N_7$, 261.25)

To a mixture of the hydrazino derivative **27** (0.01 mol) and $CH(OEt)_3$ (0.01 mol) in ethanol (20 ml), a few drops of acetic acid were added. The mixture was refluxed for 3 h and then allowed to cool. The solid product was collected and recrystallized from *DMF* as yellow crystals in 84% yield; m.p. > 360 °C.

4-Methyl-1,2,4-triazolo[3'',4'',:6',1']pyrimido[4',5':4,5]-7H-pyrrolo[2,3-b]quinoxaline
(**30**, $C_{14}H_9N_7$, 275.27).

A mixture of the hydrazino derivative **27** (0.01 mol) and acetic anhydride (20 ml) was refluxed for 4 h. The solid product thus formed was filtered off and recrystallized from *DMF* as yellow crystals in 80% yield; m.p.: 345 °C.

References

[1] Ohmori J, Sakamoto S, Kupota H, Shimizu-Sasamata M, Okada M, Kawassaki S, Hidaka K, Togami J, Furuya T, Murase K (1994) J Med Chem **37**: 467
[2] Milata V, Ilavsky D, Chudik M, Zalibera L, Lesko J, Seman M, Belicova A (1995) Monatsh Chem **126**: 1349
[3] Terpetschnig E, Ott W, Kollenz G, Peters K, Peters EM, Schnering HG (1988) Monatshefte fur Chemie, **119**: 367
[4] Kurasawa Y, Katoh R, Takada A (1992) J Heterocyclic Chem **29**: 1001
[5] Tian W, Grivas S (1992) J Heterocyclic Chem **29**: 1305
[6] Yamamoto H, Jap Pat 6917136 (1969) C. A. 71, 124505d
[7] Yellin TO, US Pat 3635971 (1972) C. A. 76, 99708r
[8] Makino K, Sakata O, Morimoto K, Ochiai Y (1985) Heterocycles **23**: 1729
[9] Ibid 2025
[10] Badr MZA, Mahgoub SA, Geies AA, Moustafa OS, Abd El-Latif FM (1992) Phosphorus, Sulfur, and Silicon **73**: 27
[11] Kamal El-Dean AM (1995) Phosphorus, Sulfur, and Silicon **105**: 77
[12] Yoshida K, Otomasu H (1984) Chem Pharm Bull **32**(9): 3361

Received May 17, 1996. Accepted (revised) August 20, 1996