HETEROCYCLES WITH A PYRIDO[3,2-*e*]-1,3-SELENAZINE AND PYRIDO[3,4-*e*]-1,3-SELENAZINE RING SYSTEMS

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2-Chloronicotinoyl isoselenocyanate (*IIa*) and 2,6-dimethyl-4-chloronicotinoyl isoselenocyanate (*IIb*) react with arylamines to give 2-arylimino-4-oxopyrido[3,2-*e*]-1,3-selenazines *IV* and 2-arylimino-5,7-dimethyl-4-oxopyrido[3,4-*e*]-1,3-selenazines *V*. A reaction of *IIa,b* with sodium hydrogen sulfide and hydroselenide afford the respective 2-thio- and 2-seleno-4-oxopyrido-1,3-selenazines *VI* and *VII*. Structure of these new types of heterocycles was corroborated by spectral (IR, UV, ^{1}H NMR, ^{13}C NMR, and mass) means.

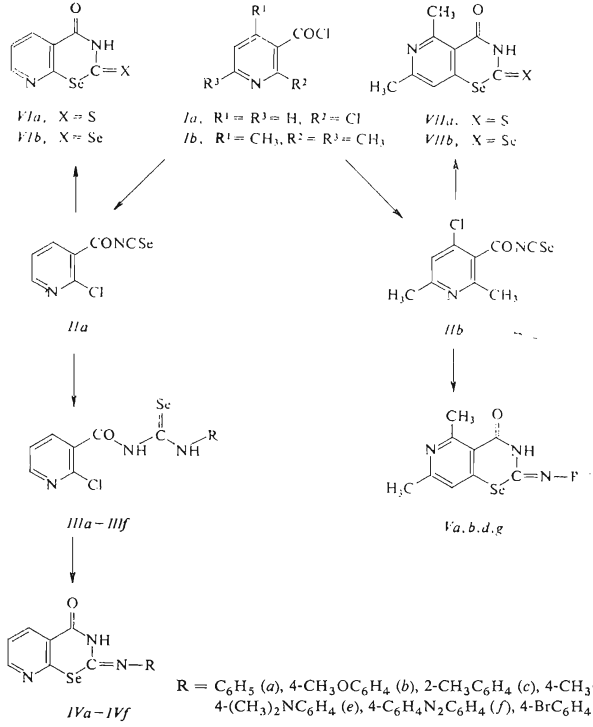
So far, no paper dealing with the synthesis of pyridoselenazines has been reported; tetrahydro-1,3-selenazines were already obtained by several methods[1–4]. The first unsaturated 1,3-selenazine derivative was prepared by cyclization of 2-selenocyanatobenzoyl chloride[5,6] with hydrogen chloride affording 2-chloro-1,3-benzoselenazin-4-one.

This paper concerns the synthesis of polycondensed derivative of pyridine with a 1,3-selenazine ring system from halogenacyl isoselenocyanates and arylamines, NaHS and NaHSe. The starting isoselenocyanates were 2-chloronicotinoyl isoselenocyanate (*IIa*) and 2,6-dimethyl-4-chloronicotinoyl isoselenocyanate (*IIb*), prepared from the corresponding acyl chlorides *Ia,b* with potassium selenocyanate. Compound *IIa* reacts with arylamines to yield selenoureas *IIIa–IIIf* which, in contrast to analogous thioureas[7] do not cyclize in the presence of strong bases to selenouracils but, afford exclusively 2-arylimino-4-oxopyrido[3,2-*e*]-1,3-selenazines *IV*. Selenoureas decompose upon thermal cyclization. Isoselenocyanate *IIb* reacts with arylamines, due to a stronger reactivity of chlorine in γ position of the pyridine ring, furnishing directly 2-arylimino-5,7-dimethyl-4-oxopyrido[3,4-*e*]-1,3-selenazines *Va,b,d,g* (Scheme 1).

Other nucleophilic reagents, as NaHS and NaHSe react instantly with isoselenocyanates *IIa,b* to form the corresponding 2-thio and 2-seleno-4-oxopyrido-1,3-selenazines *VIa,b*, *VIIa,b*. Substances *VIa,b* were also prepared from 2-chloronicotinoyl- and 2,6-dimethyl-4-chloronicotinoyl isothiocyanates[7,8] and NaHSe.

Nicotinoyl isoselenocyanates *IIa,b* are extraordinarily unstable red compounds decomposing within 5–10 min under formation of elemental selenium. Struc-

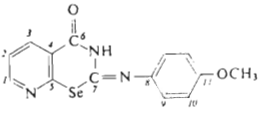
of these compounds was backed by IR and ^{1}H NMR spectra. The stability of seleno ureas *IIIa–IIIf* and oxopyridoselenazines *IV* and *V* depends on their purity. Small traces of selenium accelerate the autocatalytical decomposition of selenium derivatives already at −10°C. Isoselenocyanates *IIa,b* react with alkylamines, but the unstable products could not be isolated. Selenazines *IV*, *V* are sensitive towards heat and light and therefore, they have to be stored in a refrigerator; they are well soluble in polar organic solvents only.



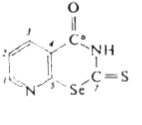
SCHEME 1

The IR spectra of *IIa,b* contain a broad absorption band ν_{as}(NCSe) at 1 945 cm^{-1} and a (C=O) one at 1 770 cm^{-1}. The selenoureas *IIIa–IIIf* reveal characteristic stretching vibrations ν(C=O) at 1 675 cm^{-1} and (NH—C=Se) at 1 485 cm^{-1}. The spectra of cyclization products *IV*, *V* display an additional absorption band of ν(C=N) stretching vibrations at 1 575 cm^{-1}. Compounds *V* have the vibrations of carbonyl groups shifted towards lower wave numbers relative to *IV* (ν(C=O) 1 675, *IV*: 1 710 cm^{-1}). The ^{1}H NMR spectra of *IV* and *V* are indicative of protons of both pyridine and benzene rings. Due to a low solubility in C^2HCl_3 the ^{13}C NMR spectra were measured in hexadeuteriodimethyl sulfoxide. The most part of selenium compounds underwent decomposition during measurement, and therefore, only spectra of *IVb* and *VIa* were recorded. The resonance signals of the particular carbons were ascribed by analogy with other sulfur derivatives[7], and from the off resonance spectra.

Since the reaction of isoselenocyanates *IIa,b* with NaHS proceeds *via* selenothiocarbamate intermediate, the cyclization product can, in principle, be either the selenazinethione or thiazinoselenone. An unambiguous proof for the structure afforded the mass spectrum of compound *VIa*, revealing the $M-HNCS^{+\cdot}$ species indicative of the presence of selenium in an endocyclic system. Likewise fragmentation displayed compounds *IVf* and *Vg*, too. The intensity of molecular ion peaks of compounds *IVf* and *Vg* is by far lower than that of *VIa* this being, however, in line with their lower stability.



IVb



VIa

SCHEME 2

EXPERIMENTAL

2-Chloronicotinoyl Isoselenocyanate (*IIa*), 2,6-Dimethyl-4-chloronicotinoyl Isoselenocyanate (*IIb*)

A solution of nicotinoyl chloride *Ia* (ref.[9]) or *Ib* (ref.[8]) (10 mmol) in acetone (20 ml) was added at 0–5°C to a stirred solution of KSeCN (10 mmol) in acetone (20 ml) in a nitrogen atmosphere. The crude *IIa,b* was after 5 min of stirring quickly filtered from the precipitated KCl and used directly in the next step. *IIa*: IR spectrum, cm^{-1}, 1 770 ν(C=O), 1 948ν(NCSe). ^{1}H NMR spectrum (δ, ppm): 8·93–9·30 (m, H_α, H_γ of the pyridine ring), 8·62 (q, H_β). *IIb*: IR spectrum, cm^{-1} 1 772ν(C=O), 1 952ν(NCSe). ^{1}H NMR spectrum: 7·12 (s, H_β), 2·50 and 2·54 (s, s CH_3)

TABLE I

Selenothioureas *III* and pyridoselenazines *IV*, *V*, *VI*, *VII*

Compound	Formula (M_r)	M.p., °C solvent	Yield, %	Calculated/Found		
				% C	% H	% N
IIIa	$C_{13}H_{10}ClN_3OSe$ (338·7)	106–108[b]	37	46·11 46·21	2·98 2·89	12·41 12·43
IIIb	$C_{14}H_{12}ClN_3O_2Se$ (368·7)	110–112[b]	53	45·62 45·71	3·25 3·33	11·39 11·41
IIIc	$C_{14}H_{12}ClN_3OSe$ (352·7)	111–113[b]	24	47·68 47·70	3·43 3·44	11·91 11·96
IIId	$C_{14}H_{12}ClN_3OSe$ (352·7)	118–121[b]	48	47·68 47·71	3·43 3·47	11·91 12·03
IIIe	$C_{15}H_{15}ClN_4OSe$ (381·7)	163–165[c]	35	47·20 47·28	3·96 3·81	14·68 14·44
IIIf	$C_{19}H_{14}ClN_5OSe$ (442·8)	148–150[b]	49	51·54 51·55	3·19 3·26	15·82 15·88
IVa	$C_{13}H_9N_3OSe$ (302·2)	226–228[d]	38	51·67 51·69	3·00 2·87	13·91 13·81
IVb	$C_{14}H_{11}N_3O_2Se$ (332·2)	231–233[a]	49	50·61 50·51	3·33 3·41	12·65 12·77
IVc	$C_{14}H_{11}N_3OSe$ (316·2)	216–218[a]	52	53·17 53·25	3·51 3·54	13·28 13·13
IVd	$C_{14}H_{11}N_3OSe$ (316·2)	258–259[d]	35	53·17 53·28	3·51 3·54	13·28 13·41
IVe	$C_{15}H_{14}N_4OSe$ (345·2)	244[a]	37	52·18 52·12	4·09 4·06	16·33 16·18
IVf[e]	$C_{19}H_{13}N_5OSe$ (406·3)	263[a]	26	56·17 56·37	3·22 3·16	17·24 17·21
Va	$C_{15}H_{13}N_3OSe$ (330·2)	140–142	32	54·55 54·60	3·97 3·88	12·72 12·70
Vb	$C_{16}H_{15}N_3O_2Se$ (360·2)	183–185[b]	35	53·34 53·31	4·20 4·21	11·66 11·51
Vd	$C_{16}H_{15}N_3OSe$ (344·2)	168–169[c]	28	55·82 55·86	4·39 4·28	12·21 12·18
Vg[f]	$C_{15}H_{12}BrN_3OSe$ (409·2)	127–128[b]	20	44·03 44·08	2·96 2·82	10·27 10·20
VIa[g]	$C_7H_4N_2OSSe$ (243·2)	225[h]	39	34·58 34·61	1·66 1·74	11·52 11·37

TABLE I
(*Continued*)

IR (cm^{-1})			^1H NMR (ppm, δ)				λ_{max}, nm (log ε)
ν(C=O) ν(C=N)	ν(NH) assoc.	ν(NH) free	H_α—H_γ[a] $CH_{3\alpha}/CH_{3\alpha'}$	H_β	NH	R	
1 676	3 230	3 380	8·50—7·97	7·42	11·42	7·25—7·40	215 (4·16)
—	3 177				12·36		250 (4·08)
1 679	3 327	3 380	8·50—7·93	7·43	—	7·25—7·40	220 (4·03)
—	3 171				12·45	3·82	247 (4·34)
1 678	3 228	3 378	8·55—8·17	7·30	8·85	7·24—7·40	213 (4·28)
—	3 176	3 378			10·03	4·01	250 (4·11)
1 675	3 230	3 380	8·50—7·96	7·42	11·51	7·35—7·50	212 (4·12)
—	3 178				12·40	2·73	250 (4·01)
1 670	3 230	3 376	8·50—7·97	7·42	11·43	7·10—7·30	210 (4·33)
—	3 165				—	2·97	265 (5·46)
1 674	3 230	3 379	8·50—7·95	7·45	11·57	7·70—7·90	210 (4·38
—	3 179				—	—	355 (5·37)
1 712	—	3 367	8·85—8·70	7·67	—	7·10—7·40	211 (4·23)
1 596						—	273 (4·46)
1 712	—	3 370	8·55—8·43	7·30	12·31	7·26—7·46	214 (4·29)
1 598						3·85	330 (4·35)
1 705	—	3 368	8·75—8·55	7·75	12·50	7·28—7·46	213 (4·40)
1 600						2·52	328 (4·21)
1 704	—	3 358	8·65—8·42	7·27	—	7·22—7·42	213 (4·46)
1 595						2·45	327 (4·16)
1 712	—	3 370	8·65—8·52	7·62	12·01	7·20—7·40	213 (3·19)
1 590						3·90	—
1 710	—	3 369	8·75—8·63	7·63	—	8·00	213 (3·33)
1 590							340 (4·11)
1 676	—	3 420	—	7·00	10·12	7·46	213 (3·03)
1 573			2·50/2·55				269 (4·96)
1 673	—	3 420	2·45/2·49	6·71	8·24	7·47; 7·90	213 (3·01)
1 576						3·77	260 (4·91)
1 673	—	3 420	2·31/2·44	6·90	8·52	7·46; 7·09	243 (4·16)
1 576						2·46	288 (4·00)
1 680	3 420	—	2·52/2·56	7·11	10·30	7·66; 7·49	245 (3·34)
1 570							270 (3·28)
1 710	—	—	8·75—8·97	7·77	—	—	226 (4·1
—							265 (3·3

TABLE I
(*Continued*)

Compound	Formula (M_r)	M. p., C° solvent	Yield, %	Calculated/Found		
				% C	% H	% N
VIb	$C_9H_8N_2OSSe$ (271·2)	209[d]	30	39·86 39·56	2·97 2·87	10·33 10·41
VIIa	$C_7H_4N_2OSe_2$ (290·0)	208[d]	34	29·00 29·11	1·39 1·34	9·66 9·67
VIIb	$C_9H_8N_2OSe_2$ (318·1)	186[d]	21	33·98 34·11	2·53 2·56	8·81 8·88

[a] Chemical shifts of pyridine ring and its substituent protons; [b] chloroform–ether; [c] chloroform–heptane; [d] chloroform–hexane; [e] mass spectrum, *m/z* (relative intensity, %): 406 (51), 327 (80), 185 (100), 157 (52), 105 (48), 77 (80); [f] mass spectrum, *m/z* (relative intensity, %): 409 (44),

N-Arylsubstituted N'-2-chloronicotinoylselenoureas *IIIa–IIIf*

Arylamine (8 mmol) in acetone (15 ml) was reacted with the crude *IIa* with stirring and under nitrogen. The mixture was after 10 min poured into a 4-fold volume of cold water, the precipitate was filtered off, purified using charcoal and crystallized from an appropriate solvent (Table I).

2-Arylimino-4-oxopyrido[3,2-*e*]-1,3-selenazines *IVa–IVf*

Selenourea *IIIa–IIIf* (10 mmol) was added to the stirred emulsion of lithium hydride (11 mmol) in dimethylformamide (35 ml) during 3–5 min. The mixture was stirred at 20°C until the turbidity disappeared, then it was gently heated to 50–60°C and left to cool. The crude product, which separated after pouring the cooled mixture into a 3-fold amount of ice-cold water, was crystallized (Table I).

2-Arylimino-5,7-dimethyl-4-oxopyrido[3,4-*e*]-selenazines *Va,b,d,g*

A solution of the respective arylamine (8 mmol) in acetone (15 ml) was added under a nitrogen atmosphere into the crude *IIb* as prepared from the chloride *Ib* (10 mmol). The hydrogenium chloride was filtered off after 20 min and suspended in benzene (25 ml). The free base liberated by an equimolar amount of pyridine was extracted by water and the product was crystallized (Table I).

2-Thio-4-oxopyrido[3,2-*e*]-1,3-selenazine (*VIa*), 2-Thio-5,7-dimethyl-4-oxopyrido[3,4-*e*]-1,3-selenazine (*VIb*)

a) Sodium hydrogen sulfide, prepared by introducing hydrogen sulfide (13·5 mmol) into a methanolic sodium hydroxide (13·5 mmol in 25 ml), was reacted with an equivalent amount

TABLE I
(*Continued*)

IR (cm^{-1})			^1H NMR (ppm, δ)				λ_{max}, nm (log ε)
ν(C=O) ν(C=N)	ν(NH) assoc.	ν(NH) free	H_α - H_γ[a] $CH_{3\alpha}/CH_{3\gamma}$	H_β	NH	T	
1 695	3 316	—	2·55/2·86	6·95	—	—	220 (3·30)
—							305 (4·10)
1 712	—	—	8·75 – 8·97	8·77	—	—	228 (4·16)
—							—
1 685	3 300	—	2·55/2·85	7·20	–	–	217 (4·01)
—							365 (4·10)

212 (30), 105 (42), 91 (24), 77 (85), 184 (40), 168 (100); [g] mass spectrum, *m/z* (relative intensity, %); 243 (71), 242 (55), 185 (100), 157 (57), 122 (31), 105 (18), 91 (15), 77 (17); [h] chloroform–light petroleum.

of *IIa* or *IIb* with stirring and in a nitrogen atmosphere. The separated product was filtered off washed with water, dried and crystallized (Table I).

b) To a solution of sodium hydrogen selenide obtained in a nitrogen atmosphere from powdered selenium (11·4 mmol) and $NaBH_4$ (13 mmol) in acetone (5 ml) within a 15 min-stirring *IIb*, or *IIa* (prepared from *Ia*, or *Ib* and ammonium isothiocyanate in acetone according to [7,8]) was dropwise added. The solvent was removed under reduced pressure and the solid was washed and crystallized (Table I).

2-Seleno-4-oxopyrido[3,2-*e*]-1,3-selenazine (*VIIa*).
2-Seleno-5,7-dimethyl-4-oxopyrido[3,4-*e*]-1,3-selenazine (*VIIb*)

Isoselocyanate *IIa*, or *IIb* was added to a solution of sodium hydrogen selenide (*cf.* the preceding procedure, method *b*). The mixture was acidified by dilute (1 : 1) hydrochloric acid and the precipitated product was rapidly filtered off and crystallized (Table I).

Spectral Measurements

The IR spectra of chloroform solutions were measured with a Specord 75 IR (Zeiss, Jena) apparatus, the UV spectra of methanolic solutions were taken with a Perkin–Elmer, model 402 spectrophotometer in 1 cm-cells, the ^1H NMR spectra were recorded with a Tesla BS 497 operating at 80 MHz, and the ^{13}C NMR spectra with a Tesla BS 567 A apparatuses operating at 25·2 MHz. The chloroform–hexadeuteriodimethyl sulfoxide solutions contained tetramethylsilane as an internal reference. The mass spectra were run with a JMS D-100 (Jeol) instrument at 70 eV ionizing electron energy and 295°C (*IVf*), 190°C (*Vg*) and 220°C (*VIa*). ^{13}C NMR spectra: *IIb*: $C_{(1)}$ 154·10, $C_{(2)}$ 120·72, $C_{(3)}$ 136·84, $C_{(4)}$ 113·92, $C_{(5)}$ 158·12, $C_{(6)}$ 149·24, $C_{(7)}$ 179·92, $C_{(8)}$

133·81, $C_{(9)}$ 130·12, $C_{(10)}$ 114·30, $C_{(11)}$ 152·92, OCH_3 55·24; *VIa*: $C_{(1')}$ 154·46, $C_{(2')}$ 124·03, $C_{(3')}$ 138·85, $C_{(4')}$ 120·94, $C_{(5')}$ 149·08, $C_{(6')}$ 162·37, $C_{(7')}$ 193·14. (Scheme 2).

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REFERENCES

1. Baringer W.: Chem. Ber. *23*, 103 (1980).
2. Luknitskii F. I., Taube D. O., Vovsi B. A.: Dokl. Akad. Nauk SSSR *184*, 355 (1969).
3. Luknitskii F. I., Taube D. O., Vovsi B. A.: Zh. Org. Khim. *5*, 1844 (1969).
4. Dzurilla M., Kristian P.: This Journal *41*, 1388 (1976).
5. Simchen G.: Angew. Chem., Int. Ed. Engl. *7*, 464 (1968).
6. Simchen G., Wenselburger J.: Chem. Ber. *103*, 413 (1970).
7. Koščik D., Kristian P., Gonda J.: This Journal, in press.
8. Koščik D., Kristian P., Forgáč O.: This Journal *48*, 3426 (1983).
9. Taylor E. C., Crovetti A. I.: J. Org. Chem. *19*, 1633 (1954).

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