Condensed Pyridines; 1. A Convenient Method for Synthesis of Novel 3-Cyanopyridine-2(1*H*)-selenones and 3-Aminoselenolo[2,3-*b*]pyridines

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The most common methods for the synthesis of pyridine-2-(1*H*)-selenones are based on the reaction of 2-halopyridines with sodium selenide under harsh conditions[1,2]. The present paper describes the use of the new cyanoselenoacetamide **(1)** for the synthesis of 4,6-disubstituted 3-cyanopyridine-2(1*H*)-selenones **(4)**. The selenoacetamide **(1)** is readily obtained in high yield by the reaction of malononitrile with hydrogen selenide in ether containing triethylamine.

Compound **1** reacts with 1,3-diketones **(3)** in the presence of triethylamine to give the desired products **4** in good yields (Method A, Table). Selenones **4** are also obtained in excellent yields by the reaction of 2-chloro-3-cyanopyridines **(2)** with selenourea (Method B) or sodium hydrogen selenide (Method C).

The reaction of the selenones **4** with the halides **5** in the presence of excess potassium hydroxide gives 3-aminoselenolo[2,3-*b*]pyridines **(7)**. However, application of an equimolar quantity of potassium hydroxide furnishes 3-cyano-2-alkylselenopyridines **(6)** which can subsequently be converted to compounds **7**. This cyclization can be classified as a Thorpe-Ziegler type reaction and considered as the first example in the 3-aminoselenophene series.

Product **7a** can be further converted to 4-amino-7,9-dimethylpyridino[2',3':2,3]selenolo[4,5-*d*]pyrimidine **(8)** by cyclocondensation with formamide.

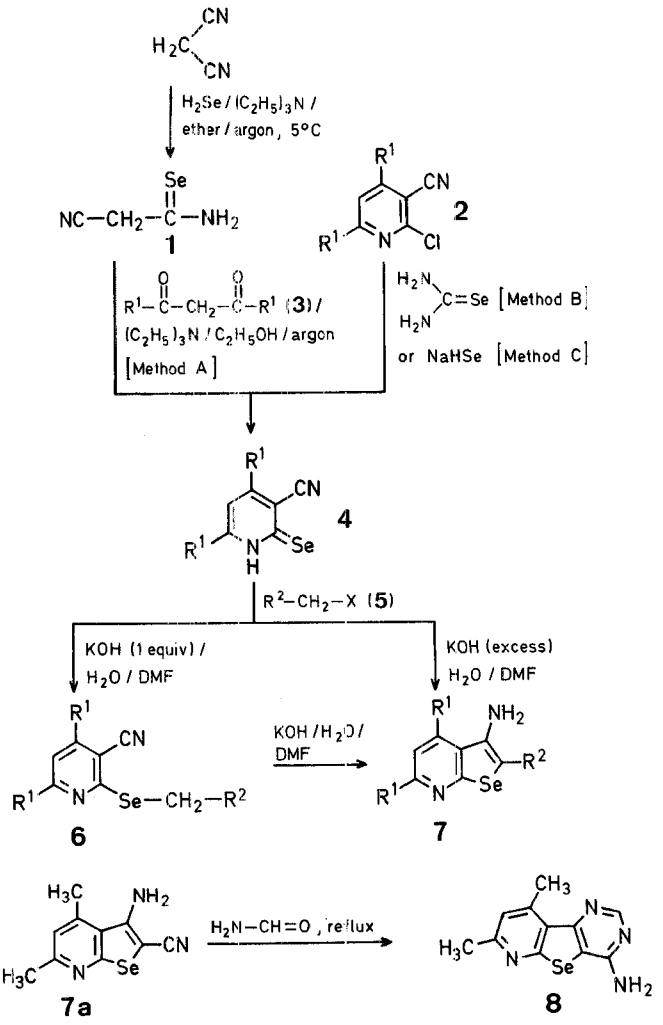
The structures of all new products were assigned on the basis of their microanalytical, I.R., U.V., and ^{1}H-N.M.R. spectral data.

Cyanoselenoacetamide (1):
Dry hydrogen selenide is passed through a solution of malononitrile (16.5 g, 0.25 mol) in dry ether (150 ml) for 5–10 min at 5°C under

Table. Compounds **4**, **6**, and **7** prepared

Product No	R^1	R^2	Method	Yield [%]	m.p. [°C] (solvent)
4a	CH_3	–	A	86	214–216°
			B	74	(dec.)
			C	67	
4b	C_6H_5	–	A	62	280–283°
			B	92	(dec.)
			C	84	
6a	CH_3	CN	–	80	110–111° (*n*-hexane)
6b	CH_3	$COOC_2H_5$	–	80	62° (*n*-hexane)
6c	CH_3	C_6H_5—CO—	–	73	134–135° (C_2H_5OH)
7a	CH_3	CN	–	76[c] (82)[f]	208–209° (C_2H_5OH)
7b	CH_3	$COOC_2H_5$	–	88[c] (90)[f]	155–156° (C_2H_5OH)
7c	CH_3	C_6H_5—CO—	–	81 (88)	155–156° (C_2H_5OH)
7d	C_6H_5	CN	–	72	226–227° (C_2H_5OH)

[a] Satisfactory microanalysis obtained: C ± 0.30, H ± 0.25, N ± 0.26, Se ± 0.38.
[b] UR-20 spectrophotometer.



Molecular formula[a]	I.R. (KBr)[b] ν[cm^{-1}]	U.V. (C_2H_5OH)[c] λ_{max}(log ε_{max})[nm]	^{1}H-N.M.R. (DMSO-d_6/TMS) δ[ppm]
$C_8H_8N_2Se$ (211.2)	2223	202 (4.32), 263 (3.70), 335 (4.20), 395 (3.28)	2.36 (s, 3H); 2.40 (s, 3H); 6.68 (s, 1H); 14.23 (s, 1H)
$C_{18}H_{12}N_2Se$ (335.3)	2207	205 (4.34), 251 (4.04), 278 (4.08), 400 (3.00)	7.10 (s, 1H); 7.3–8.0 (m, 10H$_{arom}$)
$C_{10}H_9N_3Se$ (250.2)	2220, 2250	202 (4.66), 230 (4.60), 261 (4.30), 304 (3.97)	2.40 (s, 3H); 2.51 (s, 3H); 4.09 (s, 2H); 7.18 (s, 1H)
$C_{12}H_{14}N_2O_2Se$ (297.3)	1728, 2220	210 (3.95), 226 (3.83), 240 (3.65), 276 (3.74), 305 (3.66)	1.16 (t, 3H, J = 7.2 Hz); 2.35 (s, 3H); 2.43 (s, 3H); 4.00 (s, 2H); 4.05 (q, 2H, J = 7.2 Hz); 7.08 (s, 1H)
$C_{16}H_{14}N_2OSe$ (331.3)	1690, 2220	202 (4.70), 232 (4.42), 250 (4.30), 275 (4.80), 312 (3.78)	2.25 (s, 3H); 2.36 (s, 3H); 4.72 (s, 2H); 7.05 (s, 1H); 7.70 (m, 5H$_{arom}$)
$C_{10}H_9N_3Se$ (250.2)	1636, 2183, 3205, 3308, 3453	202 (4.36), 227 (4.27), 283 (4.37), 302 (3.71)	2.45 (s, 3H); 2.69 (s, 3H); 6.26 (s, 2H); 7.07 (s, 1H)
$C_{12}H_{14}N_2O_2Se$ (297.3)	1667, 1610, 3332, 3438	210 (4.38), 230 (4.09), 245 (4.00), 290 (4.51), 375 (3.89)	1.25 (t, 3H, J = 7.2 Hz); 2.45 (s, 3H); 2.70 (s, 3H); 4.19 (q, 2H, J = 7.2 Hz); 6.68 (s, 2H); 7.00 (s, 1H)
$C_{16}H_{14}N_2OSe$ (331.3)	1595, 3260–3370, 3497	220 (4.30), 304 (4.24), 418 (3.96)	2.48 (s, 3H); 2.73 (s, 3H); 7.01 (s, 1H); 7.4–7.7 (m, 5H$_{arom}$); 8.15 (s, 2H)
$C_{20}H_{13}N_3Se$ (374.3)	1632, 2189, 3220, 3330, 3468	201 (4.43), 256 (4.19), 304 (4.34), 333 (4.02), 388 (3.63)	5.49 (s, 2H); 7.78 (s, 1H), 7.2–8.2 (m, 10H$_{arom}$)

[c] Specord UV-Vis spectrophotometer.
[d] Varian FT-80A spectrometer.
[e] Preparation from compounds **4**.
[f] Preparation from compounds **6**.

argon. Triethylamine (0.2 ml) is then added and hydrogen selenide (7.8 l) passed through. The yellowish-brown solid obtained by decantation is dissolved in ethanol and used immediately; crude yield: 27.6 g (75%).

Due to its instability compound **1** was used for the next step without further purification. Analytical data were taken from a sample obtained by recrystallization from ethanol; m.p. 96–98 °C (dec.).

$C_3H_4N_2Se$ (147.2) calc. C 24.50 H 2.74 N 19.05 Se 53.71
found 24.26 2.50 19.30 53.94

I.R. (KBr): ν = 1619, 2257, 3143, 3262, 3323 cm^{-1}.

U.V. (C_2H_5OH): λ_{max} (log ε_{max}) = 306 (4.04) nm.

^{1}H-N.M.R. (DMSO-d_6/TMS): δ = 3.93 ppm (s).

3-Cyanopyridine-2(1*H*)selenones (4); General Procedure:

Method A: Triethylamine (0.2 ml) is added to a solution of **1** (1.47 g, 10 mmol) and the 1,3-diketone **3** (11 mmol) in anhydrous ethanol (20 ml) at 50 °C under argon. The mixture is allowed to cool to room temperature during 3 h. The crystals are filtered off and washed with dry ethanol to give pure selenones **4** (Table).

Method B: A solution of 4,6-disubstituted 2-chloro-3-cyanopyridine **2** (10 mmol) and selenourea (1.9 g, 15 mmol) in dry ethanol (50 ml) under argon is refluxed for 6 h and a solution of 10% potassium hydroxide in ethanol (4 ml) added. The mixture is heated under reflux for 1 h, allowed to cool to room temperature, and acidified with 17% hydrochloric acid. The resultant precipitate is isolated by filtration, washed with water, ethanol, and hexane (Table).

Method C: A mixture of the corresponding 2-chloro-3-cyanopyridine **2** (10 mmol) and sodium hydroselenide (1.24 g, 12 mmol) in ethanol (40 ml) is refluxed with stirring under argon for 1 h. After cooling to room temperature, the mixture is acidified with 17% hydrochloric acid. The resultant precipitate is isolated by filtration, washed with water, ethanol, and hexane (Table).

2-Alkylseleno-3-cyanopyridines (6a–c); General Procedure:

3-Cyanopyridine-2(1*H*)-selenone (**4**; 10 mmol) is dissolved in 10% aqueous potassium hydroxide (5.6 ml) and dimethylformamide (20 ml). To this solution the alkyl halides **5** (10–11 mmol) are added under argon at 8–10 °C. After stirring for 10–15 min, water (5–15 ml) is added dropwise. The alkylselenopyridines **6** are collected by filtration (Table).

3-Aminoselenolo[2,3-*b*]pyridines (7); Preparation from Compounds 4:

To a solution of compounds **4** (5 mmol) in 10% aqueous potassium hydroxide (2.8 ml) and dimethylformamide (20 ml), the halides **5** (5 mmol) are added under argon. The mixture is stirred at room temperature for 30 min, 10% aqueous potassium hydroxide (5 ml) is added, and the solution stirred for further 2 h. The resultant precipitate is isolated by filtration (Table).

3-Aminoselenolo[2,3-*b*]pyridines (7); Preparation from Compounds 6:

To a solution of the 2-alkylseleno-3-cyanopyridines **6** (5 mmol) in dimethylformamide (15 ml) 10% aqueous potassium hydroxide (15 ml) is added. The mixture is stirred at room temperature for 2 h and water (5–15 ml) is added. The resultant precipitate is isolated by filtration (Table).

4-Amino-7,9-dimethylpyrido[2′,3′:2,3]selenolo[4,5-*d*]pyrimidine (8):

The solution of 3-amino-4,6-dimethyl-2-cyanoselenolo[2,3-*b*]pyridine (**7a**; 0.4 g, 1.6 mmol) in formamide (10 ml) is refluxed for 3.5 h. After cooling, the precipitate is collected; yield: 0.33 g (79%); m.p. 274–274 °C (from acetic acid).

$C_{11}H_{10}N_4Se$ (277.2) calc. C 47.50 H 3.41 N 20.04 Se 28.13
found 47.67 3.64 20.22 27.88

I.R. (KBr): ν = 1638, 3200, 3330, 3410 cm^{-1}.

^{1}H-N.M.R. (DMSO-d_6/TMS): δ = 2.54 (s, 3H); 2.89 (s, 3H); 7.17 (s, 1H); 7.32 (s, 2H); 8.45 ppm (s, 1H).

Received: April 11, 1984

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