Synthesis and crystal structure of 7-allylseleno-5-amino-8-cyano-3-ethoxycarbonyl-4-(2-furyl)-1,4-dihydro-2-methyl-1,6-naphthyridine

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The reaction of 2-furylmethylideneacetoacetic ester with cyanoselenoacetamide afforded 7-allylseleno-5-amino-8-cyano-3-ethoxycarbonyl-4-(2-furyl)-1,4-dihydro-2-methyl-1,6-naphthyridine, the structure of which has been established by X-ray structural study.

Key words: α,β-unsaturated nitriles, cyanoselenoacetamide, 1,6-naphthyridine, X-ray structural study.

As part of continuing studies of reactions of α,β-unsaturated nitriles with cyanoselenoacetamide,[1,2] we found for the first time that the reaction of 2-furylideneacetoacetic ester (**1**) with cyanoselenoacetamide (**2**) in anhydrous ethanol under an argon atmosphere in the presence of a two-fold excess of 1-methylmorpholine affords the corresponding salt of 5-amino-8-cyano-3-ethoxycarbonyl-4-(2-furyl)-1,4-dihydro-2-methyl-1,6-naphthyridine (**6**). Apparently, the reaction proceeds according to Scheme 1 with the successive formation of adduct (**3**) and 1,4-dihydropyridines (**4**, **5**). Compound (**6**) was not isolated; instead, we obtained naphthyridine (**7**) by alkylation of **6** with allyl bromide. The structure of **7** has been unambiguously established by X-ray structural study. The overall view of molecule **7** and the bond lengths are shown in Fig. 1.

The bond lengths and bond angles in molecule **7** have normal values[3] (Table 1). The 1,4-dihydropyridine cycle

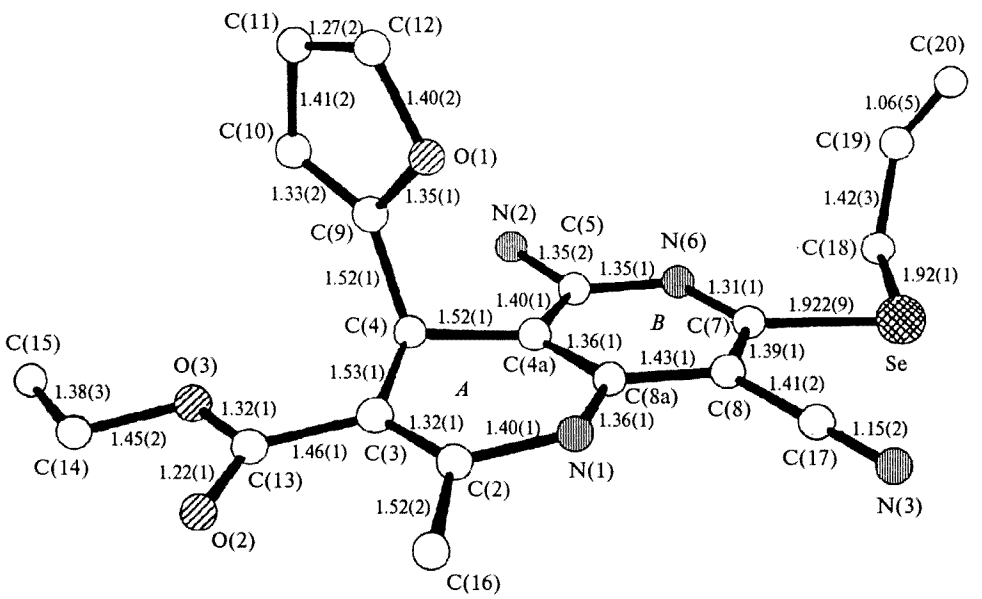

Fig. 1. Overall view and bond lengths in molecule **7**.

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Scheme 1

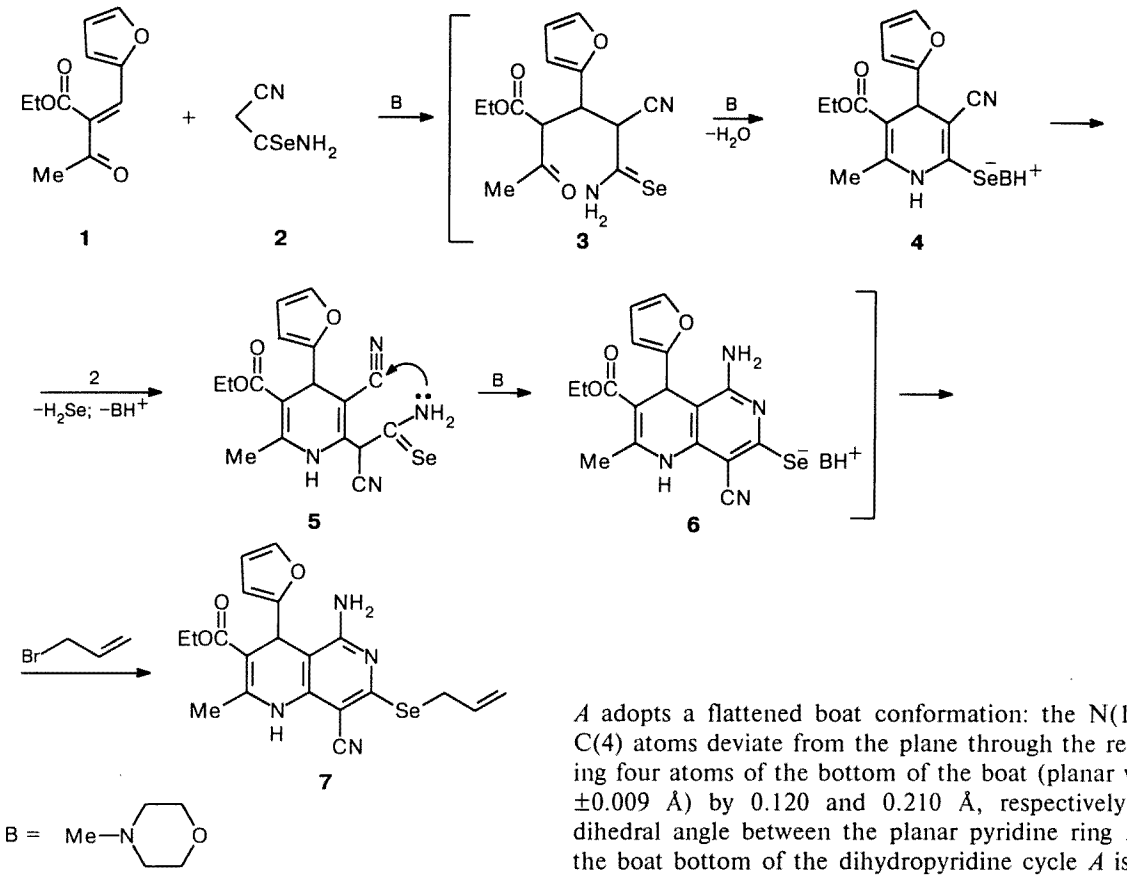

Table 1. Bond angles (ω) in molecule **7**

Angle	ω/deg	Angle	ω/deg
C(7)—Se—C(18)	99.6(5)	Se—C(7)—C(8)	116.7(7)
C(9)—O(1)—C(12)	103.2(9)	N(6)—C(7)—C(8)	124.9(9)
C(13)—O(3)—C(14)	117.2(10)	C(8a)—C(8)—C(7)	117.0(9)
C(2)—N(1)—C(8a)	121.6(8)	C(17)—C(8)—C(7)	122.4(8)
C(5)—N(6)—C(7)	117.2(9)	C(17)—C(8)—C(8a)	120.5(9)
C(3)—C(2)—N(1)	121.1(9)	C(4a)—C(8a)—N(1)	120.8(8)
N(1)—C(2)—C(16)	112.2(9)	C(4a)—C(8a)—C(8)	119.3(8)
C(3)—C(2)—C(16)	126.7(9)	N(1)—C(8a)—C(8)	119.9(8)
C(2)—C(3)—C(13)	121.5(9)	O(1)—C(9)—C(4)	115.5(8)
C(4)—C(3)—C(2)	121.0(8)	O(1)—C(9)—C(10)	110.9(9)
C(4)—C(3)—C(13)	117.5(8)	C(4)—C(9)—C(10)	133.6(9)
C(3)—C(4)—C(4a)	111.5(8)	C(9)—C(10)—C(11)	106.9(12)
C(3)—C(4)—C(9)	110.5(8)	C(12)—C(11)—C(10)	106.6(13)
C(4a)—C(4)—C(9)	110.5(7)	O(1)—C(12)—C(11)	112.4(12)
C(4)—C(4a)—C(5)	121.2(8)	O(3)—C(13)—O(2)	121.2(9)
C(4)—C(4a)—C(8a)	120.6(8)	C(3)—C(13)—O(2)	125.9(10)
C(5)—C(4a)—C(8a)	118.1(8)	C(3)—C(13)—O(3)	112.9(9)
N(6)—C(5)—N(2)	114.2(9)	O(3)—C(14)—C(15)	111.8(13)
N(6)—C(5)—C(4a)	123.3(9)	C(8)—C(17)—N(3)	179.1(11)
C(4a)—C(5)—N(2)	122.4(9)	Se—C(18)—C(19)	114.7(15)
Se—C(7)—N(6)	118.3(7)	C(18)—C(19)—C(20)	147.9(35)

A adopts a flattened boat conformation: the N(1) and C(4) atoms deviate from the plane through the remaining four atoms of the bottom of the boat (planar within ±0.009 Å) by 0.120 and 0.210 Å, respectively. The dihedral angle between the planar pyridine ring *B* and the boat bottom of the dihydropyridine cycle *A* is 5.9°, *i.e.*, the bicyclic fragment of the molecule is approximately planar. The pseudoaxial furyl substituent is twisted by 85.5° relative to the planar part of heterocycle *A*, apparently because of shortened nonvalent intramolecular contacts O(1)...C(3) 3.05(1) Å and O(1)...C(4a) 2.89(1) Å (the sum of the van der Waals radii[4] of O and C atoms is 3.22 Å).

As in the case of the molecules of compounds containing the allyl-S(Se) fragment, which we have studied previously,[5–7] the Se—C(18) bond in naphthyridine **7** has a cisoid orientation with respect to the N(6)—C(7) bond of the cycle (the N(6)—C(7)—Se—C(18) torsion angle is 1.9(1)°), whereas the allyl group is approximately perpendicular to the plane of the pyridine cycle *B* (the C(7)—Se—C(18)—C(19) and Se—C(18)—C(19)—C(20) torsion angles are 96.3 and 61.0°, respectively).

The methyl group is coplanar with the carbonyl group, which results in the short nonbonded O(2)...C(16) contact (2.78(1) Å, the sum of the van der Waals radii[4] is 3.22 Å); this contact can be considered as a C—H...O hydrogen bond (C(16)—H(16a) 1.0(1), H(16a)...O(2) 2.31(5) Å, C(16)—H(16a)...O(2) angle 107(3)°).[8]

In the crystal, molecules **7** are linked *via* weak intermolecular hydrogen bonds N(1)—H(1)...N(3) (1—*x*, 1—*y*, 1—*z*) [N(1)...N(3) 3.15(1), N(1)—H(1) 0.98(7), H(1)...N(3) 2.21(8) Å, the N(1)—H(1)...N(3) angle

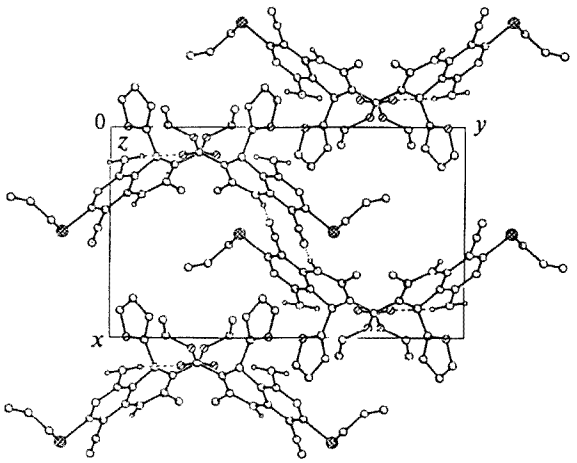

Fig. 2. The *ab* projection of the crystal structure of **7**. Dashed lines indicate intermolecular N—H...O and N—H...N hydrogen bonds.

162(2)°] and N(2)—H(2a)...O(2) (x, $1.5-y$, $-0.5+z$) [N(2)...O(2) 3.04(1), N(2)—H(2a) 0.92(7), H(2a)...O(2) 2.16(7) Å, the N(2)—H(2a)...O(2) angle 158(2)°] to form a three-dimensional framework (Fig. 2).

Experimental

The IR spectra were obtained on a Specord M 40 spectrometer using KBr pellets. The ^{1}H NMR spectra were recorded on a Bruker WP-100 SY instrument (100 MHz) in DMSO-d_6. The identity and purity of the compound was controlled by TLC on Silufol UV-254 plates in an acetone—hexane system (1 : 3).

7-Allylseleno-5-amino-8-cyano-3-ethoxycarbonyl-4-(2-furyl)-1,4-dihydro-2-methyl-1,6-naphthyridine (7). Compound **2** (1.47 g, 10 mmol) and then *N*-methylmorpholine (1 mL, 10 mmol) were added with stirring to a solution of ester **1** (1.04 g, 5 mmol) in 20 mL of anhydrous ethanol under argon at 25 °C. The reaction mixture was stirred for 10 min and was allowed to stand at ~20 °C for 5 h; then allyl bromide (0.43 mL, 5 mmol) was added, and the reaction mixture was stirred for 4 h. The precipitate was filtered off and washed with ethanol and hexane. The yield of product **7** was 1.42 g (64 %), m.p. 203—205 °C (from MeOH). Found (%): C, 53.98; H, 4.45; N, 12.69; Se, 18.01. $C_{20}H_{20}N_4O_3Se$. Calculated (%): C, 54.18; H, 4.55; N, 12.64; Se, 17.81. IR, ν/cm^{-1}: 2198 (CN), 3310, 3365, 3422 (NH_2, NH), 1683 (CO), 1620 (δ, NH_2). ^{1}H NMR, δ: 8.79 (s, 1 H, NH); 6.15, 6.24, 7.39 (m, 1 H, H(3), H(4), H(5), furyl); 6.94 (br.s, 2 H, NH_2); 5.13 (s, 1 H, H(4)); 5.93 (m, 1 H, CH=); 4.98 (m, 2 H, CH_2=); 3.84 (d, 2 H, $SeCH_2$); 4.07 (q, 2 H, OCH_2); 2.37 (s, 3 H, Me); 1.21 (t, 3 H, Me).

X-ray structural study of compound 7. The crystals of compound **7** are monoclinic, at 20 °C a = 10.935(2) Å, b = 18.092(3) Å, c = 10.345(4) Å, β = 100.91(2)°, V = 2010(2) Å^3, d_{calc} = 1.473 g cm^{-3}, Z = 4, space group $P2_1/c$. The unit cell parameters and intensities of 2642 independent reflections were measured on a four-circle automated Siemens P3/PC diffractometer (Mo-Kα radiation, graphite monochromator, $\theta/2\theta$ scanning technique to θ_{max} = 28°). The absorption correction was applied using the DIFABS program.[9] The structure was solved by the direct method and refined by the full-matrix least-squares method with anisotropic temperature factors for nonhydrogen atoms using 1592 reflections with $I > 2\sigma(I)$. All hydrogen atoms were revealed from the difference syntheses; however, because of high thermal vibrations, these atoms were included in the refinement with fixed thermal parameters U = 0.08 Å^2. The final value of the R factor was 0.061 (R_w = 0.061). All calculations were carried out using the SHELXTL PLUS program[10] (Version PC). Atomic coordinates are given in Table 2 (thermal parameters of the atoms can be obtained from authors).

Table 2. Atomic coordinates of molecule **7** (×10^4; ×10^3 for H)

Atom	x	y	z
Se	5043(1)	3668(1)	751(1)
O(1)	10028(6)	5488(4)	3676(7)
O(2)	8688(9)	7967(4)	4399(8)
O(3)	9519(6)	7679(4)	2670(7)
N(1)	6812(7)	5885(4)	3804(8)
N(2)	8442(10)	5392(5)	−88(10)
N(3)	4502(9)	4506(6)	3821(9)
N(6)	6932(8)	4653(4)	440(8)
C(2)	7403(8)	6573(5)	4039(9)
C(3)	8229(8)	6796(5)	3338(8)
C(4)	8595(8)	6302(5)	2268(8)
C(4A)	7672(8)	5676(5)	1895(8)
C(5)	7661(9)	5254(5)	753(9)
C(7)	6162(9)	4485(5)	1222(10)
C(8)	6077(8)	4858(5)	2372(9)
C(8A)	6870(8)	5484(5)	2700(9)
C(9)	9901(8)	6000(5)	2713(9)
C(10)	10983(11)	6126(7)	2344(13)
C(11)	11868(12)	5666(9)	3117(15)
C(12)	11294(13)	5306(8)	3872(16)
C(13)	8816(9)	7524(5)	3541(10)
C(14)	10098(16)	8401(7)	2752(15)
C(15)	10841(18)	8489(10)	1821(17)
C(16)	7008(11)	6983(7)	5171(12)
C(17)	5205(9)	4663(6)	3161(10)
C(18)	5568(15)	3352(8)	−833(12)
C(19)	6441(23)	2759(14)	−660(30)
C(20)	6641(36)	2204(22)	−372(44)
H(1)	634(10)	567(6)	442(10)
H(2A)	861(10)	589(6)	1(11)
H(2B)	832(9)	497(6)	−82(10)
H(4)	859(9)	660(6)	153(10)
H(10)	1094(10)	644(6)	158(10)
H(11)	1284(10)	571(5)	285(9)
H(12)	1137(11)	494(6)	445(11)
H(14A)	1069(10)	846(6)	368(11)
H(14B)	967(10)	886(6)	281(11)
H(15A)	1118(9)	910(6)	170(10)
H(15B)	1148(9)	789(6)	176(10)
H(15C)	1060(11)	839(7)	102(11)
H(16A)	686(9)	752(6)	493(10)
H(16B)	634(10)	692(6)	530(12)
H(16C)	718(9)	661(6)	597(10)
H(18A)	567(10)	370(6)	−141(10)
H(18B)	483(9)	302(5)	−159(10)
H(19)	710(11)	299(7)	−58(13)
H(20A)	664(14)	237(9)	39(13)
H(20B)	764(10)	187(6)	−6(10)

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