PROPERTIES OF 4H-[1]BENZOPYRANO[3,4-c]-[1,2,5]-SELENODIAZOL-4-ONE

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UDC 547.814.07'794.-3'818.5.04

4H-[1]benzopyrano[3,4-c][1,2,5]selenodiazol-4-one has been synthesized by the reaction of 3,4-diaminocoumarin with selenous acid and its reaction with several nucleophiles (alkali, ammonia, amines, hydrazine hydrate) and its nitration have been studied. Using PMR spectroscopy, a comparative kinetic study of the opening of the lactone ring in 6,8-dinitro-4H-[1]benzopyrano[3,4-c][1,2,5]seleno- and thiadiazol-4-ones has been carried out.

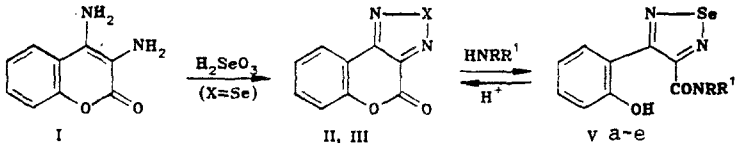
In a series of syntheses of condensed systems based on 3,4-diaminocoumarins [1-3] we have described 4H-[1]benzopyran[3,4-c][1,2,5]selenodiazol-4-one (II), prepared from the coumarin I and selenous acid.

In the present work we have examined the properties of this new heterocyclic system in comparison with its sulfur analog III [3].

In the UV spectrum (in MeCN) of compound II a bathochromic shift of the longwave absorption maximum is observed (Table 1) in comparison with the longwave maximum of the thioanalog III [λ_{max} 318 nm (log ε 4.01)] which is characteristic also for 2,1,3-seleno- and thiaazoles [5]. In the IR spectrum of the selenodiazole II in addition to the vibrational band of the carbonyl group (Table 1) vibrations of the double bonds of the coumarin fragment are also recorded at 1615 cm^{-1}. In the PMR spectrum of this compound a multiplet of the 9-H proton is observed at 8.11 ppm and multiplet signals, close in terms of chemical shift, at 7.64 (7-H), 7.42 (6-H), and 7.40 ppm (8-H). Assignment of the signals was effected by comparing them with the data for coumarin PMR [6] with allowance for spin–spin coupling.

The selenodiazole II is soluble, like the thioanalog III, in cold dilute alkali, forming a yellow-green solution of the sodium salt of 4-(2-hydroxyphenyl)-1,2,5-selenodiazole-3-carboxylic acid IV from which, as in the case of compound III, we did not succeed in isolating the free acid; on acidification of the alkaline solution a precipitate of the original lactone II gradually forms. However, it was found possible to follow the opening of the pyrone ring of compound II from its electronic absorption spectrum (Fig. 1). Thus, the disappearance of the band at 268 nm and the hypsochromic displacement of the maximum at 347 nm to 312 nm on addition of alkali to a solution of compound II in 50% aqueous ethanol provide evidence of a disturbance of the p–π conjugation on rupture of the lactone ring in compound II. This same process is also observed on keeping the coumarin II in an aqueous alcohol solution (Fig. 1).

Reaction of compound II with ammonia, amines, and hydrazine hydrate leads to the formation of the corresponding amides Va-d or the hydrazide Ve, which on treatment with hydrochloric acid are cyclized into the original lactone II. The ease with which the pyrone ring is opened in compound II, as also in the thio analog III [3], is a result of the electron-acceptor effect of the heterodiazole ring [5] which increases the electrophilicity of the carbonyl center.



I II, III V a-e

II X=Se; III X=S; V a R=R¹=H, b R=H, R¹=—C_4H_9, c R=R¹=—C_4H_9, d R+R¹= =—$(CH_2)_5$—, e R=H, R¹=NH_2

Scientific-Research Institute for Pharmacology, Academy of Medical Sciences of the USSR, Moscow 125315. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 1, pp. 128-133, January, 1991. Original article submitted January 10, 1989; revision submitted May 21, 1990.

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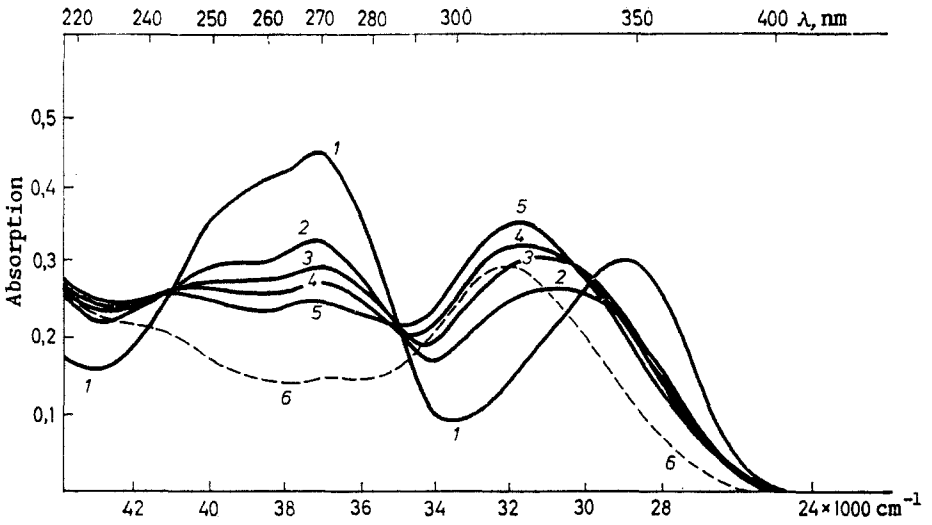
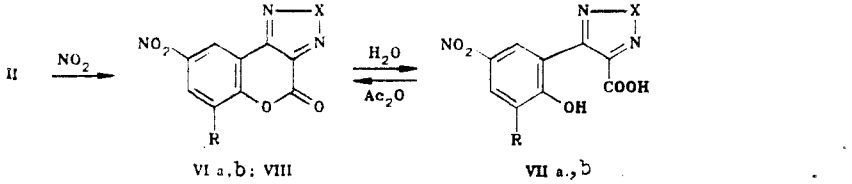


Fig. 1. Electronic absorption spectra of compound II in 50% ethanol. 1) Immediately after preparation; 2) after 18 h; 3) after 48 h; 4) after 66 h; 5) after 99 h; 6) spectrum of compound II after addition of an equimolar quantity of NaOH.

TABLE 1. Spectroscopic Characteristics of Compounds II, VI, and VII

Compound	IR spectrum, $\nu_{C=O}$, cm^{-1}	UV spectrum (in MeCN), λ_{max}, nm (log ε)
II	1758	266 (4,24), 344 (4,10)
VIa	1768	258 (4,51), 338 (4,29)
VIb	1778, 1767	259 (4,56), 334 (4,37)
VIIa	1695	304 (4,49)
VIIb	1706	295 (4,46)

The results of the nitration of the selenodiazole II and the properties of the nitration products are in general similar to those of the corresponding thio analogs [3]. Thus, on nitration of compound II with an equimolar quantity of nitrating mixture the 8-nitroderivative VIa is formed and this, on boiling in water or on treatment with dilute alkali, is converted into the acid VIIa. Use of an excess of the nitrating agent leads to the formation of the 6,8-dinitroderivative VIb, the lactone ring of which is prone to nucleophilic attack to the extent that, on treating the reaction mixture with water, a product of ring opening (the acid VIIb) is immediately precipitated. The acids VIIa, b differ from the acid IV in being stable in neutral and acid media; cyclization of these compounds to the original lactones VIa, b occurs on boiling with acetic anhydride.



VI, VII X=Se, a R=H, b R=NO_2; VIII X=S, R=NO_2

The presence of a nitrogroup on the benzene ring of the coumarin fragment leads to a hypsochromic shift of both absorption maxima in the UV spectra (in MeCN) of compounds VIa, b and an increase in their intensity (Table 1). We were not able to obtain the UV spectra of these nitro-compounds in aqueous ethanol on account of rapid opening of the coumarin ring, especially in the case of compound VIb. Comparison of the absorption spectra of compounds VIa, b and VIIa, b showed considerable differences, similar to those observed in the spectrum of coumarin II on addition of alkali or on standing in 50% ethanol (Fig. 1).

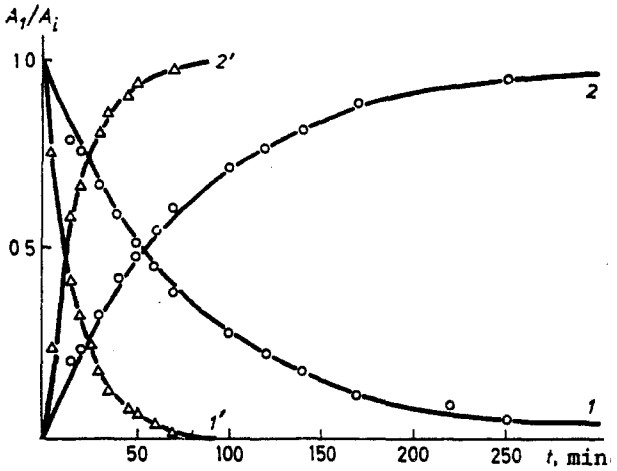


Fig. 2. Kinetic curves of the decomposition of the original compounds (1, 1') and the formation of reaction products (2, 2') against time (in solution in DMSO-D_6, c = 10%): 1, 2) compound VIb; 1', 2') compound VIII.

TABLE 2. Characteristics of Amides Va-e

Compound	Empirical formula	Mp, °C	IR spectrum, cm^{-1}	UV spectrum, λ_{max}, nm (log ε)	Yield, %
Va	$C_9H_7N_3O_2Se$	—**	3298, 3290, 3120, 1656, 1617, 1585	305 (4,15)	95
Vb	$C_{13}H_{15}N_3O_2Se$	120...122	3285, 1654, 1618, 1585	307 (4,10)	78
Vc	$C_{17}H_{23}N_3O_2Se$	113...114	3055, 1616, 1596	310 (4,26)	79
Vd	$C_{14}H_{15}N_3O_2Se$	148...150	3155, 1624, 1598	312 (4,19)	77
Ve	$C_9H_8N_4O_2Se$	156 decomp.	3319, 3259, 3185, 1675, 1628, 1608, 1595	310 (4,15)	88

*Compound Va was purified by reprecipitating with petroleum ether from ethanol; Vb was recrystallized from benzene; Vc from a mixture of ethyl acetate and petroleum ether, Vd from a mixture of benzene and petroleum ether, and Ve from isopropanol.

**Cyclizes to form compound II.

In the IR spectra of compounds VIa, b the carbonyl group vibrations are displaced to a higher frequency region in comparison with the coumarin II while in the acids VIIa, b the carbonyl vibrations are observed at a lower frequency (Table 1). From this, one can readily identify the cyclic and open compounds both in the crystalline state and in solution.

The position of the nitrogroups in compounds VIa, b was established from the PMR spectra by analogy with their thio analogs [3]. Thus, in the PMR spectrum of the 8-nitro-derivative VIa doublets at 8.80 and 7.70 ppm were assigned to the 9-H and 6-H protons, respectively, and a doublet of doublets at 8.45 ppm to the 7-H proton (J_{67} = 9 Hz, J_{79} = 3.0). In the PMR spectrum of the dinitrocoumarin VIb, run immediately after preparing the solution, doublets at 8.93 and 9.03 ppm (J = 3.0 Hz) corresponded to the 9-H and 7-H protons [3]. With the passage of time, two new doublet signals appeared in this spectrum at 8.45 and 8.75 ppm (J = 3.0 Hz), the integral intensities of which gradually increased while the intensities of the first two doublets fell. After several hours the spectrum obtained was completely identical with that of the acid VIIb which points to opening of the pyrone ring in the coumarin VIb. A similar picture was observed in the case of the dinitrothiadiazole VIII [3].

A comparative kinetic study of the rate of opening of the pyrone ring in compounds VIII and VIb was carried out by measuring the PMR spectra in solution in DMSO-D_6 against time at 30°C. Integral intensities of the proton signals, proportional to the concentration of the reactants, were obtained by examination of the spectra. These integral intensities were used directly in calculating the rate constants of the reactions. The rate constants were evaluated on the basis of a comparison of the ratio of the summed integral area of the 9-H and 7-H signals of the initial coumarins VIII and VIb at the initial point in

time (A_1), taken as standard, to the area of the signals at the given point in time (A_i). The linear relationship of the natural logarithm of the ratio A_1/A_i to reaction time for compounds VIII and VIb shows that the opening of the lactone ring in both compounds can be described by a pseudo first-order equation in the reactant [7] $c = c_1e^{-kt}$, where $c_1 = \alpha A_1$ and $c = \alpha A_i$ (the initial and instantaneous concentrations of the compounds studied), α is the proportionality coefficient, k is the rate constant for the reaction. The values of k, calculated from the angle of slope of the line, were $5.58 \cdot 10^{-1}$ and $1.23 \cdot 10^{-2}$ min^{-1} for compounds VIII and VIb, respectively. Kinetic curves were plotted for the consumption of the starting material and the formation of the new reaction product against time for both compounds (Fig. 2). It can be seen from an examination of the results that the rate of lactone ring opening is 4.5 times greater for compound VIII than for compound VIb.

EXPERIMENTAL

UV spectra were run on a Specord M 20 in MeCN or 50% ethanol ($c = 1 \cdot 10^{-4}$ mole/liter, $l = 0.5$ cm). A Perkin–Elmer 580 instrument was used for the IR spectra with 1-200 mg samples in KBr disks. PMR spectra were obtained on a Varian T-60 spectrometer in DMSO-D_6 at 30°C with TMS as internal standard. Mass spectra were run on a Varian MAT-112 with direct introduction of the sample, the ion source at 100-120°C, and an ionizing potential of 70 eV. Monitoring of the progress of the reactions and the purity of the products was effected by TLC on Silufol UV-254 plates in 2:1 hexane–ethyl acetate and visualization by UV light.

Elemental analyses for C, H, and N corresponded to the calculated results.

The diamine I was prepared by the method of [3].

4H-[1]Benzopyrano[3,.4-c][1,2,5]selenodiazol-4-one (II, $C_4H_9N_2)_2Se$). To a suspension of 3 g (17 mmoles) diamine I in 150 ml dioxane was added, dropwise with stirring, a solution of 4 g selenous acid in 10 ml water. The mixture was stirred 3 h at room temperature, diluted with water, and the precipitate filtered off, washed with water, and dried. Yield 3.8 g (89%) compound II, mp 236-238°C (from toluene). Found: M^+ 251. Calculated: M 251.11.

Amides of 4-(2-Hydroxyphenyl)-1,2,5-selenodiazole-3-carboxylic Acid (Va-e). A. A current of dry ammonia was passed through a suspension of 1.2 g (4.7 mmoles) compound II in 35 ml dry benzene and the mixture kept overnight at room temperature until all the original compound had disappeared. The precipitated material was filtered off and washed with benzene and water, and dried. It was purified by reprecipitating from ethanol–water solution with hexane. Yield 1.22 g amide Va (Table 2).

B. To a suspension of 0.75 g (3 mmoles) compound II in 10 ml dry benzene was added, dropwise with stirring, 6 mmoles of the appropriate amine. The mixture was stirred for 2-3 h (in the case of amine Vc, 30 h) at room temperature to completion of the reaction. The solution was washed with 5% HCl and with water, dried, and evaporated. Amides Vb-d were obtained (Table 2).

Hydrazides of 4-(2-Hydroxyphenyl)-1,2,5-selenodiazol-3-carboxylic Acid (Ve). To a suspension of 0.75 g (3 mmoles) compound II in 8 ml absolute ethanol was added, with stirring, a solution of 0.16 ml hydrazine hydrate in 3 ml absolute ethanol. The mixture was stirred 3 h at room temperature. The solvent was distilled off under vacuum and the residue rubbed with a small quantity of water, filtered off, and dried to yield 0.75 g compound Ve (Table 2).

Cyclization of Amide Va. A solution of 0.1 g (0.3 mmole) compound Va in 5 ml concentrated HCl was kept for 3 h at room temperature. The precipitate which settled was filtered off, washed with water, and dried to yield 0.065 g (86%) coumarin II.

3-Nitro-4H-[1]benzopyrano[3,4-c][1,2,5]selenodiazol-4-one (VIa, $C_9H_3N_3O_4Se$). A. A mixture of 0.54 ml (13 mmoles) HNO_3 (d 1.5) and 4 ml concentrated H_2SO_4 was added, dropwise while stirring at 0-5°C, to a solution of 3 g (12 mmoles) compound II in 12 moles concentrated H_2SO_4. The mixture was stirred for 2 h at 20°C and poured into ice water. The precipitate which formed was filtered off, washed with water, dried, and crystallized from glacial acetic acid. Yield 2.84 g (80%) compound VIa, mp 230-232°C. Found: M^+ 296. Calculated: M^+ 296.10. IR spectrum: 1768 (C=O), 1622, 1589 ($C = C_{arom}$), 1515, 1347 cm^{-1} (NO_2).

B. A mixture of 0.47 g (1.5 mmoles) acid VIIa and 1.5 ml acetic anhydride was heated at bp for 30 min. The solution was cooled and the deposit which formed was filtered off, washed with water, and dried to yield 0.39 g (88%) coumarin VIa.

4-(2-Hydroxy-5-nitrophenyl)-1,2,5-selenodiazole-3-carboxylic Acid (VIIa, $C_9H_5N_3O_5Se$). A. A solution of 0.8 g (2.7 mmoles) compound VIa in 10 ml 10% NaOH was left to stand for 1 h at 20°C and then acidified with 10% HCl. The precipitate which formed was filtered off and dissolved in 30 ml saturated $NaHCO_3$ solution, which was filtered and carefully acidified with 10% HCl. The precipitate was filtered off, washed with water, and dried. Yield 0.76 g

(90%) acid VIIa, mp 155°C (decomp.). IR spectrum: 1695 (C=O), 1626 (C = C_{arom}), 1510, 1335 cm^{-1} (NO_2). Found: M^+ 314. Calculated: M 314.12.

B. A suspension of 0.5 g (1.7 mmoles) coumarin VIa in 100 ml distilled water was heated at bp until solution was complete (1 h) and then for a further hour, and cooled. The precipitate which formed was filtered off and dried to yield 0.36 g (67%) acid VIIa.

4-(2-Hydroxy-3,5-dinitrophenyl)-1,2,5-selenodiazole-3-carboxylic Acid (VIIb, $C_9H_4N_4O_7Se$). A. A mixture of 1 ml (24 mmoles) HNO_3 (d 1.5) and 4 ml concentrated H_2SO_4 was added, dropwise with stirring at 0-5°C, to a solution of 2 g (8 mmoles) compound II in 8 ml concentrated H_2SO_4. The mixture was left to stand 28 h at room temperature and then poured into ice water. The precipitate which formed was filtered off, washed with a small quantity of cold water, dried, and recrystallized from 50% ethanol. Yield 2.2 g (77%) acid VIIb, mp 157°C (decomp.). IR spectrum: 1706 (C=O), 1612 (C = C_{arom}), 1552, 1542, 1838 cm^{-1} (NO_2). Found: M^+ 359. Calculated: M 359.11.

B. A mixture of 0.17 g (4 mmoles) HNO_3 (d 1.5) and 1 ml concentrated H_2SO_4 was added, dropwise with stirring at 0-5°C, to a solution of 0.59 g (2 mmoles) compound VIa in 3 ml concentrated H_2SO_4. The mixture was left to stand at room temperature for 28 h and then poured into ice water. The precipitate which formed was filtered off, washed with a small quantity of cold water, dried, and recrystallized from 50% ethanol. Yield 0.5 g (70%) acid VIIb.

6,8-Dinitro-4H-[1]benzopyrano[3,4-c][1,2,5]selenodiazol-4-one (VIb, $C_9H_2N_4O_6Se$). A mixture of 0.72 g (2 mmoles) compound VIIb and 2 ml acetic anhydride was heated at bp for 30 min. The solution was cooled, and the precipitate which formed was filtered off, washed with hexane, and dried. Yield 0.56 g (82%) coumarin VIb, mp 233-235°C (from dry benzene). Found: M^+ 341. Calculated: M 341.10.

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