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Bisbenzisoselenazol-3(2H)-ones, a New Group of Ebselen Analogues

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The title compounds with benzisoselenazolone moieties connected by spacers such as phenylene, bisphenylene, alkylene, oxaalkylene, azaalkylene and dithiaalkylene groups have been obtained in the reaction of 2-(chloroseleno)benzoyl chloride with compounds having two primary amine groups, while the secondary amines gave products of their selenenylation and/or acylation. Bisbenzisoselenazol-3(2H)-ones were found, in the antiviral assay *in vitro*, to be inhibitors of cytopathic activity of RNA and DNA viruses: EMCV, HSV-1 and VSV.

Key words: bisbenzisoselenazol-3(2H)-ones, 2-(chloroseleno)benzoyl chloride, diselenides, ebselen analogues, virucides

Seventeen years ago it was revealed that the simple, synthetically available organoselenium compound 2-phenylbenzisoselenazol-3(2H)-one named ebselen (**2**) could act against oxidative stress in a similar way as common enzyme glutathione peroxidase [1,2]. Extensive studies of the chemistry and biology of ebselen demonstrated its antiinflammatory, antisclerotic and cytoprotective properties [3,4]. In our previous papers we reported that ebselen, as well as some other 2-substituted benzisoselenazol-3(2H)-ones and related bisaryldiselenides, were inhibitors of viral cytopathogenicity and replication [5] and active immunostimulants inducing cytokines, such as interferons (IFNs), tumor necrosis factors (TNFs) and interleukin (IL-2) in human peripheral blood leukocytes [5,7]. Moreover, carboxyebselen (2-(4-carboxyphenyl)benzisoselenazol-3(2H)-one) was found to be a potent and selective inhibitor of endothelial nitric oxide synthase [8,9].

In this paper we present a synthetic approach to a novel group of organoselenium compounds, which have been designed as new cytokine inducers and virucides. They are bisbenzisoselenazol-3(2H)-ones (**4**), in which both of heterocyclic moieties are bridged with arylene (**4a–d**), alkylene (**4e–i**), oxaalkylene (**4j, k**), azaalkylene (**4l–p**) or dithiaalkylene groups (**4g**). The distance between both of benzisoselenazolyl moieties and hydrophilic/lipophilic properties was varied using different spacers, thus,

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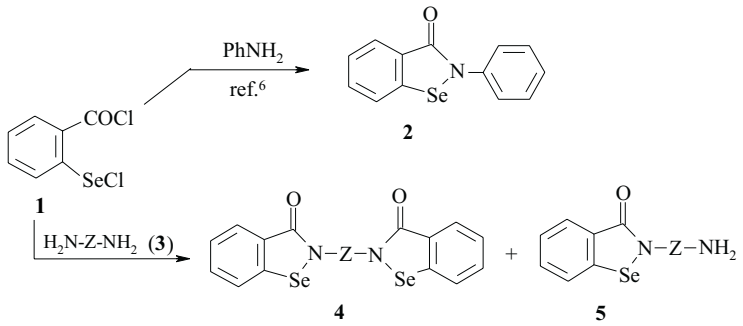
this series of compounds should be a good material for biological studies. Moreover, our chemical interest was focused on the reactivity of 2-(chloroseleno)benzoyl chloride (**1**) as a model electrophile, having two different electrophilic centers, towards bisnucleophiles such as aromatic and aliphatic diamines.

RESULTS AND DISCUSSION

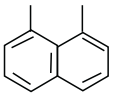
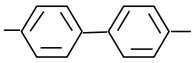
The general strategy for synthesis of bisbenzisoselenazol-3(2H)-ones (**4**) (presented in Scheme 1) was similar as for synthesis of ebselen and its analogues reported in our earlier works [6,9]. The key substrate was 2-(chloroseleno)benzoyl chloride (**1**) obtained in the four-step synthesis from anthranilic acid [6] and the appropriate diamine **3**. The molar ratio of chloride to amine was 1:3. When arylene diamines **3a–d** were used as substrates (Table 1), the results depended strongly on the structure of diamine. Thus, acylation-selenenylation of *m*-phenylenediamine resulted only in a complex mixture of tarry products. *o*-Phenylenediamine (**3a**) and 1,8-diaminonaphthalene (**3b**) gave 2-(2-aminophenyl)benzisoselenazol-3(2H)-one (**5a**) and 2-[1-(8-aminonaphthyl)]benzisoselenazol-3(2H)-one (**5b**) respectively, since for steric reasons only one amino group could react with chloride **1**. When *p*-phenylenediamine (**3c**) was a substrate, one or both amino groups reacted with chloride **1** and expected bisbenzisoselenazolone **4c** as well as 2-(4-aminophenyl)benzisoselenazol-3(2H)-one **5c** was produced. Formation of bisbenzisoselenazolones **4c** and **4d**, as the sole products, can be explained in the light of the known fact that the acylation of both amino groups in diamines with acyl chlorides is very fast; much faster than the diffusion of the acylating agent [10]. This assumption was supported by the additional experiment when diamine **3c** was used in a ten-fold excess in a high-dilution. In this case the ratio of product **4c** to **5c** substantially decreased. At the same reaction conditions ethylenediamine (**3e**) gave a mixture of bisbenzisoselenazolone **4e** and benzisoselenazolone **5e**. When various alkylenediamines (**3e–h**), oxyalkylenediamines (**3j,k**), azaalkylenediamines (**3l,n–p**) and dithiaalkylenediamine (**3q**) were used as substrates, and the reaction was carried out under standard conditions, corre-

Scheme 1



sponding bisbenzisoselenazol-3(2H)-ones (**4e–l,n–q**) were produced in a satisfactory to fair yields (Table 2). Quaternization of compound **4l**, having tertiary amino group in the alkylene moiety with iodomethane, gave methiodide **4m**, while no methylation of selenium atoms was observed.

Table 1. The results of the reaction of 2-(chloroseleno)benzoyl chloride (**1**) with aromatic diamines **3a–d**.

Diamine	Z	Compd.	Products		
			Yield, %	Compd.	Yield, %
3a		–	–	**5a**	46
3b		–	–	**5b**	87
3c		**4c** **4c**	29 49[a]	**5c** **5c**	15 51[a]
3d		**4d**	80	–	–

[a]Amine used in ten-fold excess in high dilution conditions.

Table 2. The results of the reaction of 2-(chloroseleno)benzoyl chloride (**1**) with aliphatic di- and polyamines **3e–q**.

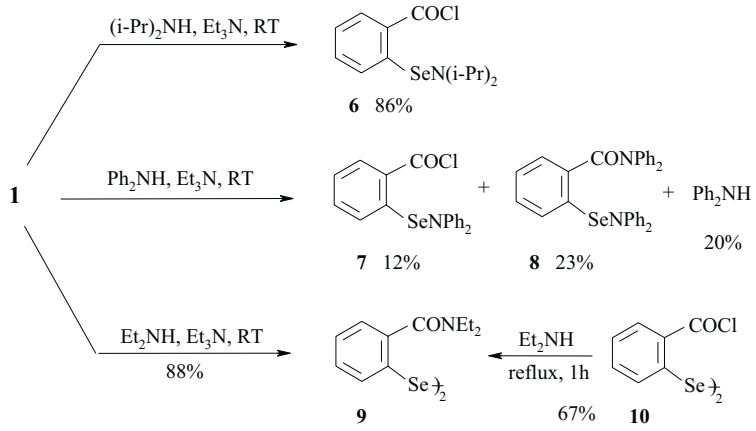
Amine	Z	Product		Amine	Z	Product	
		Compd.	Yield, %			Compd.	Yield, %
3e	$-(CH_2)_2-$	**4e**	68	**3k**	$-CH_2(CH_2CH_2O)_3CH_2CH_2CH_2-$	**4k**	25
		4e	22[a]	**3l**	$-(CH_2)_2N(CH_3)(CH_2)_2-$	**4l**	61
3f	$-(CH_2)_3-$	**4f**	76	**3m**	$-[(CH_2)_2N(CH_3)_2(CH_2)_2]-^{+}I^{-}$	**4m**	52
3g	$-(CH_2)_6-$	**4g**	54	**3n**	$-(CH_2)_2NH(CH_2)_2-$	**4n**	37
3h	$-(CH_2)_{12}-$	**4h**	71	**3o**	$-(CH_2)_2(NHCH_2CH_2)_2-$	**4o**	41
3i	$-CH_2CH(CH_3)-$	**4i**	54	**3p**	$-(CH_2)_2(NHCH_2CH_2)_3-$	**4p**	58
3j	$-(CH_2CH_2O)_2CH_2CH_2-$	**4j**	83	**3q**	$-(CH_2)_2SS(CH_2)_2-$	**4q**	46

[a]When amine **3e** was used in ten-fold excess in the high dilution conditions, the compounds **5e** was a major product formed in 49% yield.

2-(Chloroseleno)benzoyl chloride (**1**), used as a key substrate, is a biselectrophile bearing two different centers reactive towards nucleophiles such as amines. One of them (hard electrophilic center) is localized on the carbonyl carbon atom and the sec-

ond one (soft electrophilic center) is the selenium atom. When secondary amines were used as nucleophiles, the competition between both of these centers was observed, since cyclization into isoselenazole ring could not take place. The results depended on the amine used and in consequence on the reactivity of intermediate N-selenenylation product (Scheme 2). When chloride **1** was treated with di(*iso*-propyl)amine in the presence of triethylamine as a base, N-selenenylation proceeded faster than N-acylation and the stable selenenylamide **6** was formed almost exclusively, while diphenylamine produced selenenylamide **7**, accompanied with diamide **8**, being a product of its subsequent N-acylation. Surprisingly, dichloride **1** treated with diethylamine produced 2,2′-diselenobis(N,N-diethylbenzamide) (**9**) obtained also on the alternative way from 2,2′-diselenobisbenzoyl chloride (**10**).

Scheme 2



Compounds **4c**, **4e–4g**, **4i–4m**, **5a** and **5c** were tested as cytokine inducers. The compounds or phytohemagglutinin (PHA, used as positive control) were added to human peripheral blood leukocytes cultures and incubated for 24 h at 37°C. The levels of interferon (IFN) and tumor necrosis factor (TNF) were determined in culture supernatants. Only **4e**, **4g** and **5a** were found to induce TNF production. No statistically significant enhancement of IFN production was detected.

Antiviral effects of compounds **4c–4q**, **5a–5c** and **5e** were measured against encephalomyocarditis virus (EMCV, non-enveloped RNA virus), vesicular stomatitis virus (VSV, enveloped RNA virus) and herpes simplex virus type 1 (HSV-1, enveloped DNA virus). Strong anti-EMCV activity was found in the case of **4e–4g**, **4i–4p** and **5c** (Minimal virus-inhibiting dose 0.6–8.0 μg/ml). High anti-HSV-1 effect was determined for **4e–4g**, **4i–4n**, **5a**, **5c** and **5e** (Minimal virus-inhibiting dose 0.6–6.0 μg/ml). Among the compounds tested only **4f**, **4k**, **4n**, **4q** and **5b** were found to exhibit weak anti-VSV activity. Compound **4c** had negligible and compound **4d** no antiviral activities. More advanced antiviral tests are in progress.

EXPERIMENTAL

All reagents and solvents were purchased from Aldrich or Fluka. 2-(Chloroseleno)benzoyl chloride (**1**) and 2-diselenobisbenzoyl chloride (**10**) were obtained according to [9]. Melting points were determined with a Digital Melting Point Apparatus Electrothermal IA 9100. ^{1}H NMR spectra were recorded in DMSO-d_6 (except spectra of compounds **4h,j,k** measured in $CDCl_3$) on a Bruker DRX 300 spectrometers 300 MHz. Chemical shifts δ are reported in ppm relative to TMS. IR spectra were measured on a Perkin-Elmer 2000 FT spectrometer. The procedure for the determination of the ability to induce TNF and IFN was the same as described in [5,11]. In the antiviral assay the organoselenium compounds were incubated with the viruses for 2 h at room temperature. The virus titer was measured on human A549 cells and minimal virus inhibiting dose was determined [5].

Synthesis of arylenebisbenzisoselenazol-3(2H)-ones (4c,d) and 2-aminoarylbisbenzisoselenazol-3(2H)-ones (5a–c): A solution of chloride **1** (1.27 g, 5 mmol) in dry acetonitrile (15 ml) was added dropwise in room temperature over a period of 30 min. to a stirred solution of diamine (**3a–d**) (16.5 mmol) in dry acetonitrile (45 ml) and the reaction was continued for additional 2 h. When the reaction was finished, acetonitrile was evaporated *in vacuo*. Water (100 ml) was added to the residue, the mixture was stirred for 12 h and the solid precipitate was filtered off and dried in air. The solid was extracted with boiling solvent – ethanol (**4d**), ethyl acetate (**5a**), and purified on silica gel column (chloroform), or directly recrystallized (**5b**). When mixture of **4c** and **5c** was formed, the compound **5c** was extracted from the solid with boiling methanol and recrystallized from the same solvent. The residue after extraction recrystallized from DMSO gave pure **4c**. In the additional experiment (high dilution conditions) a solution of chloride **1** (0.64 g, 2.5 mmol) in dichloromethane (100 ml) was added dropwise at room temperature to a solution of diamine **3c** and the reaction was continued for additional 2 h. The obtained mixture of the products **4c** and **5c** was worked up as decsribed above.

1,4-Bis[2-benzisoselenazol-3(2H)-onyl]benzene (4c): White powder. M.p. 228–238°C (decomp.). IR (KBr) 1598 cm^{-1} (CO). ^{1}H NMR: 7.49 (t, 2H, J = 7.5 Hz, ArH); 7.69 (t, 4H, J = 7.6 Hz, ArH); 7.72 (d, 2H, J = 7.7 Hz, ArH); 7.92 (d, 2H, J = 7.6 Hz, ArH); 8.09 (d, 2H, J = 7.9 Hz, ArH). Anal. Calcd for $C_{20}H_{12}N_2O_2Se_2$ (74.80) C, 51.10; H, 2.57; N, 5.96. Found: C, 49.62%; H, 2.84%; N, 5.62%.

4,4′-Bis[2-benzisoselenazol-3(2H)-onyl]biphenyl (4d): Grey powder. M.p. 310–313°C. IR (KBr) 1629 cm^{-1} (CO). ^{1}H NMR: 7.27 (d, 2H, J = 4.2 Hz, ArH), 7.45 (t, 2H, J = 7.4 Hz, ArH), 7.60–7.76 (m, 8H, ArH), 7.88 (d, 2H, J = 3.9 Hz, ArH), 8.32 (d, 2H, J = 3.9 Hz, ArH). Anal. Calcd for $C_{26}H_{16}N_2O_2Se_2$ (545.8) C, 57.13; H, 2.95; N, 5.13. Found: C, 56.76; H, 3.21; N, 5.16.

2-(2-Aminophenyl)benzisoselenazol-3(2H)-one (5a): Yellow powder. M.p. 159°C. IR (KBr) 1642 cm^{-1} (CO); 3384, 3384 cm^{-1} (NH_2). ^{1}H NMR: 4.05 (s, 2H, NH_2); 6.84 (d, 2H, J = 7.6 Hz, ArH); 7.16–7.26 (m, 2H, ArH); 7.44–7.52 (m, 1H, ArH); 7.62–7.69 (m, 2H, ArH); 8.12, (d, 1H, J = 7.7 Hz, ArH). Anal. Calcd. for $C_{13}H_{10}N_2OSe$ (288.90) C, 53.97; H, 3.49; N, 9.69; Found: C, 53.82; H, 3.52; N, 9.80.

2-[1-(8-Aminonaphtyl)]benzisoselenazol-3(2H)-one (5b): Violet tiny prisms. M.p. 290–300°C (decomp.). IR (KBr) 1637 cm^{-1} (CO), 3405 cm^{-1} (NH_2). ^{1}H NMR: 3.44 (s, 2H, NH2); 7.07–7.29 (m, 2H, ArH); 7.36–7.44 (m, 4H, ArH); 7.69 (t, 1H, J = 7.5 Hz, ArH); 7.83 (t, 1H, J = 7.4 Hz, ArH); 8.49 (d, 1H, J = 3.9 Hz, ArH); 8.68 (d, 1H, J = 4.0 Hz, ArH). Anal. Calcd. for $C_{17}H_{12}N_2OSe$ (338.90) C, 60.19; H, 3.54; N, 8.26; Found: C, 60.62; H, 4.02; N, 8.50.

2-(4-Aminophenyl)benzisoselenazol-3(2H)-one (5c): White tiny needles. M.p. 237–247°C (decomp.). IR (KBr) 1621, 1639 cm^{-1} (CO), 3213 cm^{-1} (NH_2). $_1$H NMR: 5.23 (s, 2H, NH2); 6.60 (d, 2H, J = 9.2 Hz, ArH); 7.16 (d, 2H, J = 7.6 Hz, ArH); 7.44 (t, 1H, J = 7.2 Hz, ArH); 7.63 (t, 1H, J = 7.6 Hz, ArH); 7.84 (d, 1H, J = 7.3 Hz, ArH); 8.04 (d, 1H, J = 8.0 Hz, ArH). Anal. Calcd. for $C_{13}H_{10}N_2OSe$ (288.90) C, 63.97; H, 3.49; N, 9.69. Found: C, 53.98; H, 3.58; N, 9.75.

Synthesis of alkylenebisbenzisoselenazol-3(2H)-ones (4e–h) and azaalkylenebisbenzisoselenazol-3(2H)-ones (4l,n–p). General procedure: A solution of chloride 1 (1.27 g, 5 mmol) in dry acetonitrile (15 ml) was added dropwise at room temperature over a period of 30 min to a stirred solution of diamine **3e–h,l,n–p** (16.5 mmol) in dry acetonitrile (50 ml) and the reaction was continued for additional 2 h. After the reaction finished, acetonitrile was evaporated *in vacuo*. Water (100 ml) was added to the residue, the mixture was stirred for 12 h and the crude product was filtered off and recrystallized from DMSO-acetonitrile 1:1 (**4e**), DMSO (**4f**) chloroform-hexane 5:2 (**4g**), chloroform (**4h**), methanol (**4l**) or washed with methanol (**4o,p**). When diamine **3n** was a substrate the solid formed after the reaction was

filtered off, extracted with boiling methanol and filtered again. From the filtrate methanol was evaporated *in vacuo* and the residue was a pure product **4n**. In the additional experiment (high solution condition) a solution of chloride **1** (0.64 g, 2.5 mmol) in dichloromethane (100 ml) was added dropwise at room temperature to a solution of diamine **3e** (1.51 g, 25 mmol) in dichloromethane (300 ml) and the reaction was continued for additional 2 h. After the reaction finished the solid was filtered off. It was treated with water (100 ml) and the mixture was stirred for 12 h and the crude product **4a** was recrystallized from DMSO-acetonitrile (1:1). The filtrate obtained was concentrated *in vacuo* to a small volume and crystallized pure **5e** was collected.

1,2-Bis[2-benzisoselenazol-3(2H)-onyl]ethane (4e): White tiny needles. M.p. 321°C. IR (KBr) 1600 cm^{-1} (CO). ^{1}H NMR: 4.0 (s, 4H, CH_2); 7.38 (t, 2H, J = 7.4 Hz, ArH); 7.66 (t, 2H, J = 7.6 Hz, ArH); 7.79 (d, 2H, J = 7.9 Hz, ArH); 7.96 (d, 2H, J = 8.0 Hz, ArH). Anal. Calcd for $C_{16}H_{12}N_2O_2Se_2$ (421.80) C, 45.5; H, 2.84; N, 6.64. Found: C, 45.35; H, 2.83; N, 6.69.

2-(2-Aminoethyl)benzisoselenazol-3(2H)-one (5e): White tiny needles. M.p. 85–87°C. IR (KBr) 1605, 1633 cm^{-1} (CO), 3280 cm^{-1} (NH_2). ^{1}H NMR: 2.81 (t, 2H, J = 6.0 Hz, CH_2); 3.26 (s, 2H, NH_2); 3.26 (s, 2H, NH_2); 3.71 (t, 2H, J = 6.3 Hz, CH_2); 7.39 (dt, 1H, J = 7.4 Hz and 0.4 Hz, ArH); 7.58 (dt, 1H, J = 7.6 Hz and 0.6 Hz, ArH); 7.81 (d, 1H, J = 3.9 Hz, ArH); 8.03 (d, 1H, J = 4.0 Hz, ArH) Anal. Calcd for $C_9H_{10}N_2OSe$ (240.90) C, 44.81; H, 4.15; N, 11.62. Found: C, 44.21; H, 4.20; N, 11.51.

1,3-Bis[2-benzisoselenazol-3(2H)-onyl]propane (4f): White tiny crystal. M.p. 252–255°C. IR (KBr) 1593 cm^{-1} (CO). ^{1}H NMR: 1.99 (q, 2H, J = 6.9 Hz, CH_2); 3.79 (t, 4H, J = 6.9 Hz, NCH_2); 7.41 (dd, 2H, J = 7.8 Hz, ArH); 7.60 (dd, 2H, J = 7.6 Hz and 7.3 Hz, ArH); 7.78 (d, 2H, J = 7.3 Hz, ArH); 8.04 (d, 2H, J = 7.6 Hz, ArH). Anal. Calcd for $C_{17}H_{14}N_2O_2Se_2$ (435.80) C, 46.80; H, 3.20; N, 6.42. Found: C, 46.62; H, 3.34; N, 6.39.

1,12-Bis[2-benzisoselenazol-3(2H)-onyl]dodecane (4h): White powder. M.p. 156–159°C. IR (KBr) 1595 cm^{-1} (CO). ^{1}H NMR: 1.22 (m, 16H, CH_2); 1.68 (m, 4H, CH_2); 3.86 (t, 4H, J = 7.2 Hz, NCH_2); 7.42 (dt, 2H, J = 7.4 Hz and 0.5 Hz, ArH); 7.58 (dt, 2H, J = 7.4 Hz and 0.6 Hz, ArH); 7.64 (d, 2H, J = 7.8 Hz, ArH); 8.05 (d, 2H, J = 7.8 Hz, ArH). Anal. Calcd for $C_{26}H_{32}N_2O_2Se_2$ (561.80) C, 55.56; H, 5.70; N, 4.98. Found: C, 55.46; H, 5.76; N, 5.08.

1,5-Bis[2-benzisoselenazol-3(2H)-onyl]-3methyl-3-azapentane (4l): White tiny needles. M.p. 180–182°C. IR (KBr) 1615 cm^{-1} (CO). ^{1}H NMR: 2.42 (s, 3H, NCH_3); 2.73 (t, 4H, J = 6.1 Hz, CH_2N); 3.89 (t, 4H, J = 6.1 Hz, NCH_2); 7.38 (dt, 2H, J = 7.4 Hz and 0.6 Hz, ArH); 7.56 (dt, 2H, J = 7.5 Hz and 0.6 Hz, ArH); 7.59 (d, 2H, J = 7.5 Hz, ArH); 7.89 (d, 2H, J = 7.6 Hz, ArH). Anal. Calcd for $C_{19}H_{19}N_3O_2Se_2$ (478.80) C, 47.60; H, 4.00; N, 8.77. Found: C, 47.90; H, 4.28; N, 8.81.

1,5-Bis[2-benzisoselenazol-3(2H)-onyl]-3-azapentane (4n): White powder. M.p. 190–192°C. IR (KBr) 1603 (CO), 3309 cm^{-1} (NH). ^{1}H NMR: 2.87 (t, 1H, J = 6.1 Hz, NH); 3.36–3.47 (m, 4H, CH_2); 3.76–4.07 (m, 4H, CH_2); 7.39 (t, 2H, J = 7.2 Hz, ArH); 7.59 (dt, 2H, J = 7.5 Hz and 0.6 Hz, ArH); 7.81 (d, 2H, J = 3.8 Hz, ArH) 7.98 (d, 2H, J = 3.9 Hz, ArH). Anal. Calcd. for $C_{18}H_{17}N_2O_2Se_2$ (450.80) C, 46.47; H, 3.47; H, 3.66; N, 9.04. Found: C, 46.20; H, 3.88; N, 8.80.

1,8-Bis[2-benzisoselenazol-3(2H)-onyl]-3,6-diazaooctane (4o): Yellow powder. M.p. 226–229°C; IR (KBr) 1625 cm^{-1} (CO), 3438 cm^{-1} (NH). ^{1}H NMR: 2.71–2.73 (m, 8H, CH_2); 2.82 (s, 4H, NCH_2); 3.78–3.88 (m, 2H, NH); 7.37 (t, 2H, J = 7.4 Hz, ArH); 7.57 (t, 2H, J = 7.3 Hz, ArH); 7.80 (d, 2H, J = 3.7 Hz, ArH); 8.01 (d, 2H, J = 3.9 Hz, ArH). Anal. Calcd for $C_{20}H_{22}N_4O_2Se_2$ (507.80) C, 47.26; H, 4.33; N, 11.02. Found: C, 47.00; H, 4.13; N, 11.33.

1,11-Bis[2-benzisoselenazol-3(2H)-onyl]-2,6,9-triazaundecane (4p): Yellow tiny crystal. Mp. 249–250°C; ^{1}H NMR: 2.49–2.60 (m, 4H, CH_2); 2.62 (t, 3H, J = 5.0 Hz, NH); 2.63–2.76 (m, 8H, CH_2); 3.88 (t, 4H, J = 4.8 Hz, CH_2); 7.37 (dd, 2H, J = 7.7 Hz, ArH); 7.57 (dd, 2H, J = 7.8 Hz, ArH); 7.80 (d, 2H, J = 7.7 Hz, ArH); 8.01 (d, 2H, J = 7.8 Hz, ArH); IR: 1626 cm^{-1} (CO); 3441 cm^{-1} (NH). Anal. Calcd for $C_{22}H_{27}N_5O_2Se_2$ (522.80): C, 47.93; H, 4.90; N, 12.70. Found: C, 47.78; H, 4.99; N, 12.50.

Synthesis of oxaalkylenebisbenzisoselenazol-3(2H)-ones (4j,k): A solution of chloride **1** (1.27 g, 5 mmol) in dichloromethane (15 ml) was added dropwise at room temperature over a period 30 min to a stirred solution of diamine **4j,k** (16.5 mmol) in dichloromethane (50 ml) and the reaction was continued for 3 days. After the reaction finished the mixture was filtered, the filtrate was washed with 5% hydrochloric acid (2×50 ml) and the solvent was evaporated *in vacuo*. The residue was recrystallized from dichloromethane-hexane 1:1 (**4j**) or product **4k** was separated by silica gel chromatography (ethyl acetate-methanol 5:1).

1,8-Bis[2-benzisoselenazol-3(2H)-onyl]-3,6-dioksaoctane (4j): White powder. M.p. 97°C. IR (KBr) 1622 cm^{-1}(CO). ^{1}H NMR: 3.74 (s, 4H, OCH_2O); 3.78 (t, 4H, J = 4.8 Hz, CH_2O); 4.13 (t, 4H, J = 4.8 Hz, NCH_2), 7.39 (dt, 2H, J = 7.5 Hz and 0.5 Hz, ArH); 7.57 (dt, 2H, J = 7.5 Hz and 0.6 Hz, ArH); 7.69 (d, 2H, J = 8.2 Hz, ArH); 8.03 (d, 2H, J = 8.1 Hz, ArH). Anal. Calcd for $C_{20}H_{20}N_2O_4Se_2$ (509.80) C, 47.00; H, 3.95; N, 5.53. Found: C, 47.03; H, 3.58; N, 5.20.

1,13-Bis[2-benzisoselenazol-3(2H)-onyl]-4,7,10-trioksatridecane (4k): White powder. M.p. 103–105°C. IR (KBr) 1592 cm^{-1} (CO). ^{1}H NMR: 1.97–2.06 (m, 4H, $N(CH_2)_2$; 3.56 (t, 4H, J = 6.8 Hz, CH_2O); 3.60–3.69 (m, 8H, $O(CH_2)_2O$); 3.94 (t, 6H, J = 6.8 Hz, NCH_2); 7.39 (dt, 2H, J = 7.4 Hz and 0.6 Hz, ArH); 7.54 (dt, 2H, J = 7.5 Hz and 0.7 Hz ArH); 7.62 (d, 2H, J = 3.9 Hz, ArH); 8.02 (d, 2H, J = 3.9 Hz, ArH). Anal Calcd for $C_{22}H_{24}N_2O_5Se_2$ (521.80) C, 49.50; H, 4.85; N, 4.81. Found: C 49.80; H, 5.18, N, 5.14.

1,5-Bis[2-benzisoselenazol-3(2H)-onyl]-3-azapentane methiodide (4m): The solution of compound **4l** (0.24 g, 5.2 mmol) in methanol (20 ml) and iodomethane (10 ml, 37 mmol) were stirred under reflux for 12 h. The formed solid filtered off and washed with methanol gave pure **4m**. Yellow powder. M.p. 226–228°C. IR (KBr) 1631 cm^{-1} (CO). ^{1}H NMR: 3.21 (s, 6H, CH_3); 3.69 (t, 4H, J = 6.9 Hz, CH_2N); 4.23 (t, 4H, J = 6.9 Hz, NCH_2); 7.44 (t, 2H, J = 7.4 Hz, ArH); 7.64 (dt, 2H, J = 7.6 Hz and 0.6 Hz, ArH); 7.83 (d, 2H, J = 7.7 Hz, ArH); 8.12 (d, 2H, J = 7.7 Hz, ArH). Anal. Calcd for $C_{20}H2_2IN_3O_2Se_2$ (620.70) C, 38.68; H, 3.57; N, 6.76. Found: C, 38.30; H, 3.57; N, 6.76.

1,6-Bis[2-benzisoselenazol-3(2H)-onyl]-3,4-dithiahexane (4q): A solution of chloride **1** (0.635 g, 2.5 mmol) in dry acetonitrile (15 ml) was added dropwise at room temperature over a period 30 min to a stirred solution of cystamine hydrochloride (**3q**) (0.38 g, 7.5 mmol) and triethylamine (2.1 ml, 150 mmol) in dry acetonitrile (25 ml) and the reaction was continued for additional 2 h. After the reaction finished, acetonitril was evaporated *in vacuo*. Water (50 ml) was added to the residue, the mixture was stirred for 12 h and the crude product was filtered off and recrystallized from acetonitrile-DMSO 4:1. Yiellow prisms. M.p. 215–217°C. IR (KBr) 1601 cm^{-1} (CO). ^{1}H NMR: 3.07 (t, 4H, J = 6.5 Hz, CH_2S); 4.02 (t, 4H, J = 6.5 Hz, NCH_2); 7.40 (t, 2H, J = 7.3 Hz, ArH); 7.61 (dt, 2H, J = 7.5 Hz, and 0.6 Hz, ArH); 7.81 (d, 2H, J = 3.8 Hz, ArH); 8.03 (d, 2H, J = 3.9 Hz, ArH). Anal. Calcd for $C_{18}H_{16}N_2O_2S_2Se_2$ (513.92) C, 42.02; H, 3.11; N, 5.45; Found: C, 42.10; H, 3.15; N, 5.50.

Reaction of 2-(chloroselenium)benzoyl chloride (1) with secondary amines. A solution of chloride **1** (0.507 g, 2 mmol) and triethylamine (7ml 5mmol) in dry ethyl acetate (15 ml) was added dropwise at room temperature over a period 30 min to a stirred solution of secondary amines (4 mmol) in dry ethyl acetate (25 ml) and the reaction was continued for 2 h. After the reaction finished the solid was filtered off. The solution was evaporated *in vacuo* and the crude product was recrystallized from ethyl acetate (**6,9**) or purified by silica gel chromatography using dichloromethane as an eluent (**7,8**). The compound **9** was also obtained by treating of the solution of 2-diselenobisbenzoyl chloride (**10**) (1.09 g; 2.5 mmol) in dichlorometane (70 ml) with diethylamine (1.1 ml, 5 mmol) and the reaction was continued for 2 h. After the reaction finished the mixture was washed with water (100 ml), the solvent was evaporated *in vacuo* and the residue was recrystallized from dichloromethane-hexane (1:3).

2-[(N,N-Diisopropyloamino)selenium]benzoyl chloride (6): Yellow prisms. M.p. 96–98°C. IR (KBr) 1658 cm^{-1} (CO). ^{1}H NMR: 1.21 (d,12H, J = 3.3 Hz, CH_3); 3.29–3.33 (m, 2H, CH); 7.33 (t, 1H, J = 7.3 Hz, ArH); 7.58 (t, 1H, J = 7.4 Hz, ArH); 7.74 (d,1H, J = 3.8 Hz, ArH); 8.19 (d, 1H, J = 4.0 Hz, ArH). Anal. Calcd for $C_{13}H_{18}NOSeCl$ (318.40): C, 48.98; H, 5.65; N, 4.40; Found: C, 48.77; H, 5.80; N, 4.40.

2-[(N,N-Diphenylamino)selenium]benzoyl chloride (7): Blue plates. M.p. 183–185°C. IR (KBr) 1594 cm^{-1} (CO). ^{1}H NMR: 7.29 (t, 4H, J = 6.5 Hz, ArH); 7.38 (t, 5H, J = 6.5 Hz, ArH); 7.53 (d, 5H, J = 3.8 Hz, ArH). Anal. Calcd for $C_{19}H_{14}NOSeCl$ (386.50): C, 59.00; H, 3.62; N, 3.62; Found: C, 58.87; H, 3.80; N, 3.49.

2-[(N,N-Diphenylamino)selenium]N′,N′-diphenylbenzamide (8): Yellow prisms. M.p. 155°C. IR (KBr) 1635 cm^{-1} (CO). ^{1}H NMR: 6.88–7.16 (m, 9H, ArH); 7.18–7.39 (m., 13H, ArH); 7.45 (d, 2H, J = 4.3 Hz, ArH). Anal. Calcd for $C_{31}H_{24}N_2OSe$ (518.90): C,71.68 ; H, 4.62; N, 5.39 ; Found: C, 71.05; H, 4.89 ; N, 5.49.

Diselenobis(N,N-diethylbenzamide) 9: White tiny needles. M.p. 88–89°C. IR (KBr) 1613 cm^{-1} (CO). ^{1}H NMR: 1.01 (broad s, 6H, CH_3); 1.16 (broad s, 6H, CH_3); 3.10 (broad s, 4H, CH_2); 3.46 (broad s, 4H, CH_2); 7.26–7.38 (m, 2H, ArH); 7.71–7.74 (m.,6H, Ar-H). Anal. Calcd for $C_{22}H_{28}N_2O_2Se_2$ (509.80): C, 51.38; H, 5.45; N, 5.45 ; Found: C, 51.52; H, 5.60; N, 5.21.

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