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Synthesis of 2,2′-Diselenobisbenzamides and 4,4′-Diselenobisbutyramides with Sulfamoyl Groups as New Potential Virucides and Cytokine Inducers

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The synthesis of 2,2′-diselenobisbenzamides and 4,4′-diselenobisbutyramides with sulfamoyl functions, two new groups of potential antiviral agents and cytokine inducers, based on the acylation of the 4-aminobenzenosulfonamides with corresponding chlorocarbonylaryl or chlorocarbonylalkyl diselenides, has been elaborated. In a similar way dithiobenzamide and diphenic acid bisbenzamide were obtained from dithio-2,2-bisbenzoic acid and diphenic acid dichlorides respectively.

Key words: γ-butyrolactone, 2,2′-diselenobisbenzamides, 4,4′-diselenobisbutyramides, sulfonamides, organic diselenides

The new strategy for the chemotherapy of AIDS led to discovery of 2,2′-dithiobenzamides with sulfonamide function (DIBAs), which are promising candidates for HIV treatment. They attack the protein zinc fingers, inactivate cell-free virions, inhibit acute and chronic infections, and exhibit broad antiretroviral activity. Among them DIBA-1 (**3**) was found to be the most active compound [1–3]. On the other hand, 2,2′-diselenobis(benzenesulfonamides) and their cyclic analogs 1,3,2-benzothiaselenazolone 1,1-dioxides, synthesized recently in our laboratory [4], were found as cytokine inducers in human peripheral blood leucocytes, similarly to other bisaryl diselenides and benzisoselenazolon-3(2H)-ones reported earlier [5,6].

These findings open some questions: Is the disulfide group a crucial factor responsible for biological activity of these compounds or can it be replaced by diselenide group? Can the DIBAs and their selenium analogues act as virucides active against various types of RNA and DNA viruses? Do they act as immunostimulants by induction of cytokines in a similar way as some other organoselenium compounds [7]? With these questions in mind we elaborated a simple synthesis for the model compounds with sulfamoyl group: 2,2′-diselenobisbenzamides (**4**), 4,4′-diselenobisbutyramides (**10**) and bisbenzamide (**6**), having neither disulfide or diselenide group. The reference DIBA-1 (**3**) was also synthesized.

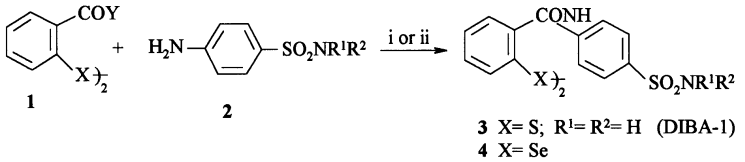
RESULTS AND DISCUSSION

2,2′-Disulfobenzamide (**3**), 2,2′-diselenobisbenzamides (**4**) and di(4-sulfamidophenyl)-2,2′-benzamide (**6**) were synthesized on two alternative methods presented in Scheme 1. The first of them (Method A) was based on the direct acylation of the corresponding 4-aminobenzenesulfonamide (**2**) [8] with acid chloride **1** (X = S, Se; Y = Cl) or **5** (Y = Cl) in the presence of pyridine used as a base in refluxing toluene. The alternative route (Method B) was based on HOBT-DCC (1-hydroxybenzotriazolo – dicyclohexylcarbodiimide) method [9] with DMAP used as cocatalyst. The starting acids were commercially available (**1**, X= S; **5**) or prepared according to known method (**1**, X = Se) [6]. From the acids their chlorides were obtained using the known procedures [3,6,10].

For the synthesis of DIBA-1 (**3**) and bisbenzamide (**6**) the more effective was Method B. The products **3** and **6** were obtained in 83% and 85% yield, respectively, while using of Method A led to both of these compounds in the yields about 20% lower. On the contrary, for synthesis of 2,2′-diselenobisbenzamides (**4**) Method A gave better results (yields 47–84%) than Method B.

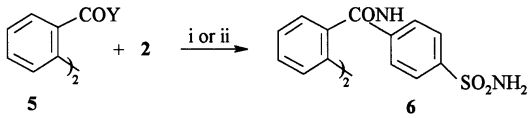
4,4′-Diselenobisbutyramides (**10**) were synthesized according to procedure presented in Scheme 2. The starting substrate was γ-butyrolactone (**7**). It was converted into 4,4′-diselenobisbutyric acid (**8**) by treatment with dilithium diselenide, generated *in situ* from elemental lithium and selenium, in the way similar to described

Scheme 1



4	R^1	R^2
a	H	H
b	COMe	H
c	Me	H
d	Me	Me
e	Bu	H

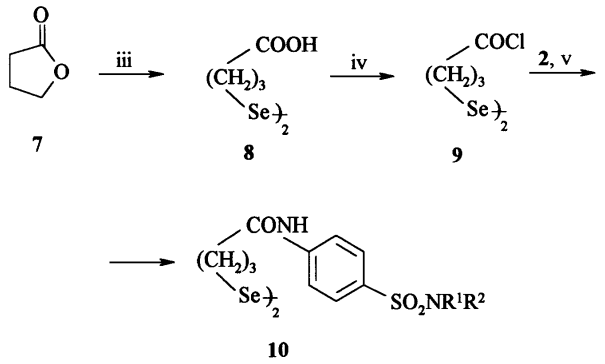
4	R^1	R^2
f		H
g	Oct	H
h		H
i	$-CH_2CH_2$ 	H



i: (Y=Cl), toluene, pyridine, reflux, 3-48h (Method A);
ii: (Y=OH), DCC, HOBT, DMAP, CH_2Cl_2, DMF (Method B).

earlier [11]. The formation of dilithium diselenide was catalysed by 4,4′-di(tert-butyl)biphenyl being catalyst, more effective than previously used diphenylacetylene, and the reaction was carried out using the ultrasonic bath. In the next step, acid (**8**) treated with oxalyl chloride gave chloride (**9**) subsequently used as a reagent for acylation of 4-aminobenzenesulfonamide (**2**), in the presence of 4-methylmorpholine as a base.

Scheme 2



10	R^1	R^2
a	H	H
b	Bu	H
c	Hex	H
d	Oct	H
e	$-(CH_2)_5-$	

iii: 1. Li_2Se_2, THF, RT; 2. HCl, H_2O; iv: ClCOCOCl, benzene, RT;
v: THF, 4-methylmorpholine, RT

Compounds **3**, **4a–i**, **6** and **10a–e** were tested as cytokine inducers. The compounds were added to human peripheral blood cultures and incubated for 24 hrs at 37°C. Phytohemaglutinin (PHA) was used as positive control. The levels of interferon (IFN), tumor necrosis factor (TNF) and interleukin 10 (IL-10) were determined in culture supernants [7,12]. Only **4d**, **4f** and **4g** were found to induce TNF production. There was no statistically enhancement of IFN or IL-10 production. Antiviral effects of compounds **3**, **4a–i**, **6** and **10a–e** were measured against encephalomyocarditis virus (EMCV, non-enveloped RNA virus), vesicular stomatitis virus (VSV, enveloped DNA virus) and herpes simplex virus type 1 (HSV-1, enveloped DNA virus). Strong anti-EMCV and anti-HSV-1 activities were found in the case of **4b**, **4c** and **4h**. Moreover, compounds **4d** and **4i** demonstrated anti-HSV-1 effect. Among the compounds tested only **4a** had weak anti-VSV activity. More advanced biological studies, including structure – activity relationship and mechanism of antiviral action of 2,2′-diselenobisbenzamides, are in progress.

EXPERIMENTAL

All reagents and solvents were purchased from Aldrich or Fluka. Reaction progress was monitored by Thin Layer Chromatography (TLC) on silica gel $60F_{254}$ coated aluminum TLC plates from Merck. 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 compound **8** and **9** 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.

Sulfonamides 3, 4 and 6. General procedure (Method A): The solution of acid chloride **1** (X = S, Se) or **5** (2.3 mmol), sulfanilamide **2** (5 mmol) and pyridine (1 ml) in toluene (40 ml) was refluxed for 3 to 48 h until dichloride was consumed. (The reaction progress was controlled by TLC). After the reaction finished the solvent was evaporated *in vacuo* and the residue was washed with 5% HCl and then with water. The crude product was recrystallized from DMF (**4a**, **6**), water (**4c**), DMF-water (**3**, **4d**, **4f**), acetone-cyclohexane (**4g**), purified on silicagel column using ethyl acetate-hexane 4:1 as an eluent (**4b**) or washed with hot water (**4e**).

Sulfonamides 3 and 6. (Method B): The solution of acid **1** (X = S; Y = OH) or **5** (Y = OH) (4.0 mmol), sulfanilamide (**2**) (8.0 mmol), DCC (1.8 g, 8.0 mmol), HOBT (1.13 g, 8.0 mmol) and DMAP (0.05 g, 0.4 mmol) in dichloromethane (40 ml) and DMF (20 ml) was stirred at room temperature for 3 h. Then the solid was filtered off and from the filtrate solvents were evaporated *in vacuo*. The residue was washed with water and the crude product was recrystallized from DMF (**6**) or DMF-water (**3**).

2,2′-Dithiobis[benz(p-sulfonamido)anilide] (3): White plates. Yield 64% (Method B 83%), m.p. 310°C (decomp.), ref. [3] 311–312°C.

2,2′-Diselenobis[benz(p-sulfonamido)anilide] (4a): White needles. Yield 59%, m.p. 315–318°C (decomp.). IR (KBr) 3342, 3302 cm^{-1} (NH), 1647 (CO), 1321, 1155 (SO_2). ^{1}H NMR: 7.05 (s, 4H, SO_2NH_2), 7.42–7.51 (m, 4H, ArH), 7.85 (q, J = 9.0 Hz, 6H, ArH), 7.98 (d, J = 9.0 Hz, 6H, ArH), 10.84 (s, 2H, CONH), Anal. Calcd. for $C_{26}H_{22}N_4O_6S_2Se_2$ (708.54); C, 44.92; H, 3.60; N, 7.52; S, 12.04. Found: C, 44.85; H, 3.35; N, 7.35; S, 11.90.

2,2′-Diselenobis{benz[p-(N-acetylsulfonamido)]anilide} (4b): Pale yellow needles. Yield 47%, m.p. 183–186°C. IR (KBr) 3293 cm^{-1} (NH), 1655 (CO), 1312, 1169 (SO_2). ^{1}H NMR: 1.98 (s, 6H, CH_3), 7.45 (dq, J = 8.0, 2.0 Hz, 4H, ArH), 7.80 (dd, J = 7.6, 2.0 Hz, 2H, ArH), 8.01–7.91 (m,10H, ArH), 10.94 (s, 2H, CONH), 12.00 (s, 2H, SO_2NHCO); Anal. Calcd. for $C_{30}H_{26}N_4O_8S_2Se_2$ (792.61) C, 45.71; H, 4.16; N, 6.79; S, 8.03 . Found: C, 45.72; H, 4.08; N, 6.94; S, 7.94.

2,2′-Diselenobis{benz[p-(N-methylsulfonamido)]anilide} (4c): Pale yellow prisms. Yield 58%, m.p. 201–203°C. IR (KBr) 3303 cm^{-1} (NH), 1611 (CO), 1329, 1161 (SO_2).^{1}H NMR: 2.43 (d, J = 5.0 Hz, 6H, CH_3), 7.43–7.51 (m, 4H, ArH, SO_2NH), 7.70 (t, J = 7.0 Hz, 2H, ArH), 7.82 (d, J = 8.0 Hz, 4H, ArH), 7.92–7.95 (m, 6H, ArH), 8.09 (d, J = 8.0 Hz, 2H, ArH),. Anal. Calcd. for $C_{28}H_{26}N_4O_6S_2Se_2$ (736.59) C, 44.03 ;H, 3.56; N, 7.69; S, 8.79 . Found: C, 44.32; H, 3.61; N, 7.86; S, 8.94.

2,2′-Diselenobis{benz[p-(N,N-dimethylsulfonamido)]anilide} (4d): Pale yellow prisms. Yield 56%, m.p. 254–259°C (decomp.). IR (KBr) 3365 cm^{-1} (NH), 1659 (CO), 1331, 1158 (SO_2). ^{1}H NMR: 2.59 (s, 12H, CH_3), 7.30–7.50 (m, 4H, ArH), 7.65–7.80 (m, 6H, ArH), 7.90–8.20 (m, 6H, ArH), 10.90 (s, 2H, CONH). Anal. Calcd. for $C_{30}H_{30}N_4O_6S_2Se_2$ (764.64); C, 46.96; H, 3.95; N, 7.02; S, 9.50. Found: C, 46.63; H, 4.11; N, 6.77; S, 9.85.

2,2′-Diselenobis{benz[p-(N-butylsulfonamido)]anilide} (4e): Pale yellow prisms. Yield 49%, m.p. 197–200°C. IR (KBr) 3276 cm^{-1} (NH), 1655 (CO), 1318, 1158 (SO_2). ^{1}H NMR: 0.78 (t, J = 7.0 Hz, 6H, CH_3), 1.16–1.26 (m, 4H, CH_2), 1.29–1.39 (m, 4H, CH_2), 2.71 (q, J = 6.0 Hz, 4H, NCH_2), 7.39–7.49 (m, 6H, ArH and SO_2NH), 7.88 (dd, J = 9.0 Hz, 6H, ArH), 7.95 (d, J = 9.0 Hz, 6H, ArH), 10.87 (s, 2H, CONH). Anal. Calcd. for $C_{34}H_{38}N_4O_6S_2Se_2$ (764.64); C, 49.76; H, 4.64; N, 6.83; S, 7.8. Found: C, 49.50; H, 4.60; N, 7.14; S, 7.93.

2,2′-Diselenobis{benz[p-(N-cyclohexylsulfonamido)]anilide} (4f): Pale yellow powder. Yield 55%, m.p. 285–288°C (decomp.). IR (KBr) 3366, 3295 cm^{-1} (NH), 1646 (CO), 1326, 1151 (SO_2), ^{1}H NMR: 0.90–1.25 (m, 10H, CH_2), 1.40–1.60 (m, 10H, CH_2), 2.91 (m, 2H, NCH), 7.38–7.49 (m, 2H, ArH), 7.54 (d, J = 7.2 Hz, 2H, SO_2NH), 7.77–7.82 (m, 6H, ArH), 7.92–7.99 (m, 6H, ArH), 10.83 (s, 2H, CONH). Anal. Calcd. for $C_{38}H_{42}N_4O_6S_2Se_2$ (872.83); C, 52,29; H, 4.85; N, 6.42; S, 7.35. Found: C, 51.61; H, 5.06; N, 6.16; S, 7.86.

2,2′-Diselenobis{benz[p-(N-octylsulfonamido)]anilide} (4g): White prisms. Yield 84%, m.p. 193–195°C. IR (KBr) 3270 cm^{-1} (NH), 1646 (CO), 1325, 1153 (SO_2). ^1H NMR : 0.82 (t, J = 6.45 Hz, 6H, CH_3), 1.09–1.38 (m, 24H, CH_2), 2.73 (q, J = 6.72 Hz, 4H, NCH_2), 7.37–7.51 (m, 6H, ArH), 7.77–7.82 (m, 6H, ArH and SO_2NH), 7.96–8.00 (m, 6H, ArH),10.88 (s, 2H, CONH). Anal. Calcd. for $C_{42}H_{54}N_4O_6S_2Se_2$ (932.97); C, 54.07; H, 5.83; N, 6.01; S, 6.87. Found: C, 54.29; H, 5.90; N, 6.21; S, 7.19.

2,2′-Diselenobis{benz[p-(N-(2-pyridyl)sulfonamido)]anilide} (4h): Yellow prisms. Yield 50%, m.p. 173–180°C. IR (KBr), 3232 cm^{-1} (NH), 1629 (CO), 1326, 1156 (SO_2). ^1H NMR: 6.88 (t, J = 6.21 Hz, 2H, Ar), 7.17 (d, J = 8.61 Hz, 2H, ArH), 7.33–7.54 (m, 4H, ArH), 7.68–7.81 (m, 4H, ArH), 7.85–8.11 (m, 12H, ArH), 10.84 (s, 2H, SO_2NH), 12.07 (s, 2H, CONH). Anal. Calcd. for $C_{36}H_{28}N_6O_6S_2Se_2$ (862.71); C, 50.12; H, 3.27; N, 9.74; S, 7.43. Found: C, 49.94; H, 3.00; N, 9.39; S, 7.38.

2,2′-Diselenobis{benz[p-(N-(ethyl-2-pyridyl)sulfonamido)]anilide} (4i): Yellow needles. Yield 49%, m.p. 210–217°C. IR (KBr) 3289 cm^{-1} (NH), 1644 (CO), 1320, 1157 (SO_2). ^1H NMR: 2.85 (t, J = 7.5 Hz, 4H, CH_2), 3.12 (q, J = 7.2 Hz, 4H, CH_2), 7.18–7.24 (m, 4H, ArH), 7.37–7.52 (m, 4H, ArH), 7.63–7.71 (m, 4H, ArH), 7.79–7.83 (m, 6H, ArH and SO_2NH), 7.96–8.04 (m, 6H, ArH), 8.45 (d, J = 4.5 Hz, 2H, ArH), 10.88 (s, 2H, CONH), ArH). Anal. Calcd. for $C_{40}H_{36}N_6O_6S_2Se_2$ (917.89); C, 52.29; H, 3.95; N, 9.15; S, 6.98. Found: C, 52.4 2; H, 3.62; N, 8.90; S, 7.65.

2,2′-Diphenicbis[(p-sulfonamido)anilide] (6): White plates. Yield 67% (Method B 85%), m.p. 319°C. IR (KBr) 3295 cm^{-1} (NH), 1648 (CO), 1332, 1158 (SO_2). ^1H NMR: 7.21–7.23 (m, 6H, ArH, SO_2NH_2), 7.47–7.52 (m, 4H, ArH), 7.62 (d, J = 8.82 Hz, 4H, ArH), 7.71 (d, J = 8.82 Hz, 6H, ArH), 10.79 (s, 2H, CONH). Anal. Calcd. for $C_{26}H_{22}N_4O_6S_2$ (550.62); C, 56.72; H, 4.03; N, 10.18; S, 11.65. Found: C, 56,40; H, 4.26; N, 10.03; S, 11.48.

4,4′-Diselenobisbutyric acid (8). To anhydrous tetrahydrofuran (50 ml), freshly distilled from a mixture potassium-benzophenone pleaced into dry 100 ml round-bottom long-neck flask, the fine slices of lithium (0.75 g, 0.107 mol) and 4,4′-di(tert-butyl)biphenyl (0.1 g, 0.4 mmol) were added. The flask was connected to the vacuum (water jet pump) until THF started to boil. Then vacuum was turn out and the flask was immersed into an ultrasonic bath, until the permanent deep green color appeared (*ca* 15 min). Selenium powder (7.89 g, 100 mmol) was added to the flask in one portion and it was degassed *in vacuo*, stoppered and sonificated at 30–40°C until all lithium was consumed (*ca* 4 h).

To a stirred reddish-brown suspension of dilithium diselenide, thus obtained, the solution of γ-butyrolactone (**7**) (9.4 g, 0.110 mmol) in anhydrous THF (20 ml) was added under nitrogen at room temperature during 15 min. The reaction was continued for additional 1 h, then the mixture was refluxed for 30 min. It was cooled, poured into water (200 ml) and shaken with ethyl ether. The layers were separated, the ethereal solution was washed with 10% aqueous KOH, and the water solutions were combined, acidified with 10% HCl to pH 3, and extracted with dichloromethane. The extract was washed with water, dried over Na_2SO_4, the solvent was evaporated *in vacuo* and the crude acid **8** (obtained in 84% yield) was recrystallized from isopropyl ether. Yellow powder. Yield 66%, m.p. 81–82°C (lit. [11] 74°C). IR (KBr), 3250–2600 cm^{-1} (OH), 1690, 1716 (CO). ^1H NMR: 2.09 (quintet, 4H, J = 7.2 Hz, CH_2), 2.51 (t, 4H, J = 7.2 Hz, $\underline{CH_2}COOH$), 2.96 (t, 4H, J = 7.2 Hz, $SeCH_2$), 11.3 (brs, 2H, COOH).

4,4′-Diselenobisbutyric acid chloride (9): To a stirred mixture of acid **8** (1.66 g, 5 mmol) in benzene (30 ml) oxalyl chloride (1.270 g, 10 mmol) was added at room temperature and the reaction was continued until all solid was dissolved (*ca* 1 h) and then for additional 0.5 h. After this period the solvent was evaporated *in vacuo*. Benzene (20 ml) was added to the residue and procedure was repeated twice in order to completely remove other volatile substances. The chloride **9** (yellow oil) was used in the next reactions without purification. Yield 1.830 g (99%). IR (CCl_4), ν 1797 cm^{-1}, ^1H NMR: 2.16 (quintet, J = 7.0 Hz, 4H, CH_2), 2.93 (t, J = 7.1 Hz, 4H, CH_2, 3.06 (t, J = 7.1 Hz, 4H, CH_2).

4,4′-Diselenobisbutyramides (10a–e). **General procedure:** To a solution of crude chloride **9** (1.830 g, 5 mmol) in anhydrous tetrahydrofuran (60 ml), sulfanilamide **2** (10.2 mmol) and N-methylmorpholine (1.032 g, 10.2 mmol) was added. The reaction was controlled by TLC on silica gel plates using: ethyl acetate for **10a**, ethyl acetate:hexane (2:3) for **10b–d** and ethyl acetate:hexane (1:1) for **10e** as a eluent. After the reaction was completed (1–3 days) the solvent was evaporated *in vacuo* and aqueous 5% HCl (100 ml) was added to the residue. Products **10a–e** were extracted using ethyl acetate (3 × 60 ml). The extracts were washed with 5% HCl (2 × 60 ml), then 5% $NaHCO_3$ (3 × 60 ml), water (3 × 60 ml) and dried over anhydrous sodium sulphate. The solvent was evaporated *in vacuo* and the crude products were recrystallized from DMF-water (**10a**), acetone (**10b**), acetonitrile (**10c**,**d**), toluene-chloroform (**10e**).

4,4′-Diselenobis{butyr[p-(sulfonamido)]anilide} (10a): Pale yellow powder. Yield 1.047 g (33%), m.p. 243–245°C, IR (KBr) 3295 cm^{-1} (NH), 1676 (CO), 1332, 1160 (SO_2). ^{1}H NMR: 2.02 (quintet, J = 7.0 Hz, 4H, CH_2), 2.48 (t, J = 6.8 Hz, 4H, CH_2), 2.98 (t, J = 7.1 Hz, 4H, CH_2), 7.24 (s, 4H, SO_2NH_2), 7.74 (s, 8H, ArH), 10.28 (s, 2H, CONH). Anal. Calcd. for $C_{20}H_{26}O_6N_4S_2Se_2$ (640.28); C, 37.50; H, 4.09; N, 8.75; S, 10.01. Found C, 36.64; H, 4.26; N, 8.26; S, 11.79.

4,4′-Diselenobis{butyr[p-(N-butylsulfonamido)]anilide} (10b): Pale yelow prisms. Yield 0.884 g (24%), m.p. 158–160°C, IR (KBr) 3277 cm^{-1} (NH), 1663 (CO), 1324, 1155 (SO_2). ^{1}H NMR: 0.84 (t, J = 7.2 Hz, 6H, CH_3), 1.21–1.42 (m, 8H, CH_2), 2.08 (quintet, J = 7.1 Hz, 4H, CH_2), 2.55 (t, J = 7.3 Hz, 4H, CH_2), 2.74 (q, J = 6.5 Hz, 4H, CH_2), 3.04 (t, 7.2 Hz, 4H, CH_2), 7.45 (t, J = 6.0 Hz, 2H, SO_2NH), 7.79 (dd, J = 12.6 and 8.7 Hz, 8H, ArH), 10.35 (s, 2H, CONH). Anal. Calcd. for $C_{28}H_{42}O_6N_4S_2Se_2$ (752.72); C, 44.68; H, 5.62; N, 7.44; S, 8.52. Found C, 44.55; H, 5.70; N, 7.32; S, 8.28.

4,4′-Diselenobis{butyr[p-(N-hexylsulfonamido)]anilide (10c): Pale yellow prisms. Yield 0.979 g (24%), m.p. 166–167°C, IR (KBr) 3272 cm^{-1} (NH), 1667 (CO), 1322, 1153 (SO_2). ^{1}H NMR: 0.80 (t, J = 6.5 Hz, 6H, CH_3), 1.14–1.33 (m, 16H, CH_2), 2.01 (quintet, J = 7.1 Hz, 4H, CH_2), 2.47 (t, J = 7.3 Hz, 4H, CH_2), 2.67 (dd, J = 6.7 and 6.2 Hz, 4H, CH_2), 2.97 (t, J = 7.2 Hz, 4H, CH_2), 7.38 (t, J = 6.0 Hz, 2H, SO_2NH), 7.72 (dd, J = 12.9 and 9.0 Hz, 8H, ArH), 10.28 (s, 2H, CONH). Anal. Calcd. for $C_{32}H_{50}O_6N_4S_2Se_2$ (808.82); C, 47.52; H, 6.23; N, 6.93; S, 7.93. Found C, 47.42; H, 6.11; N, 6.72; S, 7.74.

4,4′-Diselenobis{butyr[p-(N-octylsulfonamido)]anilide} (10d): Pale yellow prisms. Yield 1.479 g (34%), m.p. 172–173°C, IR (KBr) 3289 cm^{-1} (NH), 1663 (CO), 1328, 1158 (SO_2). ^{1}H NMR: 0.89 (t, J = 6.6 Hz, 6H, CH_3), 1.21–1.40 (m, 24H, CH_2), 2.08 (quintet, J = 7.2 Hz, 4H, CH_2), 2.54 (t, J = 7.3 Hz, 4H, CH_2), 2.75 (q, J = 6.5 Hz, 4H, CH_2), 3.04 (t, J = 7.2 Hz, 4H, CH_2), 7.44 (t, J = 6.0 Hz, 2H, SO_2NH), 7.79 (dd, J = 13.8 and 9.0 Hz, 8H, ArH), 10.36 (s, 2H, CONH). Anal. Calcd. for $C_{36}H_{58}O_6N_4S_2Se_2$ (864.93); C, 49.99; H, 6.76; N, 6.48; S, 7.41. Found C, 49.87; H, 6.50; N, 6.31; S, 7.69.

4,4′-Diselenobis{butyr(p-piperidylsulfonamido)anilide} (10e): Pale yellow prisms. Yield 1.549 g (40%), m.p. 102–103°C, IR (KBr) 3331 cm^{-1} (NH), 1679 (CO), 1338, 1149 (SO_2). ^{1}H NMR: 1.33–1.34 (m, 4H, CH_2), 1.49–1.53 (m, 8H, CH_2), 2.02 (quintet, J = 7.1 Hz, 4H, CH_2), 2.48 (t, J = 7.3 Hz, 4H, CH_2), 7.63 (d, J = 9.0 Hz, 4H, ArH), 7.81 (d, J = 9.0 Hz, 4H, ArH), 10.32 (s, 2H, CONH). Anal. Calcd. for $C_{30}H_{42}O_6N_4S_2Se_2$ (776.74); C, 46.39; H, 5.45; N, 7.21; S, 8.26. Found C, 46.91; H, 5.78; N, 7.66; S, 10.30.

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