Pergamon

Tetrahedron 58 (2002) 7531–7537

TETRAHEDRON

The reactions of 2-(chloroseleno)benzoyl chloride with nucleophiles

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Received 4 December 2001; revised 17 June 2002; accepted 4 July 2002

Abstract—The reactions of 2-(chloroseleno)benzoyl chloride with N, O and S nucleophiles such as alkanols, aminoalkanols, phenols, thiols, aminothiols and thiophenols have been investigated. It was found that the most reactive was a primary amino group which simultaneously underwent selenenylation–acylation. Less reactive hydroxy and thiol groups were selenenylated and/or acylated depending on the structure of the substrate and reaction conditions.

1. Introduction

Organoselenium compounds have been extensively applied in organic synthesis, materials synthesis, ligand chemistry and biologically relevant processes.[1,2] Among them benzisoselenazol-3(2*H*)-ones (particularly ebselen) play an important role in biology and medicine as biological response modifiers, mainly antiinflammatory agents.[3,4] In our previous work, some of these compounds were synthesized and reported as immunostimulants and virucides. They exhibited modest activity as inducers of different cytokines, such as interferons (mainly IFN-γ), tumor necrosis factor (IFN-α), interleukines (IL-2, IL-6), and other factors in human peripheral blood leukocyte cultures.[5–9] Moreover, some of them were active as inhibitors of endothelial nitric oxide synthase (ce NOS).[9–11] Although some methods for their synthesis are known most of them were synthesized starting from 2-(chloroseleno)benzoyl chloride (**1**), a well known and easy to obtain reagent.[6,9,12–14]

This particular compound has two different electrophilic centers. One of them (hard electrophilic center) is localized on the carbonyl carbon atom and the second one (soft electrophilic center) is the selenium atom. Both of these centers may compete toward nucleophiles such as amine nitrogen, thiol sulfur and hydroxide oxygen atoms. Although many reactions of 2-(chloroseleno)benzoyl chloride with nucleophiles have been studied, the majority of the reactants were primary aromatic, aliphatic and heteroaromatic amines[6,12–16] or compounds having a primary amino group and other functional groups completely inactive toward acylation or selenylation. They inchided aminocarboxylic acids,[9] aminoalkylphosphonates,[17] carboxyamides and sulfonamides,[18] pyrrolidine *N*-oxide substituted with a phenylamino group,[19] or compounds with active methylene groups (ketones and other C–H acids).[20,21] Acylation of methanol with 2-(chloroseleno)benzoyl chloride was mentioned by Lesser et al.[22,23] but in these old papers no structural evidence was provided. Most recently, the reaction of two long-chain alkanols was reported but diselenides were found as the final products.[24]

To the best of our knowledge, no information concerning the reactions of 2-(chloroseleno)benzoyl chloride with a broad spectrum of different mono and bisnucleophiles such as phenols, diols aromatic alcohols, aminoalkanols, hydroxylamine, aminophenols, thiols, dithiols and aminothiols has been published. The main goal of the work presented here was to generalize the competition of both electrophilic centers of 2-(chloroseleno)benzoyl chloride toward N, O and S nucleophiles particularly to these having two nucleophilic centers in the molecule.

2. Results and discussion

The first group of nucleophiles used in this work were hydroxy compounds—some alkanols, diols and hydroxyarenes (phenol and catechol) (Scheme 1). The reagent (**1**) was added stepwise to the nucleophile in the ratio 1:1 or 1:3 (sometimes the nucleophile was used in a larger excess). The alkanols (ethanol and 1-dodecanol), 1,4-butanediol and benzyl alcohol reacted with the hard electrophilic center of chloride (**1**) localized on the carbonyl carbon atom. *O*-Acylation proceeded faster than *O*-selenenylation and stable 2-(chloroseleno)benzoates (**2a–2d**) were formed, even when the alcohol was used in a large excess. Acid

Keywords: nucleophiles; acylation; selenium halogen compounds; selenium heterocycles.

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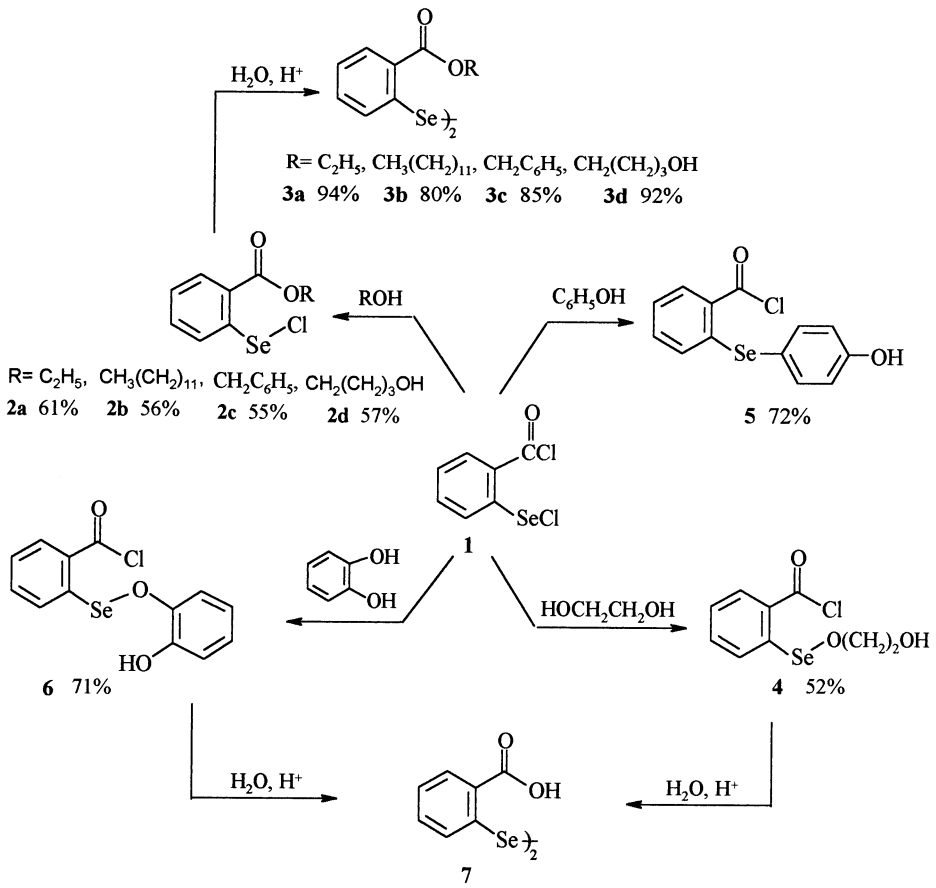
PII: S0040-4020(02)00789-5



Scheme 1.

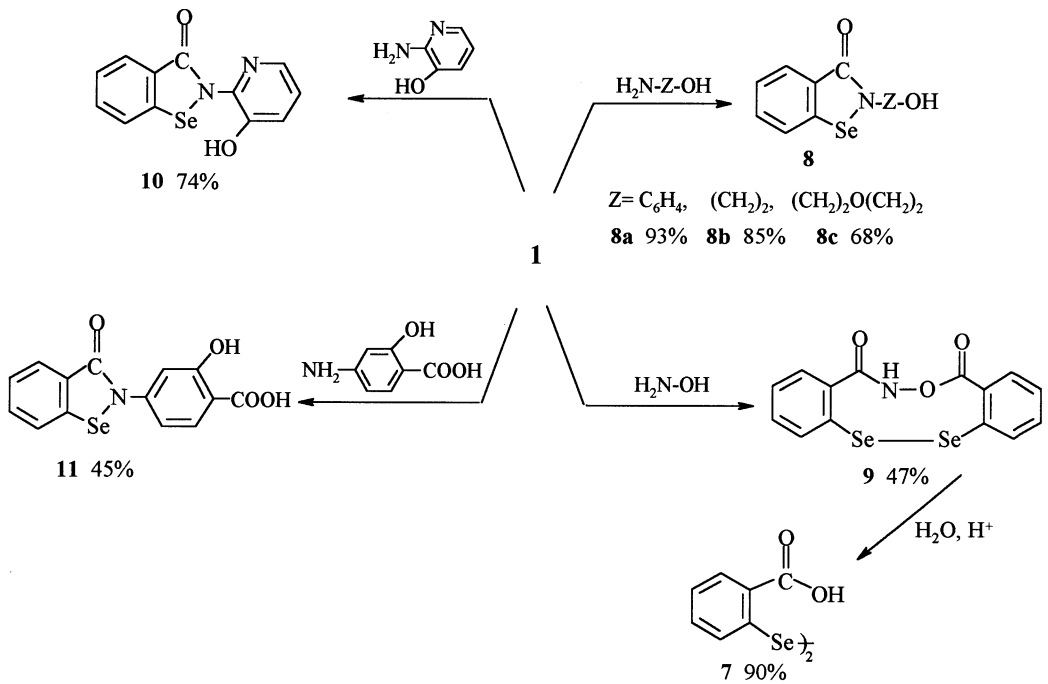
hydrolysis of these esters gave 2,2′-diselenobisbenzoates (**3a**–**3d**) (Scheme 1). This provides the evidence that the chloroseleno (and not the chlorocarbonyl group) was present in the starting **2**. Otherwise 2,2′-dielenobisbenzoic acid (**7**) should have formed.

Phenol reacted differently. *C*-Selenenylation of the aromatic ring, in the *para* position, instead of *O*-selenenylation of the hydroxy group, took place, and selenide (**5**) was produced. Catechol and ethylene glycol also reacted with 2-(chloroseleno)benzoyl chloride **1** in a different way to alkanols, 1,4-butanediol and benzyl alcohol. In this case, *O*-selenenylation proceeded faster than *O*-acylation and 2-(ethoxyseleno)benzoyl chlorides (**6**, **4**) were formed. Acid hydrolysis of the products (**6**, **4**) to known 2,2′-diseleno-bis(benzoic acid) (**7**)[25] (Scheme 1) confirmed the proposed structure.

It has been known that when diamines are treated with chloride (**1**) both amino groups react and bisbenzisoselena-zol-3(2*H*)-ones are produced.[14] We expected that in the case of compounds having amino and hydroxy groups both of them would react with the electrophilic centers of chloride (**1**). When chloride (**1**) was treated with hydroxylamine, the reaction proceeded in this way and cyclic diselenide (**9**) was produced, but it was an exception. In the IR spectrum of diselenide (**9**) two $\nu_{C=O}$ absorption bands at 1654 and 1705 cm^{-1} for O=C–N and O=C–O groups, respectively, were observed.[26] The acid hydrolysis of (**9**) resulted in 2,2′-diselenobis(benzoic acid) (**7**) and confirmed proposed structure.

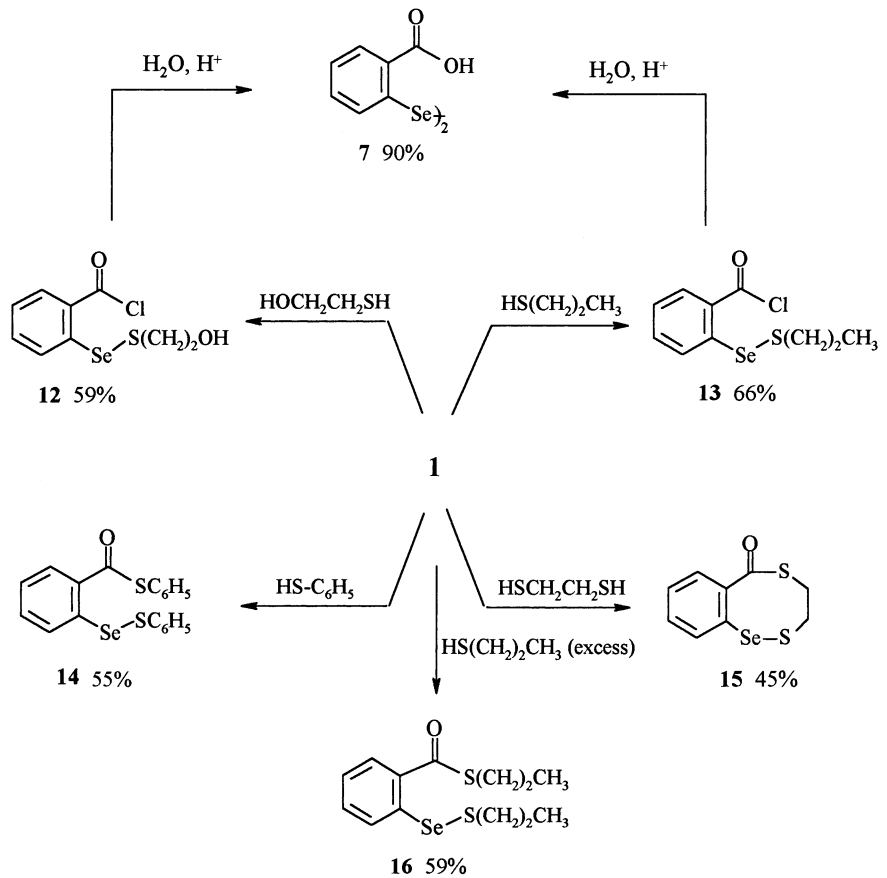
Aminoalkanols reacted with chloride (**1**) only at the amino group since its reactivity toward acylation and selenenyl-ation was substantially higher than reactivity of the hydroxy group, and 2-(hydroxyalkyl)benzisoselenazol-3(2*H*)-ones (**8a**–**8c**) were produced (Scheme 2). Reaction of *ortho* and *meta* aminophenols with 2-(chloroseleno)benzoyl chloride (**1**) gave only tarry mixtures of unidentified products but when an electron-withdrawing moiety such as a carboxylic acid group or pyridine nitrogen atom was present in the aromatic ring, the corresponding 2-substituted bensiso-selenazol-3(2*H*)-ones (**10**, **11**) were produced in high yields. The IR and ^{1}H NMR spectra of compounds (**8**, **10**, **11**) are characteristic for 2-substitued benzisoselenazol-3(2*H*)-ones and similar to these reported earlier for other compounds of this class.[6,9,14]

The third group of reactants investigated were *S*-nucleo-philes—thiols, dithiols, and thiophenol (Scheme 3). Generally, thiols reacted differently to O-nucleophiles and selenenylation of the sulfur atom was preferred. When the chloride (**1**) was treated with equimolar amount of 1-propanethiol only *S*-selenenylation, took place and selenosulfide (**13**) was formed. When the same thiol was used in a large excess, both *S*-selenenylation and *S*-acylation proceeded giving selenosulfide (**16**). 2-Mercaptoethanol and thiophenol reacted in a similar way producing the

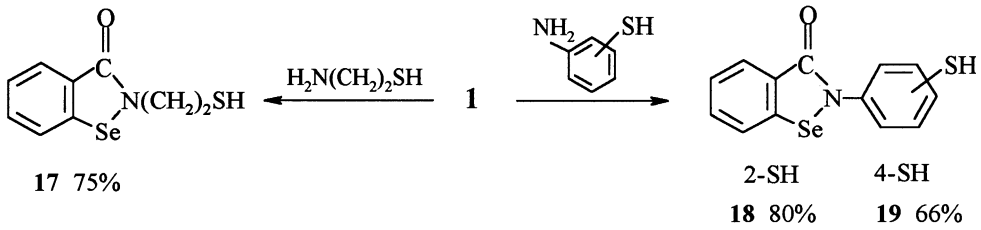


Scheme 2.

corresponding selenosulfides (**12**) and (**14**) while 1,2-ethanethiol gave cyclic product (**15**). Acid hydrolysis of the selenosulfides (**12**–**14**) to 2,2′-diselenobis(benzoic acid) (**7**) is a proof that in all of these compounds the chlorocarbonyl group is present and confirmed the proposed structures. The broad absorption bands ν_{CO}, in the IR spectra of the compounds (**14**–**16**) (1661–1745 cm^{-1}) are similar to these ν_{CO} values observed for compounds which have O=C–S group such as 3-chloropropylthioacetate (ν_{CO}=1680 cm^{-1}).[26]



Scheme 3.



Scheme 4.

Aminothiols reacted in a similar way to aminoalkanols (Scheme 4). Since reactivity of the amino group toward selenenylation–acylation was substantially higher than reactivity of the thiol group, the nitrogen atom of the amino group was incorporated into the heterocyclic ring and 2-thioalkyl or thioarylbenzisoselenazol-3(2*H*)-ones (**17**–**19**) were formed. Similarly, their IR and ^{1}H NMR spectra compared to these of other 2-substitued benzisoselenazol-3(2*H*)-ones[6,9,14] confirmed proposed structures.

3. Conclusions

It has been found that 2-(chloroseleno)benzoyl chloride reacts with N, O and S nucleophiles as selenenylating, acylating or as a tandem selenenylating–acylating bis-electrophile. The results of the reactions depend on the nucleophile and the molar ratio of the reagents. Selenenylation of thiols, catechol and ethylene glycol proceeded faster than acylation. For alkanols, 1,4-butanediol and benzyl alcohol different process was observed (*O*-acylation proceeded faster than *O*-selenenylation). In the case of phenol, selenylation took place on the carbon atom of the aromatic ring activated by the *para* hydroxy group. These results can be explained in terms of the hard and soft acid and base theory (HSAB principle).[27] The sulfur atom in thiols, being a soft nucleophilic center, is selenylated preferentially, and subsequent acylation takes place when the thiol is used in excess. The oxygen atoms in catechol, ethylene glycol or the 4-carbon atom in an aromatic ring being softer nucleophilic centers than oxygen atoms in alkanols, benzyl alcohol or 1,4-butanediol are selenylated while the later are acylated. It should be noted that compounds with Se–Cl, Se–O and Se–S bonds are susceptible toward hydrolysis producing 2,2′-diselenobis-(benzoic acid) (**7**) or its carboxyesters.

Among N, O and S nucleophiles, a primary amino group is the most susceptible towards selenenylation and acylation. Although it is difficult to predict which reaction proceeds initially, the final result is ring closure. Thus aminothiols, aminoalkanols and aminophenols form 2-thioalkyl-, 2-thioaryl-, 2-hydroxyalkyl- and 2-(hydroxyaryl)benzisoselenazol-3(2*H*)-ones. Since this reaction is highly chemoselective it opens a way for the synthesis of new biological response modifiers of this class starting from aminopolyols, aminosugars and nucleosides. We hope that the results presented in this work will be useful to those seeking new bioactive structures based on selenium-containing heterocycles.

4. Experimental

All reagents and solvents were purchased from Aldrich or Fluka. 2-(Chloro-seleno)benzoyl chloride (**1**) was prepared according to the literature.[4] Melting points were determined with a Digital Melting Point Apparatus Electrothermal IA 9100. ^{1}H NMR and ^{13}C NMR spectra were recorded in DMSO-d_6 on a Bruker DRX 300 spectrometer 300 MHz. Chemical shifts δ are reported in ppm relative to TMS. For compounds **2a**, **10**, **13**, **19**, selected as representatives of each class of compounds, ^{13}C NMR spectra were recorded. IR spectra were measured on a Perkin–Elmer 2000 FT spectrometer.

4.1. Reaction of chloride (1) with alkanols, diols and phenols

A solution of chloride (**1**) (0.51 g, 2 mmol) in dry acetonitrile (15 mL) was added dropwise at room temperature over a period of 30 min to a stirred solution of alcohol (2 mmol) (and triethylamine 0.7 mL, in the case of product **5**) in dry acetonitrile (45 mL) and the reaction was continued for an additional 2 h. When the reaction was completed, acetonitrile was evaporated in vacuo and the crude products were recrystallized from acetonitrile.

4.1.1. Ethyl 2-(chloroseleno)benzoate (2a). Yellow tiny needles (0.32 g, 61%), mp 85–88°C; [Found: C, 41.30; H, 3.70; Cl, 13.32. $C_9H_9O_2SeCl$ requires C, 41.01; H, 3.44; Cl, 13.45%]; ν_{max} (KBr) 1616, 2983, 2939 cm^{-1}; δ_H (300 MHz, DMSO-d_6) 1.46 (t, 3H, *J*=7.2 Hz, C*H*$_3$), 4.51 (q, 2H, *J*=7.2 Hz, C*H*$_2$), 7.34–7.39 (m, 1H, Ar-*H*), 7.65–7.70 (m, 1H, Ar-*H*), 8.02–8.07 (m, 2H, Ar-*H*); δ_C (300 MHz, DMSO-d_6) 13.89, 64.21, 124.03, 125.97, 126.84, 131.6, 135.26, 142.60, 172.00.

4.1.2. Dodecyl 2-(chloroseleno)benzoate (2b). Yellow tiny needles (0.45 g, 56%), mp 43–45°C; [Found: C, 56.22; H, 6.95; Cl, 8.54. $C_{19}H_{29}O_2SeCl$ requires C, 56.52; H, 7.19; Cl, 8.80%]; ν_{max} (KBr) 1635, 2855, 2927, 2955 cm^{-1}; δ_H (300 MHz, DMSO-d_6) 1.45 (t, 3H, *J*=7.3 Hz, C*H*$_3$), 4.30–4.55 (m, 22H, C*H*$_2$), 7.30–7.45 (m, 2H, Ar-*H*), 8.05–8.10 (m, 2H, Ar-*H*).

4.1.3. Benzyl 2-(chloroseleno)benzoate (2c). Yellow powder (0.36 g, 55%), mp 66–69°C; [Found: C, 51.36; H, 3.94. $C_{14}H_{11}O_2SeCl$ requires C, 51.61; H, 3.38%]; ν_{max} (KBr) 1629, 3030 cm^{-1}; δ_H (300 MHz, DMSO-d_6) 5.47 (s, 2H, C*H*$_2$), 7.30–7.55 (m, 6H, Ar-*H*), 7.69 (t, 1H, *J*=7.5 Hz, Ar-*H*), 8.06 (t, 2H, *J*=7.6 Hz, Ar-*H*).

4.1.4. 4-Hydroxybutyl 2-(chloroseleno)benzoate (2d).

Yellow tiny crystals (0.35 g, 57%), mp 60–62°C; [Found: C, 45.14; H, 4.93; Cl, 12.12. $C_{11}H_{13}O_2SeCl$ requires C, 45.30; H, 4.50; Cl, 12.68%]; ν_{max} (KBr) 1630, 2874, 2942, 3067, 3358 cm^{-1}; δ_H (300 MHz, DMSO-d_6) 1.59–1.92 (m, 8H, C*H*$_2$), 4.49 (s, 1H, O*H*), 7.36–8.03 (m, 4H, Ar-*H*).

4.1.5. 2-[(2-Hydroxyethyloxy)selena]benzoyl chloride (4). White prisms (0.29 g, 52%), mp 128–129°C; [Found: C, 38.50; H, 3.31; Cl, 12.72. $C_9H_9O_3SeCl$ requires C, 38.62; H, 3.25; Cl, 12.68%]; ν_{max} (KBr) 1698, 2878, 2948, 3285 cm^{-1}; δ_H (300 MHz, DMSO-d_6) 3.76 (t, 2H, *J*=4.7 Hz, C*H*$_2$), 4.38 (t, 2H, *J*=4.8 Hz, C*H*$_2$), 4.38 (s, 1H, O*H*), 7.41 (t, 1H, *J*=7.4 Hz, Ar-*H*); 7.54 (t, 1H, *J*=7.3 Hz, Ar-*H*), 7.69 (d, 1H, *J*=4.0 Hz, Ar-*H*), 8.14 (d, 1H, *J*=4.0 Hz, Ar-*H*).

4.1.6. 2-[(2-Hydroxyphenyl)selena]benzoyl chloride (5). Yellow powder (0.45 g, 72%), mp 173–174°C; [Found: C, 50.22; H, 2.70; Cl, 11.28. $C_{13}H_9O_2SeCl$ requires C, 50.10; H, 2.89; Cl, 11.40%]; ν_{max} (KBr) 1605, 3368 cm^{-1}; δ_H (300 MHz, DMSO-d_6) 7.03 (d, 2H, *J*=4.4 Hz, Ar-*H*), 7.66 (t, 1H, *J*=7.7 Hz, Ar-*H*), 7.89 (d, 2H, *J*=4.4 Hz, Ar-*H*), 7.96 (t, 1H, *J*=7.7 Hz, Ar-*H*), 8.33 (d, 1H, *J*=4.0 Hz, Ar-*H*), 8.38 (d, 1H, *J*=3.9 Hz, Ar-*H*), 10.78 (s, 1H, O*H*).

4.1.7. 2-[(2-Hydroxyphenoxy)selena]benzoyl chloride (6). Beige powder (0.66 g, 71%), mp 159–161°C; [Found: C, 47.80; H, 2.87; Cl, 10.80. $C_{13}H_9O_3SeCl$ requires C, 47.66; H, 2.77; Cl, 10.82%]; ν_{max} (KBr) 1715, 3422 cm^{-1}; δ_H (300 MHz, DMSO-d_6) 6.16–8.33 (m, 8H, Ar-*H*), 9.67 (bs, 1H, O*H*).

4.2. Acid hydrolysis of esters (2) and compounds (4, 6, 9, 12, 13)

The hydrolyzed compound (2 mmol) was poured into water (30 mL), the reaction mixture was stirred for 24 h and formed solid was filtered off. Diselenides (**3a**–**3d**) or 2,2′-diselenobis(benzoic acid) (**7**) thus obtained were dried in vacuo and recrystallized from hexane–ethyl acetate.

4.2.1. Diethyl 2,2′-diselenobisbenzoate (3a). Beige powder (0.86 g, 94%), mp 132°C;[24] 132°C.

4.2.2. Didodecyl 2,2′-diselenobisbenzoate (3b). Yellow powder (1.18 g, 80%), mp 72°C;[24] 72°C.

4.2.3. Dibenzyl 2,2′-diselenobisbenzoate (3c). White powder (0.95 g, 85%), mp 108°C; [Found: C, 57.80; H, 3.84. $C_{28}H_{22}O_4Se_2$ requires C, 57.95; H, 3.79%]; ν_{max} (KBr) 1690 cm^{-1}; δ_H (300 MHz, DMSO-d_6) 5.42 (s, 4H, C*H*$_2$), 7.20–7.52 (m, 12H, Ar-*H*), 7.65–8.05 (m, 6H, Ar-*H*).

4.2.4. Di(4-hydroxybutyl) 2,2′-diselenobisbenzoate (3d). Yellow powder (1.00 g, 92%), mp 125–127°C; [Found: C, 48.11; H, 4.35. $C_{22}H_{26}O_6Se_2$ requires C, 48.55; H, 4.78%]; ν_{max} (KBr) 1686, 3330 cm^{-1}; δ_H (300 MHz, DMSO-d_6) 1.45–1.80 (m, 16H, C*H*$_2$), 4.45 (s, 2H, O*H*), 7.30–8.09 (m, 8H, Ar-*H*).

4.2.5. 2,2′-Diselenobisbenzoic acid (7). White powder (84–90%), mp 295°C;[25] 296–297°C.

4.3. Reaction of chloride (1) with hydroxylamine and aminoalkanols

A solution of chloride (**1**) (0.51 g, 2 mmol) (and 6 mmol CaO in case **9**) in dry acetonitrile (15 mL); (in case of **11**, 15 mL DMF) was added dropwise at room temperature over a period of 30 min to a stirred solution of hydroxylamine hydrochloride and aminoalkanol or aminophenol (2 mmol) in dry acetonitrile (45 mL) (in case **11**, 45 mL DMF) and the reaction was continued for additional 2 h. When the reaction was completed, acetonitrile (DMF in case **11**) was evaporated in vacuo. Product **8b** was recrystallized from water; product **9** from acetonitrile. Water (100 mL) was added to the residue, the mixture was stirred for 12 h and the product **10** was filtered off, dried in air and recrystallized from DMSO/acetonitrile (4:1). Product **11** was extracted with ethanol (30 mL) and recrystallized from the same solvent; the compounds **8a**, **8c** were extracted with dichloromethane (30 mL) and recrystallized from acetonitrile.

4.3.1. 2-(4-Hydroxyphenyl)benzisoselenazol-3(2*H*)-one (8a). White powder (0.54 g, 93%), mp 94–96°C; [Found: C, 53.80; H, 3.10; N, 4.85. $C_{13}H_9O_2NSe$ requires C, 53.81; H, 3.13; N, 4.83%]; ν_{max} (KBr) 1639, 3260 cm^{-1}; δ_H (300 MHz, DMSO-d_6) 6.84–6.79 (m, 2H, Ar-*H*), 7.31–7.35 (m, 2H, Ar-*H*), 7.44 (t, 1H, *J*=7.5 Hz, Ar-*H*), 7.64 (t, 1H, *J*=7.6 Hz, Ar-*H*), 8.06 (d, 1H, *J*=3.9 Hz, Ar-*H*), 8.86 (d, 1H, *J*=3.9 Hz, Ar-*H*), 9.57 (s, 1H, Ar-O*H*).

4.3.2. 2-(4-Hydroxyethyl)benzisoselenazol-3(2*H*)-one (8b). Yellow tiny crystals (0.30 g, 85%), mp 142–145°C; [Found: C, 44.52; H, 3.64; N, 5.87. $C_9H_9NO_2Se$ requires C, 44.67; H, 3.72; N, 5.79%]; ν_{max} (KBr) 1593, 2842, 2921, 3224 cm^{-1}; δ_H (300 MHz, DMSO-d_6) 3.58–3.63 (m, 2H, C*H*$_2$), 3.79 (t, 2H, *J*=5.4 Hz, N–C*H*$_2$), 5.07 (s, 1H, O*H*), 7.39 (t, 1H, *J*=7.4 Hz, Ar-*H*), 7.58 (t, 1H, *J*=7.5 Hz, Ar-*H*), 7.80 (d, 1H, *J*=7.8 Hz, Ar-*H*), 8.01 (d, 1H, *J*=7.8 Hz, Ar-*H*).

4.3.3. 2-(4-Hydroxyethoxyethyl)benzisoselenazol-3(2*H*)-one (8c). White needles (0.39 g, 68%), mp117–119°C; [Found: C, 46.12; H, 4.58; N, 5.10. $C_{11}H_{13}NO_2Se_2$ requires C, 46.00; H, 4.55; N, 4.89%]; ν_{max} (KBr) 1578, 2902, 3486 cm^{-1}; δ_H (300 MHz, DMSO-d_6) 3.64–3.67 (m, 2H, C*H*$_2$), 3.73–3.83 (t, 4H, *J*=5.4 Hz, C*H*$_2$–O–C*H*$_2$), 4.12 (t, 2H, N–C*H*$_2$), 7.39–7.44 (m, 1H, Ar-*H*), 7.56–7.64 (m, 2H, Ar-*H*), 8.06 (d, 1H, *J*=7.8 Hz, Ar-*H*).

4.3.4. Compound 9. Orange powder (0.37 g, 47%), mp 85–86°C; [Found: C, 42.27; H, 2.30; N, 3.20. $C_{14}H_9NO_3Se_2$ requires C, 42.31; H, 2.27; N, 3.52%]; ν_{max} (KBr) 1654, 1705, 3433 cm^{-1}; δ_H (300 MHz, DMSO-d_6) 4.42 (bs, 1H, O*H*), 7.35–8.37 (m, 8H, Ar-*H*).

4.3.5. 2-[2-(3-Hydroxypyridyl)]benzisoselenazol-3(2*H*)-one (10). Beige powder (0.22 g, 74%), mp 199–201°C; [Found: C, 49.32; H, 2.77; N,9.39. $C_{12}H_8N_2O_2Se$ requires C, 49.50; H, 2.75; N, 9.63%]; ν_{max} (KBr) 1624, 2573, 3056 cm^{-1}; δ_H (300 MHz, DMSO-d_6) 7.18–7.26 (m, 1H, Ar-*H*), 7.36 (d, 1H, *J*=4.0 Hz, Ar-*H*), 7.49 (t, 1H, *J*=7.5 Hz, Ar-*H*), 7.71 (t, 1H, *J*=7.6 Hz, Ar-*H*), 7.92–8.03 (m, 2H, Ar-*H*), 8.09 (d, 1H, *J*=4.0 Hz, Ar-*H*), 12.15 (s, 1H,

O*H*); δ_C (300 MHz, DMSO-d_6) 123.70, 126.26, 126.73, 127.59, 128.53, 129.78, 133.43, 138.87, 140.89, 142.87, 145.11, 165.59.

4.3.6. 2-(4-Carboxy-3-hydroxyphenyl)benzisoselenazol-3(2*H*)-one (11). White powder (0.39 g, 45%), mp 190–195°C; [Found: C, 50.26; H, 2.74; N, 4.41. $C_{14}H_9NO_2Se$ requires C, 50.30; H, 2.69; N, 4.19%]; ν_{max} (KBr) 1605, 1651, 3055, 3421 cm^{-1}; δ_H (300 MHz, DMSO-d_6) 7.26–7.29 (m, 1H, Ar-*H*), 7.43–7.52 (m, 2H, Ar-*H*), 7.69 (t, 1H, *J*=7.5 Hz, Ar-*H*), 7.83 (d, 1H, *J*=4.1 Hz, Ar-*H*), 7.91 (d, 1H, *J*=4.0 Hz, Ar-*H*), 8.07 (d, 1H, *J*=4.0 Hz, Ar-*H*), 10.43–14.00 (m, 2H, O*H*; COO*H*).

4.4. Reaction of chloride (1) with thiols and thiophenol

A solution of chloride (**1**) (0.51 g, 2 mmol) in dry dichloromethane (15 mL) were added stepwise at room temperature over a period of 30 min to a stirred mixture of thiol (2 mmol) and BaO (0.31 g, 4 mmol) in dry dichloromethane (45 mL) and the reaction was continued for additional 2 h. The insoluble $Ba(OH)_2$ and $BaCl_2$ were filtered off. From the filtrate, dichloromethane was evaporated in vacuo. Products **12** and **13** were recrystallized from dichloromethane; **14** from toluene; **15** and **16** from acetonitrile.

4.4.1. 2-[(2-Hydroxyethylthio)seleno]benzoyl chloride (12). Yellow tiny prisms (0.31 g, 59%), mp 94–96°C; [Found: C, 36.02; H, 3.10; S, 11.04. $C_9H_9O_2SSeCl$ requires C, 36.56; H, 3.05; S, 10.83%]; ν_{max} (KBr) 1635, 2950, 3055, 3436 cm^{-1}; δ_H (300 MHz, DMSO-d_6) 2.86 (s, 1H, O*H*), 3.16–3.26 (m, 2H, CH_2), 4.48–4.62 (m, 2H, CH_2), 7.37 (t, 1H, *J*=7.5 Hz, Ar-*H*), 7.47 (d, 1H, *J*=3.6 Hz, Ar-*H*), 7.67 (d, 1H, *J*=3.6 Hz, Ar-*H*), 8.22 (t, 1H, *J*=7.5 Hz, Ar-*H*).

4.4.2. 2-(2-Propylthioseleno)benzoyl chloride (13). Beige powder (0.39 g, 66%), mp 67–68°C, [Found: C, 40.90; H, 3.80; S, 10.95; Cl, 12.11. $C_{10}H_{11}OSSeCl$ requires C, 40.90; H, 3.78; S, 10.92; Cl, 12.07%]; ν_{max} (KBr) 1636, 2872, 2931, 2964, 3060 cm^{-1}; δ_H (300 MHz, DMSO-d_6) 1.04 (t, 3H, *J*=7.2 Hz, CH_3), 1.76 (t, 2H, *J*=7.2 Hz, CH_2), 3.16–3.19 (m, 2H, CH_2), 7.38 (d, 1H, *J*=3.4 Hz, Ar-*H*), 7.68 (d, 1H, *J*=3.4 Hz, Ar-*H*), 8.12 (t, 2H, *J*=8.0 Hz, Ar-*H*). δ_C (300 MHz, DMSO-d_6) 13.21, 22.22, 22.31, 64.20, 126.61, 126.72 129.82, 131.60, 133.96, 144.97.

4.4.3. *S*-Phenyl 2-[(phenylthio)seleno]benzoate (14). Yellow powder (0.34 g, 55%), mp 278–279°C; [Found: C, 56.00; H, 3.39; S, 16.05. $C_{19}H_{14}OS_2Se$ requires C, 56.87; H, 3.49; S, 15.93%]; ν_{max} (KBr) 1745 cm^{-1}; δ_H (300 MHz, DMSO-d_6) 7.27–7.43 (m, 4H, Ar-*H*) 7.59 (t, 1H, *J*=7.7 Hz, Ar-*H*), 7.66 (d, 2H, *J*=4.0 Hz, Ar-*H*), 7.73 (d, 1H, *J*=4.0 Hz, Ar-*H*), 8.03 (t, 2H, *J*=7.8 Hz, Ar-*H*), 8.17 (d, 1H, *J*=4.0 Hz, Ar-*H*).

4.4.4. 1,2,5-Selenadithiabenzcyclooctan-6-one (15). White prisms (0.33 g, 45%), mp124–126°C; [Found: C, 39.30; H, 3.00; S, 23.66. $C_9H_8OS_2Se$ requires C, 39.27; H, 2.91; S, 23.27%]; ν_{max} (KBr) 1661 cm^{-1}; δ_H (300 MHz, DMSO-d_6) 2.96–3.09 (m, 2H, CH_2), 3.36–3.43 (m, 2H, CH_2), 7.30 (t, 1H, *J*=8.0 Hz, Ar-*H*), 7.60 (t, 1H, *J*=8.0 Hz, Ar-*H*), 8.07–8.15 (m, 1H, Ar-*H*), 8.26–8.35 (m, 1H, Ar-*H*).

4.4.5. *S*-Propyl 2-[(propylthio)seleno]benzoate (16). Yellow oil (59%); [Found: C, 46.82; H, 5.09; S, 19.11. $C_{13}H_{18}OS_2Se$ requires C, 43.28; H, 4.59; S, 19.23%]; ν_{max} (KBr) 1694, 2929, 2961 cm^{-1}; δ_H (300 MHz, DMSO-d_6) 0.95 (t, 6H, *J*=15 Hz, CH_3), 1.55–1.68 (m, 4H, CH_2), 2.76 (t, 2H, *J*=7.2 Hz, S–CH_2), 3.07 (t, 2H, *J*=7.2 Hz, S–CH_2), 7.47 (t, 1H, *J*=4.0 Hz, Ar-*H*), 7.72 (d, 1H, *J*=4.0 Hz, Ar-*H*), 8.15 (t, 1H, *J*=4.0 Hz, Ar-*H*), 8.24 (d, 1H, *J*=4.0 Hz, Ar-*H*).

4.5. Reaction of chloride (1) with aminothiol and aminothiophenols

A solution of chloride (**1**) (0.51 g, 2 mmol) in dry acetonitrile (15 mL) was added dropwise at room temperature over a period of 30 min to a stirred solution of aminothiol or aminophenol (6 mmol) in dry acetonitrile (45 mL) and the reaction was continued for additional 2 h. When the reaction was completed, acetonitrile was evaporated in vacuo. Water (100 mL) was added to the residue, the mixture was stirred for 12 h and the precipitate solid was filtered off and dried in air. The products **17**–**19** were recrystallized from DMSO/acetonitrile (3:1).

4.5.1. 2-(2-Mercaptoethyl)benzisoselenazol-3(2*H*)-one (17). Bright beige powder (0.44 g, 75%), mp 150–152°C; [Found: C, 39.16; H, 3.45; N, 5.55. C_8H_9NOSeS requires C, 39.04; H, 3.66; N, 5.69%]; ν_{max} (KBr) 1630, 2925 cm^{-1}; δ_H (300 MHz, DMSO-d_6) 2.07 (s, 1H, SH), 2.98–3.16 (m, 2H, CH_2), 3.19–3.32 (m, 2H, CH_2), 7.35–8.23 (m, 4H, Ar-*H*).

4.5.2. 2-(2-Mercaptophenyl)benzisoselenazol-3(2*H*)-one (18). Brown powder (0.47 g, 80%), mp 179–181°C; [Found: C, 51.51; H, 2.58; N,4.60. $C_{13}H_9NOSe$ requires C, 51.00; H, 2.94; N, 4.58%]; ν_{max} (KBr) 1621, 3055 cm^{-1}; δ_H (300 MHz, DMSO-d_6) 7.22–7.93 (m, 8H, Ar-*H*), 10.67 (s, 1H, S*H*).

4.5.3. 2-(4-Mercaptophenyl)benzisoselenazol-3(2*H*)-one (19). Yellow powder (0.40 g, 66%), mp 139–141°C; [Found: C, 51.22; H, 3.16; N, 4.70. $C_{13}H_9NOSe$ requires C, 51.00; H, 2.94; N, 4.58%]; ν_{max} (KBr) 1646, 3286 cm^{-1}; δ_H (300 MHz, DMSO-d_6) 7.27–8.03 (m, 8H, Ar-*H*), 10.67 (s, 1H, S*H*); δ_C (300 MHz, DMSO-d_6) 122.00, 122.40, 126.80, 127.84, 129.41, 130.24, 130.64, 131.50, 132.54, 133.00, 134.04, 136.45, 174.00.

Acknowledgments

This work was supported by the Polish State Committee for Scientific Research (grant No 3T09A 097 17).

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