Oxidation of α-sulfonyl selenides: Formation of selenolesters

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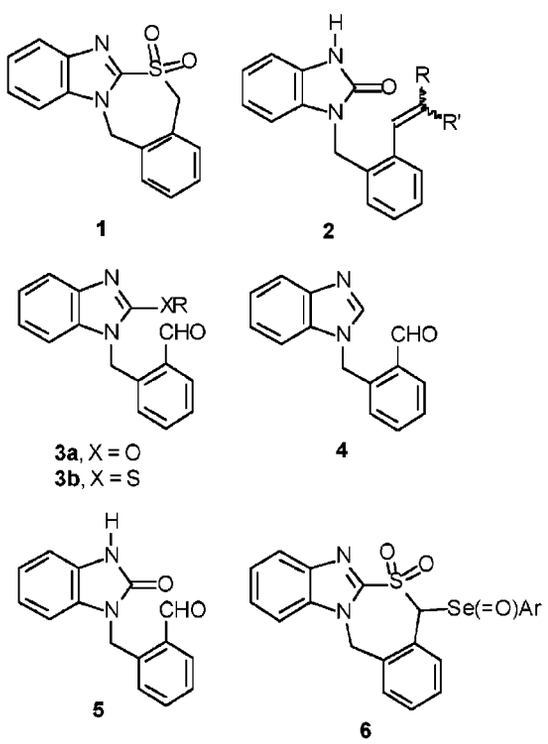
Treatment of 7-phenylseleno-7,12-dihydrobenzo[5,6][1,3]thiazepino[3,2-*a*]benzimidazole 6,6-dioxide **7a** in CH_2Cl_2 with *m*-chloroperbenzoic acid (MCPBA) and 28% H_2O_2 at room temperature gave *Se*-phenyl 2-[(benzimidazol-1-yl)methyl]selenobenzoate **8a**. Similarly, the oxidation of sulfone **7a** in THF with aqueous Oxone® at room temperature gave the same selenolester **8a**. The formation of selenolesters **8** can be explained by assuming either the involvement of oxaseleniranium cation **13**, having a sulfinate group at C-2 of the benzimidazole moiety, as an intermediate which is believed to be formed by an intramolecular nucleophilic attack of the polarized oxygen of the Se=O bond of selenoxide **6** to the α-carbon next to the sulfonyl group, or Pummerer-type reactions.

Introduction

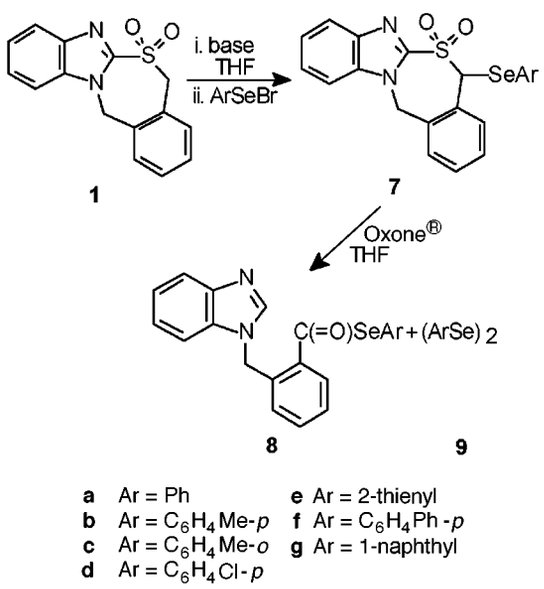
We have previously shown that 7,12-dihydrobenzo[5,6]-[1,3]thiazepino[3,2-*a*]benzimidazole 6,6-dioxide **1**[1] can be utilized for the synthesis of various benzimidazole derivatives such as 1-(2-vinylbenzyl)benzimidazolin-2-ones **2**,[1] 2-alkoxy-1-(2-formylbenzyl)benzimidazoles **3a**, 2-alkylthio-1-(2-formylbenzyl)benzimidazoles **3b**, 1-(2-formylbenzyl)benzimidazole **4**, and 1-(2-formylbenzyl)benzimidazol-2-one **5**.[2]



In continuing to explore new functionalized benzimidazole derivatives, which are of biological interest,[3] we became interested in an α-sulfonyl selenoxide **6**, characterized by bonding of sulfonyl and areneseleninyl moieties to the same carbon atom with a hydrogen atom and a phenyl group, because the chemistry of such a system has never been studied despite extensive research on the oxidation of α-sulfonyl selenides having an alkyl group at the α-position.[4] One might envisage the formation of α-sulfonyl selenenate as an intermediate, as proposed in the thermal decomposition of benzyl phenyl selenoxide into benzaldehyde,[5] or displacement of the sulfonyl group by nucleophilic attack of the polarized oxygen of a Se=O bond of the dipolar selenoxide functionality, although only rarely have sulfones been usefully employed as leaving groups in reactions forming new carbon–carbon bonds.[6] With this in mind, we have undertaken the selenation of sulfone **1**, followed by oxidation reactions.

Results and discussion

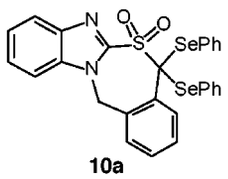
Treatment of compound **1** in THF with *n*-BuLi (1–1.5 equiv.) at −78 °C, followed by addition of benzeneselenenyl bromide, gave α-sulfonyl selenide **7a** (18%) (Scheme 1). Substitution of



Scheme 1

n-BuLi for LDA (2 equiv.) as a base afforded **7a** (19%). The yield of **7a** increased to 65% when NaH followed by *n*-BuLi was used. Treatment of compound **1** with NaH, followed by the addition of benzenselenenyl bromide, gave a reaction mixture which showed two spots corresponding to compound **7a** (R_f = 0.6, EtOAc–*n*-hexane 1:2) and bis(phenylseleno) sulfone **10a** (R_f = 0.7, EtOAc–*n*-hexane 1:2) on TLC in spite of the use of equimolar amounts of NaH and substrate **1**. The top spot corresponding to bisselenide **10a** disappeared after the addition of *n*-BuLi, and intensified fluorescence was observed from the

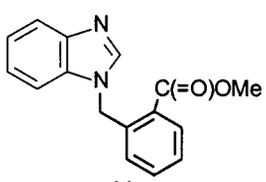
bottom spot corresponding to compound **7a** by visualization with a mineral UV lamp.



10a

Since compound **10a**, formed in minute amounts, was able to be removed by carefully performed column chromatography without using *n*-BuLi, analogous monoselenide products **7b–g** were isolated by chromatographic separation of the reaction mixture without using *n*-BuLi.

Oxidation of selenide **7a** with MCPBA in CH_2Cl_2 at rt gave selenolester **8a** (36%), diphenyl diselenide **9a** (25%), and unchanged reagent **7a** (34% recovery). Selected oxidants such as 28% H_2O_2, Oxone®, and sodium periodate were employed to see if the yield of selenolester **8a** could be increased. The reaction of compound **7a** with 28% H_2O_2 in CH_2Cl_2 (1.2 equiv.) for 5 h at rt gave selenolester **8a** (25%) together with diselenide **9a** (21%). However, treatment of compound **7a** in MeOH with aq. Oxone® (1.1 equiv.) for 20 h at rt gave methyl 2-[(benzimidazol-1-yl)methyl]benzoate **11** (38%). In contrast, treatment of compound **7a** in THF with the same oxidant (1.1 equiv.) in water for 24 h at rt gave compound **8a** (21%) along with diselenide **9a** (39%). Interestingly, compound **7a** in MeOH reacted with aq. $NaIO_4$ (1.1 equiv.) at reflux to give ester **11** (31%) and methyl 2-[(2-methoxybenzimidazol-1-yl)methyl]-benzoate **12** (14%).



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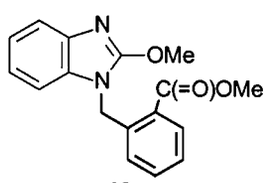

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Although MCPBA was a better oxidant than the other oxidants employed, it was more laborious to separate the desired product from the MCPBA-mediated oxidation mixture than from the other oxidant-mediated reaction mixtures. Therefore, Oxone® in THF was used for the other oxidation reactions.

The structures of selenolesters **8** were determined on the basis of their spectroscopic data and elemental analyses. There have been a variety of methods for the synthesis of selenolesters.[7] Nevertheless, the formation of aryl selenolesters **8** from the oxidation of α-sulfonyl areneselenides **7** is of interest from a mechanistic point of view. The formation of selenolesters **8** may be explained by assuming the involvement of oxaseleniranium cation **13** having a sulfinate group at C-2 of the benzimidazole moiety as an intermediate, which is believed to be formed by an intramolecular nucleophilic attack of the polarized oxygen of a Se=O bond of selenoxide **6** to the α-carbon next to the sulfonyl group (Scheme 2). To the best of our knowledge, neither oxaselenirane nor oxaseleniranium cation has appeared in the literature, although there are a number of literature reports in which oxathiiranes, analogous to oxaselenirane, have been proposed as intermediates.[8] Loss of sulfur dioxide from the intermediate **13** to give a carbanion **14**, followed by protonation, which is analogous to the formation of the parent benzimidazole *via* benzimidazol-2-ylsulfinate as an intermediate in alkaline autoxidation of benzimidazole-2-thione with oxygen and *tert*-butoxide in *tert*-butanol,[9] would give a new oxaseleniranium cation **15**, which undergoes deprotonation concomitant with a bond cleavage between oxygen and selenium atoms to give selenolesters **8**. Alternatively, first ring opening, followed by loss of a sulfur dioxide, which is in reverse order of the preceding path (**13** ⟶ **14** ⟶ **15**) would give a carbanion **17** (**13** ⟶ **16** ⟶ **17**). Protonation of **17** would give selenolesters **8**. On the other hand, one may consider the possible involvement of a Pummerer-type of reaction on compound **6**, which would lead to seleninium ion **18**.[10] Nucleophilic attack of water to give the alcohol **19**, followed by a C–S bond cleavage would give sulfinate **16**. Surprisingly, there is no precedent for this type of bond cleavage yielding selenolesters in the reported Pummerer reactions.

The possibility of an intramolecular proton transfer from an oxaseleniranium moiety to the carbanion at C-2 of the benzimidazole moiety of an intermediate **14** was ruled out owing to the failure of the isolation of a deuterium incorporated compound **8** from its deuterated precursor **7a-D**, which was prepared as shown in Scheme 3.

Treatment of compound **1** with NaH in THF under nitrogen at rt, followed by addition of D_2O, gave deuterated compound **1-D** (27%) and undeuterated **1** (63%). The deuterium content of product **1-D** increased to 60% by performing one more deuteration under the same conditions as in the first one. Compound **1-D** (60% D content) was converted into selenide **7a-D** (55%). Deuterium content of **7a-D** (30%) was determined by comparing the intensities of the proton signal of an NCH_2 and a methine proton signal of the $SO_2CHSePh$ moiety. Treatment of compound **7a-D** with MCPBA afforded compound **8** of which the ^1H NMR spectrum did not indicate the incorporation of D at C-2 (δ-value of H at C-2: 7.91) of the benzimidazole moiety. Therefore, it may be reasonable to assume that either *m*-chlorobenzoic acid or water acts as a proton donor depending on the oxidants employed. In view of this, pathway **13** ⟶ **14** ⟶ **15** may be more plausible than the alternative pathway **13** ⟶ **16** ⟶ **17** if oxaseleniranium ions are involved because, for the former, protonation of the carbanion of **14** precedes deprotonation of the oxaseleniranium cation of intermediate **14**, whereas for the latter, deuteration of a carbanion **17** may be possible owing to the precedent deprotonation of an oxaseleniranium cation **13**.

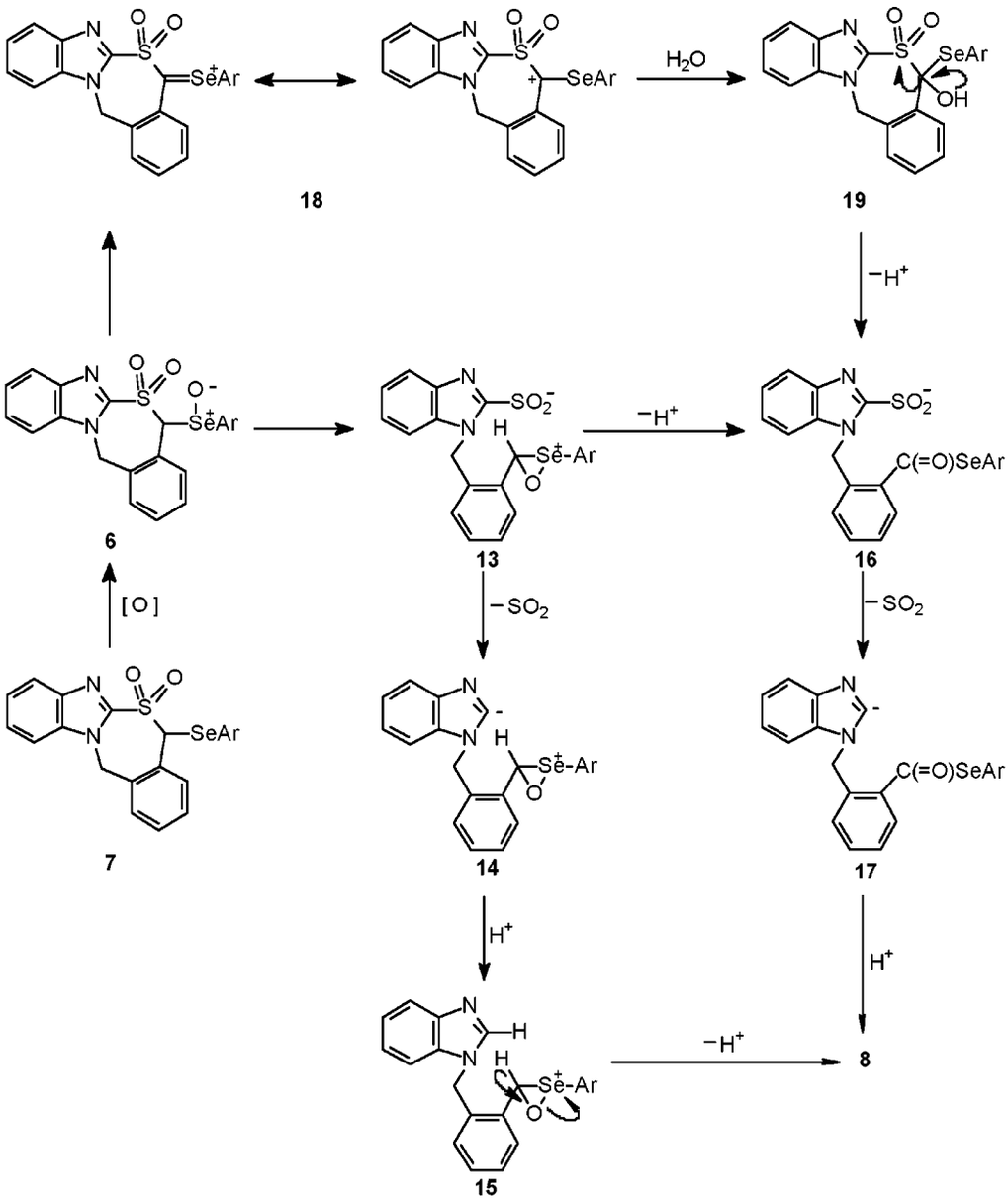
In order to test the generality of the reaction, phenyl α-phenylsulfonylbenzyl selenide **21** was prepared from benzyl phenyl sulfone **20**, benzeneselenenyl bromide, and LDA. Treatment of sulfone **21** with Oxone® in a mixture of THF and water (5 : 2) for 10 min gave selenolester **22** (44%) (Scheme 4).

However, the same oxidation of α-sulfonyl-α-methyl selenide **23** with Oxone® gave an elimination product **24** (65%) (Scheme 5).

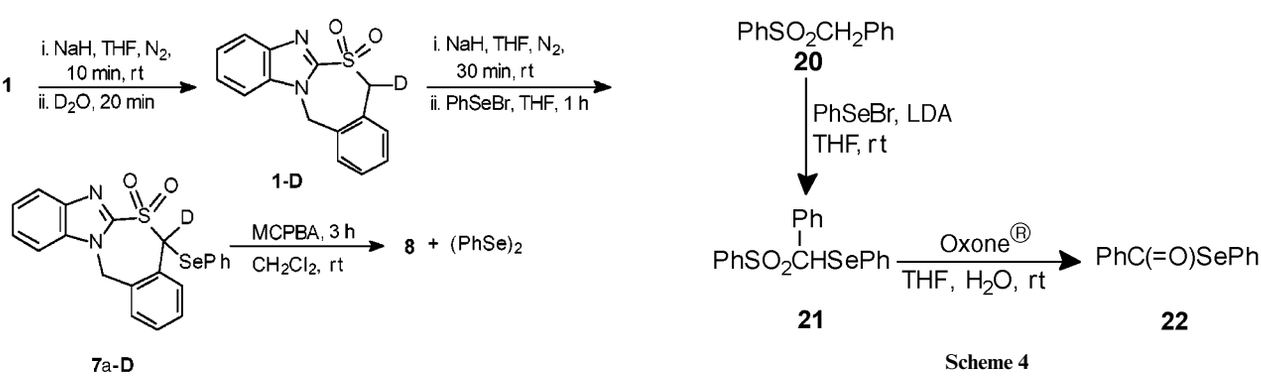
In summary, treatment of α-sulfonyl selenides having one α-hydrogen but without β-hydrogens, *i.e.*, 7-phenylseleno-7,12-dihydrobenzo[5,6][1,3]thiazepino[3,2-*a*]benzimidazole **7a** and phenyl α-phenylsulfonylbenzyl selenide **21**, with oxidants such as MCPBA, 28% H_2O_2, and Oxone® in THF gives the corresponding selenolesters **8** and **22**, respectively. The formation of selenolesters can be explained by the involvement of either an oxaseleniranium cation or Pummerer type of reaction, in which the former, to the best of our knowledge, has never been proposed in the literature and there is no precedent for the formation of selenolester in Pummerer reactions.

Experimental

The ^1H NMR spectra were recorded at 80, 200, or 300 MHz in $CDCl_3$ solution containing tetramethylsilane as an internal standard; *J*-values are given in Hz. IR spectra were recorded in KBr or for thin-film samples on KBr plates. Mass spectra were obtained by electron impact at 70 eV. Elemental analyses were determined by the Korea Basic Science Center. Column chromatography was performed using silica gel (Merck, 70–230 mesh, ASTM). Mps were determined on a Fisher-Johns melting point apparatus and are uncorrected. Solvents were pre-dried over sodium.



Scheme 2

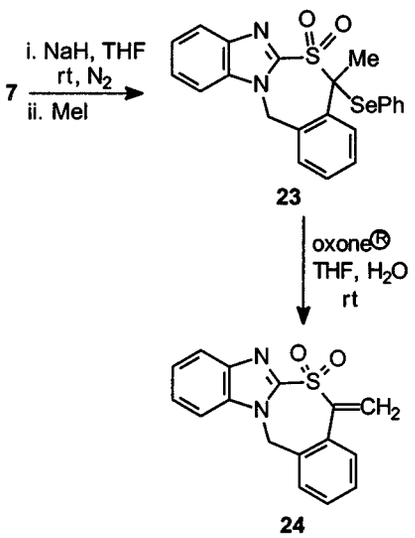


Scheme 3

Scheme 4

Reaction of 7,12-dihydrobenzo[5,6][1,3]thiazepino[3,2-*a*]benzimidazole 6,6-dioxide 1 with NaH

To a solution of compound **1** (284 mg, 1.00 mmol) in dried THF (25 ml) at rt under nitrogen was added NaH (36 mg, 1.50 mmol). The mixture was stirred for 10 min, followed by dropwise addition of a solution of benzeneselenenyl bromide (354 mg, 1.50 mmol) in THF (30 ml) for 30 min and subsequently *n*-BuLi (0.3 ml of 2.5 M solution in *n*-hexane, 0.120 mmol) was added during 5 min. The mixture was additionally stirred for 30 min at rt, followed by quenching with water. The reaction mixture was extracted with EtOAc (40 ml × 3). The extracts were dried over $MgSO_4$. After removal of the solvent *in vacuo*, the residue was chromatographed on a silica gel column (2 × 10 cm). Elution with a mixture of *n*-hexane and EtOAc (2:1) gave diphenyl diselenide **9a** (78 mg, 33%), *7,7-bis(phenylseleno)-7,12-dihydrobenzo[5,6][1,3]-*



Scheme 5

thiazepino[3,2-a]benzimidazole 6,6-dioxide **10a** (14 mg, 2%), mp 180–181 °C (from CH_2Cl_2–*n*-hexane) (Found: C, 53.9; H, 3.2; N, 4.9; S, 5.4. $C_{27}H_{20}N_2O_2SSe_2$ requires C, 54.10; H, 3.36; N, 4.67; S, 5.35%); ν_{max}(KBr)/cm^{-1} 3056, 1690, 1321, 1148, 822 and 736; δ_H(80 MHz) 5.53 (2H, s, NCH_2), 6.48–7.57 (16H, m, ArH), 7.57–8.13 (1H, m, ArH) and 8.47–8.74 (1H, m, ArH), and *5-phenylseleno-7,12-dihydrobenzo[5,6][1,3]thiazepino[3,2-a]benzimidazole 6,6-dioxide* **7a** (284 mg, 65%), mp 108–111 °C (from EtOH) (Found: C, 57.3; H, 3.8; N, 6.5; S, 7.3. $C_{21}H_{16}N_2O_2SSe$ requires C, 57.40; H, 3.67; N, 6.38; S, 7.30%); ν_{max}(KBr)/cm^{-1} 3056, 2912, 1456, 1427, 1318, 1142 and 822; δ_H(80 MHz) 5.43 (2H, s, NCH_2), 5.88 (1H, s, SO_2CH), 7.06–7.15 (2H, m, ArH), 7.21–7.53 (10H, m, ArH) and 7.91–7.98 (1H, m, ArH). Elution with the same solvent mixture (1 : 2) gave unchanged substrate **1** (41 mg, 14% recovery).

General procedure for the synthesis of 7-(arylseleno)-7,12-dihydrobenzo[5,6][1,3]thiazepino[3,2-*a*]benzimidazole 6,6-dioxides 7b–g

To a solution of compound **1** in THF (100 ml) under nitrogen was added NaH. The mixture was stirred for 1 h at rt followed by dropwise addition of di-*p*-tolyl diselenide and di-*o*-tolyl diselenide for products **7b** and **7c**, respectively, during 5 min. For products **7d**–**g**, the corresponding areneselenenyl bromide, which was prepared *in situ* by treatment of the corresponding diarene diselenide **9** with bromine in THF (10–15 ml) for 5 min at rt under nitrogen, was added dropwise. The mixture was additionally stirred for 1 h. After removal of the solvent *in vacuo*, the residue was extracted with CH_2Cl_2 (150 ml × 2), and dried over $MgSO_4$. Chromatography (230–400 mesh, 2 × 10 cm) of the residue using a mixture of EtOAc and *n*-hexane (1 : 2) gave the corresponding diselenide **9d**–**g** and selenides **7b**–**g** and **10c**,**d**.

7-(4-Tolylseleno)-7,12-dihydrobenzo[5,6][1,3]thiazepino[3,2-*a*]benzimidazole 6,6-dioxide 7b. The reaction of compound **1** (284 mg, 1.00 mmol), NaH (29 mg, 1.21 mmol), and di-*p*-tolyl diselenide (275 mg, 1.10 mmol) gave *title compound* **7b** (153 mg, 33%), mp 170–171 °C (from CH_2Cl_2–*n*-hexane) (Found: C, 58.0; H, 4.1; N, 6.2; S, 7.0. $C_{22}H_{18}N_2O_2SSe$ requires C, 58.28; H, 4.00; N, 6.18; S, 7.07%); ν_{max}(KBr)/cm^{-1} 3040, 2912, 1321, 1142 and 819; δ_H(80 MHz) 2.20 (3H, s, CH_3), 5.40 (2H, s, NCH_2), 5.80 (1H, s, SO_2CH), 6.61–6.96 (2H, m, ArH), 6.96–7.57 (9H, m, ArH) and 7.64–8.01 (1H, m, ArH).

7-(2-Tolylseleno)-7,12-dihydrobenzo[5,6][1,3]thiazepino[3,2-*a*]benzimidazole 6,6-dioxide 7c. The reaction of compound **1** (200 mg, 0.703 mmol), NaH (17 mg, 0.708 mmol), and di-*o*-tolyl diselenide (175 mg, 0.700 mmol) gave *title compound* **7c** (97 mg, 31%), mp 196–198 °C (from CH_2Cl_2–*n*-hexane) (Found: C, 58.5; H, 3.9; N, 6.25; S, 7.1%); ν_{max}(KBr)/cm^{-1} 3056, 2928, 1452, 1318, 1142 and 1120; δ_H(80 MHz) 2.44 (3H, s, CH_3), 5.50 (2H, s, NCH_2), 5.76 (1H, s, SO_2CH), 6.67–7.74 (11H, m, ArH) and 7.74–8.01 (1H, m, ArH), and *7,7-bis(2-tolylseleno)-7,12-dihydrobenzo[5,6][1,3]thiazepino[3,2-a]benzimidazole 6,6-dioxide* **10c** (13 mg, 3%), mp 221–223 °C (from CH_2Cl_2) (Found: C, 56.1; H, 3.9; N, 4.4; S, 5.1. $C_{29}H_{24}N_2O_2SSe_2$ requires C, 55.95; H, 3.89; N, 4.50; S, 5.15%); ν_{max}(KBr)/cm^{-1} 3056, 2912, 1320, 1142, 1082, 819, 624 and 430; δ_H(80 MHz) 2.48 (6H, s, $2CH_3$), 5.73 (2H, s, NCH_2), 6.56–7.66 (14H, m, ArH), 7.78–8.14 (1H, m, ArH) and 8.14–8.48 (1H, m, ArH).

7-(4-Chlorophenylseleno)-7,12-dihydrobenzo[5,6][1,3]thiazepino[3,2-*a*]benzimidazole 6,6-dioxide 7d. The reaction of compound **1** (284 mg, 1.00 mmol), NaH (26 mg, 1.08 mmol), and 4-chlorobenzeneselenenyl bromide, which was prepared *in situ* from di-4-chlorophenyl diselenide (209 mg, 0.548 mmol) and bromine (88 mg, 0.551 mmol), gave *title compound* **7d** (205 mg, 43%), mp 116–118 °C (from CH_2Cl_2–*n*-hexane) (Found: C, 53.5; H, 3.3; N, 5.7; S, 6.9. $C_{21}H_{15}ClN_2O_2SSe$ requires C, 53.23; H, 3.19; N, 5.91; S, 6.76%); ν_{max}(KBr)/cm^{-1} 3056, 2484, 1459, 1318, 1142, 1120, 1081, 1011 and 909; δ_H(80 MHz) 5.44 (2H, s, NCH_2), 5.86 (1H, s, SO_2CH), 6.70–7.64 (11H, m, ArH) and 7.76–8.06 (1H, m, ArH), and *7,7-bis(4-chlorophenylseleno)-7,12-dihydrobenzo[5,6][1,3]thiazepino[3,2-a]benzimidazole 6,6-dioxide* **10d** (11 mg, 2%), mp 202–204 °C (from CH_2Cl_2–*n*-hexane) (Found: C, 49.0; H, 2.7; N, 4.2; S, 5.0. $C_{27}H_{18}Cl_2N_2O_2SSe_2$ requires C, 48.98; H, 2.74; N, 4.22; S, 4.83%); ν_{max}(KBr)/cm^{-1} 3056, 1462, 1328, 1142, 1123 and 742; δ_H(80 MHz) 5.52 (2H, s, NCH_2), 6.58–6.99 (4H, m, ArH), 6.99–7.77 (10H, m, ArH), 7.77–8.08 (1H, m, ArH) and 8.43–8.73 (1H, m, ArH).

7-(2-Thienylseleno)-7,12-dihydrobenzo[5,6][1,3]thiazepino-[3,2-*a*]benzimidazole 6,6-dioxide 7e. The reaction of compound **1** (284 mg, 1.00 mmol), NaH (24 mg, 1.00 mmol), and thiophene-2-selenenyl bromide, which was prepared *in situ* from di-2-thienyl diselenide (194 mg, 0.598 mmol) and bromine (96 mg, 0.601 mmol), gave *title compound* **7e** (172 mg, 39%), mp 160–161 °C (from EtOAc–*n*-hexane) (Found: C, 51.0; H, 3.2; N, 6.35; S, 7.1. $C_{19}H_{14}N_2O_2S_2Se$ requires C, 51.24; H, 3.17; N, 6.29; S, 7.20%); ν_{max}(KBr)/cm^{-1} 3056, 2912, 1430, 1321, 1123, 1094, 819 and 793; δ_H(80 MHz) 5.49 (2H, s, NCH_2), 5.86 (1H, s, SO_2CH), 6.50–6.75 (2H, m, ArH), 7.18–7.63 (8H, m, ArH) and 7.83–8.06 (1H, m, ArH).

7-(Biphenyl-4-ylseleno)-7,12-dihydrobenzo[5,6][1,3]thiazepino[3,2-*a*]benzimidazole 6,6-dioxide 7f. The reaction of compound **1** (193 mg, 0.678 mmol), NaH (17 mg, 0.708 mmol), and biphenyl-4-ylselenenyl bromide, which was prepared *in situ* from bis(biphenyl-4-yl) diselenide (157 mg, 0.328 mmol) and bromine (54 mg, 0.338 mmol), gave *title compound* **7f** (115 mg, 33%), mp 206–208 °C (from MeOH–CH_2Cl_2) (Found: C, 63.15; H, 4.0; N, 5.6; S, 6.2. $C_{27}H_{20}N_2O_2SSe$ requires C, 62.91; H, 3.91; N, 5.43; S, 6.22%); ν_{max}(KBr)/cm^{-1} 3056, 2960, 1321, 1235, 1142, 1004, 826 and 611; δ_H(80 MHz) 5.39 (2H, s, NCH_2), 5.89 (1H, s, SO_2CH), 6.87–7.63 (16H, m, ArH) and 7.69–8.02 (1H, m, ArH).

5-(1-Naphthylseleno)-7,12-dihydrobenzo[5,6][1,3]thiazepino-[3,2-*a*]benzimidazole 6,6-dioxide 7g. The reaction of compound **1** (300 mg, 1.06 mmol), NaH (28 mg, 1.17 mmol), and naphthalene-1-selenenyl bromide, which was prepared *in situ* from di-1-naphthyl diselenide (263 mg, 0.637 mmol) and bromine (102 mg, 0.638 mmol), gave *title compound* **7g** (193 mg, 37%), mp 204–206 °C (from CH_3CN) (Found: C, 61.4; H, 3.6; N, 5.9; S, 6.6. $C_{25}H_{18}N_2O_2SSe$ requires C, 61.13; H, 3.71;

N, 5.72; S, 6.55%); ν_{max}(KBr)/cm^{-1} 3056, 2912, 1325, 1241, 1146, 1126 and 720; δ_H(80 MHz) 5.42 (2H, s, NCH_2), 5.79 (1H, s, SO_2CH) and 6.39–8.49 (15H, m, ArH).

Oxidation of compound 7a

(i) Using MCPBA. To a solution of compound **7a** (500 mg, 1.14 mmol) in dried CH_2Cl_2 (60 ml) was added dropwise a solution of MCPBA (302 mg, 1.25 mmol) in CH_2Cl_2 (40 ml) during 10 min. The mixture was stirred for 1 h at rt. After removal of the solvent, the residue was chromatographed on a silica gel column (2 × 15 cm). Elution with a mixture of EtOAc and *n*-hexane (1 : 2) gave diselenide **9a** (45 mg, 25%) and unchanged reagent **7a** (168 mg, 34% recovery). Elution with EtOAc–*n*-hexane (1 : 1) gave *Se-phenyl 2-[(benzimidazol-1-yl)methyl]selenobenzoate* **8a** (162 mg, 36%), mp 54–55 °C (CH_2Cl_2–*n*-hexane) (Found: C, 64.7; H, 4.2; N, 7.2. $C_{21}H_{16}N_2OSe$ requires C, 64.45; H, 4.12; N, 7.16%); ν_{max}(neat)/cm^{-1} 3040, 2912, 1683, 1437, 1350, 1270 and 1187; δ_H(300 MHz) 5.56 (2H, s, NCH_2), 6.87–6.90 (1H, m, ArH), 7.17–7.35 (3H, m, ArH), 7.37–7.45 (5H, m, ArH), 7.55–7.58 (2H, m, ArH), 7.83–7.87 (1H, m, ArH), 7.91 (1H, s, N=CH) and 8.04–8.07 (1H, m, ArH).

(ii) Using 28% H_2O_2. To solution of compound **7a** (385 mg, 0.876 mmol) in CH_2Cl_2 (50 ml) was added 28% H_2O_2 (128 mg, 1.05 mmol). The mixture was stirred for 5 h at rt, followed by quenching with aq. sodium hydrogen carbonate (10%), and the mixture was extracted with CH_2Cl_2 (100 ml × 2). The extracts were worked up as usual. Chromatography (2 × 10 cm) of the reaction mixture with a mixture of EtOAc and *n*-hexane (1 : 1) gave diselenide **9a** (29 mg, 21%), starting material **7a** (18 mg, 5% recovery), and selenobenzoate **8a** (88 mg, 25%).

(iii) Using Oxone® (potassium peroxymonosulfate) in MeOH. To a solution of compound **7a** (610 mg, 1.39 mmol) in MeOH (50 ml) was added dropwise aq. Oxone® (940 mg, 1.53 mmol in 50 ml) during 30 min. The mixture was stirred for 20 h at rt and worked up as usual. Chromatography (2 × 15 cm) of the reaction mixture using EtOAc–*n*-hexane (1 : 1) gave compound **9a** (21 mg, 10%), unchanged substrate **7a** (192 mg, 31% recovery), and methyl 2-[(benzimidazol-1-yl)methyl]benzoate **11** (142 mg, 38%), mp 130–131 °C (from EtOAc–*n*-hexane) (Found: C, 71.9; H, 5.4; N, 10.6. $C_{16}H_{14}N_2O_2$ requires C, 72.17; H, 5.30; N, 10.51%); ν_{max}(neat)/cm^{-1} 3056, 2944, 1702, 1594, 1484, 1446, 1418, 1347, 1280, 1088 and 883; δ_H(200 MHz) 3.90 (3H, s, OCH_3), 5.83 (2H, s, NCH_2), 6.65–6.82 (1H, m, ArH), 7.20–7.42 (5H, m, ArH), 7.85–7.97 (1H, m, ArH), 7.90 (1H, s, N=CH) and 8.02–8.15 (1H, m, ArH); δ_C(50 MHz) 47.1, 52.3, 110.0, 120.4, 122.2, 123.1, 127.6, 127.9, 131.3, 133.0, 134.0, 137.9, 143.8 and 167.1.

(iv) Using Oxone® in aq. THF. To a solution of compound **7a** (210 mg, 0.478 mmol) in THF (40 ml) was added dropwise aq. Oxone® (323 mg, 0.525 mmol in 30 ml) during 10 min. The mixture was stirred at rt for 24 h and worked up as usual. Chromatography (1 × 15 cm) of the reaction mixture using EtOAc–*n*-hexane (1 : 1) gave diselenide **9a** (29 mg, 39%), unchanged starting material **7a** (47 mg, 22% recovery) and selenobenzoate **8a** (39 mg, 21%).

(v) Using $NaIO_4$. To a solution of compound **7a** (239 mg, 0.544 mmol) in MeOH (25 ml) was added dropwise aq. $NaIO_4$ (128 mg, 0.598 mmol in 15 ml) during 15 min. The reaction mixture was stirred for 3 h at reflux and worked up as usual. Chromatography (2 × 15 cm) of the reaction mixture using EtOAc–*n*-hexane (1 : 1) gave methyl 2-[(2-methoxybenzimidazol-1-yl)methyl]benzoate **12** (23 mg, 14%) and analogue **11** (46 mg, 31%).

General procedure for the synthesis of *Se*-aryl 2-[(benzimidazol-1-yl)methyl]selenobenzoates 8

A solution of a sulfone **7** (0.165–0.225 mmol) in THF (30 ml) was treated with aq. Oxone® (0.182–0.281 mmol in 20 ml) for 10 min, and the mixture was stirred for 20–36 h at rt. The mixture was worked up as described in method (iv) above.

***Se*-4-Tolyl 2-[(benzimidazol-1-yl)methyl]selenobenzoate 8b.** The reaction of compound **7b** (75 mg, 0.165 mmol) and Oxone® (112 mg, 0.182 mmol) gave unchanged substrate **7b** (24 mg, 32% recovery), diselenide **9b** (7 mg, 24%), and *title compound* **8b** (24 mg, 35%), as a liquid (Found: C, 65.0; H, 4.3; N, 7.0. $C_{22}H_{18}N_2OSe$ requires C, 65.19; H, 4.48; N, 6.91%); ν_{max}(neat)/cm^{-1} 3056, 2928, 1683, 1485, 1363, 803 and 762; δ_H(80 MHz) 2.39 (3H, s, CH_3), 5.59 (2H, s, NCH_2), 6.68–7.62 (11H, m, ArH) and 7.62–8.19 (2H, m, ArH, N=CH).

***Se*-2-Tolyl 2-[(benzimidazol-1-yl)methyl]selenobenzoate 8c.** The reaction of compound **7c** (95 mg, 0.210 mmol) and Oxone® (141 mg, 0.229 mmol) gave diselenide **9c** (45 mg, 63%) and *title compound* **8c** (28 mg, 33%), as a liquid (Found: C, 65.0; H, 4.6; N, 6.9. $C_{22}H_{18}N_2OSe$ requires C, 65.19; H, 4.48; N, 6.91%); ν_{max}(neat)/cm^{-1} 3056, 2928, 1690 and 883; δ_H(80 MHz) 2.40 (3H, s, CH_3), 5.56 (2H, s, NCH_2), 6.72–7.01 (1H, m, ArH), 7.01–7.68 (9H, m, ArH), 7.11–7.99 (2H, m, ArH, N=CH) and 7.99–8.29 (1H, m, ArH).

***Se*-4-Chlorophenyl 2-[(benzimidazol-1-yl)methyl]selenobenzoate 8d.** The reaction of compound **7d** (100 mg, 0.211 mmol) and Oxone® (143 mg, 0.233 mmol) gave unchanged starting material **7d** (53 mg, 53% recovery) and *title compound* **8d** (35 mg, 38%) as a liquid (Found: C, 59.0; H, 3.8; N, 6.2. $C_{21}H_{15}ClN_2OSe$ requires C, 59.24; H, 3.55; N, 6.58%); ν_{max}(neat)/cm^{-1} 3056, 2928, 1686, 1277 and 813; δ_H(80 MHz) 5.57 (2H, s, NCH_2), 6.74 (11H, m, ArH) and 7.64–8.19 (2H, m, ArH, N=CH).

***Se*-2-Thienyl 2-[(benzimidazol-1-yl)methyl]selenobenzoate 8e.** The reaction of compound **7e** (100 mg, 0.225 mmol) and Oxone® (173 mg, 0.281 mmol) gave unchanged starting material **7e** (41 mg, 41% recovery) and *title compound* **8e** (27 mg, 31%) as a liquid (Found: C, 57.2; H, 3.6; N, 7.1; S, 7.85. $C_{19}H_{14}N_2OSSe$ requires C, 57.43; H, 3.55; N, 7.05; S, 8.07%); ν_{max}(neat)/cm^{-1} 1680, 1475, 748, 730 and 681; δ_H(300 MHz) 5.61 (2H, s, NCH_2), 6.65–6.82 (2H, m, ArH), 6.85–7.18 (5H, m, ArH), 7.23 (1H, s, N=CH), 7.32–7.53 (3H, m, ArH) and 7.81–7.96 (1H, m, ArH).

***Se*-Biphenyl-4-yl 2-[(benzimidazol-1-yl)methyl]selenobenzoate 8f (attempted preparation).** A solution of compound **7f** (90 mg, 0.175 mmol) in THF (25 ml) was treated with aq. Oxone® (118 mg, 0.192 mmol in 20 ml) for 10 min, and the mixture was stirred for 24 h at rt. Work-up as usual gave bis(biphenyl-4-yl) diselenide **9f** (12 mg, 30%) and unchanged substrate **7f** (17 mg, 19% recovery). No title compound **8f** was formed.

***Se*-1-Naphthyl 2-[(benzimidazol-1-yl)methyl]selenobenzoate 8g.** The reaction of compound **7g** (100 mg, 0.204 mmol) and Oxone® (135 mg, 0.220 mmol) gave starting material **7g** (36 mg, 36% recovery) and *title compound* **8g** (38 mg, 42%) as a liquid (Found: C, 68.25; H, 4.0; N, 6.4. $C_{25}H_{18}N_2OSe$ requires C, 68.29; H, 4.11; N, 6.35%); ν_{max}(neat)/cm^{-1} 3136, 2720, 1686, 1190 and 860; δ_H(300 MHz) 5.65 (2H, s, NCH_2), 6.75–6.85 (1H, m, ArH), 6.97–7.24 (6H, m, ArH), 7.30 (1H, s, N=CH), 7.40–7.62 (5H, m, ArH) and 7.82–8.08 (3H, m, ArH).

7-Deuterio-7,12-dihydrobenzo[5,6][1,3]thiazepino[3,2-*a*]benzimidazole 6,6-dioxide 1-D

To a solution of compound **1** (700 mg, 2.46 mmol) in THF (100 ml) under nitrogen was added NaH (65 mg, 2.71 mmol).

The mixture was stirred for 10 min at rt, followed by the addition of D_2O (98 mg, 4.90 mmol), and the mixture was additionally stirred for 20 min. After removal of the solvent, the residue was extracted with EtOAc (400 ml × 3). The extracts were dried over $MgSO_4$. Removal of the solvent, followed by recrystallization of the residue, gave compound **1** (600 mg, 85%) in which yield of labelled isomer **1-D** was calculated to be 27%. Compound **1-D** (560 mg, 1.96 mmol; D content 27%) was treated with NaH (52 mg, 2.17 mmol) and D_2O (78 mg, 3.90 mmol) for 20 min under the same conditions as in the first reaction. Work-up gave back compound **1-D** (500 mg, 89%) having 60% D content.

7-Deuterio-7-phenylseleno-7,12-dihydrobenzo[5,6][1,3]thiazepino[3,2-*a*]benzimidazole 6,6-dioxide 7a-D

Compound **1-D** (400 mg, 1.41 mmol; 60% D content) was treated with NaH (41 mg, 1.71 mmol) and benzeneselenenyl bromide (354 mg, 1.50 mmol) under the same conditions as for the preparation of compound **7a**. From the reaction mixture were isolated title compound **7a-D** (342 mg, 55%; 30% D content) and diselenide **9a** (75 mg, 32%).

Oxidation of sulfone 7a-D with MCPBA

A solution of compound **7a-D** (297 mg, 0.653 mmol; 30% D content) in CH_2Cl_2 (100 ml) was treated with MCPBA (180 mg, 0.745 mmol) for 3 h at rt. The mixture was worked up according to the same procedure as described for the reaction of the parent sulfone **7a** with MCPBA. From the reaction mixture were isolated selenobenzoate **8a** (140 mg, 52%), diselenide **9a** (37 mg, 35%), and unchanged starting material **7a-D** (27 mg, 9% recovery; 30% D content).

Preparation of benzyl phenyl sulfone 20

To a solution of benzyl phenyl sulfide (3.00 g, 15.0 mmol) in diethyl ether (100 ml) at rt was added MCPBA (11.0 g, 45.0 mmol) during 30 min. The mixture was stirred for 10 h. After removal of the solvent *in vacuo*, the residue was neutralized with aq. sodium hydrogen carbonate (10%). The mixture was extracted with EtOAc (200 ml × 2) and the extracts were dried ($MgSO_4$). Removal of the solvent *in vacuo*, followed by chromatography (2 × 10 cm) using a mixture of *n*-hexane and EtOAc (2:1) as eluant, gave title sulfone **20** (3.35 g, 96%), mp 142–144 °C (lit.,[11] 144–145 °C).

Phenyl α-phenylselenobenzyl sulfone 21

To a solution of sulfone **20** (930 mg, 4.01 mmol) in THF (60 ml) at rt was added dropwise LDA (514 mg, 4.80 mmol). The mixture was stirred for 1 h, followed by the addition of a solution of benzeneselenenyl bromide (944 mg, 4.00 mmol) in THF (30 ml), and the mixture was stirred for 30 min before being extracted with EtOAc (100 ml × 2), and the extracts were dried over $MgSO_4$. After removal of the solvent *in vacuo*, the residue was chromatographed on a silica gel column (2 × 10 cm). Elution with a mixture of EtOAc and *n*-hexane (1:2) gave diselenide **9a** (263 mg, 42%), and a mixture of starting sulfone **20** (465 mg, 50% recovery) and seleno sulfone **21** (585 mg, 38%) of which the ratio was determined on the basis of ^1H NMR spectroscopic data, δ_H(80 MHz) 4.26 (2H, s, CH_2SO_2), 5.13 (1H, s, $CHSO_2$) and 6.81–7.93 (25H, s, ArH).

Oxidation of a mixture of sulfones 20 and 21 with oxone®

To a solution of the mixture of sulfones **20** (465 mg, 2.00 mmol) and **21** (585 mg, 1.51 mmol) in THF (50 ml) was added aq. Oxone® (928 mg, 1.51 mmol in 20 ml) during 5 min. The mixture was stirred for 10 min and then was extracted with EtOAc (100 ml × 2), and the extract was worked up as usual. Elution with a mixture of *n*-hexane and EtOAc (2:1) gave diselenide **9a** (43 mg, 18%). Continued elution with the same solvent mixture gave phenyl selenobenzoate **22** (175 mg, 44%), mp 38–39 °C (from CH_2Cl_2–*n*-hexane) (lit.,[12] 38–40 °C).

7-Methyl-7-phenylseleno-7,12-dihydrobenzo[5,6][1,3]thiazepino-[3,2-*a*]benzimidazole 6,6-dioxide 23

To a solution of compound **7** (120 mg, 0.265 mmol) in THF (25 ml) at rt under nitrogen was added NaH (6.6 mg, 0.28 mmol), the mixture was stirred for 10 min and then methyl iodide (383 mg, 2.70 mmol) was added. The mixture was stirred for 30 min and worked up as usual. Elution with a mixture of EtOAc and *n*-hexane (1:2) gave diselenide **9a** (4 mg, 9%). Elution with EtOAc–*n*-hexane (1:1) gave *title compound* **23** (88 mg, 72%), mp 84–86 °C (from EtOAc–*n*-hexane) (Found: C, 58.0; H, 3.9; N, 6.3; S, 7.1. $C_{22}H_{18}N_2O_2SSe$ requires C, 58.28; H, 4.00; N, 6.18; S, 7.07%); ν_{max}(KBr)/cm^{-1} 1456, 1427, 1318 and 1145; δ_H(80 MHz) 2.09 (3H, s, CH_3), 5.29–6.05 (2H, q, *J* 7.5, NCH_2) and 6.65–8.12 (13H, m, ArH).

7-Methylene-7,12-dihydrobenzo[5,6][1,3]thiazepino[3,2-*a*]benzimidazole 6,6-dioxide 24

To a solution of selenide **23** (71 mg, 0.157 mmol) in THF (20 ml) at rt was added aq. Oxone® (96 mg, 0.156 mmol in 10 ml). The mixture was stirred for 1 h and worked up as usual. Elution with a mixture of EtOAc and *n*-hexane (1:2) gave *title compound* **24** (31 mg, 65%), mp 218–220 °C (from CH_2Cl_2–*n*-hexane) (Found: C, 64.9; H, 4.1; N, 9.4; S, 10.8. $C_{16}H_{12}N_2O_2S$ requires C, 64.85; H, 4.08; N, 9.45; S, 10.82%); ν_{max}(KBr)/cm^{-1} 1452, 1305 and 1139; δ_H(300 MHz) 5.55 (2H, s, NCH_2), 6.32 (1H, s, =CH), 6.87 (1H, s, =CH) and 7.57–7.91 (8H, m, ArH); *m*/*z* (EI) 296 (M^+, 54%), 231 (100) and 232 (97).

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