Pergamon

Tetrahedron, Vol. 52, No. 34, pp. 11163-11176, 1996

0040-4020/96 $15.00 + 0.00

PII: S0040-4020(96)00665-5

The Invention of Radical Reactions. Part XXXVII.[1] A Convenient Radical Synthesis of Dialkyl Diselenides from Carboxylic Acids.

Derek H. R. Barton* and Giovanni Fontana*

Department of Chemistry, Texas A&M University, College Station, Texas 77843-3255, U.S.A.

Abstract: A new and convenient synthesis of dialkyl diselenides from carboxylic acids by Barton PTOC ester based radical chemistry is described. This method was especially successful when *O*-cholestan-3β-yl-2,2,2-trichloroselenoacetate and *O-neo*pentyl selenobenzoate were used as radical traps. Copyright © 1996 Elsevier Science Ltd

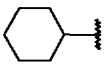
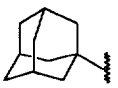
INTRODUCTION

Organoselenium compounds have received considerable attention as useful synthetic reagents and intermediates in organic synthesis.[2,3] Since diselenides are versatile intermediates for other organoselenium compounds, convenient high yield syntheses are desirable. The simplest preparation of dialkyl diselenides is the alkylation of diselenide anions, prepared by the reduction of selenium, with various electrophiles.[4-12] Other previous preparations have involved the oxidation of selenols,[13] hydrolysis of $RSeMgX$[14,15] or $ArSeCN$,[16,17] and reduction of carbonyl compounds with H_2Se.[18] However, most of the existing methods of preparation of diselenides suffer from certain disadvantages such as low yields and toxic intermediates. Moreover, in the synthesis of many complex molecules, radical chain reactions have advantages over conventional ionic processes: neutral conditions, lower steric effects and compatibility with various sensitive functional groups.

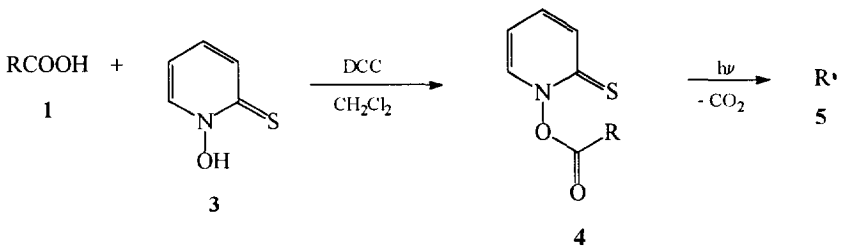
In this communication we would like to report a new radical method for the conversion of carboxylic acids into the corresponding symmetrical dialkyl diselenides.

$$\underset{\mathbf{1}}{RCOOH} \longrightarrow \underset{\mathbf{2}}{R\text{-}Se\text{-}Se\text{-}R}$$

Table 1. Radical Reaction Conversion of Carboxylic Acids **1** to Dialkyl Diselenides **2**.

	R	RSeSeR
1a	$PhCH_2CH_2$-	**2a**
1b		**2b**
1c		**2c**

O-Acyl-*N*-hydroxy-2-thiopyridone derivatives **4** (Barton PTOC esters) are a convenient and inexpensive source of carbon radicals of synthetic utility.[19] Upon photolysis, homolytic cleavage of the Barton PTOC ester and decarboxylation of the derived acyloxy radical occurs affording carbon radicals **5** (**Scheme 1**).

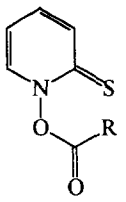


Scheme 1

Recently we found that radicals obtained by photolysis of Barton PTOC esters **4** react with white phosphorus[20] to give, after oxidation with H_2O_2, the corresponding phosphonic acids, and with elemental sulfur[21] to afford, after reduction with $NaBH_4$, the corresponding thiols in excellent yields. These results initially prompted us to investigate the reaction of Barton PTOC esters with elemental red and black selenium in order to obtain the corresponding dialkyl diselenides.

RESULTS AND DISCUSSION

When **4a** was photolysed in the presence of red selenium[22] in carbon disulfide or toluene, it afforded (after reduction of the crude product with $NaBH_4$ followed by oxidation by air) the corresponding di-(2-phenylethyl)diselenide (**2a**) in low to moderate yield (35%). The use of commerciable black selenium did not give better results (21%). This is probably due to the insufficient solubility of red and black selenium in any organic solvents and their poor solubility in carbon disulfide (**Scheme 2**).



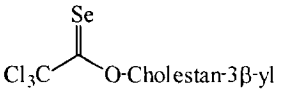
4a + Se $\xrightarrow[2.\ NaBH_4,\ THF\ \ 3.\ O_2,\ Et_2O]{1.\ h\nu,\ CS_2}$ R-Se-Se-R

2a: 35%, Se = Red-Selenium

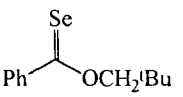
2a: 21%, Se = Black-Selenium

Scheme 2

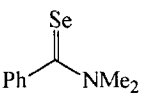
We also examined the possible use of alloys of sulfur and selenium made by fusing the two elements in variable proportions mostly with an excess of sulfur. Although some of these alloys were more soluble in carbon disulfide, they rapidly deposited red selenium on standing. So, we decided to examine the reactivity of Barton PTOC esters with particular substrates that could react as efficient traps for carbon radicals and as "good sources" of selenium, to afford the desired dialkyl diselenides. Selenoester derivatives **6a** and **7** and selenobenzamide derivative **8** were synthesized and investigated for this radical reaction.



6a

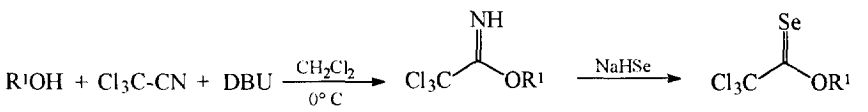


7



8

Alcohols **9** were converted into the corresponding trichloroacetimido derivatives **10** by treating with trichloroacetonitrile and 1,8-diazabicyclo[5,4,0]undec-7-ene (DBU). Reaction of compounds **10** with a solution of sodium hydrogenselenide afforded *O*-alkyl-2,2,2-trichloroselenoacetate derivatives **6** (**Scheme 3**). None of these yields were optimized.



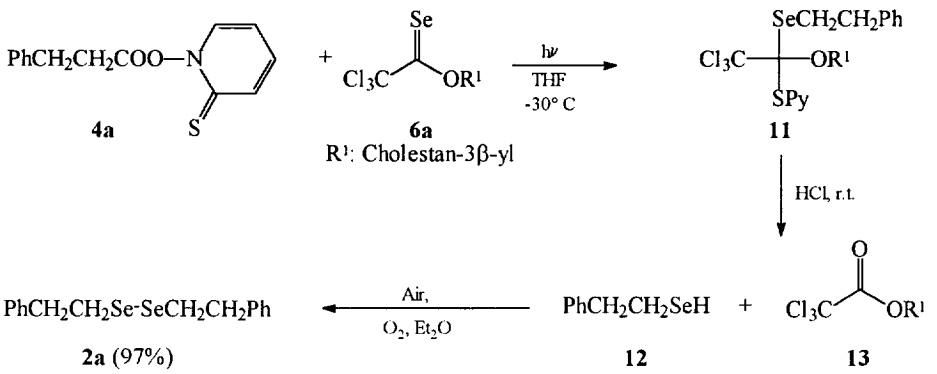
9 **10** **6**

	R^1	yield (%) of 10	yield(%) of 6
a:	cholestan-3β-yl	92[a]	50[a]
b:	*Neo*pentyl	82[a]	40[b]
c:	*Iso*propyl	70[a]	35[b]

[a] Isolated yield. [b] Determined by NMR

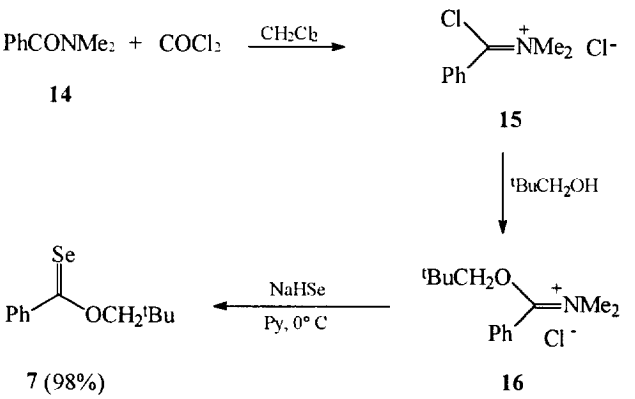
Scheme 3

N-Hydroxythiopyridone derivative **4a** was photolysed in presence of **6a** at -30°C to furnish adduct **11**. This was not isolated but hydrolysed *in situ* in the presence of aqueous hydrochloric acid followed by oxidation with air to the corresponding di-(2-phenylethyl)diselenide (**2a**) (97%) (**Scheme 4**).



Scheme 4

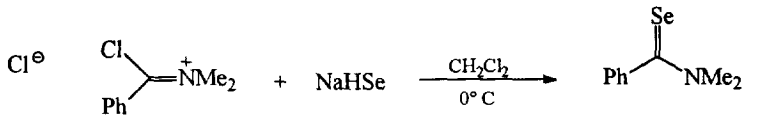
We then considered the use of different derivatives **6b** and **6c** as traps for the carbon radicals. Following the same procedure reported in **Scheme 3** and using *iso*propanol and *neo*pentanol the corresponding imidates **10b** and **10c** were synthesized. These products reacted with a solution of NaHSe to afford the desired products **6b** and **6c**. Unfortunately, derivatives **6b** and **6c** were very unstable and readily eliminated red selenium. So, we considered other plausible radical traps such as the *O-neo*pentyl selenobenzoate **7** and *N,N*-dimethyl selenobenzamide **8**. Product **7** was prepared according to the literature method described by Barton and McCombie[23] (**Scheme 5**).



Scheme 5

Treatment of *N,N*-dimethylbenzamide **14** with phosgene gave the imidoyl chloride methochloride **15**. Reaction with *neo*pentanol at room temperature gave the salt **16**, which was converted in excellent yield into the *O-neo*pentyl selenobenzoate **7** (deep red, low melting solid) by reaction *in situ* with a solution of sodium hydrogenselenide (prepared from selenium with $NaBH_4$ in ethanol).[24]

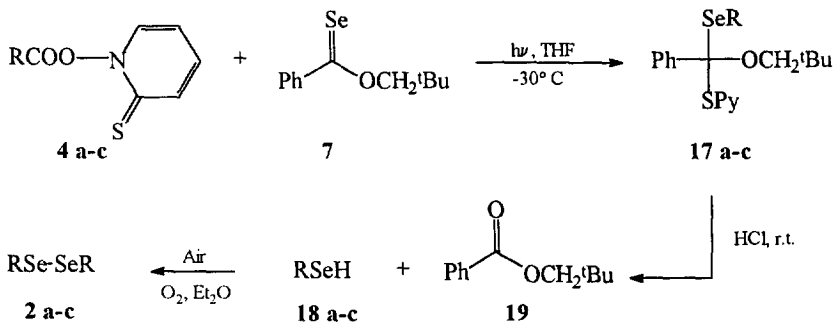
Moreover, by *in situ* reaction of such a solution of sodium hydrogenselenide with the previously described imidoyl chloride methochloride salt **15**, we obtained a high yield of *N,N*-dimethyl selenobenzamide **8** as a yellow, stable and crystalline substance (**Scheme 6**). Previous preparations of **8** gave only low to moderate yields.[25]



15 **8** (92%)

Scheme 6

Irradiation of *N*-hydroxythiopyridone derivatives **4 a-c** in the presence of *O-neo*pentyl selenobenzoate **7** afforded adducts **17 a-c**. These intermediates **17 a-c** were not isolated, but were hydrolysed *in situ* with aqueous hydrochloric acid to furnish the corresponding selenols **18 a-c** and *neo*pentyl benzoate **19**. Oxidation of the crude residue by air/O_2 provided, after purification, the desired dialkyl diselenides **2 a-c** in good to high yields (**Scheme 7**).



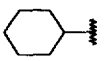
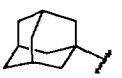
4 a-c **7** **17 a-c**

2 a-c **18 a-c** **19**

Scheme 7

The reaction was studied at different temperatures: (20 °C; 0 °C; -30 °C) and we found that it works better at low temperature (-30 °C). The influence of the amount of the radical trap was also investigated and better yields were obtained in the presence of a slight excess of compound **7** (**Table 2**).

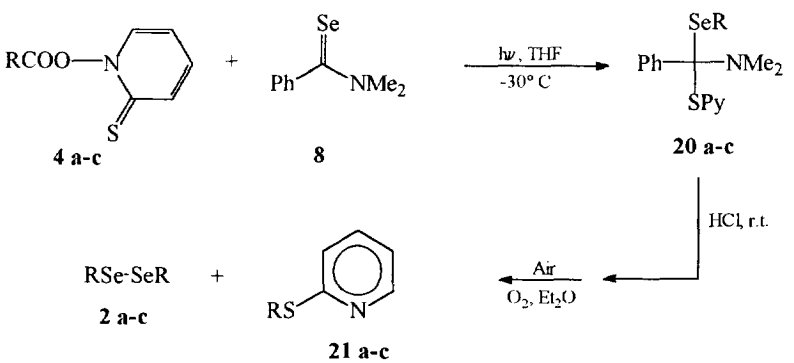
Table 2: Radical Reaction from Carboxylic Acids **1** to Dialkyl Diselenides **2** *via* O-*Neo*pentyl selenobenzoate **7** as Radical Trap.

	R	Compound 7 (equiv.)[b]	R-Se-Se-R 4 → 2 Total yield (%)[a]
a	$PhCH_2CH_2$-	1.5 0.67	70 35
b		1.1	48
c		1.2 0.67	87 40

[a] Isolated yield. [b] Equivalents of 7 with respect to **4 a-c**.

Although we could not isolate the adducts **17 a-c**, the course of the reaction of Barton PTOC ester **4b** with compound **7** as radical trap was conveniently followed by ^{1}H- ^{13}C- and ^{77}Se-NMR analyses. The ^{77}Se-NMR (C_6D_6) of compound **7** showed a peak at 933.2 ppm (NMR spectrometer referenced to external Ph-Se-Se-Ph, δ= 460 ppm).[26] After photolysis of Barton PTOC ester derivate **4b** in C_6D_6 in the presence of compound **7**, the ^{77}Se-NMR spectrum showed a new peak at 458.6 ppm. After hydrolysis with D_2O, followed by oxidation by air, the spectrum showed the complete disappearance of the signal at 458.6 ppm and the appearance of a signal at 369.1 ppm due to the formation of the dicyclohexyl diselenide (**2b**).[27] It is then reasonable to assume that the signal at 458.6 ppm is due to the formation of the adduct **17b**.

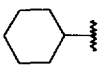
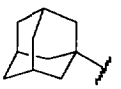
The same reactions were examined with *N,N*-dimethyl selenobenzamide **8** as trap for the carbon radicals. As previously described, Barton PTOC esters **4 a-c** were photolysed in the presence of **8**. This was followed by hydrolysis with aqueous hydrochloric acid and oxidation by air to afford dialkyl diselenides **2 a-c** (**Scheme 8**).



Scheme 8

However, the use of substrate **8** as a radical trap gave lower yields than those observed in the case of substrate **7** (**Table 3**).

Table 3: Radical Reaction from Carboxylic Acids **1** to Dialkyl Diselenides **2** *via* *N,N*-Dimethyl selenobenzamide **8** as Radical Trap.

	R	Compound **8** (equiv.)[c]	**R-Se-Se-R** **4 → 2** Total yield (%)
a	$PhCH_2CH_2$-	1.2	20[a]
b		1.2	18[b]
c		1.2	15[b]

[a] Isolated yield. [b] Determined by NMR. [c] Equivalents of **8** with respect to **4 a-c**.

When selenobenzamide **8** was used in this reaction, after irradiation we isolated the Barton PTOC ester rearranged compound **21**[19] as the major product and the substrate **8** remained mostly unreacted (**Scheme 8**). In the selenobenzamide the presence of the nitrogen decreases the reactivity of C=Se towards nucleophilic radicals by delocalization of its lone pair electrons on the selenium atom. Moreover, we found that the addition of the carbon radicals to *O*-alkyl selenoesters is enhanced by the use of strongly electron-withdrawing α-substituents on the C=Se. In fact, as expected, compound **6a** was found to be a better radical trap than **7**.

CONCLUSIONS

The direct transformation of carboxylic acids **1 a-c** into the corresponding dialkyl diselenides **2 a-c** by reaction of Barton PTOC esters **4 a-c** and elemental red or black selenium has been demonstrated. The use of *O*-cholestan-3β-yl-2,2,2-trichloroselenoacetate (**6a**). and *O-neo*pentyl selenobenzoate (**7**) as efficient traps for carbon radicals and as good sources of selenium afforded the desired dialkyl diselenides **2 a-c** in good to high yields. The mild conditions required for the reaction and the following hydrolysis should find application in the synthesis of sensitive products. Furthermore, these transformations are suitable for primary, secondary and tertiary carbon radicals.

EXPERIMENTAL

General Procedures and Starting Materials.

Melting points were determined on a Kofler hot-stage melting point apparatus and are uncorrected. IR spectra were recorded on a Perkin-Elmer 881 spectrophotometer. ^{1}H- and ^{13}C-NMR spectra were determined for solutions in deuterochloroform (unless specified otherwise) with TMS as internal reference on a Varian Gemini 200, Varian XL 200E or a Varian XL 200 spectrometers.^{77}Se-NMR spectra were recorded for solutions in $CDCl_3$ or C_6D_6 on a Varian XL 200 spectrometer with diphenyl diselenide as external reference[26] (Ph-Se-Se-Ph (1M) in $CDCl_3$, δ = 460 ppm). Gas chromatographic-mass spectroscopic analyses (GC-MS) were performed on a Hewlett-Packard 5790A GC interfaced with a 5970A mass selective detector and a Hewlett-Packard model 9133 computer. Specific rotations were determined on a Jasco Model DIP-360 digital polarimeter. The concentrations reported as *c* for the specific rotations are in g/mL. Microanalyses were performed by Atlantic Microlab, Inc., Norcross, Georgia. Thin-layer chromatography (TLC) was performed on aluminum sheets precoated with silica gel (Merck, Kieselgel 60 F-254). Column chromatography was performed on silica gel (Merck, Kieselgel 60 230-440 mesh). Solvents were used either as purchased or dried and purified by standard methodology under argon. Other reference compounds and starting materials were purchased from Aldrich Chemical Co., Inc., Milwaukee,WI.

General Procedure for the Synthesis of *N*-hydroxy-pyridine-2-thione Esters (4a-c)[28]. 1,3-Dicyclohexylcarbodiimide (DCC, 1 eq.) and *N*-hydroxypyridine-2-thione (1 eq.) were dissolved in dry CH_2Cl_2 under an argon atmosphere. The solution was protected from light and kept at or below 0 °C. The appropriate carboxylic acid (1 equiv.) in dry CH_2Cl_2 was added dropwise to the solution, and the reaction mixture was then allowed to warm up to room temperature. The yellow solution was quickly filtered through a bed of silica gel (again protected from light) and the silica gel was washed with some more CH_2Cl_2. The organic layers were then combined and concentrated to give a yellow crystalline product. The product can be further purified by recrystallization from CH_2Cl_2/hexanes and stored in a cool dark place until further use.
4a: yield 85%, m.p.: 136-137 °C (lit.[28] 135 °C). **4b**: yield 88%, m.p.: 108-109 °C(lit.[28] 110 °C). **4c**: yield 87%, m.p.:164-165 °C (lit.[28] 166 °C).

General Procedure for the Photolysis of *N*-hydroxypyridine-2-thione Ester Derivative 4a with Red or Black (shot) Selenium. To an ice-cooled suspension of red selenium[22] (amorphous) (0.80 g, 10.10 mmol) in anhydrous CS_2 (200 mL), under an argon atmosphere was added the phenylethyl-*N*-hydroxypyridine-2-thione derivative **4a** (0.5 g, 2.02 mmol). The reaction mixture was irradiated at 0 °C with a 150W tungsten lamp until starting material was no longer detectable (1h). After evaporation *in vacuo* of the solvent, the crude mixture

was dissolved in Et_2O and filtered through a bed of silica to remove the excess of red selenium. After removal of the solvent, the residue was dissolved in anhydrous THF (20 mL) and $NaBH_4$ (0.13 g, 3.43 mmol) was added in small portions over 30 min. The mixture was stirred at room temperature for 1h, then poured into sulfuric acid (1N, 60 mL) and the aqueous phase extracted with AcOEt (3x50 mL) and dried over $MgSO_4$. Evaporation of the solvent, followed by oxidation by air (open flask) over 1-2 days at room temperature (t.l.c. control) gave a residue that was purified by flash chromatography on silica gel (eluent: AcOEt/hexanes 1/9) to give the di-(2-phenylethyl)diselenide (**2a**)[29] (0.13 g, 35%) as a yellow oil. When phenylethyl-*N*-hydroxypyridine-2-thione derivative **4a** was photolysed in CS_2 in the presence of black (shot) selenium, following the previously described procedure, 21% yield of desired di-(2-phenylethyl)diselenide (**2a**) was obtained. All physical and spectral data of **2a** are reported below.

Trichloroacetimido-3β-cholestanol 10a.[30] To a solution of cholestan-3β-ol (2 g, 5.15 mmol) and trichloroacetonitrile (7.43 g, 51.46 mmol) in dry CH_2Cl_2 (15 mL) at 0 °C under an argon atmosphere was added 1,8-diazabicyclo[5,4,0]undec-7-ene (0.86 g, 5.51 mmol) and the reaction was stirred at 0 °C for two hours. After evaporation of the solvent, the residue was purified by flash chromatography on silica gel (eluent: CH_2Cl_2/Et_2O 8/2). Recrystallization from $EtOH/CH_2Cl_2$ afforded derivative **10a** (2.45 g, 92%) as a white solid: m.p.: 158-160 °C; IR (KBr): 2945, 1657, 1528, 1431, 1078 cm^{-1}; ^{1}H-NMR ($CDCl_3$, δ, ppm): 8.20 (s, 1H), 4.85 (m, 1H), 2.10-0.70 (m, 47H); ^{13}C-NMR ($CDCl_3$, δ, ppm): 162.8, 91.9, 78.7, 56.4, 56.2, 54.2, $C_{aliphatics}$; $[\alpha]^{25}_D$ = +8.3° (*c* = 1.81, $CHCl_3$); m/z (%): 370 (100), 355 (39), 215 (97), 161 (26), 147 (47), 121 (43). Anal. calcd. for $C_{29}H_{48}Cl_3NO$: C, 65.27; H, 9.01; N, 2.63. Found: C, 65.35; H, 9.06; N, 2.46 %.

Trichloroacetimido derivatives **10b** and **10c** were synthesized following the same procedure.

Trichloroacetimido-*neo*pentanol 10b: Purification by column chromatography on silica gel (eluent: CH_2Cl_2/Et_2O 8/2) gave compound **10b** (82%) as a low melting solid: IR (neat): 3345, 2960, 1659, 1474, 1366, 1307, 1086 cm^{-1}; ^{1}H-NMR ($CDCl_3$, δ, ppm): 8.20 (s, 1H), 3.95 (s, 2H), 1.03 (s, 9H); ^{13}C-NMR ($CDCl_3$, δ, ppm): 163.2, 91.8, 78.7, 31.8, 26.4; m/z (%): 216 (12), 162 (40), 111 (38), 71 (100), 57 (70), 43 (90).

Trichloroacetimido-*iso*propanol 10c: Purification by column chromatography on silica gel (eluent: CH_2Cl_2/Et_2O 8/2) gave compound **10c** (70%) as a viscous liquid: IR (neat): 3331, 2973, 1749, 1644, 1457, 1351, 1077 cm^{-1}; ^{1}H-NMR ($CDCl_3$, δ, ppm): 8.22 (s, 1H), 5.14 (m, 1H), 1.37 (d, 6H, J= 6.2 Hz); ^{13}C-NMR ($CDCl_3$, δ, ppm): 162.1, 91.8, 72.8, 21.1; m/z (%): 204 (2), 162 (5), 126 (8), 83 (25), 59 (34), 43 (100).

***O*-Cholestan-3β-yl-2,2,2-trichloroselenoacetate (6a).** Selenium powder (0.37 g, 4.68 mmol) was stirred in absolute ethanol (10 mL) in an inert atmosphere during addition of sodium borohydride (0.23 g, 6.11

mmol). After the initial vigorous foaming had subsided (15 min.) and a clear almost colorless solution had formed (more $NaBH_4$ was added if necessary), acetic acid (0.25 mL) was added and the solution cooled to 0 °C. A solution of the derivative **10a** (0.5 g, 0.94 mmol) in CH_2Cl_2 (10 mL) was added dropwise. After stirring at 0 °C for 1 h, the solvent was evaporated and the residue purified quickly by flash chromatography on silica gel (eluent: Et_2O/hexanes 15/85). Recrystallization from CH_2Cl_2/acetone gave the *O*-Cholestan-3β-yl-2,2,2-trichloro selenoacetate (**6a**) (0.27 g, 50%) as a yellow solid: m.p.: 106-108 °C; IR (KBr): 2938, 1465, 1275, 1034, 718 cm^{-1}; ^{1}H-NMR ($CDCl_3$, δ, ppm): 5.53 (m, 1H), 2.12-0.60 (m, 47H); m/z (%): 371 (89), 370 (100), 355 (31), 106 (24), 121 (31), 119 (22), 95 (82), 81 (81); $[\alpha]^{25}_D$: -15.2 (*c* = 1.80, $CHCl_3$). Owing to its thermal instability a satisfactory analysis of compound **6a** could not be obtained.

***O-Neo*pentyl selenobenzoate (7).** *N,N*-Dimethylbenzamide (4.5 g, 0.03 mol) was kept for 15 h at room temperature in dry dichloromethane (80 mL) containing phosgene (6 g, 0.061 mol) under argon. The solution was evaporated *in vacuo* and the imidoyl chloride **15** was stirred in dry dichloromethane (50 mL) during addition of *neo*pentyl alcohol (2.64 g, 0.03 mol) in dichloromethane (20 mL). After stirring at room temperature for 0.5 h, the salt **16** in dichloromethane was treated with dry pyridine (5 mL) and this solution was added to a solution of sodium hydrogenselenide,[24] prepared from selenium (2.4g), ethanol (50 mL), sodium borohydride (1.5 g) with subsequent addition of acetic acid (1 mL), kept at 0 °C under argon. After stirrring at room temperature for 1 h, the reaction mixture was diluted with dichloromethane (200 mL), washed with H_2O (100 mL), dilute HCl (10%, 100 mL), $NaHCO_3$ saturated solution (2x100 mL), H_2O (100 mL) and dried over $MgSO_4$. After evaporation of the solvent the residue was purified by flash chromatography on silica gel (eluent: AcOEt/hexanes 2/8) to give the *O-neo*pentyl selenobenzoate **9** (7.74 g, 98%) as deep red, low melting solid: IR (neat): 2949 ,2862, 1442, 1217, 1171, 996 cm^{-1}; ^{1}H-NMR ($CDCl_3$, δ, ppm): 8.22 (m, 2H), 7.61 (m, 1H), 7.35 (m, 2H), 4.41 (s, 2H), 1.13 (s, 9H); ^{13}C-NMR ($CDCl_3$, δ, ppm): 222.3, 142.9, 132.6, 128.9, 128.3, 86.5, 31.9, 26.8; ^{77}Se-NMR (C_6D_6, δ, ppm, refer. Ph-Se-Se-Ph, δ= 460): 933.2; m/z (%): 256 (M^+, 24), 254 (12), 186 (36), 169 (12), 105 (100), 77 (47), 71 (61); Anal. calcd. for $C_{12}H_{16}OSe$: C, 56.48; H, 6.31. Found: C, 56.34; H, 6.34 %.

***N,N*-Dimethyl selenobenzamide (8).** *N,N*-Dimethylbenzamide (2.25 g, 15.08 mmol) in dichloromethane (20 mL) was converted into the imidoyl chloride **15** by stirring overnight at room temperature under an argon atmosphere with a solution of phosgene (2.5 g) in dichloromethane (15 mL). The solution was evaporated *in vacuo* and the salt **15** in dichloromethane (30 mL) was added at 0 °C under argon atmosphere to a solution of sodium hydrogenselenide, prepared as previously described from selenium (1.2 g), ethanol (25 mL) and $NaBH_4$ (0.75 g). After stirring at room temperature for 3 h, the mixture was diluted with CH_2Cl_2 (100 mL), washed with H_2O (100 mL), dilute HCl (10%, 100 mL), $NaHCO_3$ saturated solution (2x100 mL), H_2O (100 mL) and

dried over $MgSO_4$. The crude product obtained after removal of the solvent was purified by flash chromatography on silica gel (eluent: AcOEt/hexanes 2/8) affording pure *N,N*-dimethyl selenobenzamide **(8)**[25] (2.94 g, 92%) as yellow crystals: m.p.: 83-85 °C; IR (KBr): 1496, 1367, 1248, 1109, 744 cm^{-1}; ^{1}H-NMR ($CDCl_3$, δ, ppm): 7.30 (m, 5H), 3.69 (s, 3H), 3.10 (s, 3H); ^{13}C-NMR ($CDCl_3$, δ, ppm): 205.2, 146.1, 128.4, 128.0, 124.6, 47.2, 44.7; ^{77}Se-NMR ($CDCl_3$, δ, ppm, refer. Ph-Se-Se-Ph, δ= 460): 735.2; m/z (%): 213 (M^+, 100), 169 (48), 131 (28), 118 (46), 104 (17), 91 (22), 77 (32).

Typical Procedure for the Preparation of Dialkyl Diselenides from *N*-hydroxypyridine-2-thione Esters and Substrate 6a. A typical procedure is described for the preparation of di-(2-phenylethyl)diselenide **2a**. To a solution of *O*-cholestan-3β-yl selenotrichloroacetate **(6a)** (0.20 g, 0.35 mmol) in dry THF (25 mL) at -30 °C under an inert atmosphere was added the phenylethyl-*N*-hydroxy-2-thiopyridone derivate **4a** (0.12 g, 0.50 mmol) and the reaction mixture was irradiated at -30 °C with a 150 W tungsten lamp (25 cm from the reaction flask), until the reaction was complete by TLC. The crude product was hydrolyzed without purification with a 10% solution of HCl (3 mL) overnight. Evaporation of the solvent, followed by oxidation with air gave a residue that was purified by flash chromatography on silica gel (eluent: Et_2O/hexanes 5/95) to afford the di-(2-phenylethyl)diselenide **(2a)**[29] (0.06 g, 97%) as a pale yellow oil and *O*-Cholestan-3β-yl trichloroacetate **13**. **2a** had : IR (neat) : 3061, 3031, 2932, 1600, 1497, 1453, 1243,1030 cm^{-1}; ^{1}H-NMR ($CDCl_3$, δ, ppm): 7.23 (m, 10H), 3.15-3.05 (m, 8H); ^{13}C-NMR ($CDCl_3$, δ, ppm): 141.2, 128.4, 128.3, 126.3, 37.2, 24.9; ^{77}Se-NMR ($CDCl_3$, δ, ppm, refer. Ph-Se-Se-Ph, δ= 460): 330.4; m/z (%): 370 (M^+, $^{80}Se_2$, 10), 207 (15), 105 (100), 77 (20).

General Procedure for the Radical Addition of the *N*-hydroxypyridine-2-thione Esters 4a-c to the Substrates 7 and 8 to give Dialkyl Diselenides 2a-c. A typical procedure is described for the preparation of di-(2-phenylethyl)diselenide (**2a**). To a solution of seleno ester derivative 7 (0.50 g, 1.96 mmol) in dry THF (20 mL) at -30 °C under argon, the phenylethyl-*N*-hydroxy-2-thione derivative **4a** (0.32 g, 1.31 mmol) was added and the reaction mixture was irradiated at -30 °C with a 150 W tungsten lamp (25 cm from the reaction flask) until the reaction was complete by TLC. The crude product was treated with a 10% solution of HCl (5 mL) and stirred for 3 h at room temperature. After removing the solvent, the residue was dissolved in Et_2O (50 mL), washed with H_2O (50 mL), brine (50 mL), dried over $MgSO_4$ and then left to be oxidized under air for two days. After evaporation of the solvent, the product was purified by flash chromatography on silica gel (eluent: Et_2O/hexanes 5/95) to afford the di-(2-phenylethyl)diselenides **(2a)**[29] (0.17 g, 70%) as pale yellow oil as well as O-*neo*pentylbenzoate **19**. All physical and spectral data of **2a** were identical to those previously reported (*vide supra*). Dicyclohexyl diselenide (**2b**) and di-(1-adamantyl)diselenide (**2c**) were similarly prepared.

The same procedure was followed with substrate **8** as a radical trap. Yields are listed in **Table 2** and **Table 3** and the physical and spectral data are as follows.

Dicyclohexyl diselenide (2b)[27,31], viscous liquid: ^{1}H-NMR ($CDCl_3$, δ, ppm): 2.98 (m, 2H), 2.35-1.37 (br, 20H); ^{13}C-NMR ($CDCl_3$, δ, ppm): 43.4, 34.7, 27.1, 25.7; ^{77}Se-NMR (C_6D_6, δ, ppm, refer. Ph-Se-Se-Ph, δ= 460): 369.1; m/z (%): 326 (M+, $^{80}Se_2$).

Di-(1-adamantyl) diselenide (2c)[32]: an analytical sample was recrystallized from hexane; m.p.: 148-150 °C; IR (KBr): 2898, 2844, 1435, 1283, 1096, 1023 cm^{-1}; ^{1}H-NMR ($CDCl_3$, δ, ppm): 2.03 (bs, 3H), 1.97 (bs, 6H), 1.69 (bs, 6H); ^{13}C-NMR ($CDCl_3$, δ, ppm): 45.1, 44.3, 36.3, 31.2; ^{77}Se-NMR ($CDCl_3$, δ, ppm, refer. Ph-Se-Se-Ph, δ= 460): 437,7; m/z (%): 430 (M+, $^{80}Se_2$, 7), 428 (6), 136 (22), 135 (100), 93 (21), 79 (28); Anal. calcd. for $C_{20}H_{30}Se_2$: C, 56.08; H, 7.06. Found: C, 56.15; H, 7.12 %.

Acknowledgements: We thank the Robert A. Welch Foundation, the N.I.H. and the Schering-Plough Corp. for their financial support of the work described in this article.

REFERENCES

1) a) Part XXXV: Barton, D.H.R.; Fontana, G.; Yang, Y. *Tetrahedron* **1996**, *52*, 2705. b) Part XXXVI: Barton, D.H.R.; Jaszberenyi, J.Cs.; Liu, W.; Shinada, T. *Tetrahedron* **1996**, *52*, 2717.

2) For a comprehensive treatment of organoselenium chemistry see "*Organoselenium Compounds: Their Chemistry and Biology*", Klayman, D.L.; Günther, W.H.H., Wiley Ed., New York, NY 1973.

3) For reviews: a) Reich, H.J. *Acc. Chem. Res.* **1979**, *12*, 22. b) Clive, D.L.J. *Tetrahedron* **1978**, *34*, 1048. c) Liotta, D. *Acc. Chem. Res.* **1984**, *17*, 28.

4) a) Bergstrom, F.W. *J. Am. Chem. Soc.* **1926**, *48*, 146. b) Bird, M.L.; Challenger, L. *J. Chem. Soc.* **1942**, 570.

5) Tschugaeff, L.; Chlopin, W. *Chem. Ber.* **1914**, *47*, 1269.

6) a) Klayman, D.L.; Griffin, T.S. *J. Am. Chem. Soc.* **1973**, *95*, 197. b) Gladysz, J.; Hornby, J.L.; Garbe, J.E. *J. Org. Chem.* **1978**, *43*, 1204. c) Bergman, J.; Engman, L. *Synthesis* **1980**, *7*, 596.

7) Clive, D.L.J.; Menchen, S.M. *J. Org. Chem.* **1979**, *44*, 4279.

8) Syper, L.; Mlochowski, J. *Synthesis* **1984**, 439.

9) Wagner, G.; Nuhn, P. *Arch. Pharm. (Weinheim)* **1964**, *297*, 401.

10) Günther, W.H.H.; Mautner, H.G: *J. Am. Chem Soc.* **1965**, *87*, 2708.

11) Li, J.Q.; Bao, W.L.; Lue, P.; Zhan, X. *Synth. Comm.* **1991**, *21* (6), 799.

12) Lue, P.; Zhan, X. *Synth. Comm.* **1993**, *23* (12), 1721.

13) a) Ward, H.P.; O'Donnel, I.L. *J. Am. Chem Soc.* **1945**, *67*, 883. b) Backer, H.J.; Hurenkamp, J.B.G. *Recl. Trav. Chim. Pay-Bas.* **1942**, *61*, 802.

14) Günther, W.H.H. *J. Org. Chem.* **1967**, *32*, 3929.

15) Jeu, K.Y.; Cava, M.P. *J. Org. Chem.* **1983**, *48*, 1449.

16) Waitkins, G.R.; Shutt, R. *Inorg. Synth.* **1946**, *2*, 186.

17) Hari, T.; Sharpless, K.B. *J. Org. Chem.* **1978**, *43*, 1689.

18) a) Cohen, V.I. *J. Org. Chem.* **1977**, *42*, 2510. b) Nishiyama, Y.; Hamanaka, S. *Synth. Comm.* **1986**, *16*, 1059.

19) a) Barton, D.H.R.; Zard, S.Z. *Pure Appl. Chem.* **1986**, *58*, 675. b) Idem, *Janssen Chimica Acta* **1987**, *4*, 3. c) Barton, D.H.R. *Aldrichimica Acta* **1990**, *23*, 3. d) Barton, D.H.R.; Chern, C.-Y.; Jaszberenyi, J.Cs. *Aust. J. Chem.* **1995**, *48*, 407. e) Barton, D.H.R.; Crich, D.; Motherwell, W.B. *J. Chem. Soc., Chem. Comm.* **1983**, 931. f) Barton, D.H.R.; Crich, D.; Motherwell, W.B.*Tetrahedron* **1985**, *41*, 3901. g) Newcomb, M.; Weber, K.A. *J. Org. Chem.* **1991**, *56*, 1309.

20) Barton, D.H.R.; Zhu, J. *J. Am. Chem. Soc.* **1993**, *115*, 2071.

21) Barton, D.H.R.; Castagnino, E.; Jaszberenyi, J.Cs. *Tetrahedron Lett.* **1994**, *35*, 6057.

22) a) Richter, H.; Kulcke, W.; Specht, H.Z. *Naturforsch* **1952**, *7a*, 511. b) Burbank, R.D. *Acta Cryst.* **1951**, *4*, 140. c) *ibid.* **1952**, *5*, 236. d) Bagnall, K.W. in *Comprehensive Inorganic Chemistry* 1973, Pergamon Press, New York, Ch. 24, p 940. e) see ref. 2.

23) Barton, D.H.R.; McCombie, S.W. *J. Chem. Soc., Perkin Trans. 1* **1975**, 1574.

24) a) Klayman, D.H.; Griffin, T.S. *J. Am. Chem. Soc.* **1973**, *95*, 197. b) see ref. 2 and ref. 23.

25) a) Jensen, K.A.; Nielsen, P.H. *Acta Chem. Scand.* **1966**, *20*, 597. b) Ogawa, A.; Miyake, J; Kambe, N; Sonoda, N *J. Bull. Chem. Soc. Jpn.* **1985**, *58*, 1448. c) Rae, I.D. *Aust. J. Chem.* **1979**, *32*, 567. d) Cullen, E.R.; Guziec, F.S.; Murphy, C.J.; Wong, T.C. *J. Chem. Soc., Perkin Trans. 2* **1982**, *4*, 473.

26) Harris, R.K.; Mann, B.E.; *NMR and the Periodic Table*, Academic Press, 1978, Ch. 12, p. 405 and references cited therein.

27) Eggert, H.; Nielsen, O.; Henriksen, L. *J. Am. Chem. Soc.* **1986**, *108(8)*, 1725.

28) a) Barton, D.H.R.; Ozbalik, N.; Vacher, B. *Tetrahedron* **1988**, *44*, 3501. b) Idem, *ibid.* **1988**, *44*, 7385.

29) a) Higuchi, H.; Otsubo, T.; Oguna, F.; Yamaguchi, H.; Sakata, Y.; Misumi, S. *Bull. Chem. Soc. Jpn.* **1982**, *55*, 182. b) Thompson, D.P.; Boudjouk, P. *J. Org. Chem.* **1988**, *53*, 2109. c) Yoshimatsu, M.; Sato, T.; Shimizu, H.; Hori, M.; Kataoka, T. *J. Org. Chem.* **1994**, *59*, 1011. d) Kataoka, T.; Ohe, Y.; Umeda, A.; Iwamura, T. *Chem. Pharm. Bull.* **1994**, *42(4)*, 811.

30) a) Sato, S.; Ogawa, T. *Carbohydr. Res.* **1987**, *167*, 197. b) Pascal Langlois' thesis, Université de Paris Sud, September 15, 1989.

31) see ref. 6b and ref. 18b.

32) Palacios, S.M.; Santiago, A.N.; Rossi, R.A. *J. Org. Chem.* **1984**, *49*, 4609.

(*Received in USA* 27 *May* 1996; *accepted* 10 *July* 1996)