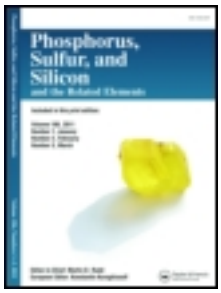


Phosphorus, Sulfur, and Silicon and the Related Elements

Publication details, including instructions for authors and subscription information:
http://www.tandfonline.com/loi/gpss20

SYNTHESIS, CHARACTERIZATION AND STRUCTURES OF α-SUBSTITUTED SELENENYL-ACETOPHENONES

Ananda S. Hodage [a] , Prasad P. Phadnis [a] , Amey Wadawale [a] , K. I. Priyadarsini [b] & Vimal K. Jain [a]

[a] Chemistry Division, Bhabha Atomic Research Centre , Trombay , Mumbai , 400 085 , India
Phone: +91-22-2559-5095 Fax: +91-22-2559-5095

[b] Radiation and Photochemistry Division, Bhabha Atomic Research Centre , Trombay , Mumbai , 400 085 , India

Accepted author version posted online: 30 Sep 2013.

To cite this article: Phosphorus, Sulfur, and Silicon and the Related Elements (2013): SYNTHESIS, CHARACTERIZATION AND STRUCTURES OF α-SUBSTITUTED SELENENYL-ACETOPHENONES, Phosphorus, Sulfur, and Silicon and the Related Elements, DOI: 10.1080/10426507.2013.844144

To link to this article: http://dx.doi.org/10.1080/10426507.2013.844144

SYNTHESIS, CHARACTERIZATION AND STRUCTURES OF α-SUBSTITUTED SELENENYL-ACETOPHENONES

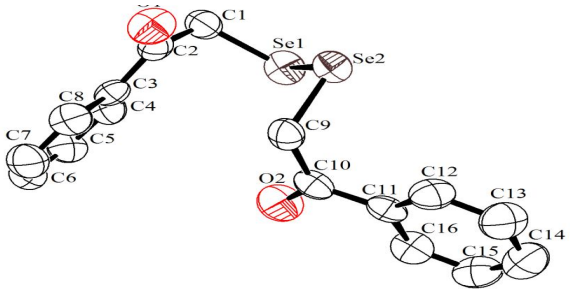
Ananda S. Hodage,[a] Prasad P. Phadnis,[a] Amey Wadawale,[a] K. I. Priyadarsini,*[b] and Vimal K. Jain*[a]

[a]*Chemistry Division, Bhabha Atomic Research Centre, Trombay, Mumbai 400 085, India, Email: jainvk@barc.gov.in, Fax: +91-22-2550-5151; Tel: +91-22-2559-5095*

[b]*Radiation and Photochemistry Division, Bhabha Atomic Research Centre, Trombay, Mumbai 400 085, India, Email: kindira@barc.ernet.in*

Abstract

A series of α-substituted selenenyl acetophenone derivatives of the types, $[PhC(OCH_2CH_2O)CH_2Se]_2$, $[PhC(OCH_2CH_2O)CH_2SeR]$, $(PhCOCH_2Se)_2$ and $[PhCOCH_2SeR]$ have been prepared. These compounds have been characterized by elemental analyses, IR and NMR (^1H, ^{13}C, ^{77}Se) spectroscopy. The compounds, $[PhC(OCH_2CH_2)CH_2Se]_2$ and $(PhCOCH_2Se)_2$ have been structurally characterized by single crystal X-ray diffraction analyses. The former shows intra-molecular Se---O interaction while the latter exhibits inter-molecular non-bonding Se---O interaction.



Keywords Selenenyl acetophenone, selenium, NMR, X-ray structure, Se---O non-bonding interaction

INTRODUCTION

The chemistry of organoselenium compounds has witnessed a rapid growth in the last two decades or so owing to their applications in the diverse area like organic synthesis, materials science and biology.[1-3] Metal selenolates have emerged as versatile precursors for the synthesis of metal selenide nanocrystals and for deposition of thin films.[4]

Biological relevance of selenium has now been well recognized as an essential micro-nutrient.[5,6] In general selenium is primarily present in the form of selenocysteine in selenoenzymes in biological systems.[7] The physiological functions of several selenoenzymes have now been identified. Among these selenoenzymes, glutathione peroxidase (GPx), an antioxidant enzyme, has received an extensive attention. To mimic GPx like activity, different families of organoselenium compounds have been designed and synthesized,[8,9] *e.g.,* ebselen act as glutathione peroxidase (GPx) mimic, antioxidant, radioprotector and an anti-inflammatory drug.[10] The potent applications of ebselen prompted researchers to design and synthesize organoselenium compounds incorporating intra-molecular non-bonding Se---N/O interactions (**I-III**) (Scheme 1) which have shown promising GPx mimicking activity.[11-19] In this context, α-phenylselenenyl acetophenone (**IV**) exhibit GPx like activity both *in-vitro* and *in-vivo*,[20-22] whereas diphenylselenide shows hardly any activity. We have recently reported GPx like activity in alkyl mono- and di-selenides, $\{X(CH_2)_n\}_2Se$ and $\{X(CH_2)_nSe\}_2$ (X = HO, NH_2, HOOC; n = 2 or 3).[23-26] Thus it was envisioned to design organoselenium compounds containing both acetophenone and $X(CH_2)_n$ fragments with the hope to develop potent GPx mimics. Accordingly

we have synthesized a series of α-substituted selenenyl acetophenone derivatives and structurally characterized two such derivatives. Results of this work are reported herein.

RESULTS AND DISCUSSION

Synthesis and spectroscopy

The reaction of 2-(bromomethyl)-2-phenyl-1,3-dioxolane ethylene with Na_2Se_2 (prepared from elemental Se with hydrazine hydrate and NaOH in DMF as a solvent) gave a greenish solution which, after work-up, afforded pale yellow crystals of diselenide $[PhC(OCH_2CH_2O)CH_2Se]_2$ (**1**) in 74 % yield. Treatment of $PhC(OCH_2CH_2O)CH_2SeNa$, prepared by reductive cleavage of Se-Se bond in **1** with $NaBH_4$ in methanol, with bromo compounds gave unsymmetrical seleno ethers (**2**-**9**). The reactions with $HO(CH_2)_nBr$, however afforded a mixture of both protected (**6**, **7**) as well as deprotected (**8**, **9**) compounds which could be easily separated by column chromatography. Acid hydrolysis of **6** and **7** with dil. HCl readily gave **8** and **9**, respectively. Deprotection of carbonyl group in **1** with ceric ammonium nitrate (CAN) yielded the corresponding keto compound $(PhCOCH_2Se)_2$ (**10)**. Synthetic routes for these compounds are depicted in Schemes 2 and 3. These compounds were purified by column chromatography and were characterized by microanalyses, IR and NMR spectroscopy and mass spectrometry.

The IR spectra of carbonyl compounds **8**-**11** displayed a strong absorption in the region 1654-1685 cm^{-1} attributable to $\upsilon_{C=O}$ stretchings. The ^1H and $^{13}C\{^1H\}$ NMR spectra exhibited expected resonances and peak multiplicities. The glycolic protons (OCH_2CH_2O) appeared as multiplets in the regions 3.72-3.89 and 4.02-4.19 ppm. The $SeCH_2$ protons appeared as a singlet

in the region 2.99-4.93 ppm. The resonance in the cyano derivative (**11**) is highly deshielded (δ 4.93 ppm). Similarly in the $^{13}C\{^{1}H\}$ NMR spectrum a singlet is observed in the region 26.4-42.7 ppm with $^{1}J_{Se\text{-}C}$ couplings (65-83 Hz) for CH_2Se. The $^{1}J_{Se\text{-}C}$ for the cyano derivative (**11**) is significantly reduced (43 Hz), owing to the strong electron withdrawing nature of CN group. The carbonyl resonance in **8**-**11** appeared in the region 193.2-195.5 ppm, with the cyano compound being most shielded.

The $^{77}Se\{^{1}H\}$ NMR spectra displayed a single resonance in the region 80-372 ppm and the shifts showed pronounced influence of the substituents. The resonances for diselenides are most deshielded.[27] Due to electron withdrawing C=O group in **10** the $^{77}Se\{^{1}H\}$ NMR resonance appeared at lower field (δ 372 ppm) than that for **1** (δ 310 ppm). Similarly the $^{77}Se\{^{1}H\}$ resonance for compounds containing carbonyl group (**8** and **9**) are deshielded as compared to the corresponding glycolic derivatives (**6** and **7**). The resonances for monoselenides containing aliphatic side chain with two carbon atoms are shielded (**2** (91 ppm) and **6** (80 ppm)) than the signals for the corresponding derivative containing three carbon atoms (**3** (128 ppm) and **7** (123 ppm)).

Molecular structures

The molecular structures of $[PhC(OCH_2CH_2O)CH_2Se]_2$ (**1**) and $[PhCOCH_2Se]_2$ (**10**) have been established unambiguously by single crystal X-ray diffraction analyses. ORTEP drawings with numbering scheme are shown in Figures 1 and 2 while selected interatomic parameters are given in Table 2. The Se-Se distances of ~ 2.31 Å are well in agreement with the values reported in diorganodiselenides (2.29-2.39 Å).[28-30] The Se-C distances (~ 1.96 Å) are as expected.[31-34] The

C-Se-Se-C torsion angles in **1** and **10** are 78.1 and 90.3°, respectively. The C-Se-Se-C torsion angles in diselenides, in general, vary between 70 and 100º.[35] The five-membered "$COOC_2$" glycolic ring is puckered. There are weak secondary Se---O interactions in both the molecules. In the case of **1** both the glycolic oxygen atoms (O1 and O2) are equidistant from Se1 (3.177 Å). In the case of **10** the carbonyl oxygen atom of one of the carbonyl groups (O1) makes a short contact with the Se2 of the neighboring molecule (3.221 Å) so as to form a dimer. The Se---O separations in both the molecules are shorter than the sum of their van der Waals radii (3.42 Å)

[Insert Figure 1]

[Insert Figure 2]

CONCLUSIONS

The α-substituted selenenyl acetophenone derivatives with OH / NH_2 functionalized aliphatic chains on Se atom have been synthesized. There are weak intra- and inter-molecular Se---O interactions in **1** and **10,** respectively.

EXPERIMENTAL

Materials and Methods

Elemental selenium (99.99 %), sodium borohydride, 2-bromoethylamine hydrobromide, 3-chloropropylamine hydrochloride, 2-bromoethanol, 3-bromopropanol, potassium selenocynide (KSeCN), ceric ammonium nitrate (CAN), picolyl chloride hydrochloride were purchased from commercial sources (Aldrich / Fluka). The starting compound for all the selenides, 2-(bromomethyl)-2-phenyl-1,3-dioxolane *i.e.,* $PhC(OCH_2CH_2O)CH_2Br$[36] was prepared by

literature procedure (*supplementary materials*). All reactions were carried out under a nitrogen atmosphere. Solvents were purified and distilled prior to use. The compounds were purified by column chromatography on silica gel 60/ 120 mesh size. Melting points were determined in capillary tubes and are uncorrected. Elemental analyses were carried out on Flash EA 1112 Series CHNS Analyzer. NMR spectra were recorded on a Bruker Avance-II 300 MHz spectrometer operating at 300.13 (^{1}H), 75.47 (^{13}C{^{1}H}) and 57.25 (^{77}Se{^{1}H}) MHz. ^{1}H and ^{13}C{^{1}H} NMR chemical shifts were relative to internal chloroform peak (δ = 7.26 ppm for ^{1}H and δ = 77.0 for ^{13}C{^{1}H} NMR). The ^{77}Se{^{1}H} NMR chemical shifts were relative to external diphenyl diselenide (Ph_2Se_2) in $CDCl_3$ (δ 463.0 ppm relative to Me_2Se (0 ppm)). The mass spectra were recorded on a MS-500 Ion Trap (IT) Varian mass spectrometer at Sophisticated Analytical Instrumentation Facility (SAIF), Indian Institute of Technology-Bombay, Mumbai. Selected ^{1}H, ^{13}C and ^{77}Se NMR spectra for 1, 2 and 10 are presented in the Supplemental Materials (Figures S 1 – S 9)

Synthesis

Synthesis of $[PhC(OCH_2CH_2O)CH_2Se]_2$ (1). To a greenish brown solution of Na_2Se_2 in DMF (200 mL) (prepared by stirring a mixture of Se (20 g, 253 mmol), crushed NaOH (10.1 g, 253 mmol) and $N_2H_4{\cdot}H_2O$ (65 % v/v, 4.70 mL, 61.3 mmol) for 2 h) at 90 ºC, solution of $PhC(OCH_2CH_2O)CH_2Br$ (61.8 g, 254 mmol) in DMF (100 mL) was added drop wise over a period of 30 min and the reaction mixture was further stirred at ~ 100 ^{o}C for 3 h. The reaction was monitored by TLC. A clear yellow solution was cooled to room temperature and diluted with water while the product was precipitated in the form of yellow crystals. It was filtered,

washed several times with water and cold methanol and recrystallized from hot methanol to yield yellow crystals of the title compound (45.9 g, 74 %). m.p.: 95-96 ^{o}C. Anal. Calcd. for $C_{20}H_{22}O_4Se_2$: C, 49.60; H, 4.58; Found: C, 49.74; H, 4.55 %. ^{1}H NMR ($CDCl_3$) δ: 3.53 (s, $^2J_{Se\text{-}H}$ = 11 Hz, 2H, -SeCH_2-), 3.78-3.83 (m, 2H, -OCH_2CH_2O-), 4.06-4.10 (m, 2H, -OCH_2CH_2O-), 7.28-7.36 (m, 3H, C_6H_5), 7.45-7.82 (m, 2H, C_6H_5); ^{13}C{^{1}H} NMR ($CDCl_3$) δ: 42.7 ($^1J_{Se\text{-}C}$ = 83 Hz, -Se*C*H_2-), 65.1 (-O*C*H_2*C*H_2O-), 108.9 (-*C*(OCH_2CH_2O)-), 125.6, 128.0, 128.1, 141.1 (-Ph); ^{77}Se{^{1}H} NMR ($CDCl_3$) δ: 310 ppm. MS (IT) m/z: 487 $[M+1]^+$, 332 [M-2C_6H_5], 283 [M/2+K].

Synthesis of PhC(OCH_2CH_2O)CH_2SeCH_2CH_2NH_2 (2) Pale yellow oil (91 %)**.** To a suspension of **1** (1.2 g, 2.48 mmol) in ethanol, $NaBH_4$ (209 mg, 5.5 mmol) was added in a flow of nitrogen. The reaction mixture was stirred for 2 h to form a clear colorless solution. To this, solid 2-bromo ethylamine hydrobromide (1.01 g, 4.93 mmol) was added with stirring which continued for 3 h whereupon a white slurry formed. The reaction was monitored with TLC. The solvent was evaporated on a rotavapor. The residue was dissolved in water and extracted with ethyl acetate. The organic layer was dried over sodium sulfate, evaporated on rotavapor and the residue was purified by column chromatography with ethyl acetate:hexane mixture (20:80) as eluent to afford a thick yellow oil (1.29 g, 91 %). Anal. IR (υ cm^{-1}): 3375, 2949, 2888, 1488, 1447, 1042, 980, 703. ^{1}H NMR ($CDCl_3$) δ: 1.62 (s, 2H, -NH_2), 2.56 (t, *J* = 6.5 Hz, 2H, -SeCH_2CH_2-), 2.80 (t, *J* = 6.5 Hz, 2H, -CH_2NH_2), 2.99 (s, $^2J_{Se\text{-}H}$ =11 Hz, 2H, -SeCH_2-), 3.73-3.78 (m, 2H, -OCH_2CH_2O-), 4.03-4.08 (m, 2H, -OCH_2CH_2O-), 7.28-7.31 (m, 3H, C_6H_5), 7.42-7.45 (m, 2H, C_6H_5); ^{13}C{^{1}H} NMR ($CDCl_3$) δ: 29.7 ($^1J_{Se\text{-}C}$ = 61 Hz, -Se*C*H_2CH_2-), 33.8 ($^1J_{Se\text{-}C}$ = 73 Hz, -*C*H_2Se-), 41.4 (-*C*H_2NH_2), 65.0 (-O*C*H_2*C*H_2O-), 109.0 (-*C*(OCH_2CH_2O)-), 125.5, 127.8, 127.9, 141.4 (-Ph); ^{77}Se{^{1}H} NMR ($CDCl_3$) δ: 91 ppm.

Compounds **3-5** were synthesized in a similar mannar using the corresponding organic halide.

PhC(OCH$_2$CH$_2$O)CH$_2$SeCH$_2$CH$_2$CH$_2$NH$_2$ (3). Pale yellow oil (86 %). IR (υ cm^{-1}): 2934, 2887, 1560, 1486, 1043, 704. ^{1}H NMR ($CDCl_3$) δ: 1.75 (qn, *J* = 6.8 Hz, 2H, -CH$_2$C*H*$_2$CH$_2$-), 2.02 (bs, 2H, -NH$_2$), 2.55 (t, *J* = 7.1 Hz, 2H, -SeC*H*$_2$CH$_2$-), 2.74 (t, *J* = 6.1 Hz, -C*H*$_2$NH$_2$), 3.04 (s, 2H, -C*H*$_2$Se-), 3.77-3.88 (m, 2H, -OC*H*$_2$CH$_2$O-), 4.06-4.17 (m, 2H, -OCH$_2$C*H*$_2$O-), 7.30-7.37 (m, 3H, -C$_6$*H*$_5$), 7.47-7.51 (m, 2H, -C$_6$*H*$_5$); ^{13}C{^{1}H} NMR ($CDCl_3$) δ: 22.3 ($^1J_{Se-C}$ = 59 Hz, -Se*C*H$_2$CH$_2$-), 33.8 (-CH$_2$*C*H$_2$CH$_2$-), 34.1 ($^1J_{Se-C}$ = 68 Hz, -Se*C*H$_2$-), 41.7 (-*C*H$_2$NH$_2$), 65.0 (-OCH$_2$*C*H$_2$O-), 109.2 (-*C*(OCH$_2$CH$_2$O)-), 125.6, 127.9, 141.4 (-Ph); ^{77}Se{^{1}H} NMR ($CDCl_3$) δ: 128 ppm.

PhC(OCH$_2$CH$_2$O)CH$_2$SeCH$_2$py (4). Pale yellow oil (75 %); IR (υ cm^{-1}): 2944, 2886, 1590, 1566, 1473, 1434, 1028, 982, 766, 704. ^{1}H NMR ($CDCl_3$) δ: 3.06 (s, $^2J_{Se-H}$ = 11 Hz, 2H, -C*H*$_2$Se-), 3.79-3.83 (m, 2H, -OC*H*$_2$CH$_2$O-), 3.90 (s, $^2J_{Se-H}$ = 14 Hz, 2H, -C*H*$_2$py), 4.09-4.14 (m, 2H, -OCH$_2$C*H*$_2$O-), 7.13 (t, *J* = 6.2 Hz, 1H, -py), 7.25-7.29 (m, 1H, -py), 7.31-7.36 (m, 3H, -Ph), 7.47-7.50 (m, 2H, -Ph), 7.62 (td, *J* = 7.9, 1.8 Hz, 1H, -py), 8.50 (d, *J* = 4.8 Hz, 1H, -py); ^{13}C{^{1}H} NMR ($CDCl_3$) δ: 29.3 ($^1J_{Se-C}$ = 61 Hz, -Se*C*H$_2$py), 33.5 ($^1J_{Se-C}$ = 74 Hz, -*C*H$_2$Se-), 64.8 (-OC*H*$_2$*C*H$_2$O-), 109.1 (-*C*(OCH$_2$CH$_2$O)-), 121.0, 122.6, 125.3, 127.7, 127.7, 136.0, 141.4, 148.8, 159.2 (-Ph + -py); ^{77}Se{^{1}H} NMR ($CDCl_3$) δ: 219 ppm.

PhC(OCH$_2$CH$_2$O)CH$_2$SeC$_6$H$_4$(*o*-NO$_2$) (5). Yellow crystalline solid (86 %). m. p.: 88-90 ^{o}C. Anal. Calcd. for $C_{16}H_{16}NO_4Se$: C, 52.61; H, 4.41%; Found: C, 52.63; H, 4.42% . IR (υ cm^{-1}): 2986, 2889, 1588, 1565, 1505, 1328, 1039, 708. ^{1}H NMR ($CDCl_3$) δ: 3.48 (s, $^2J_{Se-H}$ = 11 Hz, 2H, -C*H*$_2$Se-), 3.84-3.89 (m, 2H, -OC*H*$_2$CH$_2$O-), 4.15-4.19 (m, 2H, -OCH$_2$C*H*$_2$O-), 7.28-7.33 (m, 1H,

aromatic), 7.35-7.43 (m, 3H, aromatic), 7.45-7.51 (m, 1H, aromatic), 7.57-7.60 (m, 2H, aromatic), 7.67 (dd, J = 8.1 Hz, 1H, aromatic), 8.25 (dd, J = 8.1 Hz, 1H, aromatic); $^{13}C\{^{1}H\}$ NMR ($CDCl_3$) δ: 37.5 ($^{1}J_{Se\text{-}C}$ = 79 Hz, -*C*H_2Se-), 65.4 (-O*C*H_2*C*H_2O-), 125.3, 128.4, 128.5, 141.6 (-Ph); 125.5, 126.0, 126.4, 128.8, 129.9, 133.4 (-$C_6H_4NO_2$); $^{77}Se\{^{1}H\}$ NMR ($CDCl_3$) δ: 328 ppm.

Synthesis of PhC(OCH$_2$CH$_2$O)CH$_2$SeCH$_2$CH$_2$OH (6) and PhCOCH$_2$SeCH$_2$CH$_2$OH (8). To a suspension of **1** (2.0 g, 4.13 mmol) in ethanol, $NaBH_4$ (350 mg, 9.21 mmol) was added in a flow of nitrogen. The reaction mixture was stirred for 2 h to form a clear colorless solution. To this 2-bromo ethanol (0.6 mL, 8.26 mmol) was added and the contents were stirred for 3 h until a white slurry formed. The reaction was monitored by TLC. The solvent was removed on a rotavapor, residue was dissolved in water and extracted with ethyl acetate. Organic layer was dried over sodium sulfate, evaporated on rotavapor and the residue was purified by column chromatography eluting with ethyl acetate and hexane to give two fractions (by TLC). The first fraction after solvent evaporation gave **6** while the second one afforded **8**.

PhC(OCH$_2$CH$_2$O)CH$_2$SeCH$_2$CH$_2$OH (6). Pale yellow oil (710 mg, 30 %). IR (υ cm^{-1}): 3328 (-OH), 2932, 2875, 1595, 1578, 1448, 1277, 1042, 709. ^{1}H NMR ($CDCl_3$) δ: 2.73 (t, J = 5.9 Hz, 2H, -SeC*H*$_2$CH$_2$OH), 3.03 (bs, 1H, -OH), 3.08 (s, $^{2}J_{Se\text{-}H}$ = 10.5 Hz, 2H, -C*H*$_2$Se-), 3.76 (t, J = 5.6 Hz, 2H, -SeCH$_2$C*H*$_2$OH), 3.79-3.87 (m, 2H, -OC*H*$_2$CH$_2$O-), 4.10-4.15 (m, 2H, -OCH$_2$C*H*$_2$O-), 7.28-7.36 (m, 3H, -C$_6$*H*$_5$), 7.44-7.48 (m, 3H, -C$_6$*H*$_5$); $^{13}C\{^{1}H\}$ NMR ($CDCl_3$) δ: 29.4 ($^{1}J_{Se\text{-}C}$ = 64 Hz, -Se*C*H_2CH$_2$OH), 34.5 ($^{1}J_{Se\text{-}C}$ = 73 Hz, -Se*C*H_2-), 61.7 (-*C*H_2OH), 65.2 (-O*C*H_2*C*H_2O-), 109.1 (-*C*(OCH$_2$CH$_2$O)-), 125.5, 128.1, 128.3, 141.3 (-Ph); $^{77}Se\{^{1}H\}$ NMR ($CDCl_3$) δ: 80 ppm.

$PhCOCH_2SeCH_2CH_2OH$ (8). Pale yellow oil (840 mg, 42 %); IR (υ cm^{-1}): 3358 (-OH), 2926, 1685 (C=O), 1276, 710. ^1H NMR ($CDCl_3$) δ: 2.03 (bs, 1H, -O*H*), 2.87 (t, *J* = 5.9 Hz, 2H, -SeC*H*$_2$CH$_2$-), 3.86 (t, *J* = 6.0 Hz, 4H, -C*H*$_2$SeC*H*$_2$-), 7.45-7.50 (m, 2H, -C_6H_5), 7.56-7.61 (m, 1H, -C_6H_5), 7.96 (dd, *J* = 6.6, 1.5 Hz, 2H, -C_6H_5); $^{13}C\{^1H\}$ NMR ($CDCl_3$) δ: 26.3 ($^1J_{Se-C}$ = 65 Hz, -Se*C*H$_2$CH$_2$-), 28.4 ($^1J_{Se-C}$ = 65 Hz, -*C*H$_2$Se-), 61.4 (-*C*H$_2$OH), 128.5, 128.6, 134.7 (-Ph), 195.5 (*C*=O); $^{77}Se\{^1H\}$ NMR ($CDCl_3$) δ: 171 ppm.

Compounds **7** and **9** were synthesized in a similar mannar using 3-bromo propanol.

$PhC(OCH_2CH_2O)CH_2SeCH_2CH_2CH_2OH$ (7). Pale yellow oil (14 %), IR (υ cm^{-1}): 3407 (-OH), 2934, 2874, 1595, 1578, 1447, 1276, 1009, 709. ^1H NMR ($CDCl_3$) δ: 1.78 (qn, *J* = 6.6 Hz, 2H, -CH$_2$C*H*$_2$CH$_2$-), 2.55 (t, *J* = 7 Hz, 2H, -SeC*H*$_2$CH$_2$-), 3.00 (s, $^2J_{Se-H}$ = 11 Hz, 2H, -C*H*$_2$Se-), 3.07 (br, 1H, -O*H*), 3.58 (t, *J* = 6.2 Hz, 2H, -C*H*$_2$OH), 3.72-3.77 (m, 2H, -OC*H*$_2$CH$_2$O-), 4.02-4.07 (m, 2H, -OCH$_2$C*H*$_2$O-), 7.22-7.31 (m, 3H, -C_6H_5), 7.41-7.45 (m, 2H, -C_6H_5); $^{13}C\{^1H\}$ NMR ($CDCl_3$) δ: 21.3 ($^1J_{Se-C}$ = 59 Hz, -Se*C*H$_2$CH$_2$-), 32.4 (-CH$_2$C*H*$_2$CH$_2$-), 33.9 ($^1J_{Se-C}$ = 73.3 Hz, -Se*C*H$_2$-), 61.5 (-*C*H$_2$OH), 64.8 (-OC*H*$_2$*C*H$_2$O-), 109.0 (-*C*(OCH$_2$CH$_2$O)-), 125.3, 127.8, 127.8, 141.2 (-Ph); $^{77}Se\{^1H\}$ NMR ($CDCl_3$) δ: 123 ppm.

$PhCOCH_2SeCH_2CH_2CH_2OH$ (9). Pale yellow oil (52 %); IR (υ cm^{-1}): 3408 (-OH), 2933, 2874, 1666 (C=O), 1595, 1578, 1447, 1276, 1010, 709. ^1H NMR ($CDCl_3$) δ: 1.78 (qn, *J* = 6.5 Hz, 2H, -SeCH$_2$C*H*$_2$-), 2.17 (br, 1H, -O*H*), 2.76 (t, *J* = 7.1 Hz, 2H, -SeC*H*$_2$-), 3.70 (t, *J* = 6.1 Hz, 2H, -C*H*$_2$OH), 3.79 (s, 2H, -SeC*H*$_2$-), 7.43-7.48 (m, 2H, C_6H_5), 7.54-7.60 (m, 1H, C_6H_5), 7.94-7.96 (m, 2H, C_6H_5); $^{13}C\{^1H\}$ NMR ($CDCl_3$) δ: 21.7 ($^1J_{Se-C}$ = 63 Hz, -Se*C*H$_2$-), 26.4 ($^1J_{Se-C}$ = 65 Hz, -CO*C*H$_2$-), 32.3, 61.3 (each s -*C*H$_2$*C*H$_2$-), 128.4, 128.5, 133.1, 134.7 (-Ph), 195.3 (-*C*=O); $^{77}Se\{^1H\}$ NMR ($CDCl_3$) δ: 211 ppm.

Synthesis of $[PhCOCH_2Se]_2$ (10). To a hot acetonitrile solution (10 mL) of **1** (60 mg, 0.12 mmol), an excess of ceric ammonium nitrate (CAN) (140 mg, 0.38 mmol), dissolved in water (5 mL) was added slowly until the orange color of CAN persisted for a long time. The reaction mixture was refluxed until a white precipitate was formed. The reaction was monitored by TLC. The solvents were evaporated under vacuum and the residue was extracted with ethyl acetate, organic layer was dried over sodium sulfate and concentrated on rotavapor to yield a pale yellow solid which was further purified on column chromatography as yellow crystals (30 mg, 61 %). m.p.: 125-126 ^oC. Anal. Calcd. for $C_{16}H_{14}O_2Se_2$: C, 48.50; H, 3.56; Found: C, 48.30; H, 3.49. IR (υ cm^{-1}): 1654 (C=O), 1447, 1415, 1274, 1011, 704. ^1H NMR ($CDCl_3$) δ: 4.30 (s, $^2J_{Se\text{-}H}$ = 14.7 Hz, 2H, -SeCH_2-), 7.45 (t, J = 7.7 Hz, 2H, C_6H_5), 7.57 (t, J = 7.4 Hz, 1H, C_6H_5), 7.92 (d, J = 7.8 Hz, 2H, C_6H_5); $^{13}C\{^1H\}$ NMR ($CDCl_3$) δ: 34.0 ($^1J_{Se\text{-}C}$ = 77 Hz, -CH$_2$Se-), 128.6, 128.7, 133.5, 135.1 (-Ph), 195.3 (-C=O); $^{77}Se\{^1H\}$ NMR ($CDCl_3$) δ: 372 ppm.

X-ray Crystallography

Single crystal X-ray data on $[PhC(OCH_2CH_2)CH_2Se]_2$ (**1**) and $(PhCOCH_2Se)_2$ (**10**) were collected at room temperature (298 ± 2 K) on a Rigaku AFC 7S diffractometer using graphite monochromated Mo-Kα (λ = 0.71069 Å) radiation so that $\theta_{max} = 27.5^o$. The unit cell parameters (Table 1) were determined from 25 reflections measured by a random search routine. The intensity data were corrected for Lorenz, polarization and absorption effects with an empirical procedure.[38] The structures were solved by direct methods using SHELX-97[39] and refined by full-matrix least squares methods. The non-hydrogen atoms were refined anisotropically. The

hydrogen atoms were fixed in their calculated positions. The molecular structures were drawn by ORTEP.[40] X-ray data and selected bond and angles are presented in Tables 1 and 2 respectively.

[Insert Table 1]

[Insert Table 2]

SUPPLEMENTARY DATA

Crystallographic data for the structural analyses have been deposited with the Cambridge Crystallographic Data Centre, CCDC Nos. 937751 $[PhC(OCH_2CH_2O)CH_2Se]_2$ (**1**) and 937750 $[PhCOCH_2Se]_2$ (**10**). Copies of this information may be obtained free of charge from: The Director, CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [fax: (int. code) +44 1223-336-033; e-mail: deposit@ccdc.cam.ac.uk or www: http://www.ccdc.cam.ac.uk].

SUPPORTING INFORMATION (see footnote on the first page of this article):

Synthesis and characterization of $Ph(OCH_2CH_2O)CH_2Br$, NMR (^1H, $^{13}C\{^1H\}$ and $^{77}Se\{^1H\}$) and mass spectra of all organoselenium compounds and the cif files of the single crystal X-ray diffraction analyses of compounds **1** and **10** are available.

ACKNOWLEDGEMENTS

One of the authors (ASH) is grateful to Board of Research in Nuclear Sciences (BRNS), Department of Atomic Energy (DAE) for a Junior Research Fellowship awarded to him. We are also grateful to BRNS for the research grant under the Prospective Research Fund (PRF) Scheme (Grant No. BRNS/2007/38/5).

REFERENCES

1. Kedarnath, G.; Jain, V. K. *Coord. Chem. Rev.* **2013**, 257, 1409-1435; Akhtar, J.; Malik, M. A.; Stubbs, S.K.; O'Brien, P.; Helliwell, M.; Binks, D. J. *Eur. J. Inorg. Chem.* 2011, 19, 2984-2990.

2. Nogueira, C.W.; Zeni, G.; Rocha, J.B.T. *Chem. Rev.* **2004**, 104, 6255-6285; Brigelius-Flohé, R. *Chem. Biodiv.* **2008**, 5, 389-395.

3. Mugesh, G.; duMont, W.-W.; Sies, H. *Chem. Rev.* **2001**, 101, 2125-2179.; Yoshida, S.; Kumakura, F.; Komatsu, I.; Arai, K.; Onuma, Y.; Hojo, H.; Singh, B. G.; Priyadarsini, K. I.; Iwaoka, M. *Angew. Chem. Int. Ed.* **2011**, 50, 2125-2128.

4. Sharma, R. K.; Kedarnath, G.; Jain, V. K.; Wadawale, A.; Pillai, C. G. S.; Nalliath, M.; Vishwanadh, B. *Dalton Trans.* **2011**, 40, 9194-9201; Sharma, R. K.; Kedarnath, G.; Wadawale, A.; Betty, C. A.; Vishwanadh, B.; Jain, V. K. *Dalton Trans.* 2012, 41(39):12129-12138;. Sharma, R. K.; Kedarnath, G.; Jain, V. K.; Wadawale, A.; Nalliath, A.; Pillai, C. G. S.; Vishwanadh, B. *Dalton Trans.* **2010**, 39, 8779-8787.

5. Hatfield, D. L. Ed. Selenium: Its molecular biology and role in human health, Boston, Kluwer Academic Publisher, (2001) 219-233.

6. Battin, E. E.; Brumaghim, J. L. *Cell Biochem. Biophys.* **2009**, 55, 1-23.

7. Jacob, C.; Giles, G. I.; Giles, N. M.; Sies, H. *Angew. Chem. Int. Ed.* 42 (2003) 4742-4758.

8. Mugesh, G.; DuMont, W. W.; Sies, H. *Chem. Rev.* **2001**, 101, 2125-2179.

9. Nogueira, C. W.; Zeni, G.; Rocha, J. B. T. *Chem. Rev.* **2004**, 104, 6255-6268.

10. Wendel, A.; Fausel, M.; Safayhi, H.; Tiegs, G.; Otter, R. *Biochem. Pharmacol.* **1984**, 33, 3241-3245; Sies, H.; Masumoto, H. *Adv. Pharmacol.* **1997**, 38, 229-246; Müller, A.; Cadenas, E.; Graf, P.; Sies, H. *Biochem. Pharmacol.* **1984**, 33, 3235-3239.

11. Wilson, S. R.; Zucker, P. A.; Huang, R. R. C.; Spector, A. *J. Am. Chem. Soc.* **1989**, 111, 5936-5939.

12. Iwaoka, M.; Tomoda, S. *J. Am. Chem. Soc.* **1994**, 116, 2557-2561.

13. Bhabak, K. P.; Mugesh, G. *Chem. Eur. J.* **2008**, 14, 8640-8651.

14. Bhabak, K. P.; Mugesh, G. *Chem. Eur. J.* **2009**, 15, 9846-9854.

15. Mukherjee, A. J.; Zade, S. S.; Singh, H. B.; Sunoj, R. B. *Chem. Rev.* **2010**, 110, 4357-4416.

16. Hodage, A. S.; Phadnis, P. P.; Wadawale, A.; Priyadarsini, K. I.; Jain, V. K. *Phosphorus, Sulfur, and Silicon and Relat. Elem.* **2012**, 187, 1419-1433.

17. Wirth, T. *Molecules* **1998**, 3, 164-166.

18. Bayse, C. A.; Pavlou, A. *Org. Biomol. Chem.* **2011**, 9, 8006-8015.

19. Tripati, S. K.; Patel, U.; Roy, D.; Sunoj, R. B.; Singh, H. B.; Wolmershauer, G.; Butcher, R. J. *J. Org. Chem.* **2005**, 70, 9237-9247.

20. Cotgreave, I. A.; Moldéus, P.; Brattsand, R.; Hallberg, A.; Andersson, C. M.; Engman, L. *Biochem. Pharmacol.* **1992**, 43, 793-802.

21. Engman, L.; Anderson, C.; Morgenstern, R.; Cotgreave, I. A.; Andersson, C. M.; Hallberg, A. *Tetrahedron* **1994**, 50, 2929-2938.

22. Gerzson, M. F. B.; Victoria, F. N.; Radatz, C. S.; de Gomes, M. G.; Bocira, S. P.; Jacob, R. G.; Alves, D.; Jesse, C. R.; Savegnago, L. *Pharmacol. Biochem. Be.* **2012**, 102, 21-29.

23. Mishra, B.; Kumbhare, L. B.; Jain, V. K.; Priyadarsini, K. I. *J. Phys. Chem.* B **2008**, 112, 4441-4446.

24. Kumar, B. S.; Kunwar, A.; Ahmad, A.; Kumbhare, L. B.; Jain, V. K.; Priyadarsini, K. I. *Radiat. Environ. Biophys.* **2009**, 48, 379-384.

25. Jain, V. K.; Priyadarsini, K. I. *Proceed. Nat. Acad. Sci.* **2010**, 80, 269-280.

26. Prabhu, P.; Bag, P. P.; Singh, B. G.; Hodage, A.; Jain, V. K.; Iwaoka, M.; Priyadarsini, K. I. *Free Radical Research* **2011**, 45, 461-468.

27. Duddeck, H. Selenium-77 nuclear magnetic resonance spectroscopy, *Progress in NMR Spectroscopy* **1995**, 27, 1-323.

28. Hodage, A. S.; Prabhu, C. P.; Phadnis, P. P.; Wadawale, A.; Priyadarsini, K. I.; Jain, V. K. *J. Organomet. Chem.* **2012**, 720, 19-25.

29. Prabhu, C. P.; Phadnis, P. P.; Wadawale, A.; Priyadarsini, K. I.; Jain, V. K. *J. Organomet. Chem.* **2012**, 713, 42-50.

30. Dhau, J. S.; Sigh, A.; Dhir, R. *J. Organomet. Chem.* **2011**, 696, 2008-2013; Bhasin, K. K.; Singh, J. *J. Organomet. Chem.* **2002**, 658, 71-76.

31. Mugesh, G.; Panda, A.; Singh, H. B.; Butcher, R. *J. Chem. Eur. J.* **1999**, 5, 1411-142.

32. Hodage, A. S.; Phadnis, P. P.; Wadawale, A.; Priyadarsini, K. I.; Jain, V. K. *Org. Biomol. Chem.* **2011**, 9, 2992-2298.

33. Kumar, S.; Kandasamy, K.; Singh, H. B.; Wolmershäuse, G.; Butcher, R. J. *Organometallics* **2004**, 23, 4199-4208.

34. Bhalla, A.; Nagpal, Y.; Kumar, R.; Mehta, S. K.; Bhasin, K. K.; Bari, S. S. *J. Organomet. Chem.* **2009**, 694, 179-189.

35. Jeske, J.; von Salzen, A. M.; DuMont, W. W.; Jones, P. G. *Acta Cryst.* **1998**, C54, 1873-1875.

36. Carlson, R.; Gautun, H.; Westerlund, A. *Adv. Synth. Catal.* **2002**, 344, 57-60.

37. Otero, M. D.; Batanero, B.; Barba, F. *Tetrahedron* **2004**, 60, 4609-4612.

38. Higashi, T. ABSCOR-Empirical absorption Correction based on Fourier Series approximation, Rigaku Corporation, 3-9-12 Matsubara, Akishima, Japan, 1995.

39. Sheldrick, G. M. SHELX-97-Program for Crystal Structure Analysis, Göttingen, Germany, 1997.

40. Johnson, C. K. ORTEP II, Report ORNL-5136, Oak Ridge National Laboratory, Oak Ridge, TN 1976.

Table 1 Crystallographic and structural refinement data for selenoacetophenone derivatives $[PhC(OCH_2CH_2O)CH_2Se]_2$ (**1**) and $[PhCOCH_2Se]_2$ (**10**).

	1	**10**
Empirical formula	$C_{20}H_{22}O_4Se_2$	$C_{16}H_{14}O_2Se_2$
Formula weight	484.30	396.19
Crystal system/ space group	Monoclinic/ I 2/a	Orthorhombic/ P*bca*
a / Å	11.934 (3)	8.705 (3)
b / Å	10.872 (2)	17.760 (9)
c / Å	15.133 (6)	19.517 (7)
α / ^{o}	90.00	90.00
β / ^{o}	95.00 (3)	90.00
γ / ^{o}	90.00	90.00
V / (Å^3)	1955.3 (10)	3017 (2)
Z	4	8
D_c (g/cm^3)	1.645	1.744
μ(Mo-*K*α) mm^{-1}/ *F* (000)	3.804/ 968	4.899/ 1552
Crystal size	0.25 x 0.15 x 0.10	0.30 x 0.30 x 0.10
Color / Shape	Yellow/ Prismatic	Colorless/ Block
Temp (K)	298	298
Theta range of data collection	2.54-27.50	2.52-27.48
Reflections collected	2239	3453
Independent reflections	1199	1184
Data/ Restraints/ Parameters	2239/ 0/ 118	3453/ 0/ 181
Goodness-of-fit on F^2	0.993	0.935
Final R indices [I>2σ(I)]	R_1 = 0.0385	R_1 = 0.0490
R indices (all data)	R_1 = 0.1151	R_1 = 0.2308
Largest difference peak/hole	0.391, -0.396	0.422, -0.586

Table 2 Selected bond lengths (Å) and bond angles (°) for compound **1** and **10**

$[PhC(OCH_2CH_2O)CH_2Se]_2$ (**1**)		$[PhCOCH_2Se]_2$ (**10**)	
Se(1)-Se(1′)	2.3152 (11)	Se(1)-Se(2)	2.3118 (12)
Se(1)-C(1)	1.962 (4)	Se(1)-C(1)	1.975 (6)
C(1)-C(2)	1.511 (5)	Se(2)-C(9)	1.965 (6)
C(2)-O(1)	1.429 (4)	C(2)-O(1)	1.231 (6)
C(2)-O(2)	1.426 (4)	C(10)-O(2)	1.200 (6)
Se(1)-C(1)-C(2)	113.0 (3)	Se(1)-C(1)-C(2)	110.9 (4)
C(1)-Se(1)-Se(1′)	100.45 (13)	C(1)-C(2)-O(1)	119.3 (6)
C(1)-C(2)-C(3)	110.3 (3)	C(1)-C(2)-C(3)	120.6 (6)
C(1)-C(2)-O(1)	110.8 (3)	C(1)-Se(1)-Se(2)	101.12 (18)
C(1)-C(2)-O(2)	108.6 (3)	Se(1)-Se(2)-C(9)	101.27 (16)
C(1)-Se(1)-Se(1′)-C(1')	78.1	Se(2)-C(9)-C(10)	110.2 (4)
		C(9)-C(10)-O(2)	120.5 (6)
		C(9)-C(10)-C(11)	119.6 (6)
		C(1)-Se(1)-Se(2)-C(9)	90.3 (3)

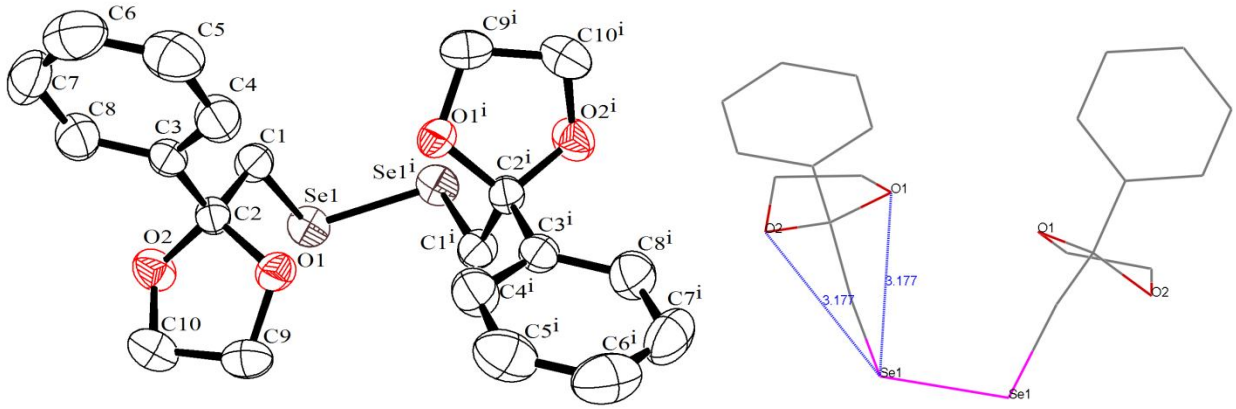


Figure 1 Molecular crystal structure of $[PhC(OCH_2CH_2O)CH_2Se]_2$ (**1**). Thermal ellipsoids are drawn with 30% probability. Inset shows intra-molecular Se---O non-bonding interactions.

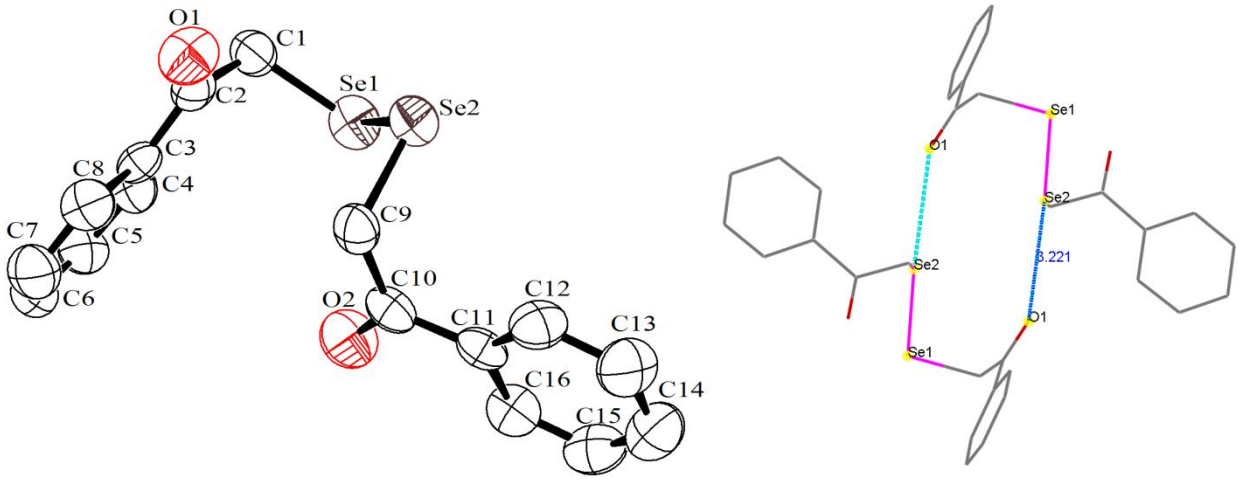
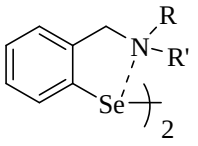
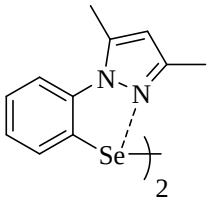


Figure 2 Molecular crystal structure of $[PhCOCH_2Se]_2$ (**10**). Thermal ellipsoids are drawn with 30% probability. Inset shows inter-molecular Se---O non-bonding interactions.

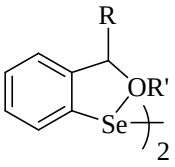


R = H, Me, Et, Pr
R' = Me, Et, Pr
R, R' = Me or c-Hx

(**I**)

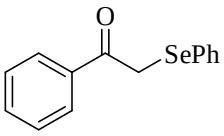


(**II**)



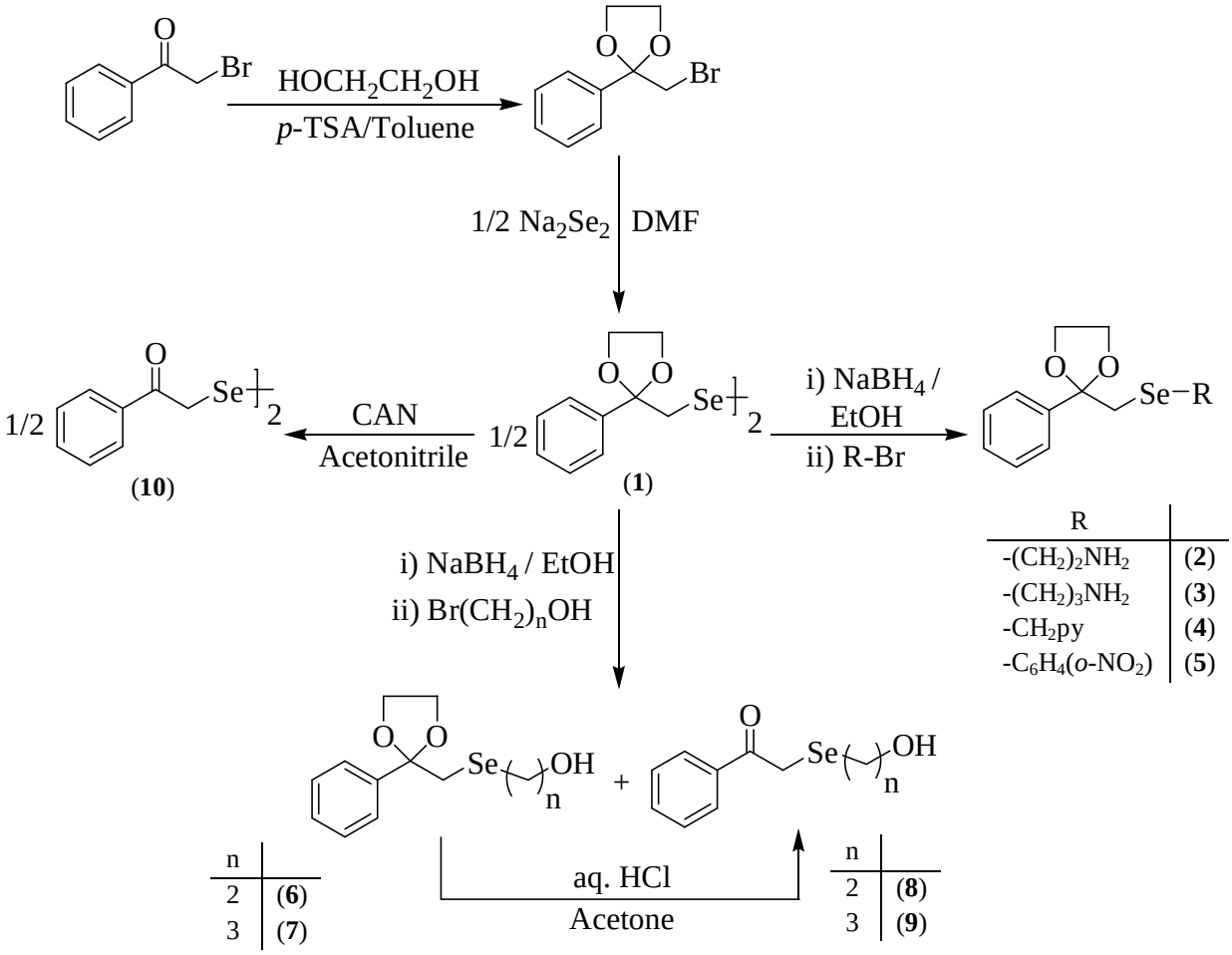
R / R' = H / H; Me / H;
Et / H; Et / Me

(**III**)

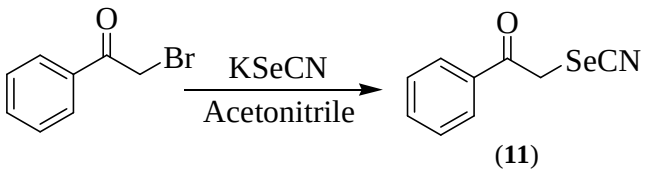


(**IV**)

Scheme 1



Scheme 2. Synthesis of Compounds **1-10**



Scheme 3