

Synthesis and Structure of Eight-, Nine-, and Ten-Membered Rings with P–Se–Se–P Linkages

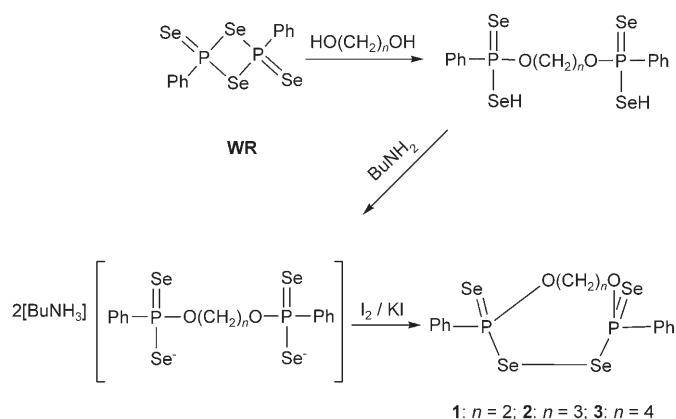
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Organoselenium compounds are studied because of their interesting reactivities and potential biological or pharmaceutical significance. Organic diselenides, as useful synthetic reagents and intermediates, have played an important role in organoselenium chemistry, as they are stable, easily handled, and reactive enough to generate electrophilic, nucleophilic, and radiophilic species.^[1] There are only a few examples of macrocycles containing diselenide linkages,^[2] and many of the known routes to diselenides in general suffer from the use of highly toxic H₂Se, harsh reaction conditions, low yields, or complicated manipulations.

We are developing the chemistry of 2,4-bis(phenyl)-1,3-diselenadiphosphetane-2,4-diselenide [PhP(Se)(μ-Se)]₂ (known as Woollins' reagent, WR).^[3] Herein, we report the synthesis of five novel P–Se diselenides with eight-, nine- and ten-membered rings; this is the first reported synthesis of such large-ring diselenides bearing the P–Se–Se–P linkage.

Cleavage of the four-membered P₂Se₂ ring in WR by alkyl diols affords the corresponding bis(diselenophosphonic) acids quantitatively as yellow oils. These acids were converted into the corresponding amine salts by treatment with butylamine and were oxidized using I₂/KI to give eight-, nine- and ten-membered-ring diselenides **1–3** (70–90% yields, Scheme 1).

Compounds **1–3** are soluble in common polar organic solvents and were crystallized from dichloromethane solutions with slow diffusion of hexane to give transparent, colorless, cubic crystals. The compounds are stable to air and moisture for several months. The ³¹P NMR spectra of **1–3** exhibit sharp singlets at δ ≈ 67 ppm, which are accompanied by two sets of satellites for the endocyclic and exocyclic selenium atoms (¹J(P,Se_{endo}) and ¹J(P,Se_{exo}): 444 and 822 Hz for **1**, 465 and 812 Hz for **2**, and 460 and 808 Hz for **3**), thus indicating the presence of single and double P–Se bonds in each compound. Detailed NMR spectroscopic analysis reveals the relatively small coupling constant between phosphorus atoms (³J(P,P) = 3.0–4.7 Hz), supporting the presence of the P–Se–Se–P group (cf. ³J(P,P) = 4 Hz for the analogous P–S–S–P system).^[4] The ⁷⁷Se NMR spectra for **1–3** contain signals arising from exocyclic (δ = –75, –61, and



Scheme 1. Synthesis of **1–3**.

–80 ppm; ¹J(P,Se_{exo}) = 822, 810, and 806 Hz, respectively) and endocyclic selenium atoms (δ = 491, 441, and 441 ppm). The X-ray structures of **1–3** (Figure 1) confirm the presence of the eight-, nine-, and ten-membered rings. Both *R,R* and *S,S* enantiomers are present in all the structures, and no *R,S,S,R* diastereomers are observed. The macrocyclic framework is highly puckered with the two phenyl rings on opposite sides of the heterocycle. The Se–Se bond (2.3393(12), 2.3518(7), and 2.3475(6) Å in **1–3**, respectively) is slightly shorter than that in acyclic structures containing the P–Se–Se–P linkage (2.384(1) Å).^[5] The geometry around P(1) and P(2) is distorted tetrahedral (Se(1)–P(1)–Se(2) and Se(3)–P(2)–Se(4): 103.94(9) and 105.25(9), 105.49(6) and 105.76(6), 103.94(9) and 106.04(5)° for **1–3**, respectively).

Heating equimolar amounts of aromatic diol and WR at reflux in toluene for 15 h affords, after workup in air, diselenides **4** and **5** as white crystals in 61% and 65% yields (Scheme 2). **4** and **5** are soluble in organic solvents, are air-stable, and display the expected NMR spectra. The X-ray structures of **4** and **5** (Figure 2) are similar to the structures of **1–3**, although the P(1)–Se–Se angles (106.83(4), 107.27(4)° for **4** and 106.22(5), 108.18(5)° for **5**) are larger than in **1–3**.

Since the Se–Se bond is labile and can be broken easily, studies to use these P–Se heterocyclic diselenides as multi-donor ligands and as synthetic precursors are now underway.

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Experimental Section

General procedure for synthesis of **1–3**: A mixture of the appropriate alkyl diol (1.0 mmol) and WR (0.54 g, 1.0 mmol) in toluene (20 mL) was stirred at room temperature for 20 h. The red suspension changed to a green solution along with a trace amount of black elemental

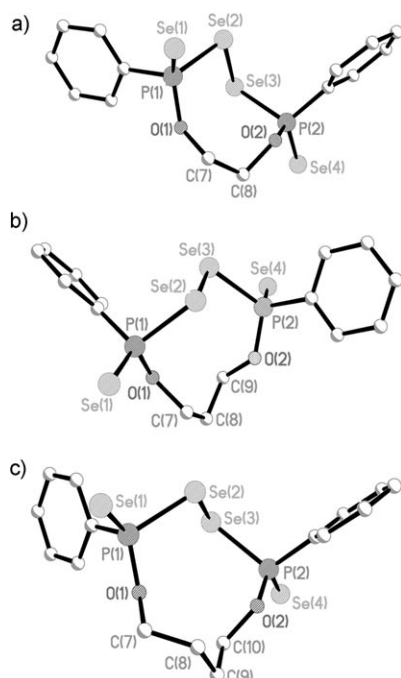
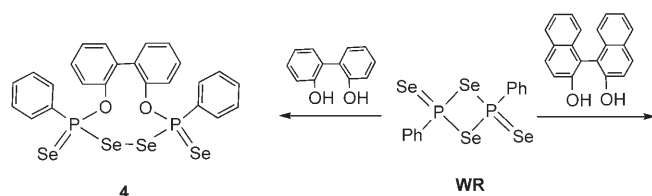


Figure 1. Molecular structure (H atoms omitted for clarity), of a) **1**; selected bond lengths [Å]: Se(1)–P(1) 2.089(2), Se(2)–P(1) 2.253(2), O(1)–P(1) 1.573(6), Se(2)–Se(3) 2.3393(12), Se(4)–P(2) 2.085(2), Se(3)–P(2) 2.243(2), O(2)–P(2) 1.586(6); b) **2**; selected bond lengths [Å]: Se(1)–P(1) 2.0788(13), Se(2)–P(1) 2.2605(13), O(1)–P(1) 1.584(3), Se(2)–Se(3) 2.3518(7), Se(3)–P(2) 2.0821(14), Se(4)–P(2) 2.2468(14), O(2)–P(2) 1.587(3); and c) **3**; selected bond lengths [Å]: Se(1)–P(1) 2.0894(12), Se(2)–P(1) 2.2455(12), O(1)–P(1) 1.583(3), Se(2)–Se(3) 2.3475(6), Se(3)–P(2) 2.0869(12), Se(4)–P(2) 2.2488(12), O(2)–P(2) 1.581(3).



Scheme 2. Synthesis of **4** and **5**.

selenium. The resulting mixture was filtered and concentrated in vacuo to give a green paste, which was dissolved in diethyl ether (20 mL), and butylamine (0.5 mL) was added dropwise. This resulted intermediately in a brown suspension and then a gray suspension after 30 min stirring at room temperature. The gray, solid dibutylammonium bisdiselenophosphonates were obtained by filtration and washed with diethyl ether.

A solution of KI/I₂ (1.5 mmol) was added dropwise to a stirred solution of the dibutylammonium bisdiselenophosphonate (0.5 mmol) in THF (10 mL). An obvious white precipitate formed immediately. The mixture was then stirred at room temperature for another 1 h to ensure complete reaction and then reduced to dryness in vacuo. The residue was dissolved in dichloromethane and filtered to give a yellow solution and gray insoluble solid (polymer side product). The filtrate was purified by silica gel chromatography (dichloromethane as eluent) to give **1–3**. Crystals were obtained from dichloromethane solutions by diffusion of hexane.

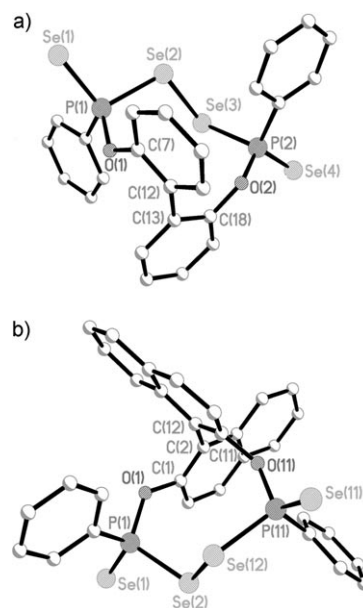


Figure 2. Molecular structure (H atoms omitted for clarity) of a) **4**; selected bond lengths [Å]: Se(1)–P(1) 2.0888(14), Se(2)–P(1) 2.2371(13), O(1)–P(1) 1.612(3), Se(2)–Se(3) 2.3555(8), Se(3)–P(2) 2.0797(13), Se(4)–P(2) 2.2545(13), O(2)–P(2) 1.616(3); and b) **5**; selected bond lengths [Å]: Se(1)–P(1) 2.0745(17), Se(2)–P(1) 2.2413(17), O(1)–P(1) 1.612(4), Se(2)–Se(12) 2.3474(9), Se(11)–P(11) 2.0808(16), Se(12)–P(11) 2.2372(16), O(11)–P(11) 1.613(4).

1: 90% yield. M.p. 110°C. Selected IR (KBr): $\tilde{\nu}$ = 1437(m), 1105(s), 1068(s), 1023(vs), 944(vs), 745(s), 711(m), 689(m), 537 cm^{−1} (s, P=Se). ¹H NMR (CD₂Cl₂): δ = 8.02–7.53 (m, 10H, ArH), 5.30 (t, J = 12 Hz, 2H, CH₂), 4.22 ppm (t, J = 12 Hz, 2H, CH₂). ¹³C NMR (CD₂Cl₂): δ = 132.9 (d, J (P,C) = 100 Hz), 130.4 (d, J (P,C) = 3 Hz), 128.5 (d, J (P,C) = 12 Hz), 126.5 (d, J (P,C) = 15 Hz), 66.1 ppm (s, CH₂). ³¹P NMR (CD₂Cl₂): δ = 66.77 ppm, singlet with ⁷⁷Se satellites (2 × AXX' pattern) (¹J(P,Se_{exo}) = 822 Hz, ¹J(P,Se_{endo}) = 444 Hz, ³J(P,P) = 3.0 Hz; lines for ²J(P,Se_{endo}) were hidden under the intensive central line, prohibiting calculation of the coupling constant). ⁷⁷Se NMR (CD₂Cl₂): δ = 490.66 (dd, J (P,Se_{endo}) = 443 Hz, ²J(P,Se_{endo}) = 24.7 Hz), −74.59 ppm (d, J (P,Se_{exo}) = 822 Hz). EI⁺ MS m/z : 592 [M]⁺. Elemental analysis calcd (%) for C₁₄H₁₄O₂P₂Se₄: C 28.4, H 2.4; found: C 28.0, H 2.6.

2: 85% yield. M.p. 162–163°C. Selected IR (KBr): $\tilde{\nu}$ = 1433(m), 1262(m), 1103(s), 987(s), 804(m), 740(m), 684(m), 538 cm^{−1} (s, P=Se). ¹H NMR (CD₂Cl₂): δ = 8.00–7.56 (m, 10H, ArH), 4.66 (m, J = 12 Hz, 2H, CH₂), 4.30 ppm (t, J = 12 Hz, 4H, CH₂). ¹³C NMR (CD₂Cl₂): δ = 135.1 (d, J (P,C) = 103 Hz), 133.2 (d, J (P,C) = 3 Hz), 130.7 (d, J (P,C) = 12 Hz), 128.6 (d, J (P,C) = 15 Hz), 62.4 (d, J (P,C) = 15 Hz, CH₂); 28.4 ppm (t, ³J(P,C) = 10 Hz, CH₂). ³¹P NMR (CD₂Cl₂): δ = 67.21 ppm (s, ¹J(P,Se_{exo}) = 812 Hz, ¹J(P,Se_{endo}) = 465 Hz, ³J(P,P) = 4.2 Hz; lines for ²J(P,Se_{endo}) were hidden under the intensive central line, prohibiting calculation of the coupling constant). ⁷⁷Se NMR (CD₂Cl₂): δ = 441.17 (dd, ¹J(P,Se_{endo}) = 465, ²J(P,Se_{endo}) = 21.5 Hz), −61.15 ppm (dd, ¹J(P,Se_{exo}) = 810 Hz). High-resolution mass spectrometry (EIMS): 609.7284, calculated mass for C₁₅H₁₆O₂P₂Se₄: 609.7281. Elemental analysis calcd (%) for C₁₅H₁₆O₂P₂Se₄: C 29.7, H 2.7; found C 29.5, H 2.8.

3: 70% yield. M.p. 108°C. Selected IR (KBr): $\tilde{\nu}$ = 2948(m), 2882(w), 1435(s), 1381(w), 1105(s), 962(bs), 745(s), 711(s), 687(s), 532 cm⁻¹ (s, P=Se). ¹H NMR (CD₂Cl₂): δ = 8.04 m, 4H, ArH), 7.56 (m, 6H, ArH), 4.39 (m, ³J(P,H) = 40 Hz, ³J(H,H) = 8.9 Hz, 4H, CH₂), 2.04 ppm (m, ³J(H,H) = 8.9 Hz, 4H, CH₂). ¹³C NMR (CD₂Cl₂): δ = 137.5 (d, ¹J(P,C) = 98 Hz), 132.3 (d, ¹J(P,C) = 3 Hz), 129.6 (d, ³J(P,C) = 13 Hz), 128.4 (d, ²J(P,C) = 15 Hz), 65.9 (²J(P,C) = 32 Hz, CH₂), 25.1 ppm (³J(P,C) = 8 Hz, CH₂). ³¹P NMR (CD₂Cl₂): δ = 68.28 ppm, (s, ¹J(P,Se_{exo}) = 808 Hz, ¹J(P,Se_{endo}) = 460 Hz, ³J(P,P) = 4.7 Hz; lines for ²J(P,Se_{endo}) were hidden under the intensive central line, prohibiting calculation of the coupling constant). ⁷⁷Se NMR (CD₂Cl₂): δ = 474.21 (dd, ¹J(P,Se_{endo}) = 463 Hz, ²J(P,Se_{endo}) = 21.5 Hz), -80.17 ppm (d, ¹J(P,Se_{exo}) = 806 Hz). High-resolution mass spectrometry (EIMS): 621.7450, calculated mass for C₁₆H₁₈O₂P₂Se₄: 621.7445. Elemental analysis calcd (%) for C₁₆H₁₈O₂P₂Se₄: C 31.0, H 2.9; found: C 30.5, H 2.8.

General Procedure for synthesis of **4** and **5**: A mixture of aromatic diol (1.0 mmol) and WR (0.54 g, 1 mmol) in toluene (20 mL) was heated at reflux for 15 h under N₂. Upon cooling to room temperature the mixture was purified by silica gel chromatography (toluene as eluent) to afford diselenides **4** and **5** as white crystals.

4. 61% yield. M.p. 172–173°C. Selected IR (KBr): $\tilde{\nu}$ = 1577(w), 1502(m), 1452(m), 1469(m), 1435(m), 1182(s), 1099(s), 916(vs), 769(s), 743(s), 684(m), 557(m), 528 cm⁻¹ (s, P=Se). ¹H NMR (CDCl₃): δ = 8.70 (d, ³J(H,H) = 8.2 Hz, 4H, ArH), 7.61 (d, ³J(H,H) = 6.7 Hz, 2H, ArH), 7.48 (m, ³J(H,H) = 8.2 Hz, 6H, ArH), 7.32 (dd, ³J(H,H) = 6.7 Hz, 2H, ArH), 7.16 ppm (m, ³J(H,H) = 6.7 Hz, 4H, ArH). ¹³C NMR (CDCl₃): δ = 134.0, 133.2, 132.5, 131.3, 131.2, 131.1, 129.5, 128.3, 128.2, 128.1, 125.6, 119.8, 119.7 ppm. ³¹P NMR (CDCl₃): δ = 67.21 ppm (s, ¹J(P,Se_{exo}) = 826 Hz, ¹J(P,Se_{endo}) = 507 Hz, ³J(P,P) = 4.7 Hz; lines for ²J(P,Se_{endo}) were hidden under the intensive central line, prohibiting calculation of the coupling constant). ⁷⁷Se NMR (CDCl₃): δ = 505.36 (dd, ¹J(P,Se_{endo}) = 498 Hz, ²J(P,Se_{endo}) = 23.9 Hz), 22.31 ppm (d, ¹J(P,Se_{exo}) = 826 Hz). High-resolution mass spectrometry (EIMS): 717.7444, calculated mass for C₂₄H₁₈O₂P₂Se₄: 717.7445. Elemental analysis calcd (%) for C₂₄H₁₈O₂P₂Se₄: C 40.1, H 2.5; found C 40.3, H 2.9.

5: 65% yield. M.p. 140–141°C. Selected IR (KBr): $\tilde{\nu}$ = 1586(w), 1504(w), 1434(m), 1219(m), 1199(m), 1099(m), 1071(m), 986(s), 829(s), 812(m), 745(m), 695(m), 535(s), 481 cm⁻¹ (m). ¹H NMR (CD₂Cl₂): δ = 8.97 (d, ³J(H,H) = 9.1 Hz, 2H, NapH), 8.24 (d, ³J(H,H) = 9.1 Hz, 2H, NapH), 8.13 (d, ³J(H,H) = 8.2 Hz, 2H, PhH), 7.90 (d, ³J(H,H) = 8.2 Hz, 4H, PhH), 7.59–7.28 (m, 8H, NapH + PhH), 7.10 ppm (d, ³J(H,H) = 9.1 Hz, 2H, NapH). ¹³C NMR (CD₂Cl₂): δ = 152.9, 133.4 (d, ¹J(P,C) = 33.2 Hz), 131.4, 130.8 (d, ¹J(P,C) = 13.5 Hz), 130.1, 129.6, 128.5, 128.2, 127.8, 127.4, 126.4, 125.6, 124.1 (d, ¹J(P,C) = 7.3 Hz), 118.9, 117.8 ppm. ³¹P NMR (CD₂Cl₂): δ = 65.79 ppm (s, ¹J(P,Se_{exo}) = 822 Hz, ¹J(P,Se_{endo}) = 502 Hz, ³J(P,P) = 4.7 Hz; lines for ²J(P,Se_{endo}) were hidden under the intensive central line, prohibiting calculation of the coupling constant). ⁷⁷Se NMR (CD₂Cl₂): δ = 498.94 (dd, ¹J(P,Se_{endo}) = 501 Hz, ²J(P,Se_{endo}) = 23 Hz), 37.56 ppm (d, ¹J(P,Se_{exo}) = 820 Hz). EI⁺ MS m/z : 816 [M]⁺. Elemental analysis calcd (%) for C₃₂H₂₂O₂P₂Se₄: C 47.1, H 2.7; found C 46.3, H 2.6.

X-ray crystal data for compounds **1–5** were collected at 93 K using a Rigaku MM007 high-brilliance RA generator/confocal optics and Mercury CCD system. Intensities were corrected for Lorentz polarization and for absorption. The structures were solved by direct methods. Hydrogen atoms bound to carbon were idealized. Structural refinements were obtained with full-matrix least-squares based on F^2 using the program SHELXTL.^[6] CCDC-663349 (**1**), 663350 (**2**), 663351 (**3**), 663352 (**4**), and 663353 (**5**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

Crystal data for **1**: C₁₄H₁₄O₂P₂Se₄, M_r = 592.03, triclinic, space group $P\bar{1}$, a = 11.154(3), b = 13.120(2), c = 13.245(3) Å, α = 105.945(12), β = 90.097(14), γ = 92.998(13)°, U = 1860.9(6) Å³, Z = 4, μ = 8.059 mm⁻¹, 12 374 reflections collected, 5465 observed independent reflections (R_{int} = 0.0355) gave R = 0.0692 for $I > 2\sigma(I)$ and $wR(F^2)$ = 0.1766.

Crystal data for **2**: C₁₅H₁₆O₂P₂Se₄, M_r = 606.06, triclinic, space group $P\bar{1}$, a = 8.9823, b = 9.5401, c = 11.8295 Å, α = 78.391(6), β = 88.090(7), γ = 78.328(6)°, U = 972.4(2) Å³, Z = 2, μ = 7.714 mm⁻¹, 6910 reflections collected, 3030 observed independent reflections (R_{int} = 0.0402) gave R = 0.0443 for $I > 2\sigma(I)$ and $wR(F^2)$ = 0.0989.

Crystal data for **3**: C₁₆H₁₈O₂P₂Se₄, M_r = 620.08, monoclinic, space group $P2_1/n$, a = 15.3206(17), b = 9.3686(9), c = 15.3675(18) Å, β = 109.91(2)°, U = 2074.8(4) Å³, Z = 4, μ = 7.240 mm⁻¹, 14 276 reflections collected, 3422 observed independent reflections (R_{int} = 0.0604) gave R = 0.0426 for $I > 2\sigma(I)$ and $wR(F^2)$ = 0.0779.

Crystal data for **4**: C₂₄H₁₈O₂P₂Se₄, M_r = 716.16, triclinic, space group $P\bar{1}$, a = 9.2156(12), b = 9.9004(12), c = 14.797(2) Å, α = 72.569(14), β = 80.164(19), γ = 72.384(17)°, U = 1222.9(3) Å³, Z = 2, μ = 6.151 mm⁻¹, 8627 reflections collected, 3762 observed independent reflections (R_{int} = 0.0322) gave R = 0.0433 for $I > 2\sigma(I)$ and $wR(F^2)$ = 0.0694.

Crystal data for **5**: C₃₃H₂₄Cl₂O₂P₂Se₄, M_r = 901.20, triclinic, space group $P\bar{1}$, a = 11.1080(7), b = 11.5793(10), c = 14.2126(10) Å, α = 87.875(8), β = 70.601(6), γ = 74.137(6)°, U = 1655.7(2) Å³, Z = 2, μ = 4.720 mm⁻¹, 10 839 reflections collected, 4543 observed independent reflections (R_{int} = 0.0322) gave R = 0.0756 for $I > 2\sigma(I)$ and $wR(F^2)$ = 0.1049.

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