From Phenylalkylcyanamides to Heterocyclic Selenazadiphospholaminediselenides and Carbamidoyl(phenyl)phosphinodiselenoic Acids

*Guoxiong Hua, Qingzhi Zhang, Yang Li, Alexandra M. Z. Slawin and J. Derek Woollins**

Case for Publication

This manuscript describes the facile synthesis of new P_2SeCN heterocycles

Furthermore the synthesis of unusual zwitterionic carbamidoyl(phenyl)phosphinodiselenoic acids is reported

All four new compounds have been fully characterised including X-ray structures.

We believe this work will be of interest to molecular synthetic chemists and the increasing group of scientists who are studying selenium chemistry as well as structural chemists

From Phenylalkylcyanamides to Heterocyclic Selenazadiphospholaminediselenides and Carbamidoyl(phenyl)phosphinodiselenoic Acids

*Guoxiong Hua, Qingzhi Zhang, Yang Li, Alexandra M. Z. Slawin and J. Derek Woollins**

School of Chemistry, University of St Andrews, Fife, KY16 9ST, UK

*Corresponding author. Tel: (+44)-1334-463384; email: jdw3@st-and.ac.uk

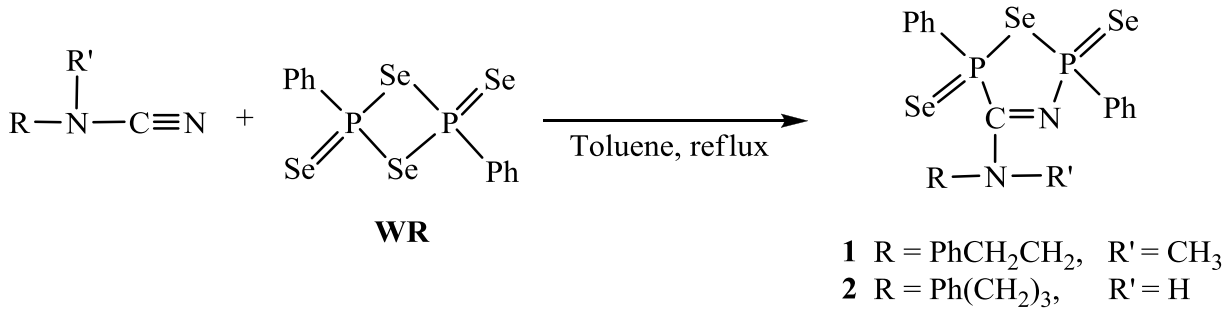
Reaction of 2,4-bis(phenyl)-1,3-diselenadiphosphetane-2,4-diselenide (Woollins' Reagent, WR) with phenylalkylcyanamides (RR'NC≡N, R = $PhCH_2CH_2$, R' = CH_3 and R = $PhCH_2CH_2CH_2$, R' = H) in refluxing toluene led to novel heterocyclic selenazadiphospholaminediselenides 1 and 2 (43% and 42% yields), the latter were hydrolyzed to unusual zwitterionic carbamidoyl(phenyl)phosphinodiselenoic acids 3 and 4 in excellent yields (96% and 98%).

Organoselenium compounds occupy a uniquely important role in synthetic chemistry due to their rich and versatile chemistry.[1] In particular, this class of compounds has long been of widespread interest by virtue of their ubiquitous biological activity.[2] The compounds derived from cyanides are known as tumor inhibitors[3] and are also very important intermediates or precursors in the synthesis of *N*-alkyl or *N*-aryl imides.[4] The conversion of the cyano group to selenocarbonyl, is a useful procedure for the synthesis of organoselenium compounds. In recent years, 2,4-bis(phenyl)-1,3-diselenadiphosphetane-2,4-diselenide $[PhP(Se)(\mu\text{-}Se)]_2$, (which has been known as Woollins' reagent, WR, a selenium counterpart of the well-known Lawesson's reagent $[p\text{-}MeOC_6H_4P(S)(\mu\text{-}S)]_2$) has received increasing attention due to its efficiency and broad utility in the preparation of P-Se heterocycles and the related organoselenium compounds.[5] For example, WR has been used to prepare a series of selenium-containing compounds, such as large P/Se molecular aggregates or metal complexes by nucleophilic ring-opening reactions with alkali-metal thiolates,[6] a wide range of selenoamides and selenoaldehydes by simple oxygen/selenium exchange reaction or reaction with ArCN followed by hydrolysis and a variety of P-Se heterocycles.[7,8] WR is also efficient coupling reagent for syntheses of symmetrical and unsymmetrical (*E*)-olefins from the corresponding ketones or aldehydes[9] and a promising deoxygenation reagent for the synthesis of phenylsulfides from the corresponding phenylsulfoxides.[10] Use of WR for the synthesis of 8-10 membered ring macrocyclic diselenides bearing P-Se-Se-P linkage has been reported recently.[11]

As a continuation of our interest in exploring the reactivity of WR towards different organic substrates, here we report the synthesis of heterocyclic selenazadiphospholaminediselenides

[$PhCH_2CH_2N(CH_3)C{=}N(PhP(Se)SeP(Se)Ph)$ (**1**) and $Ph\ CH_2CH_2CH_2N(H)C{=}N(PhP(Se)SeP(Se)Ph)$ (**2**)], and carbamidoyl(phenyl)phosphinodiselenoic acids [$PhCH_2CH_2N(CH_3)C(NH_2)P(Se)(Se)Ph$ **(3)** and $PhCH_2CH_2CH_2N(H)C(NH_2)P(Se)(Se)Ph$ (**4**)] and their X-ray crystal structures.

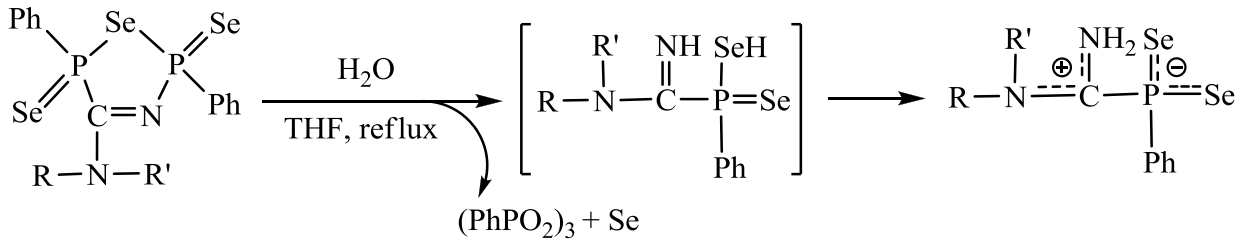
Phenylalkylcyanamides were synthesised with a modified method by reaction of cyanogen bromide with crystalline primary or secondary amine in dry methanol in the presence of excess of anhydrous CH_3COONa.[12] Compounds **1** and **2** were prepared by cleavage of the four-membered P_2Se_2 ring WR with RR'NC=N (43% and 42% yields, respectively, Scheme 1). Both compounds, which are stable in air for several months, are soluble in common non-polar organic solvents and were crystallised from dichloromethane\hexane to give transparent yellowish cubic crystals. The identifying ^{31}P NMR characteristics of **1** and **2** are two sets of doublets (δ = 76.65 and 75.08 ppm, $^2J_{(P,P)}$ = 11.7 Hz for **1**; δ = 76.36 and 74.91 ppm $^2J_{(P,P)}$ = 14.1 Hz for **2)**, accompanied by two sets of satellites for the endocyclic and exocyclic selenium atoms ($^1J_{(P,Seendo)}$ and $^1J_{(P,Seexo)}$: 455/457 and 793/798 Hz for **1**; 477/479 and 789/825 Hz for **2**). The ^{77}Se NMR spectra, consist of doublet of doublets (δ = 502.01 ppm, $^1J_{(P,Seendo)}$ = 455/457 Hz for **1**; δ = 414.70 ppm, $^1J_{(P,Seendo)}$ = 477/479 Hz for **2**), two doublets (δ = 13.38 and -79.52 ppm, $^1J_{(P,Seexo)}$ = 827 and 792 Hz for **1**; δ = 10.90 and -125.77 ppm, $^1J_{(P,Seexo)}$ = 825 and 790 Hz for **2)**. Detailed NMR spectroscopic analysis and iterative simulation reveal the coupling constant between phosphorus atoms and exocyclic selenium atoms ($^3J_{(P,Seexo)}$: *ca*. 9.5 Hz) in **1** and **2**. The chemical shifts and coupling constants are comparable to the related compounds in the literatures.[13]



Scheme 1

Hydrolysis of compounds **1** and **2** (Scheme 2) was carried out in refluxing tetrahydrofuran with water to give the unusual zwitterionic carbamidoyl(phenyl)phosphinodiselenoic acids **3** and **4** in high yields (96% and 98%, respectively) as green solids which were subsequently recrystallised from dichloromethane\hexane before further analyses. **3** and **4**, which are soluble in dichloromethane, tetrahydrofuran and chloroform, are stable at room temperature in air for months without any observed decomposition. **4** is only formed in *E* configuration, whilst **3** was formed as a mixture of *E/Z* isomers in the ratio of 7 : 3. The ^{31}P NMR spectra of **3** and **4** display sharp singlets at 27.35 and 24.90 ppm for **3** and 29.94 ppm for **4**, and each signal is flanked by a single pair of selenium satellites with a ^{31}P-^{77}Se coupling constants of 700 Hz for **3** and 703 Hz for **4**,

indicating a single P-Se bond order of approximately 1.5. However, the values are slightly bigger than that in phosphonodiselenoate salts (*ca*. 657 - 680 Hz),[14] indicating the presence of the zwitterionic structures in compounds **3** and **4**. The ^{77}Se NMR spectra show doublets at 31.59 and 29.92 ppm for **3** and -95.18 ppm for **4** with matching coupling constants. Compared to compound **3**, the ^{77}Se signal in **4** appears sharply downfield at -95.18 ppm with the similar coupling constant, in accord with the presence of hydrogen bonding in **4** which cannot occur in **3** due to the substitution of H in the nitrogen cation by CH_3. The broad ^{1}H NMR spectrum for NH in **4** further supports the occurrence of H bonding (*See notes and references section*). This is perhaps related to the presence of N-H ··· Se=P hydrogen bonding interactions in the solid state, as noted in the crystal structure of **3** (*See below*).



3 R = $PhCH_2CH_2$, R' = CH_3, *E*/*Z* = 70% : 30%
4 R = $Ph(CH_2)_3$, R' = H, *E*/*Z* = 100% : 0%

Scheme 2

X-ray crystallography (Figures 1 and 2) reveals the frameworks in **1** and **2** contain five-membered P_2SeCN rings with P(Se)-Se-P(Se) linkages and exocyclic P=Se groups orientated *trans* to one another. The bond lengths and angles are normal and comparable with the related structures.[7h,8,11, 13e,15] The geometry around P(1) [Se(1)-P(1)-Se(2): 118.17(8) and 118.40(6)˚ for **1** and **2**, respectively] and P(3) [Se(2)-P(3)-Se(3): 110.35(8) and 114.38(6)˚ for **1** and **2**, respectively] is distorted tetrahedral due to the steric hindrance of phenyl groups. The transannular P ··· P bond distances are 3.17(3) and 3.23(2) Å for **1** and **2**, being marginally longer than those observed in the four-membered P_2Se_2 ring system (3.1 Å Å) and considerably shorter than those in six-membered P_2Se_4 ring system (4.3 Å).[16]

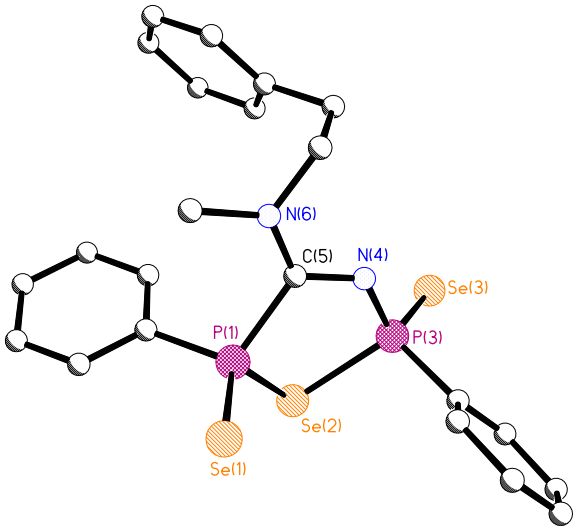
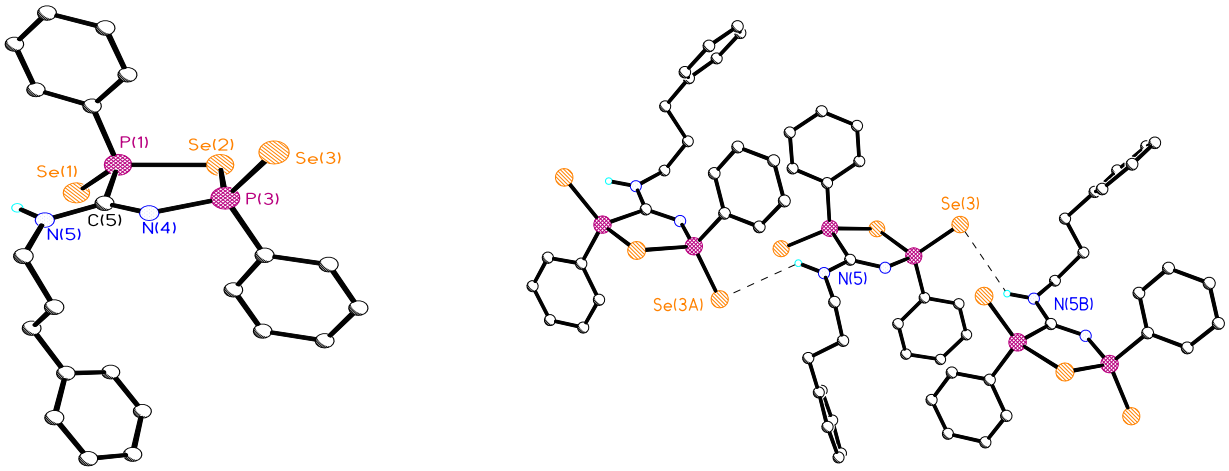


Fig. 1 X-ray crystal structure of **1** (C-H bonds omitted for clarity). Selected bond lengths (Å) and angles (˚) (esds in parentheses): Se(1)-P(1) 2.0768(18), Se(2)-P(1) 2.2267(19), Se(2)-P(3) 2.2637(18), Se(3)-P(3) 2.075(2), P(3)-N(4) 1.626(5), P(1)-C(5) 1.884(6), N(4)-C(5) 1.298(8), N(6)-C(5) 1.320(8), P(1)-Se(2)-P(3) 89.93(7), N(4)-P(3)-Se(3) 116.1(2), N(4)-P(3)-Se(2) 103.0(2), Se(3)-P(3)-Se(2) 110.35(8), C(5)-P(1)-Se(1) 111.16(18), C(5)-P(1)-Se(2) 97.6(2), Se(1)-P(1)-Se(2) 118.17(8), C(5)-N(4)-P(3) 125.1(4).

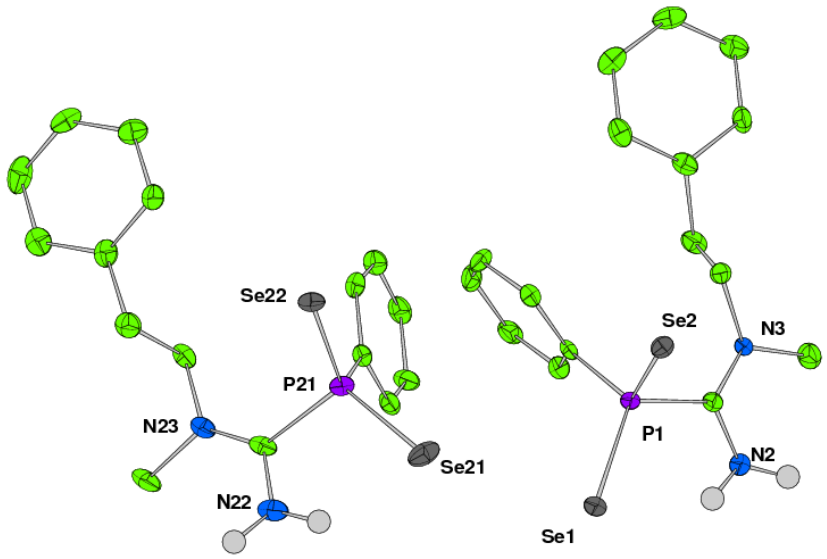


(a) (b)

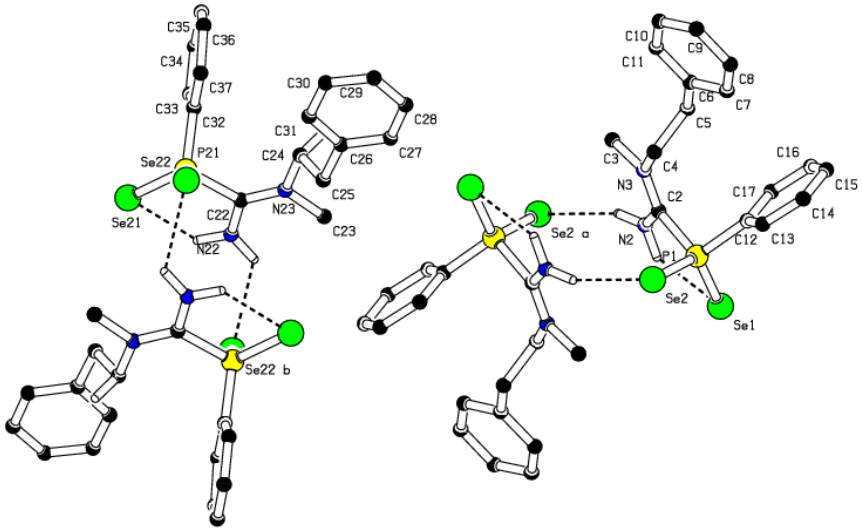
Fig. 2 (a) X-ray crystal structure of **2** (C-H bonds omitted for clarity). Selected bond lengths (Å) and angles (˚) (esds in parentheses): Se(1)-P(1) 2.0833(13), Se(2)-P(1) 2.2334(13), Se(2)-P(3) 2.2976(12), Se(3)-P(3) 2.0943(14), P(3)-N(4) 1.647(3), P(1)-C(5) 1.901(4), N(5)-C(5) 1.331(5), N(4)-C(5) 1.283(5), P(1)-Se(2)-P(3) 90.99(4), N(4)-P(3)-Se(3) 116.10(16), N(4)-P(3)-Se(2) 103.59(13), Se(3)-P(3)-Se(2) 114.38(6), C(5)-P(1)-Se(1) 111.02(16), C(5)-P(1)-Se(2) 97.41(14), Se(1)-P(1)-Se(2) 118.40(6), C(5)-N(4)-P(3) 123.2(3). (b) Hydrogen bonding interaction between exocyclic selenium atom and H atom of the secondary amine nitrogen.

The structure of **3** crystallises in the monoclinic space group *P2(1)/n* with two crystallographically independent molecules in the asymmetric unit. Meanwhile, the structure of **4** crystallises in the orthorhombic space group *Pca2(1)/n* with two crystallographically independent molecules in the asymmetric unit. Both

structures adopt a skewed 'U' shape conformation and reveal that two molecules are in unusually zwitterionic structures. The two P-Se bonds are statistically invariant: P(1)-Se(1) and P(1)-Se(2): 2.1302(12) [2.1313(14)] and 2.1319(13) [2.1343(13)] Å for **3**, and 2.0142(2) [2.1492(19)] and 2.147(2) [2.138(2)] Å for **4**. These values are slightly longer than those in other double bond P=Se systems (2.08 – 2.12 Å) but still considerably shorter than those in single bonded P-Se systems (2.2 – 2.3 Å).[16,17] The two C-N bonds are also essentially equal (C(2)-N(2) and C(2)-N(3): 1.314(6) [1.316(7)] and 1.317(6) [1.309(7)] Å for **3**, 1.339(9) [1.316(9)] and 1.307(9) [1.321(9)] Å for **4**. As was the case for two P-Se bonds, the distances are longer than the C=N bond distances (C(5)-N(4): 1.298(8) and 1.283(5) Å for **1** and **2**, respectively but considerably shorter than those of single C-N bond (1.320(8) and 1.331(5) Å for **1** and **2**, respectively). The Se-P-Se angles are considerably enlarged compared to idealized tetrahedral (Se(1)-P(1)-Se(2): 119.30(6) [118.55(6)] Å for **3** and 120.66(9) [121.44(9)] Å for **4**).



(a)



(b)

Fig. 3 (a) X-ray crystal structure of **3** (*Z*) (some C-H bonds omitted for clarity). Selected bond lengths (Å) and angles (˚) (esds in parentheses): Se(2)-P(1) 2.1319(13) [2.1343(13)], Se(1)-P(1) 2.1302(12) [2.1313(14)], P(1)-C(2) 1.902(5) [1.913(5)], C(2)-N(2) 1.314(6) [1.316(7)], C(2)-N(3) 1.317(6) [1.309(7)], C(2)-P(1)-Se(1) 106.70(15) [104.68(17)], C(2)-P(1)-Se(2) 103.48(15) [108.49(15)], Se(1)-P(1)-Se(2) 119.30(6) [118.55(6)], N(2)-C(2)-N(3), 120.5(4) [120.6(5)], N(2)-C(2)-P(1) 113.8(4) [113.7(4)], N(3)-C(2)-P(1) 125.6(4) [125.8(4)]. (b) Hydrogen bonding interactions leading to chains of dimers.

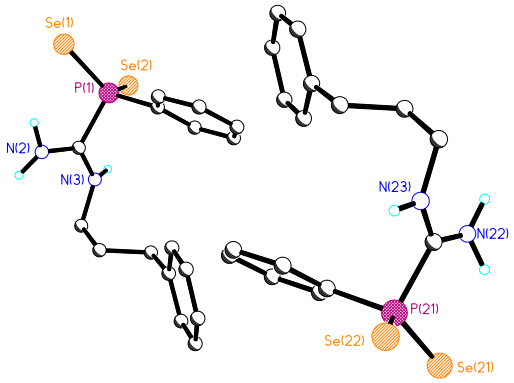


Fig. 4 X-ray crystal structure of **4** (*E*) (C-H bonds omitted for clarity). Selected bond lengths (Å) and angles (˚) (esds in parentheses): Se(2)-P(1) 2.147(2) [2.138(2)], Se(1)-P(1) 2.142(2) [2.1492(19)], P(1)-C(2) 1.884(7) [1.886(7)], C(2)-N(2) 1.339(9) [1.316(9)], C(2)-N(3) 1.307(9) [1.321(9)], C(2)-P(1)-Se(1) 105.9(2) [104.5(2)], C(2)-P(1)-Se(2) 104.7(2) [106.3(2)], Se(1)-P(1)-Se(2) 120.66(9) [121.44(9)], N(2)-C(2)-N(3), 123.8(6) [123.6(7)], N(2)-C(2)-P(1) 117.4(5) [119.1(5)], N(3)-C(2)-P(1) 118.7(5) [117.1(5)].

In summary, the results reported here provide a new approach to five-membered P_2SeCN rings, and novel carbamidoyl(phenyl)phosphinodiselenoic acids with unusually zwitterionic structures. Studies to explore the carbamidoyl(phenyl)phosphinodiselenoic acids as synthetic precursors for efficient stereoselective transformations in organic chemistry are now underway.

Acknowledgement

The authors are thankful to the Engineering and Physical Science Research Council (EPSRC, U.K.) for financial support.

Notes and references

Unless otherwise stated, all reactions were carried out under on oxygen free nitrogen atmosphere using pre-dried solvents and standard Schlenk techniques, subsequent chromatographic and work up procedures were performed in air. Solvents were dried, purified, and stored according to common procedures. ^{1}H (270 Hz), ^{13}C (67.9 Hz), ^{31}P-{^{1}H} (109 Hz) and ^{77}Se-{^{1}H} (51.4Hz referenced to external Me_2Se) NMR spectra were

recorded at 25 °C (unless stated otherwise) on a JEOL GSX 270. IR spectra were recorded as KBr pellets in the range of 4000 - 250 cm^{-1} on a Perkin-Elmer 2000 FTIR/Raman spectrometer. Microanalysis was performed by the University of St-Andrews microanalysis service. Mass spectrometry was performed by the EPSRC National Mass Spectrometry Service Centre, Swansea (U.K.) and the University of St Andrews Mass Spectrometry Service. X-ray crystal data for compounds **1** - **4** were collected at 93 K by using a Rigaku MM007 High brilliance RA generator/confocal optics and Mercury CCD system. Intensities were corrected for Lorentz-polarisation and for absorption. The structure was solved by direct methods. Hydrogen atoms bound to carbon were idealised. Structural refinement was obtained with full-matrix least-squares based on F^2 by using the program SHELXTL.[18] CCDC contain the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/conts/retrieving.html or from the Cambridge Crystallographic Data centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax (+44) 1223-336-033; e-mail: deposit@ccdc.cam.ac.uk.

***N*-phenethyl-*N*-methyl-2,5-diphenyl-2,5-dihydro-1,2,3,5,-selenazadiphosphol-4-amine-2,5-diselenide (1)**. A mixture of *N*-methyl-*N*-phenethylcyanamide (0.64 g, 4.0 mmol) and WR (2.14 g, 4.0 mmol) in 50 ml of dry toluene was heated at 130 °C for 7 h. The red suspension disappeared and a red solution was formed along with a small amount of grey selenium after cooling to room temperature. The resulting mixture was concentrated to *ca.* 10 ml and purified by silica gel (1 : 9 = ethyl acetate / toluene as eluent) to give **1** as pale green solid (1.68 g, 42%). Elemental analysis: Found C, 43.67, H, 3.45, N, 4.50; $C_{22}H_{22}N_2P_2Se_3$ requires C, 43.09, H, 3.62, N, 4.57. IR: (KBr, ν_{max}/cm^{-1}): 3425(w), 2921(w), 1561(vs, C=N), 1434(s), 1355(m), 1094(s), 869(m), 746(m), 687(m), 554(m, P=Se), 539(m, P=Se). ^{1}H NMR (CD_2Cl_2, δ): 8.16-8.08 (m, 4H, ArH), 7.72-7.53 (m, 6H, ArH), 7.22-7.19 (m, 7H, ArH) ppm. ^{13}C NMR (CD_2Cl_2, δ): 137.8, 137.0, 133.4, 133.1, 132.4, 132.2, 132.0, 131.9, 131.3, 131.1, 129.6, 129.4, 129.2, 129.0, 128.7, 128.6, 128.5, 128.3, 126.7, 57.9, 38.8, 33.6 ppm. ^{31}P NMR (CD_2Cl_2, δ): 76.65 (d, $^2J_{(P,P)}$ = 11.7 Hz, $J_{(P,Seendo)}$ = 455 Hz, $J_{(P,Seexo)}$ = 793 Hz), 75.08 (d, $^2J_{(P,P)}$ = 11.7 Hz, $J_{(P,Seendo)}$ = 457 Hz, $J_{(P,Seexo)}$ = 798 Hz) ppm. ^{77}Se NMR (CD_2Cl_2, δ): 502.01 (dd, $J_{(P,Seendo)}$ = 455 Hz, $J_{(P,Seendo)}$ = 457 Hz), 13.38 (d, $J_{(P,Seexo)}$ = 827 Hz), -79.52 (d, $J_{(P,Seexo)}$ = 792 Hz) ppm. MS (EI^+, m/z), 616 $[M]^+$, 536 $[M\text{-}Se]^+$. Accurate mass measurement (EI, m/z): 615.8745, calculated mass for $C_{22}H_{22}N_2P_2Se_3$: 615.8748.

***N*-(3-phenylpropyl)-2,5-diphenyl-2,5-dihydro-1,2,3,5,-selenazadiphosphol-4-amine -2,5-diselenide (2)**. In an analogous fashion to **1**, a mixture of *N*-(3-phenylpropyl)cyanamide (0.64 g, 4.0 mmol) and WR (2.14 g, 4.0 mmol) in 50 ml of dry toluene was refluxed for 4 h. Work-up led to **2** as pale green solid (1.05 g, 43%). Elemental analysis: Found C, 43.01, H, 3.45, N, 4.51; $C_{22}H_{22}N_2P_2Se_3$ requires C, 43.09, H, 3.62, N, 4.57. IR: (KBr, ν_{max}/cm^{-1}): 3225(dw), 2924(w), 1586(vs, C=N), 1508(m), 1434(m), 1354(m), 1252(m), 1181(m),

1093(m), 935(m), 910(m), 748(m), 678(m), 549(m, P=Se). ^{1}H NMR ($CDCl_3$, δ): 8.28 (dd, $J_{(H,H)}$ = 6.2 Hz, $^{3}J_{(P,H)}$ = 9.9 Hz, 2H, ArH), 8.05 (dd, $J_{(H,H)}$ = 6.8 Hz, $^{3}J_{(P,H)}$ = 15.1 Hz, 2H, ArH), 7.57 (m, 3H, ArH), 7.51 (m, 3H, ArH), 7.22 (d, $J_{(H,H)}$ = 7.7 Hz, 2H, ArH), 7.04 (d, $J_{(H,H)}$ = 7.7 Hz, 2H, ArH), 6.55 (s, 1H, NH), 3.52 (m, 2H, NCH_2), 2.54 (m, 2H, CH_2), 1.88 (m, 2H, CH_2) ppm. ^{13}C NMR ($CDCl_3$, δ): 166.8 (d, $^{1}J_{(P,C)}$ = 33.2 Hz), 140.5, 137.0 (d, $^{1}J_{(P,C)}$ = 91.4 Hz), 133.2 (d, $^{4}J_{(P,C)}$ = 3.1 Hz), 132.6, 132.4, 131.6 (d, $^{3}J_{(P,C)}$ = 13.5 Hz), 129.2 (d, $^{3}J_{(P,C)}$ = 13.5 Hz), 128.7, 128.4 (d, $^{4}J_{(P,C)}$ = 2.1 Hz), 126.4, 45.4, 32.7, 30.1 ppm. ^{31}P NMR ($CDCl_3$, δ): 76.36 (d, $^{2}J_{(P,P)}$ = 14.1 Hz, $J_{(P,Seendo)}$ = 477 Hz, $J_{(P,Seexo)}$ = 789 Hz), 74.91 (d, $^{2}J_{(P,P)}$ = 14.1 Hz, $J_{(P,Seendo)}$ = 479 Hz, $J_{(P,Seexo)}$ = 825 Hz) ppm. ^{77}Se NMR ($CDCl_3$, δ): 414.70 (dd, $J_{(P,Seendo)}$ = 477 Hz, $J_{(P,Seendo)}$ = 479 Hz), 10.90 (d, $J_{(P,Seexo)}$ = 825 Hz), -125.77 (d, $J_{(P,Seexo)}$ = 790 Hz) ppm. MS (CI, m/z), 617 $[M+H]^{+}$.

***N*'-phenethyl-*N'*-(methyl)carbamidoyl(phenyl)phosphinodiselenoic acid** (**3**). A mixture of **1** (0.62 g, 1.0 mmol) and 1 ml of water in 20 ml of tetrahydrofuran was refluxed for 3 hs. Upon cooling to room temperature the mixture was extracted by dichloromethane. The organic layers were dried over $MgSO_4$ overnight. After concentrated to 5 ml the organic layers were purified by silica gel (1 : 9 = ethyl acetate / dichoromethane as eluent) to afford **3** as greenish white solid (0.52 g, 98%). Elemental analysis: Found C, 44.55, H, 4.59, N, 6.45; $C_{16}H_{19}N_2PSe_2$ requires C, 44.88, H, 4.47, N, 6.54. IR: (KBr, ν_{max}/cm^{-1}): 3202(w), 3091(w), 1613(vs, C=N), 1562(m), 1453(w), 1435(m), 1088(m), 748(m), 702(m), 552(s, P=Se). One pair of *E/Z* configurations: ^{1}H NMR (CD_3CN, ppm): 9.22 (s, 2H, NH_2), 7.96 (m, 2H, ArH), 7.46 (m, 3H, ArH), 7.20 (m, 3H, ArH), 6.94 (m, 2H, ArH), 3.77 (t, *J* = 8.4 Hz, 2H, $PhCH_2$), 3.15 (s, 3H, CH_3), 2.47 (t, *J* = 8.4 Hz, 2H, NCH_2) ppm. ^{13}C NMR ($CDCl_3$, δ): 137.4, 131.2, 130.4, 130.2, 129.1, 128.8, 128.5, 126.7, 117.4, 54.8, 39.4, 32.2 ppm. ^{31}P NMR (CD_3CN, δ): 27.35 (*Z* configuration, 30%) (s, $J_{(P,Seexo)}$ = 700 Hz), δ = 24.90 (*E* configuration, 70%) (s, $J_{(P,Seexo)}$ = 700 Hz) ppm. ^{77}Se NMR (DMF-d_7, δ): 31.59 (*E* configuration, 70%) and 29.92 (*Z* configuration, 30%) (d, $J_{(P,Seexo)}$ = 700 Hz) ppm. MS (ES^{+}, m/z), 453 $[M+Na]^{+}$. MS (ES^{-}, m/z), 429$[M-H]^{+}$.

***N*'-(3-phenylpropyl)carbamidoyl(phenyl)phosphinodiselenoic acid (4)**. In an analogous fashion to **3**, a mixture of **2** (0.62 g, 1.0 mmol) and 1 ml of water in 20 ml of tetrahydrofuran was refluxed for 3 h. Work-up led to **4** as green solidd (0.51 g, 96%). Elemental analysis: Found C, 44.67, H, 4.50, N, 6.19; $C_{16}H_{19}N_2PSe_2$ requires C, 44.88, H, 4.47, N, 6.54. IR: (KBr, ν_{max}/cm^{-1}): 3243(s), 3150(s), 3117(s), 1642(vs, C=N), 1577(s), 1490(m), 1454(m), 1434(m), 1346(m), 1303(m), 1233(m), 1083(m), 1010(m), 743(s), 697(s), 557(s, P=Se). ^{1}H NMR (CD_2Cl_2, δ): 8.75 (brs, 2H, NH_2), 8.20 (m, 2H, ArH), 7.45 (m, 3H, ArH), 7.23 (d, $J_{(H,H)}$ = 7.2 Hz, 2H, ArH), 7.05 (d, $J_{(H,H)}$ = 7.2 Hz, 2H, ArH), 6.89 (brs, H, NH), 3.27 (t, $J_{(H,H)}$ = 6.4 Hz, 2H, NCH_2), 2.60 (t, $J_{(H,H)}$ = 6.4 Hz, 2H, $ArCH_2$), 1.97 (m, 2H, CH_2) ppm. ^{13}C NMR (CD_2Cl_2, δ): 167.3 (d, $^{1}J_{(P,C)}$ = 29.1 Hz), 139.7, 131.8, 131.6, 131.5, 128.7, 128.4, 128.2, 126.6, 43.7, 32.2, 29.0 ppm. ^{31}P NMR (CD_2Cl_2, δ): 29.94 (s, $J_{(P,Seexo)}$

= 703 Hz) ppm. ^{77}Se NMR (CD_2Cl_2, δ): -95.18 (d, $J_{(P,Seexo)}$ = 703 Hz) ppm. MS (ES^+, m/z), 453 $[M+Na]^+$. MS (ES^-, m/z), 429 $[M-H]^+$.

Crystal data for **1**: $C_{22}H_{22}N_2P_2Se_3$, M = 613.24, orthorhombic, space group Pbca, a = 18.865(7) Å, b = 10.616(3) Å, c = 23.670(8) Å, α = 90, β = 90, λ = 90, U = 4741(3) Å^3, Z = 8, μ = 4.802 mm^{-1}, 44226 reflections collected, 4367 independent reflections (R_{int}) = 0.0869, final R indices [I › 2σ(I)] R1 = 0.0713, wR2 = 0.1792.

Crystal data for **2**: $C_{22}H_{22}N_2P_2Se_3$, M = 613.25, orthorhombic, space group P2(1)2(1)2, a = 14.813(3) Å, b = 16.104(2) Å, c = 9.7349(16) Å, α = 90, β = 90, λ = 90, U = 2322.3(7) Å^3, Z = 4, μ = 4.901 mm^{-1}, 15131 reflections collected, 4249 independent reflections (R_{int}) = 0.0408, final R indices [I › 2σ(I)] R1 = 0.0382, wR2 = 0.0638.

Crystal data for **3**: $C_{16}H_{19}N_2PSe_2$, M = 428.22, monoclinic, space group P2(1)/n, a = 21.784(3) Å, b = 6.8434(7) Å, c = 23.320(4) Å, α = 90, β = 98.307(4), λ = 90, U = 3440.1(8) Å^3, Z = 8, μ = 4.390 mm^{-1}, 22373 reflections collected, 6871 independent reflections (R_{int}) = 0.108, final R indices [I › 2σ(I)] R1 = 0.0575, wR2 = 0.1680.

Crystal data for **4**: $C_{16}H_{19}N_2PSe_2$, M = 428.22, orthorhombic, space group Pca2(1), a = 13.1547(7) Å, b = 7.4543(4) Å, c = 35.8185(19) Å, α = 90, β = 90, λ = 90, U = 3440.1(8) Å^3, Z = 8, μ = 4.297 mm^{-1}, 30063 reflections collected, 3220 independent reflections (R_{int}) = 0.0740, final R indices [I › 2σ(I)] R1 = 0.0322, wR2 = 0.0741.

1 a) T. Wirth, *Tetrahedron* 1999, **55**, 1; b) Y. Xu, E. T. Kool, *J. Am. Chem. Soc.* 2000, **122**, 9040; c) G. L. Sommen A. Linden, H. Heimgartner, *Helv. Chim. Acta* 2005, **88**, 766.

2 a) Y. Ogasawara, G. Lacourciere, T. C. Stadtman, *Proc. Natl. Acad., Sci.* USA 98, 2001, 9494; b) H. E. Ganther, *Bioorg. Med. Chem.* 2001, **9**, 1459; c) G. Mugesh, W. W. Du Mont, H. Sies, *Chem. Rev*. 2001, **101**, 2125; d) P. Ximenez-Embun, I. Alonso, Y. Madrid-Albarran, C. Camara, *J. Agric. Food Chem*. 2004, **52**, 832; e) D. B. Vickerman, J. T. Trumble, G. N. Grorge, I. J. Pickering, H. Nichol, *Environ. Sci. Technol*. 2004, **38**, 3581.

3 a) W. T. Bradner, D. A. Clarke, *Cancer Res.* 1958, **18**, 299; b) M. Saneyoshi, R. Tokuzen, M. Maeda, F. Fukuoka, *Chem. Pham. Bull.* 1968, **16**, 505.

4 a) J. R. Robinson, H. Brown, *Can. J. Chem*. 1951, **29**, 1069; b) R. W. Stephens, L. A. Domeier, M. G. Todd, V. A. Nelson, *Tetrahedron Lett.* 1992, **33**, 733.

5 G. Hua, J. D. Woollins, *Angew. Chem., Int. Ed. (In press).*

6 (a) W. Shi, M. S. Fallah, C. E. Anson and A. Rothenberger, *Dalton Trans*. 2006, 2979. (b) W. Shi, M. S. Fallah, L. Zhang, C. E. Anson, E. Matern and A. Rothenberger, *Chem. Eur. J.* 2007, **13**, 598.

7 a) I. Baxter, A. F. Hill, J. M. Malget, A. J. P. White, D. J. Williams, *J. Chem. Soc., Chem. Commun.* 1997, 2049; b) A. F. Hill, J. M. Malget, *J. Chem. Soc., Chem. Commun.* 1996, 1177; c) P. Bhattacharyya, J. D. Woollins, *Tetrahedron Lett.* 2001, **42**, 5949; d) P. Bhattacharyya, A. M. Z. Slawin, J. D. Woollins, *Inorg. Chem. Commun*. 2004, **7**, 1171; e) J. Bethke, K. Karaghiosoff, L. A. Wessjohann, *Tetrahedron Lett.* 2003, **44**, 6911; f) G. Hua, Y. Li, A. M. Z. Slawin, J. D. Woollins, *Org. Lett*. 2006, **8**, 5251; g) K. E. Darout, *Org. Lett*. 2005, **7**, 203; h) P. Bhattacharyya, A. M. Z. Slawin, J. D. Woollins, *Chem. Eur. J*. 2002, **8**, 2705; i) P. Bhattacharyya, A. M. Z. Slawin, J. D. Woollins, *Angew. Chem., Int. Ed*. 2000, **39**, 1973.

8 a) G. Hua, Y. Li, A. M. Z. Slawin, J. D. Woollins, *Eur. J. Inorg. Chem*. 2007, 891; b) G. Hua, Y. Li, A. M. Z. Slawin, J. D. Woollins, *Chem. Commun*. 2007, 1465.

9 G. Hua, Y. Li, A. M. Z. Slawin, J. D. Woollins, *Dalton Trans*. 2007, 1477.

10 G. Hua, J. D. Woollins, *Tetrahedron Lett*. 2007, **48**, 3677.

11 G. Hua, Yang Li, Alexandra M. Z. Slawin, J. D. Woollins. *Angew. Chem., Int. Ed*. 2008, **47**, 2857.

12 a) R. C. Axelle, D. Sylvie, P. Celine, L. G. David, B. Jean-Luc, A. Roger, S. Marie-Agnes, S. Dennis, M. Daniel, *J. Med. Chem*. 2002, **45**, 944 ; b) K. Hiroyo, I. Masako, S. Masahiro, H. Keiro, Y. Keiko, S. Hiroko, T. Tatsuhiro, I. Tsutomu, *Helv. Chim. Acta* 2002, **85**, 2636.

13 a) K. Karaghiosoff, K. Eckstein, *Phosphorus, Sulfur Silicon Relat. Elem*. 1993, **75**, 257; b) K. Karaghiosoff, K. Eckstein, R. Motzer, *Phosphorus, Sulfur Silicon Relat. Elem*. 1994, **93/94**, 185; c) M. J. Pilkington, A. M. Z. Slawin, D. J. William, J. D. Woollins, *Heteroat. Chem*. 1990, **1**, 351; d) P. Kilian, P. Bhattacharyya, A. M. Z. Slawin, J. D. Woollins, *Eur. J. Inorg. Chem*. 2003, 1461.

14 a) I. P. Gray, A. M. Z. Slawin, J. D. Woollins, *Dalton Trans*. 2005, 2188; b) G. Hua, Y. Li, A. M. Z. Slawin, J. D. Woollins, *Tetrahedron*. 2008, **64**, 5442.

15 a) P. Jutzi, N. Brusdielins, H. G. Stammler, B. Neumann, *Chem. Ber*. 1994, **127**, 997; b) M. Yoshifuji, N. Higeta, D. L. An, K. Toyota, *Chem. Lett*. 1998, 17; c) S. M. F. Asmus, U. Bergstraber, M. Regitz, *Synthesis* 1999, 1642; d) P. B. Hitchcock, J. F. Nixton, N. Sakaray, *Chem. Commun*. 2000, 1642.

16 S. Parveen, P. Kilian, A. M. Z. Slawin, J. D. Woollins, *Dalton Trans*. 2006, 2586.

17 P. Kilian, A. M. Z. Slawin, J. D. Woollins, *Chem. Commun*. 2001, 2288.

18 SHELXTL 6.11 Bruker AXS Madison 2004.