Tetrahedron 65 (2009) 6074–6082

Contents lists available at ScienceDirect

Tetrahedron

journal homepage: www.elsevier.com/locate/tet

Novel heterocyclic selenazadiphospholaminediselenides, zwitterionic carbamidoyl(phenyl)-phosphinodiselenoic acids and selenoureas derived from cyanamides

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

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

ARTICLE INFO

Article history:
Received 12 February 2009
Received in revised form 5 May 2009
Accepted 21 May 2009
Available online 27 May 2009

Keywords:
Woollins' reagent
Cyanamides
Carbamidoyl(phenyl)phosphinodiselenoic acids
Selenazadiphospholaminediselenides
Selenoureas

ABSTRACT

2,4-Bis(phenyl)-1,3-diselenadiphosphetane-2,4-diselenide (Woollins' reagent, **WR**) reacts with cyanamides (**1a**–**h**) in refluxing toluene to afford a series of novel selenazadiphospholaminediselenides (RR′NC=N(PhP(Se)SeP(Se)Ph, R=$C_6H_5(CH_2)_{1-3}$, 4-*n*-$C_{10}H_{21}C_6H_4$ and 4-$BrC_6H_4CH_2$; R′=H, CH_3, C_2H_5 and $C(O)OC_2H_5$ **2a**–**g**). Post-treatment of the reaction mixture with water led to the formation of carbamidoyl(phenyl)phosphinodiselenoic acids (RR′NC(NH_2)P(SeH)$_2$Ph, R=$C_6H_5(CH_2)_{2-3}$, 4-*n*-$C_{10}H_{21}C_6H_4$ and 4-$BrC_6H_4CH_2$; R′=H and CH_3, **3b**, **3c**, **3e** and **3f**) and selenoureas (RR′NC(Se)NH_2, R=$C_6H_5(CH)_{1-2}$; R′=CH_3 and $OC(O)C_2H_5$, **4f** and **4h**) in moderate to excellent yields. All new compounds are characterised spectroscopically and five X-ray crystal structures are reported.

1. Introduction

Cyanamides, cyanates, thiocyanates and their derivatives are known as tumour inhibitors[1] and important intermediates for herbicides[2] as well as *N*-alkyl or *N*-aryl imides.[3] Conversion of the cyano group to selenocarbonyl by selenation is a useful approach to organoselenium derivatives. Typical selenium reagents include SeO_2, $PhSeO_2H$, PhSeCl, $PhSe^-$,[4–6] selenoethers and phosphine selenides.[7] 2,4-Bis(phenyl)-1,3-diselenadiphosphetane-2,4-diselenide [PhP(Se)(μ-Se)]$_2$, the selenium counterpart of the well-known Lawesson's reagent [*p*-$MeOC_6H_4$P(S)(μ-S)]$_2$, known as Woollins' reagent (**WR**), has become of increasing interest in selenium chemistry due to its high efficiency and broad utility.[8] Compared with other selenium reagents, **WR** has less unpleasant properties and can be prepared readily and handled safely in air.[9] Selenoamides and selenoaldehydes have been obtained by simple oxygen/selenium exchange using **WR** and corresponding carbonyl compounds or ArCN followed by hydrolysis.[10–13] **WR** has been used as an efficient coupling reagent for syntheses of symmetrical and unsymmetrical (*E*)-olefins from the corresponding ketones or aldehydes.[14] As a deoxygenating agent, **WR** has converted phenylsulfoxides into phenylsulfides.[15] **WR** was also found application in the synthesis of 8-, 9- and 10-membered diselenides bearing P–Se–Se–P linkage.[16]

As part of our broader study into the reactivity of **WR** here we report the preparation of a series of novel selenazadiphospholaminediselenides, carbamidoyl(phenyl)phosphinodiselenoic acids and selenoureas from the selenation of cyanamides (RR′NC≡N, R=$C_6H_5(CH_2)_{1-3}$, 4-$BrC_6H_4CH_2$ and 4-*n*-$C_{10}H_{21}C_6H_4$; R′=H, CH_3, CH_2CH_3 and $C(O)OC_2H_5$) with **WR**.

2. Results and discussion

Cyanamides **1a**–**h** were prepared from cyanogen bromide with primary or secondary amines in dry methanol in the presence of excess of anhydrous CH_3COONa at room temperature in almost quantitative yields.[17]

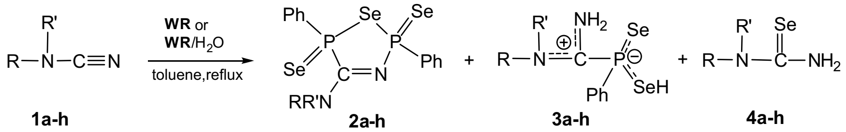
As shown in Scheme 1 and Table 1, heating the mixture of equal molar amount of **WR** and cyanamides **1a**–**g** in toluene under anhydrous condition led to the formation of selenazadiphosphoaminediselenides **2a**–**g** in moderate to good yields (28–71%) after column chromatography (silica gel, 9:1 toluene/ethyl acetate eluent) and recrystallisation by diffusion of a dichloromethane solution to *n*-hexane.

Modification of the reaction by post-treatment of the mixture of **WR** and cyanamides in refluxing toluene with water showed a diverse product distribution. The selenazadiphosphoaminediselenides **2a**, **2d** and **2g** seem very stable as the addition of water did

---

* Corresponding author. Tel./fax: +44 1334 463384.
E-mail address: jdw3@st-and.ac.uk (J.D. Woollins).

0040-4020/$ – see front matter
doi:10.1016/j.tet.2009.05.056



Scheme 1. Reaction of cyanamides and **WR** in toluene at reflux with or without post-water-treatment.

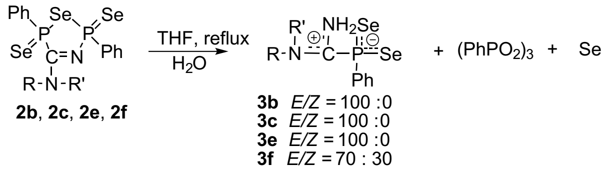
Table 1
Products of the reaction of **WR** and cyanamides in toluene at reflux with or without post-water-treatment

		Reactant	Products in reaction A		Products in reaction B					
R	R′	**1**	**2**	Yield (%)	**2**	Yield (%)	**3**	Yield (%)	**4**	Yield (%)
$C_6H_5CH_2CH_2$	H	**1a**	**2a**	45	**2a**	30	**3a**			
4-*n*-$C_{10}H_{21}C_6H_4$	H	**1b**	**2b**	71	**2b**	41	**3b**	57		
4-$BrC_6H_4CH_2$	H	**1c**	**2c**	29	**2c**	11	**3c**	47		
$C_6H_5CH_2$	H	**1d**	**2d**	28	**2d**	15				
$C_6H_5(CH_2)_3$	H	**1e**	**2e**	43	**2e**	25	**3e**	29		
$C_6H_5CH_2CH_2$	CH_3	**1f**	**2f**	42	**2f**	31	**3f**	48	**4f**	20
$C_6H_5CH_2$	CH_3CH_2	**1g**	**2g**	50	**2g**	38	**3g**			
$C_6H_5CH_2CH_2$	$EtCO_2$	**1h**			**2h**		**3h**		**4h**	91

Reaction A: **WR**, toluene, reflux for 10 h; reaction B: **WR**, toluene, reflux for 10 h, then addition of water, further reflux for 1 h.

not lead to any hydrolysed products. However, similar post-treatment of the reaction mixture of cyanamides **1b**, **1c** and **1e** and **WR** with water resulted in carbamidoyl(phenyl)phosphinodiselenoic acids **3b** (57%), **3c** (47%), **3e** (29%) and **3f** (48%), and the hydrolysed products of heterocyclic compounds **2b**, **2c** and **2e**. In the case of **1f**, water led to the formation of the third product **4f** (20%) apart from the selenazadiphosphoaminediselenide **2f** (31%) and carbamidoyl(phenyl)phosphinodiselenoic acids **3f** (48%). Meanwhile treatment of the refluxing mixture of **1g** and **WR** in toluene with water gave selenourea **4h** as the only product in 91% yield.

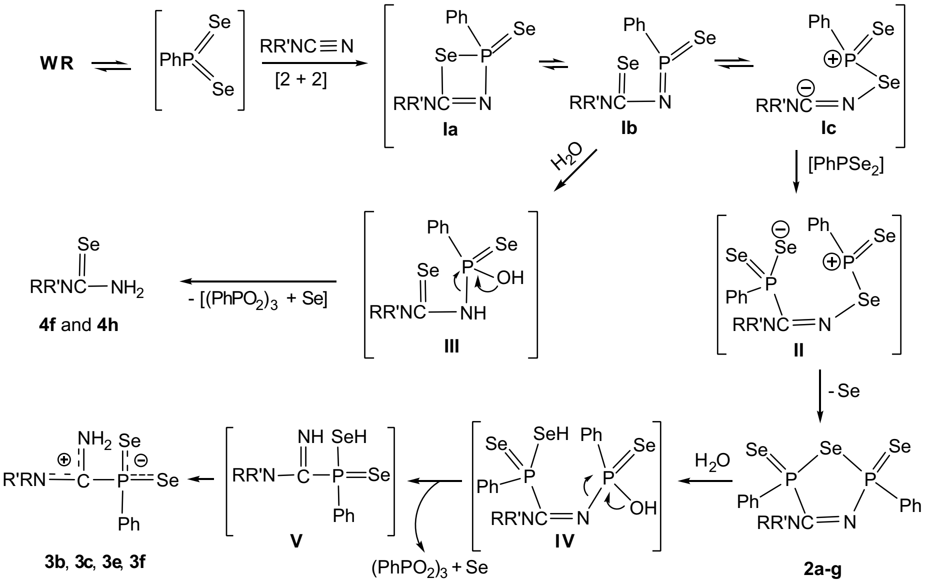
In order to gain mechanistic insight, the hydrolysis of isolated selenazadiphospholaminediselenides **2b**, **2c**, **2e** and **2f** was carried out straightforwardly in refluxing tetrahydrofuran with excess of water, giving the corresponding zwitterionic carbamidoyl(phenyl)-phosphinodiselenoic acids **3b**, **3c**, **3e** and **3f** in almost quantitative yields (Scheme 2).



Scheme 2. Hydrolysis of selenazadiphospholaminediselenides to zwitterionic carbamidoyl(phenyl)-phosphinodiselenoic acids **3b**, **3c**, **3e** and **3f**.

Therefore, we propose possible pathways for the formation of **2a–g**, **3b**, **3c**, **3e**, **3f**, **4f** and **4h** as shown in Scheme 3. **WR** at elevated temperature is in equilibrium with a diselenaphosphorane $PhP(Se)_2$, which is believed to be a true reactive species in refluxing toluene.[8] The initial step for the formation of **2a–g**, **3b**, **3c**, **3e**, **3f**, **4f** and **4h** is a typical [2+2] cycloaddition of a P═Se bond from diselenaphosphorane $PhP(Se)_2$ across the C≡N bond of cyanamide to give an intermediate **I**, which is in equilibrium in solution in three tautomeric forms: the 1,2-selenaphospacyclobutene **Ia**, the selone **Ib** and the dipolar species **Ic**. The intermediate **Ic** reacts further with another molecule of $PhP(Se)_2$ to generate a second dipolar intermediate **II**, which extrudes selenium to afford selenazadiphospholaminediselenides **2a–g**. Furthermore, reaction of selenazadiphospholaminediselenides with one molecule of H_2O gives rise to carbamidoyl(phenyl)phosphinodiselenoic acids **3b**, **3c**, **3c** and **3f** with unusual zwitterionic structures via the intermediates **IV** and **V** while eliminating PhP(Se)(O), the latter can readily decompose to give $(PhPO_2)_3$ and Se. On the subject of the formation of **4f** and **4h**, the hydrolysis of the intermediate **Ib** with one molecule of H_2O can afford selenoureas via the intermediate **III** by further loss of $(PhPO_2)_3$ and Se.

Preparation and characterisation of the compounds **2e**, **2f**, **3e** and **3f** have been reported in our recent communication,[18] thus, the



Scheme 3. Suggested mechanism for the formation of selenazadiphospholaminediselenides, carbamidoyl(phenyl)phosphinodiselenoic acids and selenoureas.

Table 2
^{31}P and ^{77}Se NMR data for compounds **2a–d** and **2g**

Compound	δ(P) [ppm]	^1J(Se–P) [Hz]	^1J(Se=P) [Hz]	δ(Se) [ppm]	^1J(Se–P) [Hz]	^1J(Se=P) [Hz]
2a	76.4	475	792	414.1	465/477	
	74.8	477	825	11.8		825
				−126.7		792
2b	89.1	484	789	391.4	310/484	
	74.9	310	831	14.3		831
				−126.2		789
2c	80.7	420	789	391.9	310/420	
	75.3	310	833	13.6		833
				−124.5		789
2d	76.5	486	825	419.1	486/477	
	74.4	477	791	15.3		825
				−126.4		791
2g	76.1	458	794	499.66	458/455	822
	[75.7]	[460]	[794]	[492.6]		[822]
	59.8	458	822	17.54	[460/458]	794
	[59.6]	[455]	[822]	[8.1]		[794]
				−70.57		
				[−74.5]		

Dimension for another diastereomeric molecule in square parentheses.

four compounds will not be discussed here in details. The characterisation of **2a–d**, **2g**, **3b**, **3c**, **4f** and **4h** is based on elemental microanalysis, ^1H, ^{13}C, ^{31}P and ^{77}Se NMR spectra, IR spectroscopy and mass spectrometry. The elemental microanalyses for all compounds were satisfactory, and all compounds showed the anticipated $[M]^+$ or $[M-H]^+$ or $[M+H]^+$ or $[M+Na]^+$ peak in their mass spectra. The ν(C=N) vibrations are observed in the range 1503–1549 cm^{-1}, while the range 550–557 cm^{-1} shows the presence of ν(P=Se) vibrations for compounds **2a–d** and **2g**, these values are comparable with similar heterocycles.[12c,d] For compounds **3b** and **3c**, the strong bands in the range 1636–1639 cm^{-1}, from the ν(N–H) vibration were observed together with the typical ν(C=N) vibrations (1512 and 1557 cm^{-1}) and the ν(P=Se) vibrations (551 and 559 cm^{-1}). However, the IR spectra of **4f** and **4h** show asymmetrical and symmetrical ν(NH_2) vibration in the range 3375–3166 cm^{-1} along with strong bands at 1612 and 1598 cm^{-1} resulting from the ν(N–H) vibrations and medium bands at 699 and 656 cm^{-1} characteristic of the C=Se group.[11,19]

^{31}P NMR characteristics of **2a–d** and **2g** exhibit two sets of double resonances with two sets of satellites for the endocyclic and exocyclic selenium atoms as showed in Table 2. Slightly different chemical shifts indicate the presence of two slightly different single P–Se and two slightly different double P=Se bonds in each compounds due to the two different phosphorus atoms. The difference is further substantiated by the ^{77}Se NMR spectra, which exhibit a doublet of doublets. One pair of diastereomers with the same intensity was identified in compound **2g**. Detailed NMR spectroscopic analysis and iterative simulation reveal the coupling constant between phosphorus atoms and exocyclic selenium atoms ($^2J_{(P,P)}$=9.4–16.4 Hz and $^3J_{(P,Se\mathit{exo})}$: ca. 9.0 Hz) in **2a–d** and **2g**. The chemical shifts and coupling constants are comparable to those in the literature.[20] Molecular structures of **2a**, **2d** and **2g** are also confirmed by single crystal X-ray analysis.

^{31}P NMR spectra of **3b** and **3c** display sharp singlets at 30.2 and 30.5 ppm, respectively, flanked by selenium satellites with ^{31}P–^{77}Se coupling constants of 702 and 695 Hz, 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),[21] indicating the presence of the zwitterionic structures for both compounds. ^{77}Se NMR spectra show doublets at −83.7 ppm for **3b** and −78.2 ppm for **3c** with matching coupling constants. All NMR spectroscopic characterisations in **3b** and **3c** are comparable with those documented in **3e** and **3f**.[18] For **4f** and **4h**, ^{77}Se NMR spectra show single signals at 607.7 and 382.1 ppm, respectively, while ^{13}C NMR spectra contain signals for the group C=Se at 207.1 and 186.7 ppm, respectively, together with the expected signals for related carbon atoms.

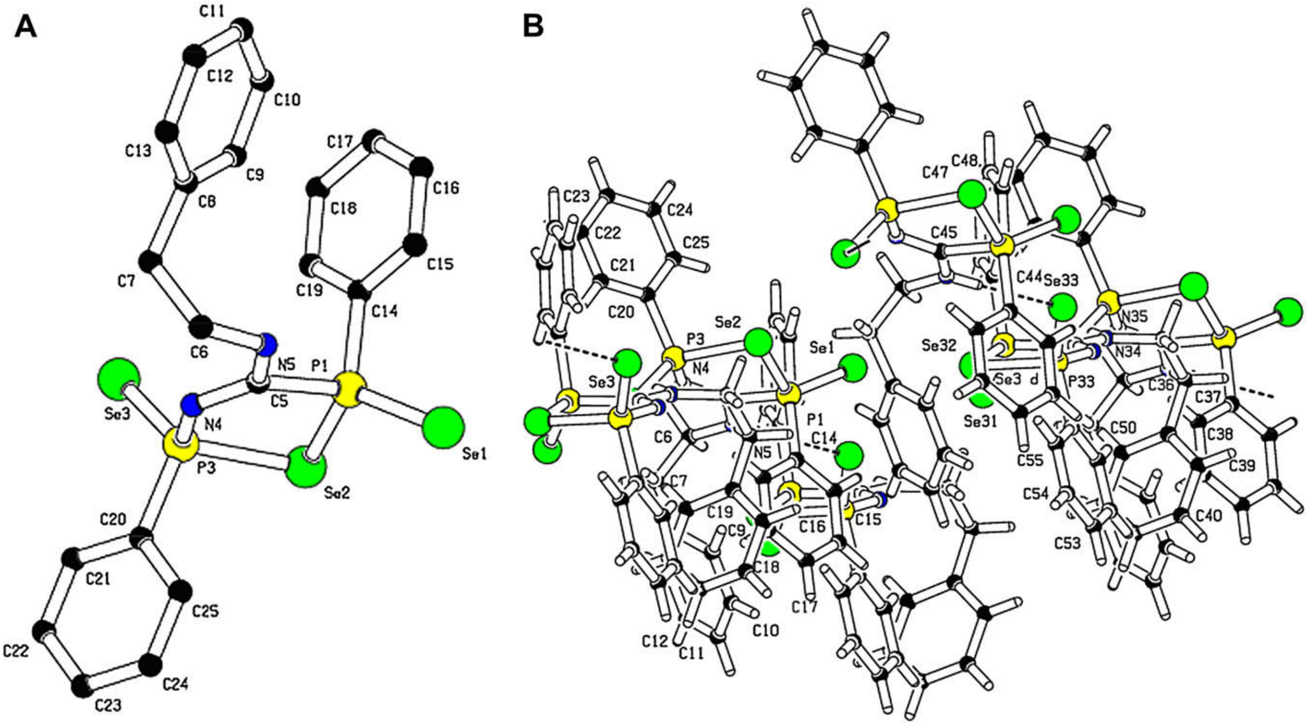


Figure 1. (A) Crystal structure of **2a** (C–H bonds omitted for clarity); (B) X-ray structure showing the intramolecular hydrogen bonding interactions of P=Se···H–N leading to chains of the polymer.

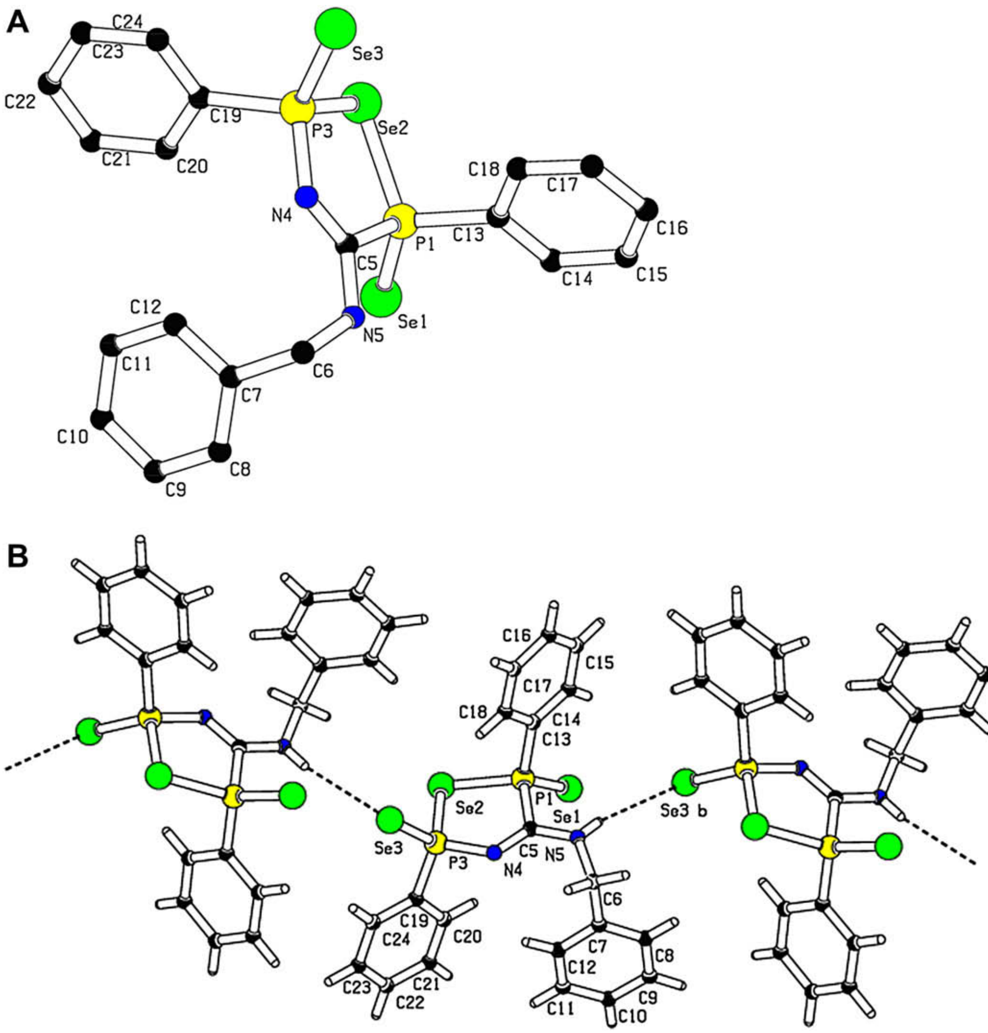


Figure 2. (A) Crystal structure of **2d** (C–H bonds omitted for clarity); (B) X-ray structure showing the intramolecular hydrogen bonding interactions of P═Se···H–N leading to chains of the polymer.

2.1. X-ray crystal structures

Perspective views of the X-ray crystallographic structures of the compounds **2a**, **2d** and **2g** with selected parameters are shown in Figures 1–3. Crystal data and details of the structure determination are given in Tables 3 and 4. The structure of **2a** contains two independent molecules within the unit cell, the differences in metric parameters in the two molecules resulting from the rotation of aryl–alkyl group [$C_6H_5CH_2CH_2$) C(14)–C(21)] leading to some steric interactions in the second independent molecule. The frame works of all compounds contain a five-membered P_2SeCN ring bearing a P(Se)–Se–P(Se) linkage with the exocyclic P═Se groups orientated trans to each other. The P═Se bond lengths and angles are normal and comparable with those found in the literature.[8,12c,13,22] The geometry around P(1) [Se(1)–P(1)–Se(2): 117.24(9)° [116.66(9)°] for

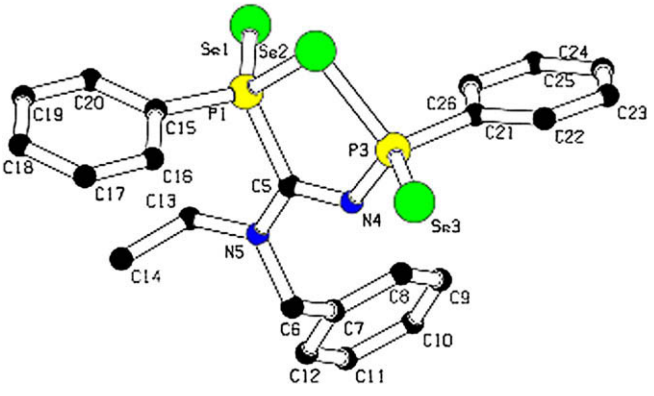


Figure 3. Crystal structure of **2g** (C–H bonds omitted for clarity).

Table 3
Details of the X-ray data collections and refinements for compounds **2a**, **2d** and **2g**

Compound	**2a**	**2d**	**2g**
Formula	$C_{21}H_{20}N_2P_2Se_3$	$C_{20}H_{18}N_2P_2Se_3$	$C_{22}H_{22}N_2P_2Se_3$
M	599.21	585.18	613.24
Crystal system	Triclinic	Monoclinic	Monoclinic
Space group	*P*-1	*P*21/*n*	*P*21/*n*
a/Å	8.8864(5)	9.7105(8)	14.7395(18)
b/Å	9.7663(14)	16.3577(13)	10.6811(10)
c/Å	13.739(2)	13.5571(11)	15.6539(18)
α	84.651(13)	90	90
β	74.529(12)	98.815(2)	109.845(2)
γ	73.472(12)	90	90
U/Å^3	1101.5(2)	2128.0(3)	2318.1(4)
Z	2	4	4
μ/mm^{-1}	5.165	5.344	4.910
Reflections collected	7616	14,859	16,162
Independent reflections (R_{int})	0.0541	0.0253	0.0418
$R1$, $wR2$ [$I>2\sigma(I)$]	0.0422, 0.0987	0.0478, 0.0611	0.0613, 0.0762

Table 4
Details of the X-ray data collections and refinements for compounds **4f** and **4h**

Compound	**4f**	**4h**
Formula	$C_{10}H_{14}N_2Se$	$C_{12}H_{16}N_2O_2Se$
M	241.19	299.23
Crystal system	Orthorhombic	Monoclinic
Space group	*Pca*2(1)	*C*2/*c*
a/Å	12.067(2)	17.695(3)
b/Å	5.9432(13)	6.7719(10)
c/Å	29.023(6)	24.199(4)
α	90	90
β	90	109.772(4)
γ	90	90
U/Å^3	2081.5(7)	2728.7(7)
Z	8	8
μ/mm^{-1}	3.564	2.745
Reflections collected	9033	8634
Independent reflections (R_{int})	0.0961	0.0406
$R1$, $wR2$ [$I>2\sigma(I)$]	0.0623, 0.1348	0.0710, 0.1819

2a, 118.16(4)° for **2d** and 114.12(4)° for **2g**, respectively] and around P(3) [Se(2)–P(3)–Se(3): 113.06(9)° [112.92(9)°] for **2a**, 112.93(3)° for **2d** and 113.06(9)° for **2g**, respectively] are distorted tetrahedral due to the effects of the steric hindrance of phenyl groups.[12e] The transannular P···P bond distances are 3.24, 3.24 and 3.21 Å for **2a**, **2d** and **2g**, respectively, being marginally longer than those observed in the four-membered P_2Se_2 ring system (3.1 Å) and considerably shorter than those measured in six-membered ring system P_2Se_4 ring system (4.3 Å).[23] It should be noted that there is a intramolecular N–H···Se=P hydrogen bonding interaction to form chains of polymer in the solid state in **2a** and **2d**.

The X-ray crystal structures of selenoureas **4f** and **4h** are shown in Figures 4 and 5. The crystallographic data, selected bond lengths and bond angles are listed in Tables 5 and 6. The structure of **4f** shows two independent molecules within the unit cell. The C–Se bond lengths in **4f** and **4h** are 1.877(7) [1.872(7)] and 1.850(4) Å, respectively, which are slightly longer than the values in arylselenoamides [1.820(4)–1.848(2)],[11] while the shortness of the C–N bond lengths in which the C–N bonds are adjacent to the C=Se double bond [C(1)–N(1) and C(1)–N(2): 1.342(8) [1.351(8)] and 1.325(8) [1.311(8)] Å for **4f**, 1.319(5) and 1.400(5) Å for **4h**], compared to the normal C–N bond distances [N(2)–C(2) and N(2)–C(3): 1.459(8) [1.460(8)] and 1.480(7) [1.454(7)] Å for **4f**, 1.401(5) and 1.490(5) Å for **4h**], suggests some multiple bonding character. It should be noted that the C(1)–N(1) bond length [1.342(8) [1.351(8)] Å] in **4f** is slightly longer than that [1.319(5) Å] in **4h**, meanwhile C(1)–N(2) bond distance [1.325(8) [1.311(8)] Å] in **4f** is much shorter than that [1.400(5) Å] in **4h**, indicating the effect of the presence of $C(O)OC_2H_5$ versus CH_3. In both structures, N(1)–N(2)–C(1)–Se(1) is approximately planar, while Se(1) lies 0.04 Å [0.03 Å for molecule 2] for **4f** and 0.02 Å for **4h** out of this plane. Furthermore, the aryl and N(1)–N(2)–C(1)–Se(1) interplanar angle in **4f** and **4h** is 15.30° [15.21°] and 17.44°, respectively. There are weak C=Se···H–N hydrogen bonding interactions in the structure of **4f** [the hydrogen bonding Se(1)···H(1A), Se(11)···H(1B), Se(11)···H(11A) and Se(1)···H(11B) distances are 2.79(6), 2.61(4), 2.80(6) and 2.59(4) Å, respectively, along with N(1)–H(1A)···Se(1), N(1)–H(1B)···Se(11), N(11)–H(11A)···Se(11) and N(11)–H(11B)···Se(1) angles of 129(5)°, 147(6)°, 126(5)° and 152(6)°]. However, in **4f**, apart from the weak C=Se···H–N hydrogen bonding interactions [Se(1)···H(1B) distance is 2.638(11) Å with N(1)–H(1B)···Se(1) angle of 162(4)°], there is another stronger hydrogen bonding interaction between C=O···H–N [H(1A)···O(1) and H(1A)···O(1^i) distances are 1.88(4) and 2.38(3) Å, respectively, with N(1)–H(1A)···O(1) and N(1)–H(1A)···O(1^i) angles of 129(4)° and 146(4)°]. For both compounds, the hydrogen bonding interactions result in discrete dimeric pairs, with additional secondary

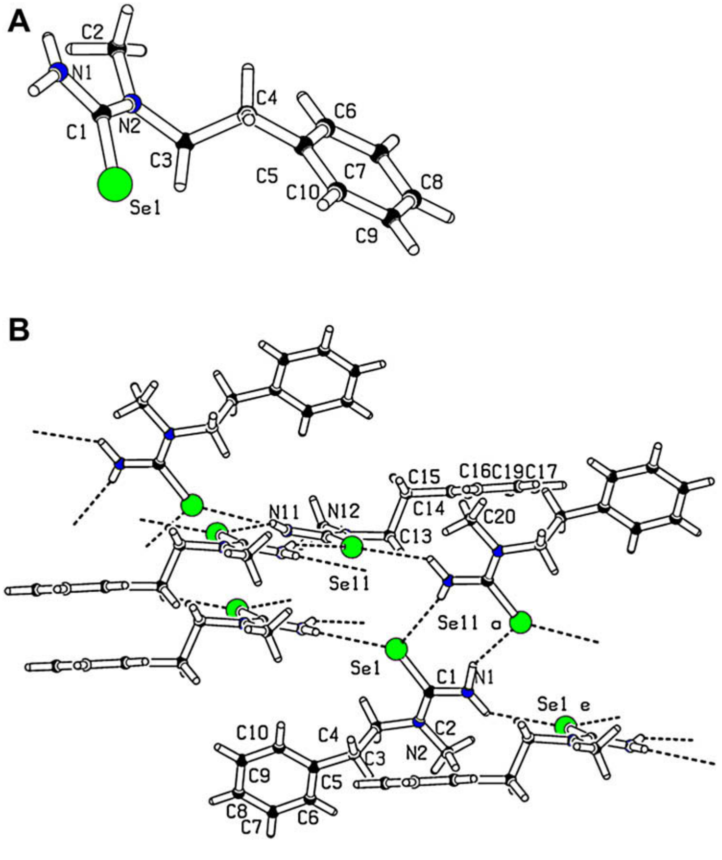


Figure 4. (A) Crystal structure of **4f** (C–H bonds omitted for clarity); (B) X-ray structure showing hydrogen bonding interaction of Se···H–N leading to clusters of the polymer.

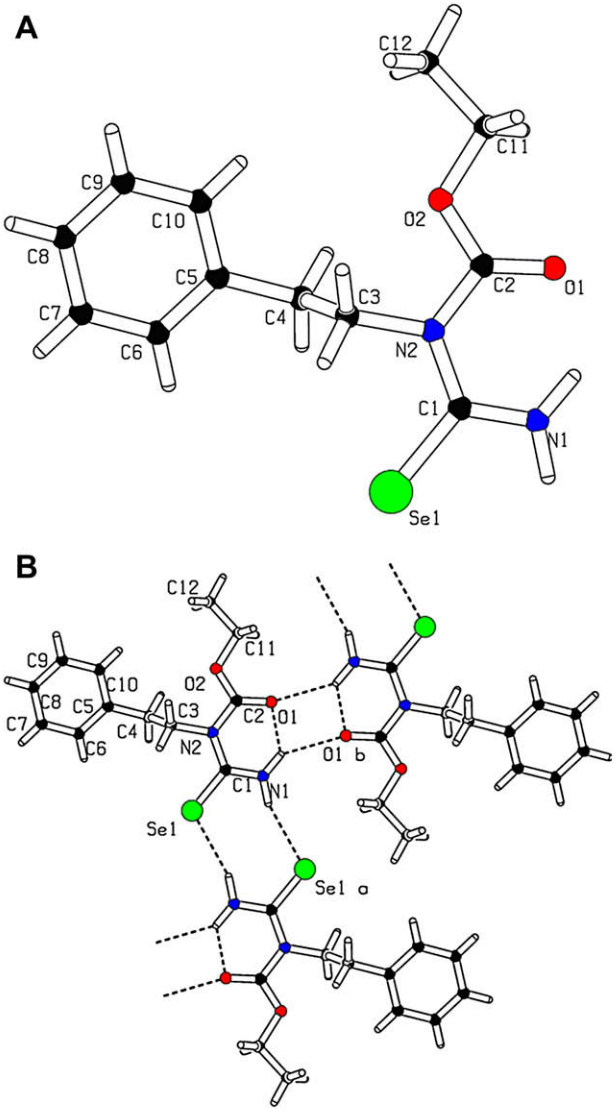


Figure 5. (A) Crystal structure of **4h** (C–H bonds omitted for clarity); (B) X-ray structure showing hydrogen bonding interactions of C=Se···H–N and C=O···H–N leading to clusters of the polymer.

Table 5
Selected bond lengths (Å) and angles (°) for compounds **2a**, **2d** and **2g**

	2a[a]	**2d**	**2g**
Se(1)–P(1)	2.098(2) [2.089(2)]	2.0892(8)	2.0976(10)
Se(2)–P(1)	2.236(2) [2.247(2)]	2.2409(8)	2.2288(10)
Se(2)–P(3)	2.311(2) [2.291(2)]	2.2883(8)	2.2791(10)
Se(3)–P(3)	2.096(2) [2.104(2)]	2.1031(8)	2.0865(10)
P(3)–N(4)	1.647(6) [1.636(6)]	1.652(2)	1.644(3)
P(1)–C(5)	1.882(8) [1.889(8)]	1.889(3)	1.890(3)
N(5)–C(5)	1.326(9) [1.336(10)]	1.339(3)	1.337(4)
N(4)–C(5)	1.303(9) [1.301(10)]	1.283(3)	1.304(4)
P(1)–Se(2)–P(3)	90.70(8) [91.03(7)]	91.44(3)	90.91(3)
N(4)–P(3)–Se(3)	116.3(3) [114.9(3)]	115.71(9)	115.41(11)
N(4)–P(3)–Se(2)	102.2(3) [104.1(3)]	103.22(8)	103.41(10)
Se(3)–P(3)–Se(2)	113.06(9) [112.92(9)]	112.93(3)	112.59(4)
C(5)–P(1)–Se(1)	114.0(2) [114.6(2)]	112.60(9)	112.71(11)
C(5)–P(1)–Se(2)	97.9(3) [98.1(2)]	97.80(9)	99.49(11)
Se(1)–P(1)–Se(2)	117.24(9) [116.66(9)]	118.16(4)	114.12(4)
C(5)–N(4)–P(3)	124.0(6) [123.9(6)]	123.95(19)	125.6(2)

[a] Dimensions for second independent molecule in square parentheses.

Table 6
Selected bond lengths (Å) and angles (°) for compounds **4f** and **4h**

	4f[a]	**4h**
N(1)–C(1)	1.342(8) [1.351(8)]	1.319(5)
N(2)–C(1)	1.325(8) [1.311(8)]	1.400(5)
N(2)–C(2)	1.459(8) [1.460(8)]	1.401(5)
N(2)–C(3)	1.480(7) [1.454(7)]	1.490(5)
Se(1)–C(1)	1.877(7) [1.872(7)]	1.850(4)
C(1)–N(2)–C(2)	121.0(5) [120.5(5)]	122.5(3)
C(1)–N(2)–C(3)	122.7(5) [121.9(6)]	119.5(3)
C(2)–N(2)–C(3)	116.2(5) [116.9(5)]	117.8(3)
N(2)–C(1)–N(1)	117.6(6) [117.8(6)]	119.1(3)
N(2)–C(1)–Se(1)	124.6(5) [124.6(5)]	120.7(3)
N(1)–C(1)–Se(1)	117.8(5) [117.6(5)]	120.1(3)

[a] Dimensions for second independent molecule in square parentheses.

interactions of the same type between dimeric pairs to finally give a polymeric structure in the solid state.

In summary, a convenient and efficient approach to synthesise a series of new heterocyclic selenazadiphospholaminediselenides, zwitterionic carbamidoyl(phenyl)phosphinodiselenoic acids and selenoureas has been developed from the reaction of Woollins reagent with the corresponding cyanamide following with or without further treatment with H_2O. The biological activity of **2a**–**2h** will be investigated in due course.

3. Experimental section

3.1. General

Unless otherwise stated, all reactions were carried out under an oxygen free nitrogen atmosphere using pre-dried solvents and standard Schlenk techniques, subsequent chromatographic and work up procedures were performed aerobically. Solvents were dried, purified, and stored according to common procedures. ^1H (270 MHz), ^{13}C (67.9 MHz), ^{31}P–{^1H} (109 MHz) and ^{77}Se–{^1H} (51.4 MHz 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 (UK) and the University of St. Andrews Mass Spectrometry Service. X-ray crystal data for compounds **2a**, **2d**, **2g**, **4f** and **4h** 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.[24] CCDC 720091–720095 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.

3.2. Reaction of cyanamides with WR (method A)

A mixture of cyanamide (4.0 mmol) and **WR** (2.15 g, 4.0 mmol) in 50.0 mL of dry toluene was heated at 130 °C for 10 h. The red suspension disappeared and a pale yellow solution was formed along with a small amount of grey selenium after cooling to room temperature. The resulting mixture was concentrated to ca. 5.0 mL and purified by silica gel (1:9=ethyl acetate/toluene as eluent) to give **2a**–**g**.

3.3. Reaction of cyanamides with WR/H_2O (method B)

A red toluene (30 mL) suspension of **WR** (2.0 mmol) and cyanamide (2.0 mmol) were refluxed for 10 h. The red suspension disappeared and a pale yellow solution was formed. After cooling to 90 °C to the mixture was added 2.0 mL of water and refluxing continued for another 1 h. A yellow suspension was obtained along with a mixture of dark and white precipitate. Toluene and excess water were removed in vacuo, the residue was then extracted by dichloromethane (3×30 mL). The organic layers were dried over $MgSO_4$, concentrated in vacuo and further purified by silica gel chromatography to give selenazadiphospholaminediselenides **2a**–**g** (1:9=ethyl acetate/dichloromethane as eluent), carbamidoyl (phenyl)phosphinodiselenoic acids **3b**, **3c**, **3e** and **3f** (1:5=ethyl acetate/dichloromethane as eluent), and selenoureas **4f** and **4h** (1:5=ethyl acetate/dichloromethane as eluent).

3.4. Hydrolysis of selenazadiphospholaminediselenides to carbamidoyl(phenyl)phosphinodiselenoic acids (method C)

A solution of selenazadiphospholaminediselenides (1.0 mmol) and 1.0 mL of water in 20.0 mL of tetrahydrofuran was refluxed for 3 h. Upon cooling to room temperature the resulting mixture was extracted with dichloromethane (2×25 mL). The organic layers were dried over $MgSO_4$ overnight. After concentration in vacuo the residue was purified by silica gel chromatography (1:5=ethyl acetate/dichloromethane as eluent) to afford the corresponding carbamidoyl(phenyl)phosphinodiselenoic acids.

*3.4.1. N-(Phenylpropyl)-2,5-diphenyl-2,5-dihydro-1,2,3,5-selenazadiphosphol-4-amine-2,5-diselenide (**2a**)*

Yellow solid (45% yield from method A and 30% yield from method B); mp 133–134 °C. Elemental analysis: Found C, 41.81; H, 3.05; N, 4.55. $C_{21}H_{20}N_2P_2Se_3$ requires C, 42.09; H, 3.36; N, 4.67. IR (KBr, ν_{max}/cm^{-1}): 3226 (w), 1579 (vs), 1503 (w, C═N), 1434 (m), 1357 (w), 1260 (m), 1095 (m), 1084 (m), 920 (m), 747 (m), 549 (s, P═Se). ^{1}H NMR ($CDCl_3$, ppm): 8.19 (dd, $J_{(H,H)}$=8.2 Hz, $J_{(P,H)}$=16.1 Hz, 2H, ArH), 7.96 (dd, $J_{(H,H)}$=8.4 Hz, $J_{(P,H)}$=9.6 Hz, 2H, ArH), 7.56–7.52 (m, 3H, ArH), 7.52–7.50 (m, 3H, ArH), 7.21–7.19 (m, 2H, ArH), 7.00–6.96 (m, 3H, ArH), 3.73 (t, $J_{(H,H)}$=6.7 Hz, 2H, $ArCH_2$), 2.82 (t, $J_{(H,H)}$=6.7 Hz, 2H, NCH_2), 0.06 (s, 1H, NH). ^{13}C NMR ($CDCl_3$, ppm): 166.58 (d, $J_{(P,C)}$=34.3 Hz), 137.4, 133.2, 132.6, 132.4, 131.5 (d, $J_{(P,C)}$=14.3 Hz), 129.2, 129.0, 128.9, 128.7, 128.5, 127.0, 47.2, 47.1, 34.8. ^{31}P NMR ($CDCl_3$, ppm): 76.4 (d, $^{2}J_{(P,P)}$=14.1 Hz, $J_{(P,Se)}$=475, 792 Hz), 74.8 (d, $^{2}J_{(P,P)}$=14.1 Hz, $J_{(P,Se)}$=477, 825 Hz). ^{77}Se NMR ($CDCl_3$, ppm): 414.1 (dd, $J_{(P,Se)}$=475, 477 Hz), 11.8 (d, $J_{(P,Se)}$=825 Hz), −126.7 (d, $J_{(P,Se)}$=792 Hz). MS (EI, *m*/*z*), 602 $[M]^+$.

*3.4.2. N-(4-Decylphenyl)-2,5-diphenyl-2,5-dihydro-1,2,3,5-selenazadiphosphol-4-amine-2,5-diselenide (**2b**)*

Yellow oil (71% yield from method A and 41% from method B); mp 158–159 °C. Elemental analysis: Found C, 49.10; H, 4.81; N, 3.65. $C_{29}H_{35}N_2P_2Se_3$ requires C, 49.03; H, 4.97; N, 3.94. IR (KBr, ν_{max}/cm^{-1}): 2922 (s), 2850 (m), 1581 (s), 1511 (m, C═N), 1434 (m), 1411 (m), 1305 (w), 1260 (w), 1180 (w), 1087 (m), 940 (s), 821 (m), 745 (m), 685 (m), 554 (s, P═Se). ^{1}H NMR ($CDCl_3$, ppm): 8.67 (ws, 1H, NH), 8.65 (ws, 1H, NH), 8.34 (dd, $^{3}J_{(H,H)}$=7.4 Hz, $^{3}J_{(P,H)}$=15.6 Hz, 4H, ArH), 8.05 (m, 6H, ArH), 7.58 (d, $^{3}J_{(H,H)}$=8.2 Hz, 2H, ArH), 7.11 (d, $^{3}J_{(H,H)}$=8.2 Hz, 2H, ArH), 2.54 (t, $^{3}J_{(H,H)}$=7.2 Hz, 2H, CH_2), 1.53–1.50 (m, $^{3}J_{(H,H)}$=7.2 Hz, 2H, CH_2), 1.24–1.22 (m, 14H, CH_2), 0.88 (t, $^{3}J_{(H,H)}$=7.2 Hz, 3H, CH_3). ^{13}C NMR ($CDCl_3$, ppm): 161.5 (d, $^{1}J_{(P,C)}$=34.3 Hz, P–C), 141.5, 137.3, 136.0, 134.9 (d, $^{2}J_{(P,C)}$=9.3 Hz), 133.4 (d, $^{4}J_{(P,C)}$=3.1 Hz), 132.8 (d, $^{3}J_{(P,C)}$=4.2 Hz), 132.5 (d, $^{1}J_{(P,C)}$=13.5 Hz), 131.6 (d, $^{1}J_{(P,C)}$=13.5 Hz), 129.4, 129.2, 128.7, 128.4, 120.1, 35.5, 32.0, 31.5, 29.7, 29.6, 29.4, 29.3, 22.8, 14.3. ^{31}P NMR ($CDCl_3$, ppm): 81.0 (d, $^{2}J_{(P,P)}$=16.4 Hz, $J_{(P,Se)}$=484, 789 Hz), 74.9 (d, $^{2}J_{(P,P)}$=16.4 Hz, $J_{(P,Se)}$=310, 831 Hz). ^{77}Se NMR ($CDCl_3$, ppm): 391.4 (dd, $J_{(P,Se)}$=310, 484 Hz), 14.3 (d, $J_{(P,Se)}$=831 Hz), −126.2 (d, $J_{(P,Se)}$=789 Hz). MS (EI, *m*/*z*), 713 $[M]^+$.

*3.4.3. N-(4-Bromobenzyl)-2,5-diphenyl-2,5-dihydro-1,2,3,5-selenazadiphosphol-4-amine-2,5-diselenide (**2c**)*

Green solid (29% yield from method A and 11% yield from method B); mp 163–164 °C. Elemental analysis: Found C, 36.01; H, 2.43; N, 4.11. $C_{20}H_{17}BrN_2P_2Se_3$ requires C, 36.17; H, 2.58; N, 4.22. IR (KBr, ν_{max}/cm^{-1}): 3264 (w), 3047 (w), 1596 (s), 1565 (s), 1525 (m, C═N), 1486 (m), 1434 (m), 1395 (m), 1306 (m), 1180 (m), 1084 (m), 943 (m), 819 (m), 744 (m), 702 (m), 702 (m), 683 (m), 551 (s, P═Se). ^{1}H NMR ($CDCl_3$, ppm): 8.32 (d, $^{3}J_{(H,H)}$=7.2 Hz, 2H, ArH), 8.28 (dd, $^{3}J_{(H,H)}$=7.2 Hz, $^{3}J_{(P,H)}$=10.1 Hz, 2H, ArH), 8.00 (dd, $^{3}J_{(H,H)}$=7.2 Hz, $^{3}J_{(P,H)}$=10.1 Hz, 2H, ArH), 7.59 (dd, $^{3}J_{(H,H)}$=7.2 Hz, $^{4}J_{(P,H)}$=3.7 Hz, 2H, ArH), 7.57 (dd, $^{3}J_{(H,H)}$=7.2 Hz, $^{4}J_{(P,H)}$=3.0 Hz, 2H, ArH), 7.52 (dd, $^{3}J_{(H,H)}$=7.2 Hz, 1H, ArH), 7.41 (dd, $^{3}J_{(H,H)}$=7.2 Hz, 1H, ArH), 7.22 (d, $^{3}J_{(H,H)}$=7.2 Hz, 2H, ArH), 2.35 (s, 2H, CH_2), 0.07 (s, 1H, NH). ^{13}C NMR ($CDCl_3$, ppm): 165.0 (d, $^{1}J_{(P,C)}$=32.6 Hz), 136.2 (d, $^{3}J_{(P,C)}$=9.3 Hz), 133.5 (d, $^{4}J_{(P,C)}$=4.2 Hz), 132.9 (d, $^{4}J_{(P,C)}$=3.1 Hz), 132.5 (d, $^{2}J_{(P,C)}$=14.5 Hz), 132.4, 131.6 (d, $^{2}J_{(P,C)}$=13.5 Hz), 129.3 (d, $^{2}J_{(P,C)}$=13.5 Hz), 129.1, 128.7 (d, $^{2}J_{(P,C)}$=14.5 Hz), 128.3, 125.4, 121.8, 40.8. ^{31}P NMR ($CDCl_3$, ppm): 80.7 (d, $^{2}J_{(P,P)}$=14.1 Hz, $J_{(P,Se)}$=420, 789 Hz), 75.3 (d, $^{2}J_{(P,P)}$=14.1 Hz, $J_{(P,Se)}$=310, 833 Hz). ^{77}Se NMR ($CDCl_3$, ppm): 391.9 (dd, $J_{(P,Se)}$=310, 420 Hz), 13.6 (d, $J_{(P,Se)}$=833 Hz), −124.5 (d, $J_{(P,Se)}$=789 Hz). MS (EI, *m*/*z*), 666 $[M]^+$.

*3.4.4. N-Benzyl-2,5-diphenyl-2,5-dihydro-1,2,3,5-selenazadiphosphol-4-amine-2,5-diselenide (**2d**)*

Yellow solid (28% yield from method A and 15% yield from method B); mp 108–110 °C. Elemental analysis: Found C, 40.90; H, 3.03; N, 4.65. $C_{20}H_{18}N_2P_2Se_3$ requires C, 41.05; H, 3.10; N, 4.79. IR (KBr, ν_{max}/cm^{-1}): 3249 (m), 1580 (vs), 1511 (m, C═N), 1433 (m), 1085 (m), 1017 (m), 882 (m), 550 (vs, P═Se). ^{1}H NMR ($CDCl_3$, ppm): 8.26 (dd, $^{3}J_{(H,H)}$=8 Hz, $^{3}J_{(P,H)}$=16 Hz, 4H, ArH), 7.93–7.89 (m, $^{3}J_{(H,H)}$=8 Hz, 6H, ArH), 7.59–7.15 (m, 5H, ArH), 4.79–4.57 (m, 2H, CH_2), 1.56 (s, 1H, NH). ^{13}C NMR ($CDCl_3$, ppm): 136.0 (d, $^{1}J_{(P,C)}$=30 Hz), 133.3 (d, $^{4}J_{(P,C)}$=3 Hz), 132.5 (d, $^{3}J_{(P,C)}$=14 Hz), 131.4 (d, $^{3}J_{(P,C)}$=14 Hz), 129.3, 129.1, 128.6, 128.4, 128.3, 127.7, 49.7 (s, CH_2). ^{31}P NMR ($CDCl_3$, ppm): 76.5 (d, $^{2}J_{(P,P)}$=14 Hz, $J_{(P,Se)}$=486, 825 Hz), 74.4 (d, $^{2}J_{(P,P)}$=14 Hz, $J_{(P,Se)}$=477, 791 Hz). ^{77}Se NMR ($CDCl_3$, ppm): 419.1 (dd, $J_{(P,Se)}$=486, 477 Hz), 15.3 (d, $J_{(P,Se)}$=825 Hz), −126.4 (d, $J_{(P,Se)}$=791 Hz). MS (EI^+, *m*/*z*), 588 $[M]^+$.

*3.4.5. N-(3-Phenylpropyl)-2,5-diphenyl-2,5-dihydro-1,2,3,5-selenazadiphosphol-4-amine-2,5-diselenide (**2e**)*

Pale green solid (43% yield from method A and 25% yield from method B); mp 122–123 °C. 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 ($CDCl_3$, ppm): 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), 7.58–7.56 (m, 3H, ArH), 7.52–7.49 (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). ^{13}C NMR ($CDCl_3$, ppm): 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. ^{31}P NMR ($CDCl_3$, ppm): 76.4 (d, $^{2}J_{(P,P)}$=14.1 Hz, $J_{(P,Se)}$=479, 789 Hz), 74.9 (d, $^{2}J_{(P,P)}$=14.1 Hz, $J_{(P,Se)}$=308, 825 Hz). ^{77}Se NMR ($CDCl_3$, ppm): 414.7 (dd, $J_{(P,Se)}$=479, 308 Hz), 10.9 (d, $J_{(P,Se)}$=825 Hz), −125.8 (d, $J_{(P,Se)}$=789 Hz). MS (CI, *m*/*z*), 617 $[M+H]^+$.

*3.4.6. N-Phenethyl-N-methyl-2,5-diphenyl-2,5-dihydro-1,2,3,5-selenazadiphosphol-4-amine-2,5-diselenide (**2f**)*

Pale green solid (42% yield from method A and 31% yield from method B); mp 149–150 °C. IR (KBr, ν_{max}/cm^{-1}): 3425 (dw), 2921 (w), 1561 (vs, $C{=}N$), 1434 (s), 1355 (m), 1094 (s), 869 (m), 746 (m), 687 (m), 554 (m, $P{=}Se$), 539 (m, $P{=}Se$). ^1H NMR (CD_2Cl_2, ppm): 8.16–8.08 (m, 4H, ArH), 7.72–7.53 (m, 6H, ArH), 7.22–7.19 (m, 7H, ArH). ^{13}C NMR (CD_2Cl_2, ppm): 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. ^{31}P NMR (CD_2Cl_2, ppm): 76.7 (d, $^2J_{(P,P)}$=11.7 Hz, $J_{(P,Se)}$=455, 793 Hz), 75.1 (d, $^2J_{(P,P)}$=11.7 Hz, $J_{(P,Se)}$=477, 798 Hz). ^{77}Se NMR (CD_2Cl_2, ppm): 502.0 (dd, $J_{(P,Se)}$=455, 479 Hz), 13.4 (d, $J_{(P,Se)}$=827 Hz), −79.5 (d, $J_{(P,Se)}$=792 Hz). MS (EI$^+$, *m/z*), 616 [M]$^+$, 536 [M−Se]$^+$. Accurate mass measurement (EI, *m/z*): 615.8745, calculated mass for $C_{22}H_{22}N_2P_2Se_3$: 615.8748.

3.4.7. *N-Benzyl-N-ethyl-2,5-diphenyl-2,5-dihydro-1,2,3,5-selenazadiphosphol-4-amine-2,5-diselenide (**2g**)*

Pale green solid (50% yield from method A and 38% yield form method B); mp 140–142 °C. Elemental analysis: Found C, 42.85; H, 3.44; 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}): 3432 (w), 2927 (w), 1549 (vs, $C{=}N$), 1433 (m), 1352 (m), 1302 (w), 1237 (m), 1177 (m), 1088 (m), 980 (m), 899 (m), 899 (m), 822 (m), 741 (m), 687 (m), 596 (m), 557 (s, $P{=}Se$), 554 (s, $P{=}Se$). ^1H, ^{31}P and ^{77}Se NMR confirmed that the product is one pair of diasteroisomers with the same intensity. ^1H NMR ($CDCl_3$, ppm): 8.25 (dd, $J_{(H,H)}$=6.4 Hz, $J_{(P,H)}$=20.0 Hz, 2H, ArH), 7.93 (dd, $J_{(H,H)}$=6.4 Hz, $J_{(P,H)}$=16.8 Hz, 2H, ArH), 7.59 (dd, $J_{(H,H)}$=6.4 Hz, $J_{(P,H)}$=12.6 Hz, 2H, ArH), 7.50 (dd, $J_{(H,H)}$=6.4 Hz, $J_{(P,H)}$=13.6 Hz, 2H, ArH), 7.47 (m, 1H, ArH), 7.40 (m, 1H, ArH), 7.25 (m, 2H, ArH), 7.17 (d, $J_{(H,H)}$=6.9 Hz, 2H, ArH), 6.77 (d, $J_{(H,H)}$=6.9 Hz, 2H, ArH), 5.10 (d, $J_{(P,H)}$=14.8 Hz, 2H, $ArCH_2$), 4.57 (d, $J_{(P,H)}$=14.8 Hz, 2H, $ArCH_2$), 3.97 (q, $J_{(P,H)}$=6.9 Hz, 2H, NCH_2), 3.66 (q, $J_{(P,H)}$=6.9 Hz, 2H, NCH_2), 1.07 (t, $J_{(P,H)}$=6.9 Hz, 3H, CH_3), 0.63 (t, $J_{(P,H)}$=6.9 Hz, 3H, CH_3). ^{13}C NMR ($CDCl_3$, ppm): 163.8 (d, $J_{(P,C)}$=29.1 Hz), 162.7 (d, $J_{(P,C)}$=29.1 Hz), 138.0 (d, $J_{(P,C)}$=4.2 Hz), 136.7 (d, $J_{(P,C)}$=4.2 Hz), 135.2, 134.0, 133.2 (d, $J_{(P,C)}$=3.1 Hz), 133.1 (d, $J_{(P,C)}$=3.1 Hz), 132.6, 132.5, 132.3, 132.2, 131.5 (d, $J_{(P,C)}$=13.5 Hz), 131.2 (d, $J_{(P,C)}$=14.5 Hz), 129.5, 129.3, 128.9, 128.6, 128.4, 128.2, 128.0, 127.6, 127.5, 54.9, 53.6, 47.8, 45.0, 12.4, 11.3. ^{31}P NMR (CD_2Cl_2, ppm): 76.1 (d, $^3J_{(P,P)}$=9.4 Hz, $J_{(P,Se)}$=458, 794 Hz), 75.7 (d, $^3J_{(P,P)}$=9.4 Hz, $J_{(P,Se)}$=460, 794 Hz), 59.8 (d, $^3J_{(P,P)}$=9.4 Hz, $J_{(P,Se)}$=458, 822 Hz), 59.5 (d, $^3J_{(P,P)}$=9.4 Hz, $J_{(P,Se)}$=455, 822 Hz). ^{77}Se NMR (CD_2Cl_2, ppm): 499.7 (dd, $J_{(P,Se)}$=458, 455 Hz), 492.6 (dd, $J_{(P,Se)}$=460, 458 Hz), 17.5 (d, $J_{(P,Se)}$=822 Hz), 8.1 (d, $J_{(P,Se)}$=822 Hz), −70.6 (d, $J_{(P,Se)}$=794 Hz), −74.5 (d, $J_{(P,Se)}$=794 Hz). MS (EI, *m/z*), 616 [M]$^+$.

3.4.8. *N′-(4-Decylbenzyl)carbamidoyl(phenyl)phosphinodiselenoic acid (**3b**)*

Yellow oil (310 mg) in 57% yield from method B; mp 147–148 °C. Elemental analysis: Found C, 52.39; H, 5.88; N, 5.40. $C_{23}H_{31}N_2PSe_2$ requires C, 52.68; H, 5.96; N, 5.34. IR (KBr, ν_{max}/cm^{-1}): 2923 (s), 2852 (m), 1639 (s, $C{=}N$), 1512 (s, $C{=}N$), 1463 (m), 1436 (m), 1141 (s), 1019 (m), 938 (m), 695 (m), 551 (m, P–Se). ^1H NMR ($CDCl_3$, ppm): 10.10 (ws, 1H, NH), 8.43 (ws, 1H, NH), 8.25 (dd, $^3J_{(H,H)}$=7.4 Hz, $^3J_{(P,H)}$=15.6 Hz, 2H, ArH), 7.44–7.42 (m, 3H, ArH), 7.26 (d, $^3J_{(H,H)}$=8.2 Hz, 2H, ArH), 7.06 (d, $^3J_{(H,H)}$=8.2 Hz, 2H, ArH), 2.59 (t, $^3J_{(H,H)}$=7.2 Hz, 2H, CH_2), 1.60–1.56 (m, $^3J_{(H,H)}$=7.2 Hz, 2H, CH_2), 1.25–1.18 (m, 14H, CH_2), 0.85 (t, $^3J_{(H,H)}$=7.2 Hz, 3H, CH_3). ^{13}C NMR ($CDCl_3$, ppm): 167.3 (d, $^1J_{(P,C)}$=24.9 Hz, P–C), 145.4, 135.7, 134.8, 131.9 (d, $^2J_{(P,C)}$=13.5 Hz), 131.6, 130.8, 128.4 (d, $^3J_{(P,C)}$=13.5 Hz), 124.1, 35.6, 32.0, 31.3, 29.7, 29.5, 29.4, 29.3, 22.8, 14.2. ^{31}P NMR ($CDCl_3$, ppm): 30.2 (s, $J_{(P,Se)}$=702 Hz). ^{77}Se NMR ($CDCl_3$, ppm): −83.7 (d, $J_{(P,Se)}$=702 Hz). MS (ES$^-$, *m/z*), 525 [M−H]$^+$.

3.4.9. *N′-(4-Bromobenzyl)carbamidoyl(phenyl)-phosphinodiselenoic acid (**3c**)*

Orange solid (220 mg) in 47% yield from method B; mp 135–137 °C. Elemental analysis: Found C, 34.71; H, 3.30; N, 5.75. $C_{14}H_{16}BrN_2PSe_2$ requires C, 34.95; H, 3.35; N, 5.82. IR (KBr, ν_{max}/cm^{-1}): 3045 (m), 1636 (vs, $C{=}N$), 1557 (s, $C{=}N$), 1486 (m), 1434 (m), 1399 (w), 1249 (w), 1072 (m), 1010 (m), 809 (m), 747 (m), 689 (m), 624 (m), 559 (s, P–Se). ^1H NMR ($CDCl_3$, ppm): 8.52 (s, 2H, NH_2), 8.22 (d, $J_{(H,H)}$=6.9 Hz, 2H, ArH), 8.17 (dd, $J_{(H,H)}$=7.2 Hz, $^3J_{(P,H)}$=15.6 Hz, 2H, ArH), 8.05 (s, 1H, NH), 7.55–7.50 (m, 3H, ArH), 7.05 (d, $J_{(H,H)}$=6.9 Hz, 2H, ArH). ^{13}C NMR ($CDCl_3$, ppm): 166.9 (d, $^1J_{(P,C)}$=24.9 Hz), 135.2, 134.2, 134.0, 132.2 (d, $^2J_{(P,C)}$=19.7 Hz), 131.9, 131.8, 128.6 (d, $^3J_{(P,C)}$=13.5 Hz), 126.2, 123.7, 60.5. ^{31}P NMR ($CDCl_3$, ppm): 30.5 (s, $J_{(P,Se)}$=695 Hz). ^{77}Se NMR ($CDCl_3$, ppm): −78.2 (d, $J_{(P,Se)}$=695 Hz). MS (ES$^+$, *m/z*), 505 [M+Na]$^+$; (ES$^-$, *m/z*), 481 [M−H]$^+$.

3.4.10. *N′-(3-Phenylpropyl)carbamidoyl(phenyl)-phosphinodiselenoic acid (**3e**)*

Green solid (0.51 g), 29% yield form method B and 98% yield from method C; mp 140–141 °C. 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, $C{=}N$), 1490 (m), 1454 (m), 1434 (m), 1346 (m), 1303 (m), 1233 (m), 1083 (m), 1010 (m), 743 (s), 697 (s), 557 (s, $P{=}Se$). ^1H NMR (CD_2Cl_2, ppm): 8.75 (br s, 2H, NH_2), 8.24–8.15 (m, 2H, ArH), 7.52–7.43 (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 (ds, H, NH), 3.27 (t, $J_{(H,H)}$=6.4 Hz, 2H, NCH_2), 2.60 (t, $J_{(H,H)}$=6.4 Hz, 2H, $ArCH_2$), 2.03–1.94 (m, 2H, CH_2). ^{13}C NMR (CD_2Cl_2, ppm): 167.3 (d, $^1J_{(P,C)}$=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. ^{31}P NMR (CD_2Cl_2, ppm): 29.9 (s, $J_{(P,Se)}$=703 Hz). ^{77}Se NMR (CD_2Cl_2, ppm): −95.2 (d, $J_{(P,Se)}$=703 Hz). MS (ES$^+$, *m/z*), 453 [M+Na]$^+$; (ES$^-$, *m/z*), 429 [M−H]$^+$.

3.4.11. *N′-Phenethyl-N′-(methyl)carbamidoyl(phenyl)-phosphinodiselenoic acid (**3f**)*

Greenish white solid (0.52 g), 48% yield from method B and 99% yield from method C; mp 94–96 °C. 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, $C{=}N$), 1453 (w), 1435 (m), 1088 (m), 748 (m), 702 (m), 552 (s, $P{=}Se$). One pair of diastereomers: ^1H NMR (CD_3CN, ppm): 9.22 (s, 2H, NH_2), 8.01–7.94 (m, 2H, ArH), 7.47–7.45 (m, 3H, ArH), 7.28–7.16 (m, 3H, ArH), 6.95–6.93 (m, 2H, ArH), 3.77 (t, $J_{(H,H)}$=8.4 Hz, 2H, $PhCH_2$), 3.15 (s, 3H, CH_3), 2.47 (t, $J_{(H,H)}$=8.4 Hz, 2H, NCH_2). ^{13}C NMR ($CDCl_3$, ppm): 137.4, 131.2, 130.4, 130.2, 129.1, 128.8, 128.5, 126.7, 117.4, 54.8, 39.4, 32.2. ^{31}P NMR (CD_3CN, ppm): 27.4 (30%) (s, $J_{(P,Se)}$=700 Hz), 24.9 (70%) (s, $J_{(P,Se)}$=700 Hz). ^{77}Se NMR (DMF-d_7, ppm): 31.6 (70%) and 29.9 (30%) (d, $J_{(P,Se)}$=700 Hz). MS (ES$^+$, *m/z*), 453 [M+Na]$^+$; (ES$^-$, *m/z*), 429 [M−H]$^+$.

3.4.12. *1-Methyl-1-phenethylselenourea (**4f**)*

Pink white solid, 20% yield from method B and 99% yield from method C; mp 167–169 °C. IR (KBr, ν_{max}/cm^{-1}): 3375 (w), 3263 (m), 3166 (s), 1612 (s), 1528 (s), 1495 (w), 1452 (w), 1411 (w), 1366 (m), 1280 (m), 1006 (m), 750 (m), 699 (m, $C{=}Se$). ^1H NMR ($CDCl_3$, ppm): 7.31–7.25 (m, 3H, ArH), 6.24–6.22 (m, 2H, ArH), 4.14 (s, 3H, NCH_3), 3.46 (t, J=9.6 Hz, 2H, NCH_2), 2.97 (t, J=9.6 Hz, 2H, $PhCH_2$). ^{13}C NMR ($CDCl_3$, ppm): 207.1 ($C{=}Se$), 135.1, 128.9, 127.5, 126.8, 126.0, 37.25, 33.7, 31.0. ^{77}Se NMR (CD_3CN, ppm): 607.7. MS (ES$^+$, *m/z*), 265 [M+Na]$^+$. Accurate mass measurement [CI$^+$(NH_3), *m/z*]: 239.0425 [M+H]$^+$, calculated mass for $C_{10}H_{14}N_2Se$: 239.0422 (^{76}Se).

3.4.13. *1-Phenethyl-1-(propionyloxy)selenourea (**4h**)*

Slightly yellow powder in an yield of 91% based on **WR** from method B and 98% yield from method C; mp 110–112 °C. Elemental analysis: Found C, 47.91; H, 5.17; N, 9.13. $C_{12}H_{16}N_2O_2Se$ requires C, 48.17; H, 5.39; N, 9.36. IR (KBr, ν_{max}/cm^{-1}): 3327 (m), 3205 (w), 1715 (s), 1598 (s), 1372 (s), 1256 (s), 1196 (s), 994 (m), 899 (m), 769 (m), 705 (m), 656 (m, $C{=}Se$). ^1H NMR ($CDCl_3$, ppm): 10.47 (d,

$J_{(H,H)}$=7.2 Hz, 2H, ArH); 8.24 (d, $J_{(H,H)}$=7.2 Hz, 1H, ArH), 7.26 (d, $J_{(H,H)}$=7.2 Hz, 2H, ArH), 4.62 (t, $J_{(H,H)}$=7.9 Hz, 2H, $ArCH_2$), 4.15 (q, $J_{(H,H)}$=6.9 Hz, 2H, OCH_2), 3.06 (t, $J_{(H,H)}$=7.9 Hz, 2H, NCH_2), 1.30 (t, $J_{(H,H)}$=6.9 Hz, 3H, CH_3), 0.07 (s, 2H, NH_2). ^{13}C NMR ($CDCl_3$, ppm): 186.7 (C=Se), 154.7 (C=O), 138.5 (ArC), 129.1 (ArC), 128.6 (ArC), 126.6 (ArC), 64.2 (OCH_2), 54.2 (NCH_2), 34.9 ($ArCH_2$), 14.1 (CH_3). ^{77}Se NMR ($CDCl_3$, ppm): 382.1. MS (ES^+, m/z), 323 $[M+Na]^+$.

Acknowledgements

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

References and notes

1. (a) Bradner, W. T.; Clarke, D. A. *Cancer Res.* **1958**, *18*, 299–304; (b) Snider, B. B.; Duvall, J. R. *Org. Lett.* **2005**, *7*, 4519–4522.
2. Aberle, N. S.; Lessene, G.; Watson, K. G. *Org. Lett.* **2006**, *8*, 419–421.
3. Stephens, R. W.; Domeier, L. A.; Todd, M. G.; Nelson, V. A. *Tetrahedron Lett.* **1992**, *33*, 733–734.
4. Krief, A. In *Comprehensive Organometallic Chemistry*; Abel, E. W., Stone, F. G. A., Wilkinson, G., Eds.; Pergamon: 1995; Vol. 11, p 515.
5. Back, T. G. In *Encyclopaedia of Inorganic Chemistry*; King, R. B., Ed.; 1994; Vol. 7, p 3690.
6. Wirth, T. *Angew. Chem., Int. Ed.* **2000**, *39*, 3742–3751.
7. Hope, E. G.; Levason, W. *Coord. Chem. Rev.* **1993**, *122*, 109–116.
8. Hua, G.; Woollins, J. D. *Angew. Chem., Int. Ed.* **2008**, *48*, 1368–1377.
9. (a) Fitzmaurice, J. C.; Williams, D. J.; Wood, P. T.; Woollins, J. D. *J. Chem. Soc., Chem. Commun.* **1988**, 741–743; (b) Gray, I. P.; Bhattacharyya, P.; Slawin, A. M. Z.; Woollins, J. D. *Chem.—Eur. J.* **2005**, *11*, 6221–6227.
10. (a) Baxter, I.; Hill, A. F.; Malget, J. M.; White, A. J. P.; Williams, D. J. *Chem. Commun.* **1997**, 2049–2050; (b) Hill, A. F.; Malget, J. M. *Chem. Commun.* **1996**, 1177–1178; (c) Bhattacharyya, P.; Woollins, J. D. *Tetrahedron Lett.* **2001**, *42*, 5949–5951; (d) Bhattacharyya, P.; Slawin, A. M. Z.; Woollins, J. D. *Inorg. Chem. Commun.* **2004**, *7*, 1171–1174; (e) Bethke, J.; Karaghiosoff, K.; Wessjohann, L. A. *Tetrahedron Lett.* **2003**, *44*, 6911–6913.
11. Hua, G.; Li, Y.; Slawin, A. M. Z.; Woollins, J. D. *Org. Lett.* **2006**, *8*, 5251–5254.
12. (a) Darout, K. E. *Org. Lett.* **2005**, *7*, 203–205; (b) Foreman, M. St. J.; Slawin, A. M. Z.; Woollins, J. D. *J. Chem. Soc., Dalton Trans.* **1999**, 1175–1180; (c) Bhattacharyya, P.; Slawin, A. M. Z.; Woollins, J. D. *Chem.—Eur. J.* **2002**, *8*, 2705–2711; (d) Bhattacharyya, P.; Slawin, A. M. Z.; Woollins, J. D. *Angew. Chem., Int. Ed.* **2000**, *39*, 1973–1974; (e) Bhattacharyya, P.; Slawin, A. M. Z.; Woollins, J. D. *J. Organomet. Chem.* **2001**, *623*, 116–119; (f) Bhattacharyya, P.; Slawin, A. M. Z.; Woollins, J. D. *J. Chem. Soc., Dalton Trans.* **2001**, 300–302; (g) Bhattacharyya, P.; Novosad, J.; Phillips, J. R.; Slawin, A. M. Z.; William, D. J.; Woollins, D. J. *J. Chem. Soc., Dalton Trans.* **1995**, 1607–1613.
13. (a) Hua, G.; Li, Y.; Slawin, A. M. Z.; Woollins, J. D. *Eur. J. Inorg. Chem.* **2007**, 891–897; (b) Hua, G.; Li, Y.; Slawin, A. M. Z.; Woollins, J. D. *Chem. Commun.* **2007**, 1465–1468.
14. Hua, G.; Li, Y.; Slawin, A. M. Z.; Woollins, J. D. *Dalton Trans.* **2007**, 1477–1480.
15. Hua, G.; Woollins, J. D. *Tetrahedron Lett.* **2007**, *48*, 3677–3679.
16. Hua, G.; Li, Y.; Slawin, A. M. Z.; Woollins, J. D. *Angew. Chem., Int. Ed.* **2008**, *47*, 2857–2859.
17. (a) Axelle, R. C.; Sylvie, D.; Celine, P.; David, L. G.; Jean-Luc, B.; Roger, A.; Marie-Agnes, S.; Dennis, S.; Daniel, M. *J. Med. Chem.* **2002**, *45*, 944–954; (b) Hiroyo, K.; Masako, I.; Masahiro, S.; Keiro, H.; Keiko, Y.; Hiroko, S.; Tatsuhiro, T.; Tsutomu, I. *Helv. Chim. Acta* **2002**, *85*, 2636–2643; (c) Garmaise, D. L.; Uchiyama, A. *Can. J. Chem.* **1961**, *39*, 1054–1058; (d) Bi, X.; Lopez, C.; Bacchi, C. J.; Rattendi, D.; Woster, P. M. *Bioorg. Med. Chem. Lett.* **2006**, *16*, 3229–3232; (e) Bakunov, S. A.; Rukavishnikov, A. V.; Kachev, A. V. *Synthesis* **2000**, *8*, 1148–1153.
18. Hua, G.; Zhang, Q.; Li, Y.; Slawin, A. M. Z.; Woollins, J. D. *Dalton Trans.* **2008**, 5563–5566.
19. (a) Ogawa, A.; Miyaka, J.; Karasaki, Y.; Murai, S.; Sonoda, N. *J. Org. Chem.* **1985**, *50*, 384–386; (b) Al-Rubaie, A. Z.; Yousif, L. L.; Al-Hamad, A. J. H. *J. Organomet. Chem.* **2002**, *656*, 274–280.
20. (a) Karaghiosoff, K.; Eckstein, K. *Phosphorus, Sulfur Silicon Relat. Elem.* **1993**, *75*, 257–260; (b) Pilkington, M. J.; Slawin, A. M. Z.; William, D. J.; Woollins, J. D. *Heteroat. Chem.* **1990**, *1*, 351–355; (c) Kilian, P.; Bhattacharyya, P.; Slawin, A. M. Z.; Woollins, J. D. *Eur. J. Inorg. Chem.* **2003**, 1461–1467.
21. (a) Gray, I. P.; Slawin, A. M. Z.; Woollins, J. D. *Dalton Trans.* **2005**, 2188–2194; (b) Hua, G.; Li, Y.; Slawin, A. M. Z.; Woollins, J. D. *Tetrahedron* **2008**, *64*, 5442–5448.
22. (a) Jutzi, P.; Brusdielins, N.; Stammler, H. G.; Neumann, B. *Chem. Ber.* **1994**, *127*, 997–1001; (b) Asmus, S. M. F.; Bergstraber, U.; Regitz, M. *Synthesis* **1999**, 1642–1644; (c) Hitchcock, P. B.; Nixton, J. F.; Sakaray, N. *Chem. Commun.* **2000**, 1642–1643.
23. Parveen, S.; Kilian, P.; Slawin, A. M. Z.; Woollins, J. D. *Dalton Trans.* **2006**, 2586–2590.
24. Sheldrick, G. M. *SHELXTL 6.11*; Bruker AXS: Madison, WI, 2004.