Phosphorus Hydrazides as Building Blocks for Potential Photoaffinity Labels. Synthesis and Co-ordination Chemistry of Perfluoroaryl Azide Conjugates of Phenylphosphonothioic Dihydrazide†

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The phosphorus hydrazide $PhP(S)(NMeNH_2)_2$ **1** reacted with the azido functionalized aldehyde $4\text{-}N_3C_6F_4CHO$ to give a mixture of Schiff-base adducts with one or two perfluoroaryl azido substituents on **1**. However, the reaction with R'CHO (R = $4\text{-}O_2NC_6H_4$, $3\text{-}O_2NC_6H_4$ or $2,4\text{-}Me_2C_6H_3$) resulted in a considerable selectivity of incorporating one aromatic substituent in the terminal hydrazide unit of **1** *via* Schiff-base coupling to produce $PhP(S)(NMeNH_2)(NMeN{=}CHR')$ (R' = $4\text{-}O_2NC_6H_4$ **3**, $3\text{-}O_2NC_6H_4$ **4** or $2,4\text{-}Me_2C_6H_3$ **5**). These mono-Schiff-base adducts **3**–**5** undergo further Schiff-base coupling with azidotetrafluorobenzaldehyde to produce the azido-functionalized phosphorus hydrazides $PhP(S)(NMeN{=}CHC_6F_4N_3)(NMeN{=}CHR')$ (R' = $4\text{-}O_2NC_6H_4$ **7**, $3\text{-}O_2NC_6H_4$ **8** or $2,4\text{-}Me_2C_6H_3$ **9**). The ligating properties of the representative phosphorus hydrazides **2** and **9** with palladium(II) were investigated. The crystal structure of the complex $[PdCl_2\{PhP(S)(NMeNH_2)(NMeN{=}CHC_6F_4N_3\text{-}4)\}]$ reveals that the palladium(II) is bound in a chelating *cis* arrangement to the phosphorus chalcogenide and the hydrazine nitrogen *via* a five-membered metallacyclic framework: monoclinic, space group $P2_1/n$, a = 7.826(10), b = 18.051(20), c = 18.330(3) Å, β = 98.196(7)°, Z = 4, R = 0.038 and R' = 0.053.

There is a considerable current interest in the development of new multifunctional main-group compounds because of their usefulness in providing effective chelating features to radiometals of diagnostic and therapeutic importance for the detection and treatment of human cancer. Radiopharmaceuticals, like any other drug, tend to distribute uncharacteristically into various organs in the body and may result in excessive radiation damage to healthy cells. This has necessitated the development of targeting procedures so that the radiopharmaceutical biodistributes preferentially to certain organ(s) in the body or has greater affinity for certain parts of the body.[2] Certain proteins/peptides are known to have high affinity for specific antigens in the body. Recent studies demonstrate that the radiometal conjugates of these molecular vectors (peptides and proteins) localize at desired sites in the body.[3] A need to develop more sophisticated targeting techniques has resulted in a considerable interest in the study of fundamental main-group and transition-metal chemistry of novel ligand systems to achieve covalent attachment of biomolecules to the metallic isotope-bound ligand backbone.

Traditionally, different functional groups (*e.g.*, NCS, CO_2H, *etc.*) attached to ligand frameworks have been widely used as active sites for the covalent coupling of bifunctional chelates and bifunctional chelating agents to biomolecules. However, these conjugation methods have some serious drawbacks which include: (*a*) NCS groups are hydrolytically unstable and as a result cause lower conjugation yields and (*b*) the use of a CO_2H active site on a ligand system often involves the activation of this group using dicyclohexylcarbodiimide in the presence of triethylamine. These organic substrates may denature the protein prior to its intended use. Therefore, alternative methods to incorporate biomolecules on the ligand backbones are being sought. As part of our on-going studies in the development of new conjugation approaches, we are currently investigating the efficacy of using photochemical methods to incorporate ligands and radioisotope-bound ligands on to biomolecules. This method relies on photoactivation of an azide to produce a nitrene for insertion across C–H or C–N bonds of biomolecules.[4–6] Our recent studies have demonstrated that a functionalized perfluoroaryl azide upon photolysis generates nitrene species with subsequent insertion across the unactivated C–H bonds leading to the highest C–H insertion yields ever reported.[7] Therefore, if the azide is part of a radiometal-bound ligand system, the photochemically generated nitrene intermediate can conjugate the biomolecule *via* C–H insertion to produce a covalent linkage of a radiometal complex with the peptide(s)/proteins. Such an approach could be advantageous, particularly for those receptors which do not carry reactive functional groups for coupling, but surely contain carbon–hydrogen bonds into which the photolabel can be inserted through photolysis.

Phosphorus hydrazides have been shown to be useful ligands for transition metals and metallic radioisotopes of cancer diagnostic and therapeutic potential.[8–13] Therefore, a chemical connection between a phosphorus hydrazide and a photolabel (*e.g.* perfluoroaryl azides) may become a modality in the design

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Non-SI units employed: eV ≈ 1.60×10^{-19} J, barn = 10^{-28} m^2.

of new chelating agents capable of interacting with biomolecules photochemically while at the same time retaining the ability to complex with the metallic radioisotopes. Herein, we describe the fundamental main-group chemistry of linking phosphorus hydrazides and phosphorus hydrazides functionalized with perfluoroaryl azides. In addition, we also describe the ligating properties of these new systems with a palladium(II) precursor. The results from these studies may be used to generate the corresponding analogues with ^{109}Pd. Palladium-109 is a β-emitting radionuclide (1.02 MeV, 100%) which has many desirable nuclear properties for use in radioimmunotherapy. The availability of enriched ^{109}Pd makes feasible the production of high-yield ^{109}Pd by thermal neutron irradiation methods (σ = 12 barn, resonance integral 12 barn). The 1.02 MeV β-emission classifies ^{109}Pd as a medium-range β source suitable for tumour therapy.

Experimental

All the manipulations were carried out under a nitrogen atmosphere using standard Schlenk-tube techniques. The phosphorus hydrazide $PhP(S)(NMeNH_2)_2$ **1** was prepared by the reaction of $PhP(S)Cl_2$ with an excess of methylhydrazine,[14] and further purified by recrystallization from acetonitrile. 4-Azidotetrafluoro benzaldehyde was prepared according to the literature procedure.[5e] Nuclear magnetic resonance spectra were recorded on a Bruker WH-500 spectrometer, with chemical shifts reported in ppm downfield from $SiMe_4$ for ^{1}H and positive shifts downfield with respect to 85% H_3PO_4 as an external standard for ^{31}P. Infrared spectra were recorded using Nujol mulls and KBr cells on a Mattson Galaxy 3000 spectrophotometer. Elemental analyses for some of the new compounds were done by Oneida Research Services, New York.

Syntheses.—$PhP(S)(NMeNH_2)(NMeN{=}CHC_6F_4N_3\text{-}4)$ **2**. An equimolar solution of 4-azidotetrafluorobenzaldehyde (2.19 g, 10 mmol) in absolute ethanol (100 cm^3) was added dropwise (2 h) to a solution of the hydrazide **1** (2.3 g, 10 mmol) also in absolute ethanol (100 cm^3) cooled to −70 °C using an alcoholic slush bath. The mixture was stirred for 1 h before the solvent was removed *in vacuo* to obtain a sticky yellow solid. The solid was dissolved in the minimum volume of dichloromethane and precipitated using hexane. The precipitate was washed with diethyl ether several times and the residue dissolved in hot acetonitrile, cooled to −5 °C and crystallized several times to get the pure monosubstituted product (2.46 g, 60%), m.p. 122 °C (Found: C, 40.85; H, 3.15; N, 22.60. Calc. for $C_{15}H_{14}F_4N_7PS$: C, 41.75; H, 3.25; N, 22.75%).

Compounds $PhP(S)(NMeNH_2)(NMeN{=}CHC_6H_4R)$ (R = NO_2-4 **3** *or* NO_2-3 **4**) *and* $PhP(S)(NMeNH_2)(NMeN{=}CHC_6H_3Me_2\text{-}2,4)$. To a solution of hydrazide **1** in $CHCl_3$ was added dropwise (2 h) a $CHCl_3$ solution of the corresponding aldehydes (3-$NO_2C_6H_4CHO$, 4-$NO_2C_6H_4CHO$ or 2,4-$Me_2C_6H_3CHO$) in 1:1 stoichiometry. The reaction mixture was stirred for 3 h before the solvent was removed *in vacuo* to get mono-Schiff-base adducts **3**–**5**. Further purification of the adducts was achieved by recrystallization from hot acetonitrile: **3**, yield 82.7%, m.p. 125 °C (Found: C, 49.30; H, 4.80; N, 19.30. Calc. for $C_{15}H_{18}N_5O_2PS$: C, 49.60; H, 4.95; N, 19.30%); **4**, yield 87%, m.p. 107 °C (Found: C, 49.40; H, 4.85; N, 19.40. Calc. for $C_{15}H_{18}N_5O_2PS$: C, 49.60; H, 4.95; N, 19.30%); **5**, yield 85% (Found: C, 59.20; H, 6.70; N, 16.10. Calc. for $C_{17}H_{23}N_4PS$: C, 58.95; N, 6.65; N, 16.20%).

Compounds $PhP(S)(NMeN{=}CHC_6F_4N_3\text{-}4)_2$ **6** $PhP(S)(NMeN{=}CHC_6F_4N_3\text{-}4)(NMeN{=}CHC_6H_4R)$ (R = NO_2-4 **7** *or* NO_2-3 **8**) *and* $PhP(S)(NMeN{=}CHC_6F_4N_3\text{-}4)(NMeN{=}CHC_6H_3Me_2\text{-}2,4)$ **9**. A solution of 4-azidotetrafluorobenzaldehyde in $CHCl_3$ was slowly added dropwise to the mono-Schiff-base compounds **2**–**5** at room temperature. The mixture was stirred for 3 h before the solvent was removed *in vacuo* to obtain **6**–**9**, respectively, as microcrystalline solids. The final purification was done by dissolving the crude products in dichloromethane and precipitating using hexane. Recrystallization of **6**–**9** was performed in hot acetonitrile: **6**, yield 83%, m.p. 104 °C (Found: C, 41.30; N, 2.10; N, 22.40. Calc. for $C_{22}H_{13}F_8N_{10}PS$: C, 41.75; H, 2.05; N, 22.15%); **7**, yield 81%, m.p. 68 °C (Found: C, 46.65; H, 3.15; N, 19.65. Calc. for $C_{22}H_{17}F_4N_8O_2PS$: C, 46.80; H, 3.00; N, 19.85%); **8**, yield 65%, m.p. 54 °C (Found: C, 46.80; H, 3.00; N, 19.80. Calc. for $C_{22}H_{17}F_4N_8O_2PS$: C, 46.80; H, 3.00; N, 19.85%); **9**, yield 83%, m.p. 140 °C (Found: C, 52.65; H, 4.00; N, 17.90. Calc. for $C_{24}H_{22}F_4N_7PS$: C, 52.65; H, 4.00; N, 17.90%).

Palladium complexes. A solution of $[PdCl_2(PhCN)_2]$ (0.862 g, 2.24 mmol) in dichloromethane (50 cm^3) was added dropwise (10 min) to a solution of mono Schiff-base **2** (0.968 g, 2.24 mmol) in dichloromethane (50 cm^3). The mixture was stirred for 3 h and the solvent partially removed *in vacuo*. The concentrated mixture was treated with hexane to precipitate $[PdCl_2\{PhP(S)(NMeNH_2)(NMeN{=}CHC_6F_4N_3\text{-}4)\}]$. The precipitate was washed two times with hexane (10 × 2 cm^3) to remove benzonitrile and the resulting orange-brown precipitate dissolved in hot acetonitrile and evaporated slowly at room temperature to obtain orange-red crystals (1.05 g, 85%), m.p. 122 °C (decomp.) (Found: C, 30.05; H, 2.25; N, 15.55. Calc. for $C_{15}H_{14}Cl_2F_4N_7PPdS$: C, 29.60; H, 2.30; N, 16.10%).

The complex $[PdCl_2\{PhP(S)(NMeN{=}CHC_6F_4N_3\text{-}4)(NMeN{=}CHC_6H_3Me_2\text{-}2,4)\}]$ was prepared analogously, yield 85%, m.p. 135 °C (decomp.) (Found: C, 39.60; H, 3.10; N, 13.80. Calc. for $C_{24}H_{22}Cl_2F_4N_7PPdS$: C, 39.75; H, 3.05; N, 13.55%).

X-Ray Data Collection and Processing.—Orange crystals of $[PdCl_2\{PhP(S)(NMeNH_2)(NMeN{=}CHC_6F_4N_3\text{-}4)\}]\cdot EtOH$ suitable for X-ray diffraction were obtained from slow evaporation of its ethanol solution. The data were collected on an Enraf–Nonius CAD-4 diffractometer with Cu-Kα radiation and a graphite monochromator at 22(1) °C. Crystal data and details of data collection are listed in Table 3. The cell dimensions were obtained from a least-squares fit to setting angles of 25 reflections with the 2θ angle in the range 20.0–30.0°. The crystal exhibited no significant decay under X-ray irradiation.

The structure was solved by direct methods and subsequently refined by the full-matrix least-squares method minimizing $\Sigma w(|F_o|)^2$, where $w^{-1} = \{\sigma(\text{counting}) + [0.008(F_o)^2/4F_o]\}$. Atomic scattering factors which included anomalous scattering contributions were from ref. 15. All hydrogen atoms in the structure were located in Fourier-difference maps and refined with fixed isotropic thermal parameters. The ethanol is disordered in such a way that the CH_2 is present in two principal positions and the final model includes these at 0.6 and 0.4 occupancies. The geometry of this solvent molecule is not ideal and does not present any surprising or unusual features. The final cycle of the least-squares refinement gave an agreement factor R of 0.038. The final positional parameters for all non-hydrogen atoms are listed in Table 4. The programs used for the crystallographic computations are reported in ref. 16.

Additional material available from the Cambridge Crystallographic Data Centre comprises H-atom coordinates, thermal parameters and remaining bond lengths and angles.

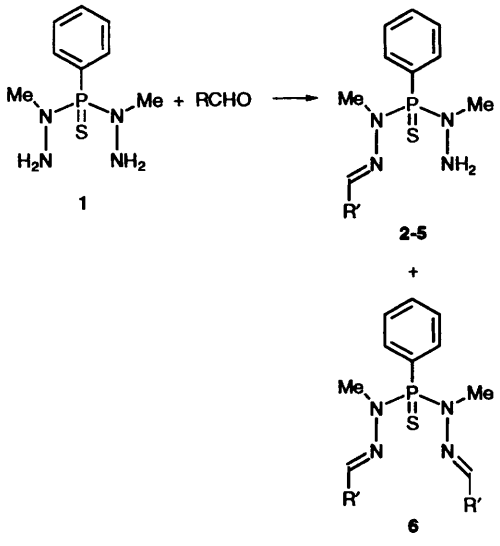
Results and Discussion

Synthesis of Azido-functionalized Phosphorus Hydrazides.—The selective introduction of one perfluoroaryl azide functionality on the phosphorus hydrazide $PhP(S)(NMeNH_2)_2$ **1** (Scheme 1) leaves the phosphorus chalcogenide (P=S) and one of the hydrazide sites for ligating interactions with a metal (and also metallic isotopes) while providing the N_3 group for photoaffinity labelling with biomolecules. However, the Schiff-base coupling reaction of azidoperfluoro benzaldehyde

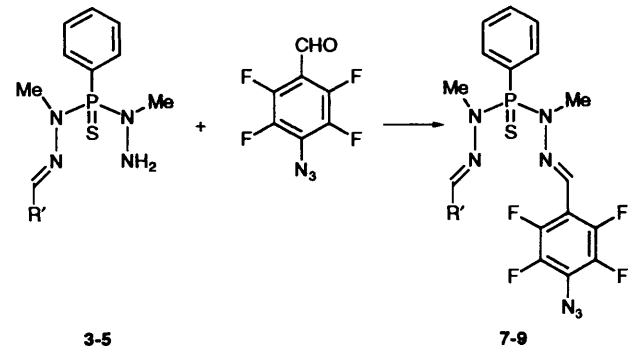
Table 1 Proton[a] and ^{31}P[b] NMR spectroscopic data

Compound	$\delta(^1H)(^3J_{P-H}/Hz)$	$\delta(^{31}P)$
1 $PhP(S)(NMeNH_2)_2$	2.84 (11.6)	86.7
2 $PhP(S)(NMeNH_2)(NMeN{=}CHC_6F_4N_3\text{-}4)$	3.25 (8.4) 2.95 (11.9)	82.7
3 $PhP(S)(NMeNH_2)(NMeN{=}CHC_6H_4NO_2\text{-}4)$	3.35 (8.5) 2.92 (12.2)	82.7
4 $PhP(S)(NMeNH_2)(NMeN{=}CHC_6H_4NO_2\text{-}3)$	3.31 (8.7) 2.85 (12.4)	83.7
6 $PhP(S)(NMeN{=}CHC_6F_4N_3\text{-}4)_2$	3.2 (9.6)	80.3
7 $PhP(S)(NMeN{=}CHC_6H_4NO_2\text{-}4)(NMeN{=}CHC_6F_4N_3\text{-}4)$	3.29 (9.2) 3.24 (9.3)	80.8
8 $PhP(S)(NMeN{=}CHC_6H_4NO_2\text{-}3)(NMeN{=}CHC_6F_4N_3\text{-}4)$	3.24 (9.3) 3.30 (9.1)	80.9
9 $PhP(S)(NMeN{=}CHC_6H_3Me_2\text{-}2,4)(NMeN{=}CHC_6F_4N_3\text{-}4)$	3.22 (9.8) 3.19 (9.0)	79.5
$[PdCl_2\{PhP(S)(NMeNH_2)(NMeN{=}CHC_6F_4N_3\text{-}4)\}]$	3.69 (9.8) 2.97 (9.7)	88.1
$[PdCl_2\{PhP(S)(NMeN{=}CHC_6F_4N_3\text{-}4)(NMeN{=}CHC_6H_3Me_2\text{-}2,4)\}]$	3.80 (10.7) 3.62 (9.5)	94

[a] Spectra recorded in $CDCl_3$ or Me_2SO; ppm *vs.* $SiMe_4$. [b] In ppm *vs.* 85% H_3PO_4. Values quoted are those determined at normal probe temperatures.



Scheme 1 R′ = $C_6F_4N_3$-4 **2** or **6**, $C_6H_4NO_2$-4 **3**, $C_6H_4NO_2$-3 **4** or $C_6H_3Me_2$-2,4 **5**

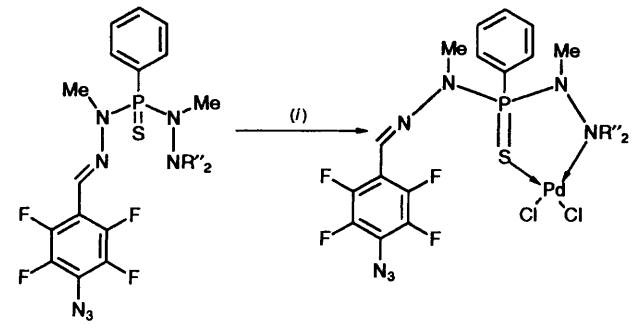


Scheme 2 R′ = $C_6H_4NO_2$-4 **3** or **7**, $C_6H_4NO_2$-3 **4** or **8**, $C_6H_3Me_2$-2,4 **5** or **9**

4-$N_3C_6F_4CHO$ with **1** even at −70 °C, generally, produced a mixture of the mono and bis adducts. In general, bis adducts carrying two photoactivable moieties are not useful in labelling biomolecules because they may induce cross-linking and aggregation and subsequently destroy their biospecificity. Hence, the selective incorporation of one perfluoroaryl azide on **1** was achieved by first blocking one of the NH_2 groups followed by subsequent Schiff-base reaction with azidoperfluorobenzaldehyde as shown in Scheme 2. It is important to note that the Schiff-base reactions of 4-$O_2NC_6H_4CHO$, 3-$O_2NC_6H_4CHO$ and 2,4-$Me_2C_6H_3CHO$ with **1** at 0 °C selectively produced the corresponding mono adducts in >80% yields. These monosubstituted phosphorus hydrazides $PhP(S)(NMeNH_2)(NMeN{=}CHR')$ (R′ = $C_6F_4N_3$-4 **2**, $C_6H_4NO_2$-4 **3**, $C_6H_4NO_2$-3 **4** or $C_6H_4Me_2$-2,4 **5**) were purified through recrystallization from acetonitrile prior to their reactions with 4-$N_3C_6H_4CHO$ to produce the corresponding azido-substituted bis adducts **6–9** respectively, as in Scheme 2. Compounds **2–9** represent a new class of functionalized phosphorus hydrazides and have been fully characterized by C, H and N analysis and ^{31}P and ^1H NMR spectroscopy (Table 1). Hydrazine derivatives containing aliphatic or aromatic substituents (*e.g.* $R^1R^2N\text{-}NH_2$; R^1 and R^2 = aliphatic or aromatic groups), generally, show instability towards air and water. However, the phosphorus(v)-functionalized hydrazides **2–9** are kinetically inert and can readily be handled in the open air. Therefore, the reactions outlined in Scheme 2 provide novel synthetic strategies to stabilize hydrazine backbones for subsequent use in aqueous media for potential radiopharmaceutical applications.

Co-ordination Chemistry of Azido-functionalized Phosphorus Hydrazides.—The reactions of the new azido-functionalized phosphorus hydrazides with a palladium(II) precursor have been investigated as models to the corresponding reactions of these compounds with ^{109}Pd. For example, the interaction of phosphorus hydrazides **2** and **9** with $[PdCl_2(PhCN)_2]$ in dichloromethane produced the complexes $[PdCl_2\{PhP(S)(NMeNH_2)(NMeN{=}CHC_6F_4N_3\text{-}4)\}]$ and $[PdCl_2\{PhP(S)(NMeN{=}CHC_6F_4N_3\text{-}4)(NMeN{=}CHC_6H_3Me_2\text{-}2,4)\}]$ respectively, in 85% yield (Scheme 3). The chemical constitutions as established by C, H and N analysis showed that these complexes have one hydrazide unit per metal centre. They are air-stable and dissolve readily in ethanol–water. The IR spectra consisted of an intense band at 2123 and 2128 cm^{-1}, respectively, indicating the presence of the azide group. These bands were nearly identical to those observed in the IR spectra of the parents **2** and **9** suggesting that the azido functionalities in the complexes are not involved in bonding interactions with the Pd. Further characterization was provided by the ^1H and ^{31}P NMR spectroscopic data summarized in Table 1.

The ^{31}P NMR data for all the compounds in Table 1 indicate



Scheme 3 R″ = H, R″$_2$ = $CHC_6H_3Me_2$-2,4. (*i*) $[PdCl_2(PhCN)_2]$

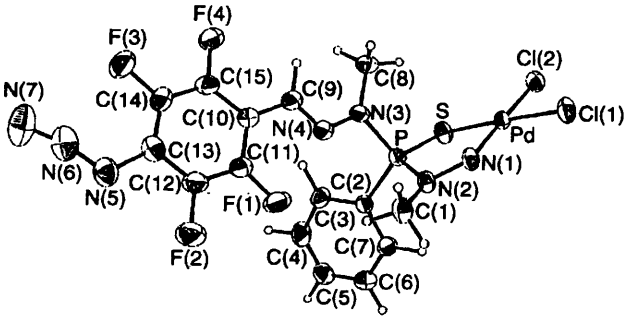


Fig. 1 An ORTEP representation of $[PdCl_2\{PhP(S)(NMeNH_2)(NMeN{=}CHC_6F_4N_3\text{-}4)\}]$. The thermal ellipsoids are drawn at the 50% probability level

Table 2 Bond distances (Å) and angles (°) for $[PdCl_2\{PhP(S)(NMeNH_2)(NMeN{=}CHC_6F_4N_3\text{-}4)\}]$

Pd–Cl(1)	2.318(1)	N(1)–N(2)	1.435(5)
Pd–Cl(2)	2.297(2)	N(2)–C(1)	1.461(7)
Pd–S	2.282(1)	N(3)–N(4)	1.374(6)
Pd–N(1)	2.026(4)	N(3)–C(8)	1.456(7)
S–P	1.993(2)	N(4)–C(9)	1.280(7)
P–N(2)	1.646(4)	N(5)–N(6)	1.234(10)
P–N(3)	1.675(5)	N(5)–C(13)	1.411(7)
P–C(2)	1.789(5)	N(6)–N(7)	1.138(11)
C(11)–Pd–Cl(2)	93.98(6)	N(2)–P–C(2)	104.5(2)
C(11)–Pd–S	177.70(6)	N(3)–P–C(2)	108.2(2)
C(11)–Pd–N(1)	86.7(1)	Pd–N(1)–N(2)	118.1(3)
C(12)–Pd–S	87.70(5)	P–N(2)–N(1)	116.4(3)
C(12)–Pd–N(1)	178.6(1)	P–N(2)–C(1)	123.6(3)
S–Pd–N(1)	91.6(1)	P–N(3)–N(4)	110.3(3)
Pd–S–P	96.89(7)	P–N(3)–C(8)	126.3(4)
S–P–N(2)	107.8(2)	N(3)–N(4)–C(9)	119.2(4)
S–P–N(3)	109.6(2)	N(6)–N(5)–C(13)	116.8(6)
S–P–C(2)	111.9(2)	N(5)–N(6)–N(7)	169.0(8)
N(2)–P–N(3)	114.8(2)		

modest upfield shifts (3–4 ppm) for the monosubstituted Schiff-base adducts **2**–**5** as compared to the free **1**. The disubstituted Schiff-base adducts **6**–**9** showed increased upfield shifts (6–7 ppm) as compared to **1**. However, the palladium complexes showed modest deshielding as compared to the parents **2** and **9** respectively. The $^3J_{P-H}$ values [due to H_3C–N–*P*(S)] of **2**–**9** are ≈2–3 Hz lower than that of **1** (Table 1). This may be rationalized in terms of an electronic effect which, presumably, decreases the s character across the P–N–CH_3 skeleton upon introduction of perfluoroaryl substituents at the terminal nitrogen *via* the Schiff base coupling reactions outlined in Schemes 1 and 2.

To obtain conclusive proof for the structures proposed in Scheme 3 an X-ray structural analysis of a representative complex $[PdCl_2\{PhP(S)(NMeNH_2)(NMeN{=}CHC_6F_4N_3\text{-}4)\}]$ was carried out. The ORTEP[17] plot is shown in Fig. 1 and the selected bonding parameters are summarized in Table 2. The structure comprises the five-membered metallacyclic unit involving *cis* co-ordination of the P=S unit and the terminal hydrazido nitrogen in a square-planar geometry around the palladium. The Pd–S (2.282 Å) and Pd–N (2.026 Å) bond

Table 3 Crystallographic data

Formula	$C_{15}H_{14}Cl_2F_4N_7PPdS{\cdot}C_2H_6O$
M	654.7
Crystal size/mm	0.10 × 0.25 × 0.45
Crystal system	Monoclinic
Space group	$P2_1/n$
a/Å	7.826(1)
b/Å	18.051(2)
c/Å	18.330(3)
β/°	98.196(7)
U/Å^3	2563.0(6)
F(000)	1304
Z	4
D_c/g cm^{-3}	1.697
$2\theta_{max}$/°	120
μ/cm^{-1}	97.6[a]
hkl ranges	−8 to 8, 0–20, 0–20
Total data	4118
Unique data[b]	3802
R[c]	0.038
R′[d]	0.053

[a] Transmission factors (φ scans) 0.74–1.00. [b] Observed data [$I > 2\sigma(I)$] 3109. [c] $\Sigma(|F_o| - |F_c|)/\Sigma|F_o|$. [d] $[\Sigma w(|F_o| - |F_c|)^2/\Sigma|F_o|^2]^{\frac{1}{2}}$, $w^{-1} = [\sigma^2|F_o| + 0.0008(F_o)]$.

Table 4 Atomic positional coordinates with estimated standard deviations in parentheses

Atom	*x*	*y*	*z*
Pd	0.519 69(5)	0.641 747(22)	0.495 868(20)
Cl(1)	0.523 32(23)	0.560 15(8)	0.398 48(8)
Cl(2)	0.753 04(19)	0.708 23(10)	0.469 00(8)
S	0.504 31(19)	0.722 36(8)	0.590 61(8)
P	0.339 07(17)	0.663 77(7)	0.640 66(7)
F(1)	0.016 7(5)	0.528 9(3)	0.768 48(23)
F(2)	−0.174 3(5)	0.463 2(3)	0.855 66(25)
F(3)	0.321 3(5)	0.391 91(23)	1.015 26(21)
F(4)	0.516 5(4)	0.459 59(21)	0.929 15(20)
N(1)	0.310 2(6)	0.585 35(23)	0.519 16(22)
N(2)	0.223 8(6)	0.612 09(23)	0.577 94(22)
N(3)	0.447 4(5)	0.616 75(25)	0.711 35(24)
N(4)	0.334 3(5)	0.579 96(25)	0.749 50(24)
N(5)	−0.053 4(8)	0.395 3(3)	0.980 0(3)
N(6)	0.004 1(9)	0.370 2(3)	1.041 2(4)
N(7)	0.030 3(12)	0.344 2(4)	1.098 3(4)
C(1)	0.075 9(8)	0.567 8(3)	0.592 4(3)
C(2)	0.184 0(6)	0.721 7(3)	0.675 7(3)
C(3)	0.195 9(8)	0.739 6(3)	0.750 4(3)
C(4)	0.081 6(9)	0.790 1(4)	0.771 0(3)
C(5)	−0.039 7(9)	0.823 2(4)	0.720 1(4)
C(6)	−0.053 5(8)	0.804 4(3)	0.647 5(4)
C(7)	0.059 7(7)	0.754 5(3)	0.624 5(3)
C(8)	0.632 3(7)	0.602 6(4)	0.723 7(3)
C(9)	0.393 8(7)	0.535 5(3)	0.801 3(3)
C(10)	0.277 9(7)	0.497 2(3)	0.845 2(3)
C(11)	0.097 7(8)	0.495 9(3)	0.828 5(4)
C(12)	−0.001 8(7)	0.461 2(4)	0.874 8(4)
C(13)	0.067 2(8)	0.426 6(3)	0.938 6(3)
C(14)	0.243 3(8)	0.426 7(3)	0.954 0(3)
C(15)	0.345 4(7)	0.460 4(3)	0.909 4(3)
O(S1)	0.965 3(6)	0.388 9(3)	0.596 1(3)
C(S2)*	0.961(3)	0.367 8(14)	0.679 7(15)
C(S2′)*	0.919 7(19)	0.351 3(9)	0.660 0(8)
C(S3)	0.865 1(12)	0.281 5(6)	0.651 3(7)

* C(S2) and C(S2′) are disordered, with occupancies 0.4 and 0.6, respectively.

lengths are in the normal range.[8-10] The presence of co-ordinated hydrazine ($MeN-NH_2$) and unco-ordinated Schiff-base hydrazine ($MeN-N=CHC_6F_4N_3$-4) within the same molecule has allowed us to make some internally consistent comparisons of bonding features. For example, the P–N bond (1.646 Å) in the five-membered metallacyclic unit is modestly shorter compared to that (1.675 Å) in the unco-ordinated part of the molecule. There is some bond lengthening observed in the P=S bond (1.993 Å) in **10** compared to the distance (1.942 Å) in the free unsubstituted phosphorus hydrazide precursor **1**.[18] This elongation is consistent with co-ordination of the phosphorus chalcogenide unit. Interestingly, the Pd–S–P bond angle (96.89°) is very narrow, a feature recently observed in a number of related metal complexes of phosphorus hydrazides.[8-11]

Conclusion

New synthetic strategies for the selective incorporation of photolabels (*e.g.* perfluoroaryl azides) into multifunctional chelating agents have been developed. The fundamental co-ordination chemistry of azido-functionalized phosphorus hydrazides with a palladium(II) precursor as demonstrated in the present investigation may be viewed as a model for the subsequent extension of this chemistry to ^{109}Pd. The application of photochemical methods to incorporate compounds **2–5** and their radiometal-bound complexes into biomolecules will form the basis of our future investigations.

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