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Nucleophilic addition to dimethylvinylphosphine sulfide as a convenient route to polydentate ligands containing the 2-dimethylphosphinoethyl unit

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Abstract—The synthesis of a range of new phosphine-containing polydentate ligands has been achieved by addition of sulfur and nitrogen nucleophiles to dimethylvinylphosphine sulfide, followed by reduction of the resulting phosphine sulfides with lithium aluminium hydride.

1. Introduction

Metal complexes containing phosphine ligands have a wide range of uses including both medical and industrial applications. Phosphines are known to coordinate well to a range of metals and their inclusion in polydentate ligands can facilitate complex formation in some circumstances. However, the tendency of alkyl substituted phosphines to oxidise in air makes it difficult to prepare pure samples of some complex phosphine-containing polydentate ligands and this has often inhibited the synthesis of polydentate ligands containing trialkylphosphine centres in favour of those containing diphenylphosphino groups.

Our interest in phosphine-containing polydentate ligands developed from our work on ^{99m}Tc-based radiopharmaceutical imaging agents.[1] Here, the ligand must be prepared in a high state of purity and the overall complex must have an appropriate lipophilicity if it is to exhibit a useful biodistribution. In this context the presence of phenyl substituents on the phosphorus is highly undesirable due to the high lipophilicity of the resulting systems while the incorporation of a terminal dimethylphosphino group is often highly desirable. In some cases, such as the bisphosphines we have prepared as potential myocardial imaging agents[2,3] incorporation of the dimethylphosphino group was achieved by nucleophilic substitution of appropriately substituted alkyl halides by the dimethylphosphide anion. However, this latter material is particularly unpleasant to handle and it often proved necessary to purify the resulting ligand via temporary formation of the corresponding sulfide or oxide in order to obtain material of sufficient purity for subsequent testing.

We now report a convenient route to a range of new polydentate ligands containing the dimethylphosphino group based on the use of dimethylvinylphosphine sulfide **1** as the precursor for the 2-dimethylphosphinoethyl unit. Previous workers[4] have reported the use of this compound in the synthesis of a number of polyphosphine ligands. We have exploited the susceptibility of the dimethylvinylphosphine sulfide to nucleophilic attack to include the use of both sulfur and nitrogen nucleophiles, thus offering scope for the synthesis of a wide range of new polydentate phosphine ligands such as those shown in Scheme 1 and Figure 1.

2. Results and discussion

In general, the nucleophilic additions to dimethylvinylphosphine sulfide **1** were carried out in ethanol and while the addition of the more nucleophilic thiolate anions could be achieved at room temperatures, addition of aliphatic amines usually required an extended period of heating under reflux. Aromatic amines were found to be unreactive towards **1** under these conditions, but they did react rapidly if first converted into their amide anions by the action of

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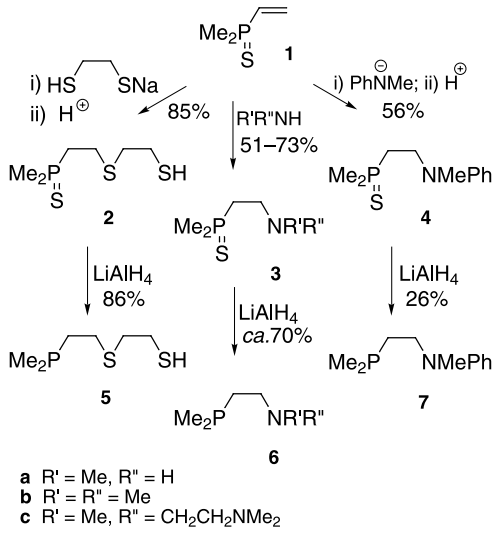


Scheme 1.

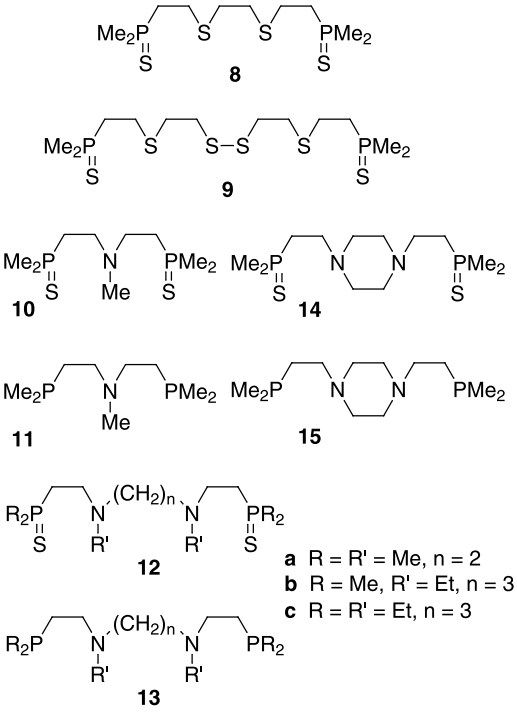


Figure 1.

n-butyllithium. Thus, for example, the lithium salt of methylaniline readily added to **1** to give the phosphine sulfide **4**.

In some cases reported here, reaction of more than one dimethylvinylphosphine sulfide molecule with the nucleophile is possible, although in general we found that this could be avoided if the nucleophile was kept in excess. This approach enabled the preparation of the phosphine sulfide **2** to be achieved from the thiolate of ethane-1,2-dithiol without significant formation of the bis(phosphine sulfide) **8**, and likewise the formation of the phosphine sulfide **3a** rather than **10** from the reaction of **1** with methylamine.

The phosphine sulfides produced in these studies were very stable, often crystalline solids, which could be readily purified. Reduction of these materials with reducing agents such as lithium aluminium hydride gave the corresponding phosphine ligands in good yield and in a high state of purity.

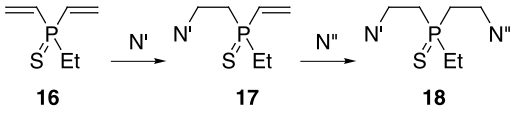
Additional support of the structure of the polydentate phosphine ligands produced in this way was obtained by adding sulfur, which led to regeneration of the phosphine sulfide precursors.

It should be noted that some of the phosphine ligands were found to readily co-distil with the dioxane used as the solvent in the reduction step. This could result in significant loss of the phosphine ligand from the distillation flask unless particular care was taken during the distillation. An alternative approach was to convert the phosphine ligand into its hydrochloride salt before removing the dioxane. The phosphine was then regenerated and recovered via extraction into diethyl ether. Fortunately, in general, this was unnecessary, as a dioxane solution of the phosphine ligand was suitable for our purposes.

We have also prepared other dialkylvinylphosphine sulfides for use in ligand synthesis. Thus, for example, diethylvinylphosphine sulfide was prepared by an analogous route to that used for the dimethyl analogue **1** and used to prepare the bisphosphine **12c**.

Preliminary work has also been carried out on the use of alkyldivinylphosphine sulfides such as **16**,[5] for the preparation of polydentate ligands containing a trialkylphosphine site at a non-terminal position.

We have already established that it is possible to react **16** with *N*,*N*,*N*′-trimethylethylenediamine to give **17** ($N'=$ $NMeCH_2CH_2NMe_2$) and that this can be converted into **18** ($N'=N''=NMeCH_2CH_2NMe_2$) in a subsequent step (Scheme 2). The stepwise addition of two different nucleophiles to the divinylphosphine sulfide **16** should therefore provide a route for the preparation of a wide range of new unsymmetrical ($N'\neq N''$) polydentate ligand systems. This is currently being investigated.



Scheme 2.

3. Conclusions

The susceptibility of dialkylvinylphosphine sulfides, such as **1**, to nucleophilic attack by both sulfur and nitrogen nucleophiles can be exploited to provide a convenient route for the synthesis of a wide range of new phosphine-containing polydentate ligands via the initial formation of the corresponding air-stable phosphine sulfide precursors. The range of ligands that are accessible by this approach can also be extended by the stepwise addition of two nucleophilic units to an alkyldivinylphosphine sulfide such as **16**.

4. Experimental

4.1. General

NMR spectra were recorded in $CDCl_3$ (on JEOL GSX270, FX100, PMX60 and Bruker AMX 600 spectrometers), dm, doublet of multiplets. Melting points were taken in open capillaries on an electrically heated Buchi SMP-20 melting point apparatus and are uncorrected. Elemental analyses were obtained on a Carlo Erba 1106 Elemental Analyser.

4.1.1. Dimethylvinylphosphine sulfide (1). Dimethylvinylphosphine sulfide was prepared by a previously reported procedure.[4]

4.1.2. Diethylvinylphosphine sulfide. Diethylvinylphosphine sulfide was obtained from diethylphosphinothioylbromide by the procedure used to prepare the corresponding dimethyl analogue **1** and isolated as a colourless oil, (0.93 g, 20% overall yield after 3 steps), bp 44 °C, 0.05 mmHg, (lit.[6] bp 98–99 °C, 1.5 mmHg). δ_P ($CDCl_3$) 48.5; δ_H (270 MHz, $CDCl_3$), 0.81 (6H, td, J_{P-H}= 19.3 Hz, J_{H-H}=7.4 Hz, CH_2*Me*), 1.57 (4H, dq, J_{P-H}= 11.4 Hz, J_{H-H}=7.4 Hz, CH_2), 5.99 (3H, m, CH=CH_2); δ_C ($CDCl_3$), 5.77 (d, J_{P-C}=4.2 Hz, CH_2*Me*), 23.9 (d, J_{P-C}= 56.1 Hz, CH_2–P), 129.1 (d, J_{P-C}=69.5 Hz, P–CH), 135.3 (s, CH=*CH_2*). EI-MS: 148 ($[M]^+$, 37%), 147 (92), 120 (84), 92 (100), 63 (52), 57 (35). ESI-HRMS: Found $[M+Na]^+$ 171.0368, $[C_6H_{13}PS+Na]^+$ requires 171.19772.

4.1.3. 2-(2-Dimethylphosphinothioylethylsulfanyl)-ethanethiol (2). 1,2-Dimercaptoethane (20 g, 213 mmol) was added to a solution of sodium ethoxide, prepared by adding sodium (1.5 g, 65 mmol) to ethanol (300 cm^3). The mixture was stirred for 1 h at room temperature and then cooled in ice before dimethylvinylphosphine sulfide **1**[4] (8 g, 66 mmol) was added. The mixture was allowed to warm to room temperature and left to stir overnight. The solvent and excess dithiol were removed under reduced pressure and water (250 cm^3) was added. The mixture was acidified by addition of hydrochloric acid and extracted with chloroform (3×200 cm^3). The chloroform extracts were dried with anhydrous $MgSO_4$, filtered and the solvent evaporated to give the phosphine sulfide **2** (12 g, 85%) as a colourless oil, containing a small quantity of the bis(phosphine sulfide) **8**. The phosphine sulfide **2** was further purified by distillation (bp 155–160 °C at 0.001 mmHg), although care was needed since some decomposition occurred at higher temperatures. δ_P ($CDCl_3$) 36.0; δ_H (270 MHz, $CDCl_3$) 1.77 (6H, d, J_{PH}= 13 Hz, P(S)Me_2), 2.10–2.20 (2H, m, α-CH_2), 2.72–2.95 (6H, m, β-CH_2 and SCH_2CH_2S); δ_C ($CDCl_3$) 21.1 (d, J_{PC}= 54 Hz, P(S)Me_2), 24.4 (CH_2), 24.8 (d, J_{PC}=2 Hz, β-CH_2), 34.3 (d, J_{PC}=49 Hz, α-CH_2), 36.0 (CH_2).

On prolonged exposure to the air the thiol **2** (R=CH_2CH_2-SH) oxidised to the corresponding disulfide **9**, a colourless waxy solid (Found: C, 33.52; H, 6.5. $C_{12}H_{28}P_2S_6$ requires C, 33.8; H, 6.6%). δ_P ($CDCl_3$) 36.2; δ_H (270 MHz, $CDCl_3$) 1.78 (12H, d, J_{PH}=13 Hz, P(S)Me_2), 2.12–2.22 (4H, m, α-CH_2) 2.92 (8H, br s, SCH_2CH_2S) 2.87–2.97 (4H, m, β-CH_2); δ_C ($CDCl_3$) 21.3 (d, J_{PC}=54 Hz, P(S)Me_2), 25.2 (d, J_{PC}= 2 Hz, β-CH_2), 31.6 (CH_2), 34.6 (d, J_{PC}=50 Hz, α-CH_2), 38.3 (CH_2).

4.1.4. 2-(2-Dimethylphosphinoethylsulfanyl)ethanethiol (5). The following reduction procedure and subsequent work-up was carried out in an inert atmosphere of nitrogen using degassed solvents. To a suspension of lithium aluminium hydride (2.2 g, 56 mmol) in dry dioxane (200 cm^3) was added 2-(2-dimethylphosphinothioylethylsulfanyl)ethane-thiol **2** (6 g, 28 mmol), and the mixture heated under reflux for 24 h (N.B. After a short initiation period a vigorous exothermic reaction often occurs which may necessitate cooling the reaction mixture). The mixture was allowed to cool and 25% aqueous dioxane (10 cm^3) was added dropwise. Aqueous sodium hydroxide (5 cm^3, 2 M) was then added followed by water (7 cm^3). The resulting mixture was filtered through a glass sinter and the solvent was removed under reduced pressure (50 °C at 40 mmHg). The residue, which contained a little solid, was redissolved in dry dioxane, filtered, and the solvent then removed under reduced pressure (50 °C at 40 mmHg) to give the phosphine **5** (ca. 4.5 g, 86%) containing a small quantity of solvent. δ_P ($CDCl_3$) −50.2; δ_H (60 MHz, $CDCl_3$) 0.94 (6H, d, J_{PH}=2 Hz, PMe_2), 1.40–1.68 (2H, m, β-CH_2), 1.70 (1H, br s, SH), 2.38–2.78 (6H, m, CH_2); δ_C ($CDCl_3$) 13.8 (d, J_{PC}=13 Hz, PMe_2), 24.7 (CH_2), 28.5 (d, J_{PC}=18 Hz, α-CH_2), 32.1 (d, J_{PC}=13 Hz, β-CH_2), 36.1 (CH_2).

4.1.5. *N*-(2′-Dimethylphosphinothioylethyl)methylamine (3a). Dry methylamine was passed into ethanol (100 cm^3) until it no longer readily dissolved. Dimethylvinylphosphine sulfide **1** (8 g, 66 mmol) was added and the mixture was heated at 80 °C overnight in a Teflon-lined (Berghof) autoclave. Volatile components were removed under reduced pressure (60 °C at 18 mmHg) and the residue distilled under vacuum, bp 100 °C at 0.1 mmHg, to give the pure phosphine sulfide **3a** as a colourless low melting solid (6 g, 60%), mp 35–36 °C (Found: C, 39.8; H, 9.53; N, 9.3. $C_5H_{14}NPS$ requires C, 39.7; H, 9.3; N, 9.3%). δ_P ($CDCl_3$) 35.2; δ_H (270 MHz, $CDCl_3$) 1.77 (6H, d, J_{PH}=13 Hz, P(S)Me_2), 1.82 (1H, br s, NH), 2.10 (2H, dt, J_{PH}=12 Hz, J_{HH}=7 Hz, α-CH_2), 2.44 (3H, s, NMe), 2.97 (2H, dt, J_{PH}= 14 Hz, J_{HH}=7 Hz, β-CH_2); δ_C ($CDCl_3$) 21.2 (d, J_{PC}= 55 Hz, P(S)Me_2), 33.6 (d, J_{PC}=53 Hz, α-CH_2), 35.4 (Me), 45.2 (β-CH_2); IR (ν max cm^{-1}, thin film): 3472, 3287, 2974, 2936, 2905, 2851, 2797, 1474, 1451, 1420, 1289, 1115, 945, 918, 856, 744.5, 713.6, 575.

4.1.6. *N*-(2′-Dimethylphosphinoethyl)methylamine (6a). *N*-(2′-Dimethylphosphinothioylethyl)methylamine **3a** (3 g, 26 mmol) was reduced cleanly to the corresponding phosphine **6a** using the method previously given for the preparation of **5**. Because the resulting *N*-(2′-dimethylphosphinoethyl)methylamine **6a** tended to co-distil when efforts were made to remove the reaction solvent, it was generally used as a solution in dioxane in subsequent studies. The dioxane could be removed carefully at 53 °C at 100 mmHg but this resulted in significant loss of product from the reaction flask.[7] δ_P ($CDCl_3$) −55.5; δ_H (270 MHz, $CDCl_3$) 0.95 (6H, d, J_{PH}=2 Hz, PMe_2), 1.50 (2H, br t, J_{HH}=8 Hz, α-CH_2), 2.08 (1H, br s, NH), 2.35 (3H, s, NMe), 2.62 (2H, dt, J_{PH}=7.5 Hz, J_{PH}=8 Hz, β-CH_2); δ_C ($CDCl_3$) 13.5 (d, J_{PC}=13 Hz, PMe_2), 32.0 (d, J_{PC}=10 Hz, α-CH_2), 35.6 (NMe), 48.2 (d, J_{PC}=17 Hz, β-CH_2).

4.1.7. *N*,*N*-Bis(2′-dimethylphosphinothioylethyl)-methylamine (10). A mixture of *N*-(2′-dimethylphosphinothioylethyl)-methylamine **3a** (11 g, 73 mmol) and dimethyl-vinylphosphine sulfide **1** (9 g, 75 mmol) in ethanol (150 cm^3) was heated under reflux for 24 h. The mixture was cooled in ice and the resulting precipitate was isolated by filtration. The solid was then recrystallised from ethanol to give the pure product **10** (11.5 g, 58%), mp 189 °C, (Found: C, 39.9; H, 8.8; N, 4.9. $C_9H_{23}NP_2S_2$ requires C, 39.8; H, 8.54; N, 5.2%), δ_P ($CDCl_3$) 36.0; δ_H (270 MHz, $CDCl_3$) 1.77 (12H, d, $J_{PH}=13$ Hz, P(S)Me_2), 2.09 (4H, dt, $J_{PH}=12$ Hz, $J_{PH}=7$ Hz, α-CH_2), 2.27 (3H, s, NMe), 2.82 (4H, dt, $J_{PH}=13$ Hz, $J_{PH}=7$ Hz, β-CH_2); δ_C ($CDCl_3$) 21.5 (d, $J_{PC}=54$ Hz, P(S)Me_2), 31.7 (d, $J_{PH}=53$ Hz, α-CH_2), 41.6 (NMe), 50.8 (β-CH_2).

4.1.8. *N*,*N*-Bis(2′-dimethylphosphinoethyl)methylamine (11). *N*,*N*-Bis(2′-dimethylphosphinothioylethyl)methylamine **10** (5 g, 18 mmol) was cleanly reduced to the phosphine **11** (3.5 g, 91%) using the procedure previously given for the preparation of **5**, allowing for the presence of two phosphine sulfide centres in the molecule. δ_P ($CDCl_3$) −53.6; δ_H (60 MHz, $CDCl_3$) 0.96 (12H, d, $J_{PH}=2$ Hz, PMe_2), 1.42 (4H, m, α-CH_2), 2.15 (3H, s, NMe), 2.42 (4H, m, β-CH_2); δ_C ($CDCl_3$) 14.0 (d, $J_{PC}=13$ Hz, PMe_2), 29.4 (d, $J_{PC}=10$ Hz, α-CH_2), 41.4 (s, NMe), 53.7 (d, $J_{PC}=19$ Hz, β-CH_2).

4.1.9. *N*-(2′-Dimethylphosphinothioylethyl)dimethylamine (3b). Dry dimethylamine was passed into ethanol (100 cm^3) until it no longer readily dissolved. Dimethyl-vinylphosphine sulfide **1** (10 g, 83 mmol) was added and the mixture was heated at 80 °C overnight in a Teflon-lined (Berghof) autoclave. The crystalline product was filtered off and purified by vacuum sublimation (100 °C at 0.1 mmHg) to give the pure product **3b** as a colourless solid (10 g, 73%), mp 79–80 °C (lit.[8] mp 125–129 °C)[9] (Found: C, 43.50; H, 9.8; N, 8.4. $C_6H_{16}NPS$ requires C, 43.6; H, 9.8; N, 8.50%). δ_P ($CDCl_3$) 35.8; δ_H (270 MHz, $CDCl_3$) 1.77 (6H, d, $J_{PH}=13$ Hz, P(S)Me_2), 2.07 (2H, dm, $J_{PH}=12$ Hz, α-CH_2), 2.56 (6H, s, NMe_2), 2.68 (2H, dm, $J_{PH}=12$ Hz, β-CH_2); δ_C ($CDCl_3$) 21.3 (d, $J_{PC}=54$ Hz, P(S)Me_2), 32.6 (d, $J_{PC}=53$ Hz, α-CH_2), 45.1 (NMe_2), 53.2 (β-CH_2).

4.1.10. *N*-(2′-Dimethylphosphinoethyl)dimethylamine (6b). *N*-(2′-Dimethylphosphinothioylethyl)dimethylamine **3b** (3 g, 26 mmol) was cleanly reduced to the corresponding phosphine **6b** using the method previously given for the preparation of **5**. Because the resulting *N*-(2′-dimethylphosphinothioylethyl)dimethylamine tended to co-distil when efforts were made to remove the reaction solvent, it was generally used as a solution in dioxane in subsequent studies. The dioxane could be removed under reduced pressure (53 °C at 100 mmHg) but this resulted in significant loss of product. δ_P ($CDCl_3$) −53.8; δ_H (60 MHz, $CDCl_3$) 0.96 (6H, d, $J_{PH}=2$ Hz, PMe_2), 1.44 (2H, m, α-CH_2), 2.17 (6H, s, NMe_2), 2.32 (4H, m, β-CH_2); δ_C ($CDCl_3$) 14.1 (d, $J_{PC}=12$ Hz, PMe_2), 30.2 (d, $J_{PC}=10$ Hz, α-CH_2), 45.2 (s, NMe_2), 56.3 (d, $J_{PC}=19$ Hz, β-CH_2).

4.1.11. *N*,*N*′-Bis(2′-dimethylphosphinothioylethyl)-*N*,*N*′-dimethylethylenediamine (12a). A mixture of *N*,*N*′-dimethylethylenediamine (5 g, 57 mmol) and dimethyl-vinylphosphine sulfide (14 g, 117 mmol) in ethanol (75 cm^3) was heated under reflux for approximately 1 week and monitored by ^{31}P NMR spectroscopy. After this time the reaction mixture was cooled to afford a crystalline solid which was isolated by filtration. The bulk of the solvent was then removed under reduced pressure (60 °C at 18 mmHg) to give a further quantity of the crystalline product. Recrystallisation of this material from ethyl acetate gave the pure product **12a** (15 g, 80%) as a colourless solid, mp 120 °C, (Found: C, 43.6; H, 9.2; N, 8.51. $C_{12}H_{30}N_2P_2S_2$ requires C, 43.9; H, 9.2; N, 8.53%). δ_P ($CDCl_3$) 36.0; δ_H (270 MHz, $CDCl_3$) 1.77 (12H, d, $J_{PH}=13$ Hz, P(S)Me_2), 2.07 (4H, dm, $J_{PH}=12$ Hz, α-CH_2), 2.26 (6H, s, NMe), 2.53 (4H, s, CH_2), 2.82 (4H, dm, $J_{PH}=13$ Hz, β-CH_2); δ_C ($CDCl_3$) 21.3 (d, $J_{PC}=55$ Hz, P(S)Me_2), 31.5 (d, $J_{PC}=53$ Hz, α-CH_2), 41.9 (NMe), 51.1 (β-CH_2), 54.8 (CH_2).

4.1.12. *N*,*N*′-Bis(2′-dimethylphosphinoethyl)-*N*,*N*′-dimethylethylenediamine (13a). *N*,*N*′-Bis(2′-Dimethylphosphinothioylethyl)-*N*,*N*′-dimethyl-ethylenediamine **12a** (6 g, 18 mmol) was cleanly reduced to the phosphine **13a** (4.0 g, 83%) using the procedure previously indicated for the preparation of **11**. δ_P ($CDCl_3$) −53.8; δ_H (60 MHz, $CDCl_3$) 0.95 (12H, d, $J_{PH}=2$ Hz, PMe_2), 1.48 (4H, m, α-CH_2), 2.17 (6H, s, NMe), 2.40 (4H, br s, CH_2), 2.42 (4H, m, β-CH_2); δ_C ($CDCl_3$) 13.8 (d, $J_{PC}=13$ Hz, PMe_2), 29.0 (d, $J_{PC}=10$ Hz, α-CH_2), 41.9 (NMe), 54.4 (d, $J_{PC}=19$ Hz, β-CH_2), 54.6 (CH_2).

4.1.13. *N*,*N*′-Bis(2′-dimethylphosphinothioylethyl)-*N*,*N*′-diethylpropylenediamine (12b). A mixture of *N*,*N*′-dimethylpropylene-1,3-diamine (5 g, 38 mmol) and dimethylvinylphosphine sulfide **1** (10.5 g, 87 mmol) in ethanol (125 cm^3) was heated under reflux for 48 h in an atmosphere of dry nitrogen. The solvent was removed under reduced pressure to give an orange oil which was recrystallised in ethyl acetate. This yielded the pure bis(phosphine sulfide) **12b** (7.9 g, 56%) as a colourless solid, mp 79 °C, (Found: C, 48.9; H, 9.9; N, 7.5. $C_{15}H_{36}N_2P_2S_2$ requires C, 48.6; H, 9.8; N, 7.56%). δ_P ($CDCl_3$) 36.1; δ_H (270 MHz, $CDCl_3$) 1.03 (6H, t, $J_{HH}=7$ Hz, Me), 1.58–1.69 (2H, m, CH_2), 1.76 (12H, d, $J_{PH}=13$ Hz, P(S)Me_2), 1.98–2.08 (4H, dm, $J_{PH}=12$ Hz, α-CH_2), 2.45 (4H, t, $J_{HH}=7$ Hz, NCH_2), 2.53 (4H, q, $J_{HH}=7$ Hz, CH_3CH_2), 2.83–2.93 (4H, dm, $J_{PH}=12$ Hz, β-CH_2); δ_C ($CDCl_3$) 11.9 (Me), 21.4 (d, $J_{PC}=55$ Hz, P(S)Me_2), 24.8 (CH_2), 31.5 (d, $J_{PC}=53$ Hz, α-CH_2), 47.0 (β-CH_2), 47.1 (CH_2), 51.3 (CH_2). EI-MS: 371 ($[M+H]^+$ 99%), 355 (15), 339 (6), 251 (8), 325 (4), 178 (21), 166 (7). ES-HRMS: Found $[M+H]^+$ 371.18762 $C_{15}H_{36}N_2P_2S_2$ requires 371.18732.

4.1.14. *N*,*N*′-Bis(2′-dimethylphosphinoethyl)-*N*,*N*′-diethyl-propylenediamine (13b). *N*,*N*′-Bis(2′-dimethylphosphinothioylethyl)-*N*,*N*′-diethyl-propylenediamine **12b** (1.9 g) was reduced to the phosphine **13b** using the procedure previously indicated for the preparation of **11**. However, to obtain a pure sample of the bisphosphine **13b** the reduction mixture was evaporated prior to hydrolysis. This caused the pure bisphosphine (0.52 g, 33%) to separated from the remaining creamy oil. δ_P ($CDCl_3$) −53.8; δ_H (270 MHz, $CDCl_3$) 0.95–1.03 (18H, m,

J_{PH}=2 Hz, Me, PMe_2), 1.46 (4H, m, α-CH_2) 1.56 (2H, m, CH_2), 2.40 (4H, m, β-CH_2), 2.49–2.56 (8H, m, NCH_2, CH_2CH_3); δ_C ($CDCl_3$) 11.4 (Me), 13.7 (d, J_{PC}=12 Hz, PMe_2), 24.2 (CH_2), 28.5 (d, J_{PC}=10 Hz, α-CH_2), 46.5 (CH_2), 49.3 (d, J_{PC}=19 Hz, β-CH_2), 50.8 (CH_2).

4.1.15. *N,N′*-Bis(2′-diethylphosphinothioylethyl)-*N,N′*-diethylpropylenediamine (12c). A mixture of *N,N′*-diethylpropylene-1,3-diamine (1.83 g, 14 mmol) and diethylvinylphosphine sulfide (4.8 g, 32 mmol) in ethanol (45 cm^3) was heated under reflux in an atmosphere of dry nitrogen for 72 h. After cooling, the solvent was removed under reduced pressure and the crude product recrystallised from diethyl ether/cyclohexane. The pure bis(phosphine sulfide) **12c** (2.75 g, 46%) was isolated as a colourless solid, mp 56 °C, (Found: C, 53.4; H, 10.5; N, 6.9. $C_{19}H_{44}N_2P_2S_2$ requires C, 53.50; H, 10.4; N, 6.6%). δ_P ($CDCl_3$) 52.2; δ_H (270 MHz, $CDCl_3$) 1.01 (6H, t, J_{HH}=7 Hz, N–CH_2CH_3), 1.18 (12H, dt, J_{PH}=19 Hz, J_{HH}=7.5 Hz, P(S)CH_2CH_3), 1.63 (2H, m, CH_2), 1.86 (8H, dm, J_{PH}=12 Hz, PCH_2CH_3), 1.90–2.00 (4H, m, α-CH_2), 2.49 (4H, m, N–CH_2), 2.53 (4H, q, J_{HH}=7 Hz, N–CH_2CH_3), 2.83 (4H, m, β-CH_2); δ_C ($CDCl_3$), 6.7 (d, J_{PC}=5 Hz, P(S)CH_2CH_3), 12.1 (N-CH_2CH_3), 24.2 (d, J_{PC}=52, P(S)CH_2CH_3), 24.9 (CH_2), 26.8 (d, J_{PC}=48 Hz, α-CH_2), 46.9 (βCH_2), 47.3 (CH_2), 51.5 (CH_2). EI-MS: 427 ($[M+H]^+$, 99%), 399 (10), 305 (30), 279 (39), 232 (10), 220 (5), 206 (69), 183 (20), 149 (68). ES-HRMS: Found $[M+H]^+$ 427.24935 $C_{19}H_{44}N_2P_2S_2$ requires 427.24992.

4.1.16. *N,N′*-(2′-Diethylphosphinoethyl)-*N,N′*-diethylethylenediamine (13c). *N,N′*-Bis(2′-diethylphosphinothioylethyl)-*N,N′*-diethyl-propylenediamine **12c** (1.45 g, 3 mmol) was cleanly reduced to the bisphosphine **13c** (0.63 g, 51%) using the procedure previously indicated for the preparation of **11**. δ_P ($CDCl_3$) −25.7; δ_H (600 MHz, $CDCl_3$) 0.95 (6H, t, J_{HH}=7.5 Hz, NCH_2CH_3), 0.99 (12H, dt, J_{PH}=14 Hz, J_{HH}=7.5 Hz, PCH_2CH_3), 1.35 (8H, q, J_{HH}=7.5 Hz, PCH_2CH_3), 1.46 (4H, m, J_{PH}=6.5 Hz, α-CH_2), 1.53 (2H, quintet, J_{HH}=7.2 Hz, CH_2), 2.37 (4H, 't', J_{HH}=7.2 Hz, $CH_2CH_2CH_2$), 2.46 (4H, q, J_{HH}=7.5 Hz, N–CH_2), 2.51 (4H, dm, J_{PH}=12 Hz, β-CH_2); δ_C ($CDCl_3$) 9.1 (d, J_{PC}=13 Hz, PCH_2CH_3), 11.6 (N-CH_2CH_3), 18.6 (d, J_{PC}=13 Hz, PCH_2CH_3), 23.4 (d, J_{PC}=16 Hz, α-CH_2), 24.8 (CH_2), 46.6 (CH_2), 49.8 (d, J_{PC}=20 Hz, β-CH_2), 50.7 (CH_2).

4.1.17. *N,N′*-(2′-Dimethylphosphinothioylethyl)piperazine (14). Piperazine (1.8 g, 21 mmol) and dimethylvinylphosphine sulfide **1** (5.1 g, 42 mmol) were dissolved in ethanol (150 cm^3) and the mixture heated under reflux for 6 days. After cooling the product was filtered off and dried to give the pure product **14** as a colourless solid (5 g, 73%), mp 212 °C, (Found: C, 44.3; H, 8.7; N, 8.4. $C_{12}H_{28}N_2P_2S_2$ requires C, 44.1; H, 8.65; N, 8.6%). δ_P ($CDCl_3$) 36.0; δ_H (270 MHz, $CDCl_3$) 1.77 (12H, d, J_{PH}=13 Hz, P(S)Me), 2.06 (4H, dt, J_{PH}=12 Hz, J_{HH}=7 Hz, α-CH_2), 2.51 (8H, br m, NCH_2), 2.77 (4H, dt, J_{PH}=14 Hz, J_{HH}=7 Hz, β-CH_2); δ_C ($CDCl_3$) 21.5 (d, J_{PC}=54 Hz, P(S)Me), 31.9 (d, J_{PC}=53 Hz, α-CH_2), 51.8 (β-CH_2), 52.9 (NCH_2).

4.1.18. *N,N′*-(2′-Dimethylphosphinoethyl)piperazine (15). *N,N′*-(2′-Dimethylphosphinothioylethyl)piperazine **14** (7 g, 21 mmol) was cleanly reduced to the phosphine **15** (4.83 g, 86%) using the procedure previously indicated for the preparation of **11** and isolated as a colourless viscous oil which solidified on standing. δ_P ($CDCl_3$) −53.1; δ_H (60 MHz, $CDCl_3$) 0.92 (12H, d, J_{PH}=2 Hz, PMe), 1.45 (4H, m, α-CH_2), 2.35 (4H, m, β-CH_2), 2.40 (8H, br s, CH_2); δ_C ($CDCl_3$) 14.0 (d, J_{PC}=12 Hz, PMe), 29.2 (d, J_{PC}=10 Hz, β-CH_2), 52.8 (NCH_2), 55.1 (d, J_{PC}=19 Hz, α-CH_2).

4.1.19. *N*-(2′-Dimethylphosphinothioylethyl)-*N,N′,N′*-trimethylethylenediamine (3c). A mixture of *N,N′,N′*-trimethylethylenediamine (8.5 g, 83 mmol) and dimethylvinylphosphine sulfide **1** (10 g, 83 mmol) in ethanol (100 cm^3) was heated under reflux for 3 days. Evaporation of the solvent gave the title product as a yellow oil, in a good state of purity. A pure sample of the product **3c** (9.6 g, 51%) was obtained by distillation (bp 114 °C at 0.1 mmHg), (Found: C, 48.6; H, 10.2; N, 12.35. $C_9H_{23}N_2PS$ requires C, 48.6; H, 10.4; N, 12.6%). δ_P ($CDCl_3$) 36.4; δ_H (270 MHz, $CDCl_3$, 30 °C), 1.57 (6H, d, J_{PH}=13 Hz, P(S)Me), 1.87 (2H, dm, J_{PH}=12 Hz, β-CH_2), 2.05 (6H, s, NMe_2), 2.08 (3H, s, NMe), 2.22 (2H, m, CH_2NMe_2), 2.32 (2H, m, CH_2NMe), 2.64 (2H, dm, J_{PH}=13 Hz, α-CH_2); δ_C ($CDCl_3$), 21.4 (d, J_{PC}=55 Hz, P(S)Me), 32.1 (d, J_{PC}=52 Hz, α-CH_2), 42.0 (N-Me), 45.8 (N-Me_2), 51.6 (CH_2), 55.3 (CH_2), 57.3 (CH_2). EI-MS: 223 ($[M+H]^+$ 99%), 207 (6), 189 (10), 178 (12), 164 (48), 150 (3). ES-HRMS: Found $[M+H]^+$ 223.13982 $C_9H_{23}N_2PS$ requires 223.13977.

4.1.20. *N*-(2′-Dimethylphosphinoethyl)-*N,N′,N′*-trimethyl-ethylenediamine (6c). *N*-(2′-Dimethylphosphinothioylethyl)-*N,N′,N′*-trimethyl-ethylenediamine **3c** (3.7 g, 17 mmol) was reduced cleanly to the phosphine **6c** using the method previously given for the preparation of **5** and isolated as a colourless oil (2.2 g, 69%), δ_P ($CDCl_3$) −53.4; δ_H (270 MHz, $CDCl_3$) 0.96 (6H, d, J_{PH}=2 Hz, PMe), 1.46–1.53 (2H, m, α-CH_2), 2.21 (3H, s, NMe), 2.24 (6H, s, NMe_2), 2.41–2.53 (6H, m, CH_2); δ_C ($CDCl_3$) 13.4 (d, J_{PC}=13 Hz, PMe), 28.8 (d, J_{PC}=11 Hz, α-CH_2), 41.5 (NMe), 45.2 (NMe), 54.2 (d, J_{PC}=19 Hz, β-CH_2), 54.5 (CH_2), 56.8 (CH_2).

4.1.21. *N*-(2′-Dimethylphosphinothioylethyl)methylamino-benzene (4). To a solution of *N*-methylaniline (1 g, 9.3 mmol) and dimethylvinylphosphine sulfide **1** (1.25 g, 10.4 mmol) in dry toluene (50 cm^3), at room temperature and under an atmosphere of dry nitrogen, was added a solution of *n*-butyl lithium in pentane (5.5 cm^3, 1.7 M). The resulting cloudy orange solution was stirred for 30 min and ethanol (20 cm^3) was then slowly added. The mixture was acidified with hydrochloric acid (2 M) and then extracted with chloroform. The aqueous layer was basified by the addition of aqueous sodium hydroxide (2 M) and re-extracted with chloroform. The latter chloroform extracts were dried with $MgSO_4$ and the solvent removed under reduced pressure to give a solid. This was recrystallised from diethyl ether to yield the phosphine sulfide **4** as a colourless solid (1.2 g, 56%) (Found: C, 57.9; H, 8.15; N, 6.2. $C_{11}H_{18}NPS$ requires C, 58.1; H, 8.0; N, 6.2%). δ_P ($CDCl_3$) 34.6; δ_H (270 MHz, $CDCl_3$) 1.67 (6H, d, J_{PH}=11 Hz, P(S)Me), 2.06 (2H, dm, J_{PH}=12 Hz, α-CH_2), 2.90 (3H, s, NMe), 3.72 (2H, dm, J_{PH}=14 Hz, β-CH_2), 6.65–6.71 (3H, m, ArH), 7.15–7.22 (2H, m, ArH); δ_C ($CDCl_3$)

21.4 (d, $J_{PC}=55$ Hz, P(S)Me), 30.6 (d, $J_{PC}=50$ Hz, α-CH_2), 38.6 (NMe), 46.9 (β-CH_2), 113.0 (C-2,6), 117.3 (C-4), 129.4 (C-3,5), 148.4 (C-1). EI-MS: 227 ($[M+H]^+$, 22%), 152 (5), 132 (100), 120 (81), 104 (63), 94 (58), 77 (65), 65 (15), 51 (12), 42 (23). ES-HRMS: Found $[M+H]^+$ 228.0970 $C_{11}H_{19}NPS$ requires 228.0976.

4.1.22. *N*-(2′-Dimethylphosphinoethyl)methylaminobenzene (7). *N*-(2′-Dimethylphossphinoethyl)methylaminobenzene **4** (0.5 g, 2.6 mmol) was reduced cleanly to the phosphine **7** using the method previously given for the preparation of **5** and isolated as a colourless oil (0.13 g, 26%), δ_P ($CDCl_3$) −54.9; δ_H (270 MHz, $CDCl_3$) 0.96 (6H, d, $J_{PH}=2$ Hz, PMe), 1.51–1.56 (2H, m, α-CH_2), 2.81 (3H, s, NMe), 3.34–3.38 (6H, m, CH_2), 6.63–6.69 (3H, m, ArH), 7.17–7.20 (2H, m, ArH); δ_C ($CDCl_3$) 13.4 (d, $J_{PC}=14$ Hz, PMe), 28.1 (d, $J_{PC}=13$ Hz, α-CH_2), 37.5 (NMe), 49.2 (d, $J_{PC}=21$ Hz, β-CH_2),), 112.0 (C-2,6), 115.8 (C-4), 128.7 (C-3,5), 148.4 (C-1)

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