The synthesis of benzylphosphine oxides *via* vicarious nucleophilic substitution and alkenes *via* VNS–Horner–Wittig reactions

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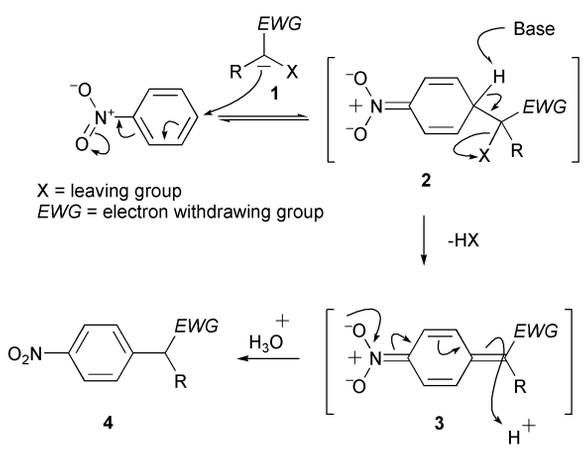
A range of substituted nitrobenzenes react with the anion of (chloromethyl)diphenylphosphinoyl oxide to give the substituted nitrobenzyldiphenylphosphine oxide by vicarious nucleophilic substitution. The novel stereoselective synthesis of *E*–stilbenes *via* a one–pot vicarious nucleophilic substitution–Horner–Wittig reaction is described.

Introduction

The direct aromatic substitution of hydrogen is an efficient method to functionalise arenes.[1] This is most often accomplished by reaction of the arene with an electrophile. An alternative route involves the substitution of hydrogen by the action of an appropriate nucleophilic species.[2] One such reaction of this type is vicarious nucleophilic substitution (VNS), an area pioneered by Makosza and co-workers.[3]

The VNS reaction is characterised by reaction of a nucleophile **1**, that also bears a nucleofugal group (X) at the same nucleophilic centre, with an electron-deficient arene, as illustrated in Scheme 1. The general mechanistic pathway of the

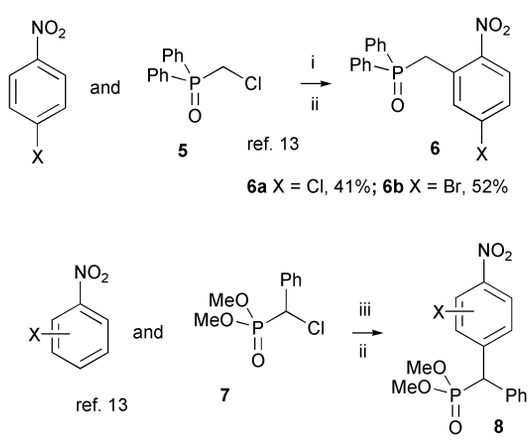


Scheme 1 Mechanism of vicarious nucleophilic substitution.

reaction has been established as a fast and reversible addition of the carbanion to the nitroarene, resulting in the formation of the σ-adduct **2**, from which base induced β-elimination takes place to generate the anion **3**.[4] In typical VNS reactions, nucleophiles are often carbanions stabilised by an adjacent electron-withdrawing species such as an alkoxy carbonyl,[5] sulfonyl,[6] cyano,[7] dialkylsulfoxonium,[8] trialkylammonium and triphenylphosphonium thioacetal[9] group. These are generally prepared *in situ* from their corresponding conjugate acid by action of a base such as KOH, NaOH, *t*-BuOH, or NaH in DMSO, liquid ammonia or DMF. Base is also consumed in the elimination step (**2** ⟶ **3**) and therefore at least two molar equivalents of base are required with respect to the conjugate acid.

The VNS reaction offers a strategy for the functionalisation of arenes complementary to existing methods such as electrophilic substitution,[1] *ortho*–lithiation,[10] and conventional nucleophilic aromatic substitution.[11]

As part of an investigation into the synthesis of alkenes *via* Wittig and Horner–Wittig chemistry[12] we were interested in the application of VNS chemistry to the synthesis of nitrobenzyl substituted phosphonium derivatives and phosphine oxides. As far as we are aware there are only two examples of the VNS reaction of the type arene ⟶ **4** with a phosphorus moiety as the electron-withdrawing group. These involve the use of chloromethyldiphenylphosphine oxide[13] (**5**) and dimethyl α-chlorobenzylphosphonate (**7**) as the VNS nucleophiles (Scheme 2). We now report the full details of our own study into the VNS synthesis of phosphine oxides.[14]



Scheme 2 *Reagents and conditions*: i, KOH, DMSO; ii, H_3O^+; iii, NaOH, liq. NH_3.

Results and discussion

We initially attempted the VNS reaction between an ylid derived from a phosphonium salt (Scheme 3). The VNS nucleophile (bromomethyl)triphenylphosphonium bromide (**9a**) was

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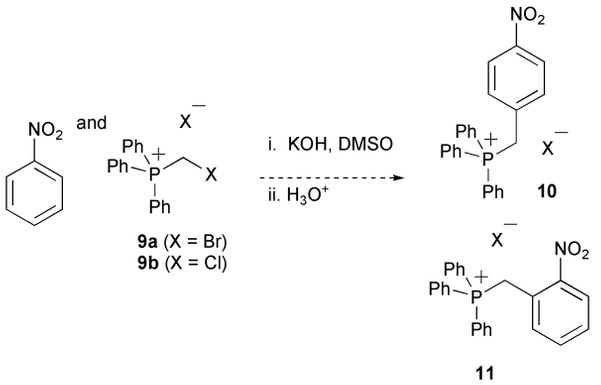
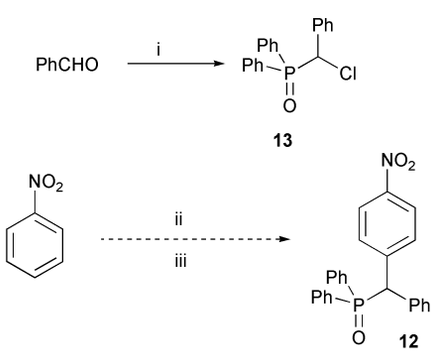


Scheme 3 VNS reactions of halomethylphosphonium salts.

prepared from triphenylphosphine and dibromomethane.[15] The expected products **10** and **11** of the VNS reaction between nitrobenzene and **9a** were prepared from their corresponding benzylbromides[16] to aid the interpretation of the NMR spectra of the VNS reaction products. We never observed the presence of **10** or **11** in the NMR spectra of the crude reaction mixtures. Unfortunately all attempts to facilitate the VNS reaction between nitrobenzene and the ylid derived from **9a** were unsuccessful. Inspection of the ^{1}H NMR spectrum of the crude reaction mixture showed that the nitrobenzene was still present. The ylid of **9a** was prepared by using LDA or potassium *tert*-butoxide,[17] either before the addition of nitrobenzene or in its presence.

We also prepared the phosphonium salt (chloromethyl)-triphenylphosphonium chloride (**9b**) by sequential treatment of triphenylphosphine with HCl–formaldehyde and thionyl chloride.[18] The ylid derived from **9b** also did not react in the VNS reaction (again the nitrobenzene did not react). The stability of the ylid was checked by treatment with 2 equivalents of LDA in THF at 0 °C for 20 minutes followed by an aqueous work-up. Analysis by NMR revealed complete decomposition of the ylid. It seems therefore that the ylid is not stable to the excess of base required to effect the VNS reaction.

We chose the phosphine oxide **12**, analogous to the known phosphonate **8a** as our next target. The required VNS nucleophile **13** was easily prepared by heating a mixture of benzaldehyde and chlorodiphenylphosphine at 150 °C (Scheme 4).[19] The



Scheme 4 *Reagents and conditions*: i, Ph_2PCl, 150 °C; ii, NaH, DMSO, **13**; iii, H_3O^+.

VNS reaction between nitrobenzene and phosphine oxide **13** was attempted using NaH in DMSO. Unfortunately the reaction was unsuccessful in our hands and ^{1}H NMR showed no signs of the expected product; the nitrobenzene remained unreacted and the starting phosphine oxide had decomposed.

We next focussed our attention on the VNS chemistry of chloromethyldiphenylphosphine oxide. Makosza has reported[13] that **5** undergoes the VNS reaction with 4-chloro and 4-bromonitrobenzene in the presence of KOH in DMSO to give **6a** and **6b** in 41% and 52% yields respectively. However in our hands the yield of **6b** was lower (26%). Sodium hydride was found to be a superior base. Addition of a mixture of **5** and 4-bromonitrobenzene to NaH in DMSO, immediately gave a deep violet coloured solution that after stirring at room temperature overnight and workup gave **6b** in 55% yield. These conditions were found to be reliable and gave consistent results. A variety of other substituted nitroarenes were reacted with **5** under the same conditions. The results are shown in Scheme 5.

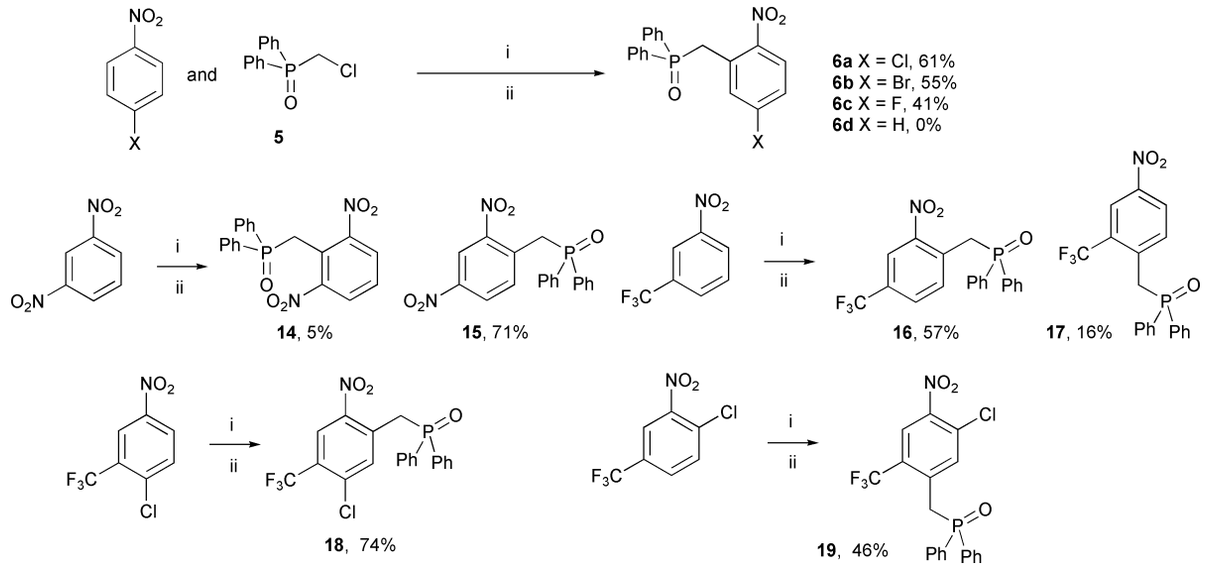
Addition to 4-chloro, 4-bromo and 4-fluoro nitrobenzenes takes place, as expected, exclusively *ortho* to the nitro group. The ^{1}H NMR signal of the hydrogen positioned *ortho* to the nitro group was especially diagnostic, since it is shifted downfield of the other aryl signals. For example the H5 signal is found at δ 7.81 (d, J 8.8 Hz) for **6a**, δ 7.74 (d, J 8.8 Hz) for **6b** and at δ 7.90 (dd, J_{HH} 9.1 and J_{HF} 5.2 Hz) for **6c**. Reaction of 4-chloronitrobenzene with **5** overnight afforded the phosphine oxide **6a** in 61% yield. 4-Fluoronitrobenzene was much less reactive towards the VNS nucleophile and gave **6c** in only 14% yield. Halogen substitution was not observed in any of the VNS reactions even though displacement of fluoride has been found to occasionally occur in VNS reactions.[20] Nitrobenzene did not undergo a VNS reaction with **5**. However, 1,3-dinitrobenzene proved to be sufficiently electrophilic to undergo the reaction efficiently. The major product of the reaction was the 6-substituted isomer **15**. A small amount of the 2-substituted isomer **14** was also isolated. The isomers were clearly identifiable from their ^{1}H NMR spectra. The 6-substituted isomer **15** has a coupling pattern expected of a 1,2,4-trisubstituted aryl group. The signal of the H3 hydrogen atom located between the two nitro groups in **15** was observed at δ 8.69 ppm (1H, J 2.3 Hz), as expected. A doublet (2H, J 8.2 Hz) at δ 8.02 ppm corresponding to H3 and H5 was observed in the ^{1}H NMR spectrum of the minor product **14**. Haglund and Nilsson have shown that the presence of pyridine and Cu(I) salts in VNS reactions of 1,3-dinitrobenzene leads to the preferential formation of the 1,2,3-trisubstituted isomer.[21] However addition of pyridine and Cu(I) chloride under our reaction conditions or using Haglund and Nilsson's procedure lead only to small amounts of the VNS products. Clearly the VNS reaction is sensitive to changes in substrates and conditions.

The VNS reaction allows the synthesis of substituted arenes bearing trifluoromethyl groups. The reaction of 3-trifluoromethylnitrobenzene with **5** was complete after 5 h and produced a 7 : 2 mixture of 6-substituted isomer **16** and the 4-substituted isomer **17** in 73% (total) yield. We were able to obtain pure **16** by recrystallisation of the mixture twice from propan-2-ol. The ^{1}H NMR spectrum of **16** clearly shows the H3 proton as a singlet at δ 8.10 ppm. The regioselectivity agrees with that found by Makosza in the reaction of 3-trifluoromethylnitrobenzene with the anion of chloromethyl phenyl sulfone.[20]

The 6-substituted isomer **18** is the exclusive product of the reaction of 3-trifluoromethyl-4-chloronitrobenzene. It is produced in 74% yield when the reaction is stirred at room temperature for four hours. The ^{1}H NMR of **18** supports the expected substitution pattern. A singlet corresponding to H5 is observed at δ 8.20 ppm. The same pattern of selectivity is observed in the reaction of 3-trifluoromethyl-4-chloronitrobenzene with chloromethyl phenyl sulfone.[22]

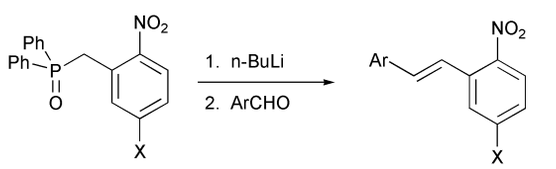
The VNS reaction of 2-chloro-5-(trifluoromethyl)nitrobenzene with **5** is much slower. After thirty hours at room temperature the yield of **19** is only 46%. Makosza has emphasised the need for rapid quenching in VNS chemistry, to avoid decomposition of the first-formed product **3** and then **4**.[2c] Most VNS reactions reported in the literature are quenched within two hours of reaction time. However it is clear that under an inert atmosphere VNS reactions of phosphinoyl anions can be left overnight to afford good to moderate yields of product.

Having prepared the series of nitrobenzyldiphenylphosphine oxides we next investigated their Horner–Wittig chemistry in the synthesis of a variety of novel stilbenes. Our own studies[12]



Scheme 5 *Reagents and conditions*: i, NaH, DMSO; ii, H_3O^+.

and those of Warren and co-workers[23] have shown that such lithiated phosphine oxides react with aromatic aldehydes generating the (*E*)-stilbene directly, without the isolation of the intermediate phosphinoyl alcohols. As expected, the lithium anion of the phosphine oxide **6a**, formed from *n*-butyllithium in THF at 0 °C, reacted with benzaldehyde giving exclusively the *trans* stilbene **20a**, but in a disappointing 31% yield (Scheme 6).

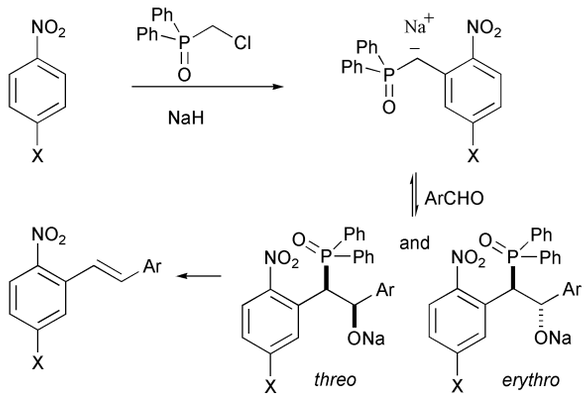


Scheme 6 Horner–Wittig reactions of nitrobenzylphosphine oxides.

On addition of the aldehyde to the deep purple coloured solution of the lithium anion, a white precipitate of lithium diphenylphosphinate slowly forms.

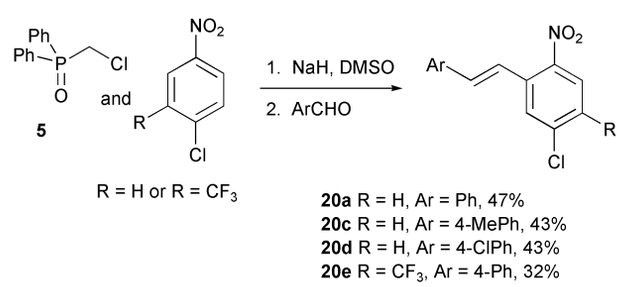
Increasing the reaction time and temperature did not increase the yield of the alkene but led to the apparent decomposition of the anion of **6a**. A ^{1}H NMR spectrum of the crude reaction mixture indicated that **6a** had been consumed. The remaining mass balance proved to be base-line material (visible by TLC). Similarly, the reaction of **6b** with 4-nitrobenzaldehyde gave the (*E*)-stilbene **20b** only, again in a moderate yield (Scheme 6). The low yield of this Horner–Wittig reaction is probably due to the high stability of the nitrobenzylic anion. Warren and co-workers have shown that the first step of the Horner–Wittig reaction is reversible (Scheme 7).[23] Addition of the phosphine oxide anion to the benzaldehyde generally produces a mixture of *erythro*- and *threo*-phosphinoyl alkoxides. Elimination of sodium diphenylphosphinate is fastest from the *threo*-precursor to produce the (*E*)-alkene. It seems that the stability of the anion of a nitrobenzylic phosphine oxide reduces the formation of the *erythro* and *threo* adducts to such an extent that undesired processes compete with aldehyde addition. The measure of this stabilisation can be seen by comparing the equilibrium acidity of *p*-$NO_2C_6H_4CH_2POPh_2$ (pK_a 17.7 in DMSO) with $PhCH_2POPh_2$(pK_a 27.5 in DMSO).[24]

The anion formed by deprotonation of the phosphine oxide **6a** in the Horner–Wittig reaction is actually the same anion of type **3** (Scheme 1) generated in the VNS reaction. It seemed possible that the anion from the VNS could be reacted directly with benzaldehyde to form a corresponding nitrostilbene. If



Scheme 7 General mechanism of the Horner–Wittig reaction.

successful this process would constitute a one-pot VNS–Horner–Wittig reaction that might improve the yields of the (*E*)-stilbenes. Our hopes were immediately met. Quenching the VNS reaction of **5** and 4-chloronitrobenzene with benzaldehyde gave the expected (*E*)-stilbene **20a** in a moderate, but improved, 47% yield (Scheme 8). The yield obtained *via* this



Scheme 8 One-pot VNS–Horner–Wittig synthesis of (*E*)-stilbenes.

one-pot process compares well with that obtained *via* the separate VNS and Horner–Wittig reaction (31% overall). The VNS reaction was carried out according to our standard conditions; chloromethyldiphenylphosphine oxide and the substituted nitrobenzene were added to a slurry of sodium hydride in DMSO under nitrogen. The disappearance of **5** was followed by proton NMR and when complete, the aldehyde was added to the reaction mixture. It was necessary to heat the mixture at this stage to effect formation of the stilbene. When the reaction was stirred overnight at ambient temperature very little stilbene was formed. When potassium or lithium hydride was used as the base no VNS reaction took place.

The one-pot VNS–Horner–Wittig reaction works with other combinations of nitroarenes and aldehydes (Scheme 8). In each case (**20c**–**20e**) the (*E*)-alkene was formed exclusively, albeit in moderate yield. On quenching the VNS reaction of 4-chloronitrobenzene and **5** with 4-tolylaldehyde the stilbene **20c** was accompanied by the alcohol by-product **21** that was isolated in 10% yield (Fig. 1). The formation of **21** is most likely associated

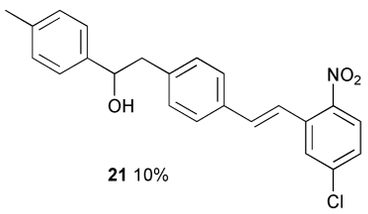
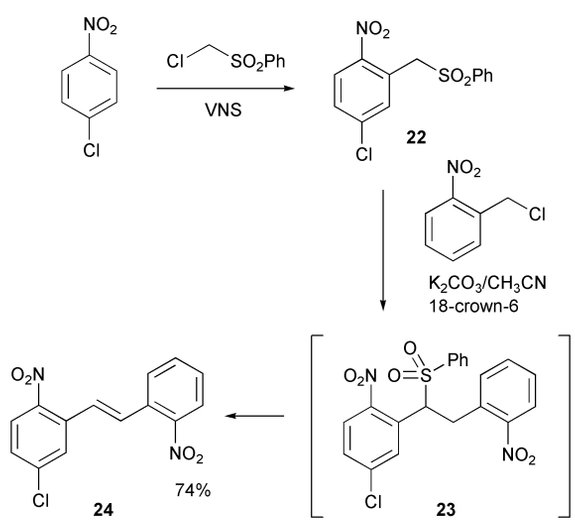


Fig. 1 Structure of the by-product from the reaction of 4-chloronitrobenzene, **5**, and 4-tolylaldehyde.

with the acidity of the methyl group in the stilbene **20c** and results from the addition of the anion of the first-formed stilbene to a second molecule of 4-tolylaldehyde.

It is worthy of note that our method joins another VNS route to nitroalkenes. Makosza and Tyrala have reported the synthesis of nitroalkenes *via* a two step process involving the initial VNS reaction of chloromethyl phenyl sulfone and a nitroarene (*e.g.* 4-chloronitrobenzene ⟶ **22**, Scheme 9).[25] Alkylation of this



Scheme 9 A route to alkenes *via* a consecutive VNS alkylation–elimination process.

isolated VNS product **22** with an alkylating agent bearing an electron-withdrawing group generates the intermediate sulfone **23** which undergoes an elimination reaction to provide the alkene **24**.

In conclusion, we have developed a convenient method for the synthesis of a range of nitrobenzyldiphenylphosphine oxides that compares favourably with current procedures. In addition, a simple route to *trans*-nitrostilbenes has been reported which effectively represents the substitution of aromatic hydrogen with a vinyl group. This stereoselective preparation of nitrostilbenes represents the first example of a VNS-derived anion **3** being quenched with anything other than a proton. This finding has subsequently led us to explore the use of other electrophiles and has led to the development of a VNS–alkylation process.[26]

Experimental

General information

The 200 MHz ^{1}H NMR spectra were recorded using a Bruker AC 200 NMR spectrometer while all 300 MHz ^{1}H and 75 MHz ^{13}C NMR spectra were recorded using a Bruker AC 300 spectrometer. ^{13}C NMR spectra were recorded using Distortionless Enhancement by Polarization Transfer. Both ^{1}H and ^{13}C spectra were recorded using $CHCl_3$ as internal standard. Chemical ionization (CI) mass spectra were recorded using a Kratos MS25 mass spectrometer; fast atom bombardment (FAB) mass spectra were recorded with a Kratos MS50 with a *m*-nitrobenzyl alcohol matrix. Accurate mass determinations were carried out on a Kratos Concept IS spectrometer. Elemental analyses were performed using a Carlo-Erba 1106 elemental analyzer. Infrared spectra were recorded using a Perkin-Elmer 783 spectrometer equipped with a PE 600 data station. Melting points were determined using an electrothermal melting point apparatus and were uncorrected. Column chromatography was conducted using silica gel 60 230–400 mesh (Merck & Co.). Silica TLC was conducted on precoated aluminum sheets (60 F_{254}) with a 0.2 mm thickness (Aldrich Chemical Co.). DMSO was distilled from calcium hydride and stored under nitrogen prior to use. Anhydrous methanol and DMF were obtained from Aldrich Chemical Co. and used as supplied.

Bromomethyltriphenylphosphonium bromide (9a)

Triphenylphosphine (15 g, 57.25 mmol) and dibromomethane (19.92 g, 114.48 mmol) were dissolved in toluene (125 cm^3) and the solution refluxed for 7 days. The mixture was cooled to 0 °C, the crystals filtered and washed with toluene to yield the phosphonium salt **9a** (16.5 g, 66%) as a white solid, mp 238–240 °C (lit.[15] mp 232–235 °C) after recrystallisation from isopropanol. ν_{max} (KBr disc)/cm^{-1} 3020 (md), 2840 (md), 2210 (w), 1590 (md), 1440 (st), 1130 (md), 1110 (st), 995 (md), 840 (md), 750 (st), 680 (st), 620 (md), 505 (st), 480 (md), 380 (w); δ_H (300 MHz; $CDCl_3$) 5.84 (2H, d, J_{PH} 5.8 Hz, CH_2), 7.65–7.82 (9H, m, aryl), 7.90–7.97 (6H, m, aryl); δ_C (75 MHz; $CDCl_3$) 18.32 (d, J_{PC} 54.6 Hz, CH_2), 116.73 (d, J_{PC} 89.2 Hz, C, *ipso*-PPh_3), 130.23 (d, J_{PC} 12.8 Hz, CH, *m*-PPh_3), 134.28 (d, J_{PC} 10.5 Hz, CH, *o*-PPh_3), 135.42 (d, J_{PC} 2.9 Hz, CH, *p*-PPh_3); *m*/*z* (FAB) 357 [(M(^{79}Br) − Br$^-$), 98], 355 [(M(^{79}Br) − Br$^-$), 100], 307 (3), 275 (22), 183 (8).

Chloromethyltriphenylphosphonium chloride (9b)

Paraformaldehyde (3.3 g, 0.11 mol) was added to an anhydrous solution of hydrochloric acid in ether (1 M solution, 100 cm^3, 0.10 mol). Triphenylphosphine (26.2 g, 0.10 mol) was dissolved in anhydrous ether (50 cm^3), added to the paraformaldehyde slurry and the mixture stirred for 2 h. The reaction mixture was filtered, the resulting hydroxymethyltriphenylphosphonium chloride was washed with ether and dried in air. The salt was dissolved in dichloromethane (40 cm^3) and filtered to remove the insoluble paraformaldehyde. Thionyl chloride (15 cm^3, 24.47 g, 0.21 mol) was added to the liquors and the mixture refluxed for 1 h. The excess thionyl chloride and dichloromethane were removed under reduced pressure and the remaining solid washed well with ether. The phosphonium salt **9b** (18.0 g, 52%) was obtained as a white solid, mp 262–264 °C (lit.[27] mp 260–263 °C) after recrystallisation from isopropanol. ν_{max}(KBr disc)/cm^{-1} 3060 (md), 2980 (md), 2850 (st), 2760 (md), 2500 (md), 1435 (st), 1160 (w), 1110 (st), 1000 (md), 840 (md), 750 (st), 730 (st), 685 (st), 520 (st), 450 (st); δ_H (300 MHz; $CDCl_3$) 6.13 (2H, d, J_{PH} 5.8 Hz, CH_2), 7.67–7.74 (6H, m, aryl), 7.79–7.84 (3H, m, aryl), 7.89–7.96 (6H, m, aryl); δ_C (75 MHz; $CDCl_3$) 33.75 (d, J_{PC} 55.8 Hz, CH_2), 116.42 (d, J_{PC} 88.4 Hz, *ipso*-PPh_3), 130.57 (d, J_{PC} 12.8 Hz, CH, *m*-PPh_3), 134.31 (d, J_{PC} 9.8 Hz, CH, *o*-PPh_3), 135.59 (d, J_{PC} 2. 9 Hz, CH, *p*-PPh_3); *m*/*z* (FAB) 313[(M(^{37}Cl) − Cl$^-$), 35], 311[(M(^{35}Cl) − Cl$^-$), 100], 275 (5), 183 (15), 165 (3), 108 (4), 77 (3).

4-Nitrobenzyltriphenylphosphonium bromide (10)

Triphenylphosphine (1.0 g, 3.82 mmol) and 4-nitrobenzyl bromide (0.82 g, 3.82 mmol) were dissolved in tetrahydrofuran

(6 cm^3) and the solution refluxed for 2 h. The solution was allowed to cool to ambient temperature, the crystals filtered and washed with tetrahydrofuran to give the phosphonium bromide **10** (1.10 g, 60%) as a white solid, mp 280–282 °C (lit.[28] 275.0–275.5 °C) after recrystallisation from methanol–ethyl acetate; ν_{max} (KBr disc)/cm^{-1} 3060 (w), 2860 (md), 1590 (md), 1480 (md), 1440 (st), 1350 (st), 1110 (st), 1000 (md), 870 (st), 750 (st), 690 (st), 630 (md), 550 (md), 505 (st), 495 (st); δ_H (300 MHz; $CDCl_3$) 5.97 (2H, d, J_{PH} 15.7 Hz, CH_2), 7.46 (2H, dd, J_{HH} 8.9 Hz, J_{PH} 2.5 Hz, H2 and H6), 7.57–7.64 (6H, m, aryl), 7.73–7.86 (11H, m, aryl); δ_C (75 MHz; $CDCl_3$) 29.80 (d, J_{PC} 47.2 Hz, CH_2), 117.08 (d, J_{PC} 86.2 Hz, C, *ipso*-PPh_3), 123.25 (d, J_{PC} 3.3 Hz, CH, C3 and C5), 130.23 (d, J_{PC} 12.7 Hz, CH, *m*-PPh_3), 132.79 (d, J_{PC} 5.3 Hz, CH, C2 and C6), 134.31 (d, J_{PC} 10.2 Hz, CH, *o*-PPh_3), 135.10 (d, J_{PC} 3.0 Hz, CH, *p*-PPh_3), 135.56 (d, J_{PC} 8.5 Hz, C, C1), 147.37 (d, J_{PC} 4.2 Hz, C, C4); *m*/*z* (FAB) 877 [(2M − Br^-), 4%], 398 [(M − Br^-), 100], 382 (7), 352 (9), 262 [(Ph_3P), 15], 183 (17), 165 (5), 108 (7), 89 (5).

2-Nitrobenzyltriphenylphosphonium bromide (11)

2-Nitrobenzyltriphenylphosphonium bromide was prepared from triphenylphosphine (2.0 g, 7.63 mmol) and 2-nitrobenzyl bromide (1.65 g, 7.64 mmol) in a similar way to the phosphonium bromide **10**. The phosphonium salt **11** (2.32 g, 64%) was obtained as a white solid, mp 172–174 °C (lit.[16] mp 161–162 °C) after recrystallisation from isopropanol; ν_{max}(KBr disc)/cm^{-1} 3460 (st), 3020 (md), 2880 (md), 1585 (md), 1520 (st), 1440 (st), 1340 (md), 1110 (st), 870 (md), 790 (md), 760 (st), 685 (st), 520 (md), 495 (md); δ_H (300 MHz; $CDCl_3$) 6.11 (2H, d, J_{PH} 14.9 Hz, CH_2), 7.45–7.51 (1H, m, aryl), 7.59–7.81 (19H, m, aryl), 7.93 (1H, d, J_{HH} 8.2 Hz, CH H2), 8.09–8.13 (1H, m, CH H6); *m*/*z* (FAB) 877 [(2M − Br^-), 48%], 398 [(M − Br^-), 100], 351 (20), 262 [(Ph_3P), 7], 183 (6), 108 (2).

(α-Chlorobenzyl)diphenylphosphine oxide (13)

Chlorodiphenylphosphine (6.24 g, 28 mmol) was added to benzaldehyde (3 g, 28 mmol) and the mixture heated at 150 °C overnight. The resulting solid was washed with hexane and dried in air to give the phosphine oxide **13** (6.3 g, 68%) as a white solid, mp 197–199 °C (lit.[29] mp 197–199 °C) after recrystallisation from ethyl acetate. Found: C, 70.0; H, 4.9; Cl, 10.9; P, 9.6. $C_{19}H_{16}ClOP$ requires C, 69.9; H, 5.0; Cl, 10.9; P, 9.5%; R_f 0.75 (silica, ethyl acetate); ν_{max} (KBr disc)/cm^{-1} 3050 (md), 2940 (md), 1590 (w), 1455 (md), 1435 (st), 1315 (w), 1200 (st), 1180 (st), 1160 (md), 1070 (md), 1000 (w), 840 (w), 745 (st), 545 (st); δ_H (300 MHz, $CDCl_3$) 5.42 (1H, d, J_{PH} 4.3 Hz, CHCl), 7.19–7.63 (13H, m, aryl), 7.87–7.93 (2H, m, aryl); *m*/*z* (FAB) 329 [(M(^{37}Cl) + H)$^+$, 32%), 327 [(M(^{35}Cl) + H)$^+$, 100], 292 [(M − Cl)$^+$, 30], 201 [(Ph_2PO), 15], 185 (17), 167 (47), 152 (5), 125 (33).

Hydroxymethyldiphenylphosphine oxide

Chlorodiphenylphosphine (6.1 g, 5.0 cm^3, 28.0 mmol) was added to 37% aqueous formaldehyde solution (50 cm^3, 617.0 mmol) and concentrated hydrochloric acid (50 cm^3) and the mixture heated at 100 °C overnight. Evaporation of the reaction mixture at reduced pressure left an oil, which was neutralised with aqueous sodium bicarbonate solution and extracted with chloroform (3 × 20 cm^3). The organic layers were combined, dried (magnesium sulfate), filtered and the solvent removed under reduced pressure to give the phosphine oxide (4.60 g, 71%) as a white solid, mp 141–143 °C (lit.[30] mp 137–139 °C) after recrystallisation from ethyl acetate. Found: C, 67.1; H, 5.5; P, 13.0. $C_{13}H_{13}O_2P$ requires C, 67.2; H, 5.7; P, 13.4%; R_f 0.45 (silica, 9 : 1, ethyl acetate : methanol, v/v); ν_{max} (KBr Disc)/cm^{-1} 3220 (st), 2900 (w), 1485 (md), 1445 (st), 1215 (st), 1150 (st), 1125 (st), 1070 (md), 850 (md), 720 (st), 545 (st), 490 (st), 435 (md); δ_H (300 MHz; $CDCl_3$) 4.40 (2H, d, J_{PH} 0.9 Hz, CH_2), 7.43–7.58 (6H, m, aromatic), 7.72–7.79 (4H, m, aromatic); δ_C (75 MHz; $CDCl_3$) 61.30 (d, J_{PC} 82 Hz, CH_2), 128.65 (d, J_{PC} 12.0 Hz, CH, *m*-Ph_2PO), 130.49 (d, J_{PC} 96.7 Hz, C, *ipso*-Ph_2PO), 131.33 (d, J_{PC} 10.5 Hz, CH, *o*-Ph_2PO), 132.12 (d, J_{PC} 2.2 Hz, CH, *p*-Ph_2PO); *m*/*z* (FAB) 465 [(2M + H)$^+$, 7%], 233 [(M + H)$^+$, 100], 183 (7), 140 (23), 91 (7).

Chloromethyldiphenylphosphine oxide (5)

Hydroxymethyldiphenylphosphine oxide (4.0 g, 17.24 mmol) was dissolved in dichloromethane (25 cm^3). Thionyl chloride was added (2.5 cm^3, 34.26 mmol) and the solution stirred for 3 h at ambient temperature. The reaction was carefully quenched with water (50 cm^3), neutralised with aqueous sodium bicarbonate and extracted with dichloromethane (3 × 20 cm^3). The organic layers were combined, dried (magnesium sulfate), filtered and the solvent removed under reduced pressure to give the phosphine oxide **5** (2.84 g, 66%) as a white solid, mp 133–135 °C (lit.[31] mp 137–138 °C) after recrystallisation from ethyl acetate. Found: C, 62.1; H, 4.5; Cl, 13.8; P, 12.2. $C_{13}H_{12}ClOP$ requires C, 62.3; H, 4.8; Cl, 14.1; P, 12.4%; R_f 0.38 (silica, ethyl acetate); ν_{max} (KBr Disc)/cm^{-1} 3070 (w), 2920 (w), 1490 (w), 1445 (st), 1435 (st), 1195 (st), 1130 (st), 1000 (w), 815 (st), 745 (md), 700 (st), 490 (st), 415 (md), 300 (md); δ_H (300 MHz; $CDCl_3$) 4.05 (2H, d, J_{PH} 6.6 Hz, CH_2), 7.50–7.63 (6H, m, aryl), 7.78–7.85 (4H, m, aryl); δ_C (75 MHz; $CDCl_3$) 37.79 (d, J_{PC} 72.0 Hz, CH_2), 128.92 (d, J_{PC} 12.0 Hz, CH, *m*-Ph_2PO), 131.11 (d, J_{PC} 90.0 Hz, C, *ipso*-Ph_2PO), 131.72 (d, J_{PC} 9.0 Hz, CH, *o*-Ph_2PO), 132.82 (d, J_{PC} 2.2 Hz, CH, *p*-Ph_2PO); *m*/*z* (FAB) 501 [(2M(^{35}Cl) + H)$^+$, 4%], 251 [(M(^{37}Cl + H)$^+$, 30], 251 [(M(^{35}Cl) + H)$^+$, 100], 215 (5), 183 (5), 91 (7).

(3-Chloro-6-nitrobenzyl)diphenylphosphine oxide (6a)

Sodium hydride (60% dispersion in oil, 800 mg, 20 mmol) was added to anhydrous dimethyl sulfoxide (9 cm^3) and the mixture flushed with nitrogen. Chloromethyldiphenylphosphine oxide (**5**) (2.0 g, 7.98 mmol) and 4-chloronitrobenzene (1.40 g, 8.89 mmol) were dissolved in anhydrous dimethyl sulfoxide (11 cm^3) and added dropwise to the sodium hydride slurry. The mixture was stirred at ambient temperature overnight. The reaction was quenched with distilled water, acidified with hydrochloric acid (1 M solution) and extracted with dichloromethane (3 × 20 cm^3). The combined extracts were washed with distilled water (3 × 20 cm^3), dried (magnesium sulfate), filtered and the solvent removed under reduced pressure to yield the phosphine oxide **6a** (1.8 g, 61%) as a cream coloured solid, mp 186–188 °C (lit.[13] mp 188–189.5 °C) after recrystallisation from ethanol. Found: C, 61.5; H, 4.1; N, 4.0; Cl, 9.7; P, 8.3. $C_{19}H_{15}ClNO_3P$ requires C, 61.4; H, 4.1; N, 3.8; Cl, 9.5; P, 8.3%; R_f (silica, ethyl acetate); ν_{max} (KBr Disc)/cm^{-1} 3110 (w), 1605 (md), 1525 (st), 1440 (md), 1415 (md), 1350 (st), 1155 (md), 1130 (md), 1110 (md), 905 (st), 750 (md), 700 (st), 610 (md), 520 (st); δ_H (300 MHz; $CDCl_3$) 4.21 (2H, d, J_{PH} 13.8 Hz, CH_2), 7.30 (1H, dt *J* 8.8 and 2.0 Hz, H4), 7.42–7.57 (7H, m, aryl), 7.65–7.72 (4H, m, aryl), 7.81 (1H, d, *J* 8.8 Hz, H5); δ_C (75 MHz; $CDCl_3$) 34.61 (d, J_{PC} 62.2 Hz, CH_2), 126.47 (d, J_{PC} 1.9 Hz, CH, C5), 127.96 (d, J_{PC} 2.2 Hz, CH, C4), 128.62 (d, J_{PC} 11.8, CH, *m*-Ph_2PO), 129.19 (d, J_{PC} 8.4 Hz, C, C1), 130.99 (d, J_{PC} 101.0 Hz, C, *ipso*-Ph_2PO), 130.88 (d, J_{PC} 9.5 Hz, CH, *o*-Ph_2PO), 132.18 (d, J_{PC} 2.9 Hz, CH, *p*-Ph_2PO), 133.02 (d, J_{PC} 4.3 Hz, CH, C2), 139.12 (d, J_{PC} 3.1 Hz, C, C3), 147.17 (d, J_{PC} 5.4 Hz, C, C6); *m*/*z* (FAB) 374 [(M(^{37}Cl) + H)$^+$, 40%], 372 [(M(^{35}Cl) + H)$^+$, 100], 325 (11), 77 (11).

(3-Bromo-6-nitrobenzyl)diphenylphosphine oxide (6b)

The phosphine oxide **6b** was prepared from chloromethyldiphenylphosphine oxide **5** (2.50 g, 9.98 mmol) and 4-bromonitrobenzene (2.20 g, 10.89 mmol) in a similar way to the diphenylphosphine oxide **6a**. The phosphine oxide **6b** (2.3 g,

55%) was obtained as a cream coloured solid, mp 193–195 °C (lit.[13] mp 195–197.5 °C) after chromatography (silica, 2 : 1, chloroform : ethyl acetate, v/v). Found: C, 55.1; H, 3.3; N, 3.6; Br, 18.9; P, 7.4. $C_{19}H_{15}BrNO_3P$ requires C, 54.8; H, 3.6; N, 3.4; Br, 19.2; P, 7.4%; R_f 0.49 (silica, ethyl acetate); ν_{max} (KBr Disc)/cm^{-1} 3000 (w), 1600 (md), 1530 (st), 1480 (w), 1435 (st), 1350 (st), 1230 (w), 1190 (st), 1120 (md), 880 (st), 820 (md), 760 (md), 740 (st), 690 (st), 520 (st); δ_H (300 MHz; $CDCl_3$) 4.20 (2H, d, J_{PH} 13.8 Hz, CH_2), 7.42–7.57 (7H, m, aryl), 7.64–7.72 (5H, m, aryl), 7.74 (1H, d, J 8.8 Hz, H5); *m*/*z* (FAB) 418 [(M(^{81}Br) + H)$^+$, 100%], 416 [(M(^{79}Br) + H)$^+$, 100], 371 (8), 369 (8), 307 (5), 210 [(Ph_2PO), 43], 165 (8), 107 (12), 89 (20).

(3-Fluoro-6-nitrobenzyl)diphenylphosphine oxide (6c)

The phosphine oxide **6c** was prepared from chloromethyldiphenylphosphine oxide (**5**) (1.71 g, 6.83 mmol) and 4-fluoronitrobenzene (1.06 g, 7.52 mmol) in a similar way to the diphenylphosphine oxide **6a**. The phosphine oxide **6c** (350 mg, 14%) was obtained as a pale brown solid, mp 189–190 °C after chromatography (silica, 4 : 1, chloroform : ethyl acetate, v/v). Found: C, 63.9; H, 4.6; N, 4.1; F, 5.3; P, 8.5. $C_{19}H_{15}FNO_3P$ requires C, 64.2; H, 4.3; N, 3.9; F, 5.4; P, 8.7%; R_f 0.63 (silica, ethyl acetate); ν_{max} (KBr Disc)/cm^{-1} 3120 (w), 1620 (md), 1530 (st), 1440 (md), 1350 (st), 1250 (md), 1190 (st), 1125 (md), 965 (md), 830 (md), 700 (st), 610 (md), 520 (st), 490 (md); δ_H (300 MHz; $CDCl_3$) 4.25 (2H, d, J_{PH} 13.9 Hz, CH_2), 6.99–7.06 (1H, m, aryl), 7.29–7.33 (1H, m, aryl), 7.42–7.57 (6H, m, aryl), 7.65–7.72 (4H, m, aryl), 7.90 (1H, dd, J_{HF} 5.2 and J_{HH} 9.1 Hz, H5); *m*/*z* (FAB) 356 [(M + H)$^+$, 100%], 340 (3), 309 (10), 201 [(Ph_2PO), 32], 183 (8), 107 (5).

(2,4-Dinitrobenzyl)diphenylphosphine oxide (15) and (2,6-dinitrobenzyl)diphenylphosphine oxide (14)

The phosphine oxide **15** was prepared from chloromethyldiphenylphosphine oxide **5** (500 mg, 2.00 mmol) and 1,3-dinitrobenzene (370 mg, 2.20 mmol) in a similar way to the diphenylphosphine oxide **6a**. The phosphine oxide **15** (540 mg, 71%) was obtained as a pale brown solid, mp 166–168 °C after chromatography (silica, 1 : 1, chloroform : ethyl acetate, v/v) and recrystallisation from isopropanol. Found: C, 59.7; H, 4.1; N, 7.6; P, 7.7. $C_{19}H_{15}N_2O_5P$ requires C, 59.7; H, 4.0; N, 7.3; P, 8.1%; R_f 0.42 (silica, 1 : 1, chloroform : ethyl acetate, v/v); ν_{max} (KBr Disc)/cm^{-1} 2930 (md), 1715 (w), 1620 (md), 1540 (st), 1440 (md), 1350 (st), 1180 (st), 1150 (md), 1120 (md), 1100 (w), 900 (md), 860 (md), 830 (md), 770 (w), 750 (md), 720 (md), 710 (md), 690 (md), 550 (md), 510 (md); δ_H (300 MHz; $CDCl_3$) 4.33 (2H, d, J_{PH} 13.9 Hz, CH_2), 7.44–7.51 (4H, m, aryl), 7.54–7.59 (2H, m, aryl), 7.64–7.71 (4H, m, aryl), 7.78 (1H, dd, J_{HH} 8.5 Hz, J_{PH} 2.1 Hz, H6), 8.33 (1H, dd, J_{HH} 2.3, 8.5 Hz, H5), 8.69 (1H, d, J_{HH} 2.3 Hz, H3); δ_C (75 MHz; $CDCl_3$) 35.31 (d, J_{PC} 59.3 Hz, CH_2), 120.47 (d, J_{PC} 2.5 Hz, CH, C3), 126.64 (d, J_{PC} 2.0 Hz, CH, C5), 128.84 (d, J_{PC} 11.7 Hz, CH, *m*-Ph_2PO), 130.51 (d, J_{PC} 101.9 Hz, C, *ipso*-Ph_2PO), 131.86 (d, J_{PC} 9.5 Hz, CH, *o*-Ph_2PO), 132.54 (d, J_{PC} 3.0 Hz, CH, *p*-Ph_2PO), 134.37 (d, J_{PC} 7.5 Hz, C, C1), 134.69 (d, J_{PC} 4.4 Hz, CH, C6), 146.58 (d, J_{PC} 2.9 Hz, C, C4), 148.83 (d, J_{PC} 5.4 Hz, C, C2); *m*/*z* (FAB) 765 [(2M + H)$^+$, 10%], 383 [(M + H)$^+$, 100], 367 (10), 336 (10), 307 (12), 201 [(Ph_2PO), 24]. The phosphine oxide **14** (40 mg, 5%) was obtained as a brown solid, 143–144 °C after chromatography (silica, 1 : 1, chloroform : ethyl acetate, v/v). R_f 0.45 (silica, 1 : 1, chloroform : ethyl acetate, v/v); ν_{max} (KBr Disc)/cm^{-1} 2930 (md), 1715 (w), 1620 (md), 1540 (st), 1440 (md), 1350 (st), 1180 (st), 1150 (md), 1120 (md), 1100 (w), 900 (md), 860 (md), 830 (md), 770 (w), 750 (md), 720 (md), 710 (md), 690 (md), 550 (md), 510 (md); δ_H (300 MHz; $CDCl_3$) 4.76 (2H, d, J_{PH} 13.2 Hz, CH_2), 7.42–7.70 (11H, m, aryl), 8.02 (2H, d, J 8.2 Hz, H3 and H5); found (CI): (M + H)$^+$, 383.0800. $C_{19}H_{16}N_2O_5P$ requires (M + H)$^+$, 383.0797; *m*/*z* (FAB) 383 [(M + H)$^+$, 100%], 201 [(Ph_2PO), 40].

[2-Nitro-4-(trifluoromethyl)benzyl]diphenylphosphine oxide (16)

The phosphine oxide **16** was prepared from chloromethyldiphenylphosphine oxide (**5**) (2.5 g, 9.98 mmol) and 3-trifluoromethylnitrobenzene (2.10 g, 10.98 mmol) in a similar way to diphenylphosphine oxide **6a**. The phosphine oxide **16** (1.5 g, 37%) was obtained as white needles, mp 188–189 °C after two recrystallisations from isopropanol. Found: C, 59.2; H, 3.4; N, 3.6; F, 13.8; P, 7.8. $C_{20}H_{15}F_3NO_3P$ requires C, 59.3; H, 3.7; N, 3.5; F, 14.1; P, 7.6%; R_f 0.36 (silica, 4 : 1, chloroform : ethyl acetate, v/v); ν_{max} (KBr Disc)/cm^{-1} 3080 (w), 2930 (md), 1630 (md), 1540 (st), 1440 (st), 1360 (md), 1330 (st), 1220 (md), 1130 (st), 1000 (md), 860 (md), 750 (md), 720 (st), 630 (st); δ_H (300 MHz; $CDCl_3$) 4.29 (2H, d, J_{PH} 13.9 Hz), 7.45–7.51 (4H, m, aryl), 7.55–7.60 (2H, m, aryl), 7.68–7.72 (4H, m, aryl), 7.76 (1H, d, J_{HH} 9.0 Hz, H5), 7.79 (1H, dd, J_{HH} 9.0 Hz and J_{PH} 1.5 Hz, H6), 8.10 (1H, s, H3); *m*/*z* (FAB) 811 [(2M + H)$^+$, 17%], 406 [(M + H)$^+$, 100], 359 (20), 201 [(Ph_2PO), 60], 89 (12), 77 (20).

[3-Chloro-6-nitro-4-(trifluoromethyl)benzyl]diphenylphosphine oxide (18)

The phosphine oxide **18** was prepared from chloromethyldiphenylphosphine oxide (**5**) (2.5 g, 9.98 mmol) and 4-chloro-3-(trifluoromethyl)nitrobenzene (2.48 g, 11.00 mmol) in a similar way to the diphenylphosphine oxide **6a**. The phosphine oxide **18** (3.62 g, 74%) was obtained as cream coloured needles, mp 243–244 °C after recrystallisation from isopropanol. Found: C, 54.5; H, 3.1; N, 3.2; F, 12.6; Cl, 8.1; P, 6.8. $C_{20}H_{14}ClF_3NO_3P$ requires C, 54.6; H, 3.2; N, 3.2; F, 13.0; Cl, 8.1; P, 7.0%; R_f 0.72 (silica, ethyl acetate); ν_{max} (KBr Disc)/cm^{-1} 3000 (w), 1620 (md), 1530 (st), 1440 (md), 1390 (st), 1350 (st), 1310 (st), 1185 (st), 1130 (st), 1000 (w), 950 (md), 835 (md), 725 (st), 650 (md); δ_H (300 MHz; $CDCl_3$) 4.26 (2H, d, J_{PH} 13.8 Hz, CH_2), 7.45–7.60 (6H, m, aryl), 7.65–7.72 (5H, m, aryl), 8.20 (1H, s, H5); *m*/*z* (FAB) 879 [(2M(^{35}Cl) + H)$^+$, 3%], 442 [(M(^{37}Cl) + H)$^+$, 40], 440 [(M(^{35}Cl) + H)$^+$, 100], 393 (8), 201 [(Ph_2PO), 27], 125 (5), 77 (7).

[3-Chloro-4-nitro-6-(trifluoromethyl)benzyl]diphenylphosphine oxide (19)

The phosphine oxide **19** was prepared from chloromethyldiphenylphosphine oxide (**5**) (2.0 g, 7.98 mmol) and 2-chloro-5-trifluoromethylnitrobenzene (1.98 g, 8.78 mmol) in a similar way to the diphenylphosphine oxide **6a**. The phosphine oxide **19** (1.61 g, 46%) was obtained as white needles, mp 175–177 °C after chromatography (silica, 4 : 1, chloroform : ethyl acetate, v/v) and recrystallisation from isopropanol. Found: C, 54.6; H, 3.0; N, 3.1; Cl, 8.0; F, 12.6; P, 7.0. $C_{20}H_{14}ClF_3NO_3P$ requires C, 54.7; H, 3.2; N 3.2; Cl, 8.1; F, 13.0; P, 7.1%; R_f 0.49 (silica, 4 : 1, chloroform : ethyl acetate, v/v); ν_{max} (KBr Disc)/cm^{-1} 3110 (w), 2920 (md), 1610 (md), 1535 (st), 1490 (md), 1440 (md), 1360 (st), 1310 (st), 1190 (st), 1120 (st), 850 (md), 720 (st), 690 (md), 590 (w); δ_H (300 MHz; $CDCl_3$) 3.84 (2H, d, J_{PH} 14.0 Hz, CH_2), 7.46–7.60 (6H, m, aryl), 7.67–7.73 (4H, m, aryl), 8.12 (1H, s, H2), 8.13 (1H, s, H5); *m*/*z* (FAB) 442 [(M(^{37}Cl) + H)$^+$, 40%], 440 [(M(^{35}Cl) + H)$^+$, 100], 374 (7), 201 [(Ph_2PO), 53], 77 (20).

(*E*)-1-(3′-Chloro-6′-nitrophenyl)-2-phenylethene (20a)

To a stirred slurry of 3-chloro-6-nitrobenzyldiphenylphosphine oxide **6a** (400 mg, 1.08 mmol) in dry THF (3 cm^3), under nitrogen at 0 °C, was added dropwise *n*-butyllithium (2.5 M solution in hexanes, 0.43 cm^3, 1.08 mmol). The reaction mixture was stirred at 0 °C for 15 min then a solution of benzaldehyde (120 mg, 1.13 mmol) in dry THF (2 cm^3) was added. The reaction mixture was stirred at rt overnight. Saturated ammonium chloride solution (10 cm^3) was added and the mixture extracted with dichloromethane (3 × 20 cm^3). The combined extracts were dried (magnesium sulfate) and the solvent removed under reduced pressure to yield the stilbene **20a** (86 mg, 31%) as

yellow needles, mp 90–93 °C after chromatography (silica, 1 : 1, hexane : chloroform, v/v) and recrystallisation from hexane. Found: C, 65.0; H, 3.9; N, 5.6; Cl, 13.4. $C_{14}H_{10}ClNO_2$ requires C, 64.8; H, 3.9; N, 5.4; Cl, 13.7%; R_f 0.74 (silica, 1 : 1, hexane : chloroform, v/v); ν_{max} (KBr Disc)/cm^{-1} 3030 (w), 1630 (w), 1600 (md), 1570 (md), 1510 (st), 1345 (st), 1300 (w), 1255 (md), 1190 (md), 960 (md), 920 (md), 900 (md), 860 (md), 760 (md), 745 (md), 720 (md), 690 (md); δ_H (300 MHz; $CDCl_3$) 7.10 (1H, d, *J* 16.1 Hz, H2), 7.32–7.43 (4H, m, aryl), 7.54–7.56 (2H, m, aryl), 7.59 (1H, d, *J* 16.1 Hz, H1), 7.74 (1H, d, *J* 2.2 Hz, H′), 7.96 (1H, d, *J* 8.8 Hz, H5′); δ_C (75 MHz; $CDCl_3$) 122.33 (CH), 126.32 (CH), 127.17 (CH), 127.77 (CH), 127.88 (CH), 128.80 (CH), 128.93 (CH), 134.86 (C), 135.01 (CH), 135.94 (C), 139.43 (C), 145.94 (C); *m*/*z* (FAB) 262 [(M(^{37}Cl) + H)$^+$, 25%] 260 [(M(^{35}Cl) + H)$^+$, 100].

(*E*)-1-(3′-Bromo-6′-nitrophenyl)-2-(4″-nitrophenyl)ethane (20b)

The stilbene **20b** was prepared from 3-bromo-6-nitrobenzyldiphenylphosphine oxide **6b** (400 mg, 0.96 mmol), *n*-butyllithium (2.5 M solution in hexanes, 0.40 cm^3, 1.00 mmol) and 4-nitrobenzaldehyde (145 mg, 0.96 mmol) in a similar way to the nitrostilbene **20a**. The stilbene **20b** (120 mg, 36%) was obtained as orange crystals, mp 84–86 °C after chromatography (silica, 4 : 1, chloroform : hexane, v/v) and recrystallisation from ethanol. Found: C, 48.5; H, 2.6; N, 7.9; Br, 22.9. $C_{14}H_9BrN_2O_4$ requires C, 48.2; H, 2.6; N, 8.0; Br, 22.9%; R_f 0.65 (silica, 4 : 1, hexane : chloroform, v/v); ν_{max} (KBr Disc)/cm^{-1} 1600 (st), 1560 (md), 1515 (st), 1345 (st), 1300 (md), 1250 (w), 1110 (w), 970 (w), 870 (md), 825 (md), 755 (md); δ_H (300 MHz; $CDCl_3$) 7.11 (1H, d, *J* 16.1 Hz, H2), 7.61 (1H, dd, *J* 2.0 and 8.7 Hz, H4′), 7.69 (2H, d, *J* 8.8 Hz, H2″ and H6″), 7.73 (1H, d, *J* 16.1 Hz, H1), 7.90 (1H, d, *J* 2.0 Hz, H2′), 7.95 (1H, d, *J* 8.7 Hz, H5′), 8.26 (2H, d, *J* 8.8 Hz, H3″ and H5″); δ_C (75 MHz; $CDCl_3$) 124.23 (CH), 126.57 (CH), 127.13 (CH), 127.72 (CH), 128.40 (C), 131.39 (CH), 131.97 (CH), 132.35 (CH), 134.02 (C), 142.25 (C), 146.59 (C), 147.64 (C); *m*/*z* (EI) 350 [M(^{81}Br)$^+$, 4%], 348 [M(^{79}Br)$^+$, 4], 333 (8), 331 (8), 259 (8), 257 (8), 197 (100), 176 (90), 150 (70).

Stilbenes *via* one-pot VNS–Horner–Wittig reactions

(*E*)-1-(3′-Chloro-6′-nitrophenyl)-2-phenylethene (20a)

Sodium hydride (60% dispersion in oil, 400 mg, 10.00 mmol) was added to anhydrous DMSO (10 cm^3) and the flask flushed with nitrogen. Chloromethyldiphenylphosphine oxide (**5**) (1.0 g, 3.99 mmol) and 4-chloronitrobenzene (690 mg, 4.38 mmol) were dissolved in anhydrous DMSO (10 cm^3) and added dropwise to the sodium hydride slurry. The mixture was stirred at ambient temperature for 30 h before benzaldehyde (0.6 cm^3, 5.91 mmol) was added and the resulting mixture stirred overnight at 60–70 °C. The reaction was quenched with distilled water, acidified with hydrochloric acid (1 M solution) and extracted with chloroform (3 × 20 cm^3). The combined extracts were washed with distilled water (3 × 20 cm^3), dried (magnesium sulfate), filtered and the solvent removed under reduced pressure to yield the stilbene **20a** (490 mg, 47%) as yellow needles, mp 91–93 °C after chromatography (silica, 1 : 1, hexane : chloroform, v/v) and recrystallisation from hexane. The ^{1}H NMR, mass and infrared spectra were identical to those of the previously prepared sample.

(*E*)-1-(3′-Chloro-6′-nitrophenyl)-2-(4″-methylphenyl)ethene (20c)

The stilbene **20c** was prepared from chloromethyldiphenylphosphine oxide (**5**) (1.0 g, 3.99 mmol), 4-chloronitrobenzene (690 mg, 4.38 mmol) and 4-tolylaldehyde (0.5 cm^3, 4.25 mmol) in a similar way to (*E*)-1-(3′-chloro-6′-nitrophenyl)-2-phenylethene **20a**. The stilbene **20c** (470 mg, 43%) was obtained as a yellow solid, mp 70–71 °C after chromatography (silica, 1 : 1, hexane : chloroform, v/v) and recrystallisation from ethanol. Found: C, 65.6; H, 4.1; N, 4.9; Cl, 12.6. $C_{15}H_{12}ClNO_2$ requires C, 65.8; H, 4.4; N, 5.1; Cl, 13.0%; R_f 0.51 (silica, 1 : 1, hexane : chloroform, v/v); ν_{max} (KBr Disc)/cm^{-1} 1600 (md), 1560 (md), 1530 (st), 1345 (st), 1295 (w), 1250 (w), 1190 (w), 1110 (w), 970 (md), 920 (md), 855 (md), 825 (w), 810 (st), 750 (w); δ_H (300 MHz; $CDCl_3$) 2.38 (3H, s, CH_3), 7.07 (1H, d, *J* 16.1 Hz, H1), 7.20 (2H, d, *J* 8.1 Hz, H3″ and H5″), 7.34 (1H, dd, *J* 2.2 and 8.8 Hz, H4′), 7.44 (2H, d, *J* 8.1 Hz, H2″ and H6″), 7.54 (1H, d, *J* 16.1 Hz, H2), 7.73 (1H, d, *J* 2.2 Hz, H2′), 7.94 (1H, d, *J* 8.8 Hz, H5′); δ_C (75 MHz; $CDCl_3$) 21.28 (CH_3), 121.45 (CH), 126.28 (CH), 127.11 (CH), 127.49 (CH), 127.69 (CH), 129.50 (CH), 133.20 (C), 135.00 (CH), 139.09 (C), 139.32 (C), 145.87 (C); *m*/*z* (FAB) 276 [(M(^{37}Cl) + H)$^+$, 95%], 275 [(M(^{37}Cl)$^+$, 95], 274 [(M(^{35}Cl) + H)$^+$, 55], 273 (M(^{35}Cl)$^+$, 40), 258 (40), 256 (60), 242 (20), 240 (48), 230 (25) 228 (70), 214 (37), 153 (56), 139 (30), 119 (44), 105 (86).

(*E*)-1-(3′-Chloro-6′-nitrophenyl)-2-(4″-chlorophenyl)ethene (20d)

The stilbene **20d** was prepared from chloromethyldiphenylphosphine oxide (**5**) (1.0 g, 3.99 mmol), 4-chloronitrobenzene (690 mg, 4.38 mmol) and 4-chlorobenzaldehyde (840 mg, 5.98 mmol), in a similar way to (*E*)-1-(3′-chloro-6′-nitrophenyl)-2-phenylethene **20a**. The stilbene **20d** (500 mg, 43%) was obtained as a yellow solid, mp 116–117 °C after chromatography (silica, 1 : 1, hexane : chloroform, v/v) and recrystallisation from hexane. Found: C, 56.9; H, 2.9; N, 4.6; Cl, 24.0. $C_{14}H_9Cl_2NO_2$ requires C, 57.2; H, 3.1; N, 4.8; Cl, 24.1%; R_f 0.74 (silica, 1 : 1, hexane : chloroform, v/v); ν_{max} (KBr Disc)/cm^{-1} 1640 (w), 1610 (md), 1595 (md), 1560 (md), 1520 (st), 1500 (st), 1360 (st), 1310 (md), 1300 (md), 1250 (md), 1090 (md), 1015 (md), 970 (md), 925 (md), 860 (md), 815 (st); δ_H (300 MHz; $CDCl_3$) 7.03 (1H, d, *J* 16.1 Hz, H1), 7.35–7.39 (3H, m, H3′, H5″ and H4′), 7.47 (2H, d, *J* 8.5 Hz, H2″ and H6″), 7.56 (1H, d, *J* 16.1 Hz, H1), 7.71 (1H, d, *J* 2.2 Hz, H2′), 7.97 (1H, d, *J* 8.7 Hz, H5′); δ_C (75 MHz; $CDCl_3$) 122.99 (CH), 126.38 (CH), 127.90 (CH), 128.00 (CH), 128.30 (CH), 129.00 (CH), 133.57 (CH), 134.45 (C), 134.55 (C), 134.64 (C), 139.54 (C), 145.90 (C); *m*/*z* (FAB) 297 [M(^{37}Cl^{37}Cl)$^+$, 10%], 296 [(M(^{35}Cl^{37}Cl) + H)$^+$, 45], 295 [M(^{35}Cl^{37}Cl)$^+$, 85], 294 [(M(^{35}Cl^{35}Cl) + H)$^+$, 80], 293 [M(^{35}Cl^{35}Cl)$^+$, 100], 276 (50), 261 (15), 250 (24), 214 (32), 199 (20), 165 (20), 153 (50), 139 (36).

(*E*)-1-[3′-Chloro-6′-nitro-4′-(trifluoromethyl)phenyl]-2-phenylethene (20e) and (*E*)-1-(3′-chloro-6′-nitrophenyl)-2-(4″-{(2‴-*p*-methylphenyl)-2‴-hydroxyethyl}phenyl)ethene (21)

Sodium hydride (60% dispersion in oil, 200 mg, 5.00 mmol) was added to anhydrous DMSO (5 cm^3) and the flask flushed with nitrogen. Chloromethyldiphenylphosphine oxide (**5**) (500 mg, 2.00 mmol) and 4-chloro-3-trifluoromethylnitrobenzene (500 mg, 2.22 mmol) were dissolved in anhydrous DMSO (5 cm^3) and added dropwise to the sodium hydride slurry. The mixture was stirred at ambient temperature for 6 h before benzaldehyde (0.4 cm^3, 3.94 mmol) was added and the resulting mixture stirred overnight at 60–70 °C. The reaction was quenched with distilled water, acidified with hydrochloric acid (1 M solution) and extracted with chloroform (3 × 20 cm^3). The combined extracts were washed with distilled water (3 × 20 cm^3), dried (magnesium sulfate), filtered and the solvent removed under reduced pressure to yield the stilbene **20e** (210 mg, 32%) as yellow needles, mp 153–155 °C after chromatography (silica, 4 : 1, hexane : chloroform, v/v) and recrystallisation from hexane. Found: C, 54.9; H, 2.6; N, 4.3; Cl, 10.9; F, 17.3. $C_{15}H_9ClF_3NO_2$ requires C, 55.0; H, 2.8; N, 4.3; Cl, 10.8; F, 17.4%; R_f 0.47 (silica, 4 : 1, hexane : chloroform, v/v); ν_{max} (KBr Disc)/cm^{-1} 1615 (md), 1580 (w), 1555 (md), 1505 (md), 1450 (w), 1380 (md), 1340 (st), 1300 (st), 1220 (w), 1150 (st), 1130 (st), 1090 (md), 960 (md), 910 (md), 750 (md), 690

(md), 665 (md), 500 (w); δ_H (300 MHz; $CDCl_3$) 7.20 (1H, d, *J* 16.3 Hz, H2), 7.35–7.45 (3H, m, aryl), 7.56–7.59 (2H, m, aryl), 7.63 (1H, d, *J* 16.3 Hz, H1), 7.92 (1H, s, H2′), 8.34 (1H, s, H5′); δ_C (75 MHz; $CDCl_3$) 120.96 (CH), 121.72 (q, J_{FC} 273.0 Hz, CF_3), 124.94 (q, J_{FC} 5.5 Hz, CH), 127.70 (CH), 127.53 (q, J_{FC} 10.0 Hz, C), 129.00 (CH), 129.68 (CH), 130.85 (CH), 135.46 (C), 137.14 (C), 137.46 (CH), 137.70 (C), 145.14 (C); *m*/*z* (FAB) 328 $[(M + H)^+$, 52%], 282 (100). Further elution gave the alcohol **21** (78 mg, 10%) as an oil, R_f 0.39 (silica, chloroform); ν_{max} (KBr Disc)/cm^{-1} 3400 (bm), 1600 (st), 1565 (md), 1520 (st), 1340 (st), 1255 (md), 1110 (md), 965 (md), 920 (md), 820 (md); δ_H (300 MHz; $CDCl_3$) 1.95 (1H, br s, OH), 2.36 (3H, s, CH_3), 3.03 (2H, d, *J* 6.6 Hz, CH_2), 4.88 (1H, t, *J* 6.6 Hz, C*H*OH), 7.07 (1H, d, *J* 16.1 Hz, H1), 7.11–7.32 (6H, m, aryl), 7.35 (1H, dd, *J* 2.2 and 8.7 Hz, H4′), 7.47 (2H, d, *J* 8.1 Hz, aryl), 7.55 (1H, d, *J* 16.1 Hz, H2), 7.72 (1H, d, *J* 2.2 Hz, H2′), 7.94 (1H, d, *J* 8.7 Hz, H5′). Found (CI): $(M + NH_4)^+$, 411.1488. $C_{23}H_{24}ClN_2O_3$ requires $(M + NH_4)^+$, 411.1475; *m*/*z* (CI using ammonia) 411 $[(M(^{35}Cl) + NH_4)^+$, 8%], 411 $[(M(^{35}Cl) + NH_4)^+$, 20%], 393 $[(M(^{35}Cl) + H)^+$, 10], 214 (60), 188 (100).

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