N–H Insertion reactions of rhodium carbenoids. Part 1. Preparation of α-amino acid and α-aminophosphonic acid derivatives

Enrique Aller,[a] Richard T. Buck,[a] Martin J. Drysdale,[b] Leigh Ferris,[a] David Haigh,[c] Christopher J. Moody,*,†,[a] Neil D. Pearson[d] and J. Bobby Sanghera[a]

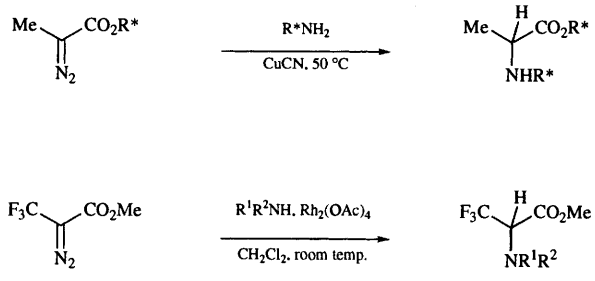
[a] *Department of Chemistry, Loughborough University, Loughborough, Leicestershire LE11 3TU, UK*
[b] *GlaxoWellcome Medicines Research Centre, Gunnels Wood Road, Stevenage, Hertfordshire SG1 2NY, UK*
[c] *SmithKline Beecham Pharmaceuticals, Great Burgh, Yew Tree Bottom Road, Epsom, Surrey KT18 5XQ, UK*
[d] *SmithKline Beecham Pharmaceuticals, Brockham Park, Betchworth, Surrey RH3 7AL, UK*

Rhodium(II) acetate-catalysed decomposition of diazophenylacetates 1 and 3 in the presence of a range of N–H compounds results in an N–H insertion reaction of the intermediate carbenoids and formation of *N*-substituted phenylglycine derivatives 2 and 4. The corresponding reactions of dimethyl α-diazobenzylphosphonate 5 constitute a simple route to aminophosphonates 6.

The synthesis of α-hydroxy and α-amino carboxylic acid derivatives and the corresponding phosphonates remains a topic of considerable importance and current interest. We have recently reported a new approach to α-hydroxy carboxylic acid derivatives based on the O–H insertion reaction of rhodium carbenoids[1–10] derived from diazo esters containing chiral auxiliaries.[11] We now describe the corresponding N–H insertion reactions of diazo esters and diazophosphonates as a route to α-amino acid and α-aminophosphonic acid derivatives.

The N–H insertion reaction of a metallocarbenoid intermediate was first described by Yates in the copper bronze-catalysed decomposition of diazoacetophenone in the presence of aniline or piperidine to give α-anilinoacetophenone and α-piperidinoacetophenone in 33 and 80% yield respectively.[12] Further copper-mediated intermolecular N–H carbenoid insertion reactions were subsequently reported,[13–19] along with photochemical[20] and protic and Lewis acid-catalysed[21–23] reactions of diazo compounds leading to N–H insertion products. However, it was the 1974 report by Paulissen and co-workers that rhodium(II) acetate was an effective catalyst for N–H insertion reactions of carbenoids that has stimulated much of the subsequent work in this area.[24] Although a number of other intermolecular N–H insertion reactions of rhodium carbenoids have been reported,[25–31] including work from our own group,[32,33] it is the intramolecular reaction that has found the widest use in synthesis. Since the original report from the Merck group in 1978,[34] the intramolecular rhodium carbenoid insertion into a β-lactam N–H bond has become a standard synthetic route to a range of bicyclic β-lactams and is widely used.[35–38] The intramolecular reaction is not limited to insertion into the β-lactam N–H, and many other examples leading to 4-, 5- and 6-membered rings have been reported.[39–46]

Hence, the insertion of metallocarbenoids derived from diazocarbonyl compounds into the N–H bond of a variety of nitrogen compounds (amines, amides, carbamates, lactams) is apparently a facile reaction, although in cases where competing pathways exist, then O–H insertion often supervenes over insertion into the N–H bond of amides and carbamates.[47–49] Therefore, it is surprising that the reaction has not been extensively investigated as a route to α-amino acids and their derivatives, although some work with this express aim in mind has been published (Scheme 1). Thus Kagan reported a new synthesis of alanine derivatives based on the copper(I) cyanide-catalysed decomposition of diazopropionates, including chiral menthyl esters, in the presence of chiral amines, R^*NH_2, although the observed asymmetric induction was modest,[14] and very recently a related rhodium(II)-catalysed N–H insertion reaction has been used as a route to α,α,α-trifluoroalanine derivatives (Scheme 1).[31]

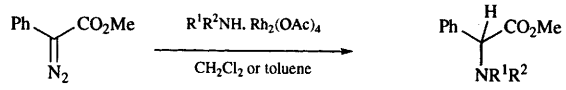


Scheme 1

Results and discussion

The diazo esters selected for study were the 2-diazo-2-phenylacetates **1** and **3**, which were readily prepared from phenylglyoxylic acid by esterification followed by the Bamford–Stevens reaction.[11,50] A range of N–H compounds was investigated: amines, anilines, amides and carbamates. Rhodium(II) acetate-catalysed decomposition of methyl 2-diazo-2-phenylacetate **1** in dichloromethane in the presence of 4-methoxyaniline, isovaleramide, benzyl carbamate or diethylamine gave the corresponding products **2a–2d** of carbenoid N–H insertion in good yield (Scheme 2), thereby extending the work of Nicoud and Kagan[14] and Osipov *et al.*[31] in the alanine series to the preparation of *N*-substituted phenylglycine derivatives. The nucleophilic amines clearly coordinate to the metal (colour change from green to red-brown) and to a certain extent poison the catalyst. In the case of diethylamine, the reaction did

† Present address: Department of Chemistry, University of Exeter, Stocker Road, Exeter EX4 4QD, UK



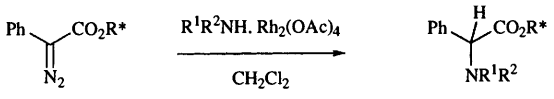
1

2a R^1 = 4-$MeOC_6H_4$, R^2 = H (79%)
b R^1 = $COCH_2CHMe_2$, R^2 = H (83%)
c R^1 = CO_2CH_2Ph, R^2 = H (74%)
d R^1 = R^2 = Et (67%)
e R^1 = (*S*)-$CH(CO_2Me)CH_2Ph$, R^2 = H (71%)
f R^1 = (*S*)-CHMePh, R^2 = H (64%)

Scheme 2

proceed in the absence of the rhodium catalyst, although the yield was lower (30–40%) and a number of unidentified by-products were formed. In an attempt to effect some asymmetric induction in such reactions, the N–H insertion reactions of (*S*)-phenylalanine methyl ester and of (*S*)-1-phenylethylamine were investigated. Both reactions gave the desired phenylglycine derivative **2e** and **2f** in reasonable yield (Scheme 2), but in both cases the induction was negligible (*ca.* 6 and 10% respectively as measured from the ^1H NMR spectrum of the mixture of diastereomers). This result is similar to that reported by Nicoud and Kagan, where only modest induction was observed in related copper-catalysed processes.[14]

In order to investigate further the possibility of diastereoselectivity in the N–H insertion reactions of rhodium carbenoids, the 2-diazo-2-phenylacetates **3** of (−)-borneol, (+)-menthol and (−)-8-phenylmenthol were studied.[11] Rhodium(II) acetate-catalysed decomposition in the presence of diethylamine, acetamide or methyl carbamate gave the corresponding *N*-substituted phenylglycine esters **4** in reasonable yield (Scheme 3), but in all cases the diastereoselectivity was



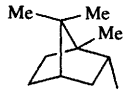
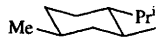
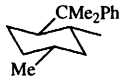
3 4a – 4e

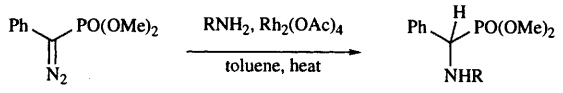
Scheme 3

very low (13% de maximum) (Table 1). This is in contrast to the closely related O–H insertion reactions of the rhodium carbenoids derived from the same diazo esters **3**, where des of over 50% could be obtained in some cases.[11]

Having established the N–H insertion reactions of rhodium carbenoids derived from diazo esters as a simple route to amino acid derivatives, we next investigated the corresponding reaction of diazophosphonates as a route to aminophosphonate derivatives. Diazophosphonates are readily available[50] and the derived rhodium carbenoids undergo a range of reactions including intramolecular C–H insertion[51,52] and O–H insertion.[10] However, apart from our own work,[32,33] there are only two reports of N–H insertion reactions of carbenoids from diazophosphonates and both of these involve the ubiquitous intramolecular insertion into the β-lactam N–H.[53,54] Therefore we investigated the simple intermolecular N–H insertion reactions of dimethyl α-diazobenzylphosphonate **5**, readily prepared by the literature method,[55,56] as a route to aminophosphonates. Diazophosphonates are more stable thermally and towards rhodium(II) catalysts than diazo esters and higher reaction temperatures are often needed.[57] Therefore, the rhodium(II) acetate-catalysed decomposition of diazophosphonate **5** in the presence of various NH compounds was carried out in boiling toluene and gave the corresponding N–H insertion products **6** (Scheme 4). The reaction with simple amides was low-yielding and the acetamide derived product **6a** could never be obtained

Table 1 Synthesis of compounds **4a–4e**

Diazo ester	R*	R^1	R^2	Product	Yield (%)	De (%)
3a		Et	Et	**4a**	49	4
3b		Et	Et	**4b**	42	3
		COMe	H	**4c**	71	10
		CO_2Me	H	**4d**	68	13
3c		COMe	H	**4e**	37	0



5

6a R = COMe (13%)
b R = COEt (33%)
c R = CO_2CH_2Ph (96%)
d R = CO_2Bu^t (95%)
e R = 4-ClC_6H_4 (76%)
f R = 4-MeC_6H_4 (16%)
g R = 4-$MeOC_6H_4$ (52%)

Scheme 4

completely pure. On the other hand, reaction with benzyl and *tert*-butyl carbamates gave the known[58–60] *N*-protected aminobenzylphosphonates **6c** and **6d** in excellent yield. Reaction with anilines to give anilinobenzylphosphonates[61] was more variable; 4-chloroaniline gave a good yield of the N–H insertion product **6e**, whereas 4-toluidine was less satisfactory. The anilinobenzylphosphonates **6e–6g** have been reported previously[62] and although we were never able to obtain the latter two as crystalline solids, the spectroscopic data closely matched those described in the literature.

There is considerable current interest in aminophosphonates and a number of methods have been developed for their synthesis.[63–78] The above route based on diazophosphonates complements existing methods and efforts are in hand to develop an asymmetric synthesis of aminophosphonates using diazophosphonate chemistry.

Experimental

Commercially available reagents were used throughout without further purification; solvents were dried by standard procedures. Analytical thin layer chromatography was carried out using aluminium-backed plates coated with Merck Kieselgel 60 GF_{254}. Plates were visualised under UV light (at 254 and/or 360 nm). Flash chromatography was carried out using Merck Kieselgel 60 H silica or Matrex silica 60. Pressure was applied at the column head with hand bellows. Samples were applied pre-adsorbed on silica.

Fully characterised compounds were chromatographically homogeneous. IR spectra were recorded in the range 4000–600 cm^{-1} using a Nicolet FT-205 spectrometer, with internal calibration. ^1H, ^{13}C and ^{31}P NMR spectra were recorded in deuteriochloroform (unless otherwise stated) using Bruker AC-250 and Bruker DPX-400 instruments; *J* values are given in Hz. High- and low-resolution mass spectra were recorded on a Kratos MS80 instrument.

Ether refers to diethyl ether and light petroleum refers to the fraction of bp 40–60 °C.

Methyl 2-(4-methoxyphenylamino)-2-phenylacetate 2a
A stirred solution of methyl 2-diazo-2-phenylacetate **1** (200 mg, 1.13 mmol) and 4-methoxyaniline (280 mg, 2.3 mmol) in dry dichloromethane (5 ml) was treated with rhodium(II) acetate (2 mol%). The mixture was heated under reflux for 12 h, the solvent evaporated and the residue chromatographed on silica gel (light petroleum–ether; gradient elution) to give the title compound (243 mg, 79%) as a colourless crystalline solid, mp 107–108 °C (lit.,[79] no mp given) (Found: M^+, 271.1212. $C_{16}H_{17}NO_3$ requires *M*, 271.1208); $\nu_{max}(CHCl_3)/cm^{-1}$ 3405, 1736, 1513 and 1238; δ_H(360 MHz) 7.50–7.49 (2 H, m, ArH), 7.47–7.28 (3 H, m, ArH), 6.72 (2 H, d, *J* 6.8, ArH), 6.53 (2 H, d, *J* 6.8, ArH), 5.02 (1 H, s, CH), 3.72 (3 H, s, OMe) and 3.71 (3 H, s, OMe); δ_C(62.9 MHz) 172.5, 152.5, 140.2, 137.8, 128.8, 128.2, 127.2, 114.8, 114.7, 61.6, 55.6 and 52.6; *m/z* (EI) 271 (M^+, 20%), 212 (100), 196 (8), 168 (9), 151 (5), 134 (8), 122 (7), 107 (6), 91 (7), 77 (11), 64 (6), 51 (6) and 39 (4).

Methyl 2-(3-methylbutanoylamino)-2-phenylacetate 2b
A stirred solution of methyl 2-diazo-2-phenylacetate **1** (200 mg, 1.13 mmol) and isovaleramide (230 mg, 2.3 mmol) in dry dichloromethane (5 ml) was treated with rhodium(II) acetate (2 mol%). The mixture was stirred at room temperature for 24 h, the solvent evaporated and the residue chromatographed on silica gel (light petroleum–ether; gradient elution) to give the *title compound* (235 mg, 83%) as a colourless crystalline solid, mp 106–107 °C (Found: M^+, 249.1365. $C_{14}H_{19}NO_3$ requires *M*, 249.1365); $\nu_{max}(CHCl_3)/cm^{-1}$ 3271, 2956, 1747, 1690, 1262; δ_H(400 MHz) 7.29–7.23 (5 H, m, ArH), 6.43 (1 H, br d, *J* 6.4, exch D_2O, NH), 5.52 (1 H, d, *J* 7.20, CH), 3.64 (3 H, s, OMe), 2.01–2.05 (3 H, m, $CHCH_2$), 0.89 (3 H, d, *J* 6.48, Me) and 0.84 (3 H, d, *J* 6.48, Me); δ_C(100.6 MHz) 170.3, 170.0, 135.1, 128.4, 127.4, 126.9, 54.7, 51.2, 44.0, 24.5, 20.7 and 20.4; *m/z* (EI) 250 (MH^+, 15%); 217 (6), 190 (36), 164 (40), 149 (8), 121 (9), 106 (100), 85 (9), 77 (12), 57 (23), 51 (4) and 41 (16).

Methyl 2-benzyloxycarbonylamino-2-phenylacetate 2c
A stirred solution of methyl 2-diazo-2-phenylacetate **1** (200 mg, 1.13 mmol) and benzyl carbamate (343 mg, 2.3 mmol) in dry dichloromethane (5 ml) was treated with rhodium(II) acetate (2 mol%). The mixture was stirred at room temperature for 24 h, the solvent evaporated and the residue chromatographed on silica gel (light petroleum–ether; gradient elution) to give the title compound (251 mg, 74%) as a colourless crystalline solid, mp 74–75 °C (lit.,[80] mp 76–77 °C) (Found: M^+, 299.1162. Calc. for $C_{14}H_{19}NO_3$, 299.1158); $\nu_{max}(CHCl_3)/cm^{-1}$ 3368, 1745, 1710, 1514 and 1215; δ_H(400 MHz) 7.39–7.34 (10 H, m, ArH), 5.90 (1 H, br d, *J* 6.0, exch D_2O, NH), 5.42 (1 H, d, *J* 7.20, CH), 5.13 (2 H, d, *J* 6.80, OCH_2) and 3.75 (3 H, s, OMe); δ_C(100.6 MHz) 172.6, 156.7, 137.9, 137.5, 130.3, 130.0, 129.9, 129.8, 129.4, 128.5, 68.4, 59.3 and 54.1; *m/z* (EI) 299 (M^+, 1%), 240 (29), 196 (20), 163 (3), 132 (6), 104 (8), 91 (100), 77 (11), 65 (10) and 51 (7).

Methyl 2-(diethylamino)-2-phenylacetate 2d
Methyl 2-diazo-2-phenylacetate **1** (200 mg, 1.14 mmol) and diethylamine (83 mg, 1.14 mmol) were dissolved in toluene (5 ml), rhodium acetate (2 mol%) was added and the mixture was heated to reflux for 12 h. The solvent was removed *in vacuo* to yield a brown oil. Purification by flash chromatography (light petroleum–ether; gradient elution) afforded the title compound as a colourless oil (168 mg, 67%) (lit.,[81] oil) (Found: M^+, 221.1416. $C_{13}H_{19}NO_2$ requires *M*, 221.1417); $\nu_{max}(CHCl_3)/cm^{-1}$ 2971, 1740 and 1202; δ_H(400 MHz) 7.44–7.43 (2 H, m, ArH), 7.33–7.28 (3 H, m, ArH), 4.49 (1 H, s, CH), 3.70 (3 H, s, OMe), 2.65–2.60 (4 H, m, CH_2) and 1.01–0.98 (6 H, t, *J* 6.7, Me); δ_C(100.6 MHz) 173.6, 137.1, 129.3, 128.7, 127.6, 69.3, 51.7, 43.7 and 12.0; *m/z* (EI) 221 (M^+, 4%), 162 (100), 146 (5), 134 (10), 121 (9), 105 (19), 91 (17) and 77 (22).

Methyl 2-[(1*S*)-1-methoxycarbonyl-2-phenylamino]-2-phenylacetate 2e
Methyl 2-diazo-2-phenylacetate **1** (200 mg, 1.14 mmol) and (*S*)-(−)-phenylalanine methyl ester (238 mg, 1.14 mmol) were dissolved in toluene (5 ml), rhodium(II) acetate (2 mol%) was added and the mixture was heated to reflux for 12 h. The solvent was removed *in vacuo* to yield a yellow oil. Purification by flash chromatography (light petroleum–ether; gradient elution) afforded the *title compound* as a colourless oil as a mixture of diastereomers (264 mg, 71%) (Found: MH^+, 328.1549. $C_{19}H_{21}NO_4$ requires *MH*, 328.1548); $\nu_{max}(CHCl_3)/cm^{-1}$ 2952 1738, 1732 and 1203; δ_H(400 MHz) 7.30–7.12 (10 H, m, ArH), 4.37 (1 H, s, CH), 3.65 (3 H, s, OMe), 3.60 (3 H, s, OMe), 3.31 (1 H, m, CH), 3.01 (2 H, m, CH_2) and 2.72 (1 H, br s, exch D_2O, NH); δ_C(100.6 MHz) 175.2, 173.5, 138.1, 138.3, 130.2, 129.5, 129.4, 128.8, 127.6, 65.0, 64.4, 61.8, 60.6, 53.2, 52.6, 40.65 and 40.57; *m/z* (CI) 328 (MH^+, 100%).

Methyl 2-[(1*S*)-1-phenylethylamino]-2-phenylacetate 2f
Methyl 2-diazo-2-phenylacetate **1** (300 mg, 1.70 mmol) and (*S*)-2-phenylethylamine (206 mg, 1.70 mmol) were dissolved in toluene (5 ml), rhodium(II) acetate (2 mol%) was added and the mixture was heated to reflux for 12 h. The solvent was removed *in vacuo* to yield an orange oil. Purification by flash chromatography (light petroleum–ether; gradient elution) afforded the *title compound*, a colourless oil (293 mg, 64%), as a mixture of diastereomers. The faster running diastereomer was obtained pure whereas the lower running diastereomer contained a trace impurity that could not be removed (Found: M^+, 269.1403. $C_{17}H_{19}NO_2$ requires *M*, 269.1415); $\nu_{max}(CHCl_3)/cm^{-1}$ 2955, 1737 and 1206; δ_H(400 MHz) (faster-running diastereomer) 7.33–7.29 (10 H, m, ArH), 4.22 (1 H, s, CH), 3.79 (1 H, q, *J* 6.5, C*H*Me), 3.70 (3 H, s, OMe) and 1.83 (3 H, d, *J* 6.5, Me); δ_C(100.6 MHz) 172.5, 144.8, 138.5, 128.2, 128.0, 127.7, 127.4, 127.2, 126.9, 62.9, 56.7, 52.2 and 24.6; *m/z* (EI) 270 (MH^+, 100%), 265 (6), 210 (97), 194 (11), 166 (12), 149 (8), 121 (19), 105 (88), 91 (12) and 77 (20). The slower-running diastereomer shows the following signals: δ_H(400 MHz) 4.19 (1 H, s, CH), 3.59 (3 H, s, OMe), 3.54 (1 H, q, *J* 6.4, CH) and 1.33 (3 H, d, *J* 6.4, Me); δ_C(100.6 MHz) 174.2, 144.6, 138.4, 128.7, 128.5, 128.4, 127.9, 127.6, 126.9, 62.9, 52.0, 50.4 and 24.4.

(1*S*)-2-*endo*-Bornyl 2-diethylamino-2-phenylacetate 4a
A stirred solution of bornyl 2-diazo-2-phenylacetate **3a** (100 mg, 0.33 mmol) and diethylamine (49 mg, 0.66 mmol) in dry dichloromethane (5 ml) was treated with rhodium(II) acetate (2 mol%). The mixture was stirred at room temperature for 7 days, the solvent evaporated and the residue chromatographed on silica gel (dichloromethane) to give the *title compound* (56 mg, 49%) as a mixture of diastereomers (*ca.* 4% de) as a colourless oil (Found: M^+, 343.2514. $C_{22}H_{33}NO_2$ requires *M*, 343.2511); ν_{max}(neat)/cm^{-1} 2961, 1732, 1454, 1198 and 1152; δ_H(250 MHz)‡ 7.45 (4 H, m, ArH), 7.29 (6 H, m, ArH), 4.92 (2 H, m, bornyl H-2), 4.51 (1 H, s, C*H*NEt_2), 4.50 (1 H, s, C*H*NEt_2), 2.64 (8 H, q, *J* 7.1, NCH_2Me), 1.89 (2 H, m), 2.34 (2 H, m), 1.15 (5 H, m), 1.67 (4 H, m), 1.01 (12 H, t, *J* 7.1, NCH_2*Me*), 0.88 (6 H, s, Me), 0.85 (3 H, s, Me), 0.84 (3 H, s, Me), 0.82 (3 H, s, Me), 0.81 (1 H, m) and 0.70 (3 H, s, Me); δ_C(62.9 MHz) 172.7, 172.6, 137.8, 137.7, 128.7, 128.5, 128.3, 127.8, 80.3, 69.7, 69.5, 48.9, 48.8, 47.9, 44.9, 44.9, 43.8, 43.7, 36.9, 36.6, 28.1, 28.0, 27.3, 27.2, 19.7, 18.9, 13.6, 13.4, 12.1 and 12.0; *m/z* (EI) 344 (MH^+, 13%), 343 (M^+, 0.7), 162 (100), 91 (12) and 81 (11).

(1*S*,3*S*,4*R*)-3-Menthyl 2-diethylamino-2-phenylacetate 4b
A stirred solution of menthyl 2-diazo-2-phenylacetate **3b** (100 mg, 0.33 mmol) and diethylamine (49 mg, 0.66 mmol) in dry

‡ NMR data for both diastereomers given.

dichloromethane (5 ml) was treated with rhodium(II) acetate (2 mol%). The mixture was stirred at room temperature for 24 h, the solvent evaporated and the residue chromatographed on silica gel (dichloromethane) to give the *title compound* (46 mg, 42%) as a mixture of diastereomers (*ca.* 3% de) as a colourless oil (Found: M^+, 345.2660. $C_{22}H_{35}NO_2$ requires *M*, 345.2688); ν_{max}(neat)/cm^{-1} 1733, 1455, 1198 and 1164; δ_H(250 MHz)‡ 7.43 (4 H, m, ArH), 7.31 (6 H, m, ArH), 4.72 (1 H, dt, *J* 10.9 and 4.4, menthyl H-3), 4.67 (1 H, dt, *J* 10.9 and 4.4 menthyl H-3), 4.46 (1 H, s, C*H*NEt$_2$), 4.41 (1 H, s, C*H*NEt$_2$), 2.64 (8 H, m), 1.85 (1 H, m), 1.80 (2 H, m), 1.65 (3 H, m), 1.35 (6 H, m), 0.99 (12 H, t, *J* 7.2, Me), 0.89 (3 H, d, *J* 6.5, Me), 0.86 (3 H, d, *J* 6.5, Me), 0.85 (3 H, d, *J* 6.5, Me), 0.85 (6 H, m), 0.70 (3 H, d, *J* 7.0, Me), 0.69 (3 H, d, *J* 7.0 Me) and 0.51 (3 H, d, *J* 6.9, Me); δ_C(62.9 MHz) 172.0, 137.4, 137.3, 128.7, 128.7, 128.2, 127.8, 127.7, 74.7, 74.5, 69.6, 69.6, 47.0, 46.8, 43.5, 43.4, 40.9, 40.3, 34.2, 31.4, 31.3, 25.9, 25.5, 23.0, 22.0, 21.9, 20.7, 20.6, 15.8, 15.6, 11.8 and 11.6; *m/z* (EI) 345 (M^+, 0.2%), 162 (100), 91 (13) and 81 (11).

(1*S*,3*S*,4*R*)-3-Menthyl 2-acetylamino-2-phenylacetate 4c

A stirred solution of menthyl 2-diazo-2-phenylacetate **3b** (100 mg, 0.33 mmol) and acetamide (39 mg, 0.66 mmol) in dry dichloromethane (5 ml) was treated with rhodium(II) acetate (2 mol%). The mixture was stirred at room temperature for 1 h, the solvent evaporated and the residue chromatographed on silica gel (ethyl acetate–light petroleum, 1:3) to give the *title compound* (78 mg, 71%) as a mixture of diastereomers (10% de) as colourless crystals, mp 68–70 °C (Found: M^+, 331.2142. $C_{20}H_{29}NO_3$ requires *M*, 331.2147); ν_{max}(Nujol)/cm^{-1} 3341, 1729, 1709, 1680, 1655, 1273, 1178 and 728; δ_H(250 MHz)‡ 7.29 (10 H, m, ArH), 6.88 (1 H, d, *J* 7.2, NH), 6.79 (1 H, d, *J* 7.5, NH), 5.56 (1 H, d, *J* 7.5, C*H*NH), 5.52 (1 H, d, *J* 7.2, C*H*NH), 4.71 (1 H, dt, *J* 10.9 and 4.4, menthyl H-3), 4.59 (1 H, dt, *J* 10.9 and 4.4, menthyl H-3), 1.98 (6 H, s, Me), 1.95 (2 H, m), 1.47 (10 H, m), 0.95 (6 H, m), 0.88 (3 H, d, *J* 6.4, Me), 0.88 (3 H, d, *J* 6.5, Me), 0.80 (3 H, d, *J*, 6.5, Me), 0.75 (3 H, d, *J* 7.0, Me), 0.57 (3 H, d, *J* 6.9, Me) and 0.38 (3 H, d, *J* 6.8, Me); δ_C(62.9 MHz) 170.7, 170.5, 169.3, 136.9, 136.8, 128.6, 128.5, 128.2, 128.1, 127.2, 127.0, 76.0, 75.9, 56.6, 56.3, 46.8, 46.6, 40.6, 39.8, 34.0, 33.9, 31.3, 31.2, 26.0, 25.2, 23.2, 22.9, 22.8, 21.8, 21.8, 20.5, 20.3, 16.1 and 15.5; *m/z* (EI) 332 (MH^+, 19%), 331 (M^+, 0.4), 194 (30), 148 (100), 106 (97) and 83 (59).

(1*S*,3*S*,4*R*)-3-Menthyl 2-methoxycarbonylamino-2-phenylacetate 4d

A stirred solution of menthyl 2-diazo-2-phenylacetate **3b** (100 mg, 0.33 mmol) and methyl carbamate (25 mg, 0.33 mmol) in dry dichloromethane (6 ml) was treated with rhodium(II) acetate (2 mol%). The mixture was stirred at room temperature, the solvent evaporated and the residue chromatographed on silica gel (dichloromethane) to give the *title compound* (78 mg, 68%), an oil, as a mixture of diastereomers (13% de) (Found: M^+, 347.2093. $C_{20}H_{29}NO_4$ requires *M*, 347.2096); ν_{max}(neat)/cm^{-1} 3436, 3364, 1728, 1499, 1179, 1054 and 698; δ_H(250 MHz)‡ 7.32 (10 H, m, ArH), 5.91 (2 H, m, NH), 5.34 (1 H, d, *J* 7.4, NHC*H*), 5.28 (1 H, d, *J* 7.4, NHC*H*), 4.73 (1 H, dt, *J* 10.9 and 4.4 menthyl H-3), 4.62 (1 H, dt, *J* 10.9 and 4.4, menthyl H-3), 3.66 (3 H, s, OMe), 3.65 (3 H, s, OMe), 2.30 (1 H, m), 1.28 (17 H, m), 0.90 (3 H, d, *J* 6.5, Me), 0.89 (3 H, d, *J* 7.1, Me), 0.82 (3 H, d, *J* 6.5, Me), 0.76 (3 H, d, *J* 6.8, Me), 0.60 (3 H, d, *J* 6.9, Me) and 0.40 (3 H, d, *J* 7.0, Me); δ_C(62.9 MHz) 170.4, 170.3, 155.9, 137.1, 128.7, 128.6, 128.3, 128.2, 127.1, 126.9, 76.1, 75.9, 58.2, 57.8, 52.2, 46.9, 46.7, 40.6, 39.8, 34.0, 33.8, 31.3, 31.2, 26.1, 25.2, 23.2, 22.9, 21.8, 21.8, 20.6, 20.4, 15.5 and 15.2; *m/z* (EI) 347 (M^+, 0.1%), 210 (27), 164 (100), 121 (18), 95 (22) and 83 (35).

(1*R*,3*R*,4*S*)-8-Phenyl-3-menthyl 2-acetylamino-2-phenylacetate 4e

A stirred solution of 8-phenyl-3-menthyl 2-diazo-2-phenylacetate **3c** (100 mg, 0.26 mmol) and acetamide (32 mg, 0.66 mmol) in dry dichloromethane (8 ml) was treated with rhodium(II) acetate (2 mol%). The mixture was stirred at room temperature for 3 h, the solvent evaporated and the residue chromatographed on silica gel (ethyl acetate–light petroleum, 1:1) to give the *title compound* (39 mg, 37%) as a mixture of diastereomers (*ca.* 0% de) as a colourless oil (Found: M^+, 407.2453. $C_{26}H_{33}NO_3$ requires *M*, 407.2460); ν_{max}(neat)/cm^{-1} 3299, 1735, 1719, 1655, 1175 and 698; δ_H(250 MHz)‡ 7.22 (20 H, m, ArH), 6.50 (1 H, d, *J* 6.9, NH), 6.34 (1 H, d, *J* 6.9, NH), 5.39 (1 H, d, *J* 6.9, C*H*NH), 4.78 (2 H, m, menthyl H-3), 4.68 (1 H, d, *J* 6.9, C*H*NH), 2.00 (2 H, m), 1.99 (3 H, s, MeCO), 1.99 (3 H, s, MeCO), 1.81 (3 H, m), 0.50–1.70 (11 H, m), 1.28 (3 H, s, Me), 1.22 (3 H, s, Me), 0.99 (3 H, s, Me), 0.84 (3 H, d, *J* 6.4, Me), 0.78 (3 H, s, Me) and 0.77 (3 H, d, *J* 6.4, Me); δ_C(62.9 MHz) 170.0, 169.9, 169.2, 168.8, 151.5, 149.9, 136.8, 136.0, 128.6, 128.6, 128.4, 128.0, 127.9, 127.8, 127.8, 127.0, 125.6, 125.31, 125.27, 77.5, 76.0, 57.3, 56.0, 50.4, 50.2, 41.5, 40.4, 39.9, 39.4, 34.3, 31.3, 31.1, 29.4, 28.8, 27.2, 26.3, 23.6, 23.1, 21.6 and 21.6; *m/z* (EI) 408 (MH^+, 7%), 407 (M^+, 2), 214 (18), 194 (91), 148 (70), 119 (100), 105 (95), 91 (59) and 77 (37).

Dimethyl α-acetylaminobenzylphosphonate 6a

To a stirred solution of dimethyl α-diazobenzylphosphonate **5** (100 mg, 0.44 mmol) in dry toluene (2 ml) was added acetamide (261 mg, 4.40 mmol). After the addition of rhodium(II) acetate (2 mol%) the reaction mixture was stirred at reflux for 2 h. Removal of the solvent under reduced pressure and purification of the reaction mixture by flash chromatography (ether–ethyl acetate, 7:3) yielded the title compound as a pale yellow oil (15 mg, 13%) (lit.,[82] mp 138–139.5 °C); ν_{max}(film)/cm^{-1} 3471br, 2957, 1757, 1263 and 1030; δ_H(400 MHz) 7.51–7.36 (5 H, m, ArH), 6.17 (1 H, d, *J* 13.5, CHP), 3.73 [3 H, d, *J* 10.6, P(OMe)$_2$], 3.65 [3 H, d, *J* 10.6, P(OMe)$_2$], 2.19 (3 H, s, Me), NH was not observed; δ_C(100.6 MHz) 169.3 (d), 133.1, 130.0, 128.9, 127.8, 70.9 (d), 53.9 (d), 53.8 (d) and 20.9; δ_P(101.3 MHz) 19.04; satisfactory mass spectrum could not be obtained.

Dimethyl α-propionylaminobenzylphosphonate 6b

To a stirred solution of dimethyl α-diazobenzylphosphonate **5** (100 mg, 0.44 mmol) in dry toluene (2 ml) was added propionamide (162 mg, 4.40 mmol). After the addition of rhodium(II) acetate (2 mol%) the reaction mixture was stirred at reflux for 1 h. Removal of the solvent under reduced pressure and purification of the reaction mixture by flash chromatography (ether–ethyl acetate, 7:3) yielded the *title compound* as a pale yellow oil (39 mg, 33%) (Found: M^+, 272.0814. $C_{12}H_{19}NO_4P$ requires *M*, 272.1052); ν_{max}(film)/cm^{-1} 3496, 2958, 1752, 1464, 1378 and 1038; δ_H(250 MHz) 7.48–7.35 (5 H, m, ArH), 6.19 (1 H, d, *J* 13.6, CHP), 3.72 [3 H, d, *J* 10.9, P(OMe)$_2$], 3.66 [3 H, d, *J* 10.5, P(OMe)$_2$], 2.46 (2 H, m, CH_2), 1.18 (3 H, t, *J* 7.4, Me), NH was not observed; δ_C(62.9 MHz) 161.1 (d), 140.2, 128.8, 128.5, 127.6, 69.8 (d), 53.9 (d), 53.8 (d), 27.4 and 8.9; δ_P(101.3 MHz) 19.15; *m/z* 272 (MH^+, 10%), 216 (15), 166 (10), 138 (15), 110 (30), 105 (20) and 57 (100).

Dimethyl α-benzyloxycarbonylaminobenzylphosphonate 6c

To a stirred solution of dimethyl α-diazobenzylphosphonate **5** (100 mg, 0.44 mmol) in dry toluene (2 ml) was added benzyl carbamate (334 mg, 2.20 mmol). After the addition of rhodium(II) acetate (2 mol%) the reaction mixture was stirred at 80 °C for 1 h. Removal of the solvent under reduced pressure and purification of the reaction mixture by flash chromatography (ether–ethyl acetate, 7:3) yielded the title compound as a colourless solid (149 mg, 96%), mp 117–118 °C (lit.,[58] mp 117–118.5 °C; lit.,[59] mp 120–121 °C) (Found: C, 58.6; H, 5.8; N, 4.2. Calc. for $C_{17}H_{20}NO_5P$: C, 58.5; H, 5.8; N, 4.0%); ν_{max}(Nujol)/cm^{-1} 3250, 3018, 2956, 1716, 1490, 1256, 1216 and 1041; δ_H(250 MHz) 7.46–7.30 (10 H, m, ArH), 6.41 (1 H, dd, *J* 9.2, 3.4, NH), 5.24 (1 H, dd, *J* 21.7, 9.7, CHP), 5.12 (1 H, d, *J* 18.0, OCH_2), 5.05 (1 H, d, *J* 18.0, OCH_2), 3.71 [3 H, d, *J* 10.6,

$P(OMe)_2$] and 3.44 [3 H, d, J 10.5, $P(OMe)_2$]; δ_C(62.9 MHz) 155.6, 136.0, 134.8, 128.7, 128.4, 128.2, 128.1, 127.9, 127.8, 67.2, 53.8, (d), 53.5 (d) and 50.8 (d); δ_P(101.3 MHz) 22.67; *m/z* 349 (M^+, 3%), 240 (40), 196 (36), 132 (20), 104 (20), 91 (100) and 77 (25).

Dimethyl α-*tert*-butoxycarbonylaminobenzylphosphonate 6d

To a stirred solution of dimethyl α-diazobenzylphosphonate **5** (100 mg, 0.44 mmol) in dry toluene (2 ml) was added *tert*-butyl carbamate (259 mg, 2.20 mmol). After the addition of rhodium(II) acetate (2 mol%) the reaction mixture was stirred at reflux for 1 h. Removal of the solvent under reduced pressure and purification of the reaction mixture by flash chromatography (ether–ethyl acetate, 4:1) yielded the title compound as a colourless solid (132 mg, 95%), mp 115–116 °C (lit.,[60] mp 110–111 °C) (Found: C, 53.6; H, 7.25; N, 4.6. Calc. for $C_{14}H_{22}NO_5P$: C, 53.3; H, 7.0; N, 4.4%); $\nu_{max}(CHCl_3)/cm^{-1}$ 3261, 3011, 2954, 1712, 1496, 1252, 1217 and 1040; δ_H(250 MHz) 7.45–7.32 (5 H, m, ArH), 5.81 (1 H, dd, J 5.5, 9.3, NH), 5.16 (1 H, dd, J 21.5, 9.3, CHP), 3.76 [3 H, d, J 10.6, $P(OMe)_2$], 3.50 [3 H, d, J 10.5, $P(OMe)_2$] and 1.42 (9 H, s, Bu^t); δ_C(62.9 MHz) 154.9, 135.2, 128.5, 128.0, 127.7, 80.2, 53.6 (d), 53.4 (d), 51.4 (d) and 28.1; δ_P(101.3 MHz) 23.12; *m/z* 315 (M^+, 3%), 242 (8), 206 (40), 150 (85), 106 (90) and 57 (100).

Dimethyl α-(4-chlorophenylamino)benzylphosphonate 6e

To a stirred solution of dimethyl α-diazobenzylphonate **5** (100 mg, 0.44 mmol) in dry toluene (2 ml) was added 4-chloroaniline (282 mg, 2.20 mmol). After the addition of rhodium(II) acetate (2 mol%) the reaction mixture was stirred at reflux for a period of 3 h. Removal of the solvent under reduced pressure and purification of the reaction mixture by flash chromatography (ethyl acetate–light petroleum, 1:1) yielded the title compound as a pale brown solid (110 mg, 76%) which was recrystallised from ethyl acetate–light petroleum to give the title compound as colourless crystals (80 mg, 56%), mp 101–102 °C (lit.,[62] mp 101–102 °C) (Found: M^+, 325.0639. Calc. for $C_{15}H_{17}ClNO_3P$, 325.0635); ν_{max}(film)/cm^{-1} 3301, 3029, 2955, 1494, 1454, 1241, 1183 and 737; δ_H(250 MHz) 7.45–7.30 (5 H, m, ArH), 7.04 (2 H, m, ArH), 6.52 (2 H, m, ArH), 4.95 (1 H, br s, NH), 4.74 (1 H, d, J 24.2, CHP), 3.76 [3 H, d, J 10.6, $P(OMe)_2$] and 3.46 [3 H, d, J 10.5, $P(OMe)_2$]; δ_C(62.9 MHz) 141.1, 135.0, 129.0, 128.2, 127.7, 127.6, 121.9, 115.0, 56.9 (d), 54.5 (d) and 53.8 (d); δ_P(101.3 MHz) 23.56; *m/z* 325 (M^+, 5%), 216 (100), 138 (12), 111 (16), 77 (9) and 43 (21).

Dimethyl α-(4-methylphenylamino)benzylphosphonate 6f

To a stirred solution of dimethyl α-diazobenzylphonate **5** (100 mg, 0.44 mmol) in dry toluene (2 ml) was added 4-methylaniline (237 mg, 2.20 mmol). After the addition of rhodium(II) acetate (2 mol%) the reaction mixture was stirred at reflux for 3 h. Removal of the solvent under reduced pressure and purification of the reaction mixture by flash chromatography (ethyl acetate–light petroleum, 1:1) yielded the title compound as a brown oil (22 mg, 16%) (lit.,[62] mp 89–90 °C) (Found: M^+, 305.1179. Calc. for $C_{16}H_{20}NO_3P$, 305.1180); ν_{max}(film)/cm^{-1} 3311, 3028, 2954, 1493, 1454, 1240, 1183 and 733; δ_H(250 MHz) 7.48–7.33 (5 H, m, ArH), 6.91 (2 H, m, ArH), 6.52 (2 H, m, ArH), 4.77 (1 H, d, J 24.5, CHP), 4.72 (1 H, br s, NH), 3.76 [3 H, d, J 10.7 $P(OMe)_2$], 3.47 [3 H, d, J 10.5, $P(OMe)_2$] and 2.17 (3 H, s, ArMe); δ_C(62.9 MHz) 142.1, 142.0, 135.7, 129.6, 128.6, 128.0, 127.8, 114.0, 57.0 (d), 54.7 (d), 53.7 (d) and 20.3; δ_P(101.3 MHz) 24.05; *m/z* 305 (M^+, 6%), 196 (100), 91 (18) and 69 (53).

Dimethyl α-(4-methoxyphenylamino)benzylphosphonate 6g

To a stirred solution of dimethyl α-diazobenzylphonate **5** (100 mg, 0.44 mmol) in dry toluene (2 ml) was added 4-methoxyaniline (272 mg, 2.20 mmol). After the addition of rhodium(II) acetate (2 mol%) the reaction mixture was stirred at reflux for 3 h. Removal of the solvent under reduced pressure and purification of the reaction mixture by flash chromatography (ether) yielded the title compound as a brown oil (74 mg, 52%) (lit.,[62] mp 100–101 °C) (Found: M^+, 321.1133. Calc. for $C_{16}H_{20}NO_4P$, 321.1130); ν_{max}(film)/cm^{-1} 3311, 3021, 2954, 1494, 1453, 1238, 1181 and 1033; δ_H(250 MHz) 7.47–7.29 (5 H, m, ArH), 6.69 (2 H, m, ArH), 6.55 (2 H, m, ArH), 4.88 (1 H, d, J 24.1, CHP), 4.58 (1 H, br s, NH), 3.76 [3 H, d, J 10.6, $P(OMe)_2$], 3.68 (3 H, s, OMe) and 3.46 [3 H, d, J 10.5, $P(OMe)_2$]; δ_C(62.9 MHz) 154.6, 152.8, 140.1, 136.5, 128.6, 127.8, 115.2, 114.7, 57.0 (d), 56.5, 53.7 (d) and 53.5 (d); δ_P(101.3 MHz; $CDCl_3$) 24.08; *m/z* 321 (M^+, 12%), 290 (10), 212 (100), 180 (47), 108 (13), 91 (21) and 77 (17).

Acknowledgements

We thank the EC (fellowship to E. A. G.), SmithKline Beecham Pharmaceuticals for support under the CASE Scheme (to L. F.) and both SmithKline Beecham and GlaxoWellcome for support (to R. T. B. and J. B. S.) through the EPSRC/DTI Asymmetric Synthesis Link Scheme. We also thank Fisons Pharmaceuticals/Astra Charnwood for their generous support of all our research programmes and the EPSRC for funds towards the purchase of a 400 MHz NMR spectrometer. We thank the EPSRC Mass Spectrometry Centre at Swansea for mass spectra.

References

1 For reviews see the following and also refs. 2–10: M. P. Doyle, *Acc. Chem. Res.*, 1986, **19**, 348.
2 M. P. Doyle, *Chem. Rev.*, 1986, **86**, 919.
3 G. Maas, *Top. Curr. Chem.*, 1987, **137**, 75.
4 J. Adams and D. M. Spero, *Tetrahedron*, 1991, **47**, 1765.
5 A. Padwa and S. F. Hornbuckle, *Chem. Rev.*, 1991, **91**, 263.
6 A. Padwa and K. E. Krumpe, *Tetrahedron*, 1992, **48**, 5385.
7 E. A. Shapiro, A. B. Dyatkin and O. M. Nefedov, *Russ. Chem. Rev.*, 1993, **62**, 447.
8 A. Padwa and D. J. Austin, *Angew. Chem., Int. Ed. Engl.*, 1994, **33**, 1797.
9 T. Ye and M. A. McKervey, *Chem. Rev.*, 1994, **94**, 1091.
10 D. J. Miller and C. J. Moody, *Tetrahedron*, 1995, **51**, 10811.
11 E. Aller, D. S. Brown, G. G. Cox, D. J. Miller and C. J. Moody, *J. Org. Chem.*, 1995, **60**, 4449.
12 P. Yates, *J. Am. Chem. Soc.*, 1952, **74**, 5376.
13 T. Saegusa, Y. Ito, S. Kobayashi, K. Hirota and T. Shimizu, *Tetrahedron Lett.*, 1966, 6131.
14 J.-F. Nicoud and H. B. Kagan, *Tetrahedron Lett.*, 1971, 2065.
15 B. Doma, B. Vercek, B. Stanovnik and M. Tisler, *Chimia*, 1974, **28**, 235.
16 G. Bartels, R.-P. Hinze and D. Wullbrandt, *Liebigs Ann. Chem.*, 1980, 168.
17 S. B. Singh and K. N. Mehrotra, *Can. J. Chem.*, 1981, **59**, 2475.
18 G. S. Singh, S. B. Singh and K. N. Mehrotra, *Bull. Chem. Soc. Jpn.*, 1984, **57**, 1667.
19 S. Husinec, I. Juranic, A. Llobera and A. E. A. Porter, *Synthesis*, 1988, 721.
20 W. Kirmse, L. Horner and H. Hoffmann, *Annalen*, 1958, **614**, 19.
21 C. E. Blades and A. L. Wilds, *J. Org. Chem.*, 1956, **21**, 1013.
22 E. Müller, H. Huben-Emden and W. Rundel, *Annalen*, 1959, **623**, 34.
23 E. Müller and H. Huben-Emden, *Annalen*, 1961, **649**, 70.
24 R. Paulissen, P. Moniotte, A. J. Hubert and P. Teyssié, *Tetrahedron Lett.*, 1974, 3311.
25 P. G. Mattingly and M. J. Miller, *J. Org. Chem.*, 1981, **46**, 1557.
26 G. Brooks, T. T. Howarth and E. Hunt, *J. Chem. Soc., Chem. Commun.*, 1981, 642.
27 T. Kametani, N. Kanaya, T. Mochizuki and T. Honda, *Heterocycles*, 1982, **19**, 1023.
28 M. Hrytsak and T. Durst, *Heterocycles*, 1987, **26**, 2393.
29 R. J. Chorvat and K. J. Rorig, *J. Org. Chem.*, 1988, **53**, 5779.
30 Y. Landais and D. Planchenault, *Synlett*, 1995, 1191.
31 S. N. Osipov, N. Sewald, A. F. Kolomiets, A. V. Fokin and K. Burger, *Tetrahedron Lett.*, 1996, **37**, 615.
32 D. Haigh, *Tetrahedron*, 1994, **50**, 3177.
33 L. Ferris, D. Haigh and C. J. Moody, *Synlett*, 1995, 921.
34 L. D. Cama and B. G. Christensen, *Tetrahedron Lett.*, 1978, **44**, 4233.

35 For recent examples see the following and also refs. 36–38: P. Andreoli, G. Cainelli, M. Panunzio, E. Bandinin, G. Martelli and G. Spunta, *J. Org. Chem.*, 1991, **56**, 5984.
36 H. Mastalerz, M. Menard, E. Ruediger and J. Fung-Tome, *J. Med. Chem.*, 1992, **35**, 953.
37 H. Mastalerz and M. Menard, *J. Org. Chem.*, 1994, **59**, 3223.
38 G. Bouthillier, H. Mastalerz and M. Menard, *Tetrahedron Lett.*, 1994, **35**. 4689.
39 J.-M. Liu, J.-J. Young, Y.-J. Li and C.-K. Sha, *J. Org. Chem.*, 1986, **51**, 1120.
40 M. P. Moyer, P. L. Feldman and H. Rapoport, *J. Org. Chem.*, 1985, **50**, 5223.
41 G. Lawton, C. J. Moody and C. J. Pearson, *J. Chem. Soc., Perkin Trans. 1*, 1987, 899.
42 G. Emmer. *Tetrahedron*, 1992, **48**, 7165.
43 S. Hanessian, J.-M. Fu, J.-L. Chiara and R. DiFabio, *Tetrahedron Lett.*, 1993, **34**, 4157.
44 J. E. Baldwin, R. M. Adlington, C. R. A. Godfrey, D. W. Gollins and J. G. Vaughan, *J. Chem. Soc.. Chem. Commun.*, 1993, 1434.
45 J. Podlech and D. Seebach, *Helv. Chim. Acta*, 1995, **78**, 1238.
46 D. R. Adams, P. D. Bailey, I. D. Collier, J. D. Heffernan and S. Stokes, *Chem. Commun.*, 1996, 349.
47 T. Sumner, L. E. Ball and J. Platner, *J. Org. Chem.*, 1959, **24**, 2017.
48 B. Ye and T. R. Burke, *Tetrahedron Lett.*, 1995, **36**, 4733.
49 M. C. Kozlowski, N. J. Tom, C. T. Seto, A. M. Sefler and P. A. Bartlett, *J. Am. Chem. Soc.*, 1995, **117**, 2128.
50 M. Regitz and G. Maas, *Diazo Compounds. Properties and Synthesis*, Academic Press, Orlando, FL, 1986.
51 B. Corbel, D. Hernot, J.-P. Haelters and G. Sturz, *Tetrahedron Lett.*, 1987, **28**, 6605.
52 M. Mikolajczyk, R. Zurawinski and P. Kielbasinski, *Tetrahedron Lett.*, 1989, **30**, 1143.
53 C.-P. Mak, C. Mayerl and H. Fliri, *Tetrahedron Lett.*, 1983, **24**, 347.
54 A. Andrus, B. G. Christensen and J. V. Heck, *Tetrahedron Lett.*, 1984, **25**, 595.
55 D. Seyferth, R. S. Marmor and P. Hilbert, *J. Org. Chem.*, 1971, **36**, 1379.
56 H. Scherer, A. Hartmann, M. Regitz, B. D. Tunggal and H. Günther, *Chem. Ber.*, 1972, **105**, 3357.
57 G. G. Cox, D. J. Miller, C. J. Moody, E.-R. H. B. Sie and J. J. Kulagowski, *Tetrahedron*, 1994, **50**, 3195.
58 J. Szewczyk, B. Lejczak and P. Kafarski, *Synthesis*, 1982, 409.
59 C. Yuan, G. Wang and S. Chen, *Synthesis*, 1990, 522.
60 M. Hoffmann, *Pol. J. Chem.*, 1979, **53**, 1153.
61 For an alternative approach to anilinobenzylphosphonates, see: H.-J. Ha and G.-S. Nam, *Synth. Commun.*, 1992, **22**, 1143.
62 L. K. Lukanov and A. P. Venkov, *Synthesis*. 1992. 263.
63 For other approaches to aminophosphonates see the following and refs. 64–78: A. B. Smith, K. M. Yager and C. M. Taylor, *J. Am. Chem. Soc.*, 1995, **117**, 10879.
64 A. S. Demir, C. Tanyeli, Ö. Sesenoglu, S. Demiç and Ö. Ö. Evin, *Tetrahedron Lett.*, 1996, **37**, 407.
65 M. Seki, K. Kondo and T. Iwasaki, *J. Chem. Soc., Perkin Trans. 1*, 1996, 3.
66 S.-K. Chung and D.-H. Kang, *Tetrahedron: Asymmetry*, 1996, **7**, 21.
67 A. Couture, E. Deniau, P. Woisel and P. Grandclaudon, *Tetrahedron Lett.*, 1995, **36**, 2483.
68 R. Hamilton, B. Walker and B. J. Walker, *Tetrahedron Lett.*, 1995, **36**, 4451.
69 M. Drescher, Y. F. Li and F. Hammerschmidt, *Tetrahedron*, 1995, **51**, 4933.
70 C. Greck, L. Bischoff, F. Ferreira and J. P. Genêt, *J. Org. Chem.*, 1995, **60**, 7010.
71 I. C. Baldwin and J. M. J. Williams, *Tetrahedron: Asymmetry*, 1995, **6**, 679.
72 G. Cabella, G. Jommi, R. Pagliarin, G. Sello and M. Sisti, *Tetrahedron*, 1995, **51**, 1817.
73 H. Sasai, S. Arai, Y. Tahara and M. Shibasaki, *J. Org. Chem.*, 1995, **60**, 6656.
74 M. J. O'Donnell, L. K. Lawley, P. B. Pushpavanam, A. Burger, F. G. Bordwell and X.-M. Zhang, *Tetrahedron Lett.*, 1994, **35**. 6421.
75 D. Green, G. Patel, S. Elgendy, J. A. Baban, G. Claeson, V. V. Kakkar and J. Deadman, *Tetrahedron*, 1994, **50**, 5099.
76 S. Hanessian, Y. L. Bennani and Y. Herve, *Synlett*, 1993, 35.
77 C. Maury, J. Royer and H. P. Husson, *Tetrahedron Lett.*, 1992, **33**, 6127.
78 S. E. Denmark, N. Chatani and S. V. Pansare, *Tetrahedron*, 1992, **48**, 2191.
79 T. Shono, N. Kise, N. Kunimi and R. Nomura, *Chem. Lett.*, 1991, 2191.
80 K. Schlögl, J. Derkosch and E. Wawerisch, *Monatsh. Chem.*, 1954, **85**, 607.
81 L. S. Hegedus, M. A. Schwindt, S. DeLombaert and R. Imwinkelreid, *J. Am. Chem. Soc.*, 1990, **112**, 2264.
82 R. Huber and A. Vasella, *Helv. Chim. Acta*, 1987, **70**, 1461.

Paper 6/04707F
Received 5*th July* 1996
Accepted 13*th August* 1996