N–H Insertion reactions of rhodium carbenoids. Part 2.[1] Preparation of *N*-substituted amino(phosphoryl)acetates (*N*-substituted phosphorylglycine esters)[2]

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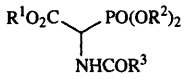
Rhodium(II) acetate-catalysed reaction of ethyl 2-diazo-2-diethoxyphosphorylacetate 2 with carbamates, amides, ureas or anilines gives a range of *N*-substituted 2-amino-2-diethoxyphosphorylacetates 3–18 by N–H insertion reaction of the intermediate rhodium carbenoid.

N-Acylaminophosphonates (phosphorylglycines) **1** are useful



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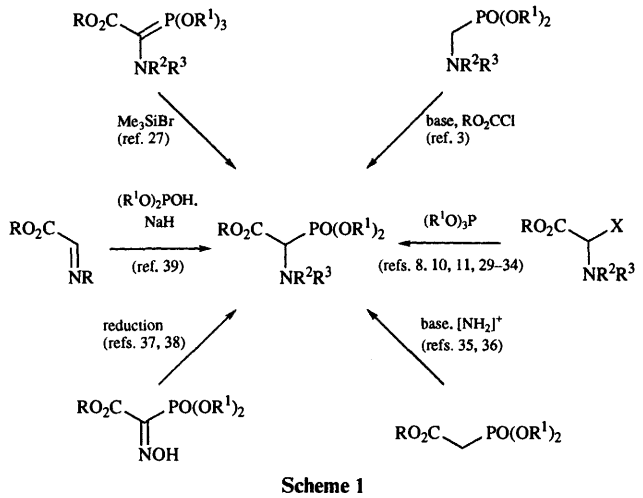
intermediates in synthesis. Originally prepared and used by the Merck group in the synthesis of cephalothin,[3,4] they have subsequently been employed in the preparation of other cephalosporins and analogues.[5–9] However, it is in the preparation of dehydro amino acids by the Wadsworth–Emmons reaction that phosphorylglycine derivatives have found the widest application.[10–28]

Phosphorylglycines were originally prepared by methoxycarbonylation of the anion of the Schiff base of diethyl (aminomethyl)phosphonate,[3] but are more commonly obtained by Michaelis–Arbusov reaction of trialkyl phosphites with α-halo- or α-alkoxy-glycine esters[8,10,11,29–33] or with aziridines.[34] Other preparative methods include the electrophilic amination of phosphorylacetates,[35,36] the oximation of phosphorylacetates followed by reduction,[37,38] the addition of diethyl phosphite anion to the Schiff base of ethyl glyoxalate[39] and the Me_3SiBr-promoted conversion of phosphoranes into phosphonates.[27] These methods are summarised in Scheme 1.



Scheme 1

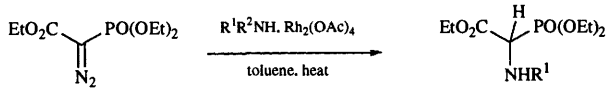
Two slightly conflicting reports also describe the preparation of amino(phosphoryl)acetates from phosphorylacetate by reaction with a sulfonyl azide followed by reduction. Thus ethyl diethoxyphosphorylacetate is reported to react with trifluoromethanesulfonyl azide to give ethyl 2-azido-2-diethoxyphosphorylacetate, $EtO_2CCHN_3PO(OEt)_2$, hydrogenation (Pd–C) of which gave the corresponding α-amino compound.[39] On the other hand, the closely related reaction of *tert*-butyl diethoxyphosphorylacetate, $Bu^tO_2CCH_2PO(OEt)_2$, with toluene-*p*-sulfonyl azide was reported to give the 2-diazo-2-diethoxyphorylacetate;[38] again hydrogenation over Pd–C gave the 2-amino-2-diethoxyphosphorylacetate.

In view of the continuing interest in phosphorylglycines and in aminophosphonates in general,[40] we decided to investigate the N–H insertion reactions of rhodium carbenoids derived from readily available ethyl 2-diazo-2-diethoxyphosphorylacetate as a simple route to a range of *N*-acyl- and *N*-aryl-amino(phosphoryl)acetates. We now report our results in detail.[2]

Results and discussion

Insertion reactions of metallocarbenoids are widely used in synthesis, and a comprehensive discussion of the N–H insertion reaction is included in the preceding paper.[1] However, very few of these reactions involve diazophosphonates, and therefore a study of the N–H insertion reactions of ethyl 2-diazo-2-diethoxyphosphorylacetate **2** was initiated. Compound **2** was prepared from ethyl diethoxyphosphorylacetate in 60–63% yield by diazo transfer reaction using toluene-*p*-sulfonyl azide.[41,42] Although both the diazo transfer reagent and the diazo compound are potentially explosive (**CAUTION**), with due regard for the hazards, we carried out the preparation on the 0.2 mol scale without incident. As an alternative to toluene-*p*-sulfonyl azide, the commercially available diazo transfer reagent, azidotris(diethylamino)phosphonium bromide,[43] can be used. This gives an improved yield of 93% (on a 8 mmol scale).[44]

The rhodium(II) acetate-catalysed decomposition of **2** was investigated in the presence of a wide range of H–H compounds (Scheme 2). The reactions were carried out in boiling



2 **3–18**

Scheme 2

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Table 1 Synthesis of compounds **3**–**18**

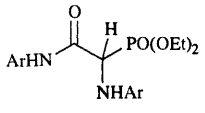
Entry	R^1	R^2	Product	Yield (%)
1	Bu^tO_2C	H	**3**	75
2	BnO_2C	H	**4**	78
3	Ac	H	**5**	79
4	EtCO	H	**6**	56
5	Bu^tCO	H	**7**	76
6	MeNHCO	H	**8**	40
7	Pr	Bu^tO_2C	**9**	46
8	Ph	H	**10**	72
9	$4\text{-}MeC_6H_4$	H	**11**	73
10	$4\text{-}MeOC_6H_4$	H	**12**	70
11	$4\text{-}NO_2C_6H_4$	H	**13**	81
12	$4\text{-}ClC_6H_4$	H	**14**	71
13	$2\text{-}MeOC_6H_4$	H	**15**	74
14	$2\text{-}BrC_6H_4$	H	**16**	70
15	$2,6\text{-}Me_2C_6H_3$	H	**17**	71
16	$2\text{-}Cl\text{-}4\text{-}CF_3C_6H_3$	H	**18**	61

toluene; diazophosphonates are generally more stable than simple diazo esters,[45] and no reaction occurred at room temperature. Likewise, there was no reaction at the elevated temperature in the absence of the rhodium catalyst.

Reaction with *tert*-butyl or benzyl carbamate gave the corresponding N–H insertion products **3** and **4** in good yield (Table 1). In the case of the Z protected phosphorylglycine, the reaction was carried out on a 2 g scale without reduction in yield. Other *N*-acyl compounds also react: simple amides such as acetamide, propionamide and isovaleramide gave the corresponding *N*-acylaminophosphorylacetates **5**–**7**, and *N*-methylurea gave the carbamoylamino derivative **8** in modest yield (Table 1), with no product resulting from insertion into the MeN–H bond being observed. Attempts to effect N–H insertion reactions on phthalimide, pyrrolidin-2-one or azetidin-2-one using **2** were unsuccessful. The lactams pyrrolidin-2-one and piperidin-2-one are known to undergo N–H insertion reactions with the carbenoid-derived by copper-catalysed decomposition of methyl diazoacetate, although the yields are poor (2 and 18% respectively).[46] Likewise, there are reports of intermolecular insertions into the N–H bond of β-lactams (azetidin-2-ones) in the rhodium(II)-catalysed reactions of more reactive diazo esters;[47–50] the intramolecular insertion into β-lactam N–H bonds is much better known and is widely used as a route to bicyclic β-lactams.[40]

Rhodium(II) acetate-catalysed decomposition of **2** in the presence of simple alkylamines did not result in the formation of the corresponding N–H insertion product, presumably as a result of catalyst poisoning. However, the overall product of insertion into the N–H bond of a primary alkylamine can readily be obtained by use of the corresponding *N*-Boc derivative, the *N*-*tert*-butoxycarbonyl group being removed during the reaction (Table 1, Entry 7).

Anilines, on the other hand, react readily to give the corresponding *N*-aryl-α-phosphorylglycines in good yield (Table 1, Entries 8–16). *N*-Aryl-α-phosphorylglycines are a poorly described group of compounds,[51] and hitherto, no general method of preparation has been developed. A range of anilines was used, and the reaction is apparently insensitive to the basicity of the aniline NH_2 group, 4-nitroaniline reacting just as readily as 4-methoxyaniline. In the case of 2-chloro-4-trifluoromethylaniline, the N–H insertion product **18** was accompanied by the amide **19**, formed by reaction of the initial carboxylate with the excess aniline.



19 Ar = $2\text{-}Cl\text{-}4\text{-}CF_3C_6H_3$

In summary, the rhodium(II)-catalysed N–H insertion reaction of compound **2** represents a simple route (two steps from ethyl diethoxyphosphorylacetate) to a wide range of *N*-substituted amino(phosphoryl)acetates.

Experimental

For general experimental points, see the preceding paper.

General procedure for N–H insertion reactions

A stirred solution of ethyl 2-diazo-2-diethoxyphosphorylacetate **2** (250 mg, 1 mmol) and the NH compound (5 mmol) in dry toluene (5 ml) was treated with rhodium(II) acetate (9 mg, 2 mol%). The mixture was heated at reflux overnight, the solvent evaporated and the residue chromatographed on silica gel (light petroleum–ether) to give the product.

Ethyl 2-*tert*-butoxycarbonylamino-2-diethoxyphosphorylacetate 3. Colourless crystalline solid (75%), mp 61–62 °C (from ether–light petroleum) (lit.,[10] 64.5–65.5 °C) (Found: C, 46.0; H, 7.9; N, 4.2. Calc. for $C_{13}H_{26}NO_7P$, C, 46.0; H, 7.7; N, 4.1%); $\nu_{max}(CHCl_3)/cm^{-1}$ 1754, 1732, 1250, 1140 and 1030; δ_H(270 MHz; $CDCl_3$) 5.35(1 H, br d, exch. CF_3CO_2D, NH), 4.80 [1 H, dd, *J* 9.07 (exch. CF_3CO_2D) and 22.55, CHP], 4.34–4.15 (6 H, m, OCH_2), 1.45 (9 H, s, Bu^t) and 1.35–1.29 (9 H, m, Me); δ_C(67.8 MHz; $CDCl_3$) 167.2, 154.9, 80.7, 63.7, 62.3, 52.2, 28.2, 16.3 (d, *J* 6.7) and 14.1; δ_P(101.3 MHz; $CDCl_3$) 15.29; *m/z* (FAB) 362 (MNa^+, 100%) and 340 (MH^+, 12).

Ethyl 2-benzyloxycarbonylamino-2-diethoxyphosphorylacetate 4. Colourless crystalline solid (78%), mp 50–51 °C (from ether–light petroleum) (lit.,[10] 47–48 °C) (Found: C, 51.5; H, 6.5; N, 3.75. Calc. for $C_{16}H_{24}NO_7P$, C, 51.55; H, 6.6; N, 3.5%); $\nu_{max}(CHCl_3)/cm^{-1}$ 2940, 1710, 1250 and 1120; δ_H(270 MHz; $CDCl_3$) 7.37–7.35 (5 H, m, ArH), 5.67 (1 H, br s, NH), 5.25 (2 H, d, *J* 3.4, $PhCH_2$), 4.97, [1 H, dd, *J* 9.07 (exch. CF_3CO_2D) and 22.27, CHP], 4.28–4.21 (6 H, m, OCH_2) and 1.35–1.29 (9 H, m, Me); δ_C(67.8 MHz; $CDCl_3$) 166.9, 155.6, 135.9, 128.9, 128.7, 128.6, 67.5, 63.8, 63.7, 62.5, 52.7 (d, *J* 146.4), 16.3 (d, *J* 6.8) and 14.1; δ_P(101.3 MHz; $CDCl_3$) 14.74; *m/z* (FAB) 374 ($M + NH_4^+$, 59%), 192(43) and 91(100).

Ethyl 2-acetylamino-2-diethoxyphosphorylacetate 5. Colourless crystalline solid (79%), mp 88–89 °C (from ether–light petroleum) (lit.,[30] 84–85 °C) (Found: C, 42.8; H, 7.4; N, 5.0. Calc. for $C_{10}H_{20}NO_6P$, C, 42.7; H, 7.2; N, 5.0%); $\nu_{max}(CHCl_3)/cm^{-1}$ 1720, 1680, 1250 and 1100; δ_H(270 MHz; $CDCl_3$) 6.27 (1 H, br s, NH, exch. D_2O), 5.17 (1 H, dd, *J* 8.8 and 21.9, CHP), 4.31–4.10 (6 H, m, OCH_2), 2.08 (3 H, s, MeCO) and 1.33 (9 H, m, Me); δ_C(67.8 MHz; $CDCl_3$) 169.6, 166.9, 63.7, 63.8, 62.4, 50.8 (d, *J* 146.6), 22.9, 16.3 (d, *J* 6.8) and 14.1; δ_P(101.3 MHz; $CDCl_3$) 14.96; *m/z* (CI) 299 ($M + NH_4^+$, 100%) and 282 (MH^+, 67).

Ethyl 2-diethoxyphosphoryl-2-propionylaminoacetate 6. Colourless crystalline solid (56%), mp 39–40 °C (Found: M^+, 295.1188. $C_{11}H_{22}NO_6P$ requires *M*, 295.1185); $\nu_{max}(CHCl_3)/cm^{-1}$ 1743, 1633 and 1250; δ_H(250 MHz; $CDCl_3$) 6.30 (1 H, br d, *J* 8, NH, exch. D_2O), 5.17 (1 H, dd, *J* 8.8 and 22.1, CHP), 4.18 (6 H, m, OCH_2), 2.30 (2 H, q, *J* 7.5, CH_2CONH), 1.33 (9 H, m, Me) and 1.18 (3 H, t, *J* 7.5, Me); δ_C(62.9 MHz; $CDCl_3$) 173.6, 167.3, 64.1, 62.8, 51.0 (d, *J* 145.4), 29.7, 16.6 (d, *J* 6.8), 14.4 and 9.7; δ_P(101.3 MHz; $CDCl_3$) 15.28; *m/z* (EI) 295 (M^+, 5%), 250 (10), 222 (11), 166 (100), 138 (80), 102 (40), 82 (20), 65 (22), 57 (80) and 44 (8).

Ethyl 2-diethoxyphosphoryl-2-(3-methylbutanoylamino)acetate 7. Pale yellow crystalline solid (76%), mp 57–58 °C (Found: C, 48.4; H, 8.3; N, 4.3. $C_{13}H_{26}NO_6P$ requires C, 48.3; H, 8.1; N, 4.3%) (Found: M^+, 323.1499. $C_{13}H_{26}NO_6P$ requires *M*, 323.1497); $\nu_{max}(CHCl_3)/cm^{-1}$ 1710, 1677, 1221 and 1025; δ_H(360 MHz; $CDCl_3$) 6.17 (1 H, br d, *J* 7.6, exch. D_2O, NH), 5.16 (1 H, dd, *J* 7.6 and 22.0, CHP), 4.20–4.16 (2 H, m, OCH_2), 4.10–4.06 (4 H, m, OCH_2), 2.09–2.05 (3 H, m, CH and CH_2), 1.25 (9 H, t, *J* 7.6, Me) and 0.90 (6 H, d *J* 7.6, Me_2CH); δ_C(67.8

MHz; $CDCl_3$) 172.0, 166.6, 63.4 (d, *J* 67.8), 63.3 (d, *J* 67.8), 62.0, 50.2 (d, *J* 162.7), 45.1, 25.8, 22.2, 16.1 (d, *J* 6.8) and 13.8; δ_P(101.3 MHz; $CDCl_3$) 15.16; *m/z* (EI) 324 (MH^+, 54%), 281 (66), 235 (42), 166 (100), 138 (72), 102 (38), 85 (65), 69 (22), 57 (99), 41 (83) and 29 (76).

Ethyl 2-diethoxyphosphoryl-2-[*N*-methylcarbamoyl]amino-acetate 8. Colourless crystalline solid (40%), mp 50–51 °C (from ether–light petroleum) (lit.,[37] 49–50 °C) (Found: M^+, 296.1137. Calc. for $C_{10}H_{21}N_2O_6P$, *M*, 296.1137); $\nu_{max}(CHCl_3)$/cm^{-1} 3350, 2930, 1720, 1675, 1250 and 1030; δ_H(270 MHz; $CDCl_3$) 6.04 (1 H, br s, exch. D_2O, NH), 5.21 (1 H, br s, exch. D_2O, NHMe), 5.09 (1 H, dd, *J* 9.3 and 22.54, CHP), 4.30–4.11 (6 H, m, OCH_2), 2.78 (3 H, d, *J* 4.4, MeNH) and 1.33 (9 H, m, Me); δ_C(67.8 MHz; $CDCl_3$) 167.9, 158.2, 64.5, 63.7, 62.1, 51.4 (d, *J* 143.5), 26.9, 16.3 (d, *J* 6.2) and 14.0; δ_P(101.3 MHz; $CDCl_3$) 16.64; *m/z* (CI) 314 ($M + NH_4^+$, 10%) and 297 (MH^+, 52).

Ethyl 2-diethoxyphosphoryl-2-propylaminoacetate 9. Colourless oil (46%) (Found: M^+, 281.1047. $C_{11}H_{24}NO_5P$ requires *M*, 281.1392); $\nu_{max}(CHCl_3)$/cm^{-1} 1740 and 1257; δ_H(250 MHz; $CDCl_3$) 5.38 (1 H, br s, exch. D_2O, NH), 5.36 (1 H, d, *J* 17.5, CHP), 4.28–4.11 (6 H, m, OCH_2), 3.12 (2 H, 2 overlapping t, CH_2N), 1.47 (2 H, m, CH_2CH_2N), 1.28 (9 H, m, 3 × Me) and 0.86 (3 H, t, *J* 7.5, Me), δ_C(62.9 MHz; $CDCl_3$) 166.1, 68.6 (d, *J* 160.4), 63.7, 62.0, 42.0, 22.8, 16.2 (d, *J* 6.7), 13.9 and 14.1; δ_P(101.3 MHz; $CDCl_3$) 12.56; *m/z* (EI) 281 (M^+, 2%), 280 (12), 240 (14), 197 (22), 167 (95), 155 (35), 138 (38), 111 (85), 69 (100) and 43 (23).

Ethyl 2-diethoxyphosphoryl-2-phenylaminoacetate 10. Colourless crystalline solid (72%), mp 56 °C (from ether–light petroleum) (lit.,[51] 55–56 °C) (Found: M^+, 315.1232. Calc. for $C_{14}H_{22}NO_5P$, *M*, 315.1236); $\nu_{max}(CHCl_3)$/cm^{-1} 1720, 1240 and 1120; δ_H(400 MHz; $CDCl_3$) 7.18 (2 H, t, *J* 8.4, ArH), 6.79 (1 H, t, *J* 7.2, ArH), 6.77 (2 H, d, *J* 8, ArH), 4.54 (1 H, s, exch. D_2O, NH), 4.51 (1 H, d, *J* 24, CHP), 4.26–4.17 (6 H, m, OCH_2) and 1.36–1.24 (9 H, m, Me); δ_C(100.6 MHz; $CDCl_3$) 168.4, 146.2, 129.3, 120.0, 114.1, 64.3, 63.6, 62.2, 56.5 (d, *J* 147.6, CHP), 22.9, 16.4 and 14.1; δ_P(101.3 MHz; $CDCl_3$) 16.14; *m/z* (FAB) 316 (MH^+, 29%), 315 (M^+, 31), 242 (12), 178 (100), 139 (6), 104 (36) and 77 (5).

Ethyl 2-diethoxyphosphoryl-2-(4-methylphenylamino)acetate 11. Beige crystalline solid (73%), mp 76–77 °C (from ether–light petroleum) (Found: C, 54.8; H, 7.4; N, 3.8. $C_{15}H_{24}NO_5P$ requires C, 54.7; H, 7.35; N, 4.25%); $\nu_{max}(CHCl_3)$/cm^{-1} 1725, 1255 and 1150; δ_H(270 MHz; $CDCl_3$) 6.99 (2 H, d, *J* 8.30, ArH), 6.60 (2 H, d, *J* 8.30, ArH), 4.72 (1 H, br s, exch. D_2O, NH), 4.46 (1 H, d, *J* 23.2, CHP), 4.30–4.12 (6 H, m, OCH_2), 2.24 (3 H, s, ArMe) 1.39–1.32 (6 H, m, Me) and 1.27 (3 H, t, *J* 7.14, Me); δ_C(67.8 MHz; $CDCl_3$) 168.6, 143.8, 129.8, 128.7, 114.2, 64.0 (d, *J* 7.2), 63.5, 62.1, 56.8 (d, *J* 149.5), 20.4, 16.4 (d, *J* 6.7) and 14.1; δ_P(101.3 MHz; $CDCl_3$) 16.21; *m/z* (FAB) 330 (MH^+, 35%), 329 (M^+, 51), 256 (13), 192 (100) and 118 (47).

Ethyl 2-diethoxyphosphoryl-2-(4-methoxyphenylamino)-acetate 12. Colourless crystalline solid (70%), mp 55–56 °C (from ether–light petroleum) (Found: M^+, 345.1344. $C_{15}H_{24}NPO_6$ requires *M*, 345.1341); $\nu_{max}(CHCl_3)$/cm^{-1} 1718, 1250 and 1130; δ_H(270 MHz; $CDCl_3$) 6.86 (2 H, d, *J* 9.1, ArH), 6.74 (2 H, d, *J* 9.1, ArH), 4.55 (1 H, d, *J* 22.3, CHP), 4.37–4.32 (6 H, m, OCH_2), 3.82 (3 H, s, OMe) and 1.46–1.27 (9 H, m, Me); δ_C(67.8 MHz; $CDCl_3$) 168.6, 153.5, 140.2, 115.7, 114.8, 64.0 (d, *J* 6.4, CH_2OP), 63.5 (d, *J* 7.3), 62.1, 57.5 (d, *J* 149.5), 55.5, 16.4 (d, *J* 6.8) and 14.1; δ_P(101.3 MHz; $CDCl_3$) 16.12; *m/z* (FAB) 346 (MH^+, 49%), 315 (12), 272 (6), 225 (8), 208 (87), 134 (74), 93 (100), 75 (33) and 57 (26).

Ethyl 2-diethoxyphosphoryl-2-(4-nitrophenylamino)acetate 13. Pale yellow solid (81%), mp 96–97 °C (from ether–light petroleum) (Found: C, 46.8; H, 5.9; N, 7.6. $C_{14}H_{21}N_2O_7P$ requires C, 46.6; H, 5.9; N, 7.8%); $\nu_{max}(CHCl_3)$/cm^{-1} 2960, 1720, 1590, 1490, 1330, 1260 and 1120; δ_H(270 MHz; $CDCl_3$) 8.22 (2 H, d, *J* 9.34, ArH), 6.75 (2 H, d, *J* 9.34, ArH), 5.38 (1 H, dd, *J* 8.25, exch. D_2O, NH), 4.68 (1 H, dd, *J* 21.75 and 8.25, CHP), 4.35–4.24 (6 H, m, OCH_2) and 1.41 (9 H, m, Me); δ_C(67.8 MHz; $CDCl_3$) 167.2, 151.2, 139.7, 126.2, 112.4, 64.2 (d, *J* 7), 63.9 (d, *J* 7), 62.8, 55.4 (d, *J* 147.4), 16.4 (d, *J* 6.8) and 14.1; δ_P(101.3 MHz; $CDCl_3$) 14.77; *m/z* (FAB) 361 (M^+, 35%), 345 (47), 287 (20), 271 (15), 259 (10), 223 (82), 207 (52), 195 (13), 178 (23), 149 (70), 139 (100), 121 (27), 111 (42), 103 (35), 93 (30), 83 (42), 77 (13) and 65 (33).

Ethyl 2-(4-chlorophenylamino)-2-diethoxyphosphorylacetate 14. Colourless crystalline solid (71%), mp 80–81 °C (from ether–light petroleum) (Found: C, 48.0; H, 6.0; N, 4.1. $C_{14}H_{21}ClNO_5P$ requires C, 48.1; H, 6.05; N, 4.0%); $\nu_{max}(CHCl_3)$/cm^{-1} 1715, 1245, 1130 and 1090; δ_H(400 MHz; $CDCl_3$) 7.14 (2 H, d, *J* 8.79, ArH), 6.61 (2 H, d, *J* 8.79, ArH), 4.57 (1 H, br s, exch. D_2O, NH), 4.44 (1 H, d, *J* 22.27, CHP), 4.22–4.17 (6 H, m, OCH_2) and 1.36–1.24 (9 H, m, Me); δ_C(100.6 MHz; $CDCl_3$) 168.1, 144.8, 129.2, 124.2, 115.2, 64.4, 64.1, 62.3, 56.6 (d, *J* 147.7), 16.4 (d, *J* 6.8) and 14.1; δ_P(101.3 MHz; $CDCl_3$) 15.78; *m/z* (FAB) 372 (MNa^+, 41%), 350 (MH^+, 27), 325 (12), 293 (8), 267 (58), 245 (35), 212 (38), 189 (24) and 167 (34).

Ethyl 2-diethoxyphosphoryl-2-(2-methoxyphenylamino)-acetate 15. Colourless oil (74%) (Found: M^+, 345.1341. $C_{15}H_{24}NO_6P$ requires *M*, 345.1341); $\nu_{max}(CHCl_3)$/cm^{-1} 1720, 1250 and 1135; δ_H(270 MHz; $CDCl_3$) 6.86–6.72 (3 H, m, ArH), 6.56 (1 H, d, *J* 7.8, ArH), 5.15 (1 H, d, *J* 9.0, exch. D_2O, NH), 4.55 (1 H, dd, *J* 11.2 and 22.6, CHP), 4.30–4.15 (6 H, m, OCH_2), 3.86 (3 H, s, OMe), 1.33 (6 H, dt, *J* 11.2 and 7.15, $MeCH_2OP$) and 1.27 (3 H, t, *J* 7.15, Me); δ_C(67.8 MHz; $CDCl_3$) 166.5, 147.6, 136.2, 121.0, 118.0, 110.9, 110.0, 63.9 (d, *J* 6.85), 63.3 (d, *J* 6.85), 62.1, 56.2, (d, *J* 147.2), 55.6, 16.4 (d, *J* 6.8) and 14.1; δ_P(101.3 MHz; $CDCl_3$) 16.18; *m/z* (CI) 346 (MH^+, 27%), 345 (M^+, 39), 272 (12), 208 (100 and 134 (42).

Ethyl 2-(2-bromophenylamino)-2-diethoxyphosphorylacetate 16. Pale yellow oil (70%) (Found: M^+, 393.0357. $C_{14}H_{21}{}^{79}BrNO_5P$ requires *M*, 393.0341); $\nu_{max}(CHCl_3)$/cm^{-1} 1720, 1250 and 1134; δ_H(400 MHz; $CDCl_3$) 7.42 (1 H, d, *J* 9.25, ArH), 7.13 (1 H, d, *J* 8.75, ArH), 6.65–6.56 (2 H, m, ArH), 5.22 (1 H, br t, *J* 8.5, NH, exch. D_2O), 4.50 (1 H, dd, *J* 22.5 and 8.5, CHP), 4.25–4.16 (6 H, m, OCH_2), 1.34–1.21 (9 H, m, Me); δ_C(100.6 MHz; $CDCl_3$) 167.7, 143.1, 132.6, 128.4, 119.7, 112.2, 110.7, 64.0 (d, *J* 6.1, CH_2OP), 63.7 (d, *J* 7.0), 62.3, 56.2 (d, *J* 156.3), 16.3 (d, *J* 6.8) and 14.0; δ_P(101.3 MHz; $CDCl_3$) 15.19; *m/z* (EI) 395/393 (M^+, 30%), 256/258 (90) and 182/184 (100).

Ethyl 2-diethoxyphosphoryl-2-(2,6-dimethylphenylamino)-acetate 17. Colourless oil (71%) (Found: M^+, 343.1546. $C_{16}H_{26}NO_5P$ requires *M*, 343.1549); $\nu_{max}(CHCl_3)$/cm^{-1} 1720, 1260 and 1130; δ_H(270 MHz; $CDCl_3$) 6.95 (2 H, d, *J* 7.24, ArH), 6.80 (1 H, dd, *J* 7.98 and 8.55, ArH), 4.44 (1 H, d, *J* 23.37, CHP), 4.26–4.10 (6 H, m, OCH_2), 2.36 (6 H, s, ArMe), 1.34 (6 H, dt, *J* 7.15 and 6.88, Me) and 1.21 (3 H, t, *J* 7.15, Me); δ_C(67.8 MHz; $CDCl_3$) 169.1, 143.3, 129.1, 128.7, 122.3, 63.7 (d, *J* 7.3), 63.3 (d, *J* 7.3), 61.9, 58.8 (d, *J* 144.3), 18.6, 16.4, (d, *J* 6.2) and 14.0; δ_P(101.3 MHz; $CDCl_3$) 16.87; *m/z* (CI) 344 (MH^+, 100%) and 206 (4).

Ethyl 2-(2-chloro-4-trifluoromethylphenylamino)-2-diethoxy-phosphorylacetate 18. Colourless oil (61%) (Found: M^+, 417.0724. $C_{15}H_{20}{}^{35}ClF_3NO_5P$ requires *M*, 417.0720); $\nu_{max}(CHCl_3)$/cm^{-1} 3370, 1743, 1293, 1241 and 1020; δ_H(270 MHz; $CDCl_3$) 7.54 (1 H, s, ArH), 7.38 (1 H, d, *J* 8.5, ArH), 6.69 (1 H, d, *J* 8.5, ArH), 5.54 (1 H, br d, *J* 8.5), 4.55 (1 H, dd, *J* 8.2 and 21.2, CHP), 4.40–4.12 (6 H, m, OCH_2) and 1.39–1.29 (9 H, m, Me); δ_C(67.8 MHz; $CDCl_3$) 167.3, 144.8, 126.7, 125.9, 125.1, 121.9, 121.3, 120.8, 120.0, 111.3, 64.2 (d, *J* 7.3), 64.0 (d, *J* 7.3), 62.7, 55.8 (d, *J* 148.4), 16.4 (d, *J* 5.2) and 14.1; δ_P(101.3 MHz; $CDCl_3$) 14.68; *m/z* (FAB) 418 (MH^+, 47%), 417 (M^+, 45), 398 (22), 344 (28), 280 (100), 206 (85) and 139 (55). Compound **19** was also formed during the reaction.

Diethyl 1,2-bis(2-chloro-4-trifluoromethylphenylamino)-2-oxoethylphosphonate 19. Colourless oil (25%) (Found: M^+, 566.0362. $C_{20}H_{19}{}^{35}Cl_2F_6N_2O_4P$ requires *M*, 566.0364);

$\nu_{max}(CHCl_3)/cm^{-1}$ 1680, 1281 and 1026; δ_H(270 MHz; $CDCl_3$) 9.22 (1 H, br s, NHCO), 8.55 (1 H, d, *J* 8.5, ArH), 7.62 (2 H, d, *J* 8.8, ArH) 7.55 (1 H, d, *J* 8.8, ArH), 7.42 (1 H, d, *J* 8.5, ArH), 6.73 (1 H, d, *J* 8.5, ArH), 5.79 (1 H, dd, *J* 5.2, *J* 9.9, CHN*H*), 4.51 (1 H, dd, *J* 5.2 and 21.7, CHP), 4.27 (4 H, dt, *J* 7.2 and 8.2, OCH_2) and 1.37 (6 H, q, *J* 7.2, Me); δ_C(67.8 MHz; $CDCl_3$) 164.4, 144.8, 136.9, 129.7, 126.8, 126.4, 125.3, 125.0, 124.5, 123.3, 122.1, 121.2, 120.6, 111.9, 64.7 (d, *J* 7.3), 64.5 (d, *J* 7.3), 57.8 (d, *J* 144.4) and 16.4 (d, *J* 5.6); δ_P(101.3 MHz; $CDCl_3$) 15.55; *m/z* (FAB) 589 (MNa^+, 67%), 567 (MH^+, 31), 429 (25), 345 (57), 206 (100) and 139 (73).

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