Preparation of alkyl- and aryl-amino[$^2H_2$]methylphosphinic acids

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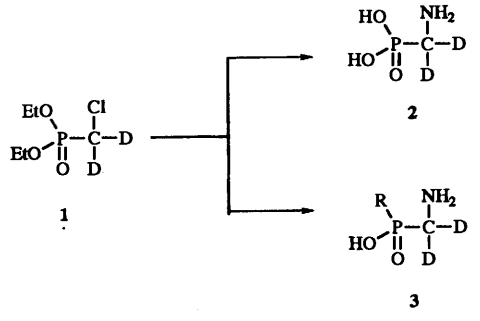
Diethyl chloro[$^2H_2$]methylphosphonate upon successive treatment with $POCl_3$ and Grignard reagents (RMgX) gave alkyl(chloro[$^2H_2$]methyl)phosphinates. Phenyl(chloro[$^2H_2$]methyl)phosphinate was prepared by deuteriolysis of the α-silylated α-phosphonylated carbanion **11** with D_2O. After conversion into trifluoroethyl phosphinic esters, the alkyl- and phenyl-(chloro[$^2H_2$]methyl)phosphinates were converted into azides and then reduced and hydrogenated into alkyl- and phenyl-(amino[$^2H_2$]methyl)phosphinic acids.

Since the discovery of 2-aminoethylphosphonic acid (AEP) from protozoa in 1959,[1] the number of known natural products containing a P–C bond has been steadily increasing. L-Phosphinothricin, a γ-aminophosphinic acid, is one of the most important members of this class of compounds. It constitutes the N-terminal amino acid of antibiotic tripeptides[2] produced by several streptomycete and actinomycete strains and exhibits high herbicidal activity.[3] The different syntheses of aminophosphinic acids were described by Maier in 1983,[4] and more recently reviewed by Kukhar and Solodenko.[5] We recently discovered the usefulness of diethyl chloro[$^2H_2$]methylphosphonate[6] **1** in the preparation of amino[$^2H_2$]methylphosphonic acid **2**. Since the ester **1** is an easily accessible starting material[7] available in high yield (95%) and with a high deuterium content (%D > 95) we decided to use it to prepare alkyl- and aryl-(amino[$^2H_2$]methyl)phosphinic acids **3** (Scheme 1), work which, we describe herein.

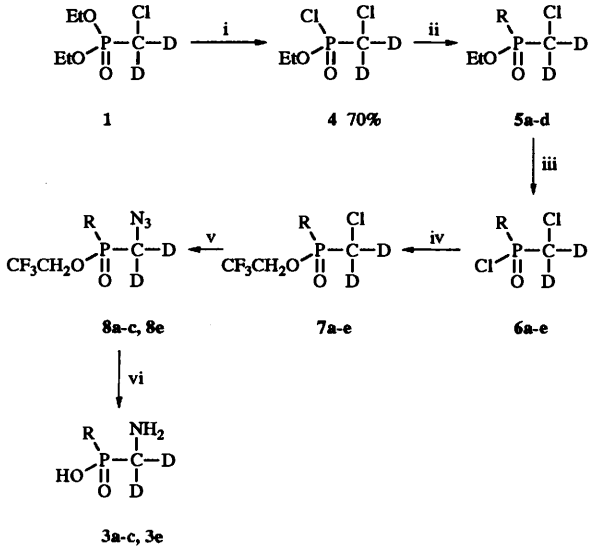


Scheme 1

Results and discussion

Two key steps in the synthesis of the acids **3** from **1** are: (*a*) selective replacement of a single P-ethoxy group by an alkyl or aryl group (R) to give the chloromethylphosphinates **5** *via* the intermediate **4** (Scheme 2); (*b*) selective nucleophilic substitution of the chlorine atom by a precursor of the amino group. The structural and experimental conditions controlling this last step have already been extensively studied in the synthesis of amino[$^2H_2$]methylphosphonic esters.[6] Initially (Scheme 2) the diester **1** was treated with an excess of phosphorus oxychloride at 75–80 °C for 4 h to give exclusively the monochlorophosphonate **4** (70%).[8] This can easily be purified since both excess of phosphorus oxychloride and the by-product ethyl dichlorophosphate can be distilled off.

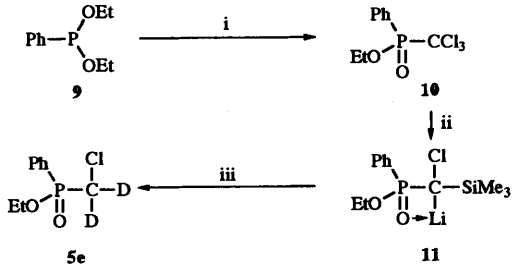
Selective substitution of the P–Cl bond of compounds **4** with Grignard reagents (RMgX) to give chloromethylphosphinates **5a–d** was possible since the magnesium reagents are neither nucleophilic enough to attack products at the phosphorus atom



a R = Me, **b** R = Et, **c** R = Pr, **d** R = CH=CH$_2$, **e** R = Ph

Scheme 2 *Reagents and conditions*: i, $POCl_3$ (1.5 mol equiv.), 80 °C, 4 h; ii, RMgX, THF–diethyl ether, −78 °C; iii, $POCl_3$ (1.5 mol equiv.), 0 °C; iv, CF_3CH_2OH, NEt_3, THF, 20 °C; v, NaN_3, DMSO, 90 °C; vi, H_2, EtOH, HCl (12 mol dm^{-3}, 3 mol equiv.), Pd/C, 1 atm

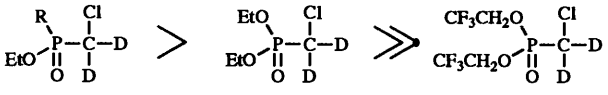
nor basic enough to abstract a deuterium of the methylene group. The reaction, carried out at low temperature in a tetrahydrofuran (THF)–diethyl ether, worked with both saturated and unsaturated aliphatic Grignard reagents except for Pr^{i}MgCl which, not unexpectedly, gave rise to halogen-metal exchange. The products **5a–c** were obtained in good yields (54–86%) after distillation, except thermally unstable **5d** which was used as obtained in the following steps. Concurrently, a simple and effective protocol for the synthesis of aryl(chloro[$^2H_2$]methyl)phosphinates was developed starting from the aryl(trichloromethyl)phosphinate **10**. The preparation is efficient but less general than the previous one since it gives complex mixtures of products when R is an alkyl group. Here it is exemplified by the preparation of ethyl phenyl(chloro[$^2H_2$]methyl)phosphinate **5e** (Scheme 3). Diethyl phenylphosphonite **9** reacted with an excess of CCl_4 in a Michaelis–Arbuzov reaction to give ethyl phenyl-(trichloromethyl)phosphinate **10** in (85%) as a crystalline material. Reaction of this with BuLi (2 equiv.) at low temperature in the presence of chlorotrimethylsilane[7] (as previously described for diethyl trichloromethylphosphonate) gave the stable carbanion **11** in quantitative yield [established by ^{31}P NMR; δ_P(THF) +51.9]. Treatment of this with an



Scheme 3 *Reagents and conditions*: i, CCl_4 (3 mol equiv.), 80 °C; ii, BuLi (2 mol equiv.), $ClSiMe_3$, THF, −80 °C; iii, D_2O, THF, −80 °C

excess of D_2O at low temperature afforded **5e** (92%) with very high deuterium incorporation [%D > 95].

Since the last step involves nucleophilic replacement of the chlorine atom by an amine-generating group we used for this purpose sodium azide in dimethyl sulfoxide (DMSO),[6] although we found that, first, replacement of the P-ethoxy groups by P-trifluoroethoxy groups was essential in order to avoid unwanted dealkylation. In the case of chloromethylphosphinic esters **5a–d**, this was effected by treatment of the compounds with phosphorous oxychloride at 0 °C to give replacement of the ethoxy group by chloride (Scheme 2). Chloromethylphosphinic esters **5a–d** are much more reactive than the chloromethylphosphonic ester **1**. The chloromethylphosphinic chlorides **6a–e**, except for **6d** were obtained in 57–71% yield after purification by vacuum distillation. A comparison of the reactions between phosphorus esters and phosphorus oxychloride reported in Scheme 2, indicates that the reactivity of phosphorus esters increases with increasing electron density at the oxygen of the P-alkoxy substituent: thus, bis(trifluoroethyl) chloromethylphosphonate was completely inert towards phosphorus oxychloride (Scheme 4).



Scheme 4 Relative reactivities of phosphorus esters

The chloromethylphosphinic chlorides **6a–e** were treated with trifluoroethanol in THF at room temperature in the presence of triethylamine to give the trifluoroethyl esters **7a–e** in good yields (75–95%). Treatment of these esters with sodium azide in DMSO at 90 °C gave generally good yields (72–84%) of the azides **11a–c**; the reaction times were variable (**7e** was longest at 7 h) and formation of by-products low (< 8% from ^{31}P NMR) compound **7d**, however, polymerised under the reaction conditions. The crude azidomethylphosphinates **8a–c** and **8e** were then subjected to Pd/C catalysed reduction under H_2 (1 atm at room temperature) in the presence of 12 mol dm^{-3} hydrochloric acid to effect simultaneous hydrogenolysis of the ester function and reduction of the azido group to an amino group. Work-up then gave the amino[$^2H_2$]methylphosphinic acids **3a–c** and **3e** (43–60%). The deuterium content [%D > 95%] was fully conserved throughout this multi-step synthesis, as verified by the absence of the methylene protons in ^1H NMR spectra.

Conclusion

Amino[$^2H_2$]methylphosphinic acids **3** have been obtained for the first time by nucleophilic amination of chloromethylphosphinates. This multi-step synthesis, using readily available starting materials with high deuterium incorporation, makes use of commercial reagents and can easily be scaled up. In this work, which confirms the advantage of the P-trifluoroethoxy group over the P-ethoxy substituent[6] in the nucleophilic amination of chloromethylphosphinic esters, only substitution of chloride was observed, no dealkylated products being detected with $R(CF_3CH_2O)P(O)CO_2Cl$; with $R(EtO)P(O)CD_2Cl$ dealkylation and amination are competitive processes.

Experimental

^{31}P NMR and ^1H NMR spectra were recorded on a Bruker AC 200 spectrometer with 85% H_3PO_4 as external standard (positive δ values are downfield of this reference) for ^{31}P NMR and $CDCl_3$ as internal standard for ^1H NMR; ^2H NMR spectra were recorded on a Bruker AM 400 spectrometer with $CDCl_3$ as internal standard; J values are quoted in Hz. High-resolution mass spectra (HRMS) were recorded on VG ZAB-HSQ or Bruker CMS 47X ICR FT mass spectrometers. All reactions, including deuteriolysis, were carried out under an inert atmosphere and rigorously anhydrous conditions. A Buchi GKR-50 apparatus with three flasks was used for distillation.

Ethyl chloro(chloro[$^2H_2$]methyl)phosphonate 4 (Scheme 2)
A mixture of diethyl chloro[$^2H_2$]methylphosphonate **1** (18.8 g, 100 mmol) and phosphorus oxychloride (23 g, 150 mmol) in a 100 cm^3 pear-shaped flask was heated for 4 h at 80 °C and then distilled under reduced pressure through an 8 cm fractionating column equipped with a condenser to give **4** (70%), bp (0.2 mmHg) 62–69 °C; $\delta_P(CDCl_3)$ +30.5; $\delta_H(CDCl_3)$ 1.43 (t, $^3J_{H,H}$ 7, OCH_2Me) and 4.36 (dq, $^3J_{P,H}$ 10 and $^3J_{H,H}$ 7, OCH_2Me); $\delta_C(CDCl_3)$ 15.95 (d, $^3J_{P,C}$ 7, OCH_2Me), 38.40 (dp, $^1J_{P,C}$ 143.6, PCD_2), 65.22 (d, $^2J_{P,C}$ 8, OCH_2Me).

Ethyl alkyl(chloro[$^2H_2$]methyl)phosphinates 5a–5d (Scheme 2)
To a stirred mixture of **4** (8.95 g, 50 mmol) in THF–diethyl ether (1:1) (200 cm^3) at −78 °C was added dropwise over the period of a few minutes a solution of the appropriate alkylmagnesium chloride (55 mmol) in THF (previously standardized before use by titration). The reaction mixture was allowed to warm to room temperature and then acidified with 5 mol dm^{-3} hydrochloric acid. The aqueous phase was extracted with CH_2Cl_2 (3 × 50 cm^3) after which the combined extracts were dried ($MgSO_4$) and evaporated under reduced pressure. The crude products were purified by bulb-to-bulb distillation.

Compound **5a** (82%), bp (20 mmHg) 150–155 °C; $\delta_P(CDCl_3)$ +48.2; $\delta_H(CDCl_3)$ 1.35 (t, $^3J_{H,H}$ 7, OCH_2Me), 1.60 (d, $^2J_{P,H}$ 15, PMe) and 4.07 (dq, $^3J_{P,H}$ and $^3J_{H,H}$ 7, OCH_2Me); $\delta_C(CDCl_3)$ 11.1 (d, $^1J_{P,C}$ 102, PMe), 15.9 (d, $^3J_{P,C}$ 5.9, OCH_2Me), 34.7 (dp, $^2J_{P,C}$ 96.5 and $^1J_{C,D}$ 23.2, PCD_2) and 60.9 (d, $^2J_{P,C}$ 6, OCH_2Me); (Found: M^+, 158.023 29. Calc. for $C_4H_8D_2{}^{35}ClO_2P$: M, 158.023 24).

Compound **5b** (60%), bp (20 mmHg) 160–165 °C; $\delta_P(CDCl_3)$ +50.6; $\delta_H(CDCl_3)$ 1.15 (dt, $^3J_{P,H}$ 19 and $^3J_{H,H}$ 7, PCH_2Me), 1.29 (t, $^3J_{H,H}$ 7, OCH_2Me), 1.85 (dq, $^2J_{P,H}$ 15.4 and $^3J_{H,H}$ 7.7, PCH_2Me) and 4.10 (dq, $^3J_{P,H}$ and $^3J_{H,H}$ 7, OCH_2Me).

Compound **5c** (54%), bp (20 mmHg) 165–170 °C; $\delta_P(CDCl_3)$ +49.2; $\delta_H(CDCl_3)$ 1.15 [t, $^3J_{H,H}$ 7, $P(CH_2)_2Me$], 1.30 (t, $^3J_{H,H}$ 7, OCH_2Me), 1.34–1.90 [m, $P(CH_2)_2Me$] and 4.10 (dq, $^3J_{P,H}$ and $^3J_{H,H}$ 7, OCH_2Me).

Compound **5d** (76%), $\delta_P(CDCl_3)$ +33.2; $\delta_H(CDCl_3)$ 1.35 (t, $^3J_{H,H}$ 7, OCH_2Me), 4.10 (dq, $^3J_{P,H}$ and $^3J_{H,H}$ 7, OCH_2Me) and 6.16–6.57 (m, $CH{=}CH_2$).

Ethyl phenyl(trichloromethyl)phosphinate 10 (Scheme 3)
A 1000 cm^3 round-bottomed flask fitted with a mechanical stirrer, a thermometer and a reflux condenser was charged with CCl_4 (46.2 g, 300 mmol) After the CCl_4 had been heated to reflux diethyl phenyl phosphonite **9** (19.8 g, 100 mmol) was added dropwise to it and the reaction mixture heated for 2 h. It was then cooled to room temp. and the excess of CCl_4 removed

by evaporation under reduced pressure to give the crude product. This was purified by treatment with hexane from which **10** spontaneously crystallized. Compound **10** (85%), mp 89–90 °C (from hexane–diethyl ether, 70:30); $\delta_P(CDCl_3)$ +24.5; $\delta_H(CDCl_3)$ 1.41 (t, $^3J_{H,H}$ 7, OCH_2Me), 4.46 (dq, $^3J_{P,H}$ and $^3J_{H-H}$ 7, OCH_2Me), 7.55 (m, 3 H, ArH) and 8.02 (m, 2 H, ArH); $\delta_C(CDCl_3)$ 17.0 (d, $^3J_{P,C}$ 5, OCH_2Me), 65.5 (d, $^2J_{P,C}$ 6.5, OCH_2Me), 93.5 (d, $^1J_{P,C}$ 105, CCl_3), 123.8 (d, $^1J_{P,C}$ 150, C_{ipso} ArC), 128.7 (d, $^3J_{P,C}$ 13.9, C_m ArC), 134.4 (d, $^4J_{P,C}$ 2.4, C_p ArC) and 135.0 (d, $^2J_{P,C}$ 9.7, C_o ArC).

Ethyl phenyl(chloro[$^2H_2$]methyl)phosphinate 5e (Scheme 3)

To a stirred mixture of BuLi (1.6 mol dm^{-3} in hexane; 132 cm^3, 210 mmol) and THF (270 cm^3) at −80 °C was added a mixture of **10** (28.7 g, 100 mmol) and chlorotrimethylsilane (11.40 g, 105 mmol) in THF (100 cm^3). The reaction mixture was stirred at −80 °C for 15 min after which D_2O (50 cm^3) was added to it at −78 °C; the mixture was then allowed to warm to 0 °C. When deuteriolysis was complete (30 min at 0 °C) the reaction mixture was acidified with 2 mol dm^{-3} hydrochloric acid and extracted with CH_2Cl_2 (3 × 50 cm^3). The combined extracts were dried ($MgSO_4$) and evaporated under reduced pressure to give the crude product. This was purified by bulb-to-bulb distillation. Compound **5e** (92%), bp (20 mmHg) 225–230 °C; $\delta_P(CDCl_3)$ +34.5; $\delta_H(CDCl_3)$ 1.35 (t, $^3J_{H,H}$ 7, OCH_2Me), 4.14 (m, $^3J_{P,H}$ and $^3J_{H-H}$ 7, OCH_2Me), 7.57 (m, ArH) and 7.84 (m, ArH); $\delta_C(CDCl_3)$ 15.9 (d, $^3J_{P,C}$ 5.4, OCH_2Me), 35.5 (dp, $^1J_{P,C}$ 105, PCD_2), 61.37 (d, $^2J_{P,C}$ 5.8, OCH_2CH_3), 127.18 (d, $^1J_{P,C}$ 136, C_{ipso} ArC), 128.30 (d, $^3J_{P,C}$ 12.6, C_m ArC), 131.70 (d, $^2J_{P,C}$ 10.2, C_o ArC) and 132.25 (s, C_p ArC); $\delta_D(H_2O–C_3D_6O)$ 3.05 (br s, CD_2); (Found: M$^+$, 220.038 94. Calc. for $C_9H_{10}D_2{}^{35}ClO_2P$: *M*, 220.038 89).

Alkyl(chloro[$^2H_2$]methyl)phosphinic chlorides 6a–6d and phenyl(chloro[$^2H_2$]methyl)phosphinic chloride 6e (Scheme 2)

Compound **5** (100 mmol) was added dropwise to phosphorus oxychloride (23 g, 150 mmol) in a 100 cm^3 pear-shaped flask cooled to 0 °C over a few minutes after which the reaction mixture was allowed to warm slowly to room temp. The residue was purified by distillation under reduced pressure using an 8 cm fractionating column equipped with a condenser. Compound **6a** (71%), bp (0.2 mmHg) 69 °C; $\delta_P(CDCl_3)$ +57.5; $\delta_H(CDCl_3)$ 2.10 (d, $^2J_{P,H}$ 14, PMe). Compound **6b** (50%), bp (0.2 mmHg) 72 °C; $\delta_P(CDCl_3)$ +63.7; $\delta_H(CDCl_3)$ 1.32 (dt, $^3J_{P,H}$ 23 and $^3J_{H,H}$ 7, PCH_2Me) and 2.35 (dq, $^2J_{P,H}$ 15.4 and $^3J_{H,H}$ 7.7, PCH_2Me). Compound **6c** (57%), bp (0.2 mmHg) 75 °C; $\delta_P(CDCl_3)$ +61.8; $\delta_H(CDCl_3)$ 1.10 (t, $^3J_{H,H}$ 7, $P(CH_2)_2Me$) and 1.65–2.35 (m, $P(CH_2)_2Me$). Compound **6d** (61%), $\delta_P(CDCl_3)$ +42.7; $\delta_H(CDCl_3)$ 6.25–6.74 (m, $CH{=}CH_2$). Compound **6e** (61%), bp (20 mmHg) 200–210 °C; $\delta_P(CDCl_3)$ +46.1; $\delta_H(CDCl_3)$ 7.63 (m, ArH) and 7.94 (m, ArH).

2,2,2-Trifluoroethyl alkyl(chloro[$^2H_2$]methyl)phosphinates 7a–7d and 2,2,2-trifluoroethyl phenyl(chloro[$^2H_2$]methyl)phosphinate 7e (Scheme 2)

2,2,2-Trifluoroethanol (10.5 g, 105 mmol) in THF (100 cm^3) was added to a stirred solution of compound **6** (100 mmol) in THF (400 cm^3) at room temp. and this was followed by triethylamine (10.6 g, 105 mmol) in THF (50 cm^3) added dropwise over a few minutes. The resulting mixture was stirred at room temperature for 2 h after which the organic salts were removed by suction filtration and the filter cake washed with THF. The combined filtrate and washings were evaporated under reduced pressure and the residue was dissolved in diethyl ether and filtered to remove insoluble triethylamine hydrochloride. After evaporation of the filtrate under reduced pressure, the crude product was purified by bulb-to-bulb distillation. Compound **7a** (75%), bp (20 mmHg) 150–155 °C; $\delta_P(CDCl_3)$ +52.8; $\delta_H(CDCl_3)$ 1.74 (d, $^2J_{P,H}$ 15, PMe) and 4.37 (m, OCH_2CF_3). Compound **7b** (90%), bp (20 mmHg) 160–165 °C; $\delta_P(CDCl_3)$ + 55.6; $\delta_H(CDCl_3)$ 1.21 (dt, $^3J_{P,H}$ 20 and $^3J_{H,H}$ 7, PCH_2Me), 2.00 (dq, $^2J_{P,H}$ 15.7 and $^3J_{H,H}$ 7.8, PCH_2Me) and 4.38 (m, OCH_2CF_3). Compound **7c** (87%), bp (20 mmHg) 165–170 °C; $\delta_P(CDCl_3)$ +61.8; $\delta_H(CDCl_3)$ 1.07 (t, $^3J_{H,H}$ 7, $P(CH_2)_2Me$), 1.56–2.05 (m, $P(CH_2)_2Me$) and 4.35 (m, OCH_2CF_3). Compound **7d** (91%), $\delta_P(CDCl_3)$ +37.6; $\delta_H(CDCl_3)$ 4.36 (m, OCH_2CF_3) and 6.12–6.63 (m, $CH{=}CH_2$). Compound **7e** (95%), bp (20 mmHg) 195–200 °C; $\delta_P(CDCl_3)$ + 38.3; $\delta_H(CDCl_3)$ 4.43 (m, OCH_2CF_3), 7.82 (m, ArH) and 7.88 (m, ArH); $\delta_C(CDCl_3)$ 36.2 (dp, $^1J_{P,C}$ 104.1, PCD_2), 34.1 (dt, $^2J_{C,F}$ 38 and $^2J_{C,P}$ 6, OCH_2CF_3), 123 (dq, $^1J_{C,F}$ 277.7 and $^3J_{P,C}$ 8.7, OCH_2CF_3), 126.6 (d, $^1J_{P,C}$ 123.9, C_{ipso} ArC), 129.15 (d, $^3J_{P,C}$ 13.4, C_m ArC), 132.2 (d, $^2J_{P,C}$ 10.5, C_o ArC) and 134.05 (s, C_p ArC); (Found: M$^+$, 274. 010 77. Calc. for $C_9H_7D_2F_3{}^{35}ClO_2P$: *M*, 274.010 62).

2,2,2-Trifluoroethyl alkyl(azido[$^2H_2$]methyl)phosphinates 8a–c, and 2,2,2-trifluoroethyl phenyl(azido[$^2H_2$]methyl)phosphinate 8e (Scheme 2)

Compound **7** (50 mmol) and sodium azide (75 mmol) in DMSO (165 cm^3) were stirred and heated at 90–95 °C for 3 h. After the reaction mixture had cooled it was treated with water (165 cm^3) and extracted with diethyl ether (3 × 80 cm^3). The combined extracts were dried ($MgSO_4$), and evaporated under reduced pressure to give the azides which were used without further purification. Compound **8a** (72%), $\delta_P(CDCl_3)$ +52.8; $\delta_H(CDCl_3)$ 1.63 (d, $^2J_{P,H}$ 14, PMe) and 4.40 (m, OCH_2CF_3). Compound **8b** (84%), $\delta_P(CDCl_3)$ +56.5; $\delta_H(CDCl_3)$ 1.23 (dt, $^3J_{P,H}$ 19 and $^3J_{H,H}$ 7, PCH_2Me), 1.93 (dq, $^2J_{P,H}$ 16 and $^3J_{H,H}$ 8, PCH_2Me) and 4.42 (m, OCH_2CF_3). Compound **8c** (80%), $\delta_P(CDCl_3)$ +63.1; $\delta_H(CDCl_3)$ 1.08 (t, $^3J_{H,H}$ 7, $P(CH_2)_2Me$), 1.60–2.98 (m, $P(CH_2)_2Me$) and 4.41 (m, OCH_2CF_3). Compound **8e** (84%), $\delta_P(CDCl_3)$ +39.4; $\delta_H(CDCl_3)$ 4.34 (m, OCH_2CF_3), 7.60 (m, ArH) and 7.85 (m, ArH).

Alkyl(amino[$^2H_2$]methyl)phosphinic acids 3a–c and phenyl(amino[$^2H_2$]methyl)phosphinic acid 3e (Scheme 2)

Compound **8** (50 mmol) in ethanol (95%, 200 cm^3), Pd/C (10%, 1.50 g), and 12 mol dm^{-3} hydrochloric acid (12.5 cm^3), under 1 H_2 (1 atm) were stirred at room temp. for 24 h. The Pd catalyst was removed by suction filtration over Celite, and the filter cake washed with hot water. After evaporation of the filtrate under reduced pressure, the crude product, dissolved in ethanol (95%), was treated with propylene oxide; the acids **3** were spontaneously precipitated.

Compound **3a** (60%), mp > 260 °C; $\delta_P(D_2O)$ +32.3; $\delta_H(D_2O)$ 1.26 (d, $^2J_{P,H}$ 14, PMe); $\delta_C(D_2O–C_3D_6O)$ 16.12 (d, $^1J_{P,C}$ 97.5, PMe), 39.1 (dp, $^1J_{P,C}$ 91.1 and $^1J_{C,D}$ 20.7, PCD_2); $\delta_D(H_2O–C_3D_6O)$ 2.90 (br s, CD_2); (Found: M$^+$, 111.0419. Calc. for $C_2H_6D_2PNO_2$: *M*, 111.0418). Compound **3b** (50%), mp > 260 °C; $\delta_P(D_2O)$ +36.5; $\delta_H(D_2O)$ 0.94 (dt, $^3J_{P,H}$ 18 and $^3J_{H,H}$ 7, PCH_2Me), 2.00 (dq, $^2J_{P,H}$ 15.5 and $^3J_{H,H}$ 7.7, PCH_2Me); $\delta_C(H_2O–C_3D_6O)$ 6.5 (d, $^2J_{P,C}$ 6, PCH_2Me), 22.8 (d, $^1J_{P,C}$ 97.9, PCH_2Me) and 37.3 (dp, $^1J_{P,C}$ 86.6 and $^1J_{C,D}$ 20.7, PCD_2); $\delta_D(H_2O–C_3D_6O)$ 2.90 (br s, CD_2); (Found: M$^+$, 125.0575. Calc. for $C_3H_8D_2PNO_2$: *M*, 125.0574). Compound **3c** (43%), mp > 260 °C; $\delta_P(D_2O)$ +34.7; $\delta_H(D_2O)$ 0.86 [t, $^3J_{H,H}$ 7, $P(CH_2)_2Me$] and 1.35–2.15 (m, $P(CH_2)_2Me$); $\delta_C(H_2O–C_3D_6O)$ 15.18 (d, $^2J_{P,C}$ 21.5, $PCH_2CH_2CH_3$), 15.28 (s, $PCH_2CH_2CH_3$), 31.25 (d, $^1J_{P,C}$ 96.5, $PCH_2CH_2CH_3$) and 37.05 (dp, $^1J_{P,C}$ 98 and $^1J_{C,D}$ 20.7, PCD_2); $\delta_D(H_2O–C_3D_6O)$ 2.87 (br s, CD_2); (Found: M$^+$, 139.0731. Calc. for $C_4H_{10}D_2PNO_2$: *M*, 139.0731). Compound **3e** (43%), mp > 260 °C; $\delta_P(D_2O)$ +27.9; $\delta_H(D_2O)$ 7.56 (m, ArH) and 7.74 (m, ArH); $\delta_C(H_2O–C_3D_6O)$ 37.1 (dp, $^1J_{P,C}$ 98 and $^1J_{C,D}$ 20.7, PCD_2), 128.9 (d, $^3J_{P,C}$ 12.2, C_m ArC),

131.4 (d, $^2J_{P,C}$ 9.3, C_o ArC), 132.2 (s, C_p ArC) and 133.6 (d, $^1J_{P,C}$ 125.3, C_{ipso} ArC); $\delta_D(H_2O–C_3D_6O)$ 3.05 (br s, CD_2); (Found: M^+, 173.0575. Calc. for $C_7H_8D_2PNO_2$: *M*, 173.0574).

Acknowledgements

We thank Dr J. P. Morizur (Universite Paris VI, ERS 72 CNRS) for the HRMS measurements.

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Paper 5/00305I
Received 18*th January* 1995
Accepted 24*th April* 1995