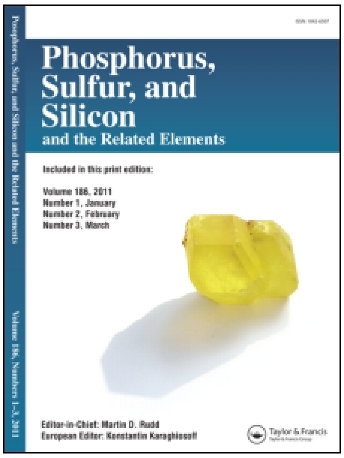

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A SIMPLE SYNTHESIS OF 1-SUBSTITUTED 2-AMINOETHYLPHENYLPHOSPHINIC ACIDS

Henryk Krawczyk[a]
[a] Institute of Organic Chemistry, Technical University (Politechnika), Łódź wirki, Poland

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A SIMPLE SYNTHESIS OF 1-SUBSTITUTED 2-AMINOETHYLPHENYLPHOSPHINIC ACIDS

HENRYK KRAWCZYK

Institute of Organic Chemistry, Technical University (Politechnika), 90-924 Łódź, Żwirki 36, Poland

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Piperidine catalysed reaction of methyl phenylphosphinylacetic acid **1** with paraformaldehyde and primary or secondary alcohols gave methyl phenyl(1-alkoxymethyl)vinylphosphinates **3a–f**. Conjugate addition of primary amines or ammonia to **3** followed by hydrolysis of the resulting 2-aminophosphinates **5** and **7** afforded 2-aminoethylphenylphosphinic acids **6** and **8** respectively.

Keywords: Vinylphosphinates; amines; conjugate addition; hydrolysis

The synthesis of functionalised phenylphosphinic acids and their esters has attracted considerable attention in recent years not only because of their potential biological activity but also because of their wide utility as useful intermediates in the preparation of various important organophosphorus compounds.[1-8] On the other hand, vinylphosphinates have proven valuable as starting materials in the synthesis of agrochemicals.[9-14] Although several methods for the preparation of vinylphosphinates have been published,[9-17] synthesis of 1-substituted vinylphosphinates remains relatively unexplored.[15-17]

Recently we reported a novel three component reaction of diethylphosphonoacetic acid with paraformaldehyde and alcohols producing diethyl 1-alkoxymethylvinylphospohonates.[18] In this paper we describe a similar approach to methyl phenyl(1-alkoxymethyl)vinylphosphinates **3** starting from readily available methyl phenylphosphinylacetic acid **1**[19] and we report a simple one-pot procedure for their transformation into (2-amino-1-alkoxymethylethyl)phenylphosphinic acids **6** and **8**. This type of acids is of biological interest.[20-22]

Reaction of the acid **1** with an excess of paraformaldehyde (3 eq.) and primary or secondary alcohols **2** in the presence of a catalytic amount of piperidine (6 mol%) (Scheme 1) produced the phosphinates **3** in yields of 52–85% (Table I).

A promising route to 2-aminoalkyl phosphinic acids seemed to be a conjugate addition of amines to vinylphosphinates followed by the standard hydrolysis of the resulting 2-aminophosphinates. Similar examples of such an addition have been reported. However, they were limited to unsubstituted vinylphosphinates and the corresponding phosphonates or phosphine oxides.[23-26] We reasoned that conjugate addition of amines to vinylphosphinates **3a–f** bearing 1-alkoxymethyl substituent (Scheme 2) would constitute a facile synthesis of 2-aminophosphinates **5**. Such a prediction was based on an analogy to the known reaction of amines with α-substituted acrylates.[27-29] It has been established that replacement of the α-methyl group in acrylates by α-hydroxymethyl substituent significantly improved the reactivity of these Michael acceptors. In contrast to methyl methacrylate which reacted with primary amines at elevated pressures in the presence of ytterbium triflate, α-hydroxymethylacrylates and their ethers were converted to the corresponding β-aminoesters at atmospheric pressure and without the use of any catalyst.

As model representatives of **3** and primary amines **4** we chose phosphinate **3a** and benzylamine **4a** respectively. Indeed, the addition of benzylamine (1.1 eq.) to **3a** proceeded readily in methanol at room temperature and was completed after three days providing 2-aminophosphinate **5aa** as a mixture of diastereoisomers in a ratio 1 : 1 (^{31}P NMR). We have not attempted to separate out particular isomers.

Base promoted hydrolysis of alkyl phosphinates is a well-known reaction.[30] Moreover, hydrolysis of diethyl β- and γ-aminoalkylphosphonates under basic conditions to give monoesters has been shown to occur with intramolecular nucleophilic catalysis by an amino group.[31] We found that heating **5aa** in aqueous ammonia at 40°C for 100h provided a gentle and effective approach to the acid **6aa**. Following this methodology we have synthesized a number of N-substituted aminophosphinic acids **6** (Table II). It has also proven useful for the preparation of N-unsubstituted aminophosphinic acids **8** (Scheme 3). In general, methanol solutions of vinylphosphinates **3** were treated with an excess of aqueous ammonia at room temperature for three weeks. After three days the addition of ammonia was completed and the forming esters **7** were then slowly hydrolysed. Only hydrolysis of ester **7b** required heating at 40°C for 100 h. In each case the acids **6** and **8** were obtained as crystalline compounds.

It is noteworthly that methyl 1-methylvinylphenylphosphinate[32] did not undergo conjugate addition with benzylamine even if the reaction mixture was heated in refluxing methanol for a prolonged time. This suggests that the reactivity of 1-substituted vinylphosphinates towards such nucleophiles as primary amines or ammonia is controlled rather by electronic effects than by steric hindrance exerted by 1-substituent.[33] Consequently one can draw the conclusion that during the addition of amines to vinylphosphinates **3** the negative charge being developed on the carbon atom adjacent to the phosphoryl group is likely to be stabilised by the inductive effect of the β-C-O bond (Scheme 4). A similar oxygen-carbon β-bond effect has already been noticed.[36]

To summarize, we described a novel route for the preparation of 1-substituted vinylphenylphosphinates and demonstrated their usefulness in the synthesis of a variety of 1-functionalised-2-aminoethylphenylphosphinic acids.

EXPERIMENTAL

NMR spectra were recorded on a Bruker DPX 250 spectrometer (250.13 MHz for ^{1}H or 101.26 for ^{31}P). TMS was used as an internal standard for ^{1}H NMR spectra, 85% H_3PO_4 was an external standard for ^{31}P NMR measurements. FAB/MS were recorded on a APO Electron (Ukraine) Modell MI 12001 E mass spectrometer equipped with FAB ion source (thioglycerol matrix). Melting points were determined in open capillaries and are uncorrected. Methyl phenylphosphinylacetic acid was prepared according to the literature procedure.[19]

Methyl Phosphinates 3a–f

General Procedure

A mixture of acid **1** (6.42 g, 0.03 mol), paraformaldehyde (2.7 g, 0.09 mol) and piperidine (153 mg, 1.8 mmol) in alcohol **2a–f** (50 ml) was heated with stirring at given temperature for a period of time as shown in Table I. The reaction mixture was concentrated under reduced pressure, the residue was taken up in chloroform (70 ml) and washed successively with water (2 × 20 ml), 5% HCl (2 × 5 ml), 5% $NaHCO_3$ (2 × 10 ml), water (2 × 20 ml) and dried over anhydrous $MgSO_4$. Removal of the solvent followed by distillation afforded phosphinates **3a–f** as colourless liquids.

Methyl (1-Methoxymethylvinyl)Phenylphosphinate 3a

yield: 85%; b.p. 125°C/0.4 Torr; ^{31}P NMR ($CDCl_3$) δ: 33.7; ^{1}H NMR ($CDCl_3$) δ: 3.27 (s, 3H, CH_3), 3.73 (d, 3H, $^{3}J_{HP}$ = 11.0, CH_3), 4.06 (dt, 2H, $^{3}J_{HP}$ = 8.0,

$^4J_{HH}$ = 1.5, CH_2), 6.09 (ddt, 1H, $^3J_{HP}$ = 40.1, $^2J_{HH}$ = $^4J_{HH}$ = 1.5, P-C=CH_{trans}), 6.12 (ddt, 1H, $^3J_{HP}$ = 22.0, $^2J_{HH}$ = $^4J_{HH}$ = 1.5, P-C=CH_{cis}), 7.43–7.60 (m, 3H, Ar), 7.75–7.85 (m, 2H, Ar); FAB/MS: m/z (%): 227 (MH^+, 100), 155 (33). Anal. Calcd for $C_{11}H_{15}O_3P$: C, 58.40; H, 6.68. Found: C; 58.52; H; 6.72.

Methyl (1-Benzyloxymethylvinyl)Phenylphosphinate 3b

yield: 54%; b.p. 150°C/0.2 Torr; ^{31}P NMR ($CDCl_3$) δ: 33.8; ^1H NMR ($CDCl_3$) δ: 3.72 (d, 3H, $^3J_{HP}$ = 11.1, CH_3), 4.18 (dt, 2H, $^3J_{HP}$ = = 8.2, $^4J_{HH}$ = 1.4, CH_2), 4.45 (s, 2H, CH_2), 6.16 (ddt, 1H, $^3J_{HP}$ = 20.4, $^2J_{HH}$ = $^4J_{HH}$ = 1.4, P-C=CH_{cis}), 6.17 (ddt, 1H, $^3J_{HP}$ = 41.6, $^2J_{HH}$ = $^4J_{HP}$ = 1.4, P-C=CH_{trans}), 7.2–7.4 (m, 5H, Ar), 7.4–7.6 (m, 3H, Ar), 7.75–7.85 (m, 2H, Ar); FAB/MS: m/z (%), 303 (MH^+, 58), 155 (11), 91 (100). Anal. Calcd for $C_{17}H_{19}O_3P$: C, 67.54; H, 6.33. Found: C, 67.69; H, 6.29.

Methyl (1-Allyloxymethylvinyl)Phenylphosphinate 3c

yield: 54%, b.p. 130°C/0.2 Torr; ^{31}P NMR ($CDCl_3$) δ: 33.7; ^1H NMR ($CDCl_3$) δ: 3.73 (d, 3H, $^3J_{HP}$ = 11.1, CH_3), 3.91 (dt, 2H, $^3J_{HH}$ = 5.55, $^4J_{HH}$ = 1.5, CH_2), 4.12 (dt, 2H, $^3J_{HP}$ = 7.87, $^4J_{HH}$ = 1.5, CH_2), 5.14 (ddt, 1H, J_{cis} = 10.4, ^2J = ^4J = 1.5, =CH_A), 5.19 (ddt, 1H, J_{trans} = 17.3, ^2J = ^4J = 1.5, =CH_B), 5.82 (ddt, 1H, ^3J = 5.55, J_{trans} = 17.3, J_{cis} = 10.4, =CH), 6.13 (ddt, 1H, $^3J_{HP}$ = 41.7, $^2J_{HH}$ = $^4J_{HH}$ = 1.5, P-C=CH_{trans}), 6.14 (ddt, 1H, $^3J_{HP}$ = 21.8, $^2J_{HH}$ = $^4J_{HH}$ = 1.5, P-C=CH_{cis}), 7.4–7.6 (m, 3H, Ar), 7.75–7.85 (m, 2H, Ar); FAB/MS: m/z (%) 253 (MH^+, 100), 155 (29), 41(25). Anal. Calcd for $C_{13}H_{17}O_3P$: C, 61.90; H, 6.79. Found: C, 61.97; H, 6.74.

Methyl (1-Propargyloxymethylvinyl)Phenylphosphinate 3d

yield: 85%; b.p. 135°C/0.2 Torr; ^{31}P NMR ($CDCl_3$) δ: 33.7; ^1H NMR ($CDCl_3$) δ: 2.4 (t, 1H, ^4J = 2.4, ≡CH), 3.74 (d, 3H, $^3J_{HP}$ = 11.0, CH_3), 4.08 (t, 2H, ^4J = 2.4, CH_2), 4.22 (dm, 2H, $^3J_{HP}$ = 8.5, CH_2), 6.13 (dm, 1H, $^3J_{HP}$ = 40.0, P-C=CH_{trans}), 6.16 (dm, 1H, $^3J_{HP}$ = 20.4, P-C=CH_{cis}), 7.4–7.6 (m, 3H, Ar), 7.75–7.85 (m, 2H, Ar); FAB/MS: m/z (%) 251 (MH^+, 100), 155 (43). Anal. Calcd for $C_{13}H_{15}O_3P$: C, 62.40; H, 6.04. Found: C, 62.49; H, 6.09.

Methyl (1-Isobutoxymethylvinyl)Phenylphosphinate 3e

yield: 64%; b.p. 120°C/0.2 Torr; ^{31}P NMR ($CDCl_3$) δ: 33.9; ^{1}H NMR ($CDCl_3$) δ: 0.85 (d, 6H, J = 6.7, 2CH_3), 1.79 (m, 1H.CH), 3.12 (d, 2H, J = 6.6, CH_2), 3.73 (d, 3H, $^{3}J_{HP}$ = 11.1, CH_3), 4.09 (dt, 2H, $^{3}J_{HP}$ = 7.6, $^{4}J_{HH}$ = 1.5, CH_2), 6.12 (1H, ddt, 1H, $^{3}J_{HP}$ = 41.8, $^{2}J_{HH}$ = $^{4}J_{HH}$ = 1.5, P-C=CH_{trans}), 6.13 (1H, ddt, $^{3}J_{HP}$ = 21.4, $^{2}J_{HH}$ = $^{4}J_{HH}$ = 1.5, P-C=CH_{cis}), 7.4–7.6 (m, 3H, Ar), 7.75-7.85 (m, 2H, Ar); FAB/MS: m/z (%) 269 (MH^+, 100), 211 (22), 155 (43). Anal. Calcd for $C_{14}H_{21}O_3P$: C, 62.67; H, 7.89. Found: C, 62.53, H, 7.96.

Methyl (1-Isopropoxymethylvinyl)Phenylphosphinate 3f

yield: 52%, b.p. 130°C/0.8 Torr; ^{31}P NMR ($CDCl_3$) δ: 34.0; ^{1}H NMR ($CDCl_3$) δ: 1.09 (d, 3H, J = 6.1, CH_3), 1.10 (d, 3H, J = 6.1, CH_3), 3.54 (sep, 1H, J = 6.1, CH), 3.73 (d, 3H, $^{3}J_{HP}$ = 11.1, CH_3), 4.10 (dt, 2H, $^{3}J_{HP}$ = 7.56, $^{4}J_{HH}$ = 1.5, CH_2), 6.14 (ddt, 1H, $^{3}J_{HP}$ = 40.8, $^{2}J_{HH}$ = $^{4}J_{HH}$ = 1.5, P-C=CH_{trans}), 6.18 (ddt, 1H, $^{3}J_{HP}$ = 20.0, $^{2}J_{HH}$ = $^{4}J_{HH}$ = 1.5, P-C=CH_{cis}), 7.4–7.6 (m, 3H, Ar), 7.75–7.85 (m, 2H, Ar); FAB/MS: m/z (%) 255 (MH^+, 100), 155 (69); Anal. Calcd for $C_{13}H_{19}O_3P$: C, 61.40; H, 7.53; Found: C, 61.52; H, 7.62.

Aminophosphinic Acids 6

General Procedure

A mixture of vinylphosphinate (4 mmol) and amine **3a**, **3d** (1.1 eq.) or **3b**, **3c** (3 eq) in methanol (5 ml) was stirred for three days at room temperature. After that time examination by ^{31}P NMR showed that all vinylphosphinate had been converted to aminophosphinate. The reaction mixture was concentrated under reduced pressure. The resulting oil was dissolved in methanol (20 ml) and added to 25% aqueous ammonia (50 ml). The reaction mixture was heated at 40°C for 100 h. The solution was evaporated to dryness to give an oily residue which after dissolving in acetone/ether (10 ml) crystallized into white solid. Crystalline acid **6** was filtered off, washed with acetone and recrystallized from methanol/acetone.

(2-N-Benzylamino-1-Methoxymethylethyl)Phenylphosphinic Acid 6aa

yield: 67%, m.p. 199–200°C ^{31}P NMR (CD_3OD) δ: 27.1; ^{1}H NMR ($CDCl_3$: CF_3COOD, 5:1) δ: 2.69 (m, 1H), 3.18 (s, 3H, CH_3), 3.3–3.7 (4H, complex), 4.23 (d, 1H, J_{AB} = 13.2), 4.35 (d, 1H, J_{AB} = 13.2), 7.3–7.6 (m, 5H, Ar); FAB/MS: m/z (%) 320 (MH^+, 90), 169 (10), 141 (8), 106 (17), 91 (100). Anal. Calcd for $C_{17}H_{22}NO_3P$: C, 63.94; H, 6.94. Found: C, 64.02; H, 6.97.

(2-N-Iso-Propylamino-1-Methoxymethylethyl)Phenylphosphinic Acid 6ab

yield: 77%, m.p. 214–215°C, ^{31}P NMR (CD_3OD) δ: 26.0; ^1H NMR ($CDCl_3$:CF_3COOD, 5:1) δ: 1.39 (d, 3H, J = 6.6, CH_3), 1.40 (d, 3H, J = 6.6, CH_3), 2.72 (m, 1H), 3.21 (s, 3H, CH_3), 3.3–3.6 (complex, 5H, 2CH_2, CH), 7.5–7.8 (m, 5H, Ar); FAB/MS: m/z (%) 272 (MH^+, 100), 169 (7), 141 (6), 72 (12), 71(11). Anal. Calc for $C_{13}H_{22}NO_3P$: C, 57.55; H, 8.17. Found C, 57.64; H, 8.23.

(2-N-tert-Butylamino-1-Methoxymethylethyl)Phenylphosphinic Acid 6ac

yield: 82%; m.p. 240°C (dec); ^{31}P NMR (CD_3OD) δ: 25.5; ^1H NMR ($CDCl_3$:CF_3COOD, 5:1)H δ: 1.45 (s, 9H, 3CH_3), 2.8 (m, 1H), 3.24 (s, 3H, CH_3), 3.35–3.75 (complex, 4H, 2CH_2), 7.5–7.8 (m, 5H, Ar); FAB/MS:m/z(%) 286 (MH^+, 100), 141(8), 71(32), 57(34). Anal. Calcd for $C_{14}H_{24}NO_3P$: C, 58.93; H, 8.48. Found: C, 58.85; H, 8.52.

(2-N-Cyclohexylamino-1-Methoxymethylethyl)Phenylphosphinic Acid 6ad

yield: 69%; m.p. 184–185°C; ^{31}P NMR (CD_3OD) δ: 26.7; ^1H NMR ($CDCl_3$:CF_3COOD, 5:1) δ: 1.4 (m, 5H), 1.9 (m, 5H), 2.8 (m, 1H), 3.1 (m, 1H), 3.25 (s, 3H, CH_3), 3.35–3.65 (complex, 4H, 2CH_2), 7.5–7.8 (m, 5H, Ar): FAB/MS: m/z(%) 312 (MH^+, 100), 141(8), 91(27), 71(28), 56(31). Anal. Calcd for $C_{16}H_{26}NO_3P$: C, 61.72; H, 8.42. Found: C, 61.66; H, 8.46.

(2-N-Benzylamino-1-Benzyloxymethylethyl)Phenylphosphinic Acid 6ba

yield: 74%; m.p. 194–195°C; ^{31}P NMR (CD_3OD) δ: 26.7; ^1H NMR ($CDCl_3$:CF_3COOD, 5:1) δ: 2.79 (m, 1H), 3.45–3.75 (complex, 4H), 4.18 (1H, d, J_{AB} = 13.1, CH_A), 4.27 (1H, d, J_{AB} = 13.1, CH_B), 4.29(1H, d, J_{AB} = 11.4, CH_A), 4.37(1H, d, J_{AB} = 11.4, CH_B), 7.1–7.9(m, 15H, Ar); FAB/MS:m/z(%) 396 (MH^+, 100), 91(89). Anal. Calcd for $C_{23}H_{26}NO_3P$: C, 69.86; H, 6.63. Found: C, 69.74; H, 6.68.

(2-N-Benzylamino-1-Allyloxymethylethyl)Phenylphosphinic Acid 6ca

Yield: 82%; m.p. 183–184°C; ^{31}P NMR (CD_3OD) δ: 26.4; ^{1}H NMR ($CDCl_3$:CF_3COOD, 5:1) δ: 2.72 (m, 1H), 3.3–3.9 (complex, 6H, $3CH_2$), 4.23 (d, 1H, J_{AB} = 13.2), 4.37 (d, 1H, J_{AB} = 13.2), 5.13 (ddt, 1H, J_{trans} = 16.9, $^2J_{HH}$ = $^4J_{HH}$ = 1.3, $=CH_A$), 5.19 (ddt, 1H, J_{cis} = 10.4, $^2J_{HH}$ = $^4J_{HH}$ = 1.3, $=CH_B$), 5.63 (ddt, 1H, ^3J = 6.2, J_{trans} = 16.8, J_{cis} = 10.4, =CH), 7.3–7.7 (m, 5H, Ar); FAB/MS:m/z(%) 346 (MH^+, 100), 91(88). Anal. Calcd for $C_{19}H_{24}NO_3P$: C, 66.07; H, 7.00. Found: C, 66.18; H, 7.08.

(2-N-tert-Butylamino-1-Allyloxymethylethyl)Phosphinic Acid 6cc

yield: 81%; m.p. 241–242°C; ^{31}P NMR(CD_3OD) δ: 26.8; ^{1}H NMR ($CDCl_3$:CF_3COOD, 5:1) δ: 1.44(s, 9H, $3CH_3$), 2.87(m, 1H), 3.5–4.0 (complex, 6H, $3CH_2$), 5.21(ddt, 1H, J_{trans} = 16.8, $^2J_{HH}$ = $^4J_{HH}$ = 1.3, $=CH_A$), 5.24(ddt, 1H, J_{cis} = 10.6, $^2J_{HH}$ = $^4J_{HH}$ = 1.3, $=CH_B$), 5.75(ddt, 1H, ^3J = 6.2, J_{trans} = 16.8, J_{cis} = 10.6, =CH), 7.4–7.5(m, 5H, Ar); FAB/MS:m/z(%) 312 (MH^+, 100), 256(8), 141(4), 58(23). Anal. Calcd for $C_{16}H_{26}NO_3P$:C, 61.69; H, 8.41. Found: C, 61:59; H, 8.46.

(2-N-tert-Butylamino-1-Propargyloxymethylethyl)Phenylphosphinic Acid 6dc

yield: 65%; m.p. 230–231°C; ^{31}P NMR (CD_3OD) δ: 26.6; ^{1}H NMR ($CDCl_3$:CF_3COOD, 5:1) δ: 1.46(s, 9H, $3CH_3$), 2.46(t, 1H, ^4J = 2.4, ≡CH), 2.88(m, 1H, CH), 3.5–3.8(complex, 4H, $2CH_2$), 4.05(d, 2H, ^4J = 2.4, CH_2), 7.5–7.8(m, 5H, Ar); FAB/MS:m/z(%) 310 (MH^+, 100), 141(8). Anal. Calcd for $C_{16}H_{24}NO_3P$:C, 62.12; H, 7.82. Found: C, 61.97; H, 7.87.

(2-N-Cyclohexylamino-1-Isobutoxymethylethyl)Phenylphosphinic Acid 6ed

yield: 63%; m.p. 206–207°C; ^{31}P NMR (CD_3OD) δ: 26.3; ^{1}H NMR ($CDCl_3$:CF_3COOD, 5:1) δ: 0.85 (d, 6H, J = 6.6, $2CH_3$), 1.2–1.6 (m, 5H), 1.7–2.2 (complex, 6H), 2.5 (m, 1H), 2.95 (m, 1H), 3.16 (m, 2H), 3.45–3.80 (complex, 4H, $2CH_2$), 7.5–7.8 (m, 5H, Ar); FAB/MS:m/z(%) 354 (MH^+, 100), 57(31). Anal. Calcd for $C_{19}H_{32}NO_3P$: C, 64.56; H, 9.13. Found: C, 64.47; H, 9.05.

(2-N-Cyclohexylamino-1-Isopropoxymethylethyl)Phenylphosphinic Acid 6fd

m.p. 202–203°C; ^{31}P NMR (CD_3OD) δ: 27.8; ^{1}H NMR ($CDCl_3$:CF_3COOD, 5:1) δ: 1.11 (d, 3H, J = 6.1, CH_3), 1.11 (d, 3H, J = 6.1, CH_3), 1.25–1.50 (m, 5H), 1.7–2.2 (m, 5H), 2.50 (sep, 1H, J = 6.1, CH), 2.87 (m, 1H, CH), 3.14 (m, 1H, CH), 3.45–3.80 (complex, 4H, $2CH_2$), 7.5–7.8 (m, 5H, Ar); FAB/MS:m/z(%) 340 (MH^+, 100), 141(7), 56(17). Anal. Calcd for $C_{18}H_{30}NO_3P$:C, 63.70; H, 8.91. Found: C, 63.61; H, 8.97.

Aminophosphinic Acids 8

General Procedure

A solution of vinylphosphinate (4 mmol) in methanol (20 ml) was added to 25% aqueous ammonia (50 ml). The reaction mixture was kept at room temperature for three weeks. The crude product was further worked up as described above.

(2-Amino-1-Methoxymethylethyl)Phenylphosphinic Acid 8a

yield: 76%; m.p. 254–255°C; ^{31}P NMR (CD_3OD) δ: 26.3; ^{1}H NMR ($CDCl_3$:CF_3COOD, 5:1) δ: 2.60 (m, 1H), 3.24 (s, 3H, CH_3), 3.4–3.7 (complex, 4H), 7.5–7.8 (m, 5H, Ar); FAB/MS:m/z(%) 230 (MH^+, 100), 141 (6). Anal. Calcd for $C_{10}H_{16}NO_3P$: C, 52.40; H, 7.04. Found: C, 52.29; H, 7.09.

(2-Amino-1-Benzyloxymethylethyl)Phenylphosphinic Acid 8b

yield 59%; m.p. 221–222°C; ^{31}P NMR (CD_3OD) δ: 26.8; ^{1}H NMR ($CDCl_3$:CF_3COOD, 5:1) δ: 2.71 (m, 1H), 3.41–3.81 (complex, 4H), 4.38 (d, 1H, J_{AB} = 11.5, CH_A), 4.47 (d, 1H, J_{AB} = 11.5, CH_B), 7.1–7.5 (m, 10H, Ar); FAB/MS:m/z(%) 306 (MH^+, 52), 91(100). Anal. Calcd for $C_{16}H_{20}NO_3P$:C, 62.94; H, 6.60. Found: C, 62.86; H, 6.67.

(2-Amino-1-Allyloxymethylethyl)Phenylphosphinic Acid 8c

yield 62%; m.p. 211–212°C; ^{31}P NMR (CD_3OD) δ: 27.3; ^{1}H NMR ($CDCl_3$:CF_3COOD, 5:1) δ: 2.68 (m, 1H), 3.50–3.95 (complex, 6H, $3CH_2$), 5.19 (ddt, 1H, J_{trans} = 16.8, $^2J_{HH}$ = $^4J_{HH}$ = 1.3, =CH_A), 5.21 (ddt, 1H, J_{cis} = 10.7, $^2J_{HH}$ = $^4J_{HH}$ = 1.3, =CH_B), 5.74 (ddt, 1H, ^3J = 6.2, J_{cis} = 10.7, J_{trans} =

16.8, =CH), 7.5–7.8 (m, 5H, Ar); FAB/MS:m/z(%) 256 (MH^+, 100), 141(14), 91(18), 73(14), 56(34). Anal.Calcd for $C_{12}H_{18}NO_3P$:C, 56.46; H, 7.10. Found: C, 56.27; H, 7.18.

(2-Amino-1-Propargyloxymethylethyl)Phenylphosphinic Acid 8d

yield: 34%; m.p. 206–207°C, ^{31}P NMR (CD_3OD) δ: 25.6; ^1H NMR ($CDCl_3$:CF_3COOD, 5:1) δ: 2.43 (t, 1H, ^4J = 2.4, ≡CH), 2.71 (m, 1H), 3.66–3.90 (complex, 4H, $2CH_2$), 4.07 (d, 2H, ^4J = 2.4, CH_2), 7.5–7.8 (m, 5H, Ar); FAB/MS:m/z(%) 254 (MH^+, 100). Anal. Calcd for $C_{12}H_{16}NO_3P$: C, 56.91; H, 6.37. Found: C, 56.75; H, 6.28.

(2-Amino-1-Isobutoxymethylethyl)Phenylphosphinic Acid 8e

yield: 47%; m.p. 232–233°C; ^{31}P NMR (CD_3OD) δ: 26.4; ^1H NMR ($CDCl_3$:CF_3COOD, 5:1) δ: 0.83 (d, 3H, J = 6.7, CH_3), 0.84 (d, 3H, 6.7, CH_3), 1.78 (m, 1H, J = 6.7. CH), 2.70 (m, 1H, CH), 3.09 (dd, 1H, ^3J = 6.7, J_{AB} = 9.2, CH_A), 3.19 (dd, 1H, ^3J = 6.7, J_{AB} = 9.2, CH_B), 3.5–3.8 (complex, 4H, $2CH_2$), 7.5–7.8 (m, 5H, Ar); FAB/MS:m/z(%), 272 (MH^+, 100), 141(9). Anal. Calcd for $C_{13}H_{22}NO_3P$: C, 57.55; H, 8.17. Found: C, 57.72; H, 8.11.

(2-Amino-1-Isopropoxymethylethyl)Phenylphosphinic Acid 8f

yield:56%; m.p. 234–235°C; ^{31}P NMR (CD_3OD) δ: 25.9; ^1H NMR ($CDCl_3$:CF_3COOD, 5:1) δ: 1.11 (d, 3H, J = 6.1, CH_3), 1.12 (d, 3H, J = 6.1, CH_3), 2.75 (m, 1H, CH), 3.50–3.85 (complex, 5H, $2CH_2$, CH), 7.5–7.8 (m, 5H, Ar); FAB/MS: m/z(%), 258 (MH^+, 100), 141(12). Anal. Calcd for $C_{12}H_{20}NO_3P$: C, 56.02; H, 7.83. Found: C, 55.93; H, 7.90.

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