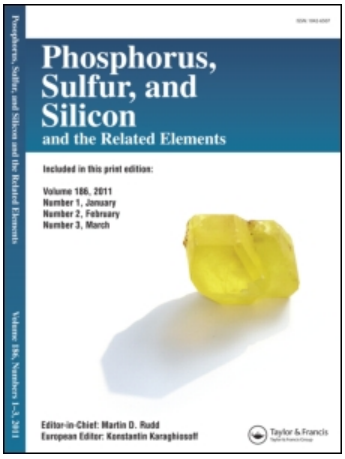

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1-AMINOPHOSPHONIC ACIDS AND ESTERS BEARING HETEROCYCLIC MOIETY. PART 2.[1] PYRIDINE, PYRROLE AND IMIDAZOLE DERIVATIVES

Bogdan Boduszek[a]
[a] Institute of Organic Chemistry, Biochemistry and Biotechnology, Technical University of Wrocław, Wrocław, Poland

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1-AMINOPHOSPHONIC ACIDS AND ESTERS BEARING HETEROCYCLIC MOIETY. PART 2.[1] PYRIDINE, PYRROLE AND IMIDAZOLE DERIVATIVES

BOGDAN BODUSZEK

Institute of Organic Chemistry, Biochemistry and Biotechnology, Technical University of Wrocław, Wybrzeże Wyspianskiego 27, 50-370 Wrocław, Poland

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The benzylic amines (benzylamine, benzhydrylamine and benzyl carbamate) were applied in the synthesis of aminophosphonates derived from pyridine, pyrrole and imidazole. The Schiff bases obtained from corresponding heterocyclic aldehydes and benzylic amines were caused to react with diphenyl phosphonate or dibenzyl phosphonate to form corresponding heterocyclic aminophosphonates in good yields. The N-(benzylamino)-phosphonates were deblocked by catalytic hydrogenolysis. The benzhydryl group from the phosphonates was removed by acidic hydrolysis, and the carbobenzyloxy group from the phosphonates can be easy removed by treatment with a solution of 30% HBr in acetic acid, as well. It was found that during acidic hydrolysis of 2- and 4-pyridylmethylaminophosphonates a rearrangement occurred, combined with a cleavage of C—P bond in the phosphonate molecules and subsequent formation of the corresponding amines.

Key words: Schiff bases, diphenyl 1-(N-benzylamino)-pyridylmethylphosphonates, dibenzyl 1-(N-benzylamino)-2-pyrrylmethylphosphonate, 1-amino-4(5)-imidazolylmethylphosphonic acid, 1-amino-3-pyridylmethylphosphonic acid.

INTRODUCTION

We reported lately, that some benzylic amines, such as benzylamine, benzhydrylamine and benzyl carbamate were effective in the preparation of various heterocyclic aminophosphonates, which were mainly derivatives of furan, thiophene and pyrazole.[1] In continuation of this research, we turned our attention to a further application of above amines for the synthesis of aminophosphonates possessing other heterocyclic systems. In this paper we wish to report a new synthetic route for the preparation of some aminophosphonates derived from heterocycles, having one or two nitrogen atoms, such as pyridine, pyrrole and imidazole.

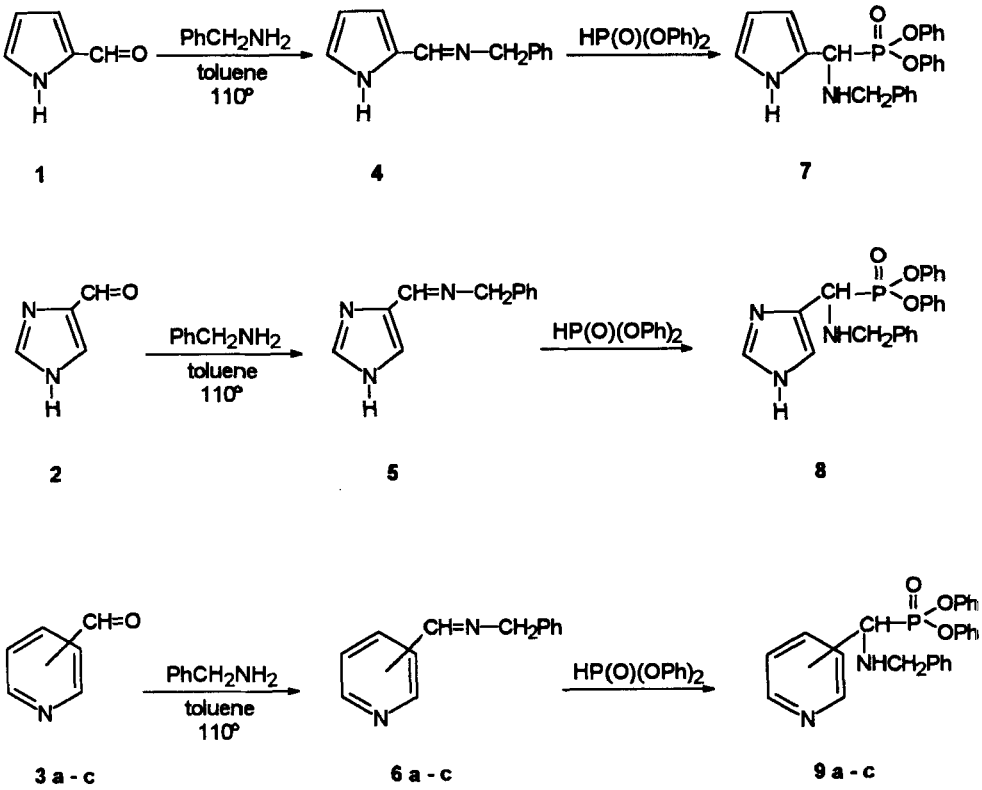
Some pyridine derivatives of the 1-aminomethylphosphonic acid, i.e. 1-(N-alkylamino)-pyridylmethylphosphonates have been previously synthesized in our laboratory.[2] At present, a corrected approach, after reinvestigation of that work,[2] is given. The discovered C—P bond cleavage in the case of hydrolysis of the 2- and 4-pyridyl derivatives, will be also a subject of a separate publication.[8]

The synthesis of pyrrole and imidazole derivatives of 1-aminomethylphosphonic acid is new, not mentioned in a literature according to the best of our knowledge. It is worthly also to underline the presented synthesis of 1-amino-4(5)-imidazolylmethylphosphonic acid; a new agent, which can be used as a potential inhibitor of enzyme histidase.[3]

RESULTS AND DISCUSSION

Benzylamine and heterocyclic aldehydes **1**, **2**, **3a–c** reacted easily (in toluene solution) to form corresponding Schiff bases, **4**, **5**, and **6a–c**. The obtained Schiff bases were used *in situ* for the subsequent reactions with diphenyl phosphonate, in the same conditions as described previously.[1] The products, diphenyl esters **7**, **8**, and **9a–c** have been crystallized out from the reaction mixture, after standing or refrigeration (Scheme 1).

The separation of pyridine derivatives **9a–c** caused some difficulties, due to a good solubility of the phosphonates **9a–c** in the reaction medium. Nevertheless, an addition of a small amount of pentane or hexane to the reaction mixture, and long refrigeration has caused the crystallization of the products **9a–c**. In all cases the obtained diphenyl esters **7**, **8**, **9a–c** were crystalline solids, pure enough for use in the next steps, without an additional purification. The yield of the phosphonates was

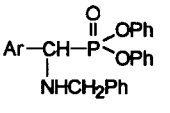
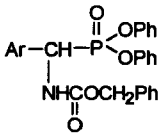
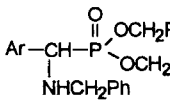


a: 2 - pyridyl
b: 3 - pyridyl
c: 4 - pyridyl

Scheme 1

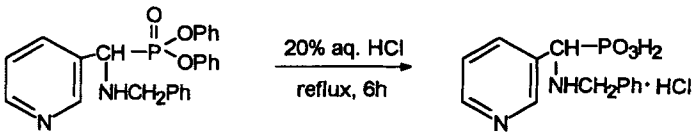
TABLE I

Physical properties of heterocyclic aminophosphonates

No. of Compd.	Ar	Yield in %	mp °C	^{1}H-NMR ($CDCl_3$) ppm	^{31}P-NMR ($CDCl_3$), ppm
					
7	2-pyrryl	71	140-141 (dec)	9.32(s, 1H, NH,pyrr.), 7.63-7.00(m, 15H, arom.), 6.60(m, 1H, arom.), 6.07(m, 2H, arom.), 4.34(d, 1H, CHP, J=20.3Hz), 3.60(dd, 2H, CH_2N) 2.25(bs, 1H, NH).	17.44(s).
8	4(5)-imidazolyl	59	194-197 (dec)	7.83(bs, 2H, arom.), 7.46-6.72(m, 15H, arom.),4.10(d, 1H, CHP, J=16.5 Hz), 3.90(dd, 2H, CH_2N). (in DMSO).	6.29(s)
9a	2-pyridyl	48	93-94	8.67(d,1H, 2-py), 7.70(t,1H,4-py), 7.56(m, 1H, 3-py), 7.32-7.04(m, 16H, arom.),4.58(d, 1H, CHP, J=21.6 Hz), 3.80(dd, 2H, CH_2N), 3.29(bs, 1H,).	16.25 (s).
9b	3-pyridyl	50	133-135	8.71(s, 1H, 2-py), 8.63(d, 1H, 6-py), 7.97(d, 1H, 4-py), 7.42-6.81(m, 16H, arom.), 4.42(d, 1H, CHP, J=19.8 Hz), 3.81(dd, 2H, CH_2N).	16.40 (s).
9c	4-pyridyl	28	61-64	8.68(d, 2H, 2,6-py), 7.59(d, 2H, 3,5-py), 7.39-6.85(m, 15H, arom.), 4.46(d, 1H, CHP, J=21.5 Hz), 3.80(dd, 2H, CH_2N).	15.26 (s).
					
13	4(5)-imidazolyl	67	>70 (dec)	8.50(bs,1H, imidazole), 7.36-6.53(m, 17H, arom.), 5.79(d, 1H, NH), 5.64(dd, 1H, CHP, J=19.6 Hz), 4.90(m, 2H, CH_2O).	15.01 (s)
14b	3-pyridyl	24	150-152	8.67(s, 1H, 2-py), 8.50(m, 1H, 6-py), 7.76(m, 1H, 4-py), 7.29-6.81(m, 16H, arom.), 6.20(d, 1H, NH), 5.54(dd, 1H, CHP, J=22.9 Hz), 5.03(dd, 2H, CH_2O).	13.93 (s)
					
15	2-pyrryl	83	64-65	9.38(bs, 1H, 1-pyrrole), 7.36-7.18(m, 15H, arom.), 6.81(m, 1H, 5-pyrrole), 6.20(m, 2H, 3,4-pyrrole), 5.15-4.62(m, 4H, CH_2O), 4.20(d, 1H, CHP, J=19.4 Hz), 3.76(dd, 2H, CH_2N), 2.80(bs, 1H, NH).	24.68 (s)
18	2-furyl	66	63-64	7.46(bs, 1H, 5-furan), 7.41-7.23(m, 15H, arom.), 6.41(m, 2H, 3,4-furan), 5.23-4.98(m, 4H, CH_2O), 4.21(d, 1H, CHP, J=22.3 Hz), 3.77(dd, 2H, CH_2N), 2.40(bs, 1H, NH).	22.80 (s)

good, usually about 50%. The physical properties of the obtained phosphonates are given in Table I.

Acidic hydrolysis of pyridyl diphenyl phosphonates **9a–c**, by means of 20% aqueous HCl gave the expected product (**10b**) only in the case of 3-pyridyl derivative **9b** (Scheme 2).

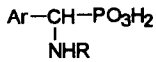


9 b **10 b**

Scheme 2

TABLE II

Physical properties of heterocyclic aminophosphonic acids

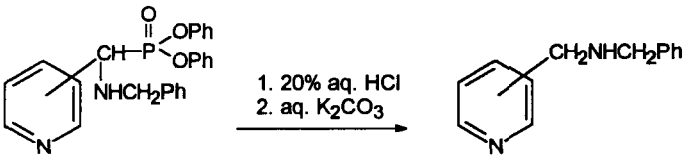


No. of compd.	Ar	R	Yield in %	mp °C	^{1}H-NMR (D_2O) ppm	^{31}P-NMR ppm
10b[a/]	3-pyridyl	Ph	63	235-240 (dec)	8.70(s, 1H, 2-py), 8.64(bs, 1H, 6-py), 8.18(d, 1H, 4-py), 7.61(m, 1H, 5-py), 7.50-7.31(m, 5H, arom.), 4.42(d, 1H, CHP, J=16.5 Hz), 4.19(m, 2H, CH_2N), (in DMSO)	10.16 (s)
11b[a/]	3-pyridyl	H	56	260-265 (dec)	8.81(s, 1H, 2-py), 8.73(d, 1H, 6-py), 8.61(d, 1H, 4-py), 8.04(t, 1H, 5-py), 4.69(d, 1H, CHP, J=16.3 Hz)	8.42 (s)
12[a/]	4(5)-imidazolyl	H	54	262-265 (dec)	8.61(s, 1H, 2-imidazole), 7.50(s, 1H, 5-imidazole), 4.53(d, 1H, CHP, J=16.5 Hz).	7.59 (s)
16	2-pyrryl	H	62	dec.>100	6.78(bs, 1H, 5-pyrrole), 6.21(bs, 1H, 3-pyrrole), 6.09(t, 1H, 4-pyrrole), 4.39(d, 1H, CHP, J=16.1 Hz)	11.20 (s)
19	2-furyl	H	64	212-215 (dec). lit[9]. 225-227 (dec).	7.48(bs, 1H, 5-furan), 6.50(bs, 1H, 3-furan), 6.41(bs, 1H, 4-furan), 4.51(d, 1H, CHP, J=16.6 Hz).	9.38 (s).

[a/] Products isolated as hydrochlorides

The product, 1-(N-benzylamino)-3-pyridylmethylphosphonic acid (**10b**) was isolated in a good yield (Table II). In the case of acidic hydrolysis of 2-pyridyl (**9a**), and 4-pyridyl diphenyl phosphonate (**9c**), new, unexpected products were formed. The above phosphonates were subjected to a C—P cleavage in acidic conditions, and rearranged to the corresponding amines. After work-up, secondary amines **10a** and **10c** were isolated (Scheme 3).

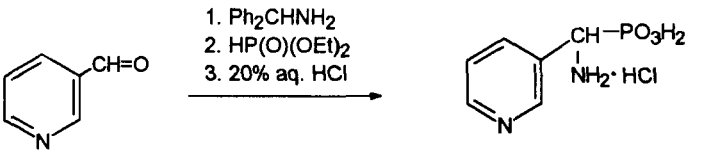
The acidic cleavage of 1-(N-alkylamino)-2-pyridylmethylphosphonates was noticed by us previously,[2] but the given explanation of this phenomenon was not correct.[2] This observed rearrangement of 1-amino-pyridylmethylphosphonates resembles an earlier described phosphonate-phosphate rearrangement, known in the cases of some hydroxyphosphonates,[4-6] and aminophosphine oxides.[7] The more detailed work and proposed mechanism of the cleavage of 2-pyridyl and 4-pyridylmethyl phosphonates in acidic conditions will be given in a separate paper.[8]



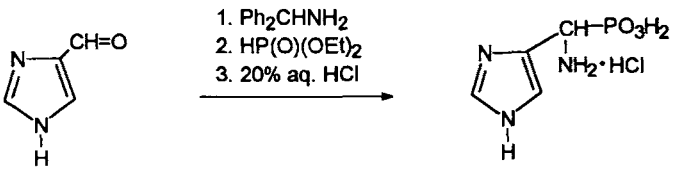
9 a, c **10 a, c**

a: 2 - pyridyl
c: 4 - pyridyl

Scheme 3

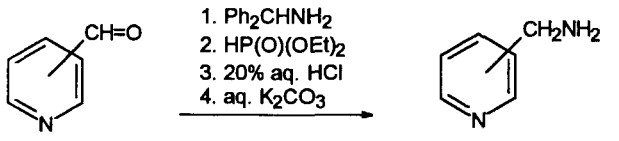


3b **11b**



2 **12**

Scheme 4



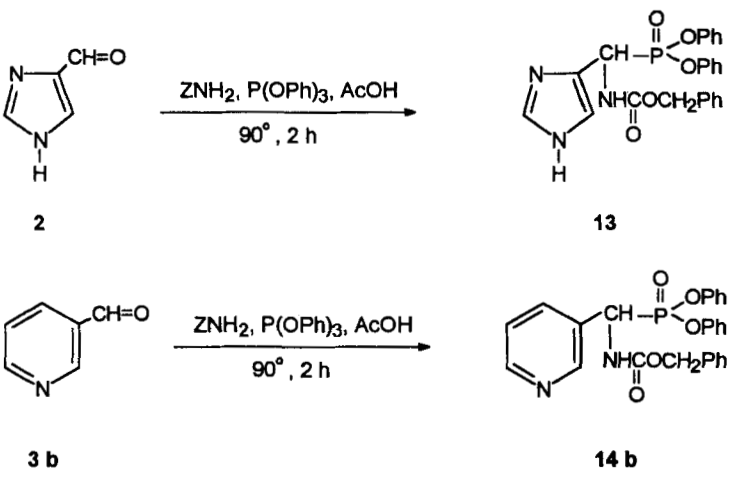
3 a, c **11 a, c**

a: 2 - pyridyl
c: 4 - pyridyl

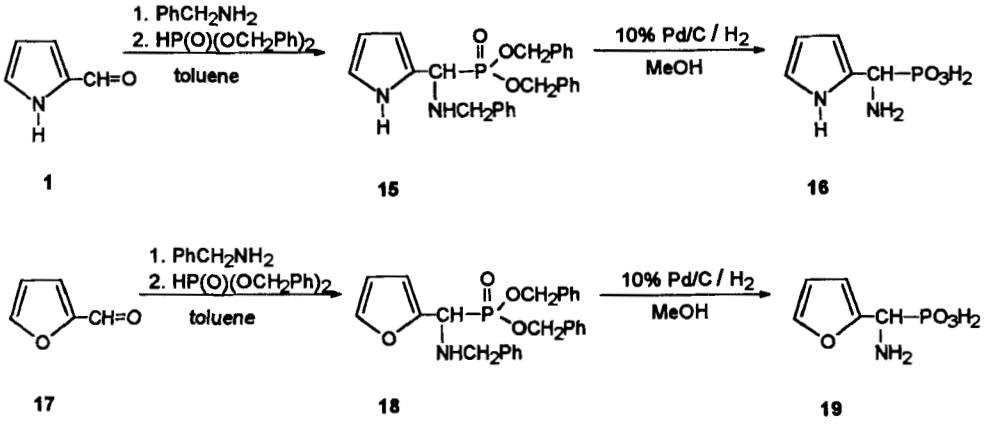
Scheme 5

The aminophosphonic acids with an unsubstituted amino group **11b** and **12** were successfully prepared using benzhydrylamine, heterocyclic aldehydes **2** and **3b**, and diethyl phosphonate in a one-pot synthesis (Scheme 4).

The similar reaction of benzhydrylamine with pyrrole-2-carboxaldehyde (**1**) and diethyl phosphonate failed completely (decomposition took place), and in the case of pyridine-2-carboxaldehyde and pyridine-4-carboxaldehyde, instead of phosphonic acids the amines **11a** and **11c** were isolated, after work-up (Scheme 5). The formation



Scheme 6



Scheme 7

of the amines **11a** and **11c** is caused as a result of the same rearrangement, likewise as it is shown on Scheme 3.

The reaction of benzyl carbamate (Z—NH_2) with heterocyclic aldehydes and triphenyl phosphite in acetic acid solution gave good results in the case of imidazole-4(5)-carboxaldehyde (**2**), and pyridine-3-carboxaldehyde (**3b**), only. The corresponding 1-N-[(benzyloxycarbonyl)amino]-phosphonates **13** and **14b** were isolated in moderate yield (Scheme 6).

No expected phosphonate products were obtained in the reaction of pyrrole-2-carboxaldehyde and pyridine 2- and 4-carboxaldehydes with benzyl carbamate and triphenyl phosphite. Pyrrole-2-carboxaldehyde was decomposed completely at that conditions, and pyridine 2- and 4-carboxaldehydes have not been reacted with above reagents, yet.

The addition of dibenzyl phosphonate to Schiff bases obtained from aldehydes **1** and **17** allowed to obtain the corresponding dibenzyl esters **15** and **18**. The addition

reaction was slower than in the case of diphenyl phosphonate, and it usually required higher temperature. The obtained dibenzyl esters **15** and **18** were utilized to synthesize 1-amino-2-pyrrylmethylphosphonic acid (**16**) and 1-amino-2-furylmethylphosphonic acid (**19**), which is not easy available,[9] The acids **16** and **19** were obtained by hydrogenolysis of the dibenzyl esters in standard conditions, using palladium on carbon, as a catalyst,[1] The amount of used gaseous hydrogen should be carefully monitored in order to avoid a hydrogenation of the pyrrole or furan ring (Scheme 7).

The pyrrole aminophosphonic acid **16** is unstable and cannot be kept for long time at room temperature. In the contrary, the furan aminophosphonic acid **19** is stable, and can be kept for long time, without any decomposition.

The physical data of the synthesized aminophosphonic acids are given in Table II. In conclusion, the benzylic amines can be used in the preparation of most heterocyclic 1-aminophosphonic acids and their esters. The application of the particular amine in the synthesis of heterocyclic aminophosphonates depends on the chemical stability of used heterocyclic aldehydes. The aldehydes with unstable heterocyclic rings as furan or pyrrole can be transformed to corresponding phosphonates via Schiff base formed from benzylamine and aldehyde, and subsequent reaction with diphenyl phosphonate. The benzyl group can be easy removed in a catalytic hydrogenolysis process. The aldehydes with more stable heterocyclic rings, (for example: thiophene, imidazole and pyridine) can react with all used benzylic amines, to form corresponding Schiff bases, which can be transformed to the corresponding phosphonates in the usual way. It has been found that 2- and 4-pyridylmethyl-(amino)-phosphonates are subjected to a rearrangement in acidic conditions, with C—P bond cleavage and formation of the corresponding amines.

EXPERIMENTAL

NMR spectra were recorded on a Bruker Avance TM DRX 300 MHz spectrometer in $CDCl_3$, DMSO or D_2O solutions, using 300.13 MHz for ^{1}H-NMR spectra, and 121.51 MHz for ^{31}P-NMR spectra, respectively. GC.-MS analyses were carried out with a Hewlett Packard HP 5971A apparatus, equipped with HP-1, 25 m capillary column. Melting points were measured on Digital Melting Point Apparatus Electrothermal 9200, and are uncorrected. Elemental analyses were performed in the Laboratory of Instrumental Analysis in the Institute. TLC was done on silica gel plates Merck (Art. 5548, HP-TLC Alufolien Kiesegel 60F 254) All commercially available reagents were used as received from the suppliers. The imidazolyl-4(5)-carboxaldehyde was prepared from 4(5)-hydroxymethylimidazole,[10] by oxidation with manganese dioxide in dioxane.[11]

Preparation of Diphenyl N-Benzylaminophosphonates **7**, **8**, *and* **9a–c**

A solution of aldehyde **1**, **2**, or **3a–c** (20 mmol) and benzylamine (2.15 g, 20 mmol) in toluene (50 mL) was heated at 110°C (reflux) for 15 min. (in the case of pyridine aldehydes the mixture was refluxed for 1 hr), and cooled. The separated drops of water were removed by shaking the solution with anh. sodium sulfate. The mixture was filtered, and to such obtained solution of imine **4**, **5** or **6a–c** neat diphenyl phosphonate (4.7 g, 20 mmol) was added. The mixture was heated to 60°C and left overnight at r.t. The diphenyl phosphonates **7** and **8** crystallized out from the reaction mixture, and were collected by filtration.

In the case of pyridine phosphonates the crystallization of the products **9a–c** was accelerated by an addition of hexane (10–15 mL) to the reaction mixture and long refrigeration (2–3 days).

The physical properties of the obtained diphenyl phosphonates are given in Table I.

Preparation of Diphenyl N-(Benzyloxycarbonyl)-aminophosphonates **13** *and* **14b**

A mixture of benzyl carbamate (1.51 g, 10 mmol), aldehyde **2** or **3b** (10 mmol), triphenyl phosphite

(3.2 g, 10 mmol) and acetic acid (6 mL, 100 mmol) was heated at 90°C for 1.5 hr. Then the volatile materials were removed by evaporation *in vacuo* and the resulting oil was dissolved in methanol (15 mL), then a small amount of water added (5–8 mL), and the solution refrigerated overnight. The product **14b** separated out from the solution and was collected by filtration. The product **13** crystallized slowly, and long time of refrigeration was required to obtain the crystals (usually several days).

The physical data of the products **13** and **14b** are given in Table I.

Preparation of Dibenzyl N-Benzylaminophosphonates **15** *and* **18**

A solution of aldehyde **1** or **17** (10 mmol) and benzylamine (1.1 g, 10 mmol) in toluene (25 mL) was refluxed for 10–15 min and cooled. Anhydrous sodium sulfate (5 g) was added to the mixture and stirred for 10 min. Then the mixture was filtered and neat dibenzyl phosphonate (2.6 g, 10 mmol) was added. The mixture was allowed to stand for 24 hr at room temperature, and the solvent was evaporated *in vacuo*. The resulting oil was heated at 80°C under argon for 30 min (for **15**), and for 3 hr (for **18**), and cooled. The oily product was dissolved in toluene (5–10 mL), the solution was mixed with an equal amount of hexane (5–10 mL) and refrigerated. The separated crystals of the product were collected by filtration and recrystallized from a mixture of toluene and hexane.

The physical data of the products **15** and **18** are given in Table I.

Hydrolysis of Diphenyl Pyridylmethyl(N-benzylamino)phosphonates **9a–c**

Diphenyl ester **9a–c** (4.3 g, 10 mmol) was mixed with 20% aq. hydrochloric acid. The mixture was refluxed for 6 hr, cooled and extracted with methylene chloride (50 mL), in order to remove the formed phenol. The aqueous layer was evaporated *in vacuo* to dryness. In the case of **9b**, the obtained crude product **10b** was dissolved in water (50 mL) and the solution was purified by heating with norite, and filtered. After evaporation of water, the aminophosphonic acid (**10b**) was obtained, which was additionally purified by recrystallization from aqueous ethanol. The physical data of the **10b** are given in Table II.

In the cases of **9a** and **9c** the resulting products (after evaporation) were treated with excess of aqueous solution of potassium carbonate and extracted with chloroform (2 × 50 mL). The combined extracts were dried (anh. K_2CO_3), filtered and evaporated to give the products, which were identified as the secondary amines **10a** and **10c**.

2-(Benzylaminomethyl)pyridine **10a**:
Oil. Yield: 74%
^{1}H-NMR ($CDCl_3$): δ = 8.57 (d, 1H, 6-py), 7.65 (m, 1H, 4-py), 7.40–7.16 (m, 7H, 3,5-py, phenyl), 3.96 (s, 2H, CH_2-2-py), 3.88 (s, 2H, CH—Ph), 2.83 (bs, 1H, NH).
G.C.-M.S.: m/e(%): 197 (M-1) (1.5), 121 (3.1), 106 (45), 93 (100), 92 (34.8), 91 (78.6).

4-(Benzylaminomethyl)pyridine **10c**:
Oil. Yield: 38%.
^{1}H-NMR ($CDCl_3$): δ = 8.54 (dd, 2H, 2,6-py), 7.38–7.26 (m, 7H, 3,5-py, phenyl), 3.85 (s, 2H, CH_2-4-py), 3.82 (s, 2H, CH_2—Ph), 2.24 (bs, 1H, NH).
G.C.-M.S.: m/e (%): 198 (M, 28.5), 197 (M-1, 24.3), 121 (14.3), 107 (46.3), 92 (58.3), 91 (100).

The amines **10a** and **10c** were also characterized as oxalate salts. The oxalate salts were obtained by treatment of the amine with oxalic acid in acetone solution, according to the method published previously.[1]

Oxalate of **10a**:
Yield: 92%. mp = 182.5–184°C (dec.)
^{1}H-NMR (D_2O): δ = 8.45 (d, 1H, 6-py), 8.03 (t, 1H, 4-py), 7.54 (m, 2H, 3,5-py), 7.20 (bs, 5H, Ph), 4.29 (s, 2H, CH_2-2-py), 4.12 (s, 2H, CH_2—Ph).
Elemental Anal. for **10a**.2·$(COOH)_2$·: Calc. C: 53.96, H: 4.80, N: 7.40%. Found: C: 53.58, H: 4.93, N: 7.02%.
M.Wt. = 378.33

Oxalate of **10c**:
Yield: 98%. mp = 214–216°C (dec.)
^{1}H-NMR (D_2O): δ = 8.56 (d, 2H, 2,6-py), 7.81 (d, 2H, 3,5-py), 7.22 (bs, 5H, Ph), 4.34 (s, 2H, CH_2-4-py), 4.14 (s, 2H, CH_2—Ph).
Elemental Anal. for **10c**.2·$(COOH)_2$·: Calc. C: 53.96, H: 4.80, N: 7.40%. Found: C: 53.38, H: 5.59, N: 7.84%
M.Wt. = 378.33

Preparation of Aminophosphonic Acids **11b** *and* **12**

A solution of aldehyde **2** or **3b** (10 mmol) and benzhydrylamine (1.83 g, 10 mmol) in toluene (60 mL) was refluxed for 30 min and filtered through a filter paper, then neat diethyl phosphonate (1.4 g, 10 mmol) was added. The mixture was refluxed for 30 min (for imidazole derivative), and for 3 hr (for pyridine derivative). The mixture was evaporated *in vacuo*, and the residue was dissolved in 20% aq. HCl (50 mL), and refluxed for 6 hr, cooled, and the mixture extracted with toluene (50 mL). The extract was discarded, and the aqueous layer evaporated *in vacuo*, to obtain crude product. The crude product was purified by heating with norite in a water solution. After filtration and evaporation of water the obtained product **11b** or **12** was recrystallized from aqueous 80% methanol or ethanol.

The physical data of the acids **11b** and **12** are given in Table II.

*Preparation of 2-(Aminomethyl)pyridine (***11a***) and 4-(Aminomethyl)pyridine (***11c***)*

A solution of pyridine aldehyde **3a** or **3c** (5.4 g, 5 mmol) and benzhydrylamine (9.2 g, 50 mmol) in toluene (100 mL) was refluxed for 1 hr and cooled. The separated drops of water were removed by adding anh. sodium sulfate (10 g) and filtration. Neat diethyl phosphonate (7.0 g, 50 mmol) was added to the filtrate and the solution was refluxed for 2 hr, then evaporated to dryness, and the residue was treated with aq. 20% HCl (150 mL) and refluxed again for 6 hr, cooled, and the mixture extracted with toluene (100 mL). The toluene extract was discarded, and the aqueous layer evaporated *in vacuo* to give a brown semi-solid. The obtained product was treated with excess of aq. potassium carbonate to make the solution alkaline, and extracted with chloroform (100 mL). The chloroform extract was dried (anh. K_2CO_3), filtered and evaporated to give the product **11a** or **11c** as a pale yellow oil.

2-(Aminomethyl)pyridine **11a**:
Oil.[14] Yield: 72%. bp. = 93–95°/16 mm Hg. Lit.[12] bp. = 91°/15 mm Hg.
^{1}H-NMR ($CDCl_3$): δ = 8.43 (dd, 1H, 6-py), 7.52 (t, 1H, 4-py), 7.16 (d, 1H, 3-py), 7.03 (m, 1H, 5-py), 3.86 (s, 2H, CH_2N), 2.25 (bs, 2H, NH_2).
G.C.-M.S.: m/e (%): 108 (M, 60.59), 107 (M-1, 45.06), 80 (100), 79 (61.47).
Oxalate of **11a**: mp = 162–164°C. Lit.[12] mp = 167°C.

4-(Aminomethyl)pyridine **11c**:
Oil.[14] Yield: 61%. bp. = 109–111°/16 mm Hg. Lit[13] bp = 112–113°/18 mm Hg.
^{1}H-NMR ($CDCl_3$): δ 8.53 (d, 2H, 2,6-py), 7.26 (d, 2H, 3,5-py), 3.90 (s, 2H, CH_2N), 2.51 (bs, 2H, NH_2).
G.C.-M.S.: m/e (%): 108 (M, 13.43), 107 (M-1, 17.91), 81 (5.88), 80 (100), 79 (27.39).
Oxalate of **11c**: mp = 174–5°C.

Preparation of Aminophosphonic Acids **16** *and* **19***; Hydrogenolysis of Dibenzyl Esters* **15** *and* **18**

A solution of dibenzyl ester **15** or **18** (2.5 mmol) in methanol (50 mL) and water (2 mL) was prepared. Then the good quality catalyst (10% Pd—C) (0.5 g) was added and the mixture was hydrogenated with monitoring of the consumption of hydrogen. When the theoretical amount of hydrogen was consumed (180 mL, ≅7.5 mmol) the hydrogenolysis was interrupted, and the catalyst filtered off, then the solvent evaporated to give crude product **16** or **19** as yellowish semi-solid. The 1-amino-2-furylmethylphosphonic acid (**19**) was purified by crystallization from 90% ethanol, to give a white, stable solid. The 1-amino-2-pyrrylmethylphosphonic acid (**16**) can be also purified from aqueous ethanol, but some decomposition takes place. It was found that the acid **16** is unstable and can not be stored for long time.

The physical data of the acids **16** and **19** are given in Table II.

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