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Application of Bromotrimethylsilane and Trialkyl Phosphites for Convenient and Effective Synthesis of Aminophosphonic Acids and Corresponding Monoalkyl and Dialkyl Esters

by B. Boduszek

Institute of Organic Chemistry, Biochemistry and Biotechnology,
Wrocław University of Technology, 50-370 Wrocław, Poland
E-mail: boduszek@kchf.ch.pwr.wroc.pl

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Application of bromotrimethylsilane (Br-TMS) in a mixture with trialkyl phosphite for synthesis of various aminophosphonic acids and esters was investigated. It was found, that appropriate mixtures of Br-TMS and trimethyl phosphite or triethyl phosphite were effective reagents for phosphorylation of various aldimines, obtained from aromatic and heteroaromatic aldehydes. Products of these reactions were corresponding aminophosphonic acids, or corresponding dialkyl or monoalkyl esters, respectively.

Key words*:* trimethyl phosphite, bromotrimethylsilane, silylation, aminophosphonic acids, monomethyl esters of aminophosphonic acids, dimethyl esters of aminophosphonic acids

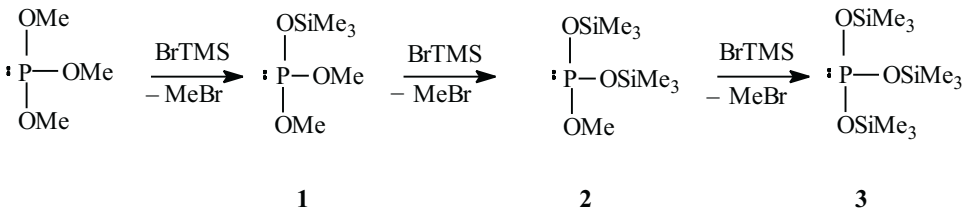
In the last three decades a considerable effort has been devoted to the synthesis of a variety of α-aminophosphonic acids, for reason of their promising biological activity related to a structural analogy with natural α-aminocarboxylic acids. One of the standard synthesis of α-aminophosphonic acids involves thermal addition of a trivalent phosphorus species to an imine, which itself is generated from the primary amine and aldehyde [1]. Over the last twenty years a new kind of the silicon-phosphorus based reagents for synthetic work on organophosphorus compounds has been developed [2–8]. Application of these reagents allowed to facilitate some synthetic routes, leading to many organophosphorus compounds. These reagents were especially significant in the synthetic procedures developed for α-aminophosphonic esters [5]. Di- and trimethylsilyl esters of phosphorous acid react with ketones [2] and aldimines under mild conditions [3,5,13]. When a completely silylated ester of H_3PO_3 is used for a reaction with an aldimine, a product, being the silylated ester of aminophosphonic acid, is obtained. Such silylated product can be easily transformed by subsequent hydrolysis or solvolysis to the final aminophosphonic acid [3,14]. However, an application of the silyl esters of phosphorous acid as definite individual compounds is rather limited, because of their instability and susceptibility for hydrolysis in reaction media. Usually, the needed silylated esters are prepared *in situ* from the commercially available chlorotrimethylsilane and appropriate dialkyl phosphites in the presence of a base [5]. The use of a basic agent for generation of the silylated esters is not an ad-

vantage synthetic method, due to the fact that the presence of a base causes difficulties in isolation of the finally formed phosphonic acids from the reaction mixture. Therefore, this method is used first of all for preparation of some dialkyl phosphonic esters [5].

We have found recently, that the silylated esters of phosphorous acid can be easily obtained from bromotrimethylsilane (Br-TMS) and trimethylphosphite, or other trialkyl phosphites without an addition of a basic agent. As it was reported earlier, the bromotrimethylsilane reacts easily with diethyl phosphite [6] or with other alkyl phosphites [7] in room temperature by a way, which was already shown for the reaction with iodotrimethylsilane [8]. This reaction was considerably fast even at a low temperature, in contrary to the reaction with chlorotrimethylsilane (frequently used as a silylating agent), which requires usually a high temperature to carry out the silylation reaction [2]. According to the ^{31}P NMR studies [7,8], iodotrimethyl- or bromotrimethylsilane react with $P(OMe)_3$ considerably fast in an inert solvent. Therefore, it seems that an addition of the Br-TMS to $P(OMe)_3$ or to the other trialkyl phosphites should result in easy *in situ* preparation of the corresponding monosilylated, disilylated or trisilylated esters of the H_3PO_3. This observation led us to elaboration of the procedure suitable for convenient and efficient preparation of various aminophosphonic acids, and corresponding mono- and dialkyl esters.

RESULTS AND DISCUSSION

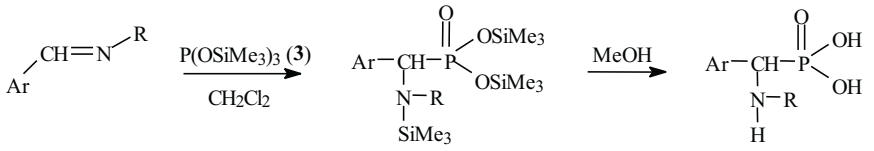
When bromotrimethylsilane was gradually added to trimethyl phosphite (in an equimolar proportion) in dry methylene chloride, the mono(trimethylsilyl)dimethyl phosphite (**1**) was preferably formed. Addition of the next equimolar amount of the Br-TMS to this solution produced mainly the di(trimethylsilyl)methyl phosphite (**2**) and when three equivalents of the Br-TMS were added, the tris(trimethylsilyl) phosphite (**3**) was finally obtained (Scheme 1).



1 **2** **3**

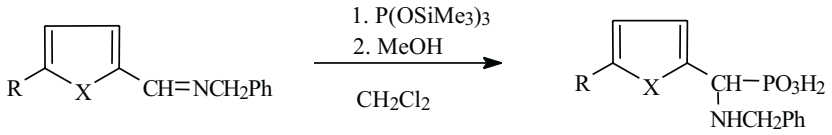
Scheme 1. Silylation of $P(OMe)_3$ by Br-TMS in methylene chloride solution.

Formation of the silylated esters **1–3** may be checked by ^{31}P NMR monitoring of the reaction, as it was reported [8]. Mechanism of the similar silylation process was described in [8], essentially for silylation of the trimethyl phosphite with iodotrimethylsilane. In the $P(OMe)_3$ – BrTMS mixtures obtained, there were also present some other minor products, as for example the $(Me_3SiO)_2P(O)H$: –12.6 (Lit. [7] –13.8) ppm). This silylated product was probably formed by hydrolysis of the tris-silylated phosphite ester (**3**) in the presence of some moisture, still existing in the solvent. Methyl bromide, which was obviously formed in these mixtures, could be easily detected by ^1H NMR (δ = 2.57 ppm; the singlet for CH_3 group). The triethyl phosphite reacted with Br-TMS similarly, but significantly slower. Such obtained silylated esters (**1–3**) were examined as the effective phosphorylating agents of many aldimines, obtained from aromatic and heteroaromatic aldehydes. Thus, when to a mixture of $P(OMe)_3$ and Br-TMS in the molar ratio 1:3 [which really contained the tris(trimethylsilyl) phosphite **3**] the aldimine **4** was added, the addition of the silylated phosphite to the double bond of imine occurred and the corresponding silylated ester of aminophosphonic acid was formed (**5**). When the silylated ester **5** was then treated with methanol, a final product, *i.e*. the aminophosphonic acid **6** ,was formed and isolated from the reaction mixture, usually in a pure state (Scheme 2).



4 a-g **5 a-g** **6 a-g**

a: Ar = Ph, R = Bu, **b:** Ar = Ph, R = CH_2Ph; **c:** Ar = 2-pyridyl, R = Bu; **d:** Ar = 2-pyridyl, R = CH_2Ph
e: Ar = 3-pyridyl, R = CH_2Ph; **f:** Ar = 4-pyridyl, R = Bu; **g:** Ar = 4-pyridyl, R = CH_2Ph.



4h,i **6h,i**

h: R = NO_2, X = O
i: R = NO_2, X = S

Scheme 2. Phosphorylation of aldimines by tris(trimethylsilyl) phosphite.

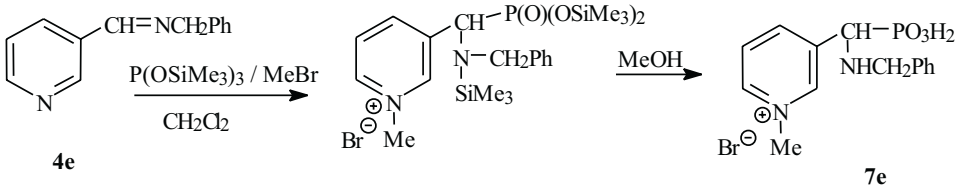
The utility of the method used here has been positively verified by the first synthesis of 5-nitrofuryl (**6h**) and 5-nitrothienyl (**6i**) derivatives of aminomethylphosphonic acid. These compounds (**6h–i**) are not available by classical methods of synthesis of aminophosphonates, presumably due to reactivity of their heterocyclic systems, increased by the presence of the nitro groups. Analytical data of the obtained products **6a–i** are summarized in Table 1.

Table 1. Analytical data of the aminophosphonic acids **6a–i**.

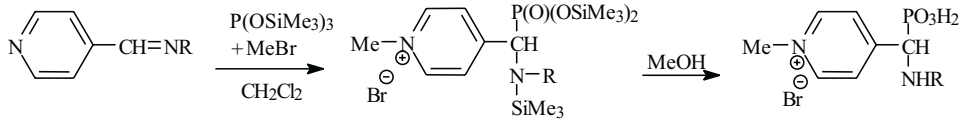
Compd.	Yield %	M.p. °C	^{1}H NMR, δ, ppm	^{31}P NMR, δ, ppm
6a	71[a]	243–4 lit. [12] 240–3	7.51 (bs, 5H, Ph), 4.60 (d, 1H, CH-P, J = 17.1 Hz), 2.97 (m, 2H, NCH_2), 1.62 (m, 2H, CH_2), 1.25 (m, 2H, CH_2), 0.80 (t, 3H, CH_3, J = 7.2 Hz).	12.289 (s)
6b	73 (68)[a]	235–7 lit. [1b] 236–7	7.40–7.19 (m, 10H, arom.), 4.30(d, 1H, CH-P, J = 16.8 Hz), 4.09 (dd, 2H, CH_2N), J = 13.5 Hz).	12.069 (s)
6c	65 (53)[a]	243–5 lit. [9,10] 244–6	8.52 (d, 1H, py-6, J = 4.9 Hz), 7.84 (t, 1H, py-4, J = 7.8 Hz), 7.48 (d, 1H, py-3, J = 8.0 Hz), 7.39 (t, 1H, py-5, J = 5.0 Hz), 4.53 (d, 1H, CH-P, J = 16.3 Hz), 3.00 (m, 2H, CH_2N), 1.60 (m, 2H, CH_2), 1.26 (m, 2H, CH_2), 0.78 (t, 3H, CH_3, J = 7.3 Hz.)	6.634 (s)
6d	78 (70)[a]	246–8 (dec.) lit [10] 244–7	8.50 (d, 1H, J =5.7 Hz), 8.37 (t, 1H, 4.925(s) J = 8.0 Hz), 7.93–7.81 (m, 2H, pyr-3 and pyr-5), 7.18 (m, 5H, Ph), 4.78 (d, 1H, CH-P, J = 17.8 Hz), 4.30 (dd, 2H, CH_2N, J = 13.3 Hz).	4.925 (s)
6e	59[a]	239–40 lit. [9] 235–40 (**6e**·HCl)	8.68 (m, 2H, py-2 and py-6), 8.55(d, 1H, J = 8.0 Hz, py-4), 8.00 (t, 1H, J = 6.3Hz, py-5) 7.28 (m, 5H, Ph), 4.82 (d, 1H, CH-P, J = 17.7Hz), 4.41–4.28 (dd, 2H, NCH_2Ph, J = 13.2 Hz).	7.141 (s)
6f	55	185–7 (dec.) lit. [10] 182–5	8.66 (m, 2H, py-2, py-6), 7.85 (m, 2H, py-3, py-5), 4.72 (d, 1H, CH-P, J = 16.5 Hz) 3.0 (m, 2H, CH_2N), 1.58, 1.23 (m, CH_2CH_2), 0.78 (t, 3H, CH_3, J = 7.1 Hz).	6.921 (s)
6g	74	208–210 (dec.) lit [10] 270–9	8.80 (d, 2H, J = 6.7 Hz, py-2, py-6), 8.02 (d, 2H, J = 5.4 Hz, py-3, py-5) 7.40 (m, 5H, Ph), 4.90 (d, 1H, CH-P, J = 17.8 Hz), 4.50 (dd, 2H, NCH_2Ph, J = 13.2 Hz).	6.255 (s)
6h	81[a]	dec. > 155 (tars formed)	7.57 (bs, 1H, furyl-4), 7.50 (m, 5H, Ph) 7.04 (bs, 1H, furyl-3), 5.05 (d, 1H, CH-P, J = 19.8 Hz), 4.49 (bs, 2H, NCH_2Ph).	5.684 (s)
6i	66[a]	dec. > 165 (tars formed)	8.00 (bs, 1H, thienyl-4), 7.42 (m, 6H, Ph and thienyl-3), 4.97 (d, 1H, CH-P, J = 18.6 Hz), 4.36 (m, 2H, NCH_2Ph).	6.939 (s)

[a]Yield of product obtained for the mixture: [$P(OEt)_3$ + 3 Me_3SiBr], used as a phosphorylating agent.

Mechanism of addition of the *O*-silylated esters of H_3PO_3 to some imines was already described in [5]. There is no doubt, that a similar mechanism should be also important in the reactions described here. It was found, that in the case of some pyridyl aldimines (**4e**, **4f**, **4g**) the main isolated products were bromides of the quarternary *N*-methyl derivatives of phosphonic acids (**7e**, **7f**, **7g**).

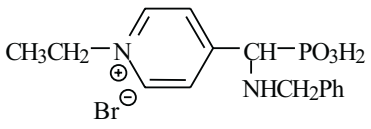


4e **7e**



4f,g **7f,g**

f: R = Bu; **g:** R = CH_2Ph



7g'

Scheme 3. Formation of quarternary *N*-alkyl derivatives of some pyridyl-aminomethylphosphonic acids.

Formation of these products was obviously caused by a subsequent *N*-methylation of the pyridine nitrogens by methyl bromide, which was still present in a reaction mixture (Scheme 3). However, the corresponding 2-pyridyl aldimines (**4c,d**) did not form such methylated products in these reactions. Supposedly, methylation of the **4c,d** did not occur, because of a lower basicity of the heterocyclic nitrogens in 2-pyridyl derivatives, in comparison with the higher basicity of parent 3- or 4-pyridyl ones. Data of the *N*-alkylated aminophosphonic acids are given in Table 2. The *N*-methylation of the pyridyl products can be avoided by removing methyl bromide formed, from the reaction mixture prior to addition of the pyridyl aldimine. It can be simply achieved by careful evaporation of the MeBr from a mixture composed with the silylated phosphorous acid esters. Application of a mixture of triethyl phosphite [$P(OEt)_3$] and Br-TMS for the phosphorylation reactions did not cause the expected *N*-ethylation of

3-pyridyl aldimine **4e**. In this case, a non-ethylated product, *i.e*. 3-pyridyl aminophosphonic acid **6e,** was obtained. However, the corresponding *N*-ethylated product was either found for the reaction with 4-pyridyl aldimine **4g**; in this case the *N*-ethyl phosphonic acid **7g′** (Table 2, Scheme 3) was obtained. Application of a mixture of $P(OMe)_3$ [or $P(OEt)_3$] and two equivalents of Br-TMS for the reaction with some aldimines **(4b**, **4d**) led mainly to the partially silylated phosphonate diesters, which could be hydrolyzed to the expected monoalkyl esters (**8b,d)** by treatment with methanol, or ethanol (Scheme 4).

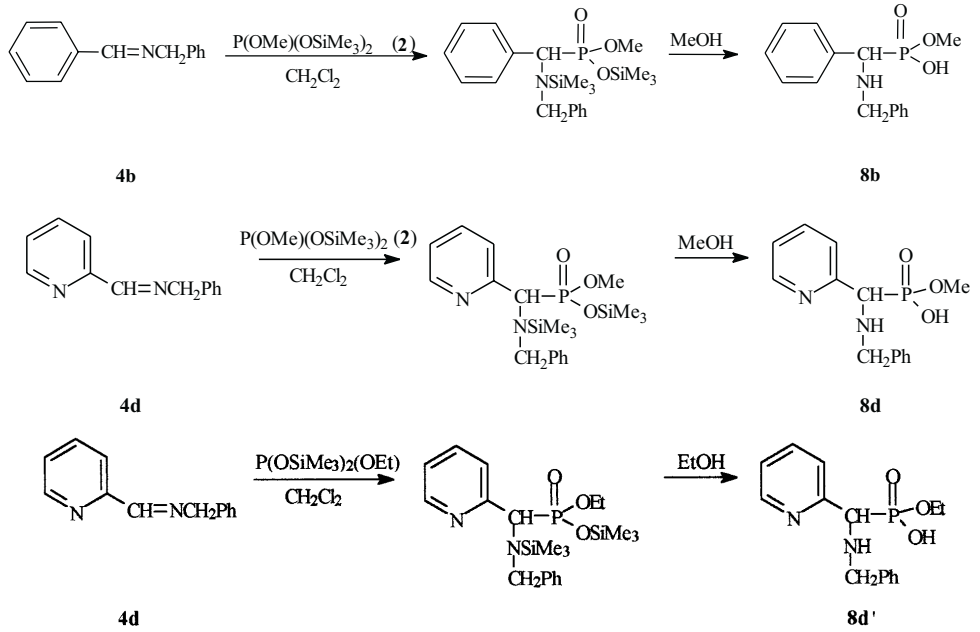
Table 2. *N*-methyl deriv.: **7e,f,g,** and *N*-ethyl deriv.: **7g′** of pyridyl aminophosphonic acids.

Compd.	Yield %	M.p. °C	^{1}H NMR, δ, ppm	^{31}P NMR, δ, ppm
7e	62	199–201	8.81 (m, 2H, py-2 and py-6), 8.61 (d, 1H, py-4, J = 8.1 Hz), 8.09 (t, 1H, py-5, J = 6.3 Hz), 7.46–7.41 (m, 5H, Ph), 4.65 (d, 1H, CH-P, J = 16.7 Hz), 4.51–4.39 (m, s, 5H, NCH_2, CH_3-N^+).	7.238 (s)
7f	42	186–92 (dec.)	8.80 (d, 2H, py-2 and py-6 J = 6.6 Hz), 8.06 (d, 2H, py-3 and py-5, J = 4.9 Hz), 4.76 (d, 1H CH-P, J = 16.8 Hz), 4.34 (s, 3H, CH_3-N^+), 3.10 (m, 2H, NCH_2), 1.65 (m, 2H, CH_2), 1.28 (m, 2H, CH_2), 0.81 (t, 3H, CH_3, J = 7.2 Hz).	6.058 (s)
7g	71	183–5 (dec.)	8.69 (d, 2H, py-2 and py-6, J = 6.45 Hz), 7.92 (d, 2H, py-3, and py-5, J = 6.1 Hz), 7.34 (m, 5H, Ph), 4.69 (d, 1H, CH-P, J = 18.0 Hz), 4.44–4.30 (m, s, 5H, NCH_2, CH_3N^+).	6.086 (s)
7g′	46[a]	212–3	8.71 (d, 2H, py-2 and py-6, J = 6.1 Hz), 7.97 (d, 2H, py-3 and py-5, J = 5.7 Hz), 7.37 (m, 5H, Ph), 4.74 (d, 1H, CH-P, J = 16.6 Hz), 4.38 (m, 2H, NCH_2Ph), 3.84 (m, 2H, N^+CH_2), 1.15 (t, 3H, J = 7.1 Hz), CH_2**CH_3**).	8.135 (s)

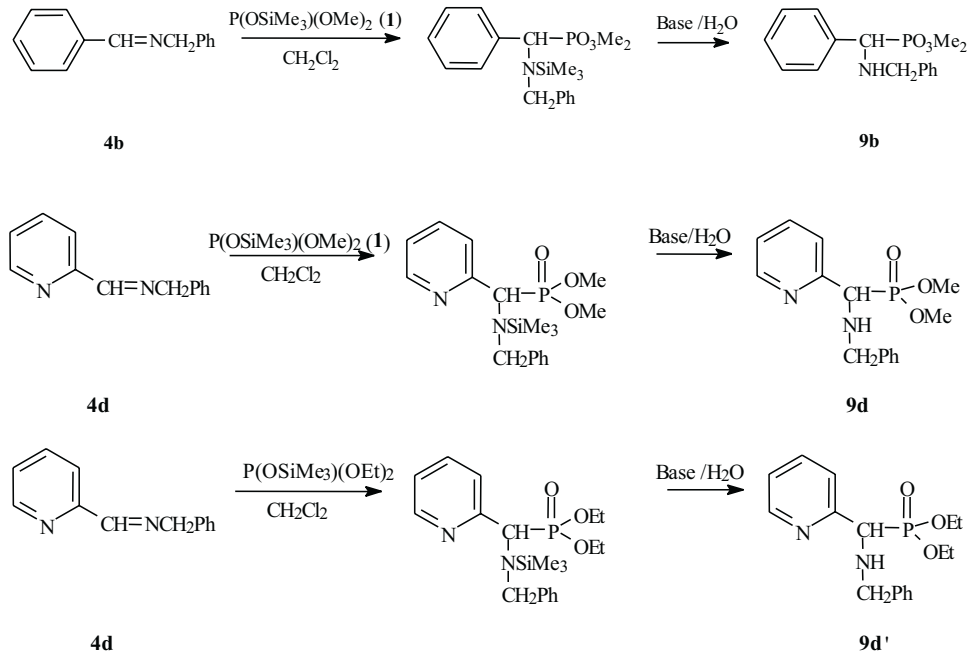
[a]Yield of product obtained for the mixture: [$P(OEt)_3$ + $3Me_3SiBr$], used as a phosphorylating agent.

In turn, an equimolar mixture of Br-TMS and trimethyl phosphite or triethyl phosphite reacted with the aldimines to form finally the phosphonic diesters (**9**), which were obtained by hydrolysis of the silylated intermediates with aqueous sodium bicarbonate (Scheme 5). Analytical data for the synthesized products **8b,d,d′** and **9b,d,d′** are given in Table 3.

In summary, the mixture of Br-TMS and trialkyl phosphite is a very effective reagent for phosphorylation of various aldimines. The use of these reagents causes a substantial improvement in the preparation of a variety of aminophosphonic derivatives. The presented method allows to obtain aminophosphonic acids, monoesters and diesters as well, by a convenient and simple way. This method is exceptionally useful for preparation of monoalkyl esters of aminophosphonic acids, which are not easily available compounds.



Scheme 4. Formation of monoalkyl esters of aminophosphonic acids.



Scheme 5. Formation of dialkyl esters of aminophosphonic acids.

Table 3. Analytical data of monoalkyl esters **8b,d,d′** and dialkyl esters **9b,d,d′**.

Compd.	Yield %	M.p. °C	^{1}H NMR, δ, ppm	^{31}P NMR, δ, ppm
8b	48	191–3 (dec.)	7.66–7.39 (m, 10H, Ph), 4.57 (d, 1H, CH-P, J = 17.1 Hz), 4.35 and 4.18 (dd, 2H, NCH_2), J = 13.2 Hz), 3.71 (d, 3H, P-OCH_3), J = 10.8 Hz).	13.766 (s)
8d	59	213–4	8.55 (d, 1H, py-6, J = 4.5 Hz), 7.83(t, 1H, py-4, J = 7.8 Hz), 7.42–7.29 (m, 7H, py-3 and py-5, Ph), 4.48 (d, 1H, CH-P, J = 17.5 Hz), 4.27–4.13 (dd, 2H, NCH_2, J = 13.2 Hz), 3.37 (d, 3H, P-OCH_3, J = 10.7 Hz).	11.731 (s)
8d′	51	203–5 lit. [11] 202–4	8.43 (d, 1H, py-6, J = 4.1 Hz), 7.71 (t, 1H, py-4, J = 7.8 Hz), 7.25 (m, 7H, Ph, py-3,5), 4.30 (d, 1H, CH-P, J = 16.6 Hz), 4.05 (dd, 2H, NCH_2Ph, J = 13.3 Hz), 3.50 (m, 2H, **OCH_2**CH_3), 0.96 (t, 3H, CH_3), J = 7.1 Hz.)	10.521 (s)
9b oxalate	66	119–121	7.47–7.20 (m, 10H, 2×Ph), 4.73 (d, 1H, CH-P, J = 17 Hz), 4.18 and 4.03 (dd, NCH_2, J = 13.2 Hz), 3.69 (d, 3H, P-OCH_3, J = 10.8 Hz), 3.54 (d, 3H, P-OCH_3, J = 10.8 Hz).	20.510 (s)
9d oxalate	47	114–5	8.61 (d, 1H, py-6, J = 4.5 Hz), 7.90(t, 1H, py-4, J = 7.5 Hz), 7.51–7.22 (m, 7H, Py-3 and py-5, Ph), 4.90 (d, 1H, CH-P, J = 18.9 Hz), 4.26–4.07 (dd, 2H, NCH_2, J = 13.2 Hz), 3.70–3.63 (dd, 6H, 2×P-OCH_3, J = 9.6 Hz).	19.765 (s)
9d′ oxalate	46	100–3 (dec.) lit. [9] 101–3	8.54 (d, 1H, py-6), J = 4.5 Hz), 7.66 (t, 1H, py-4, J = 76 Hz), 7.40–7.10 (m, 7H, Ph, py-3,5), 4.15 (d, 1H, CH-P, J = 21.4 Hz), 4.1–3.8 (m, 4H, 2×**OCH_2**CH_3), 3.65 (d, 2H, J = 13.4 Hz, NCH_2), 1.2–1.1 (t,t, 6H, 2×CH_3, J = 7.1 Hz).	23.194 (s)

EXPERIMENTAL

NMR spectra were recorded on a Bruker Avance TM DRX 300 MHz in D_2O or in D_2O-D_2SO_4 (1:1) solutions, using 300.13 MHz for ^{1}H NMR and 121.51 MHz for ^{31}P NMR spectra, respectively. Melting points were determined on a Digital Melting Point Apparatus Electrothermal 9200, and were uncorrected. Elemental analyses were done in the laboratory of Instrumental Analysis, in the Institute. All commercially available reagents were used as received from the supplier (the Aldrich Company). Aldimines **4a–i** were prepared *in situ* from the corresponding aldehydes and primary amines according the following procedure: Aromatic aldehyde (10 mmol) was dissolved in dry methylene chloride (25 mL) and an appropriate amine was added (10 mmol). The mixture was left for 24 hrs at room temperature. Then, ~ 2g anhydrous potassium carbonate was added and the mixture was filtered to give a solution of the aldimine (**4a–i**), which was used directly for the next step.

***Procedure for preparation of aminophosphonic acids* 6a–i *and* 7a–g**: Syntheses of the all aminophosphonic acids were carried out in the equipment, protected against moisture. Trimethyl phosphite (1.36 g, 11 mmol) was dissolved in dry, freshly distilled methylene chloride (25 mL). To this stirred solution, bromotrimethylsilane (5.5 g, 36 mmol) was added dropwise during 10–15 min. period. The mixture was stirred for 1 h and then to such obtained *in situ* solution of tris(trimethylsilyl) phosphite (**3**) the earlier prepared solution of aldimine **4** in methylene chloride was added. The whole mixture was stirred for 24 hrs at room temp. and evaporated. The resulting oil was treated with methanol or ethanol (20 mL) and refrigerated. Usually, after short time, the product **6** (or **7**) separated out as a white, crystalline solid. The product was filtered, washed with a small amount of methanol and diethyl ether and dried.A similar pro-

cedure was applied in the case of triethyl phosphite, used (instead of trimethyl phosphite) for generation of the corresponding silylated esters of H_3PO_3. In order to avoid undesired *N*-methylation of some pyridyl aminophosphonic acids (**6e–g**) the methylene solution of **3** was evaporated under reduced pressure at room temp. (to remove the volatile MeBr) and then the residue (after diluting again with methylene chloride) was used for reaction with the aldimine **4e–g**.

Procedure for preparation of monoalkyl esters of aminophosphonic acids **8b**,**d,d′**: Trimethyl phosphite (1.36 g, 11 mmol) was dissolved in dry, freshly distilled methylene chloride (25 mL). To this stirred solution, bromotrimethylsilane (3.6 g, 24 mmol) was added dropwise during 10–15 min. period. The mixture was stirred for 1 h and to this solution [containing the di(trimethylsilyl)methyl phosphite (**2**)], the solution of aldimine **4b,d** in methylene chloride was added. The whole mixture was stirred for 24 hrs at room temp. and evaporated. The resulted oily product was dissolved in methanol (20 mL) and refrigerated. The separated crystalline solid of monoester **8b,d** was collected by filtration, washed with a small amount of a mixture of MeOH and diethyl ether (1:1) and dried. The monoethyl ester **8d′** was prepared similarly, replacing the $P(OMe)_3$ by $P(OEt)_3$.

Procedure for preparation of dialkyl esters of aminophosphonic acids **9b,d,d′**: Trimethyl phosphite (1.36 g, 11 mmol) was dissolved in dry, freshly distilled methylene chloride (25 mL). To this stirred solution, bromotrimethylsilane (1.8 g, 12 mmol) was added dropwise during 10–15 min. period. The mixture was stirred for 1 h and then to this solution (containing the **1**), the solution of aldimine (**4b,d**) in methylene chloride was added. The whole mixture was stirred for 24 hrs at room temp., then washed with 5% aqueous sodium bicarbonate (25 mL), the organic layer was separated, dried (anh. Na_2SO_4), filtered and evaporated to give the crude oily product **9b,d**. The diethyl phosphonate **9d′** was prepared similarly, replacing the $P(OMe)_3$ by $P(OEt)_3$. Diesters obtained were characterized as the oxalate salts. Transformation of the diesters (**9b,d,d′**) into the solid oxalate salts was done as described for preparation of some other oxalates of aminophosphonates [9,11].

Elem. analyses for the new obtained compounds: **6h**, **6i**, **7e**, **7f**, **7g**, **7g′**, **8b**, **8d**, **9b**, **9d**: Anal. for **6h**; $C_{12}H_{13}N_2O_6P$ (312.212): Calc. C, 46.16; H, 4.20; N, 8.97; P, 9.92; found: C, 45.98; H, 4.32; N, 9.00; P, 9.40. Anal. for **6i**; $C_{12}H_{13}N_2O_5PS$ (328.278): Calc. C, 43.90; H, 3.99; N, 8.53; P, 9.44; found: C, 43.71; H, 3.91; N, 8.43; P, 9.22. Anal. for **7e**; $C_{14}H_{18}N_2O_3PBr$ (373.176): Calc. C, 45.06; H, 4.86; N, 7.51; P, 8.30; Br, 21.41; found: C, 44.91; H, 5.02; N, 7.16; P, 7.88; Br, 21.51. Anal. for **7f**; $C_{11}H_{20}N_2O_3PBr$ (339.162): Calc. C, 38.95; H, 5.94; N, 8.26; P, 9.13; Br, 23.56; found: C, 38.72; H, 5.98; N, 7.97; P, 8.94; Br, 23.55. Anal. for **7g**; $C_{14}H_{18}N_2O_3PBr$ (373.176): Calc. C, 45.06; H, 4.86; N, 7.51; P, 8.30; Br, 21.41; found: C, 44.89; H, 4.97; N, 7.38; P, 8.11; Br, 21.45. Anal. for **7g'**; $C_{15}H_{20}N_2O_3PBr$ (387.202): Calc. C, 46.53; H, 5.21; N, 7.23; P, 8.00; Br, 20.64; found: C, 46.37; H, 5.33; N, 7.02; P, 7.85; Br, 20.71. Anal. for **8b**; $C_{15}H_{18}NO_3P$ (291.275): Calc. C, 61.85; H, 6.23; N, 4.81; P, 10.63; found: C, 61.66; H, 6.46; N, 4.71; P, 10.54. Anal. for **8d**; $C_{14}H_{17}N_2O_3P$ (292.264): Calc. C, 57.53; H, 5.86; N, 9,59; P, 10.60; found: C, 57.34; H, 5.90; N, 9.41; P, 10.51. Anal. for **9b**·$(COOH)_2$; $C_{18}H_{22}NO_7P$ (395.337): Calc. C, 54.68; H, 5.61; N, 3.54; P, 7.83; found: C, 54.34; H, 5.82; N, 3.38; P, 7.64. Anal. for **9d**·$(COOH)_2$; $C_{17}H_{21}N_2O_7P$ (396.326): Calc. C, 51.52; H, 5.34; N, 7.07; P, 7.82; found: C, 51.37; H, 5.59; N, 7.15; P, 7.67.

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