T3P®-promoted Kabachnik–Fields reaction: an efficient synthesis of α-aminophosphonates

Mátyás Milen, Péter Ábrányi-Balogh, András Dancsó, Dávid Frigyes, László Pongó, György Keglevich

PII: S0040-4039(13)01313-0
DOI: http://dx.doi.org/10.1016/j.tetlet.2013.07.145
Reference: TETL 43343

To appear in: *Tetrahedron Letters*

Received Date: 14 June 2013
Revised Date: 5 July 2013
Accepted Date: 19 July 2013

Please cite this article as: Milen, M., Ábrányi-Balogh, P., Dancsó, A., Frigyes, D., Pongó, L., Keglevich, G., T3P®-promoted Kabachnik–Fields reaction: an efficient synthesis of α-aminophosphonates, *Tetrahedron Letters* (2013), doi: http://dx.doi.org/10.1016/j.tetlet.2013.07.145

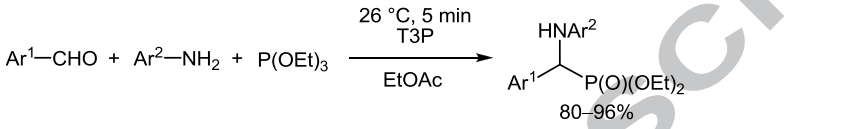
Graphical Abstract

To create your abstract, type over the instructions in the template box below.
Fonts or abstract dimensions should not be changed or altered.

T3P®-promoted Kabachnik–Fields reaction: an efficient synthesis of α-aminophosphonates

Leave this area blank for abstract info.

Mátyás Milen*, Péter Ábrányi-Balogh, András Dancsó, Dávid Frigyes, László Pongó, György Keglevich*



Ar^1 = 4-MeC_6H_4, 4-FC_6H_4, 4-ClC_6H_4, 4-$O_2NC_6H_4$, 4-$F_3CC_6H_4$, 4-$MeOC_6H_4$, 4-$BnOC_6H_4$, 3-NCC_6H_4, 1-naphthyl
Ar^2 = Ph, 4-MeC_6H_4, 4-PhC_6H_4, 4-FC_6H_4, 4-ClC_6H_4, 4-BrC_6H_4, 4-$O_2NC_6H_4$, 4-$EtO_2CC_6H_4$, 4-$MeOC_6H_4$, 3,4-$(MeO)_2C_6H_3$, 2-$MeSC_6H_4$, 2-$Ph(OC)C_6H_4$, 3-$PhOC_6H_4$, 3-$F_3CC_6H_4$, 3-$F_3COC_6H_4$, 1-naphthyl

Tetrahedron Letters
journal homepage: www.elsevier.com

T3P®-promoted Kabachnik–Fields reaction: an efficient synthesis of α-aminophosphonates

Mátyás Milen[a,b], Péter Ábrányi-Balogh[b], András Dancsó[a], Dávid Frigyes[a], László Pongó[a], György Keglevich[b,*]

[a]*Egis Pharmaceuticals PLC., Chemical Research Division, 1475 Budapest, P.O.B. 100, Hungary*
[b]*Department of Organic Chemistry and Technology, Budapest University of Technology and Economics, 1521 Budapest, Hungary*

ARTICLE INFO

Article history:
Received
Received in revised form
Accepted
Available online

Keywords:
α-aminophosphonates
T3P®
Kabachnik–Fields reaction
three-component condensation
mechanism

ABSTRACT

A simple and efficient synthesis of α-aminophosphonates has been developed via the one-pot three-component reactions of aldehydes, amines and trialkyl phosphites. The reactions occurred rapidly at room temperature in the presence of one equivalent of propylphosphonic anhydride (T3P®) as the condensing agent, and the α-aminophosphonate products were obtained in high yields.

α-Aminophosphonic acids and their derivatives are considered to be structural analogues of α-amino acids.[1] Compounds bearing an α-aminophosphonate moiety play an important role in biochemical and medicinal chemistry as enzyme inhibitors,[2] peptide mimics,[3] antibiotics,[4] herbicides,[5] plant growth regulators,[6] and haptens of catalytic antibodies.[7] Various methodologies have been reported in the literature for the preparation of α-aminophosphonates.[8] Among these, the three-component Kabachnik–Fields condensation of an aldehyde, an amine, and a dialkyl or trialkyl phosphite is one of the most important methods for the synthesis of α-aminophosphonates.[9] In general, this reaction is catalyzed by Brønsted or Lewis acids, such as trifluoroacetic acid,[10] lanthanum(III) triflate,[11] tin(II) triflate,[12] samarium(II) iodide,[13] indium(III) chloride[14] and tantalum(V) chloride on silica gel[15] using dialkyl phosphites, or by copper(II) triflate[16] and scandium tris(dodecyl sulfate),[17] where triethyl phosphite is the reagent. However, some of these species are expensive and moisture sensitive, or the methods applying them require long reaction times, heating, or special apparatus, etc. When using other Lewis acids such as $SnCl_2$, $SnCl_4$, $ZnCl_2$, $MgBr_2$ or $BF_3{\cdot}Et_2O$, the reaction does not take place in one step, because the water formed from condensation of the amine and the carbonyl compound can decompose or deactivate the catalysts.[18] It is worth mentioning that a few green protocols have been developed based on microwave (MW) irradiation,[19] ultrasound,[20] and the use of ionic liquids.[21] We have suggested that under MW conditions there is no need to use any catalyst.[22] Moreover, this procedure was solvent-free.

In continuation of our efforts to develop efficient synthetic methods in the field of α-hydroxyphosphonates and α-aminophosphonates,[23] we now describe a simple and highly efficient procedure for the preparation of α-aminophosphonates via a one-pot, three-component, T3P®-catalyzed reaction of aromatic aldehydes, aromatic primary amines and triethyl phosphite.

T3P® is a well known green coupling reagent and a powerful water scavenger with several advantages including low toxicity and low allergic potential, broad functional group tolerance, the generation of products in high yields and purity, and easy work-up procedures due to the formation of water-soluble by-products.[24] A number of applications have been developed using this reagent, such as the one-pot conversion of carboxylic acids into carbamates,[25] Beckmann rearrangement of aldoximes and ketoximes,[26] synthesis of N^{α}-protected amino thioamides,[27] acetylation and thioacetylation of aldehydes,[28] reduction of carboxylic acids to alcohols,[29] and syntheses of Weinreb amide derivatives.[30] Furthermore, T3P® has been investigated extensively in the preparation of various heterocyclic compounds.[31]

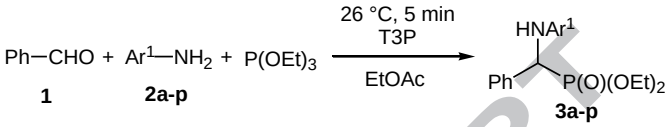
Initially, a mixture of benzaldehyde (**1**) and aniline (**2a**) was treated with triethyl phosphite in the presence of equimolar T3P® in ethyl acetate at 26 °C. The reaction took place smoothly and resulted in the formation of the corresponding α-aminophosphonate **3a** in a yield of 92% within a very short time of 5 minutes (Table 1, entry 1). The reaction proved capricious

* Corresponding author. Tel.: +36 1 463 1111/5883; fax: +36 1 463 3648; *E-mail address:* gkeglevich@mail.bme.hu (G. Keglevich).

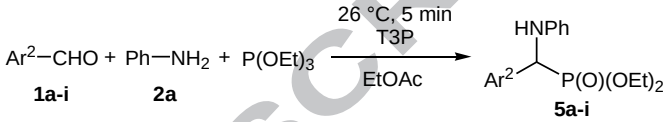
without or with a small amount of T3P®. Chandrasekhar at al. have accomplished the solvent and catalyst-free reaction of carbonyl compounds, amines and triethyl phosphite at room temperature in variable reaction times (15 min–12 h). The products were obtained in yields of 80–95%.[32] However, according to our observations, the three-component reaction of benzaldehyde, aniline and triethyl phosphite under solvent-free conditions without any catalyst gave the corresponding product in a conversion of only 80% at 26 °C after 24 hours. When this reaction was carried out under similar conditions, but using ethyl acetate as the solvent, the conversion was only 50% after 24 hours. In contrast, our results with T3P®, indicate the clear advantage of using this reagent.

As a possible extension, a series of aromatic aldehydes and aromatic amines were used in the three-component synthesis of α-aminophosphonates applying T3P® (Schemes 1 and 2). The results are summarized in Table 1[33] and Table 2.[34] Independent of the nature of the aromatic aldehyde or amine, products **3a-p** and **5a-i** were obtained in good to excellent yields (between 80% and 96%). On the other hand, this protocol was used successfully in the presence of different functional groups, such as ester (**3h**), methylsulfanyl (**3k**), keto (**3l**), benzyloxy (**5g**) and cyano (**5h**). In all cases (except **5f**), the reaction time was five minutes.

All the α-aminophosphonates prepared (**3a-p** and **5a-i**) were characterized by ^{31}P, ^{13}C and ^{1}H NMR spectroscopy and mass spectrometry. Products **3a,b,d-i,n** and **5a-d,f** have been described and characterized previously,[35–42] while compounds **3c,j-m,o,p** and **5e,g-i** have not been characterized, or are new.



Scheme 1. The condensation of benzaldehyde, aromatic amines and triethyl phosphite.



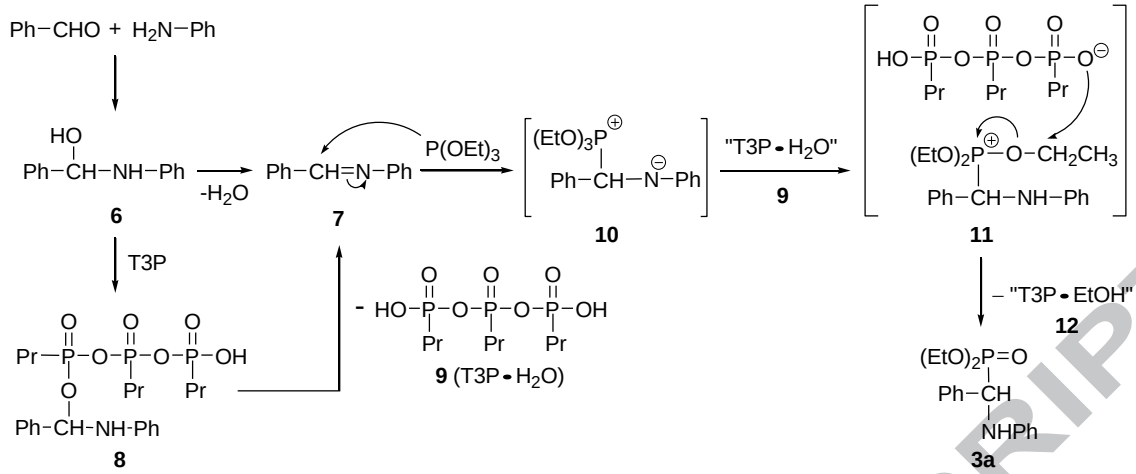
Scheme 2. The condensation of substituted benzaldehydes, aniline and triethyl phosphite.

Table 1
Results of the condensation of benzaldehyde, aromatic amines and triethyl phosphite

Entry	Ar^1	Product	Yield (%)	δ_P ($CDCl_3$)	δ_P^{Lit}	m.p. (°C)	m.p.^{Lit} (°C)
1	Ph	**3a**	92	23.2	23.3[35]	90–91	89–90[36]
2	4-MeC_6H_4	**3b**	86	23.3	-	119–120	118–120[37]
3	4-PhC_6H_4	**3c**	81	23.0	-	105–106	-
4	4-FC_6H_4	**3d**	94	23.0	23.2[38]	109–111	111–112[38]
5	4-ClC_6H_4	**3e**	89	22.8	-	120–121	119[39]
6	4-BrC_6H_4	**3f**	82	22.8	23.2[40]	118–120	122[39]
7	4-$O_2NC_6H_4$	**3g**	90	21.7	-	144–145	145–147[37]
8	4-$EtO_2CC_6H_4$	**3h**	92	22.4	-	178–180	179–180[41]
9	4-$MeOC_6H_4$	**3i**	91	23.3	23.1[42]	76–77	70–73[42]
10	3,4-$(MeO)_2C_6H_3$	**3j**	89	23.3	-	-	-
11	2-$MeSC_6H_4$	**3k**	94	22.6	-	49–51	-
12	2-$Ph(OC)C_6H_4$	**3l**	91	21.2	-	-	-
13	3-$PhOC_6H_4$	**3m**	88	23.0	-	121–122	-
14	3-$F_3CC_6H_4$	**3n**	87	22.6	22.8[38]	103–104	104–105[38]
15	3-$F_3COC_6H_4$	**3o**	96	22.6	-	69–70	-
16	1-naphthyl	**3p**	80	23.1	-	104–105	-

Table 2
Results of the condensation of substituted benzaldehydes, aniline and triethyl phosphite

Entry	Ar^2	Product	Yield (%)	δ_P ($CDCl_3$)	δ_P^{Lit}	m.p. (°C)	m.p.^{Lit} (°C)
1	4-MeC_6H_4	**5a**	90	23.4	23.5[35]	65–66	66–68[37]
2	4-FC_6H_4	**5b**	89	22.8	23.0[38]	84–85	85–86[38]
3	4-ClC_6H_4	**5c**	90	22.5	-	84.5–86	83–84[43]
4	4-$O_2NC_6H_4$	**5d**	94	21.3	21.4[35]	151–153	153–154[43]
5	4-$F_3CC_6H_4$	**5e**	89	22.1	-	122–123	-
6	4-$MeOC_6H_4$	**5f**	95	23.4	23.5[35]	99–100	102–103[43]
7	4-$BnOC_6H_4$	**5g**	87	23.4	-	92–93	-
8	3-NCC_6H_4	**5h**	94	21.5	-	114–116	-
9	1-naphthyl	**5i**	84	23.4	-	124–125	-



Scheme 3. Mechanism for the T3P®-catalyzed condensation reacion of benzaldehyde and aniline.

Three α-aminophosphonates **3a**, **3d** and **3g** were also prepared using diethyl phosphite instead of triethyl phosphite.[44] The reaction time was twice as long (10 min) as that with triethyl phosphite. The products **3a**, **3d** and **3g** were obtained in yields of 92%, 94%, and 98%, respectively.

A possible mechanism for the T3P®-promoted Kabachnik–Fields reaction is suggested in Scheme 3. In the first stage of this reaction an imine **7** is formed from the benzaldehyde and the aniline via adduct **6**. This condensation reaction may be promoted by T3P® to afford imine **7** along with *P*,*P*′,*P*″-tripropyl triphosphonic acid ("T3P·H_2O") (**9**) as the by-product. The dehydration may take place via adduct **8**. In the next step, the imine **7** reacts with triethyl phosphite in a nucleophilic addition, and after protonation by T3P·H_2O (**9**), the phosphonium salt **11** formed is stabilized by an Arbuzov fission to furnish α-aminophosphonate **3a** and T3P·EtOH (**12**) as the by-product.

In summary, a convenient and efficient method has been developed for the synthesis of α-aminophosphonates via the T3P®-promoted Kabachnik–Fields reaction using triethyl phosphite as the P-containing reagent. The advantages of this method comprise mild reaction conditions, short reaction times, and high yields.

Acknowledgment

This project was supported by the Hungarian Scientific and Research Fund (OTKA K83118).

Supplementary data

NMR spectral and HR-MS data for all compounds associated with this article can be found in the online version, at http://.....

References and notes

1. Kukhar, V.P.; Hudson, H.R. (Eds.), Aminophosphonic and Aminophosphinic Acids: Chemistry and Biological Activity, Wiley, Chichester, **2000**.
2. (a) Giannousis, P. P.; Bartlett, P. A. *J. Med. Chem*. **1987**, *30*, 1603; (b) Allen, M. C; Fuhrer, W.; Tuck, B.; Wade, R.; Wood, J. M. *J. Med. Chem.* **1989**, *32*, 1652.
3. Kafarski, P.; Lejczak, B. *Curr. Med. Chem. Anti-Cancer Agents* **2001**, *1*, 301.
4. Allerberger, F.; Klare, I. *J. Antimicrob. Chemother*. **1999**, *43*, 211.
5. Barder, A. *Aldrichim. Acta* **1988**, *21*, 15.
6. Emsley, J.; Hall, D. *Chemistry of Phosphorus*; Harper & Row: London, 1976, pp 494.
7. (a) Hirschmann, R.; Smith III, A. B.; Taylor, C. M.; Benkovic, P. A.; Taylor, S. D.; Yager, K. M.; Sprengler, P. A.; Venkovic, S. J. *Science* **1994**, *264*, 234; (b) Smith III, A. B.; Taylor, C. M.; Benkovic, S. J.; Hirschmann, R. *Tetrahedron Lett*. **1994**, *35*, 6853.
8. (a) Kukhar, V. P.; Solodenko, V. A. *Russ. Chem. Rev. (Engl. Transl.)* **1987**, *56*, 859; (b) Laschat, S.; Kunz, H. *Synthesis* **1992**, 90; (c) Kaboudin, B.; Nazari, R. *Tetrahedron Lett.* **2001**, *42*, 8211. (d) Matveeva, E. D.; Podrugina, T. A.; Tishkovskaya, E. V.; Tomilova, L. G.; Zefirov, N. S. *Synlett* **2003**, 2321. (e) Pavlov, V. Ya.; Kabachinik, M. M.; Zobnina, E. V.; Ponomarev, G. V.; Beletskaya, I. P. *Synlett* **2003**, 2193. (f) Van Meenen, E.; Moonen, K.; Acke, D.; Stevens, C. V. *ARKIVOC* **2006**, (*i*), 31-45 and refs. therein.
9. (a) Kabachnik, M.I.; Medved, T.Y. *Dokl. Akad. Nauk SSSr* **1952**, *83*, 689; *Chem. Abstr.* **1953**, *47*, 2724b; (b) Fields, E.K. *J. Am. Chem. Soc.* **1952**, *74*, 1528; (c) Keglevich, G.; Bálint E. *Molecules* **2012**, *17*, 12821; (d) Zefirov, N.S.; Matveeva, E.D. *ARKIVOC* **2008**, (*i*), 1.
10. Akiyama, T.; Sanada, M.; Fuchibe, K. *Synlett* **2003**, 1463.
11. Qian, C.; Huang, T. *J. Org. Chem*. **1998**, *63*, 4125.
12. Gallardo-Macias, R.; Nakayama, K. *Synthesis* **2010**, 57.
13. Xu, F.; Luo, Y.; Deng, M.; Shen, Q. *Eur. J. Org. Chem*. **2003**, 4728.
14. Ranu, B. C.; Hajra, A.; Jana, U. *Org. Lett*. **1999**, *1*, 1141.
15. Chandrasekhar, S.; Prakash, S. J.; Jagadeshwar, V.; Narsihmulu, C. *Tetrahedron Lett*. **2001**, *42*, 5561.
16. Paraskar, A. S.; Sudalai, A. *ARKIVOC* **2006**, (*x*), 183.
17. Manabe, K.; Kobayashi, S. *Chem. Commun*. **2000**, 669.
18. (a) Zon, J. *Pol. J. Chem*. **1981**, *55*, 643; (b) Lashat, S.; Kunz, H. *Synthesis* **1992**, 90.
19. Yadav, J. S.; Reddy, B. V. S.; Madan, C. *Synlett* **2001**, 1131; (b) Kaboudin, B.; Nazari, R. *Tetrahedron Lett*. **2001**, *42*, 8211; (c) Kabachnik, M. M.; Zobnina, E. V.; Beletskaya, I. P. *Synlett* **2005**, 1393.
20. Xia, M.; Lu, Y. D. *Ultrason. Sonochem*. **2007**, *14*, 235.
21. (a) Yadav, J. S.; Reddy, B. V. S.; Sreedhar, P. *Green Chem*. **2002**, *4*, 436; (b) Disale, S. T.; Kale, S. R.; Kahandal, S. S.; Srinivasan, T. G.; Jayaram, R. V. *Tetrahedron Lett*. **2012**, *53*, 2277.
22. Keglevich, G.; Szekrényi, A. *Lett. Org. Chem.* **2008**, *5*, 616.
23. (a) Keglevich, G.; Tóth, V. R.; Drahos, L. *Heteroatom Chem.* **2011**, *22*, 15; (b) Kiss, N. Z.; Kaszás, A.; Drahos, L.; Mucsi, Z.; Keglevich, G. *Tetrahedron Lett.* **2012**, *53*, 207; (c) Bálint, E.; Fazekas, E.; Pongrácz, P.; Kollár, L.; Drahos, L.; Holczbauer, T.; Czugler, M.; Keglevich, G. *J. Organomet. Chem.* **2012**, *717*, 75.
24. (a) Wissmann, H.; Kleiner, H.-J. *Angew. Chem., Int. Ed. Engl*. **1980**, *19*, 133; (b) Escher, R.; Bünning, P. *Angew. Chem., Int. Ed. Engl*. **1986**, *25*, 277; (c) Schwarz, M. *Synlett* **2000**, 1369; (d) García, A. L. L. *Synlett* **2007**, 1328.
25. Augustine, J. K.; Bombrun, A.; Mandal, A. B.; Alagarsamy, P.; Atta, R. N.; Selvam, P. *Synthesis* **2011**, 1477.
26. Augustine, J. K.; Kumar, R.; Bombrun, A.; Mandal, A. B. *Tetrahedron Lett*. **2011**, *52*, 1074.
27. Madhu, C.; Basavaprabhu, Vishwanatha, T. M.; Sureshbabu, V. V. *Tetrahedron Lett*. **2012**, *53*, 1406.

28. Augustine, J. K.; Bombrun, A.; Sauer, W. H. B.; Vijaykumar, P. *Tetrahedron Lett*. **2012**, *53*, 5030.
29. Nagendra, G.; Madhu, C.; Vishwanatha, T. M.; Sureshbabu, V. V. *Tetrahedron Lett*. **2012**, *53*, 5059.
30. Sharnababi, K. M.; Nagendra, G.; Vishwanatha, T. M.; Sureshbabu, V. V. *Tetrahedron Lett*. **2013**, *54*, 478.
31. (a) Desroses, M.; Wieckowski, K.; Stevens, M.; Odell, L. R. *Tetrahedron Lett*. **2011**, *52*, 4417; (b) Augustine, J. K.; Bombrun, A.; Venkatachaliah, S. *Tetrahedron Lett*. **2011**, *52*, 6814; (c) Wen, X.; Bakali, J. E.; Deprez-Poulain, R.; Deprez, B. *Tetrahedron Lett*. **2012**, *53*, 2440; (d) Augustine, J. K.; Bombrun, A.; Ramappa, B.; Boodappa, C. *Tetrahedron Lett*. **2012**, *53*, 4422; (e) Poojari, S.; Naik, P. P.; Krishnamurthy, G. *Tetrahedron Lett*. **2012**, *53*, 4639; (f) Kumar, K. S. S.; Swaroop, T. R.; Harsha, K. B.; Narasimhamurthy, K. H.; Rangappa, S. *Tetrahedron Lett*. **2012**, *53*, 5619; (g) Augustine, J. K.; Bombrun, A.; Alagarsamy, P.; Jothi, A. *Tetrahedron Lett*. **2012**, *53*, 6280; (h) Jida, M.; Deprez, B. *New J. Chem*. **2012**, *36*, 869; (i) Ramesha, A. B.; Raghavendra, G. M.; Nandeesh, K. N.; Rangappa, K. S.; Mantelingu, K. *Tetrahedron Lett*. **2013**, *54*, 95; (j) Zarei, M. *Mendeleev Commun*. **2013**, *23*, 29.
32. Chandrasekhar, S.; Narsihmulu, Ch.; Sultana, S. S.; Saritha, B.; Prakash, S. J. *Synlett* **2003**, 505.
33. **General procedure for synthesis of α-aminophosphonates (3a-p):** To the stirred mixture of benzaldehyde (0.20 mL, 2.0 mmol) and amine (2.0 mmol, aniline: 0.18 mL, 4-toluidine: 0.21 g, biphenyl-4-amine: 0.34 g, 4-fluoroaniline: 0.19 mL, 4-chloroaniline: 0.26 g, 4-bromoaniline: 0.24 g, 4-nitroaniline: 0.28 g, ethyl 4-aminobenzoate: 0.33 g, 4-methoxyaniline: 0.25 g, 3,4-dimethoxyaniline: 0.31 g, 2-(methylthio)aniline: 0.25 mL, 2-aminobenzophenone: 0.39 g, 3-phenoxyaniline: 0.37 g, 3-(trifluoromethyl)aniline: 0.25 mL, 3-(trifluoromethoxy)aniline: 0.27 mL, naphthalene-1-amine: 0.29 g) was added (1.2 mL, 2.0 mmol) of T3P (Aldrich 50% solution in EtOAc). If the mixture did not become a solution, (in the cases of the examples covered by entries 3 and 7 of Table 1) CH_2Cl_2 (2 mL) and EtOAc (2 mL) were added. After 5 min, (0.35 mL, 2.0 mmol) of $P(OEt)_3$ was added and the mixture was stirred at 26 °C. After completion of the reaction (5–10 min), the mixture was diluted with EtOAc (15 mL) and washed with 10% $NaHCO_3$ solution (15 mL). The organic phase was dried (Na_2SO_4), filtered and concentrated. The residue was purified by flash chromatography on silica gel (Merck 107736 Silica gel 60 H, CH_2Cl_2–MeOH) to afford products **3a-p**.
34. α-Aminophosphonates **5a-i** were prepared in a similar manner using aniline (0.18 mL, 2.0 mmol) and the aldehyde (2.0 mmol, 4-methylbenzaldehyde 0.24 mL, 4-fluorobenzaldehyde 0.21 mL, 4-chlorobenzaldehyde 0.28 g, 4-nitrobenzaldehyde 0.30 g, 4-(trifluoromethyl)benzaldehyde 0.27 mL, 4-methoxybenzaldehyde 0.24 mL, 4-(benzyloxy)benzaldehyde 0.41 g, 3-formylbenzonitrile 0.26 g, 1-naphthaldehyde 0.27 mL). The work-up was carried out as above to give products **5a-i**.
35. Babak, K.; Hazegh, Z. *Chem. Lett*. **2008**, *37*, 540.
36. Kassaee, M. Z.; Movahedi, F.; Masrouri, H. *Synlett* **2009**, 1326.
37. You-Ping, T.; Feng, X.; Yi, W.; Jian-Jun, W.; Hui-Li, L. *J. Chem. Res*. **2009**, 78.
38. Gruss, U.; Hägele, G. *Phosphorus, Sulfur, Silicon* **1994**, *97*, 209.
39. Jafari, A. A.; Nazarpour, M.; Abdollahi-Alibeik, M. *J. Heteroatom Chem*. **2010**, *21*, 397.
40. Thirumurugan, T.; Nandakumar, A.; Priya, N. S.; Muralidaran, D.; Perumal, P. T. *Tetrahedron Lett*. **2010**, *51*, 5708.
41. Shagidullin, R. R.; Plyamovatyi, A. Kh.; Mukhamadeeva, R. M.; Khairullin, V. K.; Pudovik, A. N. *Russ. J. Gen. Chem*. **1994**, *64*, 833.
42. Goulioukina, N. S.; Bondarenko, G. N.; Lyubimov, S. E.; Davankov, V. A.; Gavrilov, K. N.; Beletskaya, I. P. *Adv. Synth. Catal*. **2008**, *350*, 482.
43. Mohamed, Z.; Abdelhakim, E.; Abdessamad, M.; Ahmed, R.; Said, S. *J. Chem. Res.* **2005**, 324.
44. α-Aminophosphonates **3a**, **3d** and **3g** were prepared according to the general method above, using diethyl phosphite (0.26 mL, 2.0 mmol) instead of triethyl phosphite. Benzaldehyde (0.2 mL, 2.0 mmol) and the corresponding amine (2.0 mmol, aniline: 0.18 mL, 4-fluoroaniline: 0.19 mL, 4-nitroaniline 0.28 g) were the other reaction components. The reaction time was 10 min. Products **3a**, **3d** and **3g** were obtained in yields of 92%, 94%, and 98%, respectively.