Journal of Fluorine Chemistry 132 (2011) 102–106

Contents lists available at ScienceDirect

Journal of Fluorine Chemistry

journal homepage: www.elsevier.com/locate/fluor

A facile synthesis of α-aminophosphonates catalyzed by ytterbium perfluorooctanoate under solvent-free conditions

Jun Tang [a], Limin Wang [a,b,*], Wenbo Wang [a], Liang Zhang [a], Shengying Wu [a], Dan Mao [a]

[a] Key Laboratory for Advanced Materials & Institute of Fine Chemicals, East China University of Science and Technology, 130 Meilong Road, Shanghai 200237, PR China
[b] Key Laboratory of Organofluorine Chemistry, Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences, 354 Fenglin Road, Shanghai 200032, PR China

ARTICLE INFO

Article history:
Received 15 September 2010
Received in revised form 1 December 2010
Accepted 2 December 2010
Available online 9 December 2010

Keywords:
Ytterbium perfluorooctanoate
α-Aminophosphonate
Kabacknik–Fields reaction
One-pot reaction

ABSTRACT

Three-component reactions of aldehydes, amines and diethyl phosphite are efficiently catalyzed by ytterbium perfluorooctanoate [$Yb(PFO)_3$] under solvent-free conditions, giving the corresponding α-aminophosphonates in good to excellent yields. The catalyst can be recovered and reused for several times without any significant loss of activity. Furthermore, a possible mechanism for this transformation is also presented.

1. Introduction

α-Aminophosphonates have attracted much attention owing to their biological activities. Their utilities as enzyme inhibitors, antibiotics, peptide mimics, herbicides, pharmacological agents and many other applications are well documented [1–5]. Thus, a number of synthetic methods including enantioselective hydrophosphonylation reactions [6] have been developed during the last decades. The traditional Lewis acid-catalyzed addition of diethyl phosphite to aldimines has provided a useful method for the preparation of α-aminophosphonates [7–9]. However, these reactions cannot proceed smoothly by a one-pot method from aldehydes, amines, and diethyl phosphite since water generated during the reactions can deactivate or decompose the catalysts [10]. Some new type Lewis acids, such as metal triflates [11], scandium tris(dodecyl sulfate) [12], lithium perchlorate [13], zirconium compounds [14], and Brønsted acid [15] were recently reported to be effective catalysts for this one-pot reaction. However, some of these procedures suffered from drawbacks of the use of organic solvents, long reaction times, difficulties in work-up procedures and relatively low yields. Considering the wide range of biological property of α-aminophosphonates, it is still necessary to develop a new method that is simple, efficient and general for this three-component reaction.

As a part of our program aiming at developing efficient and environmentally friendly fluorous rare earth catalyst, we have developed ytterbium perfluorooctanoate [$Yb(PFO)_3$] as an easily prepared, air stable, water tolerated and recyclable catalyst in promoting condensations of indole with carbonyl compounds efficiently as well as other multicomponent condensation reactions [16]. In this paper, we report a facile and efficient method for synthesis of α-aminophosphonates via one-pot Kabacknik–Fields reaction of aldehydes, amines and diethyl phosphite promoted by $Yb(PFO)_3$ under solvent-free conditions.

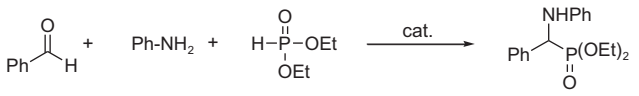
2. Results and discussion

The three-component reaction of benzaldehyde **1a**, aniline **2a**, and diethyl phosphite was selected as a model reaction for the one-pot synthesis of α-aminophosphonate **3a** promoted by a variety of Lewis acid catalysts (Scheme 1).

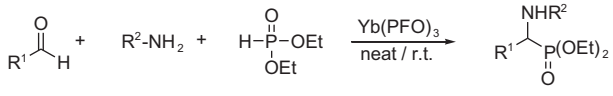
The reactions were carried out in ethanol at ambient temperature and the results are shown in Table 1. To our delight, $Yb(PFO)_3$ provided as high as 87% yield within just 1 h. No significant promoting effects were obtained even in the presence of 20 mol% of the traditional Lewis acids as predicted (entries 2 and 3). Other rare earth metal salts gave the desired product in moderate to good yields (entries 4–7). Overall, ytterbium perfluorooctanoate achieved the best result. Due to the current challenge for developing environmentally benign solvent-free synthetic systems, we tried to carry out this reaction without solvent and obtained higher yield of **3a** (92%, entry 9). The yield was not obviously changed when the amount of catalyst was reduced to

* Corresponding author at: Institute of Fine Chemicals, Lab for Advanced Materials, East China University of Science and Technology, 130 Meilong Road, Shanghai 200237, PR China. Tel.: +86 21 64253881; fax: +86 21 64253881.
E-mail address: wanglimin@ecust.edu.cn (L. Wang).

0022-1139/$ – see front matter © 2010 Elsevier B.V. All rights reserved.
doi:10.1016/j.jfluchem.2010.12.002



Scheme 1.



Scheme 2.

Table 1
Effect of different catalysts in the reaction of benzaldehyde (1 mmol), aniline (1 mmol), and diethyl phosphite (1.2 mmol)[a] via Scheme 1.

Entry	Catalyst	Amount of catalyst (mol%)	Solvent	Yield (%)[b]
1	/	/	EtOH	20
2	$AlCl_3$	20	EtOH	30
3	$ZnCl_2$	20	EtOH	26
4	$YbCl_3$	10	EtOH	68
5	$Yb(OTf)_3$	5	EtOH	84
6	$Sm(PFO)_3$	5	EtOH	76
7	$La(PFO)_3$	5	EtOH	72
8	$Yb(PFO)_3$	5	EtOH	87
9	$Yb(PFO)_3$	5	neat	92
10	$Yb(PFO)_3$	1	neat	90
11	$Yb(PFO)_3$	1	neat	90,88,88[c]

[a] All reactions were carried out at room temperature for 1 h.
[b] Isolated yields.
[c] Catalyst was reused for three times.

Table 2
Synthesis of different α-aminophosphonates in the presence of 1 mol% $Yb(PFO)_3$ via Scheme 2.[a]

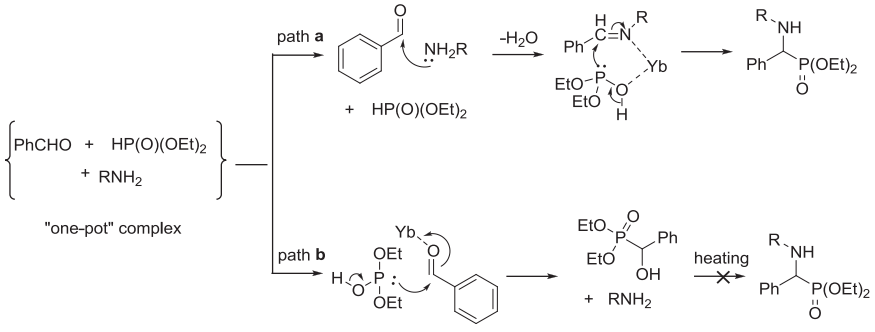
Entry	R^1	R^2	Product	Yield (%)[b]
1	Ph	Ph	3a	90
2	Ph	2-ClC_6H_4	3b	86
3	Ph	3-ClC_6H_4	3c	90
4	Ph	4-ClC_6H_4	3d	84
5	Ph	4-FC_6H_4	3e	86
6	Ph	4-$NO_2C_6H_4$	3f	84
7	Ph	4-$CH_3C_6H_4$	3g	90
8	Ph	4-$OCH_3C_6H_4$	3h	92
9	2-$NO_2C_6H_4$	Ph	3i	93
10	3-$NO_2C_6H_4$	Ph	3j	90
11	4-$NO_2C_6H_4$	Ph	3k	95
12	4-ClC_6H_4	Ph	3l	88
13	4-$CH_3C_6H_4$	Ph	3m	90
14	4-$OCH_3C_6H_4$	Ph	3n	86
15	4-$OCH_3C_6H_4$	4-$NO_2C_6H_4$	3o	90
16	$(CH_3)_2CH$-	Ph	3p	50[c]
17	Ph	Cyclohexyl	3q/4q	55/35[d]

[a] All reactions were carried out at room temperature for 1 h.
[b] Isolated yields.
[c] The reaction was heated at 50 °C for 6 h.
[d] The products are α-aminophosphonate (**3q**)/α-hydroxyphosphonate (**4q**).

1 mol%. Furthermore, recovering and reusing the catalyst for 3 times, the catalytic activities were shown without any significant loss (1st, 90%; 2nd, 88%; 3rd, 88% yield; respectively).

To establish generality, the reactions of various aldehydes and amines with diethyl phosphite in the presence of 1 mol% of $Yb(PFO)_3$ under solvent-free conditions giving the corresponding α-aminophosphonates were examined (Scheme 2). The results are shown in Table 2. Aromatic aldehydes provided excellent yields of products, whereas aliphatic aldehydes afforded phosphonates in moderate yields, which is expected that aromatic aldehydes have higher reactivity than aliphatic aldehydes. Both electron-donating and electron-withdrawing substitutions of aromatic amines provided excellent yields showing slight influences on the reactions. It is noteworthy to mention that, in the case of cyclohexylamine, the corresponding α-aminophosphonate **3q** was obtained in only 55% yield, and another solid byproduct was obtained in a very short time in 35% isolated yield, which was characterized as the corresponding α-hydroxyphosphonate **4q**. While secondary amines (e.g. piperidine, diethyl amine and morpholine) were utilized as substrates, the corresponding α-hydroxyphosphonates were the only products.

The mechanism of Kabacknik–Fields reaction was studied and explained by some researchers in recent years [17]. According to the above results, the pathway of this one-pot reaction depends on the nature of the amines. Taking benzaldehyde as an example, our proposed mechanism is depicted in Scheme 3.The amine and diethyl phosphite form a complex which either one of the partners may react with benzaldehyde. Often, the ability of the formation of imines determines the reaction pathway. Aromatic amines react with benzaldehyde very quickly, so the transformation goes to path **a** to afford the corresponding α-aminophosphonates. However, for cyclohexylamine, the imine is not immediately formed in the three component reaction and thus there is a competition between the addition of diethyl phosphite on the aldehyde and on the imine. Once α-hydroxyphosphonate is generated, it will not react with amine to form α-aminophosphonate even with long time heating (path **b**). While secondary amines are utilized, the only product α-hydroxyphosphonate is afforded, because the corresponding imines cannot be formed.



Scheme 3. The proposed mechanism of the one-pot reaction promoted by $Yb(PFO)_3$.

3. Conclusion

In summary, $Yb(PFO)_3$ was found to be an efficient catalyst in one-pot reaction of aldehydes, amines, and diethyl phosphite to afford α-aminophosphonates in good to excellent yields under solvent-free conditions. The procedure has many advantages such as short reaction time, small amount of catalyst used and easily recycled, especially the avoidance of harmful organic solvents in the reaction process, which provides a green and efficient method for synthesis of α-aminophosphonates.

4. Experimental

4.1. Method and apparatus

Melting points were determined on a Kofler hot plate.^{1}H and ^{13}C spectra were recorded on a Bruker AVANCE 400 spectrometer using TMS as internal reference, operating at 400 MHz for ^{1}H NMR, 100 MHz for ^{13}C NMR. For ^{1}H NMR, chemical shifts were reported downfield from $CDCl_3$ (δ: 7.26 ppm). For ^{13}C NMR, chemical shifts were reported in the scale relative to the solvent of $CDCl_3$ (δ: 77.0 ppm) used as an internal reference.

4.2. Catalyst preparation

The preparation and characterization of rare earth metal catalysts have been reported in our previous works [16d].

4.3. General procedure for synthesis of α-aminophosphonates

A mixture of aldehyde (1 mmol, 1.0 equiv.), amine (1 mmol, 1.0 equiv.), diethyl phosphite (1.2 mmol, 1.2 equiv.), and ytterbium perfluorooctanoate (1 mol%) under solvent-free conditions was stirred under air. After completion of the reaction as monitored by TLC, methylene chloride (5 ml) was added. The catalyst was filtered and washed with methylene chloride (5 ml). The combined filtrates and washing methylene chloride were concentrated under reduced pressure and the following purification on silica gel afforded pure α-aminophosphonate **3**. The filter residue, which was the catalyst, was dried under vacuum and reused in the next reaction. All the products were characterized by spectral methods as well as by comparison of their spectral data with those reported earlier.

4.3.1. Diethyl (phenyl)(phenylamino)methylphosphonate (3a)

White solid; Mp: 91–93 °C [11a]. ^{1}H NMR (400 MHz $CDCl_3$) δ 1.13 (t, J = 6.8 Hz, 3H), 1.30 (t, J = 6.8 Hz, 3H), 3.66–3.75 (m, 1H), 3.91–4.00 (m, 1H), 4.06–4.21 (m, 2H), 4.80 (d, J = 24.4 Hz, 1H), 4.87 (br, s, 1H), 6.62 (d, J = 8.4 Hz, 2H), 6.70 (t, J = 6.8 Hz, 1H), 7.11 (t, J = 7.6 Hz, 2H), 7.27–7.36 (m, 3H), 7.50 (d, J = 7.6 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 146.39, 146.25, 135.92, 129.17, 128.61, 128.58, 127.94, 127.88, 118.40, 113.86, 63.32, 63.29, 63.26, 63.22, 56.83, 55.33, 16.46, 16.40, 16.21, 16.16.

4.3.2. Diethyl (2-chloroaniline)(phenyl)methylphosphonate (3b)

White solid; Mp: 85–86 °C [11c]. ^{1}H NMR (400 MHz $CDCl_3$) δ 1.09 (t, J = 7.2 Hz, 3H), 1.20 (t, J = 7.2 Hz, 3H), 3.67–3.77 (m, 1H), 3.90–3.98 (m, 1H), 3.98–4.10 (m, 2H), 4.78 (dd, J = 7.6 Hz, J = 24.4 Hz, 1H), 5.41–5.46 (m, 1H), 6.43 (d, J = 8 Hz, 1H), 6.53 (t, J = 7.6 Hz, 1H), 6.68 (t, J = 8 Hz, 1H), 7.17–7.28 (m, 4H), 7.42 (d, J = 7.6 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 142.38, 142.24, 135.33, 135.30, 128.61, 128.01, 127.68, 127.63, 119.92, 118.46, 112.64, 63.44, 63.37, 63.32, 63.25, 56.52, 55.16, 16.39, 16.34, 16.20, 16.14.

4.3.3. Diethyl (3-chloroaniline)(phenyl)methylphosphonate (3c)

White solid; Mp: 122–123 °C [18a]. ^{1}H NMR (400 MHz $CDCl_3$) δ 1.09 (t, J = 7.2 Hz, 3H), 1.28 (t, J = 7.2 Hz, 3H), 3.59–3.69 (m, 1H), 3.87–3.97 (m, 1H), 4.06–4.20 (m, 2H), 4.74 (dd, J = 8.0 Hz, J = 24.4 Hz, 1H), 5.36 (br, s, 1H), 6.46 (dd, J = 2.0 Hz, J = 8.4 Hz, 1H), 6.61–6.65 (m, 2H), 6.96 (t, J = 8 Hz, 1H), 7.25–7.33 (m, 3H), 7.47 (d, J = 7.2 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.86, 147.71, 135.57, 134.80, 130.11, 128.68, 128.59, 128.10, 128.07, 127.93, 127.88, 118.07, 113.81, 111.83, 63.84, 63.41, 63.31, 63.24, 56.57, 55.07, 16.50, 16.44, 16.24, 16.19.

4.3.4. Diethyl (4-chloroaniline)(phenyl)methylphosphonate (3d)

White solid; Mp: 111–113 °C [18b]. ^{1}H NMR (400 MHz $CDCl_3$) δ 1.10 (t, J = 6.8 Hz, 3H), 1.29 (t, J = 6.8 Hz, 3H), 3.62–3.72 (m, 1H), 3.88–3.98 (m, 1H), 4.08–4.21 (m, 2H), 4.74 (d, J = 24 Hz, 1H), 5.20 (br, s,1H), 6.55 (d, J = 8.8 Hz, 1H), 7.03 (d, J = 9.2 Hz, 2H), 7.25–7.35 (m, 3H), 7.48 (d, J = 7.6 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.86, 147.71, 135.57, 134.80, 130.11, 128.67, 128.59, 128.10, 128.07, 127.93, 127.88, 118.07, 113.81, 111.83, 63.48, 63.41, 63.31, 63.24, 56.57, 55.07, 16.50, 16.44, 16.24, 16.19.

4.3.5. Diethyl (4-fluoroaniline)(phenyl)methylphosphonate (3e)

White solid; Mp: 111–112 °C [18c]. ^{1}H NMR (400 MHz $CDCl_3$) δ 1.09 (t, J = 6.8 Hz, 3H), 1.27 (t, J = 6.8 Hz, 3H), 3.62–3.72 (m, 1H), 3.87–3.97 (m, 1H), 4.05–4.19 (m, 2H), 4.71(d, J = 24.4 Hz, 1H), 4.99 (br, s,1H), 6.53–6.56 (m, 2H), 6.78 (t, J = 8.8 Hz, 2H), 7.22–7.33 (m, 3H), 7.47 (d, J = 7.2 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 146.01, 144.87, 135.43, 129.00, 128.10, 128.07, 127.85, 127.85, 127.79, 123.02, 115.00, 63.48, 63.41, 63.36, 63.29, 56.90, 55.40, 16.46, 16.39, 16.20, 16.14.

4.3.6. Diethyl (4-nitroaniline)(phenyl)methylphosphonate (3f)

Yellow solid; Mp: 145–146 °C [11c]. ^{1}H NMR (400 MHz $CDCl_3$) δ 1.12(t, J = 7.2 Hz, 3H), 1.32 (t, J = 7.2 Hz, 3H), 3.60–3.70 (m, 1H), 3.89–3.99 (m, 1H), 4.10–4.24 (m, 2H), 4.45 (dd, J = 7.6 Hz, J = 24 Hz, 1H), 6.34 (br s, 1H), 6.43 (d, J = 9.2 Hz, 1H), 7.29–7.38 (m, 3H), 7.50 (d, J = 7.2 Hz, 2H), 8.01(d, J = 9.2 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 152.23, 138.84, 134.46, 128.59, 128.88, 128.50, 128.47, 127.86, 127.81, 126.04, 112.39, 63.90, 63.83, 63.39, 63.32, 56.26, 54.74, 16.47, 16.41, 16.21, 16.15.

4.3.7. Diethyl (4-methylaniline)(phenyl)methylphosphonate (3g)

White solid; Mp: 117–118 °C [11c]. ^{1}H NMR (400 MHz $CDCl_3$) δ 1.14 (t, J = 7.2 Hz, 3H), 1.31 (t, J = 7.2 Hz, 3H), 2.21 (s, 3H), 3.66–3.76 (m, 1H), 3.92–4.01 (m, 1H), 4.07–4.21 (m, 2H), 4.77 (d, J = 24 Hz, 1H), 6.55 (d, J = 8 Hz, 2H), 6.94 (d, J = 8 Hz, 2H), 7.26–7.30 (m, 1H), 7.36 (t, J = 7.4 Hz, 2H), 7.50 (d, J = 7.2 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 136.04, 129.68,128.68, 128.59, 127.89, 127.84, 127.61, 113.99, 63.31, 63.26, 63.24, 63.19, 57.10, 55.61, 20.37, 16.48, 16.43, 16.24, 16.18.

4.3.8. Diethyl (4-methoxyaniline)(phenyl)methylphosphonate (3h)

Gray solid; Mp: 78–80 °C [18c]. ^{1}H NMR (400 MHz $CDCl_3$) δ 1.14(t, J = 6.8 Hz, 3H), 1.28 (t, J = 6.8 Hz, 3H), 3.66 (s, 3H), 3.68–3.78 (m, 1H), 3.89–3.99 (m, 1H), 4.06–4.19 (m, 2H), 4.72 (d, J = 24 Hz, 1H), 6.57 (d, J = 8.8 Hz, 2H), 6.69 (d, J = 8.8 Hz, 2H), 7.23–7.28 (m, 1H), 7.32 (t, J = 7.4 Hz, 2H), 7.47 (d, J = 7.2 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 152.64, 140.47, 140.31, 136.08, 128.56, 127.94, 127.89, 115.25, 114.72, 63.34, 63.27, 63.25, 63.18, 57.70, 56.20, 55.61, 29.68, 16.45, 16.39, 16.21, 16.15.

4.3.9. Diethyl (2-nitrobenzaldehyde)(phenylamino) methylphosphonate (3i)

White solid; Mp: 155–156 °C [18e]. ^{1}H NMR (400 MHz $CDCl_3$) δ 1.11 (t, J = 7.09 Hz, 3H), 1.33 (t, J = 7.09 Hz, 3H), 3.77–3.88 (m, 1H), 3.92–4.02 (m, 1H), 4.12–4.26 (m, 2H), 5.05(br, s, 1H), 6.20 (dd,

J = 3.8 Hz, *J* = 22.8 Hz, 1H), 6.71 (d, *J* = 8 Hz, 2H), 6.76 (t, *J* = 7.2 Hz, 1H), 7.15–7.19 (m, 2H),7.42–7.46 (m, 1H), 7.57 (t, *J* = 8 Hz, 1H), 7.76–7.78 (m, 1H), 8.03 (d, *J* = 8 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 149.48, 149.43, 145.46, 145.31, 133.54, 133.51, 131.96, 129.44, 128.94, 128.79, 128.56, 128.53, 125.27, 118.84, 113.59, 63.93, 63.86, 63.44, 63.33, 50.69, 49.19, 16.40, 16.34, 15.98, 15.92.

4.3.10. Diethyl (3-nitrobenzaldehyde)(phenylamino) methylphosphonate (3j)

Yellow solid; Mp: 95–97 °C [18e]. ^{1}H NMR (400 MHz $CDCl_3$) δ 1.20 (t, *J* = 6.8 Hz, 3H), 1.32 (t, *J* = 6.8 Hz, 3H), 3.87–3.97 (m, 1H), 4.02–4.10 (m, 1H), 4.11–4.26 (m, 2H), 4.90 (d, *J* = 24.8 Hz, 1H), 4.97 (br, s, 1H), 6.60 (d, *J* = 7.6 Hz, 2H), 6.75 (t, *J* = 7.6 Hz, 1H), 7.14 (t, *J* = 7.6 Hz, 2H), 7.54 (t, *J* = 8 Hz, 1H), 7.86 (d, *J* = 7.6 Hz, 1H), 8.15 (d, *J* = 8 Hz, 1H), 8.37–8.40 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.48, 148.76, 146.64, 138.91, 133.84, 133.79, 129.58, 129.56, 129.36, 122.97, 122.84, 122.79, 119.03, 113.03, 113.82, 63.77, 63.70, 63.46, 63.39, 56.46, 54.93, 16.49, 16.41, 16.27, 16.22.

4.3.11. Diethyl (4-nitrobenzaldehyde)(phenylamino) methylphosphonate (3k)

Yellow solid; Mp: 125–126 °C [11a]. ^{1}H NMR (400 MHz $CDCl_3$) δ 1.21(t, *J* = 6.8 Hz, 3H), 1.32 (t, *J* = 6.8 Hz, 3H), 3.85–3.95 (m, 1H), 4.02–4.10 (m, 1H), 4.11–4.26 (m, 2H), 4.88 (d, *J* = 25.2 Hz, 1H), 6.56 (d, *J* = 7.6 Hz, 2H), 6.71–6.78 (m, 1H), 7.11–7.15 (m, 2H), 7.68–7.71 (m, 2H), 8.19–8.24 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.63, .146.80, 146.66, 144.16, 129.36, 128.73, 123.75, 119.09, 113.82, 63.79, 63.70, 63.46, 63.39, 56.42, 54.49, 16.46, 16.41, 16.29, 16.24.

4.3.12. Diethyl (4-chlorobenzaldehyde)(phenylamino) methylphosphonate (3l)

White solid; Mp: 75–76 °C [12]. ^{1}H NMR (400 MHz $CDCl_3$) δ 1.21(t, *J* = 7.2 Hz, 3H), 1.32 (t, *J* = 7.2 Hz, 3H), 3.85–3.95 (m, 1H), 4.02–4.10 (m, 1H), 4.11–4.26 (m, 2H), 4.80 (d, *J* = 24.8 Hz, 1H), 5.14 (br, s, 1H), 6.61 (d, *J* = 8 Hz, 2H), 6.69 (t, *J* = 7.6 Hz, 1H), 7.09 (t, *J* = 7.8 Hz, 2H), 7.29 (d, *J* = 8 Hz, 2H), 7.43–7.46 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 146.17, 146.03, 134.68, 133.73, 129.24, 129.19, 128.81, 128.79, 118.64, 113.87, 63.53, 63.46, 63.41, 63.34, 56.27, 54.93, 16.46, 16.41, 16.30, 16.24.

4.3.13. Diethyl (4-methylbenzaldehyde)(phenylamino) methylphosphonate (3m)

White solid; Mp: 66–67 °C [11a]. ^{1}H NMR (400 MHz $CDCl_3$) δ 1.16 (t, *J* = 6.8 Hz, 3H), 1.31 (t, *J* = 6.8 Hz, 3H), 2.34 (s, 3H), 3.66–3.77 (m, 1H), 3.91–4.02 (m, 1H), 4.09–4.20 (m, 2H), 4.74–4.84 (m, 2H), 6.63 (d, *J* = 7.7 Hz, 2H), 6.72 (t, *J* = 7.2 Hz, 1H), 7.10–7.18 (m, 4H), 7.37–7.40 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 146.50, 146.35, 137.61, 137.58, 132.77, 129.34, 129.34, 129.32, 129.22, 129.16, 127.78, 127.72, 118.33, 113.88, 63.29, 63.26, 63.22, 63.19, 56.52, 55.02, 21.16, 16.49, 16.44, 16.28, 16.22.

4.3.14. Diethyl (4-methoxybenzaldehyde)(phenylamino) methylphosphonate (3n)

White solid; Mp: 101–102 °C [11a]. ^{1}H NMR (400 MHz $CDCl_3$) δ 1.13 (t, *J* = 7.2 Hz, 3H), 1.27 (t, *J* = 7.2 Hz, H), 3.73 (s, 3H), 3.90–3.99 (m, 1H), 4.04–4.21 (m, 2H), 4.75 (dd, *J* = 5.6 Hz, *J* = 24 Hz, 1H), 4.94 (br, s,1H), 6.61 (d, *J* = 7.6 Hz, 2H), 6.67 (t, *J* = 7.2 Hz, 1H), 6.86 (d, *J* = 8.4 Hz, 2H), 7.09 (t, *J* = 8 Hz, 2H), 7.38–7.41 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.31, 159.28, 146.53, 146.38, 129.10, 129.03, 128.97, 118.26, 114.03, 113.88, 63.24, 63.17, 56.08, 55.15, 46.54, 16.46, 16.40, 16.28, 16.22.

4.3.15. Diethyl (4-methoxybenzaldehyde)(4-nitroaniline) methylphosphonate (3o)

Yellow solid; Mp: 107–108 °C [18d]. ^{1}H NMR (400 MHz $CDCl_3$) δ 1.15 (t, *J* = 7.2 Hz, 3H), 1.30 (t, *J* = 7.2 Hz, 3H), 3.59–3.73 (m, 1H), 3.77 (s, 3H), 3.90–3.99 (m, 1H), 4.04–4.21 (m, 2H) 4.80 (dd, *J* = 7.6 Hz, *J* = 23.2 Hz, 1H), 6.36 (br, s, 1H), 6.63 (d, *J* = 9.2 Hz, 2H), 6.88 (d, *J* = 8.4 Hz, 2H), 7.40 (d, 2H), 7.99 (d, *J* = 9.2 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.67, 152.67, 152.31, 152.18, 138.71, 129.04, 129.00, 126.40, 126.02, 114.28, 112.38, 63.83, 63.77, 63.30, 63.24, 55.15, 54.55, 22.64, 16.46, 16.40, 16.28, 16.22, 14.11.

4.3.16. Diethyl (isobutylaldehyde)(phenylamino)methylphosphonate (3p)

Yellow oil [18d]. ^{1}H NMR (400 MHz $CDCl_3$) δ 1.07(t, 6H), 1.18 (t, *J* = 7.2 Hz, 3H), 1.29 (t, *J* = 7.2 Hz, 3H), 2.27 (t, 1H), 3.66 (dd, *J* = 3.2 Hz, *J* = 18.8 Hz, 1H), 3.94–4.18 (m, 4H), 6.67–6.74 (m, 3H), 7.17 (t, *J* = 7.6 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.79, 147.74, 129.27, 117.87, 113.30, 62.68, 62.61, 61.85, 61.78, 56.97, 55.46, 29.90, 29.84, 20.75, 20.63, 18.06, 18.01, 16.47, 16.41, 16.35.

4.3.17. Diethyl ((cyclohexylamine)phenyl)methylphosphonate (3q)

Yellow oil [18f]. ^{1}H NMR (400 MHz $CDCl_3$) δ 1.01–2.68 (t, 17H), 3.62–3.72 (m, 1H), 3.80–3.89 (m, 1H), 3.97–4.07 (m, 2H), 4.12 (d, *J* = 22 Hz, 1H), 7.18–7.33 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 136.68, 136.66, 128.36, 128.30, 128.25, 127.57, 127.54, 63.06, 62.99, 62.56, 62.49, 58.29, 56.77, 53.44, 53.29, 34.27, 31.90, 25.98, 24.77, 24.30, 16.39, 16.33, 16.13, 16.08.

4.4. Diethyl hydroxy(phenyl)methylphosphonate (4q)

White solid; Mp: 82–84 °C [18g]. ^{1}H NMR (400 MHz $CDCl_3$) δ 1.22 (t, *J* = 7 Hz, 3H), 1.27 (t, *J* = 7 Hz, 3H), 3.94–4.09 (m, 4H), 5.03 (d, *J* = 10.8 Hz, 1H), 7.29–7.39 (m, 3H), 7.47–7.49 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 136.50, 128.30, 127.08, 127.02, 71.62, 70.40, 63.40, 63.33, 63.16, 63.09, 16.40, 16.34, 16.30.

Acknowledgements

This research was financially supported by the National Nature Science Foundation of China (20672035) and Key Laboratory of Organofluorine Chemistry, Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences.

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.jfluchem.2010.12.002.

References

[1] (a) M.C. Allen, W. Fuhrer, B. Tuck, R. Wade, J.M. Wood, J. Med. Chem. 32 (1989) 1652–1661;
(b) P.P. Giannousis, P.A. Bartlett, J. Med. Chem. 32 (1987) 1603–1609.
[2] F. Allenberger, I.J. Klare, J. Antimicrob. Chemother. 43 (1999) 211–217.
[3] P. Kafarski, B. LeJczak, Phosphorus, Sulfur Silicon Relat. Elem. 53 (1991) 193–215.
[4] I.A. Natchev, Liebigs Ann. Chem. (1988) 861–867.
[5] (a) S.K. Chung, D.H. Kang, Tetrahedron: Asymmetry 7 (1996) 21–24;
(b) F.R. Atheron, C.H. Hassal, R.W. Lambert, J. Med. Chem. 29 (1986) 29–40.
[6] (a) S. Nakamura, M. Hayashi, Y. Hiramatsu, N. Shibata, Y. Funahashi, T. Toru, J. Am. Chem. Soc. 131 (2009) 18240–18241;
(b) X. Zhou, D. Shang, Q. Zhang, L. Lin, X. Liu, X. Feng, Org. Lett. 11 (2009) 1401–1404;
(c) J.P. Abell, H. Yamamoto, J. Am. Chem. Soc. 130 (2008) 10521–10523;
(d) X. Cheng, R. Goddard, G. Buth, B. List, Angew. Chem. Int. Ed. 47 (2008) 5079–5081;
(e) D. Pettersen, M. Marcolini, L. Bernardi, F. Fini, R.P. Herrera, V. Sgarzani, A. Ricci, J. Org. Chem. 71 (2006) 6269–6272;
(f) T. Akiyama, H. Morita, J. Itoh, K. Fuchibe, Org. Lett. 7 (2005) 2583–2585;
(g) G.D. Joly, E.N. Jacobsen, J. Am. Chem. Soc. 126 (2004) 4102–4103.
[7] J. Zon, Pol. J. Chem. 55 (1981) 643–646.
[8] S. Laschat, H. Kunz, Synthesis (1992) 90.
[9] J.S. Yadav, B.V.S. Reddy, K. Sarita RaJ, K. Bhaskar Reddy, A.R. Prasad, Synthesis (2001) 2277.

[10] J.P. Genet, J. Uziel, M. Port, A.M. Touzin, S. Roland, S. Thorimbert, S. Tanier, Tetrahedron Lett. 7 (1997) 33–36.
[11] (a) C.T. Qian, T. Huang, J. Org. Chem. 63 (1998) 4125–4128;
(b) J.H. Sang-gi Lee, J. Park, J.K. Kang, Lee, Chem. Commun. (2001) 1698–1699;
(c) H. Firouzabadi, N. Iranpoor, S. Sobhani, Synthesis (2004) 2692–2696.
[12] K. Manabe, S. Kobayashi, Chem. Commun. (2000) 669–670.
[13] A. Heydari, M. Zarei, R. AliJanianzadeh, H. Tavakol, Tetrahedron Lett. 42 (2001) 3629–3631.
[14] B. Srikant, K.C. Asit, J. Org. Chem. 73 (2008) 6029–6031.
[15] T. Akiyama, M. Sanada, K. Fuchibe, Synlett (2003) 1463–1464.
[16] (a) L.M. Wang, L. Hu, J. Fluorine Chem. 130 (2009) 406–409;
(b) L.M. Wang, J.H. Shao, H. Tian, B. Liu, J. Fluorine Chem. 127 (2006) 97–100;
(c) L.M. Wang, J.W. Han, H. Tian, J. Sheng, Synlett (2005) 337–339;
(d) L.M. Wang, J.W. Han, J. Sheng, H. Tian, Z.Y. Fan, Catal. Commun. 6 (2005) 201–204.
[17] (a) G. Roman, Tetrahedron 38 (1995) 10627–10632;
(b) M. Yamanaka, T.J. Hirata, J. Org. Chem. 74 (2009) 3266–3271;
(c) F.Q. Shi, B.A. Song, Org. Biomol. Chem. 7 (2009) 1292–1298;
(d) T. Akiyama, H. Morita, P. Bachu, K. Mori, M. Yamanaka, T. Hirata, Tetrahedron 65 (2009) 4950–4956;
(e) R.A. Cherkasov, V.I. Galkin, Russ. Chem. Rev. 67 (1998) 857–882.
[18] (a) M.J. Bhanushali, N.S. Nandurkar, S.R. Jagtap, B.M. Bhanage, Synth. Commun. 39 (2009) 845–859;
(b) S. Sobhani, A. Vafaee, Synthesis (2009) 1909–1915;
(c) J. Wu, W. Sun, H.G. Xia, X.Y. Sun, Org. Biomol. Chem. 9 (2006) 1663–1666;
(d) B. Srikant, K.C. Asit, J. Org. Chem. 72 (2007) 1263–1270;
(e) A. Vinu, P. Kalita, V.V. Balasubramanian, H. Oveisi, T. Selvan, A. Mano, M.A. Chari, B.V. Subba Reddy, Tetrahedron Lett. 50 (2009) 7132–7136;
(f) B.C. Ranu, A. Hajra, U. Jana, Org. Lett. 8 (1999) 1141–1143;
(g) R. Ganzarz, Tetrahedron 51 (1995) 10627–10632.