Tetrahedron xxx (2013) 1–17

Contents lists available at SciVerse ScienceDirect

Tetrahedron

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

Iron-doped single walled carbon nanotubes as an efficient and reusable heterogeneous catalyst for the synthesis of organophosphorus compounds under solvent-free conditions

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ARTICLE INFO

Article history:
Received 9 December 2012
Received in revised form 24 February 2013
Accepted 18 March 2013
Available online xxx

Keywords:
α-Aminophosphonates
Carbon nanotubes
Heterogeneous catalyst
Iron-doped
Organophosphorus
β-Phosphonomalonates
Solvent free

ABSTRACT

Iron-doped single walled carbon nanotubes (Fe/SWCNTs) is an efficient, eco-friendly, and reusable heterogeneous catalyst for the synthesis of diversely decorated α-aminophosphonates via multicomponent reaction of amines, carbonyl compounds, and phosphorus compounds under solvent-free conditions. This methodology illustrates a very simple procedure, with wide applicability, extending the scope to aliphatic and aromatic amines and carbonyl compounds. It also enabled the development of one-pot synthesis of β-phosphonomalonates during the reaction of carbonyl compounds, malononitrile and phosphorus compounds. Excellent results were obtained in each case affording the corresponding organophosphorus adducts in good yields.

1. Introduction

Organophosphorus compounds have been found a wide range of applications in the areas of industrial, agricultural, and medicinal chemistry owing to their biological and physical properties as well as their utility as synthetic intermediates.[1] In particular, compounds of tetracoordinated pentavalent phosphorus bearing heteroatomic substituents in the α- and β-position to the phosphorus atom have shown strong activities as antibiotics, anticancer drugs, antibacterial agents, antiviral agents, enzyme inhibitors, peptide mimetic, insecticides, herbicides, fungicides, as well as plant growth regulators.[2] They have also become important in the treatment of bone disorders and in medical decalcification.[3] From their physical properties, phosphonates are used as fire retardants for materials.[4] In this regard, the wide application of phosphonates has provoked the search for simple, efficient, and cost-effective procedures for the synthesis of such significant scaffolds in recent years.[2,5]

A large number of useful transformations have been achieved during the past decades, in which dialkyl/trialkyl phosphites were used as standard nucleophilic species for the construction of C–P bonds, in which various compounds can act as the acceptor, such as imines (ketimines),[6] carbonyl groups,[7] alkylidene malonates,[8] α,β-unsaturated carbonyl compounds,[9] nitroalkenes,[10] and so on.

Recently, one-pot three-component Kabachnik–Fields synthesis of α-aminophosphonates starting from aldehydes, amines, and dialkyl/trialkyl phosphites have been reported using Lewis and Brønsted acid catalysts, heteropoly acids, heterogeneous catalysts, and nano catalysts.[6] On the other hand, phospha-Michael addition, that is, the addition of a phosphorous nucleophile to an electron-deficient alkene has evoked remarkable attention by organic chemists. Synthesis of β-phosphonomalonates by this method is most commonly promoted by bases, Brønsted/Lewis acids, transition metals, and radical initiators, such as AIBN or microwaves.[8]

Although, some of these approaches are effective and for satisfactory synthesis of phosphonates, many of them cause reactor and plant corrosion problems, involve tedious separation procedures, require prolonged reaction times, and need use of toxic organic solvents and also are expensive. With regard to this, it is of great practical importance to develop a more efficient, convenient, and also an environmentally benign method using inexpensive and readily available reagents for the synthesis of these scaffolds.

Heterogeneous-reagent systems have many advantages, such as simple experimental procedures, mild reaction conditions, and the

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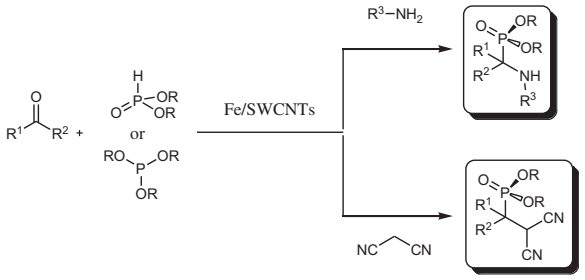
http://dx.doi.org/10.1016/j.tet.2013.03.073

minimization of chemical wastes as compared to their liquid phase counterparts.[11] Catalysis is currently recognized as a potential field of application for carbon nanotubes (CNTs), and throughout the past decade the number of publications and patents on this subject has been increasing exponentially.[12]

As a part of our program aiming at developing efficient and environmentally friendly heterogeneous catalysts for organic synthesis, we have developed iron-doped single walled carbon nanotubes (Fe/SWCNTs) as an easily prepared, air stable, water tolerated, and recyclable catalyst in promoting acylation of alcohols, phenols, acids, and amines with acid chlorides or acid anhydrides under solvent-free conditions.[13] In this paper, we report a practical, facile, and efficient method for the synthesis of α-aminophosphonates and β-phosphonomalonates via reaction of amines/malononitrile, carbonyl compounds and phosphorus compound, promoted by Fe/SWCNTs under solvent-free conditions (Scheme 1).



Scheme 1.

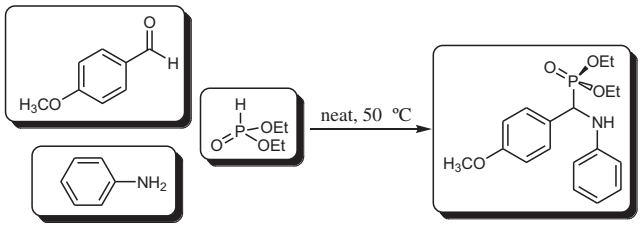
2. Results and discussion

2.1. Optimization of reaction

In search for an effective catalyst, for our initial screening experiments, the implementation of three-component strategies to obtain α-aminophosphonates in the presence of different catalysts was allowed. 4-Methoxybenzaldehyde and aniline were selected as model substrates and treated with diethyl phosphite (Table 1). When reaction was carried out in the absence of catalyst, the product yield was 25% after 1 h (Table 1, entry 1). The reaction did not proceed well when single-walled CNTs (SWCNTs) and multi-walled CNTs (MWCNTs) were employed, (Table 1, entries 2 and 3), whereas the yield of product was higher in the case of SWCNTs. The use of TiO_2-doped MWCNTs, ZnO-doped MWCNTs, TiO_2-doped SWCNTs, and Nano SnO_2 did not provide desired product in acceptable yields (Table 1, entries 4–7). Although, Nano-Fe and Fe-doped MWCNTs could accelerate the reaction to produce the target compound diethyl (4-methoxybenzaldehyde) (phenylamino) methylphosphonate, they could not provide satisfactory yields (Table 1, entries 8 and 9). We observed an increase in the reaction yield using Fe/SWCNTs (2.4 mol %). The optimum amount of nanocatalyst loading in this one-pot and three component reaction, was found to be 5.0 mol %, (Table 1, entry 11). By lowering the catalyst loading to 2.4 mol %, the desired product was obtained in lower yield while increasing of the catalyst loading to 10.0 mol % has no significant effect on reaction rate and isolated yield of product (Table 1, entries 10–13).

In the next step, the effect of solvent and temperature were surveyed (Table 2, entries 1–7). It was found that the use of 5.0 mol % of Fe-doped SWCNTs resulted in 60% formation of the corresponding α-aminophosphonates in solvent-free conditions at 30 °C within 3 h (Table 2, entry 1). Increase in the reaction temperature to 50 °C led to formation of product in higher yield, in 1 h (Table 2, entry 2). By increasing the temperature range to 80 °C the yield and time of reaction did not change significantly (Table 2, entry 3). The reaction was sluggish in H_2O probably due to the poor solubility of both the catalyst and the substrates (Table 2, entry 4). Other solvents improved yield less than neat condition (Table 2, entries 5–7). The best rate was observed when the reaction was carried out under neat condition at 50 °C (Table 2, entry 2).

Table 1
Screening of different catalyst for the synthesis of diethyl (4-methoxybenzaldehyde) (phenylamino) methylphosphonate[a]



Entry	Catalyst	Yield[b] (%)
1	—[c]	25
2	Pure SWCNTs[d]	40
3	Pure MWCNTs[d]	25
4	TiO_2/MWCNTs	35
5	ZnO/MWCNTs	35
6	TiO_2/SWCNTs	45
7	Nano SnO_2	30
8	Nano-Fe	60
9	Fe/MWCNTs	55
10	Fe/SWCNTs	80
11	Fe/SWCNTs (5.0 mol %)	95
12	Fe/SWCNTs (7.0 mol %)	97
13	Fe/SWCNTs (10.0 mol %)	97

[a] *p*-Methoxy-benzaldehyde (1.0 mmol), aniline (1.0 mmol) and diethyl phosphite (1.2 mmol), catalyst (2.4 mol %), solvent free, 50 °C, 1 h.
[b] Determined by ^{1}H NMR analysis.
[c] In the absence of catalyst.
[d] 0.02 g was used.

Table 2
The dependence of yield on the solvent and temperature[a]

Entry	Solvent	Temperature (°C)	Time (h)	Yield[b] (%)
1	—	30	3	60
2	—	50	1	95
3	—	80	0.8	98
4	H_2O	50	4	10
5	EtOH	50	4	55
6	$CHCl_3$	50	4	45
7	Dioxane	50	4	60

[a] Reaction conditions: *p*-methoxy-benzaldehyde (1.0 mmol), aniline (1.0 mmol), and diethyl phosphite (1.2 mmol) with 5.0 mol % of the catalyst.
[b] Determined by ^{1}H NMR analysis.

2.2. Characterization of Fe/SWCNTs

The recent studies have shown that, for the efficient use of CNT structural properties, particularly as catalyst in organic synthesis, CNT bundles should be activated.[14] In this study, oxygen was used for purification and functionalization of CNT bundles at 500 °C for about 2 h. To characterize the functionalized CNTs, the same amounts of each CNT sample was mixed with about 100 equiv KBr powder. The FT-IR spectrum of CNT sample is shown in Fig. 1. According to the FT-IR spectrum, the strong peak at around 3440 cm^{-1} is related to the O–H bond, whereas the peaks at ~1620 cm^{-1} are related to the carbonyl groups. Based on the back titration analysis, the amount of functionalization is ~7.2% for CVD process.

To study the amount of Fe nanoparticles doped on the CNT bundles TGA was used. The TGA instrument was adapted to study the thermal stability as well as the purity of CNT bundles. The CNT samples were analyzed according to a temperature program with

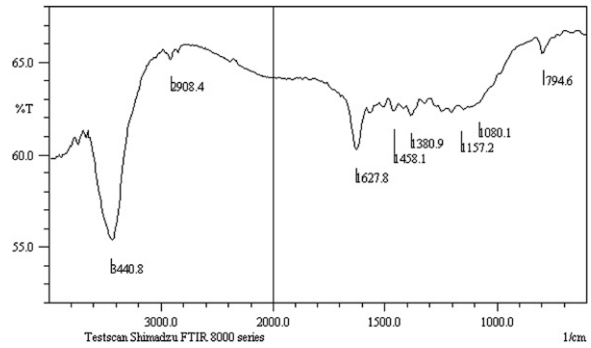


Fig. 1. FT-IR spectrum of CNTs, synthesized by high pressure CVD method.

a ramp of 2 °C min^{-1}. According to the thermogram (Fig. 2), increase in the weight percentage of the sample at temperature to ~310 °C is related to the oxidation of Fe nanoparticles and formation of iron oxides.

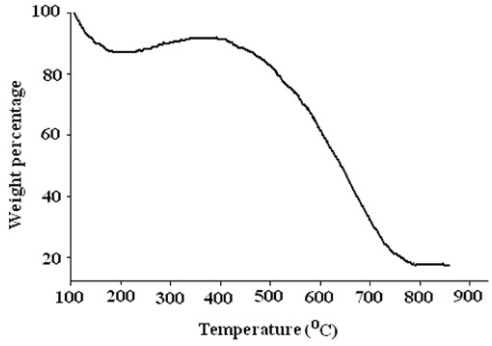


Fig. 2. Thermogram of Fe/SWCNTs.

The XRD patterns of different forms of CNTs are compared in Fig. 3. According to the XRD patterns, the strong peaks of the purified CNTs correspond to the (002), (100), and (101) planes of graphite.[15] Whereas other peaks with planes of (111) and (220) are related to γ Fe nanoparticles.

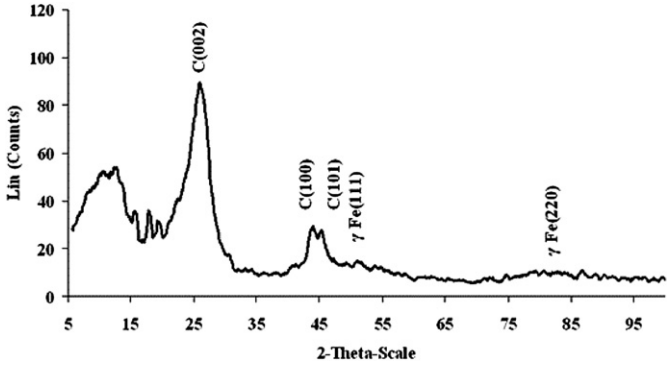


Fig. 3. XRD pattern of CNTs synthesized by CVD process.

The SEM image of Fe-doped CNTs is shown in Fig. 4.

2.3. Activity and reusability of heterogeneous catalyst

The ability to recycle and reuse of Fe/SWCNTs and the catalytic activity of Fe/SWCNTs was studied in this system. The catalyst can be so easily separated by centrifuging the reaction mixture after dispersing it in acetone. The recyclability of the heterogeneous catalytic systems was also examined for the model reactions. Fe/SWCNTs can be reused for 10 successive times in the new experiments without yield loss and generate products with purities similar to those obtained in the first run (Fig. 5).

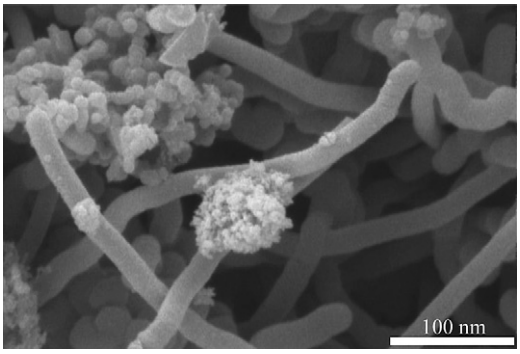


Fig. 4. SEM image of Fe-doped CNTs.

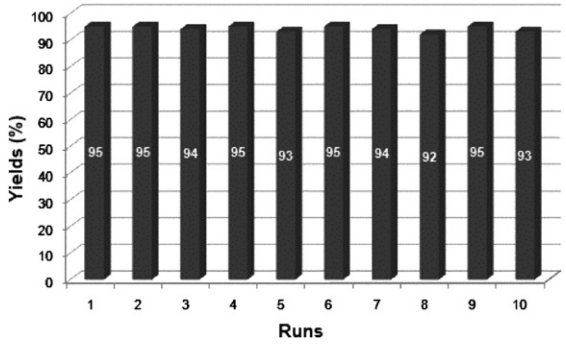


Fig. 5. Recyclability of heterogeneous catalyst for the synthesis of diethyl (4-methoxybenzaldehyde) (phenylamino) methylphosphonate. All reactions were under the same conditions for 1 h.

2.4. Comparison of the catalytic efficiency of Fe/SWCNTs with literature

In order to compare the activity of Fe/SWCNTs with other effective selected previously known catalysts, a comparison of the catalytic efficiency of different catalyst is collected in Table 3 to demonstrate that the present protocol is indeed superior to the other protocols. 4-Methoxy-benzaldehyde, aniline, and diethyl phosphite is completely reacted in 1 h at 50 °C in 95% isolated yield using the present protocol. The use of H-beta zeolite for the preparation of the same product requires reflux condition and a prolonged reaction time (Table 3, entry 1). In the presence of $TiCl_4$, $Mg(ClO_4)_2$, Tween-20, and CeO_2 the reaction completed in shorter reaction time, however, they need solvent or external source (e.g., ultrasonication) and could not recover for several times (Table 3, entries 3–6). Reaction of 4-methoxy-benzaldehyde and aniline with triethyl phosphite afforded 90% yields in 1.5 h under solvent-free condition in the presence of Fe/SWCNTs. Although, $[Cu(3,4\text{-}tmtppa)](MeSO_4)_4$ is equally effective, it requires long time to complete and the reaction carried out at 80 °C (Table 3, entry 10).

2.5. Fe/ASWCNTs catalyzed Kabachnik–Fields reaction

Encouraged by our preliminary results with respect to the phosphorus compound, 4-methoxybenzaldehyde and aniline were treated with di/tri substituted phosphites under the catalytic influence of Fe/SWCNTs (Table 4, entries 1–3). All phosphites with aliphatic and aromatic substituents worked well, giving high yields of products.

Next, to ensure the efficiency and fidelity of this catalytic system as a general methodology we subjected a series of amines and

Table 3
Comparison of protocols for the synthesis of diethyl (4-methoxybenzaldehyde) (phenylamino) methylphosphonate[a]

Entry	Conditions	Phosphorus compound	Time (h)	Yield (%)	Reuse	References
1	H-beta zeolite/ acetonitrile/reflux	$HP(O)(OEt)_2$	2	90	5	6a
2	TiO_2/20 mol %/50 °C	$HP(O)(OEt)_2$	2.5	98	5	6b
3	$TiCl_4$/acetonitrile/1 mol %	$HP(O)(OEt)_2$	0.25	90	—	6c
4	$Mg(ClO_4)_2$/5 mol %/rt	$HP(O)(OEt)_2$	0.08	95	—	6d
5	Tween-20/60 °C/water	$HP(O)(OEt)_2$	0.5	85	—	6e
6	CeO_2/5 mol %/ultrasonication	$HP(O)(OEt)_2$	0.25	91	3	6f
7	$[Yb(PFO)_3]$/rt/1 mol %	$HP(O)(OEt)_2$	1	86	3	6g
8	Fe/SWCNTs	$HP(O)(OEt)_2$	1	95	10	
9	Thiamine hydrochloride (VB1)/5 mol %	$P(OEt)_3$	1	76	—	6h
10	$[Cu(3,4\text{-tmtppa})](MeSO_4)_4$/0.16 mol %/80 °C	$P(OEt)_3$	3	90	—	6i
11	Fe/SWCNTs	$P(OEt)_3$	1.5	90	10	

[a] Reaction of *p*-methoxy-benzaldehyde, aniline, and phosphorus compound under different conditions.

aldehydes/ketones to one-pot three component reaction to obtaine desire α-aminophosphonates under the optimized conditions with the Fe/SWCNTs catalyst as summarized in Table 4. The described methodology illustrates a very simple procedure, with wide applicability, extending the scope to aliphatic and aromatic amines and carbonyl compounds. Excellent results were obtained in each case affording the corresponding phosphonate derivatives in 80–95% yields after 1–7 h at 50 °C under solvent-free condition. The reactions were clean and the products were isolated mostly in excellent yields after simple work-up using recrystallization or plate chromatography to purify.

Several functionalities present in the aromatic amines, such as alkyl, halogen, methoxy, hydroxyl, and nitro group were tolerated. It was found that, there was no remarkable electronic and position effects on the three-component couplings from the aromatic amines, since anilines with *p*-, *m*-, and *o*-substituents (Table 4, entries 4–14) resulted in the corresponding α-aminophosphonates in excellent yields. Apart from the above amines, aliphatic amines were also selected to carry out the three-component couplings. Primary aliphatic amines, such as butyl amine and 3-aminopropan-1-ol (Table 4, entries 15 and 16), was effective substrate, while secondary amines, such as morpholine was ineffective partner for this reaction.

In another attempt, we studied the reaction with substituted aromatic and aliphatic aldehydes. Various functionalities present in the aryl aldehydes, such as alkyl, halogen, methoxy, hydroxyl, and nitro groups (Table 4, entries 17–26) were compatible with the reaction. In general, aromatic aldehydes with electron-donating group could be accomplished the one-pot reaction as well as that with electron-withdrawing groups. Heteroaromatic aldehydes, such as thiophene-2-carbaldehyde and furan-2-carbaldehyde (Table 4, entries 27 and 28) were all effective substrates to successfully execute the solvent-free reactions by Fe/SWCNTs. Anthracene-9-carbaldehyde as a polynuclear aromatic aldehyde also reacted with diethyl phosphite (Table 4, entry 29) to give the desired compound in good yield. Furthermore, in the case of aliphatic aldehyde (Table 4, entries 30 and 31), the yield was quite reasonable. In addition to aldehydes, ketones were also screened to carry out the three-component couplings by Fe/SWCNTs under solvent-free conditions. Aliphatic ketone (Table 4, entry 32 and 33), smoothly produced the expected compound in acceptable yields. However, no products were gained in the case of aromatic ketones (Table 4, entry 34). The analytical and spectroscopic data for all compounds described are included in the Experimental section.

2.6. Fe/SWCNTs catalyzed synthesis of β-phosphonomalonates

Amongst the methods for P–C bond formation, phospha-Michael addition, that is, the addition of a phosphorous nucleophile to an electron-deficient alkene has evoked remarkable attention by organic chemists.[8] Spurred with the success of Kabachnik–Fields reaction, the addition of phosphite to activated conjugated alkenes that was synthesized via Knoevenagel condensation (KC) reaction,[16] was studied using this efficient nanocatalyst (Scheme 2). Previous optimized experimental protocol was required to verify that, in the presence of Fe/SWCNTs (5.0 mol %), 2-benzylidenemalononitrile with diethyl phosphite in a 1:1.2 molar ratio are smoothly converted to diethyl 2,2-dicyano-1-phenylethylphosphonate in satisfactory yield.

Since the optimal conditions for the efficient catalysis of the phospha-Michael addition had been determined, to investigate the generality and versatility of this method, the reaction was extended to different malonates. A representative selection of compounds obtained is depicted in Table 5.

As shown in Table 5, malonates with electron-donating and electron-withdrawing groups underwent successful phospha-Michael reaction with phosphites (Table 5, entries 1–10). The catalyst was compatible with functional groups, such as methoxy, halogen, and nitro (Table 5, entries 4–8). Heterocyclic malonates with furan and thiophene scaffolds underwent smooth reactions without any decomposition or polymerization under the present reaction conditions (Table 5, entries 9 and 10).

As previously demonstrated, the heterogeneous catalyst is recyclable and its activity is retained after 10 reaction cycles. The conversion yield of the reactions was generally greater than 97%, as judged by ^{1}H NMR, so the crude needed recrystallization to purify and compounds that did not reach this level, were purified by plate chromatography. The analytical and spectroscopic data for all compounds described are included in the Experimental section.

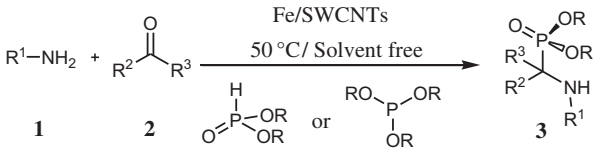
2.7. Knoevenagel condensation catalyzed by Fe/SWCNTs

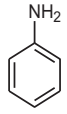
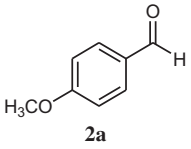
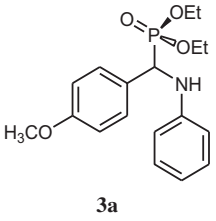
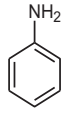
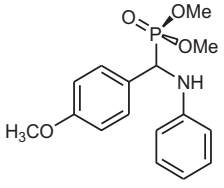
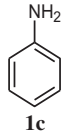
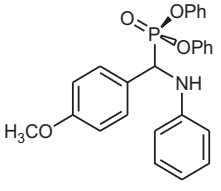
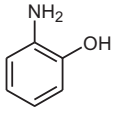
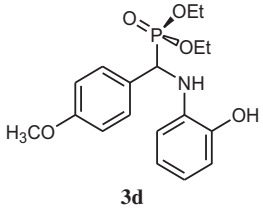
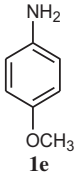
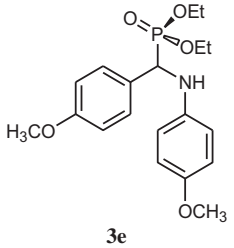
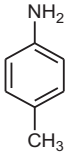
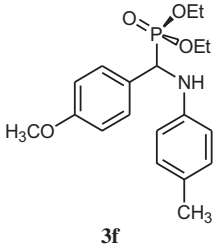
The Knoevenagel condensation (KC) has been receiving considerable attention, due to its broad spectrum of uses including perfume,[17] calcium antagonists,[18] polymers,[19] and pharmaceuticals applications.[20] Commercially this reaction was carried out using various homogeneous base catalysts, such as piperidine, amines, ammonia, and ammonium salts, which are corrosive, toxic, non-reusable, and also produce neutralization waste.[21] In last 10 years, lots of methods to achieve KC are known.[22] In general, KC is performed in organic solvents in the presence of the bases or acids. Recently, some novel heterogeneous catalysts, have been exploited as catalysts for the KC.[22a,23] However these methods are valuable, some of them suffer from some drawbacks, such as long reaction time, the use of harmful catalyst, harsh reaction conditions, stoichiometric amount of catalysts, a large amount of organic solvent as the reaction medium, and energy expenses.

The KC reaction of benzaldehyde and malononitrile as model substrates was studied at 80 °C under solvent-free condition in the presence of 5.0 mol % catalyst via ^{1}H NMR spectroscopy (Table 6,

Please cite this article in press as: Sharghi, H.; et al., Tetrahedron (2013), http://dx.doi.org/10.1016/j.tet.2013.03.073

Table 4
Fe/SWCNTs catalyzed one-pot and three component reaction of amines, carbonyl compounds, and phosphorus compounds[a]



Entry	Amine	Carbonyl compound	Phosphorus compound	Product	Time (h)	Yield[b] (%)
1	 **1a**	 **2a**	$HPO(OEt)_2$ $P(OEt)_3$	 **3a**	1.0 1.5	95 90
2	 **1b**	**2a**	$HPO(OMe)_2$ $P(OMe)_3$	 **3b**	0.3 1.0	97 95
3	 **1c**	**2a**	$HPO(OPh)_2$ $P(OPh)_3$	 **3c**	1.5 4.0	95 95
4	 **1d**	**2a**	$HPO(OEt)_2$ $P(OEt)_3$	 **3d**	3.2 5.0	82 80
5	 **1e**	**2a**	$HPO(OEt)_2$	 **3e**	1.5	92
6	 **1f**	**2a**	$HPO(OEt)_2$	 **3f**	2.0	92

(*continued on next page*)

Table 4 (*continued*)

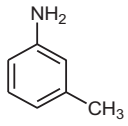
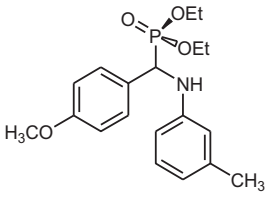
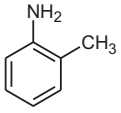
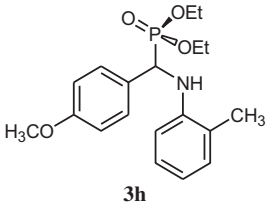
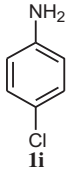
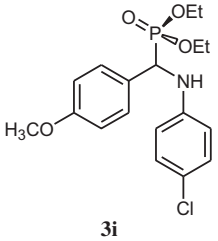
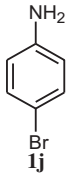
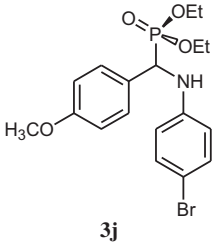
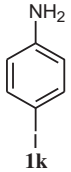
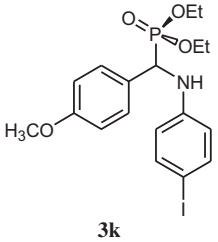
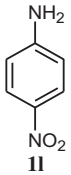
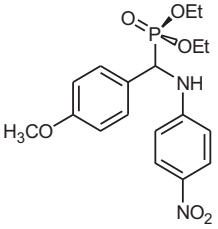
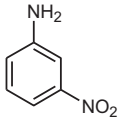
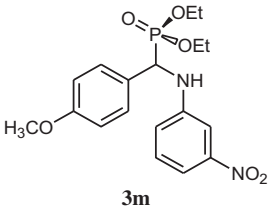
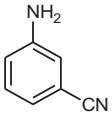
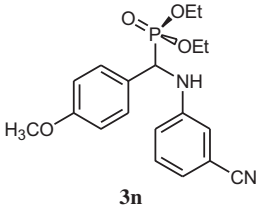
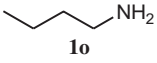
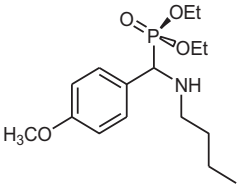
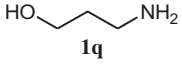
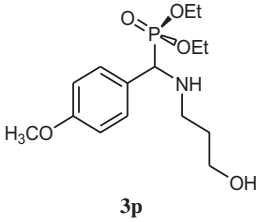
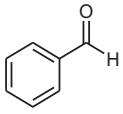
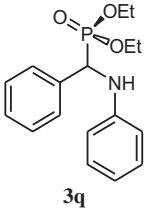
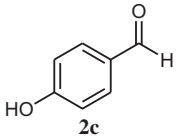
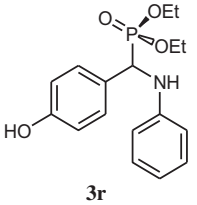
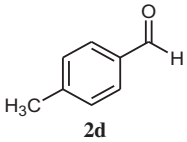
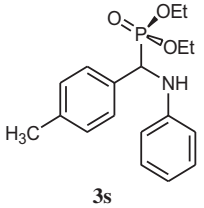
Entry	Amine	Carbonyl compound	Phosphorus compound	Product	Time (h)	Yield[b] (%)
7	 **1g**	**2a**	$HPO(OEt)_2$	 **3g**	2.0	90
8	 **1h**	**2a**	$HPO(OEt)_2$	 **3h**	2.8	90
9	 **1i**	**2a**	$HPO(OEt)_2$ $P(OEt)_3$	 **3i**	2.5 3.5	93 93
10	 **1j**	**2a**	$HPO(OEt)_2$	 **3j**	2.0	87
11	 **1k**	**2a**	$HPO(OEt)_2$ $P(OEt)_3$	 **3k**	2.5 3.0	84 80
12	 **1l**	**2a**	$HPO(OEt)_2$	 **3l**	3.0	85

Table 4 (*continued*)

Entry	Amine	Carbonyl compound	Phosphorus compound	Product	Time (h)	Yield[b] (%)
13	 **1m**	**2a**	$HPO(OEt)_2$	 **3m**	3.5	85
14	 **1n**	**2a**	$HPO(OEt)_2$	 **3n**	3.0	90
15	 **1o**	**2a**	$HPO(OEt)_2$	 **3o**	3.8	90
16	 **1q**	**2a**	$HPO(OEt)_2$	 **3p**	4.0	85
17	**1a**	 **2b**	$HPO(OEt)_2$ $P(OEt)_3$	 **3q**	1.0 1.5	95 95
18	**1a**	 **2c**	$HPO(OEt)_2$	 **3r**	2.0	88
19	**1a**	 **2d**	$HPO(OEt)_2$ $P(OEt)_3$	 **3s**	1.2 2.0	95 90

(*continued on next page*)

Table 4 (*continued*)

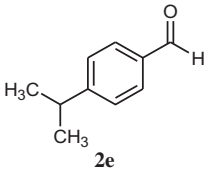
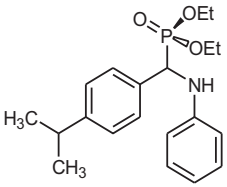
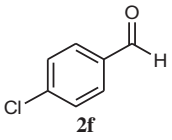
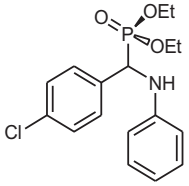
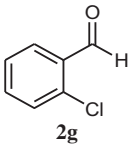
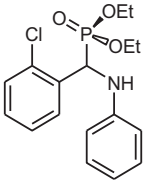
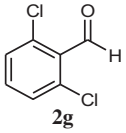
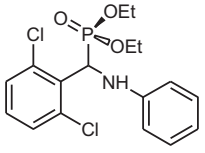
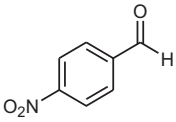
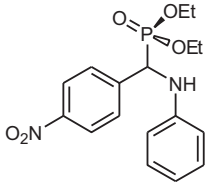
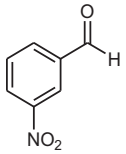
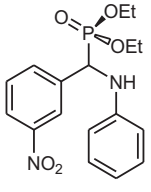
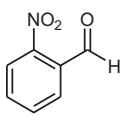
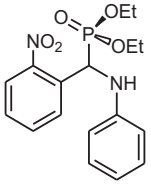
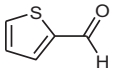
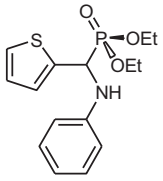
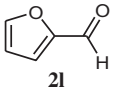
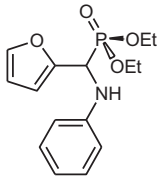
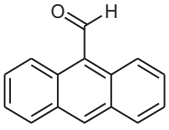
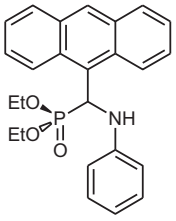
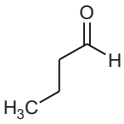
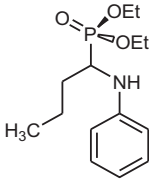
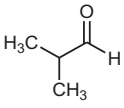
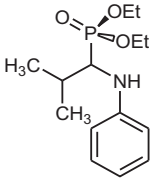
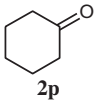
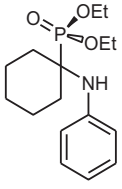
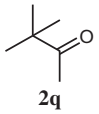
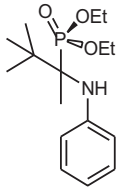
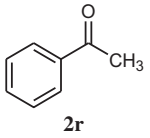
Entry	Amine	Carbonyl compound	Phosphorus compound	Product	Time (h)	Yield[b] (%)
20	**1a**	 **2e**	$HPO(OEt)_2$	 **3t**	2.0	90
21	**1a**	 **2f**	$HPO(OEt)_2$	 **3u**	3.0	90
22	**1a**	 **2g**	$HPO(OEt)_2$	 **3v**	2.0	94
23	**1a**	 **2g**	$HPO(OEt)_2$	 **3w**	3.5	92
24	**1a**	 **2h**	$HPO(OEt)_2$ $P(OEt)_3$	 **3x**	3.0 5.0	85 85
25	**1a**	 **2i**	$HPO(OEt)_2$	 **3y**	3.0	90
26	**1a**	 **2j**	$HPO(OEt)_2$	 **3z**	4.0	85

Table 4 (*continued*)

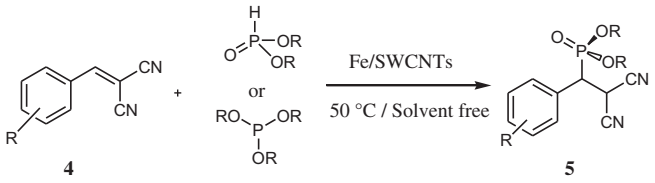
Entry	Amine	Carbonyl compound	Phosphorus compound	Product	Time (h)	Yield[b] (%)
27	**1a**	 **2k**	$HPO(OEt)_2$	 **3aa**	2.0	92
28	**1a**	 **2l**	$HPO(OEt)_2$	 **3ab**	3.5	87
29	**1a**	 **2m**	$HPO(OEt)_2$ $P(OEt)_3$	 **3ac**	4.0 6.5	87 85
30	**1a**	 **2n**	$HPO(OEt)_2$	 **3ad**	4.0	85
31	**1a**	 **2o**	$HPO(OEt)_2$	 **3ae**	5.0	82
32	**1a**	 **2p**	$HPO(OEt)_2$	 **3af**	6.0	80
33	**1a**	 **2q**	$HPO(OEt)_2$	 **3ag**	5.0	85

(*continued on next page*)

Table 4 (*continued*)

Entry	Amine	Carbonyl compound	Phosphorus compound	Product	Time (h)	Yield[b] (%)
34	**1a**	 **2r**	$HPO(OEt)_2$	Trace	10.0	—
35	**1a**	**2a**	$HPO(OEt)_2$	**3a**[c]	1.8	90

[a] Fe/SWCNTs (5.0 mol %), amine (1.0 mmol), carbonyl compound (1.0 mmol), and phosphorus compound (1.2 mmol) under solvent-free condition at 50 °C.
[b] Isolated yield.
[c] Substrates (20 mmol) have been used.



4 **5**

Scheme 2. Synthesis of β-phosphonomalonates.

entry 1). As shown in Table 6, the reaction was completed after 3.5 h to produce 2-benzylidenemalononitrile in 94% yield. Under the identical conditions, a variety of aryl aldehydes were reacted with malononitrile to afford 2-arylmethylidienemalononitrile in high yields (Table 6, entries 2–10). Both electron-rich and electron-deficient aldehydes worked well, giving high yields of products. Electron-deficient aldehydes furnished excellent yields of the corresponding arylidenes in a short reaction time, whereas electron-rich aldehydes resulted in comparatively low yields and required longer reaction times. The analytical and spectroscopic data for all compounds described are included in the Experimental section.

2.8. One-pot synthesis of β-phosphonomalonates catalyzed by Fe/SWCNTs

Since the phospha-Michael addition reaction of 2-benzylidenemalononitrile with diethyl phosphite using Fe/SWCNTs has been accomplished at 50 °C under solvent-free condition; we hypothesized that this transformation could be obtained in the same pot after the initial condensation, which is the Knoevenagel condensation of carbonyl compounds with malononitrile, was completed. So, we have explored the viability of obtaining desired β-phosphonomalonates via a KC reaction from the corresponding carbonyl compounds and malononitrile, followed directly by coupling with phosphorus compound using catalytically amount of Fe/SWCNTs.

The condensation of malononitrile and benzaldehyde was carried out at 80 °C in the presence of 5.0 mol % of Fe/SWCNTs and determined to be complete (by TLC against malononitrile with CH_2Cl_2 as eluent and $KMnO_4$ as stain) in 3.5 h. Upon completion of the first step, diethyl phosphite was added and the intermediate was converted to product in 95% yield (Table 7, entry 1). In an effort to determine the scope and limitation of this methodology various aldehydes were reacted with malononitrile, followed directly by coupling with phosphorus compound (Table 7). By using this process, the reaction times were comparable to the reaction starting from malonates, however, the yields are higher in almost all entries.

3. Conclusions

In conclusion, we have demonstrated a new, efficient, eco-friendly, chemoselective, and simple procedure for the one-pot synthesis of diversely decorated organophosphorus compounds by use of a catalytic amount of Fe/SWCNTs as catalyst under solvent-free condition. No competitive side reactions, such as the formation of α-hydroxyphosphonates were observed in these transformations. Furthermore, this catalytic system can promote Knoevenagel condensation successfully. The significant features of this method include its ease of operation, high efficiency, chemoselectivity, reusability, and avoidance of harmful organic solvents in the reaction process, which provides a green and efficient method for synthesis of α-aminophosphonates and β-phosphonomalonates. Current efforts in our research group are attempting to expand the application of Fe/SWCNTs for catalyzed organic reactions.

4. Experimental section

4.1. Instrumentation, analyses, and starting material

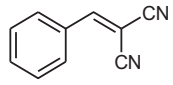
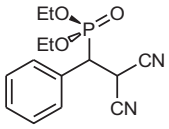
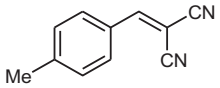
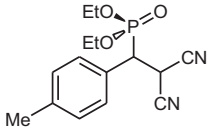
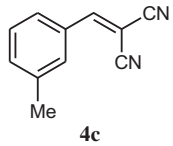
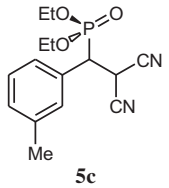
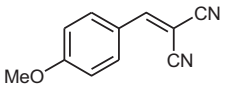
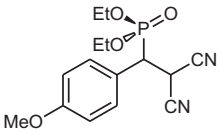
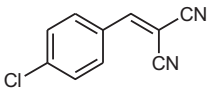
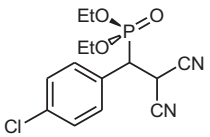
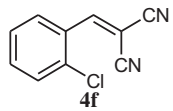
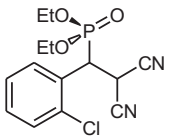
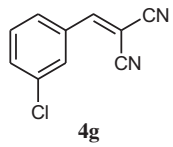
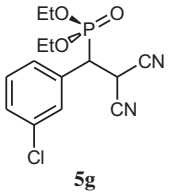
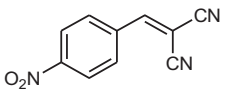
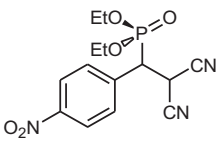
General information: scanning electron micrographs were observed by SEM instrumentation (XL-30 FEG SEM, Philips, at 20 KV). X-ray diffraction (XRD, D8, Advance, Bruker, axs) and FT-IR spectroscopy (Shimadzu FT-IR 8300 spectrophotometer) were employed for characterization of the heterogeneous catalyst. TGA of the samples was performed with a laboratory-made TGA instrument. NMR spectra were recorded on a Bruker Avance DPX-250 (^{1}H NMR 250 MHz and ^{13}C NMR 62.9 MHz) spectrometer in pure deuterated solvents with tetramethylsilane as an internal standard. Chemical shifts (δ) are reported in parts per million, and coupling constants (J) are in hertz. The following abbreviations were used to explain the multiplicities: s=singlet, d=doublet, t=triplet, q=quartet, m=multiplet, and br=broad. Mass spectra were determined on a Shimadzu GC–MS-QP 1000 EX instruments at 70 or 20 ev. Elemental analyses were performed with a Thermo Finnigan CHNS–O 1112 series analyzer. Melting points were determined in open capillary tubes in a Büchi-535 circulating oil melting point apparatus. The purity determination of the substrates and reaction monitoring was accomplished by TLC on silica gel PolyGram SILG/UV254 plates. Chemical materials were purchased from Fluka, Aldrich, and Merck Companies.

4.2. Synthesis of Fe/SWCNTs

Fe/SWCNTs were synthesized by chemical vapor disposition (CVD) method inside a quartz tube in a thermal furnace via deposition of carbon vapors at high temperature (1300 °C) at an inert atmosphere of argon. The source of SWCNTs was acetylene. Carbon vapors are then deposited on iron nanoparticles, synthesized with CVD method[24] through the decomposition of ferrocene (~14% molar percentage). The synthesized Fe/SWCNTs were then purified from any amorphous carbon or bulky nanomaterials, such as fullerenes, and activated carbon in an on-line system by hydrogen and oxygen etching process, ultraviolet (UV) and microwave irradiation. The amounts of iron nanoparticles doped on SWCNTs were

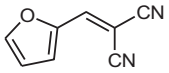
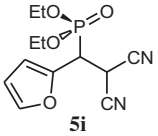
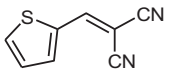
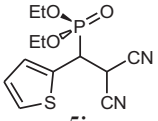
Please cite this article in press as: Sharghi, H.; et al., Tetrahedron (2013), http://dx.doi.org/10.1016/j.tet.2013.03.073

Table 5
Fe/SWCNTs catalyzed synthesis of β-phosphonomalonates[a]

Entry	Substrate	Phosphorus compound	Product	Time (h)	Yield[b] (%)
1	 **4a**	$HPO(OEt)_2$ $P(OEt)_3$	 **5a**	3.0 6.0	94 90
2	 **4b**	$HPO(OEt)_2$ $P(OEt)_3$	 **5b**	3.0 6.0	95 95
3	 **4c**	$HPO(OEt)_2$	 **5c**	3.5	90
4	 **4d**	$HPO(OEt)_2$	 **5d**	3.5	95
5	 **4e**	$HPO(OEt)_2$	 **5e**	3.0	92
6	 **4f**	$HPO(OEt)_2$	 **5f**	3.0	90
7	 **4g**	$HPO(OEt)_2$	 **5g**	2.5	90
8	 **4h**	$HPO(OEt)_2$ $P(OEt)_3$	 **5h**	6.5 9.0	85 78

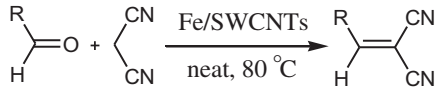
(*continued on next page*)

Table 5 (*continued*)

Entry	Substrate	Phosphorus compound	Product	Time (h)	Yield[b] (%)
9	 **4i**	$HPO(OEt)_2$	 **5i**	5.0	92
10	 **4j**	$HPO(OEt)_2$	 **5j**	4.0	90

[a] Fe/SWCNTs (5.0 mol %), malonates (1.0 mmol), and phosphorus compound (1.2 mmol) under solvent-free condition at 50 °C.
[b] Isolated yield.

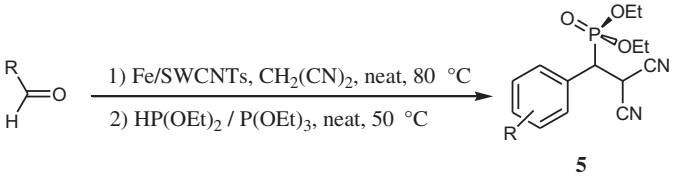
Table 6
Knoevenagel condensation using Fe/SWCNTs[a]



Entry	R	Product	Time (h)	Yield[b] (%)
1	C_6H_5	**4a**	3.5	95
2	*o*-MeO-C_6H_4	**4d**	5.0	80
3	*p*-Me-C_6H_4	**4b**	4.5	86
4	*p*-Cl–C_6H_4	**4e**	2.5	95
5	*m*-Cl–C_6H_4	**4g**	2.5	95
6	*o*-Cl–C_6H_4	**4f**	3.5	92
7	*p*-NO_2–C_6H_4	**4h**	1.5	95
8	2-Furyl	**4i**	3.5	82
9	2-Thienyl	**4j**	4.0	84
10	4-Pyridyl	**4k**	2.5	92

[a] Fe/SWCNTs (5.0 mol %), aldehyde (1.0 mmol), and malononitrile (1.0 mmol) under solvent-free condition at 80 °C.
[b] Isolated yield.

Table 7
Fe/SWCNTs catalyzed one-pot synthesis of β-phosphonomalonates[a]



5

Entry	Substrate	Phosphorus compound	Product	Time[b] (h)	Yield[c] (%)
1	C_6H_5	$HPO(OEt)_2$	**5a**	6.0	95
		$P(OEt)_3$		9.0	90
2	*p*-Me–C_6H_4	$HPO(OEt)_2$	**5b**	6.0	95
		$P(OEt)_3$		9.0	95
3	*m*-Me–C_6H_4	$HPO(OEt)_2$	**5c**	6.0	95
4	*p*-MeO–C_6H_4	$HPO(OEt)_2$	**5d**	8.5	95
5	*p*-Cl–C_6H_4	$HPO(OEt)_2$	**5e**	5.5	92
6	*o*-Cl–C_6H_4	$HPO(OEt)_2$	**5f**	5.0	90
7	*m*-Cl–C_6H_4	$HPO(OEt)_2$	**5g**	5.0	90
8	*p*-NO_2–C_6H_4	$HPO(OEt)_2$	**5h**	8.0	88
		$P(OEt)_3$		9.5	80
9	2-Furyl	$HPO(OEt)_2$	**5i**	8.0	90
10	2-Thienyl	$HPO(OEt)_2$	**5j**	8.0	95

[a] (1) Fe/SWCNTs (5.0 mol %), aldehyde (1.0 mmol), and malononitrile (1.0 mmol) under solvent-free condition at 80 °C, (2) phosphorus compound (1.2 mmol) under solvent-free condition at 50 °C.
[b] Overall one-pot time.
[c] Isolated yield.

controlled by optimization of the concentration of ferrocene and the flow rate of argon.

4.3. General procedure

4.3.1. Solvent-free synthesis of α-aminophosphonates catalyzed by Fe/SWCNTs. The required carbonyl compound (1 mmol), an amine (1 mmol), and phosphorus compound (1.2 mmol) were added to Fe/SWCNTs (0.05 g) and the mixture was heated in an oil bath at 50 °C. The progress of the reaction was monitored by TLC. After the reaction was complete, acetone (4×10 mL) was added to the reaction mixture and the catalyst was separated by centrifuging. The organic solvent was removed under reduced pressure. After purification by recrystallization (ethyl acetate/*n*-hexane 10:90) or plate chromatography (ethyl acetate/*n*-hexane 20:80) α-aminophosphonates were obtained.

4.3.2. Solvent-free synthesis of β-phosphonomalonates catalyzed by Fe/SWCNTs. The required malonates (1 mmol) and phosphorus compound (1.2 mmol) were added to Fe/SWCNTs (0.05 g) and the mixture was heated in an oil bath at 50 °C. After the reaction was complete, EtOAc (4×10 mL) was added to the reaction mixture and centrifuged to separate the catalyst. The organic solvent was removed under reduced pressure. After purification by plate chromatography (solvent: *n*-hexane/ethyl acetate, 50:50) the product was obtained.

4.3.3. Solvent-free Knoevenagel condensations over Fe/SWCNTs. The required carbonyl compound (1 mmol) and malononitrile (1 mmol) were added to Fe/SWCNTs (0.05 g) and the mixture was heated in an oil bath at 80 °C for a certain period of time as required to complete the reaction (monitored by TLC against malononitrile with CH_2Cl_2 as eluent and $KMnO_4$ as stain). The solid mass was then eluted with EtOAc (4×10 mL) and centrifuged to separate the catalyst. Evaporation of solvent furnished the corresponding practically pure product.

*4.3.4. Diethyl (4-methoxyphenyl) (phenylamino) methylphosphonate (**3a**).*[25] White crystalline solid, mp 100–102 °C (lit. 101–102); ^{1}H NMR (250 MHz, $CDCl_3$, 25 °C): δ=7.38 (d, 2H, J=7.5 Hz), 7.09 (t, 2H, J=8.0 Hz), 6.86 (d, 2H, J=7.5 Hz), 6.57–6.60 (m, 3H), 4.76 (d, 1H, J_{HP}=25.0 Hz), 4.50 (br s, 1H), 4.08–4.14 (m, 3H), 3.76–3.78 (m, 4H), 1.28 (t, 3H, J=7.2 Hz), 1.13 (t, 3H, J=7.2 Hz); ^{13}C NMR (62.9 MHz, $CDCl_3$, 25 °C) δ=159.3, 146.4, 129.1, 129.0, 128.9, 127.6, 118.3, 114.0, 113.8, 63.3 (d, $^2J_{CP}$=6.9 Hz), 63.0 (d, $^2J_{CP}$=6.9 Hz), 56.5 (d, J_{CP}=150.9 Hz), 55.2, 16.5 (d, $^3J_{CP}$=5.7 Hz), 16.3 (d, $^3J_{CP}$=5.7 Hz).

*4.3.5. Dimethyl (4-methoxyphenyl) (phenylamino) methylphosphonate (**3b**).*[6d] Greenish semisolid; ^{1}H NMR (250 MHz, $CDCl_3$, 25 °C): δ=7.35 (d, 2H, J=8.8 Hz), 7.05 (t, 2H, J=7.5 Hz), 6.84 (d, 2H, J=9.4 Hz),

6.54–6.67 (m, 3H), 4.70 (d, 1H, J_{HP}=24.0 Hz), 3.68–3.73 (m, 6 H), 3.43 (d, 3H, J=8.8 Hz); ^{13}C NMR (62.9 MHz, $CDCl_3$, 25 °C) δ=159.4, 146.8, 129.1, 128.8, 127.3, 118.4, 114.2, 114.1, 113.9, 56.1 (d, J_{CP}=153.0 Hz), 55.1, 53.7.

*4.3.6. Diphenyl (4-methoxyphenyl) (phenylamino) methylphosphonate (**3c**).*[6d] Greenish semisolid; ^{1}H NMR (250 MHz, DMSO-d_6, 25 °C): δ=7.48 (d, 2H, J=7.5 Hz), 6.98–7.31 (m, 7H), 6.85 (d, 2H, J=8.5 Hz), 6.75 (d, 2H, J=7.8 Hz), 6. 53 (t, 2H, J=7.3 Hz), 4.97 (d, 1H, J_{HP}=24.8 Hz), 3.68 (s, 3H); ^{13}C NMR (62.9 MHz, DMSO-d_6, 25 °C) δ=158.4, 151.0, 146.9, 129.5, 129.4, 128.8, 128.6, 124.1, 120.5, 116.8, 115.2, 113.4, 55.4 (d, J_{CP}=153.4 Hz), 54.9.

*4.3.7. Diethyl (2-hydroxyphenylamino) (4-methoxyphenyl) methylphosphonate (**3d**).*[6b] Off white crystalline solid, mp 77–78 °C (lit. 75); ^{1}H NMR (250 MHz, $CDCl_3$, 25 °C): δ=7.30 (d, 2H, J=7.5 Hz), 6.76 (d, 1H, J=7.5 Hz), 6.48–6.62 (m, 5H), 4.80 (d, 1H, J_{HP}=24.5 Hz), 4.22–4.28 (m, 2H), 3.87–3.95 (m, 2H), 3.62 (s, 1H), 1.29 (t, 3H, J=7.0 Hz), 1.12 (t, 3H, J=7.1 Hz); ^{13}C NMR (62.9 MHz, $CDCl_3$, 25 °C) δ=159.1, 145.2, 135.1, 134.8, 129.4, 129.2, 127.4, 124.4, 119.7, 118.1, 114.3, 113.9, 111.9, 64.1 (d, $^2J_{CP}$=6.9 Hz), 63.7 (d, $^2J_{CP}$=6.9 Hz), 56.4 (d, J_{CP}=155.8 Hz), 55.0, 16.4 (d, $^3J_{CP}$=5.7 Hz), 16.2 (d, $^3J_{CP}$=5.7 Hz).

*4.3.8. Diethyl (4-methoxyphenyl) (4-methoxyphenylamino) methylphosphonate (**3e**).*[6b] White crystalline solid, mp 116–117 °C (lit. 118); ^{1}H NMR (250 MHz, $CDCl_3$, 25 °C): δ=7.35 (d, 2H, J=7.5 Hz), 6.84 (d, 2H, J=9.0 Hz), 6.66 (d, 2H, J=7.5 Hz), 6.54 (d, 2H, J=7.5 Hz), 4.65 (d, 1H, J_{HP}=24.5 Hz), 4.03–4.12 (m, 2H), 3.87–3.92 (m, 1H), 3.62–3.70 (m, 1H), 3.56 (s, 3H), 3.52 (s, 3H), 1.26 (t, 3H, J=7.0 Hz), 1.11 (t, 3H, J=7.2 Hz); ^{13}C NMR (62.9 MHz, $CDCl_3$, 25 °C) δ=159.2, 152.5, 140.0, 132.0, 129.0, 128.9, 115.2, 114.6, 113.9, 63.3 (d, $^2J_{CP}$=6.9 Hz), 63.0 (d, $^2J_{CP}$=6.9 Hz), 57.3 (d, J_{CP}=152.8 Hz), 55.5, 55.1, 16.5 (d, $^3J_{CP}$=5.7 Hz),16.3 (d, $^3J_{CP}$=5.7 Hz).

*4.3.9. Diethyl (p-toluidino) (4-methoxyphenyl) methylphosphonate (**3f**).*[6b] White crystalline solid, mp 95–97 °C (lit. 96); ^{1}H NMR (250 MHz, $CDCl_3$, 25 °C): δ=7.29 (dd, 2H, J_1=9.5, J_2=2.5 Hz), 6.76–6.85 (m, 4H, J=8.5 Hz), 6.43 (d, 2H, J=7.5 Hz), 4.60 (d, 1H, J_{HP}=24.5 Hz), 4.04–4.11 (m, 2H), 3.79–3.95 (m, 1H), 3.70 (s, 3H), 3.55–3.60 (m, 1H), 2.10 (s, 3H), 1.20 (t, 3H, J=7.0 Hz), 1.06 (t, 3H, J=7.0 Hz); ^{13}C NMR (62.9 MHz, $CDCl_3$, 25 °C) δ=159.2, 144.1, 143.8, 129.6, 128.9, 127.9, 127.7, 114.0, 63.3 (d, $^2J_{CP}$=6.9 Hz), 63.0 (d, $^2J_{CP}$=6.9 Hz), 56.8 (d, J_{CP}=155.3 Hz), 55.2, 20.4, 16.5 (d, $^3J_{CP}$=5.7 Hz), 16.3 (d, $^3J_{CP}$=5.7 Hz).

*4.3.10. Diethyl (m-toluidino) (4-methoxyphenyl) methylphosphonate (**3g**).*[6b] Off white crystalline solid, mp 83–84 °C (lit. 86); ^{1}H NMR (250 MHz, $CDCl_3$, 25 °C): δ=7.89 (d, 2H, J=7.5 Hz), 7.16 (t, 1H, J=7.8 Hz), 6.67 (d, 2H, J=7.0 Hz), 6.55–6.58 (m, 3H), 4.65 (br s, 1H), 4.53 (d, 1H, J_{HP}=24.5 Hz), 3.66–3.91 (m, 4H), 3.40 (s, 3H), 1.91 (s, 3H), 1.02 (t, 3H, J=7.0 Hz), 0.93 (t, 3H, J=7.0 Hz); ^{13}C NMR (62.9 MHz, $CDCl_3$, 25 °C) δ=159.2, 146.7, 138.6, 128.9, 127.9, 119.0, 114.8, 113.9, 113.5, 110.8, 63.2 (d, $^2J_{CP}$=6.9 Hz), 62.9 (d, $^2J_{CP}$=6.9 Hz), 56.3 (d, J_{CP}=152.3 Hz), 55.0, 21.5, 16.4 (d, $^3J_{CP}$=5.7 Hz), 16.2 (d, $^3J_{CP}$=5.7 Hz).

*4.3.11. Diethyl (o-toluidino) (4-methoxyphenyl) methylphosphonate (**3h**).*[6b] White crystalline solid, mp 67–68 °C (lit. 65); ^{1}H NMR (250 MHz, $CDCl_3$, 25 °C): δ=7.29 (dd, 2H, J_1=8.8, J_2=2.3 Hz), 6.75–6.97 (m, 4H), 6.54 (t, 1H, J=7.3 Hz), 6.32 (d, 1H, J=8.0 Hz), 4.66 (d, 1H, J_{HP}=24.5 Hz), 4.50 (br s, 1H), 3.86–4.1(m, 3H), 3.69 (s, 3H), 3.56–3.66 (m, 1H), 2.18 (s, 3H), 1.19 (t, 3H, J=7.1 Hz), 1.06 (t, 3H, J=7.1 Hz); ^{13}C NMR (62.9 MHz, $CDCl_3$, 25 °C) δ=158.2, 143.3, 129.1, 127.8, 126.5, 125.8, 121.9, 116.9, 113.0, 112.9, 110.2, 62.3 (d, $^2J_{CP}$=6.9 Hz), 62.0 (d, $^2J_{CP}$=6.9 Hz), 55.5, 53.1 (d, J_{CP}=152.3 Hz), 16.5, 15.4, 15.3 (d, $^3J_{CP}$=5.7 Hz), 15.1 (d, $^3J_{CP}$=5.7 Hz).

*4.3.12. Diethyl (4-chlorophenylamino) (4-methoxyphenyl) methylphosphonate (**3i**).* White crystalline solid, mp 85–87 °C; R_f (AcOEt/hexane 10:90) 0.30; IR (KBr): 3294, 1596, 1512, 1242, 1180 cm^{-1}; ^{1}H NMR (250 MHz, $CDCl_3$, 25 °C): δ=7.33 (d, 2H, J=8.8 Hz), 7.02 (d, 2H, J=8.8 Hz), 6.84 (d, 2H, J=7.5 Hz), 6.51 (d, 2H, J=7.5 Hz), 5.18 (br s, 1H), 4.64 (d, 1H, J_{HP}=23.9 Hz), 4.06–4.13 (m, 2H), 3.75 (s, 3H), 3.61–4.05 (m, 2H), 1.27 (t, 3H, J=7.1 Hz), 1.11 (t, 3H, J=7.0 Hz); ^{13}C NMR (62.9 MHz, $CDCl_3$, 25 °C) δ=159.3, 145.0, 144.8, 128.9, 128.8, 127.0, 122.9, 122.0, 115.0, 114.1, 63.3 (d, $^2J_{CP}$=6.9 Hz), 63.0 (d, $^2J_{CP}$=6.9 Hz), 55.2, 54.2 (d, J_{CP}=152.8 Hz), 16.4 (d, $^3J_{CP}$=5.7 Hz), 16.2 (d, $^3J_{CP}$=5.7 Hz); Mass m/z (%): 384 (M^++1), 383 (M^+), 246, 202, 167, 138, 121, 83, 65; Anal. Calcd for $C_{18}H_{23}ClNO_4P$ (383): C, 56.33; H, 6.04. Found: C, 56.15; H, 6.30.

*4.3.13. Diethyl (4-bromophenylamino) (4-methoxyphenyl) methylphosphonate (**3j**).*[6b] White crystalline solid, mp 107–109 °C (lit. 105); ^{1}H NMR (250 MHz, $CDCl_3$, 25 °C): δ=7.27 (d, 2H, J=8.0 Hz), 6.09 (d, 2H, J=7.5 Hz), 6.77 (d, 2H, J=7.5 Hz), 6.41 (d, 2H, J=7.5 Hz), 4.57 (d, 1H, J_{HP}=25.0 Hz), 3.79–4.09 (m, 3H), 3.54–3.63 (m, 4H), 1.23 (t, 3H, J=7.1 Hz), 1.04 (t, 3H, J=7.0 Hz); ^{13}C NMR (62.9 MHz, $CDCl_3$, 25 °C) δ=159.4, 145.5, 145.2, 131.8, 128.9, 128.5, 126.9, 115.5, 110.0, 63.6 (d, $^2J_{CP}$=6.9 Hz), 63.3 (d, $^2J_{CP}$=6.9 Hz), 55.2, 54.0 (d, J_{CP}=153.5 Hz), 16.4 (d, $^3J_{CP}$=5.7 Hz), 16.2 (d, $^3J_{CP}$=5.7 Hz).

*4.3.14. Diethyl (4-iodophenylamino) (4-methoxyphenyl) methylphosphonate (**3k**).* Pale yellow crystalline solid, mp 101–103 °C; R_f (AcOEt/hexane 10:90) 0.31; IR (KBr): 3294, 1612, 1512, 1234, 1172 cm^{-1}; ^{1}H NMR (250 MHz, $CDCl_3$) δ=7.23–7.29 (m, 4H), 6.77 (d, 2H, J=7.5 Hz), 6.31 (d, 2H, J=8.5 Hz), 5.20 (br s, 1H), 4.57 (d, 1H, J_{HP}=23.8 Hz), 4.01–4.07 (m, 2H), 3.68 (s, 3H), 3.66–3.69 (m, 1H), 3.58–3.61 (m, 1H), 1.23 (t, 3H, J=7.1 Hz), 1.04 (t, 3H, J=7.0 Hz); ^{13}C NMR (62.9 MHz, $CDCl_3$, 25 °C) δ=159.4, 159.3, 145.1, 145.9, 137.6, 129.1, 128.9, 127.0, 126.9, 118.2, 116.1, 114.1, 113.8, 63.5 (d, $^2J_{CP}$=6.9 Hz), 63.2 (d, $^2J_{CP}$=6.9 Hz), 55.2, 53.9 (d, J_{CP}=155.0 Hz), 16.4 (d, $^3J_{CP}$=5.7 Hz), 16.2 (d, $^3J_{CP}$=5.7 Hz); Mass m/z (%): 476 (M^++1), 475 (M^+), 338, 230, 212, 121; Anal. Calcd for $C_{18}H_{23}INO_4P$ (475): C, 45.49; H, 4.88. Found: C, 45.63; H, 4.52.

*4.3.15. Diethyl (4-methoxyphenyl) (4-nitrophenylamino) methylphosphonate (**3l**).*[6g] Yellow crystalline solid, mp 110–112 °C (lit. 107–108); ^{1}H NMR (250 MHz, $CDCl_3$, 25 °C): δ=7.90 (d, 2H, J=9.3 Hz), 7.40 (d, 2H, J=8.5 Hz), 7.10 (br s, 1H), 6.79 (d, 2H, J=8.9 Hz), 6.65 (d, 2H, J=9.3 Hz), 4.94 (d, 1H, J_{HP}=23.8 Hz), 4.09–4.19 (m, 2H), 3.83–3.8 (m, 1H), 3.75 (s, 3H), 3.58–3.76 (m, 1H), 1.23 (t, 3H, J=7.1 Hz), 1.09 (t, 3H, J=7.0 Hz); ^{13}C NMR (62.9 MHz, $CDCl_3$, 25 °C) δ=159.5, 152.9, 138.2, 129.2, 129.1, 126.6, 126.5, 125.8, 114.1, 114.0, 112.3, 63.7 (d, $^2J_{CP}$=6.9 Hz), 63.3 (d, $^2J_{CP}$=6.9 Hz), 55.1, 53.2 (d, J_{CP}=154.5 Hz), 16.4 (d, $^3J_{CP}$=5.6 Hz), 16.2 (d, $^3J_{CP}$=5.6 Hz).

*4.3.16. Diethyl (4-methoxyphenyl) (3-nitrophenylamino) methylphosphonate (**3m**).*[6b] Yellow crystalline solid, mp 148–150 °C (lit. 148); ^{1}H NMR (250 MHz, $CDCl_3$, 25 °C): δ=7.47–7.53 (m, 2H), 7.40 (d, 2H, J=8.7 Hz), 7.13–7.25 (m, 2H), 7.16 (t, 1H, J=7.5 Hz), 6.83–6.89 (m, 3H), 5.95 (br s, 1H), 4.80 (d, 1H, J_{HP}=24.0 Hz), 4.24–4.08 (m, 2H), 3.89–4.01 (m, 1H), 3.75 (s, 3H), 3.62–3.75 (m, 1H), 1.29 (t, 3H, J=7.0 Hz), 1.13 (t, 3H, J=7.0 Hz); ^{13}C NMR (62.9 MHz, $CDCl_3$, 25 °C) δ=159.5, 149.1, 147.7, 147.5, 129.5, 129.1, 126.7, 119.9, 114.1, 112.4, 108.2, 63.7 (d, $^2J_{CP}$=6.9 Hz), 63.2, 63.2 (d, $^2J_{CP}$=6.9 Hz), 55.2, 53.7 (d, J_{CP}=154.1 Hz), 16.4 (d, $^3J_{CP}$=5.6 Hz), 16.2 (d, $^3J_{CP}$=5.6 Hz).

*4.3.17. Diethyl (3-cyanophenylamino) (4-methoxyphenyl) methylphosphonate (**3n**).*[6b] White crystalline solid, mp 120–121 °C (lit. 117); ^{1}H NMR (250 MHz, $CDCl_3$, 25 °C): δ=7.35 (d, 2H, J=8.7 Hz), 7.15 (t, 1H, J=7.5 Hz), 6.78–6.95 (m, 5H), 5.21 (br s, 1H), 6.65 (d, 1H, J_{HP}=24.0 Hz), 4.04–4.19 (m, 2H), 3.87–3.97 (m, 1H), 3.87 (s, 3H), 3.57–3.85 (m, 1H), 1.29 (t, 3H, J=7.0 Hz), 1.12 (t, 3H, J=7.0 Hz); ^{13}C NMR (62.9 MHz, $CDCl_3$, 25 °C) δ=159.5, 146.9, 129.8, 128.9, 126.5, 121.6, 119.2, 118.2, 116.1, 114.2, 112.8, 63.6 (d, $^2J_{CP}$=6.9 Hz), 63.2 (d,

$^{2}J_{CP}$=6.9 Hz), 55.2, 53.9 (d, J_{CP}=153.1 Hz), 16.4 (d, $^{3}J_{CP}$=5.7 Hz), 16.2 (d, $^{3}J_{CP}$=5.7 Hz).

*4.3.18. Diethyl (4-methoxyphenyl) (butylylamino) methylphospho nate (**3o**).*[6b] Oil; ^{1}H NMR (250 MHz, $CDCl_3$, 25 °C): δ=7.32 (d, 2H, J=8.5 Hz), 6.80 (d, 2H, J=8.5 Hz), 4.85 (d, 1H, J_{HP}=24.0 Hz), 3.40–3.71 (m, 4H), 3.71 (s, 3H), 2.28–2.46 (m, 2H), 1.05–1.37 (m, 10H), 0.77 (t, 3H, J=7.0 Hz); ^{13}C NMR (62.9 MHz, $CDCl_3$, 25 °C) δ=159.3, 132.0, 128.5, 113.6, 63.2 (d, $^{2}J_{CP}$=6.9 Hz), 63.0 (d, $^{2}J_{CP}$=6.9 Hz), 58.9 (d, J_{CP}=154.2 Hz), 55.1, 47.6, 31.8, 20.2, 16.4 (d, $^{3}J_{CP}$=5.7 Hz), 16.3 (d, $^{3}J_{CP}$=5.7 Hz), 13.9.

*4.3.19. Diethyl (3-hydroxypropylamino) (4-methoxyphenyl) methylphosphonate (**3p**).*[6b] White solid, mp 114–115 °C (lit. 113); ^{1}H NMR (250 MHz, $CDCl_3$, 25 °C): δ=8.01 (br s, 1H), 7.21 (d, 2H, J=7.5 Hz), 6.70 (d, 2H, J=7.5 Hz), 4.89 (d, 1H, J_{HP}=24.2 Hz), 3.50–3.85 (m, 4H), 3.70 (s, 3H), 3.23–3.45 (m, 2H), 2.20–2.43 (m, 2H), 1.05–1.47 (m, 5H), 1.07 (t, 3H, J=7.0 Hz); ^{13}C NMR (62.9 MHz, $CDCl_3$, 25 °C) δ=159.5, 132.2, 128.0, 113.8, 63.3 (d, $^{2}J_{CP}$=6.9 Hz), 62.9 (d, $^{2}J_{CP}$=7.0 Hz), 59.5 (d, J_{CP}=154.5 Hz), 55.4, 46.6, 30.2, 16.4 (d, $^{3}J_{CP}$=5.6 Hz), 16.2 (d, $^{3}J_{CP}$=5.6 Hz).

*4.3.20. Diethyl phenyl (phenylamino) methylphosphonate (**3q**).*[25] White crystalline solid, mp 92–93 °C (lit. 91–93); ^{1}H NMR (250 MHz, $CDCl_3$, 25 °C): δ=7.39 (d, 2H, J=7.6 Hz), 7.17–7.24 (m, 3H), 7.01 (t, 2H, J=8.0 Hz), 6.50–6.62 (m, 3H), 4.73 (br s, 1H), 4.50 (d, 1H, J_{HP}=24.6 Hz), 3.99–4.13 (m, 2H), 3.79–3.89 (m, 1H), 3.53–3.60 (m, 1H), 1.19 (t, 3H, J=7.0 Hz), 1.02 (t, 3H, J=7.0 Hz); ^{13}C NMR (62.9 MHz, $CDCl_3$, 25 °C) δ=146.4, 146.2, 130.2, 129.1, 128.6, 128.5, 127.9, 127.8, 118.6, 113.3, 63.3 (d, $^{2}J_{CP}$=6.9 Hz), 63.2 (d, $^{2}J_{CP}$=6.9 Hz), 57.2 (d, J_{CP}=151.0 Hz), 16.5 (d, $^{3}J_{CP}$=5.6 Hz), 16.2 (d, $^{3}J_{CP}$=5.6 Hz).

*4.3.21. Diethyl (4-hydroxyphenyl) (phenylamino) methylphosphonate (**3r**).*[25] Oil; ^{1}H NMR (250 MHz, $CDCl_3$, 25 °C): δ=7.89 (d, 2H, J=7.5 Hz), 7.16 (t, 1H, J=7.8 Hz), 6.67 (d, 2H, J=7.0 Hz), 6.55–6.58 (m, 3H), 4.65 (br s, 1H), 4.53 (d, 1H, J_{HP}=24.5 Hz), 3.66–3.91 (m, 4H), 3.40 (s, 3H), 1.02 (t, 3H, J=7.0 Hz), 0.93 (t, 3H, J=7.0 Hz); ^{13}C NMR (62.9 MHz, $CDCl_3$, 25 °C) δ=158.3, 157.2, 146.8, 146.2, 131.0, 130.5, 129.0, 127.6, 117.3, 114.0, 113.8, 63.5 (d, $^{2}J_{CP}$=6.9 Hz), 63.2 (d, $^{2}J_{CP}$=6.9 Hz), 56.2 (d, J_{CP}=151.5 Hz), 16.5 (d, $^{3}J_{CP}$=5.6 Hz), 16.2 (d, $^{3}J_{CP}$=5.6 Hz).

*4.3.22. Diethyl (4-methylphenyl) (phenylamino) methylphosphonate (**3s**).*[25] White crystalline solid, mp 64–65 °C (lit. 66–67); ^{1}H NMR (250 MHz, $CDCl_3$, 25 °C): δ=7.34–7.37 (m, 2H), 7.07–7.13 (m, 4H), 6.62 (t, 1H, J=7.2 Hz), 6.58 (d, 2H, J=7.7 Hz), 4.57 (d, 1H, J_{HP}=23.5 Hz), 4.50 (br s, 1H), 4.07–4.15 (m, 2H), 3.91–4.97 (m, 1H), 3.66–3.77 (m, 1H), 2.30 (s, 3H), 1.29 (t, 3H, J=7.0 Hz), 1.15 (t, 3H, J=6.9 Hz); ^{13}C NMR (62.9 MHz, $CDCl_3$, 25 °C) δ=146.7, 146.4, 137.4, 132.9, 129.3, 129.2, 127.9, 127.8, 118.1, 113.8, 63.2 (d, $^{2}J_{CP}$=6.9 Hz), 63.1 (d, $^{2}J_{CP}$=6.9 Hz), 56.9 (d, J_{CP}=151.0 Hz), 21.1, 16.4 (d, $^{3}J_{CP}$=5.6 Hz), 16.2 (d, $^{3}J_{CP}$=5.6 Hz).

*4.3.23. Diethyl (4-isopropylphenyl) (phenylamino) methylphospho nate (**3t**).*[26] (references do not report melting point) White crystalline solid, mp 101–102 °C; ^{1}H NMR (250 MHz, $CDCl_3$, 25 °C): δ=7.38 (d, 2H, J=7.5 Hz), 7.08–7.28 (m, 4H), 6.60–6.72 (m, 3H), 4.75 (d, 1H, J_{HP}=25.0 Hz), 4.07–4.15 (m, 2H), 3.88–3.95 (m, 1H), 3.62–3.72 (m, 1H), 2.82–2.90 (m, 1H), 1.20–1.31 (m, 9H), 1.07 (t, 3H, J=6.9 Hz); ^{13}C NMR (62.9 MHz, $CDCl_3$, 25 °C) δ=148.4, 144.1, 129.6, 128.9, 127.8, 127.5, 114.0, 63.2 (d, $^{2}J_{CP}$=6.9 Hz), 63.1 (d, $^{2}J_{CP}$=6.9 Hz), 56.7 (d, J_{CP}=152.2 Hz), 33.6, 23.8, 16.4 (d, $^{3}J_{CP}$=5.6 Hz), 16.2 (d, $^{3}J_{CP}$=5.6 Hz).

*4.3.24. Diethyl (4-chlorophenyl) (phenylamino) methylphosphonate (**3u**).*[25] White crystalline solid, mp 77–80 °C (lit. 75–76); ^{1}H NMR (250 MHz, $CDCl_3$, 25 °C): δ=7.35 (d, 2H, J=8.5 Hz), 7.21 (d, 2H, J=8.0 Hz), 7.02 (t, 2H, J=7.5 Hz), 6.62 (t, 1H, J=7.5 Hz), 6.48 (d, 2H, J=7.7 Hz), 4.65 (d, 1H, J_{HP}=24.8 Hz), 3.61–4.11 (m, 4H), 1.20 (t, 3H, J=7.0 Hz), 1.07 (t, 3H, J=6.9 Hz); ^{13}C NMR (62.9 MHz, $CDCl_3$, 25 °C) δ=146.1, 145.9, 134.6, 134.5, 133.7, 133.6, 129.2, 128.8, 128.7, 118.6, 113.8, 63.4 (d, $^{2}J_{CP}$=6.9 Hz), 63.3 (d, $^{2}J_{CP}$=6.9 Hz), 56.7 (d, J_{CP}=150.2 Hz), 16.4 (d, $^{3}J_{CP}$=5.6 Hz), 16.2 (d, $^{3}J_{CP}$=5.6 Hz).

*4.3.25. Diethyl (2-chlorophenyl) (phenylamino) methylphosphonate (**3v**).* White crystalline solid, mp 99–101 °C; R_f (AcOEt/hexane 10:90) 0.40; IR (KBr): 3332, 1604, 1434, 1249, 1026 cm^{-1}; ^{1}H NMR (250 MHz, $CDCl_3$, 25 °C): δ=7.99 (d, 1H, J=7.9 Hz), 7.76 (d, 1H, J=7.5 Hz), 7.54 (t, 1H, J=7.5 Hz), 7.44 (t, 1H, J=7.8 Hz), 7.14 (t, 2H, J=7.5 Hz), 6.69–6.75 (m, 3H), 6.15 (d, 1H, J_{HP}=24.0 Hz), 5.15 (br s, 1H), 4.14–4.20 (m, 2H), 3.79–3.95 (m, 2H), 1.30 (t, 3H, J=7.0 Hz), 1.09 (t, 3H, J=7.0 Hz); ^{13}C NMR (62.9 MHz, $CDCl_3$, 25 °C) δ=149.4, 145.4, 133.5, 133.4, 129.4, 129.2, 128.8, 125.2, 118.7, 113.5, 63.7 (d, $^{2}J_{CP}$=6.9 Hz), 63.2 (d, $^{2}J_{CP}$=6.9 Hz), 51.1 (d, J_{CP}=151.0 Hz), 48.6, 16.3 (d, $^{3}J_{CP}$=5.6 Hz), 16.0 (d, $^{3}J_{CP}$=5.6 Hz); Mass m/z (%):353 (M^{+}), 227, 180, 104; Anal. Calcd for $C_{17}H_{21}ClNO_3P$ (353): C, 57.71; H, 5.98. Found: C, 57.99; H, 5.89.

*4.3.26. Diethyl (2,6-dichlorophenyl) (phenylamino) methylphosphonate (**3w**).*[27] (references do not report melting point) White crystalline solid, mp 74–76 °C; ^{1}H NMR (250 MHz, $CDCl_3$, 25 °C): δ=7.19 (d, 1H, J=8.9 Hz), 6.91–7.02 (m, 4H), 6.53–6.56 (m, 3H), 5.85 (d, 1H, J_{HP}=24.5 Hz), 5.16 (br s, 1H), 4.05–4.14 (m, 2H), 3.92–3.95 (m, 1H), 3.76–3.79 (m, 1H), 1.21 (t, 3H, J=7.0 Hz), 1.01 (t, 3H, J=6.9 Hz); ^{13}C NMR (62.9 MHz, $CDCl_3$, 25 °C) δ=145.8, 145.5, 136.7, 136.6, 134.7, 131.4, 130.3, 129.2, 128.7, 118.7, 113.4, 112.9, 63.3 (d, $^{2}J_{CP}$=6.9 Hz), 63.0 (d, $^{2}J_{CP}$=6.9 Hz), 54.3 (d, J_{CP}=151.0 Hz), 16.4 (d, $^{3}J_{CP}$=5.6 Hz), 16.1 (d, $^{3}J_{CP}$=5.6 Hz).

*4.3.27. Diethyl (4-nitrophenyl) (phenylamino) methylphosphonate (**3x**).*[25] Yellow crystalline solid, mp 126–127 °C (lit. 125–126); ^{1}H NMR (250 MHz, $CDCl_3$, 25 °C): δ=8.09 (d, 2H, J=8.8 Hz), 7.55–7.61 (m, 2H), 7.01 (t, 2H, J=7.5 Hz), 6.62 (t, 1H, J=7.7 Hz), 6.45 (d, 2H, J=7.8 Hz), 4.87 (br s, 1H), 4.80 (d, 1H, J_{HP}=25.0 Hz), 3.72–4.14 (m, 4H), 1.20 (t, 3H, J=7.0 Hz), 1.09 (t, 3H, J=6.9 Hz); ^{13}C NMR (62.9 MHz, $CDCl_3$, 25 °C) δ=147.5, 145.8, 144.1, 129.3, 128.7, 128.6, 118.9, 113.7, 63.8 (d, $^{2}J_{CP}$=6.9 Hz), 63.5 (d, $^{2}J_{CP}$=6.9 Hz), 57.0 (d, J_{CP}=148.3 Hz), 16.4 (d, $^{3}J_{CP}$=5.6 Hz), 16.2 (d, $^{3}J_{CP}$=5.6 Hz).

*4.3.28. Diethyl (3-nitrophenyl) (phenylamino) methylphosphonate (**3y**).*[25] Yellow crystalline solid, mp 98–99 °C (lit. 95–97); ^{1}H NMR (250 MHz, $CDCl_3$, 25 °C): δ=8.29 (s, 1H), 8.05 (d, 1H, J=9.5 Hz), 7.76 (d, 1H, J=7.7 Hz), 7.40 (t, 1H, J=7.5 Hz), 7.01 (t, 2H, J=7.8 Hz), 6.48–6.65 (m, 3H), 5.46 (br s, 1H), 4.82 (d, 1H, J_{HP}=24.8 Hz), 3.73–4.15 (m, 4H), 1.20 (t, 3H, J=7.0 Hz), 1.09 (t, 3H, J=7.0 Hz); ^{13}C NMR (62.9 MHz, $CDCl_3$, 25 °C) δ=148.4, 145.8, 145.6, 138.9, 138.8, 133.9, 133.8, 129.2, 122.9, 122.8, 118.8, 113.7, 63.8 (d, $^{2}J_{CP}$=6.9 Hz), 63.4 (d, $^{2}J_{CP}$=6.9 Hz), 56.7 (d, J_{CP}=150.1 Hz), 16.4 (d, $^{3}J_{CP}$=5.6 Hz), 16.2 (d, $^{3}J_{CP}$=5.6 Hz).

*4.3.29. Diethyl (2-nitrophenyl) (phenylamino) methylphosphonate (**3z**).*[25] Yellow crystalline solid, mp 155–157 °C (lit. 155–156); ^{1}H NMR (250 MHz, $CDCl_3$, 25 °C): δ=8.00 (d, 1H, J=7.7 Hz), 7.70–7.73 (m, 1H), 7.43 (t, 1H, J=7.9 Hz), 7.13 (t, 2H, J=7.5 Hz), 6.66–6.75 (m, 3H), 5.27 (d, 1H, J_{HP}=23.5 Hz), 4.56 (br s, 1H), 4.14–4.20 (m, 2H), 3.82–3.96 (m, 2H), 1.30 (t, 3H, J=7.0 Hz), 1.09 (t, 3H, J=7.0 Hz); ^{13}C NMR (62.9 MHz, $CDCl_3$, 25 °C) δ=149.3, 145.5, 133.5, 133.4, 131.9, 129.4, 128.8, 125.2, 113.5, 63.7 (d, $^{2}J_{CP}$=6.9 Hz), 63.3 (d, $^{2}J_{CP}$=6.9 Hz), 51.0 (d, J_{CP}=151.0 Hz), 16.4 (d, $^{3}J_{CP}$=5.6 Hz), 16.2 (d, $^{3}J_{CP}$=5.6 Hz).

*4.3.30. Diethyl (phenylamino) (thiophen-2-yl) methylphosphonate (**3aa**).*[27] Off white semisolid, ^{1}H NMR (250 MHz, $CDCl_3$, 25 °C): δ=6.98–7.08 (m, 4H), 6.82 (t, 1H, J=4.5 Hz), 6.55–6.64 (m, 3H), 4.95

Please cite this article in press as: Sharghi, H.; et al., Tetrahedron (2013), http://dx.doi.org/10.1016/j.tet.2013.03.073

(d, 1H, J_{HP}=24.8 Hz), 4.72 (br s, 1H), 3.67–4.14 (m, 4H), 1.14 (t, 3H, J=7.0 Hz), 1.06 (t, 3H, J=6.9 Hz); ^{13}C NMR (62.9 MHz, $CDCl_3$, 25 °C) δ=146.3, 139.9, 129.2, 127.1, 126.2, 125.3, 125.2, 118.8, 113.9, 63.6 (d, $^2J_{CP}$=6.9 Hz), 63.4 (d, $^2J_{CP}$=6.9 Hz), 53.2 (d, J_{CP}=157.1 Hz), 16.5 (d, $^3J_{CP}$=5.6 Hz), 16.3 (d, $^3J_{CP}$=5.6 Hz).

*4.3.31. Diethyl furan-2-yl(phenylamino) methylphosphonate (**3ab**).*[27] Off white semisolid; ^{1}H NMR (250 MHz, $CDCl_3$, 25 °C): δ=7.28 (s, 1H), 7.05 (t, 2H, J=7.5 Hz), 6.56–6.68 (m, 3H), 6.21–6.31 (m, 2H), 4.82 (d, 1H, J_{HP}=24.8 Hz), 4.24 (br s, 1H), 3.72–4.12 (m, 4H), 1.20 (t, 3H, J=7.0 Hz), 1.11 (t, 3H, J=6.9 Hz); ^{13}C NMR (62.9 MHz, $CDCl_3$, 25 °C) δ=149.3, 146.1, 145.9, 142.4, 129.1, 118.8, 113.9, 110.8, 110.7, 108.2, 108.7, 63.5 (d, $^2J_{CP}$=6.9 Hz), 63.3 (d, $^2J_{CP}$=6.9 Hz), 51.4 (d, J_{CP}=159.1 Hz), 16.4 (d, $^3J_{CP}$=5.6 Hz), 16.2 (d, $^3J_{CP}$=5.6 Hz).

*4.3.32. Diethyl anthracen-10-yl (phenylamino) methylphosphonate (**3ac**).* Pale brown crystalline solid, mp 159–160 °C; R_f (AcOEt/hexane 10:90) 0.35; IR (KBr): 3294, 1604, 1496, 1242, 1110 cm^{-1}; ^{1}H NMR (250 MHz, $CDCl_3$, 25 °C): δ=9.11 (d, 1H, J=9.0 Hz), 8.53 (d, 1H, J=9.2 Hz), 8.43 (s, 1H), 8.05 (d, 1H, J=8.3 Hz), 7.95 (d, 1H, J=8.5 Hz), 7.59–7.44 (m, 4H), 6.98 (t, 2H, J=7.7), 6.53–6.61 (m, 3H), 6.42 (d, 1H, J_{HP}=27.0 Hz), 5.21 (br s, 1H), 4.22–4.34 (m, 2H), 3.71–3.80 (m, 1H), 3.28–3.32 (m, 1H), 1.38 (t, 3H, J=7.0 Hz), 0.69 (t, 3H, J=7.0 Hz); ^{13}C NMR (62.9 MHz, $CDCl_3$, 25 °C) δ=147.1, 146.9, 131.9, 130.5, 129.8, 129.1, 128.9, 127.8, 126.7, 125.1, 124.7, 122.7, 116.1, 113.4, 63.4 (d, $^2J_{CP}$=6.9 Hz), 63.0 (d, $^2J_{CP}$=6.9 Hz), 54.1 (d, J_{CP}=152.8 Hz), 16.6 (d, $^3J_{CP}$=5.6 Hz), 15.8 (d, $^3J_{CP}$=5.6 Hz); Mass m/z (%): 419 (M^+), 282, 104, 57; Anal. Calcd for $C_{25}H_{26}NO_3P$ (419): C, 71.59; H, 6.25. Found: C, 71.75; H, 6.17.

*4.3.33. Diethyl 1-(phenylamino) butylphosphonate (**3ad**).*[6b] Oil; ^{1}H NMR (250 MHz, $CDCl_3$, 25 °C): δ=7.08 (t, 2H, J=8.5 Hz), 6.56–6.68 (m, 3H), 3.87–4.08 (m, 4H), 3.60–3.65 (m, 2H), 1.50–1.93 (m, 4H), 1.08–1.30 (m, 6H), 0.85 (t, 3H, J=6.9 Hz); ^{13}C NMR (62.9 MHz, $CDCl_3$, 25 °C) δ=147.3, 129.2, 117.8, 113.2, 62.7 (d, $^2J_{CP}$=6.9 Hz), 61.8 (d, $^2J_{CP}$=6.9 Hz), 51.9 (d, J_{CP}=156.3 Hz), 32.8, 19.3, 19.1, 16.5 (d, $^3J_{CP}$=5.6 Hz), 16.3 (d, $^3J_{CP}$=5.6 Hz), 13.8.

*4.3.34. Diethyl (isobutylaldehyde) (phenylamino) methylphosphonate (**3ae**).*[25] Oil; ^{1}H NMR (250 MHz, $CDCl_3$, 25 °C): δ=7.72 (t, 2H, J=7.5 Hz), 6.56–6.63 (m, 3H), 3.86–4.04 (m, 5H), 3.56 (d, 1H, J_{HP}=17.8 Hz), 2.12–2.23 (m, 1H), 1.93 (t, 3H, J=7.0 Hz), 0.97–1.10 (m, 9H); ^{13}C NMR (62.9 MHz, $CDCl_3$, 25 °C) δ=147.7, 129.2, 119.8, 117.7, 113.2, 62.7 (d, $^2J_{CP}$=6.9 Hz), 61.8 (d, $^2J_{CP}$=6.9 Hz), 57.3 (d, J_{CP}=151.3 Hz), 29.8 (d, $^2J_{CP}$=5.8 Hz), 20.7 (d, $^3J_{CP}$=12.3 Hz), 18.0 (d, $^3J_{CP}$=4.5 Hz), 16.4 (d, $^3J_{CP}$=5.6 Hz), 16.3 (d, $^3J_{CP}$=5.6 Hz).

*4.3.35. Diethyl 1-(phenylamino) cyclohexylphosphonate (**3af**).*[6b] Colorless crystalline solid, mp 98–99 °C (lit. 104 °C); ^{1}H NMR (250 MHz, $CDCl_3$, 25 °C): δ=7.09 (t, 2H, J=7.5 Hz), 6.96 (d, 2H, J=8.6 Hz), 6.72 (t, 1H, J=7.4 Hz), 3.91–4.02 (m, 4H), 3.38 (br s, 1H), 2.09–2.12 (m, 2H), 1.40–1.75 (m, 8H), 1.14–1.19 (m, 6H); ^{13}C NMR (62.9 MHz, $CDCl_3$, 25 °C) δ=145.8, 128.7, 119.3, 118.4, 62.1 (d, $^2J_{CP}$=6.9 Hz), 62.0 (d, $^2J_{CP}$=6.9 Hz), 58.4 (d, J_{CP}=161.2 Hz), 30.2, 25.3, 19.9 (d, $^2J_{CP}$=11.1 Hz), 16.5 (d, $^3J_{CP}$=5.6 Hz), 16.4 (d, $^3J_{CP}$=5.6 Hz).

*4.3.36. Diethyl 3,3-dimethyl-2-(phenylamino)butan-2-ylphosphonate (**3ag**).*[6b] Colorless oil; ^{1}H NMR (250 MHz, $CDCl_3$, 25 °C): δ=7.02 (d, 2H, J=7.5 Hz), 6.81 (t, 2H, J=7.5 Hz), 6.42 (d, 2H, J=7.4 Hz), 3.98–4.12 (m, 4H), 3.85 (br s, 1H), 1.89 (d, 3H, J=10.4 Hz), 1.23–1.27 (m, 6H), 1.19 (s, 9H); ^{13}C NMR (62.9 MHz, $CDCl_3$, 25 °C) δ=149.8, 129.9, 119.5, 117.4, 71.8 (d, J_{CP}=155.2 Hz), 63.1 (d, $^2J_{CP}$=6.9 Hz), 62.9 (d, $^2J_{CP}$=6.9 Hz), 30.7, 28.6, 18.5, 16.5 (d, $^3J_{CP}$=5.6 Hz), 16.4 (d, $^3J_{CP}$=5.6 Hz).

*4.3.37. 2-Benzylidenemalononitrile (**4a**).*[29] Yellow solid, mp 83–85 °C (lit. 83); ^{1}H NMR (250 MHz, $CDCl_3$, 25 °C): δ=7.89 (d, 2H, J=7.6 Hz), 7.85 (s, 1H), 7.30–7.65 (m, 3H); ^{13}C NMR (62.9 MHz, $CDCl_3$, 25 °C) δ=160.2, 134.8, 130.8, 129.8, 129.0, 113.7, 112.4, 83.0.

*4.3.38. 2-(4-Methylbenzylidene)malononitrile (**4b**).*[31] Yellow crystalline solid, mp 134–135 C (lit. 131); ^{1}H NMR (250 MHz, $CDCl_3$, 25 °C): δ=7.79 (d, 2H, J=8.2 Hz), 7.72 (s, 1H), 7.46 (d, 2H, J=9.8 Hz), 2.47 (s, 3H), ^{13}C NMR (62.9 MHz, $CDCl_3$, 25 °C) δ=159.5, 147.1, 130.7, 130.1, 113.5, 112.7, 83.5, 22.0.

*4.3.39. 2-(4-Methoxybenzylidene)malononitrile (**4d**).*[30] Yellow crystalline solid, mp 115–117 C (lit. 119); ^{1}H NMR (250 MHz, $CDCl_3$, 25 °C): δ=7.94 (d, 2H, J=8.8 Hz), 7.57 (s, 1H), 7.03 (d, 2H, J=8.5 Hz), 3.88 (s, 3H), ^{13}C NMR (62.9 MHz, $CDCl_3$, 25 °C) δ=158.8, 133.4, 124.0, 115.1, 114.4, 55.8.

*4.3.40. 2-(4-Chlorobenzylidene)malononitrile (**4e**).*[30] Pale yellow crystalline solid, mp 166–167 °C (lit. 165); ^{1}H NMR (250 MHz, $CDCl_3$, 25 °C): δ=7.81 (d, 2H, J=8.2 Hz), 7.71 (s, 1H), 7.50 (d, 2H, J=8.5 Hz), ^{13}C NMR (62.9 MHz, $CDCl_3$, 25 °C) δ=158.1, 141.3, 131.9, 130.0, 129.3, 113.3, 112.2, 83.3.

*4.3.41. 2-(2-Chlorobenzylidene) malononitrile (**4f**).*[32] Pale yellow crystalline solid, mp 95–96 °C (lit. 95.5); ^{1}H NMR (250 MHz, $CDCl_3$, 25 °C): δ=8.26 (s, 1H), 8.19 (d, 1H, J=7.8 Hz), 7.26–7.59 (m, 3H), ^{13}C NMR (62.9 MHz, $CDCl_3$, 25 °C) δ=149.6, 148.0, 143.1, 123.7, 114.4, 113.8, 81.2.

*4.3.42. 2-(3-Chlorobenzylidene)malononitrile (**4g**).*[31] Oil; ^{1}H NMR (250 MHz, $CDCl_3$, 25 °C): δ=7.75–7.87 (m, 1H), 7.53 (s, 1H), 7.39–7.52 (m, 1H), 7.19 (s, 1H); ^{13}C NMR (62.9 MHz, $CDCl_3$, 25 °C) δ=158.3, 134.1, 130.4, 128.3, 112.2, 111.2, 80.0.

*4.3.43. 2-(4-Nitrobenzylidene)malononitrile (**4h**).*[33] Yellow solid, mp 159–160 °C (lit. 158–159), ^{1}H NMR (250 MHz, $CDCl_3$, 25 °C): δ=7.94 (d, 2H, J=7.8 Hz), 7.71 (s, 1H), 7.00 (d, 2H, J=7.5 Hz), ^{13}C NMR (62.9 MHz, DMSO-d_6, 25 °C) δ=160.0, 150.0, 136.3, 130.9, 124.6, 112.2, 85.5.

*4.3.44. 2-(2-Furylmethylidene)malononitrile (**4i**).*[34] Yellow solid, mp 69–70 °C (lit. 67–68); ^{1}H NMR (250 MHz, $CDCl_3$, 25 °C): δ=7.87 (s, 1H), 7.59 (d, 1H, J=2.5), 7.35 (d, 1H, J=3.9 Hz), 6.43 (t, 1H, J=3.8 Hz), ^{13}C NMR (62.9 MHz, $CDCl_3$, 25 °C) δ=149.3, 146.1, 144.1, 122.5, 114.0, 113.2, 111.5, 77.1.

*4.3.45. 2-(2-Thienylmethylidene)malononitrile (**4j**).*[34] Yellow solid, mp 90–93 °C (lit. 91–92); ^{1}H NMR (250 MHz, $CDCl_3$, 25 °C): δ=7.77–7.89 (m, 3H), 7.26–7.34 (m, 1H); ^{13}C NMR (62.9 MHz, $CDCl_3$, 25 °C) δ=150.2, 138.5, 137.0, 128.9, 120.2, 118.3, 81.9.

*4.3.46. 2-(4-Pyridylmethylidene)malononitrile (**4k**).*[34] Yellow solid, mp 75–76 °C (lit. 78–80); ^{1}H NMR (250 MHz, $CDCl_3$, 25 °C): δ=8.87 (m, 2H, J=7.4 Hz), 7.82 (s, 1H), 7.70 (d, 2H, J=7.3 Hz); ^{13}C NMR (62.9 MHz, $CDCl_3$, 25 °C) δ=156.1, 157.3, 151.2, 137.2, 122.7, 112.3, 111.4, 88.3.

*4.3.47. Diethyl 2,2-dicyano-1-phenylethylphosphonate (**5a**).*[28] Yellow solid, mp 53–54 °C (lit. 56–58); ^{1}H NMR (250 MHz, $CDCl_3$, 25 °C): δ=7.34–7.40 (m, 5H), 4.60 (t, 1H, J=7.9 Hz), 4.05–4.12 (m, 4H), 3.87–3.94 (m, 2H), 3.54 (dd, 1H, J_1=7.9, J_2=21.5 Hz), 1.29 (t, 3H, J=7.1 Hz), 1.13 (t, 3H, J=7.1 Hz); ^{13}C NMR (62.9 MHz, $CDCl_3$, 25 °C) δ=130.4, 129.4, 129.2, 128.8, 111.6, 111.4, 64.3 (d, $^2J_{CP}$=7.1 Hz), 63.4 (d, $^2J_{CP}$=7.2 Hz), 45.7 (d, J_{CP}=144.4 Hz), 25.6, 16.3 (d, $^3J_{CP}$=5.9 Hz), 16.1 (d, $^3J_{CP}$=5.7 Hz).

*4.3.48. Diethyl 2,2-dicyano-1-p-tolylethylphosphonate (**5b**).*[28] Yellow solid, mp 93–95 °C (lit. 88–90); ^{1}H NMR (250 MHz,

$CDCl_3$, 25 °C): δ=7.26 (d, 2H, *J*=8.3 Hz), 7.19 (d, 2H, *J*=7.2 Hz), 4.42 (t, 1H, *J*=8.4 Hz), 4.05–4.13 (m, 3H), 3.92–3.95 (m, 1H), 3.47 (dd, 1H, J_1=8.0, J_2=21.5 Hz), 2.29 (s, 3H), 1.28 (t, 3H, *J*=7.0 Hz), 1.05 (t, 3H, *J*=7.0 Hz); ^{13}C NMR (62.9 MHz, $CDCl_3$, 25 °C) δ=140.2, 130.2, 129.1, 129.0, 126.5, 111.2, 111.0, 64.4 (d, $^2J_{CP}$=7.1 Hz), 63.3 (d, $^2J_{CP}$=7.2 Hz), 45.4 (d, J_{CP}=144.4 Hz), 25.7, 21.2, 16.3 (d, $^3J_{CP}$=5.9 Hz), 16.1 (d, $^3J_{CP}$=5.7 Hz).

*4.3.49. Diethyl 2,2-dicyano-1-m-tolylethyl phosphonate (**5c**).*[28] Yellow solid, mp 55–56 °C (lit. 56–57); ^{1}H NMR (250 MHz, $CDCl_3$, 25 °C): δ=7.15–7.39 (m, 4H, *J*=8.3 Hz), 4.52 (t, 1H, *J*=7.8 Hz), 4.05–4.12 (m, 2H), 3.69–3.94 (m, 2H), 3.48 (dd, 1H, J_1=8.2, J_2=21.4 Hz), 2.28 (s, 3H), 1.27 (t, 3H, *J*=7.0 Hz), 1.01 (t, 3H, *J*=7.0 Hz); ^{13}C NMR (62.9 MHz, $CDCl_3$, 25 °C) δ=139.1, 130.3, 130.2, 129.9, 129.2, 126.2, 111.5, 111.4, 64.3 (d, $^2J_{CP}$=7.1 Hz), 63.3 (d, $^3J_{CP}$=7.2 Hz), 45.6 (d, J_{CP}=144.9 Hz), 25.5, 21.5, 16.2 (d, $^3J_{CP}$=5.9 Hz), 16.0 (d, $^3J_{CP}$=5.6 Hz).

*4.3.50. Diethyl 2,2-dicyano-1-(4-methoxyphenyl) ethyl phosphonate (**5d**).*[28] Yellow solid, mp 60–62 °C (lit. 57–58); ^{1}H NMR (250 MHz, DMSO-d_6, 25 °C): δ=7.13–7.17 (m, 2H), 6.74–6.79 (m, 2H), 3.68–3.82 (m, 5H), 3.67 (s, 1H), 0.96–1.20 (m, 6H); ^{13}C NMR (62.9 MHz, DMSO-d_6, 25 °C) δ=172.2, 129.9, 129.8, 122.3, 115.9, 113.3, 58.7 (d, J_{CP}=144.7 Hz), 55.7, 25.5, 16.3 (d, $^3J_{CP}$=5.9 Hz), 16.2 (d, $^3J_{CP}$=5.7 Hz).

*4.3.51. Diethyl 1-(4-chlorophenyl)-2,2-dicyanoethyl phosphonate (**5e**).*[28] Yellow solid, mp 93–95 °C (lit. 94–96); ^{1}H NMR (250 MHz, $CDCl_3$, 25 °C): δ=7.28–7.40 (m, 4H), 4.48 (t, 1H, *J*=8.0 Hz), 3.93–4.14 (m, 4H), 3.49 (dd, 1H, J_1=7.6, J_2=22.1 Hz), 1.31 (t, 3H, *J*=7.0 Hz), 1.13 (t, 3H, *J*=7.0 Hz); ^{13}C NMR (62.9 MHz, $CDCl_3$, 25 °C) δ=138.7, 130.3, 129.8, 128.6, 111.2, 111.0, 64.5 (d, $^2J_{CP}$=7.0 Hz), 63.6 (d, $^2J_{CP}$=7.1 Hz), 45.1 (d, J_{CP}=144.9 Hz), 25.4, 16.2 (d, $^3J_{CP}$=5.9 Hz), 16.2 (d, $^3J_{CP}$=5.6 Hz).

*4.3.52. Diethyl 1-(2-chlorophenyl)-2,2-dicyanoethyl phosphonate (**5f**).*[8a] Yellow solid, mp 75–77 °C (lit. 77); ^{1}H NMR (250 MHz, $CDCl_3$, 25 °C): δ=7.75 (d, 1H, *J*=7.5 Hz), 7.46–7.50 (m, 1H), 7.32–7.36 (m, 2H), 4.63 (t, 1H, *J*=8.5 Hz), 4.45 (dd, 1H, J_1=7.5, J_2=22.5 Hz), 4.05–4.28 (m, 2H), 3.89–3.98 (m, 1H), 3.71–3.81 (m, 1H), 1.35 (t, 3H, *J*=7.2 Hz), 1.10 (t, 3H, *J*=7.2 Hz); ^{13}C NMR (62.9 MHz, $CDCl_3$, 25 °C) δ=135.0, 130.5, 130.3, 129.6, 128.6, 127.7, 111.2, 111.0, 64.4 (d, $^2J_{CP}$=7.1 Hz), 63.6 (d, $^2J_{CP}$=7.2 Hz), 40.5 (d, $^2J_{CP}$=144.8 Hz), 24.8, 16.2 (d, $^3J_{CP}$=5.9 Hz), 16.0 (d, $^3J_{CP}$=5.7 Hz).

*4.3.53. Diethyl 1-(3-chlorophenyl)-2,2-dicyano ethyl phosphonate (**5g**).*[8a] Yellow oil; ^{1}H NMR (250 MHz, $CDCl_3$, 25 °C): δ=7.77 (s, 1H), 7.19–7.38 (m, 3H), 4.63 (t, 1H, *J*=8.5 Hz), 4.05–4.15 (m, 4H), 3.65 (dd, 1H, J_1=7.0, J_2=21.5 Hz), 1.27 (t, 3H, *J*=7.1 Hz), 1.09 (t, 3H, *J*=7.1 Hz); ^{13}C NMR (62.9 MHz, $CDCl_3$, 25 °C) δ=139.2, 130.3, 129.9, 129.1, 111.5, 111.4, 64.3 (d, $^2J_{CP}$=7.1 Hz), 63.3 (d, $^2J_{CP}$=7.2 Hz), 45.6 (d, J_{CP}=144.4 Hz), 25.5, 16.2 (d, $^3J_{CP}$=5.9 Hz), 16.0 (d, $^3J_{CP}$=5.6 Hz).

*4.3.54. Diethyl 2,2-dicyano-1-(4-nitrophenyl) ethyl phosphonate (**5h**).*[8c] (references do not report melting point) Yellow solid, mp 104–105 °C; ^{1}H NMR (250 MHz, $CDCl_3$, 25 °C): δ=8.59 (d, 2H, *J*=7.0 Hz), 7.66 (d, 2H, *J*=7.0 Hz), 4.63 (t, 1H, *J*=8.9 Hz), 4.11–4.17 (m, 4H), 3.70 (dd, 1H, J_1=7.5, J_2=22.3 Hz), 1.31 (t, 3H, *J*=7.0 Hz), 1.14 (t, 3H, *J*=7.0 Hz); ^{13}C NMR (62.9 MHz, $CDCl_3$, 25 °C) δ=137.2, 131.4, 130.6, 130.5, 124.4, 123.9, 110.4, 64.7 (d, $^2J_{CP}$=7.1 Hz), 64.2 (d, $^2J_{CP}$=7.2 Hz), 45.3 (d, $^3J_{CP}$=144.2 Hz), 25.4, 16.2 (d, $^3J_{CP}$=5.8 Hz), 16.1 (d, $^3J_{CP}$=5.6 Hz).

*4.3.55. Diethyl 2,2-dicyano-1-(furan-2-yl) ethyl phosphonate (**5i**).*[8a] Brown oil; ^{1}H NMR (250 MHz, $CDCl_3$, 25 °C): δ=7.74 (s, 1H), 7.29 (s, 1H), 6.65 (s, 1H), 4.63 (t, 1H, *J*=8.2 Hz), 4.40 (dd, 1H, J_1=7.5, J_2=24.5 Hz), 3.74–4.24 (m, 4H), 1.35 (t, 3H, *J*=7.0 Hz), 1.10 (t, 3H, *J*=7.1 Hz); ^{13}C NMR (62.9 MHz, $CDCl_3$, 25 °C) δ=149.5, 147.9, 123.7, 113.7, 112.5, 64.3 (d, $^3J_{CP}$=7.1 Hz), 63.8 (d, $^3J_{CP}$=7.2 Hz), 40.4 (d, J_{CP}=147.6 Hz), 26.7, 16.4 (d, $^3J_{CP}$=5.3 Hz), 16.2 (d, $^3J_{CP}$=5.2 Hz).

*4.3.56. Diethyl 2,2-dicyano-1-(thiophen-2-yl) ethyl phosphonate (**5j**).*[8c] Brown oil; ^{1}H NMR (250 MHz, $CDCl_3$, 25 °C): δ=7.25–7.31 (m, 2H), 7.01 (t, 1H, *J*=4.5 Hz), 4.44 (t, 1H, *J*=8.5 Hz), 4.08–4.16 (m, 4H), 3.91 (dd, 1H, J_1=7.5, J_2=22.3 Hz), 1.28 (t, 1H, *J*=7.1 Hz), 1.09 (t, 1H, *J*=7.1 Hz); ^{13}C NMR (62.9 MHz, $CDCl_3$, 25 °C) δ=140.8, 136.6, 129.5, 127.7, 111.2, 111.0, 64.6 (d, $^2J_{CP}$=7.1 Hz), 63.9 (d, $^2J_{CP}$=7.3 Hz), 41.3 (d, J_{CP}=148.2 Hz), 26.7, 16.3 (d, $^3J_{CP}$=5.1 Hz), 16.1 (d, $^3J_{CP}$=5.0 Hz).

Acknowledgements

We gratefully acknowledge the support of this work by the Shiraz University Research Council.

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Please cite this article in press as: Sharghi, H.; et al., Tetrahedron (2013), http://dx.doi.org/10.1016/j.tet.2013.03.073