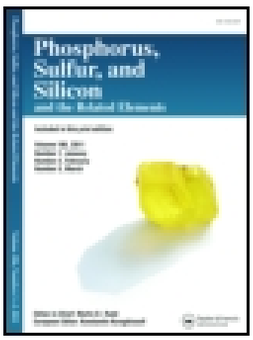

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A domino Knoevenagel-phospha-Michael reaction: one-pot synthesis of novel organophosphonates in the presence of multi-walled carbon nanotube-CO-NH$(CH_2)_2$NH-SO_3H as catalyst

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Abstract: We report a one-pot method for the synthesis of various substituted 1,3-dimethyl-2,4,6-trioxohexahydropyrimidin-5-yl phosphonate derivatives via phosphorus-carbon bond formation through domino Knoevenagel–phospha–Michael reaction. Multi-walled carbon nanotube-CO-NH$(CH_2)_2$NH-SO_3H was used as an acidic heterogeneous catalyst. The catalyst could be used four times without losing its catalytic activity. The structures of the products were determined by FT-IR spectra, ^{1}H-, ^{13}C- and ^{31}P- Nuclear Magnetic Resonance and elemental analysis. Recovery and reusability of catalyst, simplicity, applicability, good reaction time and good yields of products are the benefits of this work.

Keywords: domino Knoevenagel–phospha–Michael reaction, organophosphonates, triethylphosphite, 3,3-dimethyl barbituric acid, multi-walled carbon nanotube-CO-NH$(CH_2)_2$NH-SO_3H, heterogeneous catalyst

Introduction

Barbituric acid and its derivatives have a special place in medicinal chemistry. A literature survey shows that chemical compounds containing barbituric acid ring have biological activity such as hypnotic,[1] anaesthetic,[2] anticonvulsant,[3] antibacterial,[4] anticancer and antitumor properties.[5] In addition, this ring was used in structure of dye-sensitized solar-cells.[6] On the other hand, organophosphorus compounds are one of the most important

organic compounds that are present in human body and animals.[7] In this family, phosphonic acids and their derivatives have attracted considerable attention from organic chemists. There are many reports in literature for biological activity [8,9] and applications of phosphonic acid derivatives in industry, agriculture and medicinal chemistry.[10-14] Nowadays, multi-component reactions play an essential role in organic synthesis.[15] Domino Knoevenagel-phospho-Michael reaction is the most famous multi-component reactions for P-C bond formation.[16] Despite the extensive range of investigations on the synthesis of various types of organic phosphonates,[17] In continued our research in preparation of new phosphonates,[18] we decided to employ the domino Knoevenagel–phospha–Michael route for the synthesis of new organophosphonates by reaction between aromatic aldehydes, 3,3-dimethyl barbituric acid, triethylphosphite using multi-walled carbon nanotube-CO-NH$(CH_2)_2$NH-SO_3H as a catalyst. Lately this catalyst was synthesized and identified by our research team and was used as adsorbent for the removal of the dye from water.[19] Carbon nanotubes (CNTs) have been considered in science and technology due to simplicity and ease of synthesis. These nanostructures have the novel properties such as high surface area, good stiffness, and resilience.[20] Carbon nanotubes have the variety of applications in the area of microelectronics/nanoelectronics,[21] spintronics,[22] optics,[23] biotechnology and biomedicine.[24]These compounds are also very important in chemistry, for example, CNTs are one of the best materials for air filters,[25] water filters,[26] chemical Nanowires, [27] sensors,[28] adsorbents for the removal of dyes and metal ions in waste[29] and catalytic activity.[30]

Results and discussions

We studied the reaction between 4-nitrobenzaldehyde (1mmol), 3,3-dimethylbarbituric acid (1 mmol) and triethylphosphite (1.1 mmol) in the presence of multi-walled carbon nanotube-CO-NH$(CH_2)_2$NH-SO_3H as a catalyst. The model reaction was optimized by various experimental parameters such as solvent, temperature, reaction time and catalyst (Table 1). A mixture of products were formed in aprotic solvents such as dichloromethane, dichloroethane and dimethyl sulfoxide at room temperature (Table 1, Entries 3, 5, 6 and 10). The number of products decreased with increasing the temperature. For example, Knoevenagel product (**3a**) is the major product in halogenated solvents (Table 1, Entries 4 and 10) and minor product under solvent-free conditions (Table 1, Entries 1 and 2). On the other, one product was formed in ethanol (Table 1, Entries 7 and 8). A comparison between these results show that the use of ethanol as solvent is more suitable than the other solvents and solvent-free

conditions. The change in temperature from room temperature to 78°C increased isolated yield (from 87 to 99 %, Entries 7 and 8, Table 1) and decreased reaction time (from 1 h to 45 min., Entries 7 and 8, Table 1). Finally, decreasing the amount of catalyst decrease isolated yield and increase reaction time (Table 1, Entries 11 and 12). So, the optimal conditions were chpsen from entry 8 in Table 1.

With these optimized results in hand, we expanded the current method for the synthesis of other organophosphonates. For this purpose, a range of different aromatic aldehydes were reacted with 3,3-dimethyl barbituric acid and triethylphosphite in the presence of 0.75 mol of nano catalyst at reflux temperature in ethanol (Scheme 1, Table 2).

According to Table 2, various substituted 1,3-dimethyl-2,4,6-trioxohexahydropyrimidin-5-yl phosphonate derivatives (**2a-i**) with electron-donating and electron-withdrawing groups were synthesized from good to excellent yields. The highest yield was obtained with 4-nitro benzaldehyde, **1a** (Entry 1) and diethyl ((1,3-dimethyl-2,4,6-trioxohexahydropyrimidin-5-yl) (*p*-tolyl)methyl)phosphonate, **2i**, was detected with the lowest yield (Entry 9). Under the reaction conditions, 5-bromo-2-hydroxybenzaldehyde, **1c**, and 2-hydroxy-5-nitro benzaldehyde, **1d,** (Entries 3 and 4) converted to desired products and ring closing products were not formed. Some of *ortho*-substituted aldehydes (Entries 5 and 7) was generated of trace amount of Knoevenagel products (**3e** and **3g**).

After the centrifution of the reaction mixture, heterogeneous nanocatalyst was precipitated. This catalyst was dried and reused in the same reaction. Multi-walled carbon nanotube-CO-$NH(CH_2)_2NH$-SO_3H was used four times without losing catalytic activity. The results have shown in Table S 1 (Supplemental Materials).

Briefly, a one-pot route was introduced for the synthesis of various substituted 1,3-dimethyl-2,4,6-trioxohexahydropyrimidin-5-yl phosphonate derivatives via domino-Knoevenagel-phospha-Michael reaction between aromatic aldehydes, 3,3-dimethyl barbituric acid and triethyl phosphite catalyzed by multi-walled carbon nanotube-CO-$NH(CH_2)_2NH$-SO_3H as new heterogenous nanocatalyst. The benefits of this reaction include: recyclability and reusability of catalyst, simplicity, applicability, good reaction time and good yields of products.

Experimental

The chemical materials were supplied from Merck Chemical Company. Multi-walled carbon nanotube was supplied by Industrial Research Institute of Tehran with the following characteristics: inner diameter, 3.8 nm; outer diameter, 10-30 nm; length, 10 μm, purity 99%; special surface, 270 m^2g^{-1} and thermal conductivity 1500 $Wm^{-1}k^{-1}$. Nuclear Magnetic Resonance spectra were recorded on Ultra shield Bruker 400 and Bruker Avance 250. Melting points were determined in open capillary tubes in a Büchi-545 circulating oil melting point. Elemental analysis were recorded on a vario EL automated analyzer, model 11086109. The Supplemental Materials contains sample ^{1}H, ^{13}C and ^{31}P NMR spectra of products 2 (Figures S 1 – S 27).

General procedure for the synthesis of 1,3-dimethyl-2,4,6-trioxohexahydropyrimidin-5-yl phosphonate derivatives (2a-i)

Nano catalyst (0.75 mol) was added to a mixture of aldehyde (1 mmol), 3,3-dimethyl barbituric acid (1 mmol) and triethylphosphite (1.1 mmol) in 3 mL of ethanol. The reaction mixture was stirred at 78°C for the appropriate time according to Table 2. The progress of the reaction was monitored by TLC (eluent: *n*-hexane/ethyl acetate 5:1). Then, the mixture was centrifuged and filtrated. The filtrate was purified by silica gel column chromatography with *n*-hexane and ethyl acetate to give the pure product. The residual catalyst was dried under vacuum at 80 °C for 8 h and reused without more purification.

Spectral data:

((1,3-Dimethyl-2,4,6-trioxohexahydropyrimidin-5-yl)(4-nitrophenyl)methyl) phosphonate (2a)

FT-IR (KBr, cm^{-1}): 1608 (C=O), 1509 (C=C), 1479 (sym. str. NO_2), 1340 (C-N), 1250 (sym. str. NO_2), 1200 (P=O), 1044 (P-O). ^{1}H-NMR (250 MHz, $CDCl_3$, δ/ppm): 2.25-2.31 (t, *J*=7.4 HZ, 6H, -$OCH_2C\underline{H}_3$), 3.17 (s, 6H, CH_3), 3.26-3.28 (d, *J*=3.6 Hz, 1H, -CO-C<u>H</u>-CO-), 3.98-

4.03 (q, *J*=7.2 Hz, 4H, -OC<u>H</u>$_2$CH$_3$), 4.13-4.16 (dd, J_1=, J_2= 2.8 Hz, 1H, -C<u>H</u>-PO-), 7.06 (d, *J*= 2.7 Hz, 2H, arom.), 7.19 (d, *J*= 2.7 Hz, 2H, arom.). ^{13}C-NMR (63 MHz, $CDCl_3$, δ/ppm): 16.1, 27.3, 29.6, 31.9, 55.6, 123.9, 126.1, 137.4, 143.2, 154.4, 166.6, 167.1. ^{31}P-NMR (162 MHz, $CDCl_3$, *δ*/ppm, 85% aqueous H_3PO_4 as external reference): 19.7. Anal. Calc. for $C_{17}H_{22}N_3O_8P$ (427.35): C, 47.78; H, 5.19; N, 9.83 %. Found: C, 47.52; H, 5.13; N, 9.85 %.

Diethyl((4-bromophenyl)(1,3-dimethyl-2,4,6-trioxohexahydropyrimidin-5-yl)methyl) phosphonate (2b)

FT-IR (KBr, cm^{-1}): 1691 (C=O), 1634 (C=C), 1347 (C-N), 1205 (P=O), 1079 (P-O), 577 (C-Br). ^{1}H-NMR (250 MHz, $CDCl_3$, *δ*/ppm): 1.26-1.32 (t, *J*=7.02 HZ, 6H, -OCH$_2$C<u>H</u>$_3$), 3.32 (s, 3H, CH$_3$), 3.36 (s, 3H, CH$_3$), 3.63-3.71 (q, *J*=7.05 Hz, 4H, -OC<u>H</u>$_2$CH$_3$), 4.75 (s, 1H, -CO-C<u>H</u>-CO-), 5.32-5.37 (d, *J*= 11.7 HZ, -C<u>H</u>-PO-), 7.53-7.57 (d, *J*= 8.6 HZ, 2H, arom.), 7.87-7.91 (d, *J*= 8.6 HZ, 2H, arom.). ^{13}C-NMR (63 MHz, $CDCl_3$, *δ*/ppm):16.3, 29.6, 31.1, 31.3, 32.0, 55.1, 120.6, 121.7, 131.6, 133.7, 150.5, 169.3, 170.4. ^{31}P-NMR (162 MHz, DMSO-*d*$_6$, *δ*/ppm, 85% aqueous H_3PO_4 as external reference):19.7. Anal. Calc. for $C_{17}H_{22}BrN_2O_6P$ (461.24): C, 44.27; H, 4.81; N, 6.07 %. Found: C, 44.01; H, 4.83; N, 6.11 %.

Diethyl((5-bromo-2-hydroxyphenyl) (1,3-dimethyl-2,4,6-trioxohexahydropyrimidin-5-yl)methyl)phosphonate (2c)

FT-IR (KBr, cm^{-1}): 3492 (str. OH), 1591 (C=O), 1629 (C=C), 1369 (C-N), 1198 (P=O), 1011 (P-O), 562 (C-Br). ^{1}H-NMR (400 MHz, DMSO-*d*$_6$, *δ*/ppm): 1.02-1.06 (m, 6H, -OCH$_2$C<u>H</u>$_3$), 2.90 (s, 6H, CH$_3$), 4.00 (m, 4H, -OC<u>H</u>$_2$CH$_3$), 4.80 (s, 1H, -CO-C<u>H</u>-CO-), 5.88-5.90 (d, *J*= 8.8 Hz, 1H, -CH-PO), 7.29-7.51 (m, 2H, arom.), 7.55-7.63 (m, 1H, arom.), 10.9 (s, 1H, OH). ^{13}C-NMR (100 MHz, DMSO-*d*$_6$, *δ*/ppm): 17.1, 27.8, 28.9, 35.3, 54.3, 117.5, 118.9, 122.5, 130.6, 134.1, 151.1, 154.0, 166.7, 167.2. ^{31}P-NMR (162 MHz, DMSO-*d*$_6$, *δ*/ppm, 85% aqueous H_3PO_4 as external reference):19.6. Anal. Calc. for $C_{17}H_{22}BrN_2O_7P$ (477.24): C, 42.78; H, 4.65; N, 5.87 %. Found: C, 42.81; H, 4.69; N, 5.91 %.

Diethyl((1,3-dimethyl-2,4,6-trioxohexahydropyrimidin-5-yl)(2-hydroxy-5-nitrophenyl) methyl)phosphonate (2d)

FT-IR (KBr, cm^{-1}): 3480 (str. OH), 1667 (C=O), 1610 (C=C), 1457 (asym. str. NO$_2$), 1348 (C-N), 1254 (sym. str. NO$_2$), 1198 (P=O), 1003 (P-O), ^{1}H-NMR (400 MHz, DMSO-*d*$_6$, *δ*/ppm): 1.09-1.13 (t, *J*=7.2 Hz, 6H, -OCH$_2$C<u>H</u>$_3$), 2.99 (s, 6H, CH$_3$), 3.61-3.76 (m, 4H, -

$OC\underline{H}_2CH_3$), 4.31 (s, 1H, -CO-CH-CO-), 5.14-5.16 (d, *J*=9.2 Hz, 1H, -CH-PO-), 8.08-8.09 (m, 2H, arom.), 8.28-8.31 (m, 1H, arom.), 9.04 (1H, OH). ^{13}C-NMR (100 MHz, DMSO-d_6, *δ*/ppm): 18.5, 27.7, 29.0, 33.5, 54.3, 115.9, 125.0, 126.0, 128.6, 144.3, 148.2, 161.0, 166.6, 167.2. ^{31}P-NMR (162 MHz, DMSO-d_6, *δ*/ppm, 85% aqueous H_3PO_4 as external reference): 18.5. Anal. Calc. for $C_{17}H_{22}N_3O_9P$ (443.35): C, 46.05; H, 5.00; N, 9.48 %. Found: C, 46.43; H, 5.31; N, 9.51 %.

Diethyl((2,4-dichlorophenyl)(1,3-dimethyl-2,4,6-trioxohexahydropyrimidin-5-yl)methyl) phosphonate (2e)

FT-IR (KBr, cm^{-1}): 1594 (C=O), 1590 (C=C), 1373 (C-N), 1254 (P=O), 1160 (C-Cl), 1069 (P-O). ^{1}H-NMR (400 MHz, DMSO-d_6, δ/ppm): 1.02-1.06 (t, *J*=7.2 Hz, 6H, $-OCH_2C\underline{H}_3$), 3.11 (s, 3H, CH_3), 3.22 (s, 3H, CH_3), 3.41 (s, 1H, -CO-CH-CO), 4.40-4.45 (q, *J*=6.8 Hz, 4H, $-OC\underline{H}_2CH_3$), 5.28 (s, 1H, -CH-PO), 7.46-7.49 (m, 1H, arom.), 7.67-7.74 (m, 1H, arom.), 8.28 (s, 1H, arom.). ^{13}C-NMR (100 MHz, DMSO-d_6, δ/ppm): 17.5, 27.7, 28.5, 36.6, 54.4, 122.0, 126.7, 128.4, 131.6, 132.8, 133.8, 135.4, 149.4, 151.0, 159.6, 161.2. ^{31}P-NMR (162 MHz, DMSO-d_6, δ/ppm, 85% aqueous H_3PO_4 as external reference): 19.9. Anal. Calc. for $C_{17}H_{21}Cl_2N_2O_6P$ (451.24): C, 45.25; H, 4.69; N, 6.21 %. Found: C, 44.98; H, 4.65; N, 6.24 %.

Diethyl((4-cyanophenyl)(1,3-dimethyl-2,4,6-trioxohexahydropyrimidin-5-yl)methyl) phosphonate (2f)

FT-IR (KBr, cm^{-1}): 2229 (CN), 1567 (C=O), 1560 (C=C), 1373 (C-N), 1215 (P=O), 1012 (P-O). ^{1}H-NMR (250 MHz, $CDCl_3$, δ/ppm): 1.20-1.25 (t, *J*=6.9 Hz, 6H, $-OCH_2C\underline{H}_3$), 3.35 (s, 3H, CH_3), 3.44 (s, 3H, CH_3), 4.25 (s, 1H, -CO-CH-CO-), 4.50-4.58 (q, *J*=6.5 Hz, 4H, $-OC\underline{H}_2CH_3$), 5.62 (s, 1H, -CH-PO-), 7.26-7.32 (m, 2H, arom.), 7.58-7.73 (m, 2H, arom.). ^{13}C-NMR (100 MHz, $CDCl_3$, δ/ppm): 18.7, 27.0, 29.7, 38.0, 56.0, 115.9, 122.0, 124.5, 127.1, 128.8, 129.5, 132.4, 148.7, 150.0. ^{31}P-NMR (162 MHz, $CDCl_3$, δ/ppm,85% aqueous H_3PO_4 as external reference): 19.0. Anal. Calc. for $C_{18}H_{22}N_3O_6P$ (407.36): C, 53.07; H, 5.44; N, 10.32 %. Found: C, 52.88; H, 5.47; N, 10.35 %.

Diethyl((1,3-dimethyl-2,4,6-trioxohexahydropyrimidin-5-yl)(2-methoxyphenyl)methyl) phosphonate (2g)

FT-IR (KBr, cm^{-1}): 1591 (C=O), 1580 (C=C), 1509 (C-O), 1373 (C-N), 1251 (P=O), 1039 (P-O). ^{1}H-NMR (400 MHz, DMSO-d_6, δ/ppm): 1.06-1.08 (t, *J*=6.8 Hz, 6H, -$OCH_2C\underline{H}_3$), 3.14 (s, 3H, CH_3), 3.21 (s, 3H, CH_3), 3.86 (s, 1H, -CO-CH-CO-), 3.88 (s, 3H, -OCH_3), 4.52 (m, 4H, -$OC\underline{H}_2CH_3$), 5.25-5.28 (d, *J*=12.8 Hz 1H, -CH-PO-), 6.96-7.11 (m, 3H, arom.), 7.48-7.52 (m, 1H, arom.). ^{13}C-NMR (100 MHz, DMSO-d_6, δ/ppm): 18.4, 27.9, 28.3, 38.8, 40.1, 55.8, 110.9, 119.4, 132.1, 133.9, 150.8, 151.1, 158.8, 160.1, 162.1. ^{31}P-NMR (162 MHz, DMSO-d_6, δ/ppm, 85% aqueous H_3PO_4 as external reference): 19.4. Anal. Calc. for $C_{18}H_{25}N_2O_7P$ (412.37): C, 52.43; H, 6.11; N, 6.79 %. Found: C, 52.40; H, 6.15; N, 6.76 %.

Diethyl((1,3-dimethyl-2,4,6-trioxohexahydropyrimidin-5-yl)(4-methoxyphenyl)methyl) phosphonate (2h)

FT-IR (KBr, cm^{-1}): 1590 (C=O), 1580 (C=C), 1509 (C-O), 1371 (C-N), 1250 (P=O), 1041 (P-O). ^{1}H-NMR (400 MHz, DMSO-d_6, *δ*/ppm): 1.04-1.09 (t, *J*=6.8 Hz, 6H, -$OCH_2C\underline{H}_3$), 3.20 (s, 6H, CH_3), 3.37(s, 1H, -CO-CH-CO-), 3.88 (s, 3H, -OCH_3), 4.65-4.68 (m, 4H, -$OC\underline{H}_2CH_3$), 5.10-5.12 (d, *J*=8.0 Hz 1H, -CH-PO-), 7.06-7.07 (m, 2H, arom.), 8.30-8.34 (m, 2H, arom.). ^{13}C-NMR (100 MHz, DMSO-d_6, *δ*/ppm):17.9, 27.3, 28.0, 38.0, 52.2, 55.6, 113.8, 125.1, 137.3, 155.7, 160.7, 162.5, 163.4. ^{31}P-NMR (162 MHz, DMSO-d_6, *δ*/ppm, 85% aqueous H_3PO_4 as external reference): 27.2. Anal. Calc. for $C_{18}H_{25}N_2O_7P$ (412.37): C, 52.43; H, 6.11; N, 6.79 %. Found: C, 52.39; H, 6.13; N, 6.81 %.

Diethyl((1,3-dimethyl-2,4,6-trioxohexahydropyrimidin-5-yl)(*p*-tolyl)methyl) phosphonate (2i)

FT-IR (KBr, cm^{-1}): 1675 (C=O), 1574 (C=C), 1352 (C-N), 1267 (P=O), 1119 (P-O).^{1}H-NMR (400 MHz, DMSO-d_6, *δ*/ppm):1.11-1.15 (t, *J*=6.8 Hz, 6H, -$OCH_2C\underline{H}_3$), 2.58 (s, 3H, Ar-CH_3), 3.27 (s, 6H, CH_3), 3.35 (s, 1H, -CO-CH-CO-), 4.64-4.67(d, *J*=12.4 Hz 1H, -CH-PO-), 4.90-5.03 (m, 4H, -$OC\underline{H}_2CH_3$), 7.38 (m, 3H, arom.), 7.64-7.66 (m, 1H, arom.). ^{13}C-NMR (100 MHz, DMSO-d_6, *δ*/ppm):16.0, 18.5, 27.7, 27.8, 36.3, 54.3, 118.9, 130.6, 132.1, 148.6, 149.8, 154.0, 166.7, 167.0. ^{31}P-NMR (162 MHz, DMSO-d_6, *δ*/ppm, 85% aqueous H_3PO_4 as external reference): 21.1. Anal. Calc. for $C_{18}H_{25}N_2O_6P$ (396.37): C, 54.54; H, 6.36; N, 7.07 %. Found: C, 54.50; H, 6.34; N, 7.16 %.

5-(2,4-Dichlorobenzylidene)-1,3-dimethylpyrimidine-2,4,6(1H,3H,5H)-trione (3e)

^{1}H-NMR (400 MHz, DMSO-d_6, δ/ppm): 3.11 (s, 3H, CH_3), 3.22 (s, 3H, CH_3), 7.46-7.49 (m, 1H, arom.), 7.67-7.74 (m, 2H, arom.), 8.28 (s, 1H, CH). ^{13}C-NMR (100 MHz, DMSO-d_6, δ/ppm): 27.9, 28.5, 122.0, 126.7, 128.4, 131.6, 135.4, 149.4, 151.0, 159.6, 161.2.

5-(2-Methoxybenzylidene)-1,3-dimethylpyrimidine-2,4,6(1H,3H,5H)-trione (3g)

^{1}H-NMR (400 MHz, DMSO-d_6, δ/ppm):3.20 (s, 3H, CH_3), 3.22 (s, 3H, CH_3), 3.88 (s, 3H, -OCH_3), 7.05-7.07 (m, 2H, arom.), 8.30-8.34 (m, 2H, arom. and 1H, CH). ^{13}C-NMR (100 MHz, DMSO, δ/ppm): 27.9, 28.4, 55.8, 110.9, 118.4, 119.4, 121.6, 132.1, 133.9, 150.8, 158.8, 160.1, 162.1.

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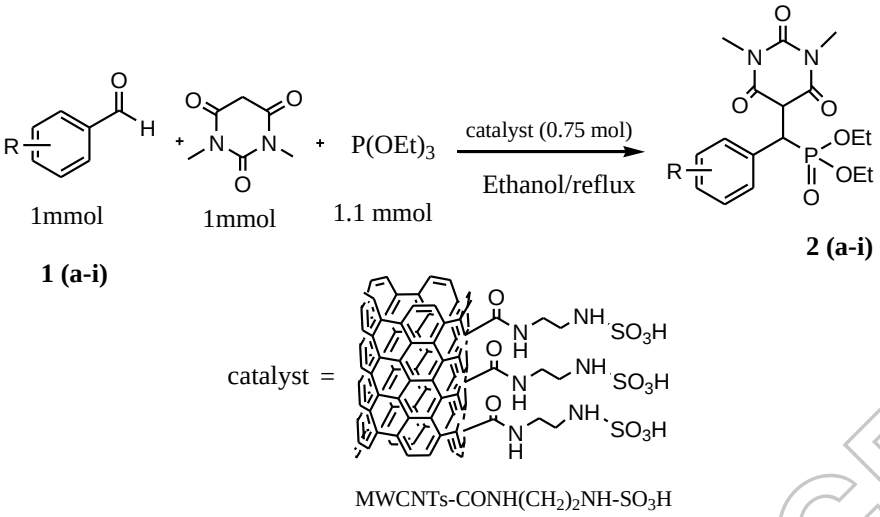
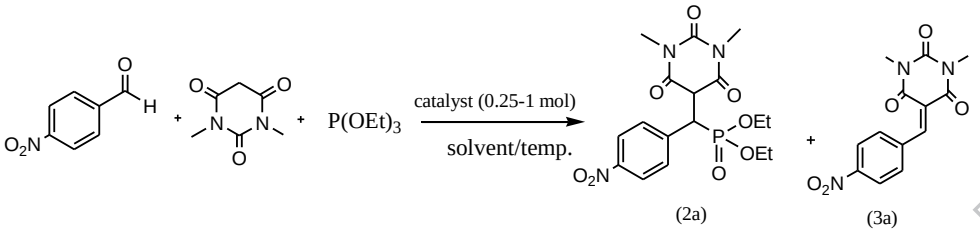


Scheme 1 Domino reaction for the one-pot synthesis of new organophosphonates

Table 1. Optimization of model reaction

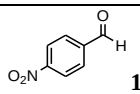
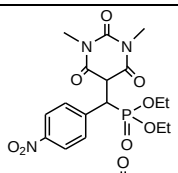
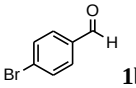
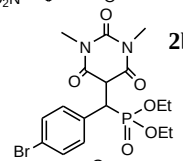
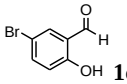
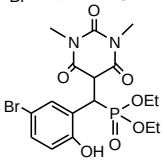
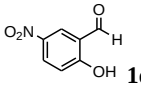
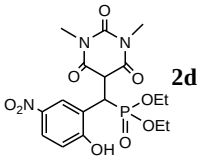
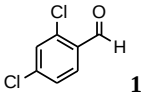
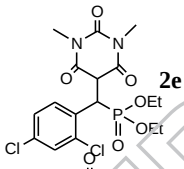
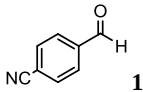
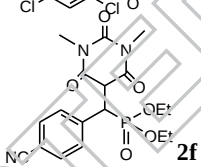
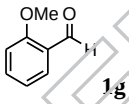
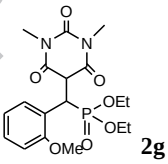
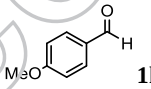
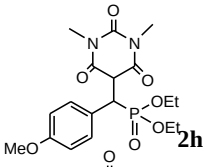
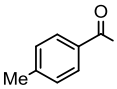
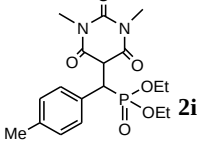


(2a) (3a)

Entry	Solvent	Amount of catalyst (mol)	Temperature (°C)	Time (h)	Isolated Yields (%)	
					2a	3a
1	Solvent-free	0.75	rt	3	50	35
2	Solvent-free	0.75	100	1	65	20
3	CH_2Cl_2	0.75	rt	24	a	
4	CH_2Cl_2	0.75	reflux	1	30	65
5	DMSO	0.75	rt	24		a
6	DMSO	0.75	reflux	24		a
7	Ethanol	0.75	rt	1	87	-
8	Ethanol	0.75	reflux	45 (min)	99	-
9	$(CH_2)_2Cl_2$	0.75	rt	24	a	
10	$(CH2)_2Cl_2$	0.75	reflux	24	20	75
11	Ethanol	0.5	reflux	2	85	-
12	Ethanol	0.25	reflux	2	70	-
13	Ethanol	1	reflux	30 (min)	99	-

[a] Mixture of products were formed

Table 2. One-pot synthesis of new organophosphonates via domino Knoevenagel–phospha–Michael reaction catalyzed by functionalized multi-walled carbon nanotube

Entry	Aldehyde **1(a-i)**	Product **2(a-i)**	Time (min)	Isolated Yield (%)	Melting Point (°C)	R_f*
1	 **1a**	 **2a**	45	99	186-188	0.37
2	 **1b**	 **2b**	60	90	175-178	0.47
3	 **1c**	 **2c**	90	56	272-274	0.34
4	 **1d**	 **2d**	60	73	240-243	0.33
5	 **1e**	 **2e**	60	87	184-186	0.31
6	 **1f**	 **2f**	60	83	176-178	0.34
7	 **1g**	 **2g**	120	58	168-170	0.30
8	 **1h**	 **2h**	90	70	141-145	0.47
9	 **1i**	 **2i**	120	53	260-258	0.47

*R_f was determined in *n*-hexane-ethyl acetate (80%-20%) on silica gel as stationary phase