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One-pot Three-component Synthesis of Phosphonate Derivatives

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Abstract

The stable phosphonate derivatives have easily synthesized by the reactions involving trialkyl(aryl) phosphites and dimethyl acetylenedicarboxylate in the presence of 4-nitrophenol and/or acid chlorides, dialkyl(aryl) phosphites and *N*-methylimidazole at 70 °C under solvent-free conditions.

Keywords: *Phosphonates, Activated acetylenes, Trialkyl phosphites, Dialkyl phosphites.*

Introduction

The use of water as a green media for organic synthesis has become an important research area. Other than the economical and environmental benefits, water also exhibits unique physical and chemical properties which lead to unique reactivity and selectivity in comparison with organic solvents. Thus, the development of organic reaction in water medium is necessary in the present days [1-8]. Phosphorus compounds containing the P–C bond are not particularly abundant in nature but they have diverse biological activity and attract considerable synthetic and pharmacological interest [9, 10]. Phosphonates have important applications in flame retardancy [11, 12], organic synthesis [13], and biological applications [14, 15]. Also, phosphonates have used as substitutes of the corresponding esters and acids of high biological activity [16, 17] and as convenient probes for designing antibodies on the basis of transition state models. These investigations have been supported by organic synthesis; therefore, development of protocols for obtaining phosphonates of complex structures is inevitably important [18-20]. Hence, a large number of methods have appeared describing novel synthesis of phosphonate systems [21-23]. Therefore, we investigate the synthesis

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of phosphonates through the reaction of trialkyl(aryl) phosphites or dialkyl(aryl) phosphite.

Experimental

Material and Equipments

All chemicals were purchased from Fluka and used without further purification. Melting points were measured on an Electrothermal 9100 aparatus. Elemental analyses for the C, H, and N were performed using a Heraeus CHN-O-Rapid analyzer. The results agreed favorably with the calculated values. Mass spectra were recorded on a FINNIGAN-MATT 8430 spectrometer operating at an ionization potential of 70 eV. IR spectra were measured on a Shimadzu IR-460 spectrometer. ^{1}H, ^{13}C, and ^{31}P NMR spectra were measured with a BRUKER DRX-500 AVANCE spectrometer at 500.1, 125.8, and 202.4 MHz.

*General Procedure for the Preparation of the Compounds **4a-4c** and **5a-5b***

To a stirred mixture of dimethyl acetylenedicarboxylate (2 mmol) and 4-nitrophenol (2 mmol) was added trialkyl(aryl) phosphite (2 mmol) at 70°C. The reaction mixture was then stirred for 5 h. After completion of the reaction [TLC (AcOEt/hexane 1:7) monitoring], the mixture of reaction was purified by column chromatography (SiO_2; *n*-Hexane/AcOEt) to afford pure title compounds.

*Physical Data for the Compounds **4a-4c** and **5a-5b***

Dimethyl 2,3-bis(dimthoxyphosphoryl) succinate (**4a**, $C_{10}H_{20}O_{10}P_2$). white powder, m.p. 73-74°C, yield 0.32 g, 88%; IR (KBr): = 2922, 1720, 1583, 1259, 1154, 1024 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 3.22 (6 H, d, $^{3}J_{HP}$ = 8.7 Hz, 2 OMe), 3.41 (6 H, d, $^{3}J_{HP}$ = 8.2 Hz, 2 OMe), 3.81 (6 H, s, 2 CO2Me), 4.75 (2 H, dd, $^{2}J_{HP}$ = 11.2 Hz and $^{3}J_{HH}$ = 8.1 Hz, 2 CH) ppm; ^{13}C NMR (125.7 MHz, $CDCl_3$): δ = 42.9, 43.2, 43.7, 44.2, 44.5 (5 lines for P-CH), 52.4 (d, $^{2}J_{CP}$ = 3.5 Hz, 2 $POCH_3$), 52.8 (d, $^{2}J_{CP}$ = 3.8 Hz, 2 POCH3), 55.6 (s, 2 CO2CH3), 167.4 (s, C=O) ppm; $_{31}P$ NMR (202 MHz, CDCl3): δ = 19.58 (P=O) ppm; MS (EI, 70 eV): *m/z* (%) = 362 (M^+, 5), 331 (35), 253 (20), 181 (48), 110 (100), 31 (78).

Dimethyl 2,3-bis(diethoxyphosphoryl) succinate (**4b**, $C_{14}H_{28}O_{10}P_2$). white powder, m.p. 85-87°C, yield 0.35 g,
83%; IR (KBr): $\bar{\upsilon}$ = 2920, 1731, 1589, 1261, 1158, 1029 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.21 (12 H, t, $^{3}J_{HH}$ = 7.0 Hz, 4 Me), 3.60 (2 H, dd, $^{2}J_{HP}$ = 10.2 Hz and $^{3}J_{HH}$ = 8.1 Hz, 2 CH), 3.83 (6 H, s, 2 OMe), 4.01 (8 H, m, 4 OCH2) ppm; ^{13}C NMR (125.7 MHz, $CDCl_3$): δ = 15.8 (d, 3JCP = 6.9 Hz, 2 CH3), 15.9 (d, $^{3}J_{CP}$ = 6.7 Hz, 2 CH_3), 39.2, 39.5, 40.3, 41.2, 41.8 (5 lines for P-CH), 54.6 (s, 2 OCH_3), 62.9 (d, $^{2}J_{CP}$ = 5.9 Hz, 2 OCH_2), 63.5 (d, $^{2}J_{CP}$ = 5.8 Hz, 2 OCH_2), 168.6 (s, C=O) ppm; ^{31}P NMR (202 MHz, $CDCl_3$): δ

= 21.09 (P=O) ppm; MS (EI, 70 eV): *m/z* (%) = 418 (M^+, 6), 387 (10), 251 (20), 223 (96), 209 (10), 138 (48), 113 (100), 45 (78).

Dimethyl 2,3-bis(diphenoxyphosphoryl) succinate (**4c**, $C_{30}H_{28}O_{10}P_2$).

Colorless crystals, m.p. 173-175°C, yield 0.52 g, 85%; IR (KBr): $\bar{\upsilon}$= 2950, 1739, 1581, 1277, 1246, 1184, 1155 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ = 3.75 (6 H, s, OMe), 4.33 (2 H, dd, $^2J_{HP}$ = 12 Hz and $^3J_{HH}$ = 6.0 Hz, CH), 7.16 (4 H, t, $^3J_{HH}$ = 8.0 Hz, 4 CH_{para} of 4 C6H5), 7.25 (8 H, d, $^3J_{HH}$ = 5.7 Hz, 8 CH_{ortho} of 4 C^6H^5), 7.31 (8 H, dd, $^3J_{HH}$ = 8.4 Hz and $^3J_{HH}$ = 7.5 Hz, 8 CH_{meta} of 4 C_6H_5) ppm; ^{13}C NMR (125.7 MHz, $CDCl_3$): δ = 44.4, 44.7, 45.2, 45.7, 46.0 (5 lines for P-CH), 53.3 (2 OCH_3), 120.8 [d, $^3J_{CP}$ = 7.5, 8 CH_{ortho} of $(C_6H_5O)_2PO$], 125.6 [d, $^4J_{PC}$ = 2.5 Hz, CH_{meta} of $(C_6H_5O)_2PO$], 129.8 [s, 4 CH_{para} of $(C_6H_5O)_2PO$], 150.0 [d, $^2J_{PC}$ = 14.6 Hz, 2 C_{ipso} of $(C_6H_5O)_2PO$], 150.1 [d, $^2J_{PC}$ = 14.4 Hz, 2 C_{ipso} of $(C_6H_5O)_2PO$], 166.3 (s, C=O) ppm; ^{31}P NMR (202 MHz, $CDCl_3$): δ = 11.73 (P=O) ppm; MS (EI, 70 eV): *m/z* (%) = 610 (M^+, 6), 579 (20), 517 (100), 485 (10), 318 (10), 285 (80), 223 (58), 140 (46), 94 (40), 77 (100).

1-Methoxy-4-nitrobenzene (**5a**, $C_7H_7NO_3$) Colorless crystals, m.p. 75-77°C, 0.14 g, yield 92%; IR (KBr): $\bar{\upsilon}$= 1683, 1492, 1333, 1261, 1173, 1105, 1016 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ = 3.89 (3 H, s, OMe), 6.93 (2 H, d, $^3J_{HH}$ = 9.1 Hz, 2 CH of C_6H_5), 8.17 (2 H, d, $^3J_{HH}$ = 9.2 Hz, 2 CH of C_6H_5) ppm; ^{13}C NMR (125.7 MHz, $CDCl_3$): δ = 55.9 (s, CH_3), 114.0 (s, 2 CH), 125.9 (s, 2 CH), 141.5 (s, Cipso of Ph), 164.6 (s, C_{ipso} of Ph) ppm.

1-Ethoxy-4-nitrobenzene (**5b**, $C_8H_9NO_3$) yellow crystals, m.p. 79-81°C, 0.13 g, yield 87%; IR (KBr): $\bar{\upsilon}$= 1585, 1490, 1329, 1257, 1177, 1102, 1033 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ = 1.45 (3 H, t, $^3J_{HH}$ = 6.9 Hz, Me), 4.12 (2 H, q, $^3J_{HH}$ = 6.9 Hz, OCH_2), 6.93 (2 H, d, $^3J_{HH}$ = 9.2 Hz, 2 CH of C_6H_5), 8.18 (2 H, d, $^3J_{HH}$ = 9.2 Hz, 2 CH of C_6H_5) ppm; ^{13}C NMR (125.7 MHz, $CDCl_3$): δ = 14.5 (s, CH_3), 64.4 (s, OCH_2), 114.4 (s, 2 CH of Ph), 125. 9 (s, 2 CH of Ph), 141.4 (s, C_{ipso} of Ph), 164.0 (s, C_{ipso} of Ph) ppm.

*General Procedure for the Preparation of the Compounds **13a-13d***

N-methylimidazole (1 mmol) was added slowly to a mixture of acid chlorides (excess) and dialkyl(aryl) phosphites (4 mmol) at 70oC. After completion of the reaction (30-45 min) as indicated by TLC (*n*-hexanes/EtOAc 8:1), the resulting solid was washed with water (5 mL) and diethylether (1 mL) and dried to afford pure title compounds. The dried product thus obtained showed a single spot on TLC and was pure enough for all analytical purposes.

*Physical Data for the Compounds **13a-13d***

Diphenyl[[diphenoxyphosphoryl)oxy]

*(4-nitrophenyl)methyl]phosphonate (**13a**)*

Yellow powder, mp 174-176ºC; yield: 1.02 g (83%). IR (KBr): 1524, 1478, 1356, 1289, 1145 and 1087. ^{1}H NMR (500.1 MHz, $CDCl_3$): 6.25 (1 H, dd, $^{2}J_{PH}$ = 14.3 Hz and $^{3}J_{PH}$ = 10.7 Hz, CH), 6.98-7.32 (20 H, m, 20 CH), 7.66 (2 H, d, ^{3}J = 8.5 Hz, 2 CH), 8.12 (2 H, d, ^{3}J = 8.5 Hz, 2 CH) ppm. ^{13}C NMR (125.7 MHz, $CDCl_3$): 74.8 (dd, $^{1}J_{CP}$ = 181.3 Hz and $^{2}J_{CP}$ = 6.7 Hz, CH), 119.8 (d, $^{3}J_{CP}$ = 5.1 Hz, 2 CH), 120.1 (d, $^{3}J_{CP}$ = 4.8 Hz, 2 CH), 120.3 (d, $^{3}J_{CP}$ = 4.1 Hz, 2 CH), 123.6 (d, $^{3}J_{CP}$ = 4.2 Hz, 2 CH), 125.7 (2 CH), 125.8 (CH), 126.4 (CH), 129.0 (2 CH), 129.1 (2 CH), 129.8 (2 CH), 129.9 (2 CH), 130.0 (d, $^{3}J_{CP}$ = 7.4 Hz, 2 CH), 131.0 (2 CH),132.5 (dd, $^{2}J_{CP}$ = 10.2 Hz and $^{3}J_{CP}$ = 6.4 Hz, C), 148.4 (d, $^{2}J_{CP}$ = 8.7 Hz, C), 149.8 (C), 149.9 (d, $^{2}J_{CP}$ = 9.6 Hz, C), 150.0 (d, $^{2}J_{CP}$ = 8.5 Hz, C), 150.3 (d, $^{2}J_{CP}$ = 8.6 Hz, C), ppm. ^{31}P NMR (202 MHz, $CDCl_3$): -10.25 ($^{3}J_{PP}$ = 40.2 Hz), 12.4 ($^{3}J_{PP}$ = 40.2 Hz) ppm. Anal. Calc. for $C_{31}H_{25}NO_9P_2$ (617.48): C, 60.30; H, 4.08; N, 2.27 found: C, 60.27; H, 3.94; N, 2.18%.

*Diethyl[[diethyloxyphosphoryl)oxy](phenyl) methyl]phosphonate (**13b**)*

Yellow powder, mp 140-142ºC; yield: 92%. IR (KBr): 1575, 1480, 1473, 1348, 1285 and 1248. ^{1}H NMR (500.1 MHz, $CDCl_3$): 1.27 (6 H, t, $^{3}J_{HH}$ = 7.3 Hz, 2 CH_3), 1.33 (6 H, t, $^{3}J_{HH}$ = 7.4 Hz, 2 CH_3), 4.25 (2 H, m, OCH_2), 4.32 (2 H, m, OCH_2), 4.48 (2 H, m, OCH_2), 4.53 (2 H, m, OCH_2), 6.16 (1 H, dd, $^{2}J_{PH}$ = 13.0 Hz and $^{3}J_{PH}$ = 10.4 Hz, CH), 6.87 (2 H, d, ^{3}J = 7.6 Hz, 2 CH), 7.45 (1 H, t, ^{3}J = 7.5 Hz, CH), 7.79 (2 H, d, ^{3}J = 7.5 Hz, 2 CH) ppm. ^{13}C NMR (125.7 MHz, $CDCl_3$): 13.4 (d, $^{3}J_{CP}$ = 5.6 Hz, 2 CH_3), 14.6 (d, $^{3}J_{CP}$ = 6.4 Hz, 2CH_3), 62.0 (d, $^{2}J_{CP}$ = 8.4 Hz, OCH_2), 62.3 (d, $^{2}J_{CP}$ = 8.5 Hz, OCH_2), 62.5 (d, $^{2}J_{CP}$ = 7.4 Hz, OCH_2), 62.7 (d, $^{2}J_{CP}$ = 7.6 Hz, OCH_2), 76.1 (dd, $^{1}J_{CP}$ = 176.5 Hz and $^{2}J_{CP}$ = 6.7 Hz, CH), 120.1 (d, $^{3}J_{CP}$ = 6.2 Hz, 2 CH), 129.4 (2 CH), 132.0 (CH), 132.8 (d, $^{2}J_{CP}$ = 9.5 Hz, C) ppm. ^{31}P NMR (202 MHz, $CDCl_3$): -11.45 (3JPP = 39.2 Hz), 9.45 ($^{3}J_{PP}$ = 39.2 Hz) ppm.

*Diethyl[[diethyloxyphosphoryl)oxy] (4-methoxyphenyl)methyl]phosphonate (**13c**)*

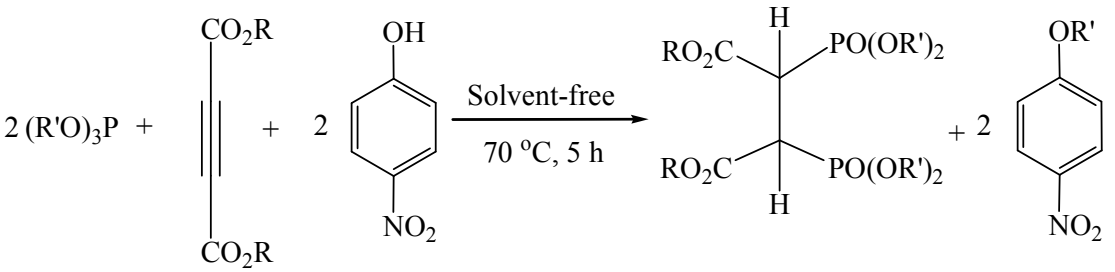
White powder, mp 155-157ºC; yield: 86%. IR (KBr)): 1534, 1477, 1342, 1315, and 1278. ^{1}H NMR (500.1 MHz, $CDCl_3$): 1.24 (6 H, t, $^{3}J_{HH}$ = 7.2 Hz, 2 CH_3), 1.37 (6 H, t, $^{3}J_{HH}$ = 7.4 Hz, 2 CH_3), 3.75 (3 H, s, MeO), 4.27 (2 H, m, CH_2), 4.32 (2 H, m, CH_2), 4.47 (2 H, m, CH_2), 4.52 (2 H, m, CH_2), 6.34 (1 H, dd, $^{2}J_{PH}$ = 14.3 Hz and 3JPH = 11.5 Hz, CH), 7.43 (2 H, d, $^{3}J_{HH}$ = 8.5 Hz, 2 CH), 8.27 (2 H, d, $^{3}J_{HH}$ = 8.4 Hz, 2 CH) ppm. ^{13}C NMR (125.7 MHz, $CDCl_3$): 13.4 (d, $^{3}J_{CP}$ = 5.6 Hz, 2 CH_3), 14.5 (d, $^{3}J_{CP}$ = 6.4 Hz, 2 CH_3), 52.4 (MeO), 62.4 (d, $^{2}J_{CP}$ = 8.5 Hz, CH_2), 62.7 (d, $^{2}J_{CP}$ = 8.6 Hz, CH2), 62.8 (d, $^{2}J_{CP}$ = 7.4 Hz, CH_2), 62.9 (d, $^{2}J_{CP}$ = 7.6 Hz, CH_2), 75.7 (dd, $^{1}J_{CP}$ = 187.4 Hz and $^{2}J_{CP}$ = 9.7 Hz, CH), 129.5 (d, $^{3}J_{CP}$ = 6.8 Hz, CH), 129.7 (d, $^{3}J_{CP}$ = 6.7 Hz, CH), 131.8 (CH),

132.0 (CH), 132.8 (dd, $^{2}J_{CP}$ = 9.5 Hz and $^{3}J_{CP}$ = 4.7 Hz, C), 140.1 (C) ppm. ^{31}P NMR (202 MHz, $CDCl_3$): -11.25 ($^{3}J_{PP}$ = 39.4 Hz), 10.34 ($^{3}J_{PP}$ = 39.4 Hz) ppm.

*Dimethyl[[dimethoxyphosphoryl)oxy]propyl] phosphonate (**13d**)*. Yellow powder, mp 115-117ºC; yield: 0.43 g (78%). IR(KBr): 1541, 1487, 1452, 1328, and 1254. ^{1}H NMR (500.1 MHz, $CDCl_3$): 1.28 (3 H, m, CH_3), 1.65 (2 H, m, CH_2), 3.72 (3 H, d, $^{3}J_{PH}$ = 5.4 Hz, CH_3), 3.78 (3 H, d, $^{3}J_{PH}$ = 5.6 Hz, CH_3), 3.80 (3 H, d, $^{3}J_{PH}$ = 6.2 Hz, CH_3), 3.82 (3 H, d, $^{3}J_{PH}$ = 6.2 Hz, CH_3), 5.24 (1 H, m, CH) ppm. ^{13}C NMR (125.7 MHz, $CDCl_3$): 12.5 (d, $^{3}J_{CP}$ = 4.8 Hz, CH_3), 28.3 (dd, $^{2}J_{CP}$ = 7.4 Hz and $^{3}J_{CP}$ = 4.2 Hz, CH_2), 51.4 (d, $^{2}J_{CP}$ = 6.0 Hz, OCH3), 51.8 (d, $^{2}J_{CP}$ = 6.2 Hz, OCH_3), 52.0 (d, $^{2}J_{CP}$ = 5.8 Hz, OCH_3), 52.3 (d, $^{2}J_{CP}$ = 5.8 Hz, OCH_3), 78.4 (dd, $^{1}J_{CP}$ = 195.2 Hz and $^{2}J_{CP}$ = 9.7 Hz, CH) ppm. ^{31}P NMR (202 MHz, $CDCl_3$): -11.65 (3JPP = 34.5 Hz), 12.32 ($^{3}J_{PP}$ = 34.5 Hz) ppm. Anal. Calc. for $C_7H_{18}O_7P_2$ (276.16): C, 30.44; H, 6.57 found: C, 30.34; H, 6.40%.

Results and Discussion

The reaction of trialkyl(aryl) phosphites **1** with dimethyl acetylenedicarboxylate **2** in the presence of 4-nitrophenol 3 as the proton source/nucleophile led to dialkyl [1-benzoyl-2-(dialkoxyphosphoryl)-3-oxo-3-phenylpropyl] phosphonates **4a-4c** in good yields (Scheme 1).



1 **2** **3**

4	R	R'	%Yield
a	Me	Me	88
b	Me	Et	83
c	Me	Ph	85

5	R'	%Yield
a	Me	92
b	Et	87

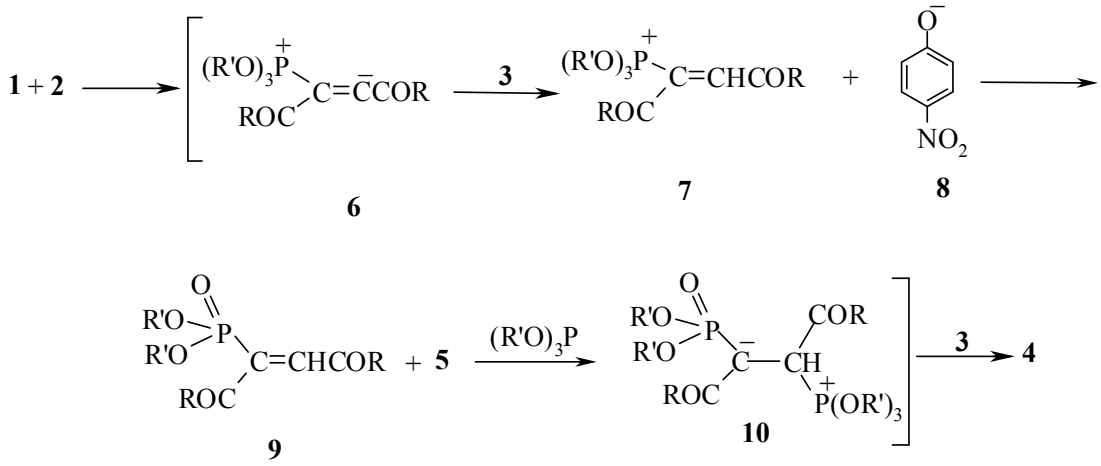
Scheme 1. The reaction between trialkyl(aryl) phosphites, dimethyl acetylenedicarboxylate, and 4-nitrophenol.

The structures of bisphosphonates **4a-4c** and **5a-5b** were deduced from their elemental analyses and their IR, ^{1}H NMR, ^{13}C NMR, ^{31}P NMR, and mass spectral data. The mass spectra of these compound displayed molecular ion peaks at appropriate *m/z* values.

The ^{1}H NMR spectrum of 4a in $CDCl_3$ showed two doublets at δ = 3.22 ($^{3}J_{HP}$ = 8.7 Hz) and 3.41 ($^{3}J_{HP}$ = 8.2 Hz) for the diastereotopic methoxy groups and a doublet of doublet at δ = 4.75 ($^{2}J_{HP}$ = 11.2 Hz and $^{3}J_{HH}$ = 8.1 Hz) for the methine moieties, along with a singlet

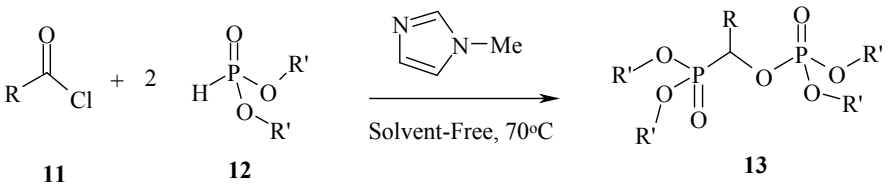
at δ = 3.81 ppm for the two CO_2Me groups. The ester carbonyl resonances in the ^{13}C NMR spectra of **4a** appear as a singlet at δ = 167.4 ppm in the ^{13}C NMR spectrum. The ^{31}P NMR signal of 4a was found at δ = 19.58 ppm. The ^{1}H and ^{13}C NMR spectra of **4b** and **4c** were similar to those for 4a except for the phosphoranyl moieties.

Although we have not yet established the mechanism of the reaction between trialkyl(aryl) phosphites and acetylenes in the presence of 4-nitrophenol in an experimental manner, a plausible explanation is proposed in Scheme **2.** On the basis of the well established chemistry of phosphorus nucleophiles [1-3], it is reasonable to assume that compounds **4** result from initial addition of phosphite to the activated acetylene and subsequent protonation of the reactive 1:1 adduct by 4-nitrophenol, followed by attack of the phenoxide ion at the alkyl group of the phosphite to generate **9** and 1-alkoxy-4-nitrobenzene **5.** Because of the higher nucleophilicity of phosphites compared to the conjugate base of 4-nitrophenol, intermediate **9** is attacked by a second phosphorus nucleophile.



Scheme 2. Proposed mechanism for the formation of **4.**

Under similar condition, we report an efficient synthetic route to phosphoryloxy phosphonate derivatives. The reaction of acid chlorides **11** with dialkyl(aryl) phosphites **12** in the presence of N-methylimidazole led to phosphoryloxy phosphonate derivatives **13** in good yield (Scheme 3).



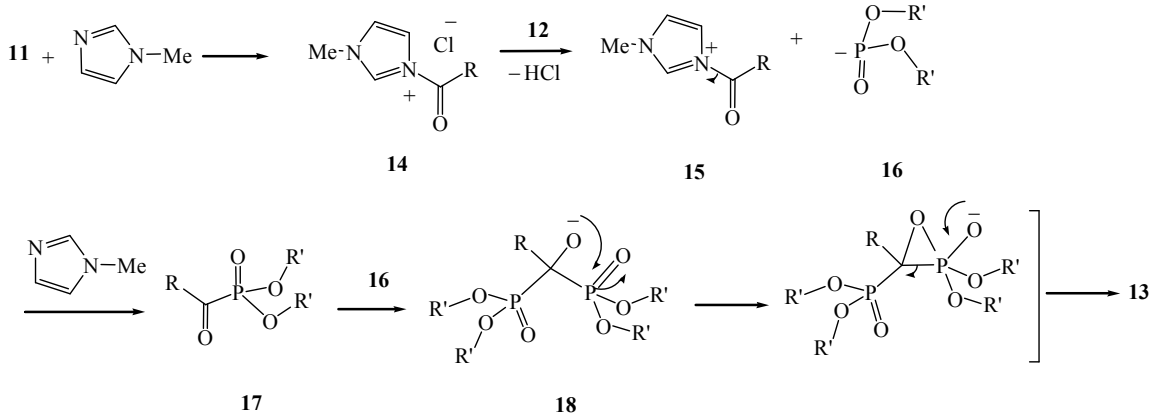
11 12 13

11, 13	R	R'	Yield % of 13
a	4-NO_2-C_6H_4	Ph	87
b	Ph	Et	85
c	4-MeO-C_6H_4	Et	90
d	Et	Me	83

Scheme 3. The reaction between acid chlorides, and dialkyl(aryl) phosphites.

The structures of compounds **13a-13d** were determined on the basis of their ^{1}H, ^{13}C, ^{31}P NMR, IR spectra, and elemental analyses data. The ^{1}H NMR spectrum of 13a in $CDCl_3$ exhibited one doublet of doublet at 6.25 (1 H, dd, $^{2}J_{PH}$ = 14.3 Hz and $^{3}J_{PH}$ = 10.7 Hz, CH), for the methine proton and multiplets at 6.98–8.12 for the aromatic protons. The ^{13}C NMR spectrum of **13a** exhibited 32 signals in agreement with the proposed structure. The ^{1}H and ^{13}C-decoupled ^{31}P NMR spectrum of **13a** exhibited two sharp singlet at -10.25 ($^{3}J_{PP}$ = 40.2 Hz), 12.4 ($^{3}J_{PP}$ = 40.2 Hz) ppm.

Mechanistically, it is conceivable that the reaction involves the initial formation of a 1:1 zwitterionic intermediate **14** between acid chlorides **11** and N-methylimidazole, which undergoes reaction with **12** to produce cationic ion **15** and anionic ion **12** after elimination of HCl. Intermediate **15** would be attacked by negative charge in **16** and loss of N-methylimidazole to produce **17** that would be attacked by negative charge in **16** again and finally compound **13** was produced in good yield (Scheme 4).



14 15 16 17 18

Scheme 4. Proposed mechanism for the formation of **13.**

The present method carries the advantage that, not only is the reaction performed under neutral conditions, but the educts can be mixed without any activation or modification. The simplicity of the present procedure for the synthesis of phosphonates makes it an interesting alternative to complex multistep approaches.

Conclusion

In summary, we have developed a simple and one-pot synthesis of phosphonate derivatives at 70 oC under solvent-free conditions. Its advantages include ease of synthesis and work-up, high yields and green conditions.

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