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Solvent-free Synthesis of Stable Oxaphosphaphenanthrene Derivatives using Multicomponent Reaction of Naphthols

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ABSTRACT

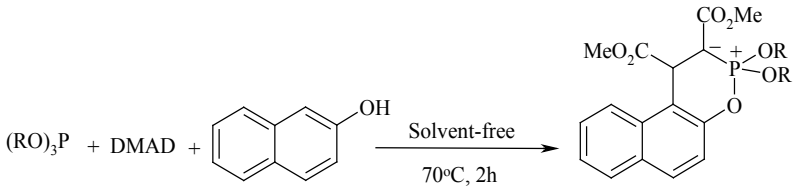
The reaction of dimethyl acetylenedicarboxylate with OH-acid such as 2-naphthol in the presence of trimethyl or triphenyl phosphite under solvent-free conditions produce oxaphosphaphenanthrene derivatives in good yields. Also, the reaction of dimethyl acetylenedicarboxylate and trimethyl phosphite in the presence of 1-naphthol leads to succinate derivatives in excellent yields. Using triethyl phosphite and dimethyl acetylenedicarboxylate in the presence of 1-naphthol or 1-naphthol produces chromene-4-carboxylate derivatives in good yields.

Key words: Dimethyl acetylenedicarboxylate; Solvent-free conditions; Oxaphosphaphenanthrene; 1-naphthol.

INTRODUCTION

Multi-component reactions (MCRs), due to their productivity, simple procedures, convergence, and facile execution, are one of the best tools in combinatorial chemistry[1]. Therefore, the design of novel MCRs has attracted great attention from research groups working in areas such as drug discovery, organic synthesis and materials science. As a result, the number of new MCRs has grown rapidly[2]. Green chemistry approaches hold out significant potential not only for reduction of byproducts, a reduction in the waste produced, and lowering of energy costs but also in the development of new methodologies toward previously unobtainable materials, using existing technologies[3-5]. Organophosphorus compounds, i.e. those bearing a carbon atom directly bound to a phosphorus atom, are synthetic targets of interest, not least because of their value for a variety of industrial, biological, and chemical synthetic uses [6-8]. As a result, a large number of methods have appeared describing novel syntheses of organophosphorus compounds. There are many studies on the reaction between trivalent phosphorus nucleophiles and α,β-unsaturated carbonyl compounds in the

presence of a proton source such as alcohol or phenol[9-11]. We describe herein the reaction of dimethyl acetylenedicarboxylate with triphenyl, triethyl and trimethylphosphit as the P-nucleophile in the presence of OH-acid such as 1-naphthol or 2-naphthol under solvent-free conditions at 70 °C in excellent yield (Scheme 1).



1, 4	R	yield % of 4
a	Ph	85
b	Me	87

Scheme 1

MATERIAL AND METHODS

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. 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, respectively. ^{1}H, ^{13}C, and 31P spectra were obtained for solutions in $CDCl_3$ using TMS as internal standard or 85% H_3PO_4 as external standard. All the chemicals used in this work were purchased from Fluka (Buchs, Switzerland) and are used without further purification.

General procedure for preparation of compounds 4a-b and 9, 17.

Dimethyl 2,2-diphenoxy-4H-1-oxa-2*l*^{5}-phosphaphenanthrene-3,4-dicarboxylate (4a)

To a magnetically stirred of 0.28 g dimethyl acethylenedicarboxylate 2 (2 mmol) and 0.29 g 2-naphthol 3 (2 mmol) was added 0.62 g triphenyl phosphite 1a (2 mmol) at 70°C. The reaction mixture was then stirred for 2 h. The reaction mixture was crystallized from diethyl ether. The product 4a was obtained as colorless crystals, m.p. 178-180 °C, 0.90 g, yield 90%. IR (KBr) (νmax/cm^{-1}): 1667, and 1722 (2 C=O). Anal. Calcd for $C_{28}H_{23}O_7P$ (502.4): C, 66.93; H, 4.61. Found: C, 66.9; H, 4.7%. ^{1}H NMR (500 MHz, $CDCl_3$): δ 3.21 and 3.72 (6 H, 2 s, 2 Me), 5.55 (1 H, d ^{3}JHP 33 Hz, CH), 6.98-9.20 (16 H, m, 16 CH). ^{13}C NMR (125.7 MHz, $CDCl_3$): δ 41.10 (d, ^{1}JCP 225 Hz, C), 41.37 (d, ^{2}JCP 9 Hz, CH), 50.32 and 52.06 (2 OMe), 118.22 (d, ^{3}JPC 6 Hz, CH of $C_{10}H_6$), 120.54 (d, ^{3}JCP 4 Hz, 2 CHortho of Ph), 120.83 (d, ^{3}JPC 9 Hz, C of $C_{10}H_6$), 121.50 (d, ^{3}JPC 4 Hz, 2 CHortho of Ph), 124.10, and 125.56 (2 CH of $C_{10}H_6$), 125.92 and 126.14 (2 CHpara of Ph), 127.49 and 128.43 (2 CH of $C_{10}H_6$), 129.71 (m, 4 CHmeta of Ph groups), 129.79 (CH of $C_{10}H_6$), 131.13 and 131.33 (2 C of $C_{10}H_6$), 148.13 (d 2JPC 8 Hz, C-O of $C_{10}H_6$), 149.96 (m, 2 Cipso of Ph groups), 168.40 (d 2JPC 17.3 Hz, C=O), 173.32 (C=O). ^{31}P NMR (202 MHz, $CDCl_3$): ´ 41.54.

Dimethyl 2,2-dimethoxy-4H-1-oxa-2*l*^{5}-phosphaphenanthrene-3,4-dicarboxylate (4b)

The procedure for preparation of 4b was similar to that for 4a. Colorless crystals, m.p. 128-130 °C, 0.64 g, yield 85%. IR (KBr) (νmax/cm^{-1}): 1652, and 1722 (2 C=O). Anal. Calcd for $C_{18}H_{19}O_7P$ (378.3): C, 57.15; H, 5.06. Found: C, 57.2; H, 5.1%. ^{1}H NMR (500 MHz, $CDCl_3$): δ 3.61 and 3.70 (6 H, 2 s, 2 Me), 3.65 (3 H, d ^{3}JPH 13 Hz, OMe), 4.07 (3 H, d ^{3}JPH 13 Hz, OMe), 5.65 (1 H, d ^{3}JHP 31 Hz, CH), 7.26 (d, 3JHH 9 Hz, CH), 7.45 (1 H, t, ^{3}JHH 9 Hz, CH), 7.59 (1 H, t, ^{3}JHH 9 Hz), 7.73 (1 H, d ^{3}JHH 9 Hz, CH), 7.79 (1 H, d 3JHH 9 Hz, CH), 8.39 (1 H, d ^{3}JHH 9 Hz, CH). ^{13}C NMR (125.7 MHz, $CDCl_3$): δ 39.20 (d, 1JCP 222 Hz, C), 41.37 (d, ^{2}JCP 9 Hz, CH), 50.37 and 52.21 (2

OMe), 55.33 (d, ^{2}JPC 6 Hz, P-OMe), 55.65 (d, ^{2}JPC 5 Hz, P-OMe), 118.35 (d, ^{3}JPC 6 Hz, CH), 121.29 (d, ^{3}JPC 9.1 Hz, C), 124.40, 125.43, 127.38, 128.40 and 129.79 (5 CH), 131.13 and 131.31 (2 C), 148.58 (d ^{2}JPC 8 Hz, C-O), 169.20 (d ^{2}JPC 18 Hz, C=O), 174.92 (C=O). ^{31}P NMR (202 MHz, $CDCl_3$): δ 42.53.

Methyl 3-oxo-2,3-dihydro-1H-benzo[f]chromene-1-carboxylate (9)

To a magnetically stirred of 0.28 g dimethyl acethylenedicarboxylate 2 (2 mmol) and 0.29 g 2-naphthol 3 (2 mmol) was added 0.33 g triethyl phosphite 1c (2 mmol) at 70 °C. The reaction mixture was then stirred for 5 h. The reaction mixture was crystallized from diethyl ether. (0.49 g, yield 96%). m.p. 151-152 °C, IR (KBr) (δmax/cm^{-1}): 1711, and 1752 (2 C=O). Anal. Calcd for $C_{15}H_{12}O_4$ (256.3): C, 70.31; H, 4.72. Found: C, 70.1; H, 4.7%. ^{1}H NMR (500 MHz, $CDCl_3$): ´ 2.82 (1 H, dd ^{2}JHH 16 Hz ^{3}JHH 6 Hz, HCH), 3.25 (1 H, d ^{2}JHH 16 Hz, HCH), 3.65 (3 H, s, OMe), 4.60 (1 H, d ^{3}JHH 6 Hz, CH), 7.26 (d, ^{3}JHH 9 Hz, CH), 7.49 (1 H, t, ^{3}JHH 8 Hz, CH), 7.59 (1 H, t, ^{3}JHH 8 Hz), 7.73 (1 H, d ^{3}JHH 8 Hz, CH), 7.79 (1 H, d ^{3}JHH 8 Hz, CH), 8.32 (1 H, ^{3}JHH 9 Hz, CH). ^{13}C NMR (125.7 MHz, $CDCl_3$): δ 31.37 (CH_2), 37.87 (CH), 52.84 (OMe), 112.73 (C), 117.70, 123.27, 125.42, 127.75, 128.76, and 130.65 (6 CH), 130.90, 131.00, and 149.96 (3 C), 166.16 and 171.22 (2 C=O). MS, m/z (%): 256 (M+·, 15), 196 (100), 168 (41).

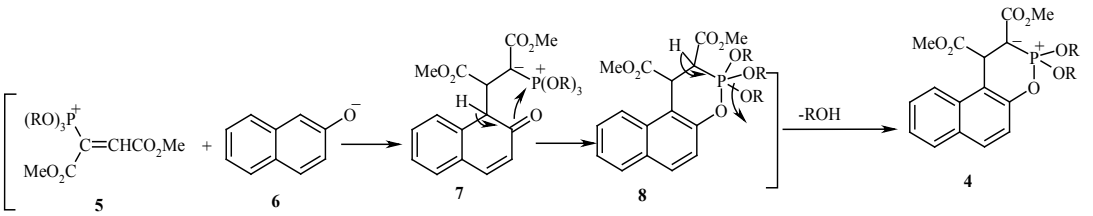
Dimethyl2-(dimethoxy-phosphoryl)-3-(1-hydroxy-naphthalene-2-yl)-succinate (17)

To a magnetically stirred of 0.28 g dimethyl acethylenedicarboxylate 2 (2 mmol) and 0.29 g 1-naphthol 16 (2 mmol) was added 0.25 g trimethyl phosphite 1b (2 mmol) at 70 °C. The reaction mixture was then stirred for 4 h. The reaction mixture was crystallized from diethyl ether. The product 17 was obtained as colorless crystals, m.p. 173-185 °C, 0.76 g, yield 96%. IR (KBr) (νmax/cm^{-1}): 3230 (OH), 1724 (C=O). Anal. Calcd for $C_{18}H_{21}O_8P$ (396.3): C, 54.55; H, 5.34. Found: C, 54.4; H, 5.3%. ^{1}H NMR (500 MHz, $CDCl_3$): δ 2.85 (3 H, d ^{3}JHP 11 Hz, OMe), 3.60 (3 H, s, OMe), 3.67 (3 H, d ^{3}JHP 11 Hz, OMe), 3.82 (3 H, s, OMe), 3.88 (1 H, dd ^{2}JHP 21 Hz ^{3}JHH 12 Hz, CH), 4.99 (1 H, dd ^{3}JHH 12 Hz ^{3}JHP 9 Hz, CH), 7.10-8.42 (6 H, m, 6 CH), 8.47 (1 H, s, OH). ^{13}C NMR (125.7 MHz, $CDCl_3$): δ 44.04 (CH), 48.51 (d ^{1}JPC 135 Hz, CH), 52.79 (OMe), 52.86 (d 2JPC 7 Hz, OMe), 53.05 (OMe), 53.97 (d ^{2}JPC 7 Hz, OMe), 116.92 (C), 121.78 and 123.42 (2 CH), 124.60 (C), 125.74, 126.82 and 127.20 (3 CH), 127.67 (C), 134.20 (CH), 150.50 (C), 168.24 (d ^{2}JPC 5 Hz, C=O), 173.01 (d ^{3}JPC 22 Hz, C=O). ^{31}P NMR (202 MHz, $CDCl_3$): δ 18.56. MS, m/z (%): 396 (M+·, 42), 305 (82), 273 (100), 168 (87),139(72).

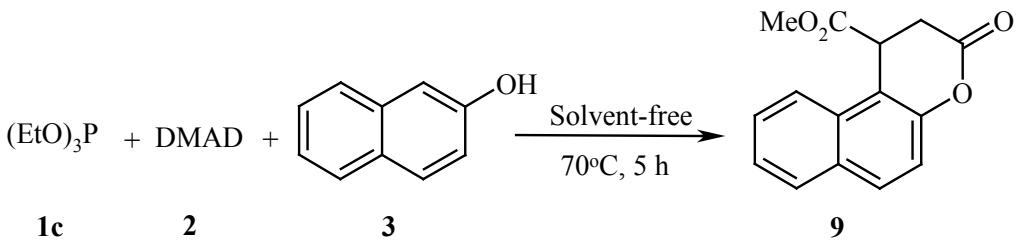
RESULT AND DISCUSSION

The reaction of dimethyl acetylene dicarboxylate 2 and 2-naphthol 3 in the presence of trimethyl or triphenyl phosphite 1 leads to oxaphosphaphenanthrene-3,4-dicarboxylate derivatives 4 in good yields (Scheme 2). The structures of 4 were determined on the basis of their ^{1}H, ^{13}C, and ^{31}P NMR spectra, IR spectra, elemental analyses, and mass spectrometric data. The ^{1}H NMR spectrum of 4a in $CDCl_3$ shows two singlets at δ = 3.21 and 3.72 ppm for the methoxy protons and one doublet at δ = 5.48 (^{3}JPH = 34 Hz) for the methine proton, along with multiplets at δ = 6.98-9.20 for the aromatic protons. Characteristic carbonyl resonances appear clearly at δ = 168.40 (d, ^{2}JPC = 17 Hz), 173.32 ppm, whereas the ylide carbon atom exhibits resonances at δ = 41.10 (d, ^{1}JPC = 225 Hz) ppm. The observed ^{1}JCP values are typical of an α-ylide ester [12]. The double bond character of the C-P bond and the presence of three electronegative oxo substituent on the phosphorus atom increases the ^{1}JCP value.11 Evidence for the presence of an oxaphosphaphenantrene skeleton in 4a was shown by the ^{13}C signals at δ = 118.22 (d, ^{3}JCP = 6 Hz) for CH of naphthalene moiety and at δ = 148.13 (d, ^{2}JCP = 8 Hz) for the C-O carbon of naphthalene. ^{31}P NMR signals was found at δ = 41.54 ppm. The ^{1}H and ^{13}C NMR spectra of 4b were similar to those for 4a except for the phosphoranyl moiety. Although we have not yet established the mechanism of the reaction between dimethylacetylene dicarboxylate and phosphites in the presence of 2-naphthol in an experimental manner, a possible explanation is proposed in (Scheme 2). On the basis of the well established chemistry of phosphorus nucleophiles2,3 it is reasonable to assume that ylide 4 results from initial addition of the phosphite to DMAD and subsequent protonation of the reactive 1:1 adduct, followed by attack of carbon atom of the anion of 2-naphthol 6 to cation 5 to generate ylide 7 which isomerises under the reaction conditions employed to produce the

oxaphosphorane 8. Elimination of ROH from 8 leads to product 4. The reaction between triethyl phosphite 1, dimethylacetylene dicarboxylate 2, and 2-naphthol 3 quantitatively gave product 9 (Scheme 3).



Scheme 2:

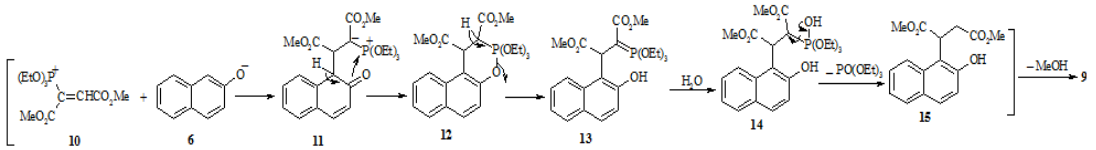


Scheme 3:

The IR spectrum of 9 exhibited the ester and lactone carbonyl groups at 1711 and 1752 cm^{-1}, respectively. The ^1H NMR spectrum of 9 showed a double doublet at δ = 2.82 (^2JHH = 16 Hz, ^3JHH = 6 Hz) for one of the methylene protons. The other methylene proton displayed a doublet (^2JHH = 16 Hz) at δ = 3.25 ppm. The methine proton showed a doublet (^3JHH = 6 Hz) at δ = 4.60 ppm. The coupling constants observed for this AMX system are consistent with a conformation in which theH-C-C-H dihedral angles for the CH-CH_2 moiety are expected to be about 90º and 30º [12]. The ^{13}C NMR spectrum of 9 displayed 15 distinct resonance in agreement with the proposed structure. A possible mechanism for the formation of compound 9 is shown in Scheme 4. The oxaphosphorane 12 is formed in similar steps shown for oxaphosphorane 8 in Scheme 2. However, since the ethoxide anion is a weaker living group, cleavage of the phosphorus-oxygen bond of the naphthol residue become favorable, giving dimethyl succinate 15. Lactonization of this hydroxy-ester gave product 9.

Under similar conditions, the reaction of dimethylacetylene dicarboxylate 2 and trimethyl phosphite 1 in the presence of 1-naphthol 16 gave succinate 17 in good yield (Scheme 5).

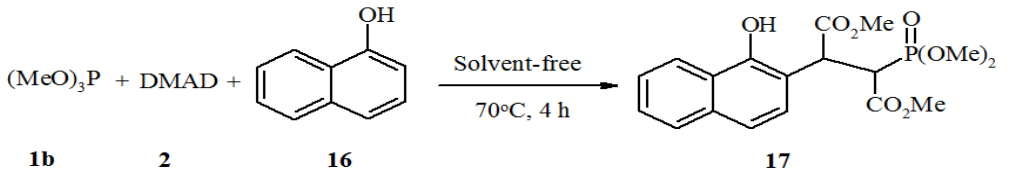
The ^1H NMR spectrum of 17 displayed signals for vicinal methine protons at δ = 3.88 and 4.99, which appeared as two set of double doublets with ^2JHP and ^3JHP values of 21 and 9 Hz, respectively. The methoxy groups of the phosphoranyl moiety are diastereotopic and show two separate doublets at δ = 2.85 and 3.67. The hydroxy proton was observed as a broad singlet at δ = 8.47 which disappeared with addition of D_2O. Observation of ^3JHH = 12 Hz for the vicinal



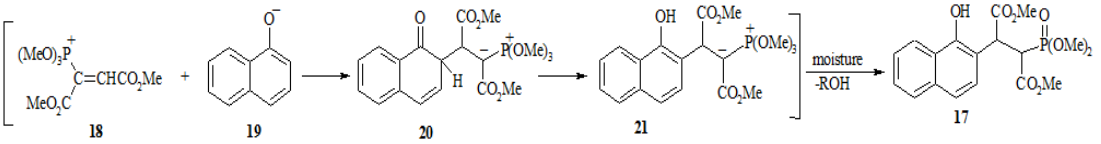
Scheme 4:

methine protons in 17 indicates the dominance of anti arrangement. A proposed mechanism for the formation of compound 17 is shown in Scheme 4.

In conclusion, we found that the reaction of dimethylacetylene dicarboxylate with trimethyl phosphite or triphenyl phosphite in the presence of 2-naphthol leads to functionalized oxaphospha phenanthrenes. The reaction of 1-naphthol with dimethylacetylene dicarboxylate and trimethyl phosphite produces, stereoselectively benzochromene derivative in high yield. The addition reaction of triethyl phosphite, dimethylacetylene dicarboxylate, and 1-naphthol or 2-naphthol leads quantitatively to benzochromene derivatives. The present method carries the advantage that, not only is the reaction performed under solvent-free conditions, but also the substances can be mixed without any activation or modification.



Scheme 5:



Scheme 6:

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