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Synthesis of Phosphorus Derivatives via Multicomponent Reactions

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Abstract

Stable derivatives of oxaphosphaphenanthrenes were prepared using multicomponent reactions of 3-bromo-2-naphthol, dialkyl acetylenedicarboxylate and trimethyl or triphenyl phosphite under microwave conditions with good yields.

Keywords: *Oxaphosphaphenanthrenes, Acetylenic compounds, Trimethyl phosphate, Triphenyl phosphate.*

Introduction

Phosphorus compounds containing P–C bonds are not mostly abundant in nature but they have diverse biological activity and have attracted significant synthetic and pharmacological interest [1, 2]. Besides precious applications, their use in the construction of the unsafe compounds sarin, soman, and VX-type chemical warfare agents (CWAs) is of note [3]. Phosphonates have important applications in flame retardancy [4, 5], organic synthesis [6], and biological applications [2c, 7]. Also, phosphonates have been used as substitutes of the corresponding esters and acids of high biological activity [8, 9] and as suitable probes for designing antibodies on the basis of transition state models.

A large number of methods have appeared describing novel syntheses of organophosphorus compounds [10-13]. Hence, we describe the reaction of dialkyl acetylenedicarboxylate with a trivalent phosphorus nucleophile such as trimethyl phosphite, or triphenyl phosphite in the presence of 3-bromo-2-naphthol under microwave conditions. This reaction was performed with the microwave irradiation as green source energy for synthesis of heterocyclic compounds.

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Experimental

Material and Equipments

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 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 ^{31}P 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 were used without further purification. The microwave instrument was applied in a type of MICROSYNTH from Mylestone Company.

General procedure for preparation of compounds **4**

To a magnetically stirred solution of dialkyl acethylenedicarboxylate **2** (2 mmol) and 3-bromo-2-naphthol **1** (2 mmol) as an OH-acid in 20 ml CH_3CN was added triphenyl phosphite or trimethyl phosphite **3** (2 mmol) under microwave conditions (In power of 800 w and T=70 ^{o}C). The reaction mixture was then stirred for 6h. After completion of reaction (monitored by TLC), the mixture of reaction was purified by preparative TLC on silica gel column chromatography (Merck 230-400 mesh) using n-hexane-EtOAc as eluent to give compound **4**.

*Spectral Data for the Compounds **4a-4d***

*Dimethyl 2,2-diphenoxy-3-bromo-4H-1-oxa-phospha phenanthrene-3,4-dicarboxylate (**4a**)*

White powder, m.p. 162-64 °C, 1.00 g, yield 87%. IR (KBr) (ν_{max}/cm^{-1}): 1665, 1723 cm^{-1}. Anal. Calcd for $C_{28}H_{22}BrO_7P$ (581.35): C, 57.85; H, 3.81. Found: C, 57.78; H, 3.76%. ^{1}H NMR (500 MHz, $CDCl_3$): 3.25 (3 H, s, MeO), 3.82 (3 H, s, MeO), 5.54 (1 H, d, $^{3}J_{HP}$ = 27.6 Hz, CH), 6.85-9.12 (15 H, m, 15 CH). ^{13}C NMR (125.7 MHz, $CDCl^3$): 42.0 (d, $^{1}J_{CP}$ = 232 Hz, C), 42.4 (d, $^{2}J_{CP}$ = 8.5 Hz, CH), 50.4 (MeO), 52.2 (OMe), 120.7 (d, $^{3}J_{CP}$ 5.2 Hz, 2 CH), 121.0 (d, $^{3}J_{PC}$ 9.6 Hz, C), 121.7 (d, $^{3}J_{PC}$ 4.6 Hz, 2 CH), 124.3 (CH), 125.7 (CH), 126.2 (CH), 126.5 (CH), 127.6 (CH), 128.5 (CH), 130.0 (m, 4 CH), 130.4 (CH), 131.3 (C), 131.8 (C), 132.2 (C), 148.5 (d $^{2}J_{PC}$ 9.2 Hz, C), 150.2 (m, 2 C), 167.6 (d $^{2}J_{PC}$ 16.8 Hz, C=O), 174.5 (C=O). ^{31}P NMR (202 MHz, $CDCl_3$): 42.4. EI-MS: m/z 581 (10, M^+), 504 (86), 428 (100), 77 (88), 31 (100).

*Diethyl 2,2-diphenoxy-3-bromo-4H-1-oxa-phospha phenanthrene Z-3,4-dicarboxylate (**4b**)*

Pale yellow powder, m.p. 170-172 °C, 0.95 g, yield 78%. IR (KBr) (ν_{max}/cm^{-1}): 1670, 1728

cm^{-1}. Anal. Calcd for $C_{30}H_{26}BrO_7P$ (609.41): C, 59.13; H, 4.30. Found: C, 59.26; H, 4.38%. ^{1}H NMR (500 MHz, $CDCl_3$): 1.32 (3 H, t, $^3J_{HH}$ = 7.4, Me), 1.37 (3 H, t, $^3J_{HH}$ = 7.3, Me), 4.22 (2 H, q, $^3J_{HH}$ = 7.4, CH_2O), 4.28 (2 H, q, $^3J_{HH}$ = 7.4, CH_2O), 5.58 (1 H, d, $^3J_{HP}$ = 28.0 Hz, CH), 6.82-9.10 (15 H, m, 15 CH). ^{13}C NMR (125.7 MHz, $CDCl_3$): 13.8 (Me), 14.2 (Me), 42.2 (d, $^1J_{CP}$ = 230 Hz, C), 42.5 (d, $^2J_{CP}$ = 8.7 Hz, CH), 61.7 (CH_2O), 62.3 (CH_2O), 121.2 (d, $^3J_{CP}$ 5.8 Hz, 2 CH), 121.4 (d, $^3J_{PC}$ 10.4 Hz, C), 122.3 (d, $^3J_{PC}$ 5.5 Hz, 2 CH), 124.8 (CH), 126.0 (CH), 126.5 (CH), 127.2 (CH), 127.8 (CH), 129.2 (CH), 130.4 (m, 4 CH), 130.7 (CH), 131.6 (C), 132.2 (C), 132.7 (C), 149.0 (d $^3J_{PC}$ 9.5 Hz, C), 150.8 (m, 2 C), 168.0 (d $^3J_{PC}$ 16.2 Hz, C=O), 174.8 (C=O). ^{31}P NMR (202 MHz, $CDCl_3$): 42.5. EI-MS: m/z 609 (10, M^+), 564 (53), 532 (74), 45 (68), 29 (100).

*Diisopropyl 2,2-diphenoxy-3-bromo-4H-1-oxa-phospha phenanthrene-3,4-dicarboxylate (***4c***)*

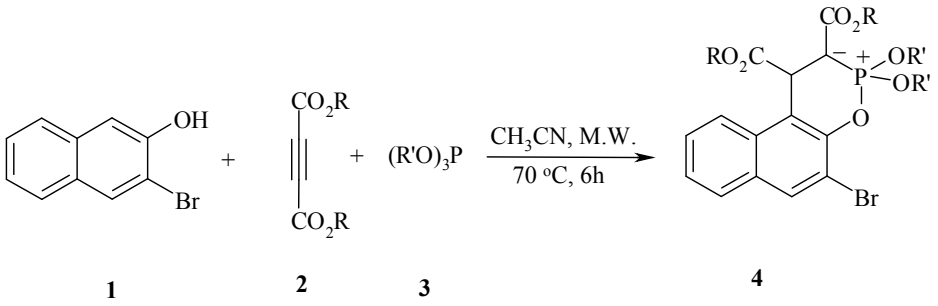
Pale Yellow powder, m.p. 182-184 °C, 0.90 g, yield 75%. IR (KBr) (ν_{max}/cm^{-1}): 1674, 1735 cm^{-1}. Anal. Calcd for $C_{32}H_{30}BrO_7P$ (637.46): C, 60.29; H, 4.74. Found: C, 60.18; H, 4.65%. ^{1}H NMR (500 MHz, $CDCl_3$): 1.35 (6 H, d, $^3J_{HH}$ = 6.5 Hz, 2 CH_3), 1.42 (6 H, d, $^3J_{HH}$ = 6.8 Hz, 2 CH_3), 5.28-5.36 (1 H, m, CH), 5.38-5.44 (1 H, m, CH), 5.62 (1 H, d, $^3J_{HP}$ = 28.4 Hz, CH), 6.85-9.15 (15 H, m, 15 CH). ^{13}C NMR (125.7 MHz, $CDCl_3$): 21.6 (2 CH_3), 22.3 (2 CH_3), 42.6 (d, $^1J_{CP}$ = 234.5 Hz, C), 42.8 (d, $^2J_{CP}$ = 9.3 Hz, CH), 68.8 ($CHMe_2$), 70.2 ($CHMe_2$), 121.6 (d, $^3J_{CP}$ 6.0 Hz, 2 CH), 122.0 (d, $^3J_{PC}$ 10.5 Hz, C), 122.5 (d, $^3J_{PC}$ 5.8 Hz, 2 CH), 125.2 (CH), 126.7 (CH), 127.3 (CH), 127.6 (CH), 128.4 (CH), 129.5 (CH), 130.8 (m, 4 CH), 131.2 (CH), 132.3 (C), 132.8 (C), 133.4 (C), 149.4 (d $^3J_{PC}$ 9.8 Hz, C), 151. (m, 2 C), 168.6 (d $^3J_{PC}$ 15.8 Hz, C=O), 175.5 (C=O). ^{31}P NMR (202 MHz, $CDCl_3$): 43.2.

*Dimethyl 2,2-dimethoxy-3-bromo-4H-1-oxa-phospha phenanthrene-3,4-dicarboxylate (***4d***)*

White crystals, m.p. 132-134 °C, 0.64 g, yield 90%. IR (KBr) (ν_{max}/cm^{-1}): 1650, 1727 cm^{-1}. Anal. Calcd for $C_{18}H_{18}BrO_7P$ (457.21): C, 47.29; H, 3.97. Found: C, 47.34; H, 4.03%. ^{1}H NMR (500 MHz, $CDCl_3$): 3.62 (3 H, s, MeO), 3.75 (3 H, s, MeO), 3.78 (3 H, d $^3J_{PH}$ 13.5 Hz, MeO), 3.97 (3 H, d $^3J_{PH}$ 13.5 Hz, MeO), 5.67 (1 H, d $^3J_{HP}$ 31.7 Hz, CH), 7.45 (1 H, t, $^3J_{HH}$ 9.4 Hz, CH), 7.62 (1 H, t, $^3J_{HH}$ 9.4 Hz), 7.82 (1 H, d $^3J_{HH}$ 9.6 Hz, CH), 7.87 (1 H, d $^3J_{HH}$ 9.6 Hz, CH), 8.12 (1 H, s, CH). ^{13}C NMR (125.7 MHz, $CDCl_3$): 39.4 (d, $^1J_{CP}$ 225.2 Hz, C), 41.6 (d, $^2J_{CP}$ 9.4 Hz, CH), 50.4 (MeO), 52.3 (MeO), 55.6 (d, $^2J_{PC}$ 6.4 Hz, P-OMe), 55.7 (d, $^2J_{PC}$ 6.4 Hz, P-OMe), 118.4 (d, $^3J_{PC}$ 6.8 Hz, C), 121.4 (d, $^3J_{PC}$ 9.5 Hz, C), 124.6 (CH), 125.5 (CH), 127.4 (CH), 128.6 (CH), 130.0 (CH), 131.4 (C), 131.7 (C), 149.2 (d $^2J_{PC}$ 8.4 Hz, C-O), 169.6 ($^2J_{PC}$ 18.4 Hz, C=O), 175.2 (C=O). ^{31}P NMR (202 MHz, $CDCl_3$): 42.8.

Results and discussion

The reaction of dialkyl acetylenedicarboxylate, 3-bromo-2-naphthol and trimethyl or triphenyl phosphite leads to 3-bromo-*4H*-1-oxa-phosphaphenanthrene-3,4-dicarboxylate derivatives **4** in excellent yields [13b] (Scheme 1).



1 **2** **3** **4**

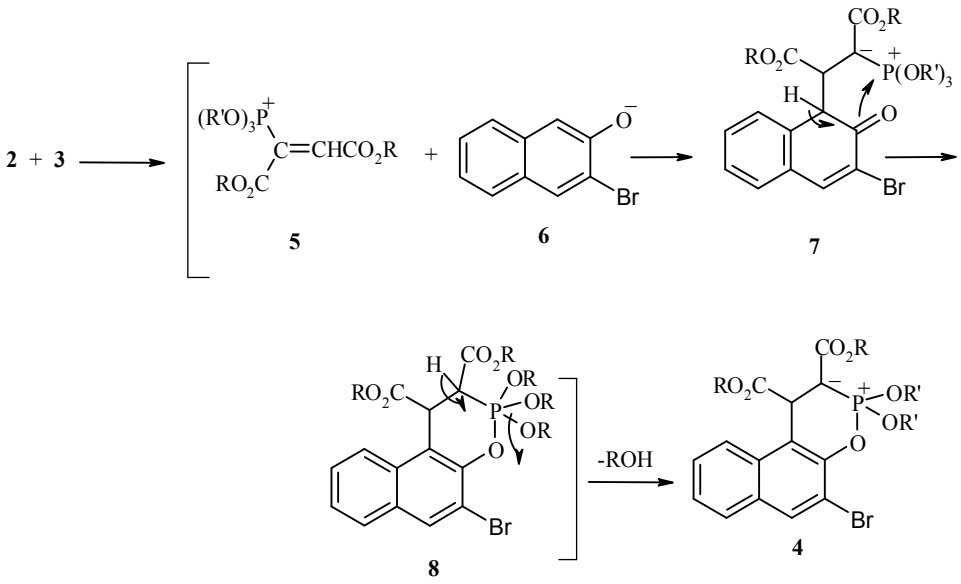
2, 3, 4	R	R'	Yield (%) of **4**
a	Me	Ph	87
b	Et	Ph	78
c	*iso*-pro	Ph	75
d	Me	Me	90

Scheme 1. The reaction between activated acetylene, 3-bromo-2-naphthol and trimethyl or triphenyl phosphite.

The structures of **4a-4d** were decided 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 for methoxy protons at 3.25 and 3.82 ppm and one doublets at δ = 5.54 ($^{3}J_{PH}$ = 27.6 Hz), for the methine proton, along with multiplets at δ = 6.85-9.12 for the aromatic protons. The presence of an ylide ester group in **4a** stabilizes by the observation of strong low-frequency carbonyl absorption at 1665 cm^{-1} in the IR spectrum [14]. The other ester carbonyl absorption in **4a** appears at 1723 cm^{-1}. The ^{13}C NMR spectrum consisted characteristic carbonyl resonances at δ = 167.6 (d, $^{2}J_{PC}$ = 16.8 Hz), and 174.5 ppm clearly, whereas the ylide carbon atom displays resonances at δ = 42.0 (d, $^{1}J_{PC}$ = 232 Hz) ppm. The observed $^{1}J_{CP}$ values are typical of a α-ylide ester [15]. The ^{31}P NMR signal was found at δ = 42.4 ppm.

Although the mechanism of this reaction has not been established, a plausible rationalization can be advanced to explain product formation (Scheme 2). On the basis of phosphorus nucleophiles chemistry, it is reasonable to presume that ylide **4** results from initial addition of the phosphite to the activated acetylenic compounds and following protonation of the reactive 1:1 adduct, followed by attack of carbon atom of the anion of 3-bromo-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**.



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

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

Conclusion

In conclusion, we found that the reaction of activated acetylenic compounds with trimethyl phosphite or triphenyl phosphite in the presence of 3-bromo-2-naphthol leads to a facile synthesis of some functionalized oxaphosphaphenanthrenes under microwave conditions without using any catalyst. Its advantages include ease of synthesis and work-up, high yields and green conditions.

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