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Multi component reaction of mercaptanols, triphenyl phosphite and acetylenic esters

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Abstract: Triphenyl phosphite reacts with dialkyl acetylene dicarboxylates in the presence of mercaptanols to produce of dialkyl 2-(diphenoxyphosphoryl)-3-[(2-hydroxy alkyl) sulfanyl] succinates in two diastromeric forms in 85- 90% yields.

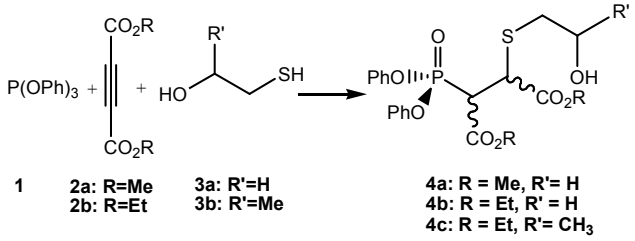
Keywords: *Triphenyl phosphite, dialkyl acetylene dicarboxilates, Mercaptanols..*

Introduction

Organophosphorus compounds, i.e. those bearing a carbon atom directly bond to a phosphorus atom, are synthetic targets of interest not least because of their value for variety of industrial, biological and chemical synthetic uses [1-3]. The successful attack by nucleophilic trivalent phosphorus on a carbon atom is facilitated when the latter is part of, or conjugated with, a carbonyl group, or when it is part of an unsaturated bond otherwise activated [1-9]. 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 [1, 9 and 10].
As part of our current studies, on the development of nucleophilic addition to acetylenic esters, we report the synthesis of dialkyl 2-(diphenoxyphosphoryl)-3-[(2-hydroxy alkyl) sulfanyl] succinates.

Results and discussion

The reaction of triphenyl phosphite **1** and dialkyl acetylene dicarboxylates **2** in the presence of mercaptanols **3** proceeds in CH_2Cl_2 at room temperature and 24 h to produce dialkyl 2-(diphenoxyphosphoryl)-3-[(2-hydroxy alkyl) sulfanyl] succinates as mixture of two diastereoisomers, in 85-90% yields (Scheme **1**).
The products were characterized based on their IR, ^{1}H NMR, ^{13}C NMR and ^{31}P NMR. The mass spectra of compounds **4a-c** displayed molecular ion peaks at appropriate values, which were consistent with 1:1:1 adducts of triphenyl phosphite, dialkyl acetylene dicarboxylates and the mercaptanols. The ^{1}H NMR spectrum in $CDCl_3$ of **4a** exhibited a multiplets for SCH_2 at δ = 3.0 - 3.12 ppm, two singlets at δ = 3.75 and 3.90 ppm for the metoxy groups, together with multiplets for vicinal methine protons and CH_2OH moiety at δ = 3.9 - 4.5 ppm, along with two broad multiplets for phenoxy moiety in **4a** at δ = 7.13 - 7.20 ppm. The proton-decoupled ^{13}C NMR spectrum of **4a** showed three teen distinct resonances in agreement with the proposed structure.



1 **2a: R=Me** **2b: R=Et** **3a: R'=H** **3b: R'=Me** **4a: R = Me, R'= H** **4b: R = Et, R' = H** **4c: R = Et, R'= CH_3**

Scheme 1.

The ^{1}H NMR, ^{13}C NMR showed that compound **4** possesses two stereogenic centers, two diastromers with *gauch* HCCH arrangements are possible (Scheme **2**).
The three-bond carbon-phosphorus coupling, $^3J_{cp}$, depends on configuration, as expected, transoid couplings being larger than cisoid ones. The karplus relation can be derived from the data for organophosphorus compounds with tetra and pentavalent phosphorus [12, 13, 14 and 15]. The observation of $^3J_{cp}$ of 10 Hz for the CO_2Me group in

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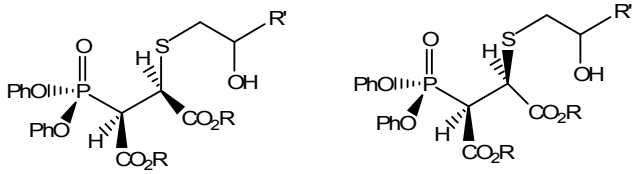
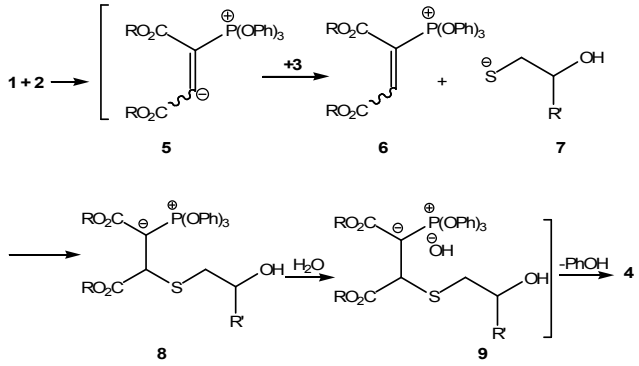
major isomer and 20.3 Hz in minor isomer is in agreement with the proposed structures.



(2R,3R)-4 or (2S*,3S*)-4 (2R,3S)-4 or (2S*,3R*)-4

Scheme 2.

Characteristic ester carbonyl resonances for the major diastereoisomer of **4a** appeared at δ = 166.9 (d, $^2J_{PC}$ = 5.1 Hz) and 171.2 (d, $^3J_{PC}$ = 10 Hz), whereas the carbon atom of the P-CH moiety appeared at δ = 48.0 (d, $^1J_{PC}$ = 129.0 Hz). The presence of three electronegative oxo substituents on the phosphorus atom increases the $^1J_{CP}$ value. Finally, the ^{31}P shifts of 11.75 - 12.70 ppm are in accord with the presence of C-P(O)(OC6H5)$_2$ groups in both diastereoisomers of **4**. Mechanistically, it is conceivable that the reaction involves initial formation of 1:1 zwitterionic intermediate [16-19] **5** between triphenyl phosphite **1** and acetylinic ester **2**. This intermediate is protonated by mercaptanol **3** and then attacked by the reaction by the conjugate base of mercaptanol **3** to produce the ylide **8** , which is then hydrolyzed to the **4** (Scheme **3**). Hydrolysis of alkyl triphenyl phosphonium salts in water has been reported to yield diphenyl alkylphosphonates [11].



Scheme 3.

In conclusion, we have reported a novel transformation involving dialkyl acetylene dicarboxylates and mercaptanols in the presence of triphenyl phosphite which affords dialkyl 2-(diphenoxyphosphoryl)-3-[(2-hydroxy alkyl) sulfanyl] succinates derivatives. The advantage of the present procedure is that reaction is performed under neutral conditions, and the starting material can be used without any activation or modification.

Experimental

Compounds **1**-3 were obtained from Fluka and were used without further purification. M.p.: Electrothermal-9100 apparatus. IR Spectra: Shimadzu IR-460 spectrometer. ^{1}H NMR and ^{13}C NMR spectra: Bruker DRX-400 AVANCE instrument; in $CDCl_3$ at 400 and 100 MHz, respectively; δ in ppm, J in Hz. EI-MS (70 eV): Finnigan-MAT-8430 mass spectrometer, in m/z. Elemental analyses (C, H, N) were performed with a Heraeus CHN-O-Rapid analyzer. The results agreed favorably with the calculated values.

General Procedure for the Preparation of Compounds 4a-4c

To a stirred solution of dialkyl acetylene dicarboxylates (2mmol) and the mercaptanols (2mmol) in CH_2Cl_2 (10 ml) was added triphenyl phosphite (0.61g, 2mmol) at room temperature. The reaction mixture was then stirred for 24 h. the solvent was removed under reduced pressure, and the residue was purified by column chromatography (SiO_2; hexan/AcOEt 3:1) to afford the pure adducts as mixture of two diastereomers.

Dimethyl 2-(diphenoxyphosphoryl)-3-[(2-hydroxy ethyl) sulfanyl]succinate (4a).

Yellow oil, yield: 0.82 g (90%), IR (KBr): ν = 1731 (C=O), 1250 (P=O), 2952 (CH), 3450 (OH) cm $^{-1}$. EI-MS: 454 (2, M+), 423 (5), 377 (35), 233 (38), 93 (100), 77 (86). Anal. Calc. for $C_{20}H_{23}O_8PS$ (454.43): C 55.75, H 5.57%; found: C 52.86, H 5.58 %. NMR data for the major isomer (60%); ^{1}H NMR: 3.0 - 3.12 (m, 2H, SCH_2), 3.75 (s, OMe), 3.90 (s, OMe), 3.90 - 4.5 (m, 2CH, CH_2OH), 7.13 - 7.20 (m, 10CH). ^{13}C NMR: 31.4 (CH_2), 43.6 (d, $^2J_{CP}$ = 2.0, CH), 47.8 (d, $^1J_{CP}$ = 131.0, CH), 53.3 (s, OMe), 60.8 (s, CH_2OH), 120.6 (d, $^3J_{CP}$ = 4.9, 4CH of $2C_6H_5$), 125.7 (s, 2CH of $2C_6H_5$), 129.5 (s, 2CH of $2C_6H_5$), 130.0 (s, 2CH of $2C_6H_5$), 149.7 (s, C_{ipso} of $2C_6H_5$), 149.8 (s, $2C_{ipso}$ of $2C_6H_5$), 166.9 (d, $^2J_{CP}$ = 5.1, C=O), 171.2 (d, $^3J_{CP}$ = 10, C=O), ^{31}P NMR: 11.75 [P(O)$(OC_6H_5)_2$]. NMR data for the minor isomer (40%); ^{1}H NMR: 2.78 – 2.90 (m, SCH_2), 3.74 (s, OMe), 3.80 (s, OMe), 3.8 – 3.95 (m, 2CH, CH_2OH), 7.30 - 7.40 (m, 10CH). ^{13}C NMR: 31.9 (CH_2), 42.4 (d, $^2J_{CP}$ = 2.0, CH), 48.0 (d, $^1J_{CP}$ = 138.0, CH), 53.1 (s, OMe), 59.7 (s, CH_2OH), 120.3 (d, $^3J_{CP}$ = 5.0, 4CH of $2C_6H_5$), 125.9 (s, 2CH of $2C_6H_5$), 129.8 (s, 2CH of $2C_6H_5$), 129.9 (s, 2CH of $2C_6H_5$), 149.6 (s, $2C_{ipso}$ of $2C_6H_5$), 149.9 (s, C_{ipso} of $2C_6H_5$), 167.3 (d,

$^{2}J_{CP}$ = 5.3, C=O), 170.0 (d, $^{3}J_{CP}$ = 20.1, C=O), ^{31}P NMR: 12.70 [P(O)(OC_6H_5)$_2$].

Diethyl 2-(diphenoxyphosphoryl)-3-[(2-hydroxy ethyl) sulfanyl]succinate (4b).

Yellow oil, yield: 0.82 g (85%), IR (KBr): ν = 1732 (C=O), 1252 (P=O), 2982 (CH), 3435 (OH) cm $^{-1}$. EI-MS: 482 (2, M+), 451 (5), 331 (35), 233 (38), 140 (41), 94 (85), 77 (100). Anal. Calc. for $C_{20}H_{23}O_8PS$ (482.50): C 54.77, H 5.64%; found: C 54.77, H 5.62%. NMR data for the major isomer (58%); ^{1}H NMR: 1.24 (t, $^{3}J_{HH}$ = 7.2, Me), 1.30 (t, $^{3}J_{HH}$ = 7.2, Me), 2.92 – 3.20 (m, SCH_2), 4.11 – 4.34 (m, 2CH, $2OCH_2$, CH_2OH), 7.14 - 7.21 (m, 10CH). ^{13}C NMR: 13.9 (Me), 14.1 (Me), 31.4 (CH_2), 43.9 (d, $^{2}J_{CP}$ = 2.0, CH), 47.9 (d, $^{1}J_{CP}$ = 129.0, CH), 60.3 (s, CH_2OH), 62.4 (OCH_2), 120.7 (d, $^{3}J_{CP}$ = 4.0, 4CH of $2C_6H_5$), 125.5 (s, 2CH of $2C_6H_5$), 129.7 (s, 2CH of $2C_6H_5$), 129.8 (s, 2CH of $2C_6H_5$), 150.0 (s, $2C_{ipso}$ of $2C_6H_5$), 166.7 (d, $^{2}J_{CP}$ = 6.0, C=O), 171.8 (d, $^{3}J_{CP}$ = 9.0, C=O), ^{31}P NMR: 12.1 [P(O)(OC_6H_5)$_2$]. NMR data for the minor isomer (42%); ^{1}H NMR: 1.22 (t, $^{3}J_{HH}$ = 7.2, Me), 1.32 (t, $^{3}J_{HH}$ = 7.2, Me), 2.74 – 2.85 (m, SCH_2), 3.70 – 4.08 (m, 2CH, $2OCH_2$, CH_2OH), 7.25 - 7.36 (m, 10CH). ^{13}C NMR: 13.8 (Me), 14.0 (Me), 31.9 (CH_2), 45.6 (d, $^{2}J_{CP}$ = 2.0, CH), 48.3 (d, $^{1}J_{CP}$ = 137.0, CH), 59.8 (s, CH_2OH), 62.1 (s, OCH_2), 120.4 (d, $^{3}J_{CP}$ = 4.0, 4CH of $2C_6H_5$), 125.4 (s, 2CH of $2C_6H_5$), 125.7 (s, 2CH of $2C_6H_5$), 129.8 (s, 2CH of $2C_6H_5$), 129.9 (s, 2CH of $2C_6H_5$), 149.6 (s, $2C_{ipso}$ of $2C_6H_5$), 166.3 (d, $^{2}J_{CP}$ = 5.0, C=O), 170.9 (d, $^{3}J_{CP}$ = 21.0, C=O), ^{31}P NMR: 13.11 [P(O)(OC_6H_5)$_2$].

Diethyl 2-(diphenoxyphosphoryl)-3-[(2-hydroxy propyl) sulfanyl]succinate (4c).

Yellow oil, yield: 0.84 g (85%), IR (KBr): ν = 1732 (C=O), 1256 (P=O), 2982 (CH), 3450 (OH) cm $^{-1}$. EI-MS: 496 (2, M+), 467 (5), 346 (35), 233 (38), 233 (38), , 94 (85), 77 (100). Anal. Calc. for $C_{20}H_{23}O_8PS$ (496.51): C 55.64, H 5.89%; found: C 55.62, H 5.85%. NMR data for the major isomer (58%); ^{1}H NMR: 1.21 (t, $^{3}J_{HH}$ = 7.2, Me), 1.25 (t, $^{3}J_{HH}$ = 7.2, Me), 1.30 (d, $^{3}J_{HH}$ = 6.1, Me), 2.45 – 2.85 (m, SCH_2), 4.13 – 4.38 (m, 2CH, $2OCH_2$, CHOH), 7.15 - 7.24 (m, 10CH). ^{13}C NMR: 13.9 (Me), 14.1 (Me), 14.2 (Me), 29.3 (CH_2), 44.3 (d, $^{2}J_{CP}$ = 1.3, CH), 47.8 (d, $^{1}J_{CP}$ = 129.8, CH), 62.3 (OCH_2), 67.3 (s, CHOH),120.7 (d, $^{3}J_{CP}$ = 4.0, 4CH of $2C_6H_5$), 125.7 (s, 2CH of $2C_6H_5$), 129.8 (s, 2CH of $2C_6H_5$), 129.9 (s, 2CH of $2C_6H_5$), 149.9 (s, $2C_{ipso}$ of $2C_6H_5$), 166.7 (d, $^{2}J_{CP}$ = 5.3, C=O), 169.1 (d, $^{3}J_{CP}$ = 11.9, C=O), ^{31}P NMR: 11.94 [P(O)(OC_6H_5)$_2$]. NMR data for the minor isomer (42%); ^{1}H NMR: 1.22 (t, $^{3}J_{HH}$ = 7.2, Me), 1.24 (t, $^{3}J_{HH}$ = 7.2, Me), 1.32 (d, $^{3}J_{HH}$ = 6.3, Me), 2.86 – 3.03 (m, SCH_2), 3.83 – 4.10 (m, 2CH, $2OCH_2$, CHOH), 7.30 - 7.35 (m, 10CH). ^{13}C NMR: 13.8 (Me), 14.0 (Me), 14.1 (Me), 31.4 (CH_2), 44.7 (d, $^{2}J_{CP}$ = 2.0, CH), 48.7 (d, $^{1}J_{CP}$ = 137.7, CH, 62.0 (s, OCH_2),), 67.5 (s, CH) 120.3 (d, $^{3}J_{CP}$ = 4.3, 4CH of $2C_6H_5$), 125.3 (s, 2CH of $2C_6H_5$), 125.3 (s, 2CH of $2C_6H_5$), 129.7 (s, 2CH of $2C_6H_5$), 130.0 (s, 2CH of $2C_6H_5$), 149.7 (s, $2C_{ipso}$ of $2C_6H_5$), 166.6 (d, $^{2}J_{CP}$ = 5.6, C=O), 169.6 (d, $^{3}J_{CP}$ = 22.5, C=O), ^{31}P NMR: 13.05 [P(O)(OC_6H_5)$_2$].

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