Efficient Synthesis of Succinate Derivatives using Mercaptoalkanols or Mercaptophenols

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A one-pot synthesis of dialkyl 2-(diphenoxyphosphoryl)-3-[hydroxy (alkyl)(aryl) sulfanyl] succinate derivatives *via* the reaction between dialkyl acetylenedicarboxylates, triphenyl phosphite and mercaptoalkanols or mercaptophenols is described. These reactions lead to the formation of dialkyl 2-(diphenoxyphosphoryl)-3-[hydroxy (alkyl)(aryl) sulfanyl] succinates as a mixture of two diastereomers without using any catalyst and in good yields.

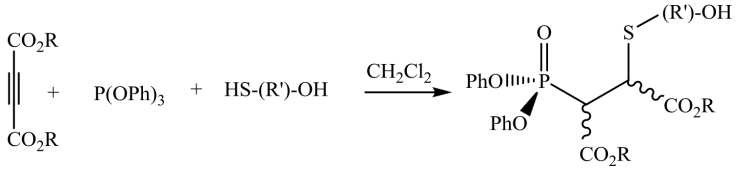
Key words: Triphenyl Phosphite, Dialkyl Acetylenedicarboxilates, Mercaptoalkanol, Mercaptophenols

Introduction

Phosphorus compounds containing P–C bonds are not particularly plentiful in nature but they have diverse biological activity and have attracted considerable synthetic and pharmacological interest [1, 2]. Besides valuable applications, their use in the production of the dangerous compounds sarin, soman, and VX-type chemical warfare agents (CWAs) is of note [3]. Phosphonates have important applications in flame retardants [4, 5], organic synthesis [6] and biological applications [2c, 7]. Phosphonates have also been used as substitutes of the corresponding esters and acids of high biological activity [8, 9] and as convenient probes for designing antibodies on the basis of transition state models. Hence, a large number of methods have appeared describing novel syntheses of phosphonate systems [10 – 13]. As part of our current studies on the development of nucleophilic addition to acetylenic esters, we report the synthesis of dialkyl 2-(diphenoxyphosphoryl)-3-[hydroxy (alkyl)(aryl) sulfanyl] succinates in good yield. Dialkyl acetylenedicarboxylates, **1**, triphenyl phosphite, **2**, and mercaptanols or mercaptophenols, **3**, undergo a smooth 1 : 1 : 1 addition reaction in CH_2Cl_2 at r. t. to give dialkyl 2-(diphenoxyphosphoryl)-3-[hydroxy (alkyl)(aryl) sulfanyl] succinates, **4**, as a mixture of two diastereoisomers, in 85 – 90 % yield (Scheme 1).

Results and Discussion

The structures of compounds **4a** – **f** were determined on the basis of their IR, ^{1}H NMR, ^{13}C NMR and ^{31}P NMR spectra. The mass spectra of these compounds display molecular ion peaks at the appropriate m/z values. The ^{1}H NMR spectrum of **4e** exhibits two



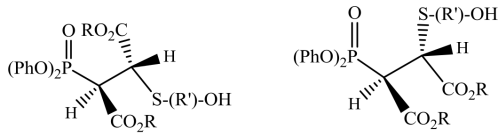
1a: R = Me
1b: R = Et

2

3a: R' = -CH_2CH_2-
3b: R' = -$CH_2CH(CH_3)$-
3c: R' = 4-OH-C_6H_4

4a: R = Me, R' = -CH_2CH_2-
4b: R = Me, R' = -$CH_2CH(CH_3)$-
4c: R = Et, R' = -CH_2CH_2-
4d: R = Et, R' = -$CH_2CH(CH_3)$-
4e: R = Me, R' = 4-OH-C_6H_4
4f: R = Et, R' = 4-OH-C_6H_4

Scheme 1. Synthesis of compounds **4a** - **f**.



major isomer
4-(*2R*,3S**)

minor isomer
4-(*2R*,3R**)

Scheme 2. Diastereomers of compound **4**.

singlets at δ = 3.70 and 3.90 ppm for two methoxy groups and two doublet of doublets at δ = 4.01 ($^2J_{PH}$ = 21.4, $^3J_{HH}$ = 11.6 Hz) and 4.23 ppm (dd, $^3J_{HP}$ = 11.2, $^3J_{HH}$ = 7.6 Hz) for the methine protons.

The presence of the ^{31}P nucleus complicates both the ^{1}H and ^{13}C NMR spectra of **4a – f** and helps in the assignment of the signals by long-range coupling with ^{1}H and ^{13}C nuclei. The observation of $^3J_{HH}$ = 7.6 – 11.6 Hz for the vicinal methine protons in **4a – f** confirms the dominance of the anti arrangement. Since compound **4** has two stereogenic centers, two diastereomers with anti HCCH arrangements are possible (Scheme 2).

Each of the diastereomers is present as racemate. Based on the Karplus relation for organophosphorus compounds with tetra- and penta-valent phosphorus, the three-bond carbon-phosphorus coupling constant, $^3J_{CP}$, depends on the conformation, and, transoid couplings are larger than cisoid ones [14, 15]. The observation of $^3J_{CP}$ = 3.7 – 6.5 Hz for the CO_2Me group is in agreement with the (2*R*, 3*S*) or (2*S*, 3*R*) diastereomer as the major isomer (58 – 64 %), and the absolute configuration of the first is depicted in Scheme 1. Since the minor diastereomer shows $^3J_{CP}$ = 19.5 – 22.6 Hz for the CO_2Me group, its configuration is (2*R*, 3*R*) or (2*S*, 3*S*). Characteristic ester carbonyl resonances for the major diastereoisomer of **4e** appeared at δ = 166.4 (d, $^2J_{PC}$ = 5.2 Hz) and 166.9 ppm (d, $^3J_{PC}$ = 3.7 Hz), whereas the carbon atom of the P–CH moiety appeared at δ = 48.2 ppm (d, $^1J_{PC}$ = 127.0 Hz). The presence of three electronegative oxo substituents on the phosphorus atom increases the $^1J_{CP}$ value. Finally, the ^{31}P shift of 11.63 – 13.14 ppm is in agreement with the presence of a phosphonate moiety in both diastereoisomers of **4**. Although the mechanism of this reaction has not been established, a plausible rationalization can be advanced to explain the product formation [16] (Scheme 3). On the basis of the well established chemistry of trivalent phosphorus nucleophiles it is reasonable to assume that phosphonate derivatives **4** results from the initial addition of triphenylphosphite to the acetylenic compound and subsequent attack of the resulting anion **5** which is protonated by mercaptanol or mercaptophenol **3** and then attacked by the conjugate base of mercaptoalkanol or mercaptophenol **3** to produce ylide **8**, which is then hydrolyzed to give **4**.

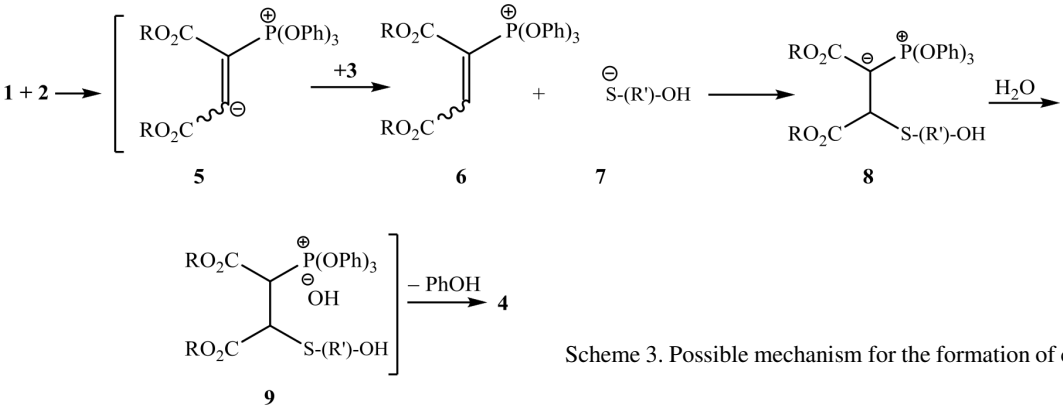
Conclusion

In conclusion, we reported a novel method involving dialkyl acetylenedicarboxylates **1** and triphenyl phosphite (**2**) in the presence of mercaptanols or mercaptophenols **3** for the synthesis of dialkyl 2-(diphenoxyphosphoryl)-3-[hydroxy (alkyl)(aryl) sulfanyl] succinates **4**. The advantages of our route are that the reaction is performed under neutral and mild condition, without using a catalyst.

Experimental Section

General

Melting points were taken on a Kofler hot stage apparatus and are uncorrected. ^{1}H, ^{13}C and ^{31}P NMR spectra were obtained on a Bruker FT-500 spectrometer in $CDCl_3$ with



Scheme 3. Possible mechanism for the formation of compounds **4**.

tetramethylsilane (TMS) as an internal standard (^{1}H, ^{13}C) or 85 % H_3PO_4 as external standard (^{31}P). Chemical shifts δ are given in ppm, coupling constants J in Hz. Mass spectra were recorded with a Finnigan Mat TSQ-70 spectrometer. Infrared (IR) spectra were recorded on a Nicolet Magna 550-FT spectrometer. Elemental analyses were carried out with a Perkin-Elmer model 240-C apparatus. The results of elemental analyses (C, H, N) were within ±0.4 % of the calculated values. Acetylenic ester, phenacyl bromide or its derivatives and triphenylphosphine were obtained from Fluka and were used without further purification.

*General procedure for the preparation of compounds **4a–f***

To a magnetically stirred solution of a dialkyl acetylenedicarboxylate **1** (2 mmol) and triphenyl phosphite (**2**) in CH_2Cl_2 (5 mL) was slowly added a mercaptoalkanol or mercaptophenol **3** (2 mmol), and the reaction mixture was stirred for 24 h at r. t. After completion of the reaction, the solvent was removed under reduced pressure and the residue was purified by chromatography over silica gel (Merck 230–400 mesh) using an *n*-hexane-AcOEt mixture (3 : 1) as eluant, to afford the pure adducts as mixture of two diastereomers.

*Dimethyl 2-(diphenoxyphosphoryl)-3-[(2-hydroxyethyl)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: m/z (%) = 454 (2) $[M]^+$, 439 (5), 377 (35), 233 (38), 93 (100), 77 (86). – Anal. for $C_{20}H_{23}O_8PS$ (454.43): calcd. C 55.75, H 5.57; found C 52.86, H 5.58 %. – NMR data for the major isomer (60 %): ^{1}H NMR: δ = 3.0–3.12 (m, 2 H, SCH_2), 3.30, (bs, 1 H, OH), 3.75 (s, 3 H, MeO), 3.90 (s, 3 H, MeO), 2.90–3.15 (m, 2 H, CH_2), 3.94 (dd, 1 H, $^2J_{PH}$ = 21.6, $^3J_{HH}$ = 9.6, CH), 4.33 (dd, 1 H, $^3J_{PH}$ = 11.4, $^3J_{HH}$ = 7.4, CH), 7.13–7.20 (m, 10 H, 10 CH). – ^{13}C NMR: δ = 31.4 (CH_2), 43.6 (d, $^2J_{CP}$ = 2.0, CH), 47.8 (d, $^1J_{CP}$ = 131.0, CH), 53.1 (s, OMe), 53.3 (s, OMe), 60.8 (s, CH_2OH), 120.6 (d, $^3J_{CP}$ = 4.9, 2 CH), 120.4 (d, $^3J_{CP}$ = 4.9, 2 CH), 125.7 (s, 2 CH), 130.0 (s, 4 CH), 149.8 (s, 2 C), 166.9 (d, $^2J_{CP}$ = 5.1, C=O), 171.2 (d, $^3J_{CP}$ = 5.8, C=O). – ^{31}P NMR: δ = 11.75 [P(O)$(OC_6H_5)_2$]. – NMR data for the minor isomer (40 %): ^{1}H NMR: δ = 2.78–2.90 (m, 2 H, SCH_2), 3.74 (s, 3 H, MeO), 3.80 (s, 3 H, MeO), 2.72–2.90 (m, 2 H, CH_2), 3.86 (dd, 1 H, $^2J_{PH}$ = 21.4, $^3J_{HH}$ = 10.2, CH), 4.22 (dd, 1 H, $^3J_{PH}$ = 11.1, $^3J_{HH}$ = 7.6, CH), 7.30–7.40 (m, 10 H, 10 CH). – ^{13}C NMR: δ = 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, 2 CH), 120.2 (d, $^3J_{CP}$ = 5.0, 2 CH), 125.9 (s, 2 CH), 129.8 (s, 4 CH), 149.6 (s, 2 C), 167.3 (d, $^2J_{CP}$ = 5.3, C=O), 170.0 (d, $^3J_{CP}$ = 20.1, C=O). – ^{31}P NMR: δ = 12.70 [P(O)$(OC_6H_5)_2$].

*Dimethyl 2-(diphenoxyphosphoryl)-3-[(2-hydroxypropyl)-sulfanyl] succinate (**4b**)*

Yellow oil, yield: 0.78 g (85 %). – IR (KBr): ν = 1735 (C=O), 1260 (P=O), 2980 (CH), 3500 (OH) cm^{-1}. – EI–MS: m/z (%) = 468 (2) $[M]^+$, 453 (8), 377 (40), 233 (43), 93 (100), 91 (85). – Anal. for $C_{21}H_{25}O_8PS$ (460.46): calcd. C 53.84, H 5.38; found C 53.80, H 5.38 %. – NMR data for the major isomer (60 %): ^{1}H NMR: δ = 1.14 (d, 3 H, $^3J_{HH}$ = 6.7, Me), 2.80–2.90 (m, 2 H, SCH_2), 3.00 (bs, 1 H, OH), 3.71 (s, 3 H, MeO), 3.75 (s, 3 H, MeO), 3.86–3.90 (m, 1 H, CH), 4.14 (dd, 1 H, $^2J_{PH}$ = 21.0, $^3J_{HH}$ = 11.0, CH), 4.23 (dd, 1 H, $^3J_{PH}$ = 11.2, $^3J_{HH}$ = 7.6, CH), 7.20–7.32 (m, 10 H, 10 CH). – ^{13}C NMR: δ = 22.4 (CH_3), 35.2 (CH_2), 37.4 (d, $^1J_{CP}$ = 129.8, CH), 42.3 (d, $^2J_{CP}$ = 2.1, CH), 52.1 (OMe), 53.3 (OMe), 68.9 (s, CH), 120.8 (d, $^3J_{CP}$ = 4.0, 2 CH), 120.7 (d, $^3J_{CP}$ = 4.3, 2 CH), 125.9 (s, 2 CH), 129.8 (s, 4 CH), 149.8 (s, 2 C), 166.6 (d, $^2J_{CP}$ = 5.3, C=O), 169.5 (d, $^3J_{CP}$ = 6.2, C=O). – ^{31}P NMR: δ = 11.83 [P(O)$(OC_6H_5)_2$]. – NMR data for the minor isomer (40 %): ^{1}H NMR: δ = 1.20 (d, 3 H, $^3J_{HH}$ = 7.0, Me), 2.92–3.02 (m, 2 H, SCH_2), 2.76 (bs, 1 H, OH), 3.72 (s, 3 H, MOe), 3.81 (s, 3 H, MeO), 3.82–3.85 (m, 1 H, CH), 4.10 (dd, 1 H, $^2J_{PH}$ = 21.2, $^3J_{HH}$ = 10.9, CH), 4.25 (dd, 1 H, $^3J_{PH}$ = 11.2, $^3J_{HH}$ = 7.6, CH), 7.11–7.21 (m, 10 H, 10 CH). – ^{13}C NMR: δ = 22.6 (CH_3), 35.0 (CH_2), 37.2 (d, $^1J_{CP}$ = 129.8, CH), 42.5 (d, $^2J_{CP}$ = 2.6, CH), 52.2 (OMe), 53.5 (OMe), 70.0 (s, CH), 120.5 (d, $^3J_{CP}$ = 4.4, 2 CH of $2C_6H_5$), 120.6 (d, $^3J_{CP}$ = 4.4, 2 CH), 125.9 (s, 2 CH), 129.8 (s, 4 CH), 149.8 (s, 2 C), 166.6 (d, $^2J_{CP}$ = 5.7, C=O), 169.5 (d, $^3J_{CP}$ = 22.0, C=O). – ^{31}P NMR: δ = 12.71 [P(O)-$(OC_6H_5)_2$].

*Diethyl 2-(diphenoxyphosphoryl)-3-[(2-hydroxyethyl)sulfanyl]succinate (**4c**)*

Yellow oil, yield: 0.82 g (85 %). – IR (KBr): ν = 1732 (C=O), 1252 (P=O), 2982 (CH), 3435 (OH) cm^{-1}. – EI–MS: m/z (%) = 482 (2) $[M]^+$, 453 (5), 405 (15), 331 (35), 233 (38), 249 (53), 94 (100), 77 (86). – Anal. for $C_{20}H_{23}O_8PS$ (482.50): calcd. C 54.77, H 5.64; found C 54.77, H 5.62 %. – NMR data for the major isomer (58 %): ^{1}H NMR: δ = 1.24 (t, 3 H, $^3J_{HH}$ = 7.2, Me), 1.30 (t, 3 H, $^3J_{HH}$ = 7.2, Me), 3.00–3.15 (m, 2 H, SCH_2), 3.30 (bs, 1 H, OH), 3.82–3.91 (m, 2 H, CH_2), 3.95–4.10 (m, 2 H, 2 OCH_2), 3.92 (dd, 1 H, $^2J_{PH}$ = 22.0, $^3J_{HH}$= 11.0, CH), 4.20 (dd, 1 H, $^3J_{PH}$ = 11.2, $^3J_{HH}$ = 7.6, CH), 7.14–7.21 (m, 10 H, 10 CH). – ^{13}C NMR: δ = 13.9 (Me), 14.1 (Me), 31.4 (CH_2), 43.9 (d, $^2J_{CP}$ = 2.0, CH), 47.9 (d, $^1J_{CP}$ = 129.0, CH), 60.3 (s, CH_2OH), 62.4 (OCH_2), 120.8 (d, $^3J_{CP}$ = 4.0, 2 CH), 120.7 (d, $^3J_{CP}$ = 4.3, 2 CH), 125.5 (s, 2 CH), 129.7 (s, 2 CH), 129.8 (s, 2 CH), 150.0 (s, 2 C), 166.7 (d, $^2J_{CP}$ = 6.0, C=O), 171.8 (d, $^3J_{CP}$ = 5.3, C=O). – ^{31}P NMR: δ = 12.1 [P(O)$(OC_6H_5)_2$]. – NMR data for the minor isomer (42 %): ^{1}H NMR: δ = 1.22 (t, 3 H, $^3J_{HH}$ = 7.2, Me), 1.32 (t, 3 H, $^3J_{HH}$ = 7.2, Me), 2.74–2.85 (m, 2 H,

SCH_2), 3.11 (bs, 1 H, OH), 3.73 – 3.82 (m, 2 H, CH_2), 3.86 – 3.95 (m, 4 H, 2 OCH_2), 3.94 (dd, 1 H, $^2J_{PH}$ = 22.2, $^3J_{HH}$ = 11.2, CH), 4.53 (dd, 1 H, $^3J_{PH}$ = 11.2, 1 H, $^3J_{HH}$ = 7.2, CH), 7.25 – 7.36 (m, 10 H, 10 CH). – ^{13}C NMR: δ = 13.8 (Me), 14.0 (Me), 31.9 (CH_2), 45.6 (d, $^2J_{CP}$ = 2.0, CH), 48.3 (d, $^1J_{CP}$ = 137.0, CH), 59.8 (s, CH_2OH), 62.1 (s, OCH_2), 120.3 (d, $^3J_{CP}$ = 4.6, 2 CH), 120.6 (d, $^3J_{CP}$ = 5.0, 2 CH), 125.4 (s, 2 CH), 125.7 (s, 2 CH), 129.8 (s, 2 CH), 129.9 (s, 2 CH), 149.6 (s, 2 C), 166.3 (d, $^2J_{CP}$ = 5.0, C=O), 170.9 (d, $^3J_{CP}$ = 21.0, C=O). – ^{31}P NMR: δ = 13.11 [P(O)$(OC_6H_5)_2$].

*Diethyl 2-(diphenoxyphosphoryl)-3-[(2-hydroxypropyl)sulfanyl]succinate (**4d**)*

Yellow oil, yield: 0.84 g (85 %). – IR (KBr): ν = 1732 (C=O), 1256 (P=O), 2982 (CH), 3450 (OH) cm^{-1}. – EI–MS: m/z = 496 (2) $[M]^+$, 467 (5), 405 (17), 346 (38), 233 (42), 94 (100), 91 (80). – Anal. for $C_{20}H_{23}O_8PS$ (496.51): calcd. C 55.64, H 5.89; found C 55.62, H 5.85 %. – NMR data for the major isomer (58 %): ^{1}H NMR: δ = 1.21 (t, 3 H, $^3J_{HH}$ = 7.2, Me), 1.25 (t, 3 H, $^3J_{HH}$ = 7.2, Me), 1.30 (d, 3 H, $^3J_{HH}$ = 7.1, Me), 2.52 – 2.93 (m, 2 H, SCH_2), 3.11 (bs, 1 H, OH), 3.74 – 3.83 (m, 2 H, CH_2), 3.93 – 4.06 (m, 4 H, 2 OCH_2), 3.95 (dd, 1 H, $^2J_{PH}$ = 21.6, $^3J_{HH}$= 9.6, CH), 4.11 (dd, 1 H, $^3J_{PH}$ = 11.6, $^3J_{HH}$ = 7.8, CH), 7.15 – 7.24 (m, 10 H, 10 CH). – ^{13}C NMR: δ = 13.9 (Me), 14.1 (Me), 14.2 (Me), 29.3 (CH_2), 44.3 (d, $^2J_{CP}$ = 1.3, CH), 47.8 (d, $^1J_{CP}$ = 129.8, CH), 62.3 (OCH_2), 67.3 (s, CHOH), 120.8 (d, $^3J_{CP}$ = 4.3, 2 CH of $2C_6H_5$), 120.7 (d, $^3J_{CP}$ = 4.3, 2 CH), 125.7 (s, 2 CH), 129.8 (s, 2 CH), 129.9 (s, 2 CH), 149.9 (s, 2 C), 166.7 (d, $^2J_{CP}$ = 5.3, C=O), 169.1 (d, $^3J_{CP}$ = 6.5, C=O). – ^{31}P NMR: δ = 11.94 [P(O)$(OC_6H_5)_2$]. – NMR data for the minor isomer (42 %): ^{1}H NMR: δ = 1.22 (t, 3 H, $^3J_{HH}$ = 7.2, Me), 1.24 (t, 3 H, $^3J_{HH}$ = 7.2, Me), 1.32 (d, 3 H, $^3J_{HH}$ = 6.3, Me), 2.42 – 2.62 (m, 2 H, SCH_2), 2.26 (bs, 1 H, OH), 3.63 – 3.71 (m, 2 H, CH_2), 3.82 – 3.92 (m, 4 H, 2 OCH_2), 3.90 (dd, 1 H, $^2J_{PH}$ = 22.0, $^3J_{HH}$= 11.0, CH), 4.09 (dd, 1 H, $^3J_{PH}$ = 11.6, $^3J_{HH}$ = 7.6, CH), 7.30 – 7.35 (m, 10 H, 10 CH). – ^{13}C NMR: δ = 13.8 (Me), 14.0 (Me), 14.1 (Me), 31.4 (CH_2), 44.7 (d, $^2J_{CP}$ = 2.0, CH), 48.7 (d, $^1J_{CP}$ = 137.7, CH, 62.0 (s, OCH_2), 67.5 (s, CH), 120.3 (d, $^3J_{CP}$ = 4.3, 2 CH), 120.4 (d, $^3J_{CP}$ = 4.3, 2 CH), 125.3 (s, 2 CH), 129.7 (s, 2 CH), 130.0 (s, 2 CH), 149.7 (s, 2 C), 166.6 (d, $^2J_{CP}$ = 5.6, C=O), 169.6 (d, $^3J_{CP}$ = 22.5, C=O). – ^{31}P NMR: δ = 13.05 [P(O)$(OC_6H_5)_2$].

*Dimethyl 2-(diphenoxyphosphoryl)-3-[(4-hydroxyphenyl)-sulfanyl]succinate (**4e**)*

Yellow oil, yield: 0.95 g (95 %). – IR (KBr): ν = 1736 (C=O), 1253 (P=O), 2983 (CH), 3415 (OH) cm^{-1}. – EI–MS: m/z = 502 (2) $[M]^+$, 443 (6), 377 (12), 296 (38), 233 (42), 93 (100). – Anal. for $C_{24}H_{23}O_8PS$ (502.47): calcd. C 57.37, H 4.61; found C 57.35, H 4.60 %. – NMR data for the major isomer (64 %): ^{1}H NMR: δ = 3.70 (s, 3 H, MeO), 3.90 (s, 3 H, MeO), 4.01 (dd, 1 H, $^2J_{PH}$ = 21.4, $^3J_{HH}$ = 11.6, CH), 4.23 (dd, 1 H, $^3J_{PH}$ = 11.2, $^3J_{HH}$ = 7.6, CH), 4.96 (bs, 1 H, OH), 6.70 (d, $^3J_{HH}$ = 8.8, 2 CH), 7.20 – 7.32 (m, 10 CH), 7.33 (d, $^3J_{HH}$ = 9.6, 2 CH). – ^{13}C NMR: δ = 48.2 (d, $^1J_{CP}$ = 127.0, CH), 49.7 (d, $^2J_{CP}$ = 3.0, CH), 52.7(s, OMe), 53.5(s, OMe), 116.4 (s, 2 CH), 120.0 (s, C), 120.6 (d, $^3J_{CP}$ = 4.3, 2 CH), 120.7 (d, $^3J_{CP}$ = 4.3, 2 CH), 125.8 (s, 2 CH), 129.8 (s, 4 CH), 137.4 (s, 2 CH), 149.8 (s, 2 C), 158.3 (s, C), 166.4 (d, $^2J_{CP}$ = 5.2, C=O), 169.9 (d, $^3J_{CP}$ = 3.7, C=O). – ^{31}P NMR: δ = 11.63[P(O)$(OC_6H_5)_2$]. – NMR data for the minor isomer (36 %): ^{1}H NMR: 3.71 (s, 3 H, MeO), 3.72 (s, 3 H, MeO), 3.92 (dd, 1 H, $^2J_{PH}$ = 22.0, $^3J_{HH}$ = 11.2, CH), 4.43 (dd, 1 H, $^3J_{PH}$ = 11.0, $^3J_{HH}$ = 10.4,CH), 5.21 (bs, 1 H, OH), 6.63 (d, 2 H, $^3J_{HH}$ = 8.8, 2 CH), 7.11 – 7.19 (m, 10 H, 10 CH), 7.40 (d, 2 H, $^3J_{HH}$ = 8.8, 2 CH). – ^{13}C NMR: δ = 47.8 (d, $^1J_{CP}$ = 138.1, CH), 49.1 (d, $^2J_{CP}$ = 2.8, CH), 52.6(s, OMe), 52.8 (s, OMe), 116.5 (s, 2 CH), 119.1(s, 2 C), 120.4 (d, $^3J_{CP}$ = 4.6, 2 CH), 120.5 (d, $^3J_{CP}$ = 4.3, 2 CH), 125.7 (s, 2 CH), 129.6 (s, 4 CH), 137.6 (s, 2 CH), 150.0 (s, 2 C), 158.4 (s, C), 167.5 (d, $^2J_{CP}$ = 5.2, C=O), 170.5(d, $^3J_{CP}$ = 19.5, C=O). – ^{31}P NMR: δ = 12.53 [P(O)$(OC_6H_5)_2$].

*Diethyl 2-(diphenoxyphosphoryl)-3-[(4-hydroxyphenyl)sulfanyl]succinate (**4f**)*

Yellow oil, yield: 0.95 g (90 %). – IR (KBr): ν = 1733 (C=O), 1247 (P=O), 2933 (CH), 3374(OH) cm^{-1}. – EI–MS: m/z = 530 (2) $[M]^+$, 501(5), 405 (5), 297 (35), 233 (45), 93 (100). – Anal. for $C_{26}H_{27}O_8PS$ (530.53): calcd. C 58.86, H 5.13; found C 58.86, H 5.12 %. – NMR data for the major isomer (63 %): ^{1}H NMR: δ = 1.20 (t, 3 H, $^3J_{HH}$ = 7.2, CH_3), 1.33 (t, 3 H, $^3J_{HH}$ = 7.2, CH_3), 4.00 (dd, 1 H, $^2J_{PH}$ = 21.6, $^3J_{HH}$ = 10.8, CH), 4.10 (q, 2 H, $^3J_{HH}$ = 7.2, CH_2), 4.13 (q, 2 H, $^3J_{HH}$ = 7.2, CH_2), 4.21 (dd, 1 H, $^3J_{PH}$ = 11.2, $^3J_{HH}$ = 7.6, CH), 5.32 (bs, 1 H, OH), 6.72 (d, 2 H, $^3J_{HH}$ = 8.4, 2 CH), 7.23 – 7.36 (m, 10 H, 10 CH), 7.38 (d, 2 H, $^3J_{HH}$ = 10, 2 CH). – ^{13}C NMR: 48.2 (d, $^1J_{CP}$ = 127.3, CH), 49.9 (d, $^2J_{CP}$ = 2.6, CH), 62.5(s, OCH_2), 116.3 (s, 2 CH), 119.6 (s, 2 C), 120.3 (d, $^3J_{CP}$ = 4.4, 2 CH), 120.6 (d, $^3J_{CP}$ = 4.4, 2 CH), 125.7 (s, 2 CH), 129.8 (s, 4 CH), 137.6 (s, 2 CH), 149.8 (s, 2 C), 158.0 (s, C), 166.0 (d, $^2J_{CP}$ = 5.0, C=O), 169.9 (d, $^3J_{CP}$ = 4.2, C=O). – ^{31}P NMR: δ = 12.05 [P(O)$(OC_6H_5)_2$]. – NMR data for the minor isomer (37 %): ^{1}H NMR: δ = 1.25 (t, 3 H, $^3J_{HH}$ = 7.2, CH_3), 1.27 (t, 3 H, $^3J_{HH}$ = 6.9, CH_3), 3.90 (dd, 1 H, $^2J_{PH}$ = 22.0, $^3J_{HH}$ = 11.6, CH), 4.32(q, 2 H, $^3J_{HH}$ = 5.6, CH_2), 4.37 (q, 2 H, $^3J_{HH}$ = 5.6, CH_2), 4.21 (dd, 1 H, $^3J_{PH}$ = 11.1, $^3J_{HH}$ = 10.0, CH), 5.31 (bs, 1 H, OH), 6.70 (d, 2 H, $^3J_{HH}$ = 8.8, 2 CH), 7.13 – 7.23 (m, 10 H, 10 CH), 7.42 (d, 2 H, $^3J_{HH}$ = 9.6, 2 CH). – ^{13}C NMR: δ = 48.1 (d, $^1J_{CP}$ = 137.5, CH), 49.9 (d, $^2J_{CP}$ = 2.6, CH), 62.4(s, OCH_2), 116.4 (s, 2 CH), 120.3 (s, 2 C), 120.6 (d, $^3J_{CP}$ = 4.3, 2 CH), 120.7 (d, $^3J_{CP}$ = 4.6, 2 CH), 125.6 (s, 2 CH), 129.9 (s, 4 CH), 137.4 (s, 2 CH), 150.0 (s, 2 C), 158.0 (s, C), 166.9 (d, $^2J_{CP}$ = 5.0, C=O), 170.1 (d, $^3J_{CP}$ = 22.6, C=O). – ^{31}P NMR: δ = 13.14 [P(O)$(OC_6H_5)_2$].

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