A Practical Synthesis of Diethyl 1-Methylthio-2-oxo-2-phenylethylphosphonates from Diethyl Methylthiomethylphosphonate

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Received 7 March 2003

Abstract: An efficient synthesis of 2′- and 3′-substituted diethyl 1-methylthio-2-oxo-2-phenylethylphosphonates **3a**–**k** from 2′- and 3′-substituted benzoyl chlorides **2a**–**k** using diethyl methylthio-1-lithiomethylphosphonate is described.

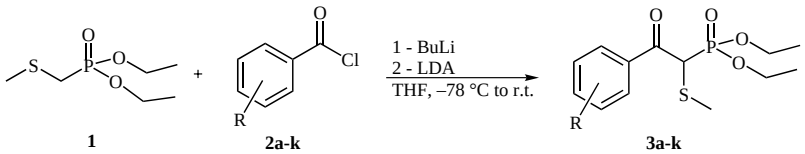
Key words: diethyl 1-methylthio-2-oxo-2-phenylethylphosphonates, diethyl methylthiomethylphosphonate, Michaelis–Arbuzov reaction, acylation reaction

β-Ketophosphonates are valuable intermediates in organic synthesis. The preparation of α,β-unsaturated carbonyl compounds by the Horner–Wadsworth–Emmons[1] reaction has been the main application of the phosphonates, which are also used as ligands in the synthesis of complexes.[2] One of the methods commonly used for the preparation of phosphonates is the Michaelis–Arbuzov reaction.[3,4] The Michaelis–Arbuzov reaction of trialkyl phosphites and α-halogenoketones leads to β-ketophosphonates, but this method is restricted to highly reactive α-halogenoketones, taking into account competition with the Perkow reaction which gives enol phosphates.[5] Many other synthetic approaches[6] for preparing β-ketophosphonates, although successful, are limited by the availability of starting materials. Other methods include Claisen condensation between α-lithioalkylphosphonates and esters,[7] acylation of 1-(trimethylsilyl)vinyl phosphonates,[8] hydrolysis of vinylogous phosphoramides,[9] acylation of α-cuprophosphonates,[10] enantioselective synthesis of γ-hydroxy-β-ketophosphonates via allenic intermediates,[11] Pd(0)-catalysed rearrangement of the 2,3-epoxyalkyl phosphonates,[12] reaction of phosphite with epoxysulfones,[13] oxidation of β-hydroxyalkyl phosphonates,[7b,14] and reaction of silyl enol ethers with phosphite using a hypervalent iodine compound.[15] Recently, β-ketophosphonates have also been obtained by: a) acylation of in situ generated trimethylsilyl diethylphosphonoacetate using $MgCl_2/Et_3N$;[16] b) acylation of triethyl phosphonoacetate and diethyl phosphonoacetic acid via the $Mg(OEt)_2$ or $MgCl_2/Et_3N$ system;[17] and c) reaction of α-halogenophosphonates with esters in the presence of a soluble Co(0) complex or magnesium.[18]

As described above, several methods for the synthesis of β-ketophosphonates have been reported, however, few studies aimed at the preparation of α-hetero-substituted β-ketophosphonates are known. This is due to the experimental limitations of the existing methods or the availability of starting reagents. In an elaborate approach, Coutrot[19] explored the reaction of 1-substituted (Me, Ph, SPh, Cl) diethyl 2-chloro-2-oxoethylphosphonate with organometallic reagents (Grignard or organocuprates reagents), in order to obtain the corresponding 2-oxoalkane phosphonates. However, the drawback of this method is the preparation of the starting reagents, which involves some steps.

The present paper, reports a simple method for the synthesis of 2′- and 3′-substituted diethyl 1-methylthio-2-oxophenylethyl-phosphonates **3a**–**k**. As shown in Scheme 1, diethyl methylthiomethylphosphonate (**1**) reacts with 1 equivalent of butyllithium. To the thus obtained carbanion, a solution of 1 equivalent of LDA in THF was added, followed by benzoyl chloride **2a**–**k** at –78 °C in THF, to give the corresponding phosphonates **3a**–**k** in moderate yields. The results are shown in Table 1.

Preparation of 2-oxoalkylphosphonates via the carbanion route is a process of limited scope. The low yields often achieved in the initial phosphonylation step are certainly due to regeneration of the starting phosphonate through



1 **2a-k** **3a-k**

R = 2'-MeO(**a**), 2'-Me(**b**), 2'-F(**c**), 2'-Cl(**d**), 2'-Br(**e**), 3'-MeO(**f**), 3'-Me(**g**), 3'-F(**h**), 3'-Cl(**i**), 3'-Br(**j**), 3'-NO_2(**k**)

Scheme 1

Synthesis 2003, No. 8, Print: 05 06 2003.
Art Id.1437-210X,E;2003,0,08,1248,1252,ftx,en;M00603SS.pdf.

Table 1 Synthesis of Phosphonates **3a–k**

Product	R	Yield (%)[a]
3a	2′-MeO	67
3b	2′-Me	58
3c	2′-F	58
3d	2′-Cl	67
3e	2′-Br	68
3f	3′-MeO	70
3g	3′-Me	55
3h	3′-F	74
3i	3′-Cl	60
3j	3′-Br	62
3k	3′-NO_2	60

[a] The yield of the isolated product is based on diethyl methylthiomethylphosphonate (**1**).

acid-base equilibrium.[7] This drawback can be overcome by proper choice of the metalating agent. The use of butyllithium and LDA (1:1 equiv) and 1 equivalent of diethyl methylthiomethylphosphonate (**1**) makes the procedure efficient, due to the conversion of **3** into the corresponding lithium enolate and shifting the equilibrium towards the reaction product, leading to the preparation of a wide range of 2′- and 3′-substituted diethyl 1-methylthio-2-oxo-2-phenylethylphosphonates **3a–k** free of by products.

Several other attempts[20] to obtain phosphonates **3** failed or gave only modest results, e.g. the sulfenylation reaction of the β-ketophosphonates gave only 20–30% yields of phosphonates **3**.

In conclusion, the present procedure is a new and practical method for the synthesis of 2′- and 3′-substituted diethyl 1-methylthio-2-oxo-2-phenylethylphosphonates **3a–k**. The compounds **3** are promising synthons in the Horner–Wadsworth–Emmons reaction for the preparation of α-methylthio-substituted α,β-unsaturated ketones, which can be used in Michael additions and Diels–Alder reactions.[21]

NMR spectra were recorded on a Varian Inova 1 spectrometer operating at 300 MHz for proton, and 75.4 MHz for carbon. ^{1}H and ^{13}C chemical shifts (δ) are reported in ppm relative to TMS as internal standard. Coupling constants (*J*) are given in Hz. IR spectra were measured on a Michelson-Bomem FTIR instrument. Elemental analyses were carried out on a Perkin-Elmer 2400 CHN-standard analyser. Low-resolution mass spectra were recorded on a Shimadzu QP5050A GC-MS spectrometer (DB5 column, EI). Column chromatography was performed on Merck silica gel 60 (230–400 mesh). Diethyl methylthiomethylphosphonate (**1**) and substituted benzoyl chlorides **2** were prepared according to the procedures described in literature.[22–24] All reactions were conducted with magnetic stirring in oven-dried glassware under dry N_2. Solvents were purified and dried according to standard procedures. Other reagents were commercially available.

Phosphonates 3a–k; General Procedure

BuLi (19.3 mL of 1.5 M solution in hexane, 29 mmol) was added to THF (20 mL) and cooled to –78 °C. A solution of diethyl methylthiomethylphosphonate (**1**; 5.55 g, 28 mmol) in THF (10 mL) was then slowly added at this temperature via a syringe. After 30 min, a solution of LDA [previously prepared from BuLi (18.6 mL of 1.5 M in hexane, 28 mmol), *i*-Pr_2NH (4.2 mL, 30 mmol) and THF (20 mL) at –78 °C] was transferred via a cannula into the first solution. To the resulting pale-yellow mixture a solution of substituted benzoyl chloride **2a–k** (30 mmol) in THF (10 mL) was added at –78 °C. This solution was allowed to reach r.t. Stirring was continued for 1 h, then cooled at 0 °C and the reaction product was quenched with aq 1 M HCl (60 mL) and extracted with CH_2Cl_2 (3 × 50 mL). The combined CH_2Cl_2 solution was washed with aq 1 M NaOH to extract the sodium enolate of **3a–k** from the starting material (3 × 15 mL). The combined alkaline solution was additionally washed with CH_2Cl_2 (20 mL), acidified with aq 1 M HCl (45 mL) to obtain the free **3a–k** and finally extracted with CH_2Cl_2 (3 × 50 mL). The combined CH_2Cl_2 solution was washed with H_2O (15 mL) and dried ($MgSO_4$). Filtration and evaporation yielded the crude compounds **3a–k**. The compounds **3f** and **3h** were purified by recrystallisation (hexane–Et_2O). In the other cases, the crude oil was purified by flash chromatography on silica gel with hexane–acetone gradient as eluent.

Diethyl 2-(2′-Methoxyphenyl)-1-(methylthio)-2-oxoethylphosphonate (3a)

Yield: 67%; colorless oil.

IR (film): 3075 (w), 2983 (m), 2928 (m), 1674 (s), 1597 (s), 1485 (s), 1299 (vs), 1246 (vs), 1164 (s), 1052 (vs), 1022 (vs) cm^{-1}.

^{1}H NMR ($CDCl_3$/TMS): δ = 7.76 (dd, 1 H, $^4J_{HH}$ = 1.8 Hz, $^3J_{HH}$ = 7.5 Hz), 7.50 (ddd, 1 H, $^4J_{HH}$ = 1.8 Hz, $^3J_{HH}$ = 7.5 Hz, $^3J_{HH}$ = 8.5 Hz), 7.00 (dt, 1 H, $^4J_{HH}$ = 0.9 Hz, $^3J_{HH}$ = 7.5 Hz), 6.97 (dd, 1 H, $^4J_{HH}$ = 0.9 Hz, $^3J_{HH}$ = 8.5 Hz), 5.00 (d, 1 H, $^2J_{HP}$ = 18.0 Hz), 4.14–4.34 ((m), 4 H), 3.93 (s, 3 H), 2.24 (d, 3 H, $^4J_{HP}$ = 0.9 Hz), 1.33 (dt, 3 H, $^4J_{HP}$ = 0.6 Hz, $^3J_{HH}$ = 7.2 Hz), 1.31 (dt, 3 H, $^4J_{HP}$ = 0.6 Hz, $^3J_{HH}$ = 7.2 Hz).

^{13}C NMR ($CDCl_3$/TMS): δ = 192.4, 157.9, 134.1, 131.1, 126.2 (d, $^3J_{CP}$ = 5.4 Hz), 120.8, 111.4, 63.2 (d, $^2J_{CP}$ = 6.8 Hz), 62.8 (d, $^2J_{CP}$ = 6.6 Hz), 55.6, 49.0 (d, $^1J_{CP}$ = 142.7 Hz), 16.2 (t, $^3J_{CP}$ = 5.4 Hz), 14.4 (d, $^3J_{CP}$ = 2.0 Hz).

MS (EI): *m/z* (%) = 332 (7), 135 (100), 92 (6), 77 (15).

Anal. Calcd for $C_{14}H_{21}O_5PS$ (332.35): C, 50.59; H, 6.37. Found: C, 50.72; H, 6.25.

Diethyl 2-(2′-Methylphenyl)-1-(methylthio)-2-oxoethylphosphonate (3b)

Yield: 58%; colorless oil.

IR (film): 3061 (w), 2984 (m), 2926 (m), 1685 (m), 1605 (w), 1569 (m), 1303 (s), 1254 (vs), 1052 (vs), 1025 (vs) cm^{-1}.

^{1}H NMR ($CDCl_3$/TMS): δ (78% ketone and 22% enol form) = 12.24 (d, 1 H, $^4J_{HP}$ = 1.2 Hz, enol), 7.23–7.72 (m, 8 H, enol + ketone), 4.39 (d, 1 H, $^2J_{HP}$ = 18.6 Hz, ketone), 4.12–4.31 (m, 8 H, enol + ketone), 2.51 (s, 3 H, ketone), 2.34 (s, 3 H, enol), 2.33 (d, 3 H, $^4J_{HP}$ = 0.9 Hz, ketone), 1.99 (d, 3 H, $^4J_{HP}$ = 0.9 Hz, enol), 1.42 (dt, 6 H, $^4J_{HP}$ = 0.9 Hz, $^3J_{HH}$ = 7.2 Hz, enol), 1.33 (dt, 3 H, $^4J_{HP}$ = 0.6 Hz, $^3J_{HH}$ = 7.2 Hz, ketone), 1.29 (dt, 3 H, $^4J_{HP}$ = 0.6 Hz, $^3J_{HH}$ = 7.2 Hz, ketone).

^{13}C NMR ($CDCl_3$/TMS): δ (78% ketone and 22% enol form) = 194.6 (ketone), 180.5 (d, $^2J_{CP}$ = 17.5 Hz, enol), 138.8 (ketone), 136.9 (d, $^3J_{CP}$ = 4.9 Hz, ketone), 135.4 (d, $^3J_{CP}$ = 15.3 Hz, enol), 134.7 (enol), 131.8 (ketone), 131.7 (ketone), 129.9 (enol), 129.0 (enol), 128.3 (ketone), 127.5 (enol), 125.5 (ketone), 125.1 (enol),

87.7 (d, $^1J_{CP}$ = 185.0 Hz, enol), 63.5 (d, $^2J_{CP}$ = 6.8 Hz, ketone), 63.2 (d, $^2J_{CP}$ = 6.5 Hz, ketone), 62.7 (d, $^2J_{CP}$ = 5.4 Hz, enol), 48.1 (d, $^1J_{CP}$ = 144.1 Hz, ketone), 20.7 (ketone), 19.6 (enol), 19.2 (enol), 16.3 (d, $^3J_{CP}$ = 6.0 Hz, ketone), 16.1 (d, $^3J_{CP}$ = 4.8 Hz, enol), 15.0 (d, $^3J_{CP}$ = 2.5 Hz, ketone).

MS (EI): *m*/*z* (%) = 316 (14), 268 (6), 162 (11), 119 (100), 115 (15), 91 (33).

Anal. Calcd for $C_{14}H_{21}O_4PS$ (316.35): C, 53.15; H, 6.69. Found: C, 52.76; H, 6.53.

Diethyl 2-(2′-Fluorophenyl)-1-(methylthio)-2-oxoethylphosphonate (3c)
Yield: 58%; light-yellow oil.

IR (film): 3070 (w), 2983 (m), 2928 (m), 1682 (m), 1609 (s), 1482 (s), 1296 (s), 1254 (vs), 1055 (vs), 1025 (vs) cm^{-1}.

^{1}H NMR ($CDCl_3$/TMS): δ = 7.90 (dt, 1 H, $^4J_{HH}$ = 1.8 Hz, $^4J_{HF}$ = 7.5 Hz), 7.56 (dddd, 1 H, $^4J_{HH}$ = 1.8 Hz, $^4J_{HF}$ = 5.1 Hz, $^3J_{HH}$ = 7.2 Hz, $^3J_{HH}$ = 8.2 Hz), 7.26 (dt, 1 H, $^4J_{HH}$ = 0.9 Hz, $^3J_{HH}$ = 7.2 Hz, $^3J_{HH}$ = 7.5 Hz), 7.15 (ddd, 1 H, $^4J_{HH}$ = 0.9 Hz, $^3J_{HH}$ = 8.2 Hz, $^3J_{HF}$ = 11.4 Hz), 4.58 (dd, 1 H, $^5J_{HF}$ = 3.6 Hz, $^2J_{HP}$ = 18.6 Hz), 4.13–4.34 (m, 4 H), 2.56 (d, 3 H, $^4J_{HP}$ = 0.6 Hz), 1.33 (dt, 3 H, $^4J_{HP}$ = 0.6 Hz, $^3J_{HH}$ = 6.9 Hz), 1.31 (dt, 3 H, $^4J_{HP}$ = 0.6 Hz, $^3J_{HH}$ = 6.9 Hz).

^{13}C NMR ($CDCl_3$/TMS): δ = 189.0 (d, $^3J_{CF}$ = 4.0 Hz), 161.2 (d, $^1J_{CF}$ = 254.1 Hz), 135.1 (d, $^3J_{CF}$ = 9.5 Hz), 131.3, 124.6 (d, $^3J_{CF}$ = 3.4 Hz), 124.5 (dd, $^3J_{CP}$ = 5.7 Hz, $^2J_{CF}$ = 11.5 Hz), 116.6 (d, $^2J_{CF}$ = 24.1 Hz), 63.5 (d, $^2J_{CP}$ = 6.9 Hz), 63.3 (d, $^2J_{CP}$ = 6.6 Hz), 49.3 (dd, $^4J_{CF}$ = 8.1 Hz, $^1J_{CP}$ = 147.6 Hz), 16.3 (d, $^3J_{CP}$ = 5.8 Hz), 16.2 (d, $^3J_{CP}$ = 6.1 Hz), 14.6 (d, $^3J_{CP}$ = 1.9 Hz).

MS (EI): *m*/*z* (%) = 320 (10), 274 (18), 166 (40), 123 (100).

Anal. Calcd for $C_{13}H_{18}FO_4PS$ (320.32): C, 48.75; H, 5.66. Found: C, 48.46; H, 5.57.

Diethyl 2-(2′-Chlorophenyl)-1-(methylthio)-2-oxoethylphosphonate (3d)
Yield: 67%; light-yellow oil.

IR (film): 3064 (w), 2985 (m), 2925 (m), 1696 (m), 1608 (vs), 1573 (vs), 1310 (vs), 1256 (s), 1052 (vs), 1023 (vs) cm^{-1}.

^{1}H NMR ($CDCl_3$/TMS): δ (50% ketone and 50 enol form) = 12.29 (d, 1 H, $^4J_{HP}$ = 1.2 Hz, enol), 7.31–7.60 (m, 8 H, enol + ketone), 4.56 (d, 1 H, $^2J_{HP}$ = 18.9 Hz, ketone), 4.12–4.33 (m, 8 H, enol + ketone), 2.30 (d, 3 H, $^4J_{HP}$ = 0.9 Hz, ketone), 2.04 (d, 3 H, $^4J_{HP}$ = 0.6 Hz, enol), 1.42 (dt, 6 H, $^4J_{HP}$ = 0.9 Hz, $^3J_{HH}$ = 7.2 Hz, enol), 1.34 (dt, 3 H, $^4J_{HP}$ = 0.6 Hz, $^3J_{HH}$ = 6.9 Hz, ketone), 1.29 (dt, 3 H, $^4J_{HP}$ = 0.6 Hz, $^3J_{HH}$ = 6.9 Hz, ketone).

^{13}C NMR ($CDCl_3$/TMS): δ (50% ketone and 50% enol form) = 192.9 (ketone), 177.1 (d, $^2J_{CP}$ = 18.4 Hz, enol), 137.5 (d, $^3J_{CP}$ = 5.5 Hz, ketone), 134.9 (d, $^3J_{CP}$ = 16.1 Hz, enol), 132.1 (ketone), 131.5 (enol), 130.9 (ketone), 130.4 (ketone), 130.3 (enol), 129.8 (ketone), 129.3 (enol), 128.9 (enol), 126.7 (ketone), 126.3 (enol), 89.1 (d, $^1J_{CP}$ = 184.2 Hz, enol), 63.6 (d, $^2J_{CP}$ = 7.1 Hz, ketone), 63.2 (d, $^2J_{CP}$ = 6.6 Hz, ketone), 62.7 (d, $^2J_{CP}$ = 4.8 Hz, enol), 49.0 (d, $^1J_{CP}$ = 144.4 Hz, ketone), 19.2 (enol), 16.2 (d, $^3J_{CP}$ = 5.7 Hz, ketone), 16.0 (d, $^3J_{CP}$ = 6.6 Hz, enol), 14.8 (d, $^3J_{CP}$ = 2.3 Hz, ketone).

MS (EI): *m*/*z* (%) = 338 (4), 336 (11), 301 (48), 182 (43), 141 (32), 139 (100), 111 (23).

Anal. Calcd for $C_{13}H_{18}ClO_4PS$ (336.77): C, 46.36; H, 5.39. Found: C, 46.40; H, 5.44.

Diethyl 2-(2′-Bromophenyl)-1-(methylthio)-2-oxoethylphosphonate (3e)
Yield: 68%; colorless oil.

IR (film): 3060 (w), 2985 (m), 2924 (m), 1697 (m), 1605 (vs), 1572 (vs), 1309 (vs), 1255 (s), 1024 (vs) cm^{-1}.

^{1}H NMR ($CDCl_3$/TMS): δ = (55% ketone and 45% enol form) = 12.30 (d, 1 H, $^4J_{HP}$ = 1.2 Hz, enol), 7.25–7.64 (m, 8 H, enol + ketone), 4.53 (d, 1 H, $^2J_{HP}$ = 18.9 Hz, ketone), 4.15–4.32 (m, 8 H, enol + ketone), 2.33 (d, 3 H, $^4J_{HP}$ = 0.9 Hz, ketone), 2.05 (d, 3 H, $^4J_{HP}$ = 1.2 Hz, enol), 1.42 (dt, 6 H, $^4J_{HP}$ = 0.9 Hz, $^3J_{HH}$ = 6.9 Hz, enol), 1.34 (dt, 3 H, $^4J_{HP}$ = 0.6 Hz, $^3J_{HH}$ = 7.2 Hz, ketone), 1.30 (dt, 3 H, $^4J_{HP}$ = 0.6 Hz, $^3J_{HH}$ = 6.9 Hz, ketone).

^{13}C NMR ($CDCl_3$/TMS): δ (55% ketone and 45% enol form) = 193.7 (ketone), 178.3 (d, $^2J_{CP}$ = 18.4 Hz, enol), 139.6 (d, $^3J_{CP}$ = 5.4 Hz, ketone), 137.1 (d, $^3J_{CP}$ = 16.4 Hz, enol), 133.6 (ketone), 132.6 (enol), 132.1 (ketone), 130.3 (enol), 129.9 (ketone), 129.0 (enol), 127.2 (ketone), 126.9 (enol), 121,0 (ketone), 119.2 (enol), 88.9 (d, $^1J_{CP}$ = 184.2 Hz, enol), 63.8 (d, $^2J_{CP}$ = 6.9 Hz, ketone), 63.4 (d, $^2J_{CP}$ = 6.8 Hz, ketone), 62.9 (d, $^2J_{CP}$ = 4.9 Hz, enol), 48.9 (d, $^1J_{CP}$ = 144.1 Hz, ketone), 19.3 (enol), 16.3 (d, $^3J_{CP}$ = 6,0 Hz, enol), 16.2 (d, $^3J_{CP}$ = 6,6 Hz, ketone), 15.0 (d, $^3J_{CP}$ = 2.3 Hz, ketone).

MS (EI): *m*/*z* (%) = 380 (5), 382 (5), 301 (100), 286 (26), 230 (30), 185 (66), 183 (74).

Anal. Calcd for $C_{13}H_{18}BrO_4PS$ (381.32): C, 40.96; H, 4.76. Found: C, 40.97; H, 4.67.

Diethyl 2-(3′-Methoxyphenyl)-1-(methylthio)-2-oxoethylphosphonate (3f)
Yield: 70%; white solid; mp 60 °C.

IR (KBr): 3075 (w), 2985 (m), 2925 (m), 1665 (vs), 1594 (vs), 1290 (vs), 1244 (vs), 1051 (vs), 1019 (vs) cm^{-1}.

^{1}H NMR ($CDCl_3$/TMS): δ = 7.59 (dt, 1 H, $^4J_{HH}$ = 0.9 Hz, $^3J_{HH}$ = 8.1 Hz), 7.54 (t, 1 H, $^4J_{HH}$ = 2.4 Hz), 7.38 (t, 1 H, $^3J_{HH}$ = 8.1 Hz), 7.14 (ddd, 1 H, $^4J_{HH}$ = 0.9 Hz, $^4J_{HH}$ = 2.4 Hz, $^3J_{HH}$ = 8.1 Hz), 4.50 (d, 1 H, $^2J_{HP}$ = 18.3 Hz), 4.14–4.37 (m, 4 H), 3.86 (s, 3 H), 2.27 (d, 3 H, $^4J_{HP}$ = 0.9 Hz), 1.33 (dt, 3 H, $^4J_{HP}$ = 0.6 Hz, $^2J_{HH}$ = 6.9 Hz), 1.32 (dt, 3 H, $^4J_{HP}$ = 0.6 Hz, $^3J_{HH}$ = 6.9 Hz).

^{13}C NMR ($CDCl_3$/TMS): δ = 191.4, 159.9, 136.8 (d, $^3J_{CP}$ = 5.5 Hz), 129.6, 121.5, 120.3, 113.2, 63.7 (d, $^2J_{CP}$ = 6.6 Hz), 63.5 (d, $^2J_{CP}$ = 6.6 Hz), 55.6, 45.7 (d, $^1J_{CP}$ = 146.7 Hz), 16.4 (d, $^3J_{CP}$ = 6.0 Hz), 15.1 (d, $^3J_{CP}$ = 2.8 Hz).

MS (EI): *m*/*z* (%) = 332 (6), 286 (10), 178 (7), 135 (100), 107 (15), 92 (6), 77 (12).

Anal. Calcd for $C_{14}H_{21}O_5PS$ (332.36): C, 50.59; H, 6.37. Found: C, 50.63; H, 6.21.

Diethyl 2-(3′-methylphenyl)-1-(methylthio)-2-oxoethylphosphonate (3g)
Yield: 55%; colorless oil.

IR (film): 3051 (w), 2983 (m), 2927 (m), 1673 (vs), 1585 (m), 1284 (vs), 1253 (vs), 1055 (vs), 1026 (vs) cm^{-1}.

^{1}H NMR ($CDCl_3$/TMS): δ = 7.81 (m, 1 H), 7.79 (m, 1 H), 7.40 (m, 1 H), 7.36 (m, 1 H), 4.53 (d, 1 H, $^2J_{HP}$ = 18.0 Hz), 4.15–4.35 (m, 4 H), 2.42 (s, 3 H), 2.27 (d, 3 H, $^4J_{HP}$ = 0.9 Hz), 1.32 (dt, 6 H, $^4J_{HP}$ = 0.6 Hz, $^3J_{HH}$ = 6.9 Hz).

^{13}C NMR ($CDCl_3$/TMS): δ = 191.6, 138.5, 135.4 (d, $^3J_{CP}$ = 5.7 Hz), 134.4, 129.3, 128.5, 126.1, 63.6 (d, $^2J_{CP}$ = 6.8 Hz), 63.4 (d, $^2J_{CP}$ = 6.6 Hz), 45.3 (d, $^1J_{CP}$ = 147.4 Hz), 21.3, 16.4 (d, $^3J_{CP}$ = 6.0 Hz), 14.9 (d, $^3J_{CP}$ = 2.3 Hz).

MS (EI): *m*/*z* (%) = 316 (6), 270 (10), 162 (8), 119 (100), 91 (26), 65 (11).

Anal. Calcd for $C_{14}H_{21}O_4PS$ (316.36): C, 53.15; H, 6.69. Found: C, 52.90; H, 6.53.

Diethyl 2-(3′-Fluorophenyl)-1-(methylthio)-2-oxoethylphosphonate (3h)
Yield: 74%; yellow solid; mp 63 °C.

IR (KBr): 3087 (w), 2984 (m), 2927 (m), 1655 (vs), 1584s, 1440 (s), 1291 (vs), 1248 (vs), 1061 (vs), 1021 (vs) cm^{-1}.

^1H NMR ($CDCl_3$/TMS): δ = 7.81 (ddd, 1 H, $^4J_{HH}$ = 0.9 Hz, $^4J_{HH}$ = 1.5 Hz, $^3J_{HH}$ = 7.9 Hz), 7.70 (ddd, 1 H, $^4J_{HH}$ = 1.5 Hz, $^4J_{HH}$ = 2.4 Hz, $^3J_{HF}$ = 9.4 Hz), 7.46 (dt, 1 H, $^4J_{HF}$ = 5.5 Hz, $^3J_{HH}$ = $^3J_{HH}$ = 7.9 Hz), 7.30 (ddt, 1 H, $^4J_{HH}$ = 0.9 Hz, $^4J_{HH}$ = 2.4 Hz, $^3J_{HH}$ = $^3J_{HF}$ = 7.9 Hz), 4.45 (d, 1 H, $^2J_{HP}$ = 18.3 Hz), 4.15–4.36 (m, 4 H), 2.27 (d, 1 H, $^4J_{HP}$ = 0.9 Hz), 1.33 (dt, 3 H, $^4J_{HP}$ = 0.6 Hz, $^3J_{HH}$ = 7.2 Hz), 1.32 (dt, 3 H, $^4J_{HP}$ = 0.6 Hz, $^3J_{HH}$ = 7.2 Hz).

^{13}C NMR ($CDCl_3$/TMS): δ = 190.3 (d, $^4J_{CF}$ = 1.9 Hz), 162.8 (d, $^1J_{CF}$ = 248.1 Hz), 137.4 (d, $^3J_{CF}$ = $^3J_{CP}$ = 5.8 Hz), 130.3 (d, $^3J_{CF}$ = 7.7 Hz), 124.7 (d, $^4J_{CF}$ = 2.9 Hz), 120.7 (d, $^2J_{CF}$ = 22.1 Hz), 115.7 (d, $^2J_{CP}$ = 23.0 Hz), 63.8 (d, $^2J_{CP}$ = 6.7 Hz), 63.6 (d, $^2J_{CP}$ = 6.7 Hz), 45.8 (d, $^1J_{CP}$ = 147.1 Hz), 16.4 (d, $^3J_{CP}$ = 4.8 Hz), 15.0 (d, $^3J_{CP}$ = 2.9 Hz).

MS (EI): *m*/*z* (%) = 320 (7), 274 (19), 166 (17), 123 (100), 95 (27).

Anal. Calcd for $C_{13}H_{18}FO_4PS$ (320.32): C, 48.75; H, 5.66. Found: C, 48.50; H, 5.65.

Diethyl 2-(3′-Chlorophenyl)-1-(methylthio)-2-oxoethylphosphonate (3i)
Yield: 60%; light-orange oil.

IR (film): 3066 (w), 2984 (m), 2928 (m), 1679 (s), 1572 (m), 1286 (s), 1252 (vs), 1055 (vs), 1025 (vs) cm^{-1}.

^1H NMR ($CDCl_3$/TMS): δ = 7.99 (t, 1 H, $^4J_{HH}$ = 1.8 Hz), 7.90 (ddd, 1 H, $^4J_{HH}$ = 1.2 Hz, $^4J_{HH}$ = 1.8 Hz, $^3J_{HH}$ = 7.8 Hz), 7.57 (ddd, 1 H, $^4J_{HH}$ = 1.2 Hz, $^4J_{HH}$ = 1.8 Hz, $^3J_{HH}$ = 7.8 Hz), 7.43 (t, 1 H, $^3J_{HH}$ = 7.8 Hz), 4.46 (d, 1 H, $^2J_{HP}$ = 18.3 Hz), 4.17–4.34 (m, 4 H), 2.27 (d, 3 H, $^4J_{HP}$ = 0.9 Hz), 1.33 (dt, 3 H, $^4J_{HP}$ = 0.6 Hz, $^3J_{HH}$ = 7.2 Hz), 1.32 (dt, 3 H, $^4J_{HP}$ = 0.6 Hz, $^3J_{HH}$ = 7.2 Hz).

^{13}C NMR ($CDCl_3$/TMS): δ = 190.1, 136.8 (d, $^3J_{CP}$ = 5.5 Hz), 134.9, 133.5, 129.9, 128.9, 126.9, 63.7 (d, $^2J_{CP}$ = 6.9 Hz), 63.5 (d, $^2J_{CP}$ = 6.6 Hz), 45.7 (d, $^1J_{CP}$ = 147.4 Hz), 16.3 (d, $^3J_{CP}$ = 6.1 Hz), 14.9 (d, $^3J_{CP}$ = 2.3 Hz).

MS (EI): *m*/*z* (%) = 338 (3), 336 (7), 290 (17), 182 (20), 180 (10), 141 (38), 139 (100), 111 (23).

Anal. Calcd for $C_{13}H_{18}ClO_4PS$ (336.77): C, 46.36; H, 5.39. Found: C, 46.58; H, 5.47.

Diethyl 2-(3′-Bromophenyl)-1-(methylthio)-2-oxoethylphosphonate (3j)
Yield: 62%; light-yellow oil.

IR (film): 3064 (w), 2981 (m), 2926 (m), 1681 (s), 1566 (m), 1285 (s), 1252 (vs), 1054 (vs), 1025 (vs) cm^{-1}.

^1H NMR ($CDCl_3$/TMS): δ = 8.14 (t, 1 H, $^4J_{HH}$ = 1.8 Hz), 7.95 (ddd, 1 H, $^4J_{HH}$ = 0.9 Hz, $^4J_{HH}$ = 1.8 Hz, $^3J_{HH}$ = 7.8 Hz), 7.72 (ddd, 1 H, $^4J_{HH}$ = 0.9 Hz, $^4J_{HH}$ = 1.8 Hz, $^3J_{HH}$ = 7.8 Hz), 7.36 (t, 1 H, $^3J_{HH}$ = 7.8 Hz), 4.44 (d, 1 H, $^2J_{HP}$ = 18.6 Hz), 4.17–4.33 (m, 4 H), 2.27 (d, 3 H, $^4J_{HP}$ = 0.9 Hz), 1.33 (dt, 3 H, $^4J_{HP}$ = 0.6 Hz, $^3J_{HH}$ = 6.9 Hz), 1.32 (dt, 3 H, $^4J_{HP}$ = 0.6 Hz, $^3J_{HH}$ = 7.2 Hz).

^{13}C NMR ($CDCl_3$/TMS): δ = 190.0, 137.0 (d, $^3J_{CP}$ = 5.5 Hz), 136.4, 131.8, 130.1, 127.4, 122.8, 63.7 (d, $^2J_{CP}$ = 7.2 Hz), 63.5 (d, $^2J_{CP}$ = 6.9 Hz), 45.6 (d, $^1J_{CP}$ = 147.1 Hz), 16.3 (d, $^3J_{CP}$ = 5.7 Hz), 14.9 (d, $^3J_{CP}$ = 2.2 Hz).

MS (EI): *m*/*z* (%) = 382 (8), 380 (8), 336 (17), 334 (18), 226 (28), 185 (90), 183 (100), 157 (20), 155 (20), 76 (17), 61 (20).

Anal. Calcd for $C_{13}H_{18}BrO_4PS$ (381.32): C, 40.96; H, 4.76. Found: C, 40.80; H, 4.91.

Diethyl 1-(Methylthio)-2-(3′-nitrophenyl)-2-oxoethylphosphonate (3k)
Yield: 60%; orange oil.

IR (film): 3089 (w), 2986 (m), 2929 (m), 1686 (s), 1615 (m), 1534 (vs), 1352 (vs), 1289 (m), 1253 (s), 1217 (s), 1053 (vs), 1025 (vs) cm^{-1}.

^1H NMR ($CDCl_3$/TMS): δ = 8.87 (t, 1 H, $^4J_{HH}$ = 1.8 Hz), 8.45 (ddd, 1 H, $^4J_{HH}$ = 1.2 Hz, $^4J_{HH}$ = 2.1 Hz, $^3J_{HH}$ = 8.1 Hz), 8.39 (ddd, 1 H, $^4J_{HH}$ = 1.2 Hz, $^4J_{HH}$ = 1.8 Hz, $^3J_{HH}$ = 8.1 Hz), 7.70 (t, 1 H, $^3J_{HH}$ = 8.1 Hz), 4.48 (d, 1 H, $^2J_{HP}$ = 19.2 Hz), 4.16–4.38 (m, 4 H), 2.28 (d, 3 H, $^4J_{HP}$ = 0.9 Hz), 1.33 (t, 3 H, $^4J_{HH}$ = 6.9 Hz), 1.32 (dt, 3 H, $^4J_{HH}$ = 6.9 Hz).

^{13}C NMR ($CDCl_3$/TMS): δ = 189.2, 148.2, 136.3 (d, $^3J_{CP}$ = 5.2 Hz), 134.5, 129.8, 127.7, 123.7, 63.8 (d, $^2J_{CP}$ = 6.9 Hz), 63.7 (d, $^2J_{CP}$ = 6.6 Hz), 46.2 (d, $^1J_{CP}$ = 146.4 Hz), 16.3 (d, $^3J_{CP}$ = 6.0 Hz), 16.2 (d, $^3J_{CP}$ = 6.0 Hz), 14.9 (d, $^3J_{CP}$ = 2.5 Hz).

MS (EI): *m*/*z* (%) = 347 (14), 301 (40), 257 (33), 193 (70), 169 (18), 150 (100), 141 (40), 123 (20), 104 (39), 76 (33), 61 (50).

Anal. Calcd for $C_{13}H_{18}NO_6PS$ (347.39): C, 44.95; H, 5.22; N, 4.03. Found: C, 44.73; H, 5.05; N, 3.96.

Acknowledgements

We thank the Fundação de Amparo à Pesquisa do Estado de São Paulo (FAPESP) for financial support of this research and a scholarship (to A.R.); the Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq) for fellowships (to P.R.O. and R.R.) and the Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES) for a scholarship (to E.V.). Professor C. H. Collins' assistance in revising this manuscript is also gratefully acknowledged.

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