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Spectral Assignments and Reference Data

Complete assignment of ^{1}H and ^{13}C NMR spectra of some 4′-substituted diethyl 1-methylthio- and diethyl 1-methylsulfonyl-2-oxo-2-phenylethylphosphonates

Adriana Karla C. A. Reis,[1] Paulo R. Olivato[1]* and Roberto Rittner[2]

[1] Conformational Analysis and Electronic Interactions Laboratory, Instituto de Química, USP, Caixa Postal 26077, 05513-970 São Paulo, SP, Brazil
[2] Physical Organic Chemistry Laboratory, Instituto de Química, UNICAMP, Caixa Postal 6154, 13084-971 Campinas, SP, Brazil

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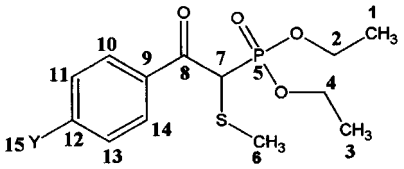
The complete assignment of ^{1}H and ^{13}C NMR spectra of some 4′-substituted diethyl 1-methylthio- and diethyl 1-methylsulfonyl-2-oxo-2-phenylethylphosphonates bearing as substituents methoxy, fluoro, chloro, bromo and nitro is reported. Copyright © 2004 John Wiley & Sons, Ltd.

KEYWORDS: NMR; ^{1}H NMR; ^{13}C NMR; diethyl phosphonates

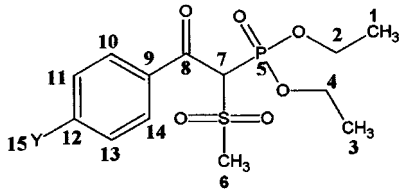
INTRODUCTION

β-Ketophosphonates bearing an α-hydrogen are valuable intermediates in organic synthesis, especially for the preparation of α,β-unsaturated ketones by Wittig–Horner condensation.[1] One of the most commonly used methods for preparation of these compounds is the classical Arbuzov reaction,[2] although recently they were prepared through reaction of an α-lithioanion of diethyl methylphosphonate with a nitrile, as an acyl cation equivalent, followed by treatment with various electrophiles.[3]

The aim of this work was to prepare some 4′-substituted diethyl 1-methylthio- and diethyl 1-methylsulfonyl-2-oxo-2-phenylethylphosphonates (Scheme 1) and to characterize them through their ^{1}H NMR and ^{13}C NMR spectra.



1 Y = MeO
2 Y = H
3 Y = F
4 Y = Cl
5 Y = Br
6 Y = NO_2



7 Y = MeO
8 Y = H
9 Y = F
10 Y = Cl
11 Y = Br
12 Y = NO_2

Scheme 1. Structures and numbering of the compounds studied.

EXPERIMENTAL

Compounds

Compounds **1–6** were obtained from an adaptation of a literature method,[4] by reaction of diethyl methylthiomethanephosphonate with 1.5 equivalents of lithium diisopropylamide (LDA), followed by addition of the corresponding benzoyl chloride in THF at −78 °C. This solution was allowed to reach room temperature. Stirring was continued for 1 h, the solution was cooled to 0 °C and the reaction product was quenched with 1 M HCl and extracted with CH_2Cl_2. The combined CH_2Cl_2 extracts were washed with water and dried over $MgSO_4$. Filtration and evaporation yielded the crude products. Compounds **2–4** were purified by recrystallization (hexane–diethyl ether). Compound **1** (a viscous oil) was purified by flash chromatography on silica gel, with a hexane–acetone (10%) gradient as eluent. The 4′-substituted diethyl 1-methylthio-2-oxo-2-phenylethylphosphonates were obtained in 42–70% yields.

Compounds **7–12** were prepared by the method of Drabowicz *et al.*[5] To a methanolic solution of the corresponding 4′-substituted diethyl 1-methylthio-2-oxo-2-phenylethylphosphonates containing selenium dioxide was added hydrogen peroxide (30%) in a 1 : 1 : 5 molar ratio at 0 °C. The reaction mixture was allowed to reach room temperature. Stirring was continued for 5 h. Cold water was added and the reaction mixture was extracted with CH_2Cl_2 and dried over $MgSO_4$. Compounds **7–12** were purified by flash chromatography on silica gel, with a hexane–acetone (10%) gradient as eluent. All 4′-substituted diethyl 1-methylsulfonyl-2-oxo-2-phenylethylphosphonates were viscous oils, except compound **11**, and were obtained in 87–90% yield.

All the compounds obtained are new, except compound **2**.[5] Elemental analyses were carried out on a Perkin-Elmer 2400-CHN-standard analyser (Table 1).

Spectra

The ^{1}H NMR and ^{13}C NMR spectra were recorded on a Varian Inova 300 spectrometer (10% in $CDCl_3$ solutions) operating at 299.947 and 75.423 MHz, respectively. Data processing was carried out on a Solaris workstation.

The ^{1}H NMR parameters were as follows: spectral width, 4507.6 Hz; data points, 32K; acquisition time, 3.73 s; digital resolution, 0.275 Hz. The ^{13}C NMR parameters were as follows: spectral width, 18 kHz; data points, 64K; acquisition time, 1.70 s; digital resolution, 0.549 Hz, with a delay of 1.0 s between transients.

Two-dimensional ^{1}H–^{1}H COSY and HETCOR were recorded from the same solutions, using the pulse programs of the Varian software library. The ^{1}H–^{1}H COSY data parameters were as follows: spectral width, 3038.1 Hz; relaxation delay, 1.0 s; acquisition time, 0.169 s; FT size, 1024 × 512. The HETCOR data parameters were as follows: spectral width, 3038.1 Hz; relaxation delay, 1.0 s; acquisition time, 0.063 s; FT size, 2048 × 512.

The ^{1}H and ^{13}C chemical shifts are given on the δ scale (ppm) and were referenced to internal tetramethylsilane (TMS); coupling constants *J* are reported in hertz. The abbreviations s, d, dd, td, dt and m were used for singlet, doublet, doublet–doublet, triplet–doublet, doublet–triplet and multiplet, respectively.

RESULTS AND DISCUSSION

As a first step, the ^{1}H NMR spectra of compounds **2** and **8** (Y=H) were fully assigned and are in agreement with literature data.[6] The remaining compounds were assigned by analogy. For compounds **1–6**, the two signals at ~1.31 and 1.33 ppm correspond to H-1 and H-3 of the diethoxyphosphoryl group (Table 2), the expected triplets

*Correspondence to: Paulo R. Olivato, Instituto de Química, USP, Caixa Postal 26077, 05513-970 São Paulo, SP, Brazil. E-mail: prolivat@iq.usp.br
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MRC

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Table 1. Physical and elemental analysis data for the 4′-substituted diethyl 1-methylthio-2-oxo-2-phenylethylphosphonates (**1–6**) and 4′-substituted diethyl 1-methylsulfonyl-2-oxo-2-phenylethylphosphonates (**7–12**)

Compound	Y	m.p. (°C)	Molecular formula	MW		Analysis (%) C	H	N
1	MeO	[a]	$C_{14}H_{21}O_5PS$	332.3	Calc.	50.6	6.4	
					Found	50.2	6.2	
2	H	55–57	$C_{13}H_{19}O_4PS$	302.3	Calc.	51.6	6.3	
					Found	51.3	6.1	
3	F	40–43	$C_{13}H_{18}FO_4PS$	320.3	Calc.	48.7	5.7	
					Found	48.8	5.5	
4	Cl	92–93	$C_{13}H_{18}ClO_4PS$	336.7	Calc.	46.4	5.4	
					Found	46.1	5.2	
5	Br	109–111	$C_{13}H_{18}BrO_4PS$	381.2	Calc.	40.9	4.8	
					Found	40.8	4.7	
6	NO_2	112–118	$C_{13}H_{18}NO_6PS$	347.3	Calc.	44.9	5.2	4.0
					Found	45.1	4.9	4.1
7	MeO	[a]	$C_{14}H_{21}O_7PS$	364.3	Calc.	46.1	5.8	
					Found	46.3	5.8	
8	H	[a]	$C_{13}H_{19}O_6PS$	334.3	Calc.	46.7	5.7	
					Found	46.9	5.4	
9	F	[a]	$C_{13}H_{18}FO_6PS$	352.3	Calc.	44.3	5.7	
					Found	44.4	5.8	
10	Cl	[a]	$C_{13}H_{18}ClO_6PS$	368.8	Calc.	42.3	4.9	
					Found	42.5	5.0	
11	Br	68–70	$C_{13}H_{18}BrO_6PS$	413.2	Calc.	37.8	4.4	
					Found	37.8	4.4	
12	NO_2	[a]	$C_{13}H_{18}NO_8PS$	379.3	Calc.	41.2	4.8	3.2
					Found	41.3	4.7	3.1

[a] An oil.

Table 2. The ^{1}H NMR chemical shifts[a] and multiplicities for the 4′-substituted diethyl 1-methylthio-2-oxo-2-phenylethylphosphonates (**1–6**) and diethyl 4′-substituted 1-methylsulfonyl-2-oxo-2-phenylethylphosphonates (**7–12**)

Compound	Y	H1[b]	H3[b]	H2/4[c]	H6	H7	H10/H14	H11/H13	H12	H15
1	MeO	1.31 td	1.32 td	4.25 m	2.26 d	4.48 d	8.01 m	6.94 m		3.88 s
2	H	1.31 td	1.32 td	4.24 m	2.27 d	4.43 d	8.02 m	7.49 m	7.60 m	
3	F	1.31 td	1.33 td	4.25 m	2.26 d	4.46 d	8.07 m	7.45 m		
4	Cl	1.31 td	1.33 td	4.24 m	2.26 d	4.44 d	7.97 m	7.45 m		
5	Br	1.31 td	1.33 td	4.25 m	2.25 d	4.43 d	7.89 m	7.62 m		
6	NO_2	1.32 td	1.34 td	4.26 m	2.26 d	4.44 d	8.32 m	8.20 m		
7	MeO	1.18 td	1.37 td	4.14 m	3.44 d	5.56 dq	7.97 m	6.98 m		3.89 s
				4.33 m						
8	H	1.17 td	1.38 td	4.14 m	3.46 d	5.61 dq	7.98 m	7.52 m	7.66 m	
				4.33 m						
9	F	1.19 td	1.38 td	4.14 m	3.45 d	5.54 dq	8.02 m	7.20 m		
				4.34 m						
10	Cl	1.21 td	1.38 td	4.14 m	3.44 d	5.52 dq	7.92 m	7.51 m		
				4.34 m						
11	Br	1.19 td	1.38 td	4.14 m	3.44 d	5.50 dq	7.84 m	7.67 m		
				4.33 m						
12	NO_2	1.21 td	1.39 td	4.18 m	3.46 d	5.55 dq	8.37 m	8.15 m		
				4.36 m						

[a] In ppm, from TMS.

[b] The assignments may be interchanged (for compounds **1–6**).

[c] The first entry corresponds to proton H2 and the second to H4 for compounds **7–12**.

being observed as triplet–doublets due to a small coupling (0.9 Hz) with the P atom $^4J_{H1,P}/^4J_{H3,P}$ (Table 3). The doublet at ~4.4 ppm corresponds to H-7 attached to the chiral carbon (C-7), showing $^2J_{H7,P} \sim 19$ Hz. It was discriminated from the signal at ~4.2 ppm, which corresponds to H-2/4, by the different multiplicity of the two signals. The upfield signal at ~2.3 is easily identified as H-6 and the aromatic protons present chemical shifts in close agreement with the empirically calculated chemical shifts.[6]

In the ^{1}H NMR spectra of compounds **7–12**, the H-1 proton present a diamagnetic shift in relation to the corresponding hydrogens of compounds **1–6**, whereas H-3 and H-2/4 show similar chemical shifts to those of compounds **1–6**. The observed diamagnetic shift is in line with the preferred conformation of compounds **7–12** obtained by HF/6-31G** computations,[7] which shows the occurrence of a short contact between the nearest methylene proton of the ethoxyl group of the diethoxyphosphoryl moiety and one of the sulphonyl oxygen atoms. A doublet–doublet at ~5.5 ppm is observed, which corresponds to H-7 attached to the center of chirality whose coupling constants are $^2J_{H7,P} \sim 20$ Hz and $^4J_{H7,H6} = 0.9$ Hz (Table 3). Although the H-7 signal should be a doublet–quartet at 300 MHz, only an unresolved doublet–doublet has been observed.

The ^{13}C NMR spectra were assigned mostly with the support of the HETCOR experiments and were checked against the data for the corresponding acetophenones.[8] The chemical shifts and coupling constants ($^nJ_{CP}$) are presented in Tables 4 and 5, respectively. The large coupling constants of ~145 Hz for the signal at ~46 ppm (compounds **1–6**) and ~129 Hz for the signal at ~69 ppm (compounds **7–12**) correspond to $^1J_{C7,P}$ (Table 5). The larger deshielding of C-6 (δ ~41 ppm) in compounds **7–12** with respect to compounds **1–6** (δ ~15 ppm) may be ascribed to the larger $-I$ inductive effect of the methylsulfonyl group ($\sigma_I = 0.50$)[9] in comparison with that of the methylthio group ($\sigma_I = 0.25$).[9] In the fluoroderivatives (**3** and **9**), coupling constants of 10, 22 and 255 Hz correspond to $^3J_{C10,F}/^3J_{C14,F}$, $^2J_{C11,F}/^2J_{C13,F}$ and $^1J_{C12,F}$, respectively.

Table 3. The ^{1}H NMR coupling constants (Hz) for the 4′-substituted diethyl 1-methylthio-2-oxo-2-phenylethylphosphonates (**1–6**) and 4′-substituted diethyl 1-methylsulfonyl-2-oxo-2-phenylethylphosphonates (**7–12**)

Compound	Y	$^3J_{H1,H2}/^3J_{H3,H4}$	$^4J_{H1,P}/^4J_{H3,P}$	$^4J_{H6,P}$	$^2J_{H7,P}$	$^4J_{H7,H6}$	$^3J_{H10,H11}/^3J_{H13,H14}$	$^4J_{H10,F}/^4J_{H14,F}$	$^3J_{H11,F}/^3J_{H13,F}$
1	MeO	6.9	0.6	0.9	18.3		9.0		
2	H	7.2	0.6	0.9	18.0				
3	F	7.2	0.6	0.9	18.6		9.0	5.4	8.6
4	Cl	6.9	0.6	0.9	18.6		9.0		
5	Br	7.2	0.6	0.9	18.6		9.0		
6	NO_2	6.9	0.6	0.6	19.2		9.0		
7	MeO	6.9	0.9	0.9	21.0	0.9	9.0		
8	H	6.9	0.9	0.9	20.0	0.9			
9	F	6.9	0.9	0.9	19.8	0.9	9.0	5.4	8.6
10	Cl	7.2	0.9	0.9	19.5	0.9	9.0		
11	Br	7.2	0.9	0.9	21.0	0.9	9.0		
12	NO_2	6.9	0.9	0.9	19.8	0.9	9.0		

Table 4. The ^{13}C NMR chemical shifts[a] and multiplicities[b] for the 4′-substituted diethyl 1-methylthio-2-oxo-2-phenylethylphosphonates (**1–6**) and 4′-substituted diethyl 1-methylsulfonyl-2-oxo-2-phenylethylphosphonates (**7–12**)

Compound	Y	C1/C3[c]	C2	C4	C6	C7	C8	C9	C10/C14	C11/C13	C12	C15
1	MeO	16.37 d	63.71 d	63.85 d	15.10 d	45.55 d	190.10 s	132.77 s	131.43 s	113.92 s	164.13 s	55.56 s
2	H	16.33 d	64.35 d	64.67 d	15.11 d	45.40 d	188.99 s	136.39 s	129.09 s	129.24 s	133.45 s	
3	F	16.26/16.41 d	63.56 d	63.71 d	15.12 d	46.19 d	190.09 s	132.69 s	131.77 d	115.77 d	166.07 d	
4	Cl	16.29/16.41 d	63.58 d	63.70 d	15.10 d	46.17 d	190.38 s	133.73 d	130.39 s	128.92 s	140.18 s	
5	Br	16.29/16.40 d	63.58 d	63.71 d	15.09 d	46.11 d	190.56 s	134.13 d	130.46 s[d]	131.93 s[d]	128.92 s	
6	NO_2	16.40/16.46 s	63.86 s	63.99 s	15.22 d	46.99 d	190.11 s	140.14 s	130.14 s	123.81 s	150.62 s	
7	MeO	15.92/16.20 d	64.29 d	64.69 d	40.95 s	69.14 d	185.89 s	129.03 s	131.70 s	114.20 s	146.70 s	55.56 s
8	H	15.95/16.27 d	64.27 d	64.93 d	41.04 s	69.65 d	187.90 s	136.32 s	128.93 s[d]	129.35 s[d]	134.48 s	
9	F	16.00/16.28 d	64.34 d	65.07 d	41.03 s	69.73 d	186.47 s	132.78 s	132.03 d	116.06 d	166.50 d	
10	Cl	16.05/16.30 d	64.31 d	65.07 d	41.14 s	69.70 d	186.94 s	134.65 s	131.09 s[d]	129.35 s[d]	141.35 s	
11	Br	16.36/16.58 s	64.41 d	65.07 d	41.18 s	69.62 d	189.68 s	136.23 s	130.64 s[d]	132.79 s[d]	149.98 s	
12	NO_2	16.27/16.58 d	64.41 d	65.18 d	41.58 s	70.09 d	189.79 s	137.32 s	132.98 s	126.56 s	151.36 s	

[a] In ppm, from TMS.

[b] Due to couplings to nuclei other than hydrogen.

[c] For compounds **1** and **2**, the signals for carbons C1 and C3 are superimposed.

[d] The assignments of C10/C14 and C11/C13 may be reversed.

Spectral Assignments and Reference Data

Table 5. The ^{13}C NMR coupling constants for the diethyl 4′-substituted 1-methylthio-2-oxo-2-phenylethylphosphonates (**1–6**) and 4′-substituted diethyl 1-methylsulfonyl-2-oxo-2-phenylethylphosphonates (**7–12**)

Compound	Y	$^3J_{C1,P}/^3J_{C3,P}$	$^2J_{C2,P}/^2J_{C4,P}$	$^3J_{C6,P}$	$^1J_{C7,P}$	$^3J_{C9,P}$	$^3J_{C10,F}/^3J_{C14,F}$	$^2J_{C11,F}/^2J_{C13,F}$	$^1J_{C12,F}$
1	MeO	6.0	6.5	2.5	146.0				
2	H	6.0	6.5	2.5	145.0				
3	F	6.0	7.0	2.0	145.0		9.0	22.0	255.0
4	Cl	6.0	6.5	2.5	146.0	5.5			
5	Br	6.0	6.5	2.5	145.0	5.0			
6	NO_2	6.0	8.2	1.5	145.0				
7	MeO	6.0	6.0		130.6				
8	H	6.0	6.5		129.7				
9	F	6.0	7.0		129.5		10.0	22.0	250.0
10	Cl	6.0	7.0		129.0				
11	Br	6.0	6.5		128.5				
12	NO_2	6.0	7.0		129.5				

Acknowledgements

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