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Synthesis of α-Phosphonylated Phosphonium and Sulfonium Ylides: Study of Their Thermal Behavior

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ABSTRACT: *The additions of two equivalents of trialkylphosphites onto phosphonodithioformates produce stabilized α-sulfanyl-α-phosphonyl phosphonium ylides. Their subsequent reaction with alkyl or benzyl halides gives stabilized sulfonium ylides. Thermal treatment of these phosphonium and sulfonium ylides leads to α-sulfanyl methylene bis-phosphonates through protonation–dealkylation intramolecular reactions.* © 2009 Wiley Periodicals, Inc. Heteroatom Chem 20:164–171, 2009; Published online in Wiley InterScience (www.interscience.wiley.com). DOI 10.1002/hc.20530

INTRODUCTION

Mixed phosphorus- and sulfur-containing compounds have been shown to be useful synthetic tools and also to exhibit interesting biologic properties, due to the diversity of functions and oxidation states involving the two heteroatoms [1]. Among them, phosphonodithioesters are versatile reagents through their use in various reactions such as thiophilic addition of nucleophiles, thioacylation of amines, and cycloaddition reactions [1a,2]. The addition of dialkyl and trialkylphosphites to phosphonodithioformates has been previously examined in our group [3] and is shown to be a convenient method to access methylene bis-phosphonate derivatives [3b,e]. Moreover, because of their hydrolytic stability and their remarkable chelating features, they have been recognized as biologically relevant materials [4].

In this paper, we describe the synthesis of α-phosphonyl phosphonium and sulfonium ylides starting from trialkylphosphites and phosphonodithioformates and their behavior under thermal conditions, leading to α-sulfanyl methylene bis-phosphonates.

RESULTS AND DISCUSSION

Synthesis of Phosphonium Ylides **4–6** *and Sulfonium Ylides* **7–9**

α-Sulfanyl-α-phosphonyl phosphonium ylides **4–6** were obtained in quantitative yields by the reaction between two equivalents of a trialkylphosphite with phosphonodithioformates **1–3**, which were easily synthesized according to the method described by Grisley [5]. The reaction proceeds by a thiophilic addition followed by desulfurization (Scheme 1) and the trialkyl thiophosphate, which is also generated in the reaction, can be efficiently removed under vacuum [3b].

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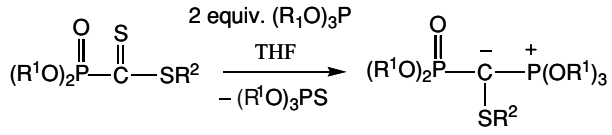


1: R^1 = Et, R^2 = Me
2: R^1 = Me, R^2 = CD_3
3: R^1 = i-Pr, R^2 = Me

4: R^1 = Et, R^2 = Me
5: R^1 = Et, R^2 = CD_3
6: R^1 = i-Pr, R^2 = Me

SCHEME 1

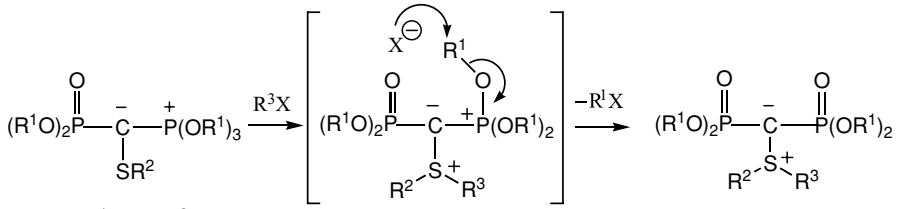
Then, the phosphonium ylides **4–5** were converted into sulfonium ylides **7–9** by S-alkylation with alkyl halides (Scheme 2). The reaction was completely selective, and no C-alkylation products were detected.

The addition at room temperature in THF of methyl iodide or benzyl bromide to phosphonium ylide **4** leads to the sulfonium ylides **7** and **8** in 65% and 76% yield, respectively. Similarly, alkylation of **5** with deuterated methyl iodide led to the expected sulfonium ylide **9**. The overall reaction involves S-alkylation and subsequently the Arbuzov-type dealkylation of the trialkoxyphosphonium intermediate [3c]. It is worth to note that ethyl iodide or ethyl bromide generated during the reaction is not reactive enough under these conditions (room temperature, THF) to react with the starting phosphonium ylides.

Reactivity of α-Methylsulfanyl Phosphonium Ylides **4** *and* **6** *under Thermal Conditions*

The phosphonium ylides **4** and **6** differ by the nature of the alkoxyphosphonium group (ethyl versus isopropyl). A high stability of these ylides was observed at room temperature, but upon heating at 110°C (Scheme 3) ylide **4** afforded, beside methylsulfanyl methylene bis-phosphonate **11**, the bis-phosphonylated sulfonium ylide **10**, and an unidentified product **A** (^{31}P NMR, $\delta = 20$ ppm). Percentages of the three products **10, 11, A**, and of the starting ylide **4** have been shown to be dependent on the heating time. Results are presented in Table 1.

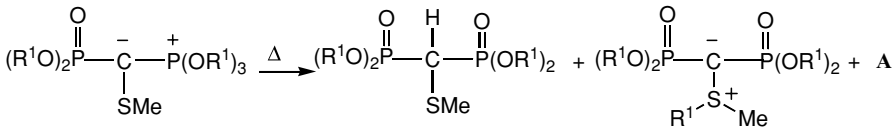
After 18 h of heating without ethyl iodide, three products were observed albeit a low conversion was achieved (Table 1, entry 1). After 150 h, the reaction was complete and only methylsulfanyl methylene bis-phosphonate **11** along with a small amount of compound **A** was formed. This result suggests the formation of methylene bis-phosphonate **11** from the intermediate sulfonium ylide **10** (Table 1, entry 2). When the phosphonium ylide **4** was heated for 18 h in refluxing toluene in the presence of 1 equiv of ethyl iodide, **11** and **10** were formed in a 3:2 ratio (Table 1, entry 3). The addition of ethyl iodide increases the reaction rate (Table 1, entry 1 versus entry 3) very likely by favoring the formation of the sulfonium ylide **10**. Prolonged heating (120 h; Table 1, entry 4) enabled the selective formation of the methylsulfanyl bis-phosphonate **11** via **10**, after addition of 1 equiv of ethyl iodide.



4: R^1 = Et, R^2 = Me
4: R^1 = Et, R^2 = Me
5: R^1 = Et, R^2 = CD_3

7: R^1 = Et, R^2 = R^3 = Me (65%)
8: R^1 = Et, R^2 = Me, R^3 = Bn (76%)
9: R^1 = Et, R^2 = R^3 = CD_3 (75%)

SCHEME 2



4: R^1 = Et
6: R^1 = i-Pr

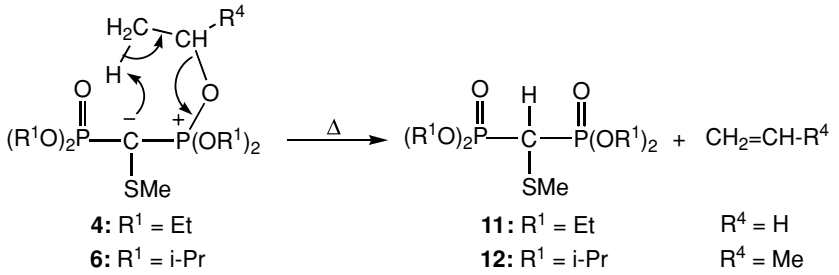
11: R^1 = Et
12: R^1 = i-Pr

10: R^1 = Et
13: R^1 = i-Pr (not observed)

SCHEME 3

TABLE 1 Transformation of Ylide **4** into **11, 10**, and **A**, under Thermal Conditions, with or without Addition of Ethyl Iodide

Entry	*Heating Time (110°C)*	*Added Ethyl Iodide*	***4*** *(%)*	***11*** *(%)*	***10*** *(%)*	***A*** *(%)*
1	18 h	0	75	13	3	5
2	150 h	0	0	83	0	10
3	18 h	1 equiv	0	60	40	0
4	120 h	1 equiv	0	100	0	0



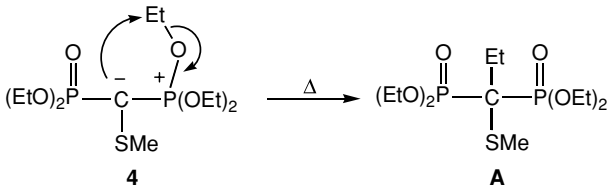
SCHEME 4

Compared to **4**, phosphonium ylide **6** led only to the methylsulfanyl tetraisopropyl methylene bis-phosphonate **12** (Scheme 3). The formation of α-phosphonylated sulfonium ylide **13** was never observed. The formation of sulfanyl methylene bis-phosphonates **11** and **12** can be explained by a mechanism involving an intramolecular protonation of the corresponding ylides with a proton coming from one alkoxy group of the phosphonium moiety producing ethylene and propylene, respectively (Scheme 4) [6,7]. This approach using phosphonodithioformates and trialkylphosphites as simple starting materials can be considered as a convenient alternative to the previously reported methods to access alkylsulfanyl methylene bis-phosphonates [3b,8].

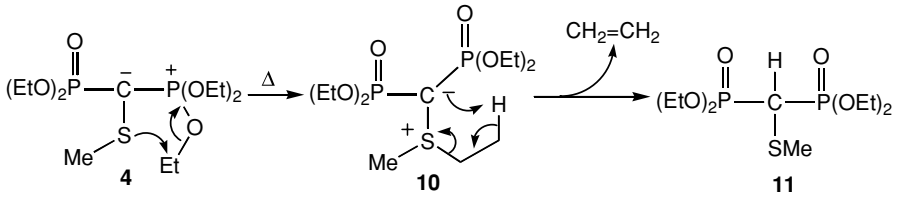
The reactivity of phosphonium ylides under thermal conditions is often related to a C-alkylation involving the transfer of an alkyl group from the phosphonium moiety to the carbon of the ylide [9]. To examine the possibility of such a reaction, the crude mixture obtained after heating the triethoxyphosphonium ylide **4** during 150 h was analyzed by GC/MS. The analysis of the mixture of bis-phosphonate **11** and **A** (Table 1, entry 2) by mass spectroscopy showed two mass peaks of 334 and 362. The mass of 362 and the observed chemical shift near 20 ppm in the ^{31}P NMR spectrum can be assigned to α-ethyl-α-methylsulfanyl methylene tetraethyl bis-phosphonate, formed from **4** by an intramolecular C-alkylation (Scheme 5).

To complete the mechanistic study of the behavior of the triethoxyphosphonium ylide **4** under thermal conditions (Scheme 3), bis-phosphonylated sulfonium ylide **10** was prepared independently in two steps following the procedures shown in Schemes 1 and 2. Thus, the reaction of triethylphosphite with ethyl diethylphosphonomethanedithioate followed by S-methylation with methyl iodide of the resulting phosphonium ylide afforded **10** in high yield. Upon heating at 110°C for 6 days, sulfonium ylide **10** generated only methylsulfanyl methylene bis-phosphonate **11** and ethylene. The ethylene gas evolving during the reaction was transformed into 1,2-dibromoethane by trapping with bromine. These results are in agreement with the mechanism proposed for the transformation of ylide **4** under thermal conditions. The reaction involves two intramolecular processes, namely S-alkylation and subsequent protonation, leading to **11** and ethylene via sulfonium ylide **10** (Scheme 6).

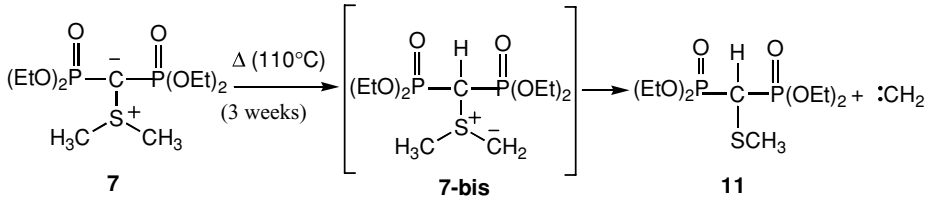
Obviously, such a mechanism based on the transfer of an alkyl group toward sulfur, is unlikely to occur with the triisopropoxyphosphonium ylide **6**. Thus, the conversion of the α-phosphonylated sulfonium ylide **10** into methylene bis-phosphonate **11** appears to be an $\alpha\beta'$ elimination-type reaction



SCHEME 5



SCHEME 6



SCHEME 7

analogue to the reaction previously reported for the analog α,α-dicarboxylated sulfonium ylide [10].

Reactivity of Bis-Phosphonylated Sulfonium Ylides **7–9** *under Thermal Conditions*

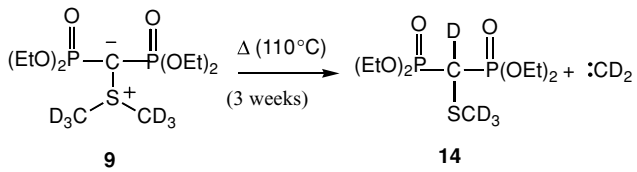
Similarly to the sulfonium ylide **10**, the stabilized ylides **7–9** led to α-alkylsulfanyl methylene bis-phosphonates upon heating.

Dimethylsulfonium ylide **7** was found to be very stable and could even be purified by flash distillation. However, submitted to a prolonged heating (3 weeks at 110°C), it led to the bis-phosphonate **11** as a single product (Scheme 7). The reaction proceeds very likely through a protonation of the ylide **7** by one proton of the methyl substituent of the sulfonium group, leading to new ylide **7-bis** (isomer of **7**), which would be decomposed upon heating into bis-phosphonate **11** and carbene. When the reaction was carried out in a sealed tube in the presence of cyclohexene, a GC/MS analysis of the mixture revealed the formation of norcarane albeit in small amount.

The reactivity of the deuterated ylide **9** under identical thermal conditions also confirmed the mechanism proposed above, as the deuterium incorporated on the central carbon of product **14** can only come from one of the CD_3 group (Scheme 8).

In the case of S-benzyl-S-methyl sulfonium ylide **8**, upon heating at 110°C during 1 week, bis-phosphonates **11** and **15** were formed in 60% and 30% yield, respectively (Scheme 9).

As in the previous studied cases, the formation of bis-phosphonate **11** can be explained by simultaneous intramolecular protonation and elimination of the corresponding carbene (PhCH:), which could,



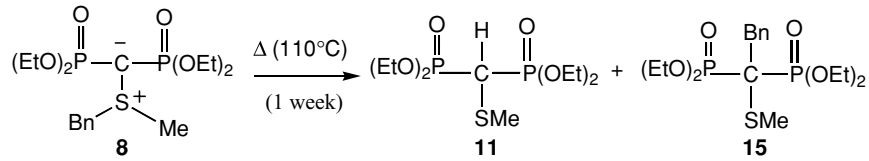
SCHEME 8

however, not be trapped with cyclohexene. The methylene bis-phosphonate **15** probably resulted from a Stevens [1,2]-rearrangement as previously reported in bis-carboxylate sulfonium ylide series [10,11].

CONCLUSION

This article described a study of the thermal behavior of stabilized α-sulfinylated phosphonium and bis-phosphonylated sulfonium ylides which enabled, beside offering a new access to alkylsulfanyl methylene bis-phosphonates, to understand the various mechanisms involved in the transformations. They were found to be largely dependent on the nature of the substituents present on the phosphonium and sulfonium moieties.

The formation of α-alkylsulfanyl methylene bis-phosphonates by thermal treatment of phosphonium and sulfonium ylides results mainly from simultaneous intramolecular protonation and elimination of an alkene or a carbene, respectively. However, we found that phosphonium ylides can be initially converted to some extent into sulfonium ylides under these conditions.



SCHEME 9

EXPERIMENTAL

General

Samples were dissolved in CCl_4, $CDCl_3$, or C_6D_6 with internal TMS. The NMR spectra were recorded in with a Bruker DPX 250 spectrometer. The chemical shifts (δ) are expressed in ppm, and the coupling constants (J) are given in hertz (Hz); conventional abbreviations are used. Infrared spectra (IR) were recorded using a Perkin–Elmer 684 spectrophotometer, absorption peaks frequencies ν are expressed in cm^{-1}. Mass spectra were performed with either a Varian CH 5 or a Nermag Riber R10 mass spectrometer. Electronic impact experiments were recorded at 70 eV (*m/z* and relative abundance in percentage are given). Chemical ionization was obtained using ammoniac. Melting points (Mp) were measured with a Köfler or a Gallzenkamp apparatus and are uncorrected. Boiling points (Bp) are given in centigrade (°C), and the corresponding pressure is expressed in mmHg. Elementary analyses were performed following the method of Debal and Levy [12]. Flash chromatography was performed with Merck 60 (63–200 μm) silica gel following the method of Zubrick [13]. All reactions were carried out using standard techniques. Solvents were purified prior to use by conventional methods.

Synthesis of Phosphonodithioformates **1–3**

Phosphonodithioformates **1–3** were synthesized according to the method of Grisley [5].

To a stirred suspension of sodium hydride (0.22 mol) in dry THF (200 mL), dialkylphosphite (0.20 mol) dropwise was added. After 3 h of stirring, the resulting solution was added onto carbon disulfide (CS_2; 0.10 mol) cooled at –10°C. Methyl iodide or CD_3I (0.21 mol) was then added to the dark red solution, and stirring was continued for 3 h. The solution was poured onto 300 mL of saturated aqueous NH_4Cl and extracted three times with ether. The combined organic layers were dried over magnesium sulfate, filtered and the solvent was evaporated. The phosphonodithioformates **1–3** (dark red liquids) were purified by distillation.

S-Methyl Diethylphosphonodithioformate **1**. $Bp_{0.1}$: 112–117°C. Yield: 57%. ^1H ($CDCl_3$) δ: 1.36 (t, $^3J_{HH} = 7$, 6H, C**H**$_3$CH$_2$—O); 2.71 (s, 3H, SC**H**$_3$); 4.22 (dq, $^3J_{HH} \sim {}^3J_{HP} = 7$, 4H, CH$_3$C**H**$_2$—O). ^{31}P ($CDCl_3$) δ: −2.41. ^{13}C ($CDCl_3$) δ: 16.15 (d, $^3J_{CP} = 7$, **C**H$_3$CH$_2$—O); 19.91 (s, S**C**H$_3$); 64.83 (d, $^2J_{CP} = 7.3$, CH$_3$**C**H$_2$—O); 241.75 (d, $^1J_{CP} = 135.5$, C=S). IR (film): 2980; 2930; 2910; 2860; 1630; 1475; 1440; 1365; 1250 (P=O); 1160 (P—OEt); 1095 (C=S). Anal.: $C_6H_{13}O_3PS_2$: S% : Calcd : 28.9; Found : 27.98.

S-Methyl(d_3)-diethylphosphonodithioformate **2**. $Bp_{0.1}$: 118°C. Yield: 60%. ^1H ($CDCl_3$) δ: 1.4 (t, $^3J_{HH} = 7$, 6H, C**H**$_3$CH$_2$—O); 4.26 (qi, $^3J_{HH} \sim {}^3J_{HP} = 7$, 4H, CH$_3$C**H**$_2$—O). ^{31}P ($CDCl_3$) δ: −2.48. ^{13}C ($CDCl_3$) δ: 16.27 (d, $^3J_{CP} = 5.89$, **C**H$_3$CH$_2$—O); 64.61 (d, $^2J_{CP} = 6.78$, CH$_3$**C**H$_2$—O); 230.05 (d, $^1J_{CP} = 175.7$, C=S). IR (film): 2985; 2920; 2900; 2240; 2110; 1640; 1470; 1440; 1390; 1255 (P=O); 1160 (P—OEt); 1100 (C=S); 1050; 970. Mass *m/z* (%): M+• 231 (30); 213 (6); 185 (4); 183 (15); 181 (18); 155 (4); 153 (13); 137 (20); 121 (6); 109 (48); 97 (4); 96 (10); 95 (32); 94 (100); 93 (21); 91 (20).

S-Methyl-diisopropylphosphonodithioformate **3**. $Bp_{0.02}$: 123°C. Yield: 58%. ^1H ($CDCl_3$) δ: 1.33 and 1.40 (d, $^3J_{HH} \sim {}^4J_{HH} = 7$, 6H, (C**H**$_3$)$_2$CH—O); 2.66 (s, 3H, SC**H**$_3$); 4.82 (octuplet, $^3J_{HH} \sim {}^3J_{HP} = 7$, 2H, (CH$_3$)$_2$C**H**—O). ^{31}P ($CDCl_3$) δ: −4.25. ^{13}C ($CDCl_3$) δ: 19.24 (d, $^3J_{HP} = 3$, S**C**H$_3$); 23.66 and 24.07 (d, $^3J_{CP} = 4.6$ (C**H**$_3$)$_2$CH—O); 73.60 (d, $^2J_{CP} = 6.7$, (CH$_3$)$_2$**C**H—O); 231.73 (d, $^1J_{CP} = 177.3$, C=S). IR (film): 1255 (P=O); 1180; 1140; 1095 (C=S); 990 (P—OiPr). Mass *m/z* (%): M+• 256 (33); 214 (43); 199 (19); 123 (61); 107 (14); 91 (100); 59 (90).

Syntheses of Trialkoxyphosphonium Ylides **4–6**

To a solution of trialkylphosphite (5.90 mmol) in THF (4 mL) at 0°C, dropwise S-methyl-dialkylphosphonodithioformate **1–3** (2.80 mmol) was added. The temperature was allowed to rise slowly to room temperature. The solvent and the trialkylthiophosphate were eliminated under reduced pressure ($Bp_{0.01} = 67$°C), and the α-sulfanyl

phosphonium ylides **4–6** (viscous oils) were obtained in quantitative yield.

Triethoxyphosphoranylidene Methylsulfanyl Diethyl Methylphosphonate **4**. ^{1}H ($CDCl_3$) δ: 1.26 (t, $^3J_{HH} = 7$, 6H, C**H**$_3$CH$_2$—O); 1.36 (t, $^3J_{HH} = 7$, 6H,C**H**$_3$CH$_2$—O); 1.93 (m, 3H, SC**H**$_3$); 3.9 (qi, $^3J_{HH} \sim {}^3J_{HP} = 7$, 4H, CH$_3$C**H**$_2$—OP); 4.2 (qi, $^3J_{HH} \sim {}^3J_{HP} = 7$, 4H, CH$_3$C**H**$_2$—OP$^+$). ^{31}P ($C_6D_6$) δ: 28.50 (d, $^2J_{PP} = 146.80$, P); 51.09 (d, $^2J_{PP} = 146.80$, P$^+$). ^{13}C (C_6D_6) δ: 16.00 (d, $^3J_{CP} = 6.8$, **C**H$_3$CH$_2$—OP); 16.74 (d, $^3J_{CP} = 6.7$, **C**H$_3$CH$_2$—OP$^+$); 23.21 (t, $^3J_{CP} = {}^3J_{CP} = 3$, S**C**H$_3$); 20.62 (t, $^1J_{CP} = 220$, P—C—P$^+$); 64.26 (d, $^2J_{CP} = 6.6$, CH$_3$**C**H$_2$—OP); 64.84 (d, $^2J_{CP} = 6.7$, CH$_3$**C**H$_2$—OP$^+$). IR (film): 2980; 2910; 1640; 1480; 1445; 1425; 1390; 1365; 1280 (P=O); 1160 (P—OEt); 1040. Mass *m/z* (%): M+• 362 (35); 334 (16); 319 (17); 306 (6); 291 (12); 288 (14); 263 (9); 235 (8); 221 (9); 204 (10); 198 (12); 152 (12); 141 (9); 121 (9); 109 (13); 99 (7); 93 (11); 81 (14); 65 (30); 45 (11); 43 (30); 32 (16); 29 (28); 25 (69); 27 (16); 18 (100).

Triethoxyphosphoranylidene Methyl(d_3)sulfanyl Diethyl Methylphosphonate **5**. ^{1}H (C_6D_6) δ: 0.98–1.37 (m, C**H**$_3$CH$_2$—O); 3.85–4.40 (m, CH$_3$CH$_2$—O). ^{31}P (C_6D_6 + CCl_4) δ: 28.66 (d, $^2J_{PP} = 147.5$, P); 51.15 (d, $^2J_{PP} = 147.5$, P$^+$). ^{13}C (C_6D_6 + CCl_4) δ: 15.99 (d, $^3J_{CP} = 2.9$, **C**H$_3$CH$_2$—OP); 16.27 (d, $^3J_{CP} = 2.5$, **C**H$_3$CH$_2$—OP$^+$); 62.54 (d, $^2J_{CP} = 4.9$, CH$_3$**C**H$_2$OP); 63.45 (d, $^2J_{CP} = 6.4$, CH$_3$**C**H$_2$OP$^+$).

Triisopropyloxyphosphoranylidene Methylsulfanyl Diisopropylmethylphosphonate **6**. ^{1}H (C_6D_6) δ: 1.28–1.40 (m, $^3J_{HH} = 7$, 12H, (C**H**$_3$)$_2$CH—O); 2.16 (m, 3H, SC**H**$_3$); 4.18 (M, (CH$_3$)$_2$C**H**—O). ^{31}P (C_6D_6) δ: 28.14 (d, $^2J_{PP} = 149.9$, P); 48.25 (d, $^2J_{PP} = 149.9$, P$^+$). ^{13}C (C_6D_6) δ: 22.85 (d, $^1J_{CP} = 220$, P—C—P); 23.12–23.85 (M, S**C**H$_3$ and (**C**H$_{3-2}$CH—O)); 68.05 (d, $^2J_{CP} = 5.2$, (CH$_3$)$_2$**C**H—OP); 73.62 (d, $^2J_{CP} = 7.5$, (CH$_3$)$_2$**C**H—OP$^+$). IR (film): 2980; 2930; 2870; 1635; 1465; 1335; 1320; 1215 (P=O); 1160 (P—OEt); 1175; 1140(P—OiPr); 1105; 1080; 990. Mass *m/z* (%): M+• 432(14); 390(21); 373(5); 348(14); 344(14); 306(23); 303(17); 264(43); 261(14); 249 (6); 247 (5); 226 (5); 224 (7); 223 (6); 222 (100); 221 (18); 219 (21); 218 (10); 207 (16); 205 (21); 204 (30); 203 (8); 177 (39); 176 (13); 159 (12); 158 (9); 146 (6); 139 (8); 125 (10); 123 (10); 99 (12).

Synthesis of Bis-Phosphonylated Sulfonium Ylides **7–9**

Dimethylsulfanylidene Methylene Tetraethyl Bis-Phosphonate **7**. Methyl iodide (0.142 g, 1 mmol) was added at room temperature to phosphonium ylide **4** (0.303 g, 0.84 mmol) in 1 mL of THF. After 48 h, the solvent was removed and the crude sulfonium ylide **7** was obtained as a viscous oil.

$Bp_{0.01}$: 165°C. Yield: 65%. ^{1}H ($CDCl_3$) δ: 1.26 (t, $^3J_{HH} = 7$, 6H,C**H**$_3$CH$_2$—O); 2.86 (s, 6H, SC**H**$_3$); 3.86 (M, CH$_3$C**H**$_2$—O). RMN ^{31}P ($CDCl_3$) δ: 24.58. ^{13}C ($CDCl_3$) δ: 16.15 (m, **C**H$_3$CH$_2$—O); 24.45 (t, $^1J_{CP} = 203$, P—C—P); 33.17 (t, $^3J_{CP} = 1.4$, S**C**H$_3$); 61.05 (m, CH$_3$**C**H$_2$—O). IR (film): 2980; 2930; 2900; 1735; 1645; 1475; 1440; 1390; 1360; 1290; 1215 (P=O); 1160 (P—OEt); 1095; 1025; 960; 795. Mass *m/z* (%): 348 (8); 333 (8); 288 (10); 277 (16); 261 (6); 242 (6); 233 (5); 221 (9); 215 (8); 152 (10); 109 (10); 58 (25); 43 (100); 42 (9). Anal.: $C_{11}H_{26}O_6P_2S$.

Element	C	H	O	S
Calcd (%)	37.20	7.52	27.50	9.20
Found (%)	37.27	7.74	26.99	9.32

Benzylmethylsulfanylidene Methylene Tetraethyl Bis-Phosphonate **8**. To a solution of phosphonium ylide **4** (3.16 g, 8.74 mmol) in THF (8 mL), 1.65 g (9.70 mmol) of benzyl bromide was added at room temperature. After 150 h of stirring, the solvent and the excess of benzyl bromide were removed under vacuum. White crystals of pure ylide **8** were obtained, washed with pentane, and dried.

Mp: 73–75°C. Yield: 76%. ^{1}H ($CDCl_3$) δ: 1.13–1.15 (m, C**H**$_3$CH$_2$—O); 2.86 (s, 3H, SC**H**$_3$); 3.50–4.18 (m, CH$_3$C**H**$_2$—O); 4.60 (s, PhC**H**$_2$); 7.30–7.50 (M, Har). ^{31}P ($CDCl_3$) δ: 25.46. ^{13}C ($CDCl_3$) δ: 16.34 (t, $^3J_{CP} = 3.7$, **C**H$_3$CH$_2$—O); 22/95 (t, $^1J_{CP} = 203.7$, P—C—P); 30.25 (t, $^3J_{CP} = 1.6$, S**C**H$_3$); 53.35 (s, Ph**C**H$_2$) 61.02 (m, CH$_3$**C**H$_2$—O); 128.9–131 (M, Car). Mass *m/z* (%): M+•424 (60); 423 (18); 378 (9); 377 (11); 333 (8); 330 (17); 304 (5); 248 (6); 22 (16); 93 (11); 91 (100); 81 (12); 65 (47); 61 (9). Anal.: $C_{17}H_{30}O_6P_2S$

Element	C	H	O	S
Calcd (%)	48.10	7.12	22.61	7.55
Found (%)	48.82	7.13	21.99	7.48

Dimethyl-(d_6)sulfanylidene Methylene Tetraethyl Bis-Phosphonate **9**. Compound **9** was obtained according to the method described for **7** using CD_3I instead of CH_3I.

Yield: 69%. ^{1}H ($CDCl_3$) δ: 1.13–1.46 (m, C**H**$_3$CH$_2$O); 3.73–4.60 (m, CH$_3$C**H**$_2$O). ^{31}P (C_6D_6+ THF) δ: 24.59. ^{13}C ($CDCl_3$) δ: 16.40 (s, **C**H$_3$CH$_2$O); 61.06 (m, CH$_3$**C**H$_2$O).

Synthesis of the Bis-Phosphonylated Sulfonium Ylide **10**

Compound **10** was obtained according to the above procedure described for **7**, starting from ethyl diethylphosphonomethanedithioate instead of its methyl analog **1**.

Yield: 92%, isolated as a viscous oil.

Ethylmethylsulfanylidene Methylene Tetraethyl Bis-Phosphonate **10**. ^{1}H ($CDCl_3$) δ: 1.30 (t, $^3J_{HH} = 7$, 12H, C**H**$_3$CH$_2$—O); 1.33 (t, $^3J_{HHA} \sim {}^3J_{HHB} = 7$, 3H, C**H**$_3CH_AH_B$—S); 2.84 (s, 3H, SC**H**$_3$); 2.98 (ddq, 1H, $^4J_{HAP} = 2$, $^2J_{HAHB} = 12$, $^3J_{HHA} = 7$, S–C**H**$_A$); 3.54 (ddq, 1H, $^4J_{HBP} = 2$, $^2J_{HAHB} = 12$, $^3J_{HHB} = 7$, S–C**H**$_B$); 3.71–4.29 (m, 6H, CH$_3$C**H**$_2$—O). ^{31}P ($CDCl_3$) δ: 26.07. ^{13}C ($CDCl_3$) δ: 9.59 (s, C**H**$_3$CH$_2$–S); 16.38 (t, $^3J_{CP} = 3.7$, **C**H$_3$CH$_2$—O); 23,08 (t, $^1J_{CP} = 203.7$, P—C—P); 31.9 (~s, S**C**H$_3$); 61.08 (t, $^2J_{CP} = 2.8$, CH$_3$**C**H$_2$—O); 67 (s, CH$_3$**C**H$_2$–S).

Synthesis of Tetraalkyl Methylsulfanyl Methylene Bis-Phosphonates **11** *and* **12**

Bis-phosphonates **11** and **12** were obtained by heating at 110°C phosphonium ylides **4** and **6** or sulfonium ylide **7**.

Tetraethyl Methylsulfanyl Methylene Bis-Phosphonate **11**. Purified by chromatography on Florisil (eluent: acetone/petroleum ether, 20/80). Yield: 68% ^{1}H ($CDCl_3$) δ: 1.35 (t, $^3J_{HH} = 7$, 6H, C**H**$_3$CH$_2$—O); 2.33 (s, 3H, SC**H**$_3$); 2.28 (t, $^2J_{HP} = 22$, 1H, P—C**H**—P); 4.16 (dq ~ qi, $^3J_{HH} \sim {}^3J_{HP} = 7$, 4H, CH$_3$C**H**$_2$—O). ^{31}P ($CDCl_3$) δ: 17.58. ^{13}C ($CDCl_3$) δ: 15.39 (m, **C**H$_3CH_2$—O); 16.3 (t, $^3J_{CP} = 2.7$, S**C**H$_3$); 37.61 (t, $^1J_{CP} = 138$, P—**C**H—P); 62.56 (m, CH$_3$**C**H$_2$—O). Off decoupling: 37.61 (q,$^1J_{CH} \sim {}^1J_{CP} = 138$ Hz, P—**C**H—P). Mass *m/z* (%): M+•334 (12); 289 (11); 288 (76); 261 (24); 233 (14); 152 (38); 141 (12); 101 (19); 58 (27); 43 (100); 28 (38). IR (film): 2970; 2930; 2910; 2870; 2230; 1700; 1470; 1440; 1420; 1390; 1245 (P=O); 1160 (P—OEt); 1095; 1035; 970. Anal.: $C_{10}H_{24}O_6P_2S$: S% Calcd : 9.59; found : 9.47.

Tetraisopropyl Methylsulfanyl Methylene Bis-Phosphonate **12**. Purified by chromatography on Florisil (eluent: ethyl acetate/ petroleum ether 15/85). Yield: 58%.

^{1}H ($CDCl_3$) δ: 1.36 (m, 6H, (C**H**$_3$)$_2$CH—O); 2.29 (s, 3H, SC**H**$_3$); 2.76 (t, $^2J_{HP} = 22$, 1H, P—C**H**—P); 4.50–5.16 (m, 2H, (C**H**$_3$)$_2$CH—O). ^{31}**P** ($CDCl_3$) δ: 15.98. ^{13}C ($CDCl_3$) δ: 17.83 (t, $^3J_{CP} = 2.8$, S**C**H$_3$); 23.71–24.32 (m, (**C**H$_3$)$_2$CH—O); 40.22 (t, $^1J_{CP} = 139.8$, P—**C**H—P); 71.90–72.40 (m, (CH$_3$)$_2$**C**H—O). Mass *m/z* (%): M+•390 (13); 345 (6); 344 (35); 303 (41); 261 (33); 260 (6); 222 (10); 221 (6); 219 (41); 218 (18); 205 (21); 204 (17); 203 (7); 177 (66); 176 (20); 159 (20); 158 (21); 142 (26); 141 (42); 127 (14); 124 (14); 123 (20); 91 (8); 78 (8); 65 (11); 43 (100). IR (film): 2980; 2930; 2870; 1725; 1640; 1465; 1450; 1385; 1370; 1355; 1315; 1250 (P=O); 1175 (P—OiPr); 1140; 1030; 975. Anal.: $C_{32}H_{24}O_6P_2S$

Element	C	H	O	S
Calcd (%)	43.06	8.26	24.58	8.21
Found (%)	42.62	8.13	25.22	8.25

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REFERENCES

[1] See for review: (a) Gulea, M.; Masson, S. Top Curr Chem 2003, 229, 161–198; (b) Mikolajczyk, M. Rev Heteroatom Chem 1993, 2, 19; (c) Cristau, H. J.; Brahic, C.; Pirat, J. L. Tetrahedron 2001, 57, 9149.

[2] See also, for example, (a) Heras, M.; Gulea, M.; Masson, S.; Philouze, C. Eur J Org Chem 2004, 160–172; (b) Urbaniak, K.; Mloston, G.; Gulea, M.; Masson, S.; Linden, A.; Heimgartner, H. Eur J Org Chem 2005, 1604–1612; (c) Mloston, G.; Urbaniak, K.; Gulea, M.; Masson, M.; Linden, A.; Heimgartner, H. Pol J Chem 2005, 79, 1483–1494; (d) Urbaniak, K.; Mloston, G.; Gulea, M.; Masson, S.; Heimgartner, H. Helv Chim Acta 2005, 88, 2582–2592.

[3] (a) Masson, S.; Sene, A.; Hutchinson, D. W.; Thornton, D. M. Phosphorus, Sulfur Silicon Relat Elem 1988, 40, 1–8; (b) Bulpin, A.; Masson, S.; Sene, A. Tetrahedron Lett 1990, 31, 1151–1154, (c) Masson, S. Phosphorus, Sulfur Silicon Relat Elem 1994, 95/96, 127–144; (d) Alberti, A.; Benaglia, M.; Guerra, M.; Gulea, M.; Dante Macciantelli, D.; Masson, S. Org Lett 2008, 10, 3327–3330; (e) Heuzé, B.; Lemarié, M.; Vazeux, M.; Gulea, M.; Masson, S.; Sene, A.; Jaffrès, P.-A.; Alberti, A. D. Macciantelli, D. Phosphorus, Sulfur Silicon Relat Elem, in press.

[4] See for recent examples: (a) Green, J. R. J Organomet Chem 2005, 690, 2439–2448; (b) Sawicki, M.; Siaugue, J. M.; Jacopin, C.; Moulin, C.; Bailly, T.; Burgada, R.; Meunier, S.; Baret, P.; Pierre, J-L.; Taran, F. Chem Eur J 2005, 11, 3689–3697; (c) Kubicek, V.; Kotek, J.; Hermann, P.; Lukes, I. Eur J Inorg Chem 2007, 333–344; (d) Ridone, S.; Bonardi, M-L.; Groppi, F., Martinotti, A.; Alfassi, Z. B. J Radioanal Nucl Chem 2008, 277, 117–123; (e) Lalatonne, Y.; Paris, C.; Serfaty, J. M.; Weinmann, P.; Lecouvey, M.; Motte, L. Chem Commun 2008, 2553–2555.

[5] Grisley, D. W., Jr. J Org Chem 1960, 26, 2544.

[6] Yoneda, S.; Kawase, T.; Yoshida, Z. I. J Org Chem 1978, 43, 1980–1985.
[7] Tomioka, H.; Ichikawa, N.; Murata, H.; J Chem Soc, Chem Commun 1992, 193.
[8] (a) Gross, M.; Seibt, H. J Prak Chem 1970, 321, 475–479; (b) Ollivier, R.; Sturtz, G.; Legendre, J. M.; Jacolot, G.; Turzo, A. Eur J Med Chim Ther 1986, 21, 103 and references cited therein; (c) Lemée, L.; Gulea-Purcarescu, M.; Masson, S.; Saquet, M.; Collignon, N. Heteroatom Chem 1999, 10, 281–289; (d) Masson, S.; Saquet, M.; Marchand, P. Tetrahedron 1998, 54, 1523.
[9] (a) Corey, E. J.; Mark, G. Tetrahedron Lett 1967, 33, 3201–3204; (b) Middelton, W. J.; Sharkey, W. H. J Org Chem 1965, 30, 1384–1390; (c) Griffiths, D. V.; Teddy, J. C. J Chem Soc, Chem Commun 1986, 871; (d) Hadjiarapoglou, L.; Varvoglis, A. Synthesis 1988, 914–915.
[10] (a) Moody, J. C.; Taylor, J. R. Tetrahedron Lett 1988, 29, 6005–6008; (b) Padwa, A.; Hornbuckle, S. Chem Rev 1991, 91(3), 264–282; (c) Wataru, A. Acc Chem Res 1977, 10, 179–185.
[11] (a) Zhang, J. J.; Schuster, G. B. J Org Chem 1988, 53, 716–719; (b) Wataru, A.; Matsuyama, G.; Nakaido, S.; Migita, T. Tetrahedron Lett 1969, 43, 3825–3828.
[12] Debal, E.; Levy, R. Bull Soc Chim Fr 1968, 426.
[13] Zubrick, J. W. The Organic Chem Lab Survival Manuel; Wiley: New York, 1998; Chap. 18.