Addition of Diazomethane to Phosphonodithioformates and Reactions of Phosphonylated Thiocarbonyl S-Methylides

Urbaniak, Katarzyna; Młoston, Grzegorz; Gulea, Mihaela; Masson, Serge; Heimgartner, Heinz

Abstract: The reaction of phosphonodithioformates 14 with diazomethane at –60°C yielded 2,5-dihydro-1,3,4-thiadiazoles 15 as unstable intermediates. Their structure was evidenced by the base-catalyzed elimination of methylsulfane leading to 1,3,4-thiadiazole-2-phosphonates. At ca. –35°C, thermal decomposition of 15 by N2-elimination led to reactive thiocarbonyl S-methylides 17. In the absence of trapping reagents, these 1,3-dipoles undergo a head-to-head dimerization leading to 1,4-dithianes 18. An intermediate zwitterionic dimer 19 was detected by 31P NMR spectroscopy. The initially formed thiocarbonyl S-methylide 17 as well as an open-chain zwitterionic dimer 20 was intercepted by methanol. Stable interception products were also obtained with S- and N-nucleophiles.

Posted at the Zurich Open Repository and Archive, University of Zurich
ZORA URL: https://doi.org/10.5167/uzh-67591
Accepted Version

Originally published at:
Addition of Diazomethane to Phosphonodithioformates and Reactions of Phosphonylated Thiocarbonyl S-Methylides

by K. Urbaniak¹, G. Młoston¹*, M. Gulea², S. Masson²* and H. Heimgartner³*

¹Section of Heteroorganic Compounds, University of Łódź, Narutowicza 68, PL-90-136
Łódź, Poland

²Laboratory of Molecular and Thio-organic Chemistry, UMR-CNRS 6507, ENSI-
Université de Caen, 6, Bd. Du Maréchal Juin, F-14050 Caen, France

³Institute of Organic Chemistry, University of Zürich, Winterthurerstrasse 190, CH-8057
Zürich, Switzerland

The reaction of phosphonodithioformates 14 with diazomethane at –60°C yielded 2,5-dihydro-1,3,4-thiadiazoles 15 as unstable intermediates. Their structure was evidenced by the base-catalyzed elimination of methylsulfane leading to 1,3,4-thiadiazole-2-phosphonates. At ca. –35°C, thermal decomposition of 15 by N₂-elimination led to reactive thiocarbonyl S-methylides 17. In the absence of trapping reagents, these 1,3-dipoles undergo a head-to-head dimerization leading to 1,4-dithianes 18. An intermediate zwitterionic dimer 19 was detected by ³¹P NMR spectroscopy. The initially formed thiocarbonyl S-methylide 17 as well as an open-chain zwitterionic dimer 20 was intercepted by methanol. Stable interception products were also obtained with S- and N-nucleophiles.

Key words: addition reactions, dimerization, thiocarbonyl ylides, 1,3-dipoles, sulfur heterocycles

The preferred method for the in-situ generation of thiocarbonyl ylides 2 is the thermal decomposition of 2,5-dihydro-1,3,4-thiadiazoles of type 1 via elimination of N₂ (Scheme 1) [1,2]. Whereas the formation of 1 from thioketones and diazomethane takes
place already at low temperature, the ease of the extrusion of N\textsubscript{2} depends on the type of the substituents R. The nature of R also determines the further transformation of 2. The systems containing aromatic substituents eliminate N\textsubscript{2} below 0°C, and the generated ylides 2 undergo preferentially head-to-head dimerization to give 1,4-dithianes 3. Recent computational studies show that the dimerization of thiobenzophenone S-methylide (2, R = Ph) occurs stepwise via a 1,6-biradical 4 [3]. However, in the presence of electron-deficient dipolarophiles, they enter [2+3] cycloaddition reactions to yield sulfur containing five-membered heterocycles [4]. On the other hand, aliphatic derivatives of 1 show enhanced stability and extrude N\textsubscript{2} only at elevated temperature. In the presence of dipolarophiles, they also undergo [2+3] cycloadditions, but in the absence of trapping agents, instead of dimerization, a 1,3-dipolar electrocyclization leading to thiiranes 5 is observed [1,2].

Scheme 1

Thio- and dithioesters show similar reactivity as thioketones and enter [2+3] cycloadditions at low temperature. Reactions of aliphatic and aromatic dithioesters with diazomethane in the absence of dipolarophiles afford 1,4-dithianes and thiiranes [5-7]. At enhanced temperature (>0°C) the reactions occur with spontaneous elimination of N\textsubscript{2}, and
1,3-dithiolanes are formed (so-called Schönberg reaction) [6,8,9]. Furthermore, C-functionalized dithioformates are attractive dienophiles and dipolarophiles. Especially C-sulfonylated dithioformates were explored in reactions with diazoalkanes as well as with dienes [10-12]. In a recent paper, an unprecedented dimerization of the thiocarbonyl ylide 6 via a conceivable [2+3] cycloaddition leading to the zwitterionic 1,3-dithiolane derivative 7, instead of products of type 3 and/or 5, has been described [13] (Scheme 2).

Scheme 2

The reaction of diazomethane with the dithiooxamide 8 yielded 11, i.e., the cyclic dimer of the thiocarbonyl S-methylide 9, via a postulated zwitterionic head-to-head dimer 10 [14] (Scheme 3). In the presence of ZnCl₂, the intermediate 10 was intercepted by methanol to give product 12. Surprisingly, the dimerization of 9 could not be suppressed completely when it was generated in a mixture of methanol and trifluoroacetic acid (TFA), and only part of 9 was trapped yielding the methanol adduct 13.

Scheme 3
These results show that the substitution pattern of the C=S compound strongly influences the behavior of the thiocarbonyl ylide. Therefore, we were aimed to investigate C-phosphonylated dithioformates. Although they have been used as phosphorylated building blocks in Diels-Alder reactions [15], there are no reports on their reactions as dipolarophiles. Only recently we reported on efficient [2+3] cycloadditions with thiocarbonyl ylides [16].

In the present paper, the results of our studies on reactions of C-phosphonylated dithioformates 14a,b with diazomethane and on the reactivity of the corresponding thiocarbonyl S-methylides with nucleophilic reagents are described. The presence of a phosphoryl group not only activates the dipolarophile but also allows the detection of less stable intermediates by $^{31}$P-NMR measurements.
RESULTS AND DISCUSSION

It is well established that [2+3] cycloadditions of diazomethane with dithioesters and aliphatic thioketones can lead to the formation of two regioisomeric cycloadducts, *i.e.*, 1,3,4- and 1,2,3-thiadiazole derivatives [5,17], and only the 1,3,4-isomers are suitable precursors of thiocarbonyl *S*-methylides. The addition of an ethereal solution of diazomethane to the orange-red solution of 14 in THF at –65°C resulted in immediate decolorization. In the case of 14a, the low temperature $^{31}$P-NMR spectra showed that only one product, showing a signal at 12.75 ppm, was formed at –60°C. Thus, the cycloaddition took place with complete regioselectivity. The structure of a 1,3,4-thiadiazole derivative 15a was confirmed by the addition of a ten-fold excess of morpholine to the crude product at –65°C. During slow warming to room temperature, no evolution of N$_2$ was observed. After workup, 1,3,4-thiadiazole-2-phosphonate 16a, formed from 15a by elimination of methylsulfane, was obtained as the only product (Scheme 4).

The decomposition of 15b at –35°C in the absence of any intercepting agent led to the formation of a crystalline product, which was identified as 1,4-dithiane 18b (Scheme 4). This product shows a single signal at 17.22 ppm in the $^{31}$P-NMR spectrum. When the reaction was monitored at low temperature by $^{31}$P-NMR spectroscopy, this signal appeared only at temperatures above +10°C. At –10°C, the spectrum revealed two signals at 28.93 and 18.96 ppm with equal intensity, indicating the existence of an intermediate containing two non-equivalent phosphonyl groups. Based on the reported data [13], we propose that the zwitterionic 1,3-dithiolane ylide 19b is this intermediate, which probably exists in equilibrium with the open-chain dimer 20b*. The latter could be the precursor of the isolated dimer 18b.

Scheme 4

* In the light of the recent studies on the dimerization of thiocarbonyl *S*-methylides [3], the intermediate 20 could also be presented as a 1,6-diradical. Furthermore, the structure of 17 can be presented as a 1,3-diradical [1,18].
In the case of 15a, the decomposition in THF in the absence of trapping reagents was also monitored by $^{31}$P-NMR spectroscopy. At –40°C, the main component was still 15a (signal at 12.70 ppm), accompanied by 19a showing two signals at 28.87 and 17.08 ppm. With increasing temperature, the ratio of 15a/19a changed in favor of the latter, and at –10°C only the signals of 19a were present. Further warming led to a mixture of new products, and the major one showed a signal at 17.99 ppm, which can be attributed by analogy with the ethoxy derivative to 1,4-dithiane 18a. However, all attempts to isolate this product were in vain. After chromatographic workup, many decomposition products were obtained. The first fraction was identified as 23a, which is the C=O analogue of 14a, with a $^{31}$P absorption at –4.84 ppm. A second fraction, which was obtained as a colorless oil, showed also a C=O absorption (IR, $^{13}$C-NMR), and its structure was
determined as 24a. Its formation can be explained by addition of water to 20a followed by elimination of methylsulfane.

In another experiment, the reaction mixture in THF, containing a few drops of water, was also analyzed by $^{31}$P-NMR spectroscopy. Between –60 and –10°C, the signals of 15a and 19a were present in analogy to the experiment carried out in absolute THF. At 0°C, only the signals of 19a were observed. After warming to room temperature, two $^{31}$P absorptions at –4.76 and –18.56 ppm remained. The signal at higher field evidenced the presence of 23a. The second product of the hydrolytic decomposition is probably the sulfane 25a. The formation of 23a–25a requires the precursor 26a, which is formed by interception of 20a by water (Scheme 5).

It is well documented that alcohols can be used as trapping agents for thiocarbonyl ylides to yield dialkyl O,S-acetals [2]. With the aim of intercepting 17, decompositions of 15 were performed in the presence of excess methanol. In the case of 15a, the $^{31}$P-NMR spectrum at –10°C showed the presence of 15a and 19a as well as of a new product with two signals at 21.74 and 16.24 ppm. The latter became the only product when the solution was warmed to +10°C. In both reactions (with 15a, 15b), stable products were isolated as colorless oils, and the spectroscopic data proved the formation of 2:1 methanol adducts 21 (Scheme 4). In order to accelerate the addition of methanol to 17, and in
regard to suppress its dimerization, the decomposition of 15a was carried out in methanol containing trifluoroacetic acid (TFA). Similar to the reaction presented in Scheme 3 [14], 2:1 and 1:1 adducts 21a and 22a, respectively, were formed side by side in a slight favor of the first one.

Thiophenol and enolizable heterocyclic thiones are also efficient trapping reagents for thiocarbonyl S-methylides [2,19]. Therefore, thiophenol, benzo-1,3-thiazole-2-thione, and 1-cyclohexyl-4,5-dimethylimidazole-2-thione were applied to capture the reactive dipolar intermediates in reactions with 15a. As in the experiments with methanol, only the 2:1 adducts 27–29 were obtained, and no 1:1-adducts could be observed (Scheme 6). Among N-nucleophiles, imidazoles and 1,2,4-triazoles are known to intercept thiocarbonyl S-methylides [20]. In the present study, the decomposition of 15a in the presence of benzimidazole gave the 2:1 adduct 30 as the only product. These results evidence once more that the dimerization of 17 is the fastest process and proceeds prior to the reaction with the trapping agent.

Scheme 6
In conclusion, the presented results show that phosphonylated dithioformates 14 react smoothly and regioselectively with diazomethane to afford 2,5-dihydro-1,3,4-thiadiazole-2-phosphonates 15, which can conveniently be used as precursors of thiocarbonyl S-methylides 17 in a one-pot procedure (Scheme 4). These 1,3-dipoles are able to enter [2+3] cycloadditions with suitable dipolarophiles [21], but generated in the absence of intercepting agents, dimerization to give 20 is the preferred reaction.

Our observations, supported by earlier reports [13,16] clearly indicate that the presence of electron-withdrawing substituents in thiocarbonyl S-methylides strongly influence their behavior. Apparently, dimerization reactions are faster then 1,3-dipolar electrocycyclization to give thiiranes. Similar to the known formation of tetraaryl-1,4-dithianes [3,8], the primarily formed dimers of 17 are the open-chain compounds 20. These intermediates exist in equilibrium with the five-membered zwitterionic cycloadducts of type 19. Their stability is limited, and only in the case described in [13] the isolation of the crystalline product was possible. On the other hand, the formation of 19 can be understood as a [2+3] cycloaddition of thiocarbonyl S-methylide 17 as a 1,3-dipole with a second molecule of 17, in which the C=S bond acts as a dipolarophile. This process shows analogies to the ‘Schönberg reaction’ [8].

The dimerization of strongly polarized thiocarbonyl S-methylides (e.g. 6, 9, and 17) to give dipolar products of type 7 and 19 has analogies in other 1,3-dipolar systems. The closest example is the dimerization of some sulfines leading to 1,2,5-oxadithiolane-2-oxides 31 [22] (Figure). Another well established example concerns the formation of 1,2,5-oxadiazole-2-oxides 32 (furoxanes) as dimers of extensively explored nitrile oxides [23,24] Analogous five-membered dimers 33 of nitrile imides are proposed as intermediates, which finally convert into 1,2,3-triazoles by elimination of a nitrene [24,25]. There are also examples known in which two different 1,3-dipoles combine in a formal [2+3] cycloaddition to give five-membered, zwitterionic heterocycles. Sulfines are especially prone to act as electron-deficient dipolarophiles, e.g., the reaction with nitrile imides yields 4,5-dihydro-1,3,4-thiadiazole-1-oxides 34 [26], diazo compounds afford 2,5-dihydro-1,3,4-thiadiazole-1-oxides 35 [28,29], and a thiocarbonyl S-methylide combines to give the 1,3-dithiolane S-oxide 36 [30].
EXPERIMENTAL

1. **General.** For general information on instruments and methods see [15]. $^{31}$P-NMR Spectra: Bruker DRX 400, in CDCl$_3$. Chemical shifts are given in ppm relative to H$_3$PO$_4$ (85%) as an external standard.

2. **Starting materials.** Methyl (diisopropoxy)phosphonyldithioformate (14a) and methyl (diethoxy)phosphonyldithioformate (14b) were prepared from the corresponding phosphites and carbon disulfide following a known protocol [30]. 1-Cyclohexyl-4,5-dimethyl-3$H$-imidazole-2-thione was syntheizized from the corresponding imidazole N-oxide and 2,2,4,4-tetramethylcyclobutane-1,3-dithione as described in [31]. Other reagents were purchased from Sigma-Aldrich and used without purification.

3. **Reactions of dithioformates 14a and 14b with diazomethane.** General procedure: A solution of 14a or 14b (1 mmol) in abs. THF (1 ml) was placed in a flask equipped with a magnetic stirring bar. The flask was cooled in an aceton/dry ice bath to –65°C. While stirring, a freshly prepared etheral solution of diazomethane was added dropwise until the orange-red color of the starting material vanished. The colorless solution was slowly warmed up, and at –35°C a rapid evolution of nitrogen was observed. The mixture was stirred at room temperature for 1 h and the solvents were evaporated in
vacuum. The thick oily residue was analysed by $^1$H-NMR spectroscopy and after removal of the solvent, the crude residue was separated chromatographically on preparative plates coated with silica gel. In the case of 14a, chromatography with diethyl ether as eluent yielded two fractions, which were identified as 23a and 24a, respectively, and in the case of 14b, the main fraction was identified as 1,4-dithiane 18b (CH$_2$Cl$_2$/MeOH 97:3). In this case, the isolated solid was additionally purified by crystallisation.

An analogous experiment carried out with 14a in a THF solution containing 3% (v/v) of water led to 23a and 24a in almost unchanged ratio.

*Tetraethyl 2,3-bis(methylsulfanyl)-[1,4]dithian-2,3-diphosphonate* (18b). Yield: 150 mg (62%), colorless crystals, m.p. 94–96°C (hexane, dry ice cooling). IR (KBr): 2981s, 2918s, 1475m, 1441s, 1390s, 1244vs, 1163s, 1028vs, 966vs, 791s, 750vs, 663m. $^1$H-NMR: 1.34–1.41 (m, 4 MeCH$_2$); 2.36 (s, MeS); 2.75–2.95 (m, 2 CH$_2$S); 4.21–4.42 (m, 4 MeC$_2$H). $^{13}$C-NMR: 15.7 (MeS); 16.7, 16.8, 16.9 (4 MeCH$_2$); 28.2, 28.9 (2 CH$_2$S); 64.2 (d, $^2$J$_{C-P}$ ≈ 8.0 Hz, 4 MeCH$_2$); 65.3, 65.4 (2 C$_q$). $^{31}$P-NMR: 17.22. MS (EI): 484 (M$^+$, 22), 390 (23), 365 (51), 256 (35), 228 (58), 181 (63), 94(100). Anal. Calc. for C$_{14}$H$_{30}$O$_6$P$_2$S$_4$ (484.04): C 34.70, H 6.24, S 26.47. Found: C 34.82, H 6.43, S 26.03.

*S-Methyl [(diisopropoxy)phosphonyl]thioformate* (23a). Yield: 50 mg (20%), pale yellow oil, which showed no differences in the IR spectrum when compared with an original sample prepared according to [29]. IR (neat): 2981s, 2933s, 1647s (C=O), 1468m, 1454m, 1387s, 1261s, 1180m, 1144m, 1103s, 993s, 881m. $^1$H-NMR: 1.36–1.41 (m, 2 Me$_2$CH); 2.41 (d, $^4$J$_{H-P}$ ≈ 1.1 Hz, MeS); 4.79–4.87 (m, 2 Me$_2$CH). $^{13}$C-NMR: 11.0 (d, $^3$J$_{C-P}$ ≈ 1.3 Hz, MeS); 23.7, 23.8, 24.0, 24.1 (2 Me$_2$CH); 73.9 (d, $^2$J$_{C-P}$ ≈ 7.0 Hz, 2 (CH$_3$)$_2$CH); 199.4 (d, $^1$J$_{C-P}$ ≈ 209 Hz, C=O). $^{31}$P-NMR: −4.85.

*Diisopropyl (2-{(diisopropyloxyphosphoryl)(methylsulfanyl)methylsulfanyl}ethylsulfanyl)oxomethanephosphonate* (24a). Yield: 100 mg (35%), thick, pale yellow oil. IR (neat): 2980s, 2933s, 1645s (C=O), 1468m, 1452m, 1387s, 1375s, 1252vs, 1178s, 1142s, 1105s, 993vs, 887m. $^1$H-NMR: 1.36, 1.39 (2 d, J = 7.5, 4 Me$_2$CH); 2.31 (d, $^4$J$_{H-P}$ ≈ 1.0 Hz, MeS); 2.94–3.31 (m, 2 CH$_2$); 3.79 (d, $^2$J$_{H-P}$ ≈ 17.0 Hz, CHP); 4.75–4.88 (m, 4 Me$_2$CH). $^{13}$C-NMR: 14.7 (d, $^3$J$_{C-P}$ ≈ 3.7 Hz, MeS); 23.6, 23.7, 23.9, 24.0, 24.1 (4 Me$_2$CH); 28.1, 30.6 (2 CH$_2$); 46.2 (d, $^1$J$_{C-P}$ ≈ 157 Hz, CHP); 72.4, 73.9 (2 d, $^2$J$_{C-P}$ ≈ 7.0 Hz, 4 Me$_2$CH); 198.9 (d, $^1$J$_{C-P}$ ≈ 209 Hz, C=O). MS (CI, NH$_3$): 511 (100, [M+1]$^+$), 479 (19), 423 (11).
4. Treatment of 2,5-dihydro-1,3,4-thiadiazole 15a with morpholine. To a cold solution (−65°C) of 15a, obtained from 1 mmol of 14a according to the general procedure, was added morpholine (10 mmol) and, while stirring, the mixture was slowly warmed up to room temperature. No evolution of nitrogen was observed. After evaporation of the solvents and removal of excess morpholine by distillation in a Kugel-Rohr, the semisolid residue was separated on preparative plates coated with silica gel (CH2Cl2/MeOH 99:1 as eluent). The main fraction was purified by crystallisation.

Diisopropyl 1,3,4-thiadiazol-2-phosphonate (16a). Yield: 160 mg (64%), colorless crystals, m.p. 36–38°C (diethyl ether/dry ice cooling). IR (KBr): 3051 m, 2983 m, 1377 m, 1250 s, 1105 s, 1005 vs, 652 m, 579 s. 1H-NMR: 1.36, 1.41 (2 d, J_H-H ≈ 6.2 Hz, 2 Me2CH); 4.88–4.99 (m, 2 Me2CH); 9.37 (d, 4 J_H-P ≈ 1.0 Hz, CH=N). 13C-NMR: 23.5, 23.6, 23.7, 23.8 (2 Me2CH); 73.9 (d, 2 J_C-P ≈ 6.3 Hz, 2 Me2CH); 154.4 (d, 3 J_C-P ≈ 3.6 Hz, CH=N); 161.0 (d, 1 J_C-P ≈ 220 Hz, CqP). MS (CI, NH3): 268 (100, [M+NH4]+), 251 (32, [M+1]+).


5. Decompositions of 2,5-dihydro-1,3,4-thiadiazoles 15a and 15b in methanol.

The reactions were performed according to the general procedure, but instead of abs. THF, MeOH (3 ml) was used as the solvent. The crude mixtures were separated chromatographically on preparative plates coated with silica gel using mixture of CH2Cl2/MeOH 98:2 as eluents yielding 21a and 21b, respectively.

Diisopropyl (2-[(diisopropoxyphosphonyl)(methylsulfanyl)methylsulfanyl]ethylsulfanyl)(methoxy)(methylsulfanyl)methanephosphonate (21a). Yield: 200 mg (70%), thick pale yellow oil. IR (neat): 2980 s, 2931 s, 1468 m, 1452 m, 1385 s, 1373 s, 1248 vs, 1178 s, 1142 s, 1105 s, 985 vs, 737 m. 1H-NMR: 1.38 (d, 4 Me2CH); 2.23 (s, MeS); 2.31 (d, 4 J_H-P ≈ 0.7 Hz, MeS); 3.00–3.15 (m, 2 CH2S); 3.42 (s, MeO); 3.80 (d, 2 J_H-P ≈ 18.0 Hz, CHP); 4.45–5.10 (m, 4 Me2CH). 31P-NMR: 13.18, 18.23. MS (CI, isobutan): 588 (23, [M+CH4]^+), 587 (100, [M+CH3]^+), 573 (8, [M+1]^+). Anal. Calc. for C19H42O7P2S4 (572.75): C 39.84, H 6.04, N 11.19, S 12.29. Found: C 39.60, H 6.39, S 12.29.

Diethyl (2-[(diethoxyphosphonyl)(methylsulfanyl)methylsulfanyl]ethylsulfanyl)-(methoxy)(methylsulfanyl)methanephosphonate (21b). Yield: 201 mg (73%), thick, pale
yellow oil. IR (film): 2981s, 2927s, 1637w, 1441m, 1390s, 1250s, 1051s, 1022s, 970s, 793m, 744m. $^1$H-NMR: 1.35 (t, 4 MeCH$_2$); 2.22 (s, MeS); 2.31 (d, $^4$J$_{H-P}$ ≈ Hz, MeS); 3.00–3.15 (m, 2 CH$_2$S); 3.50 (s, MeO); 3.95 (d, $^2$J$_{H-P}$ ≈ 18.5 Hz, CHP); 4.10–4.50 (m, 4 MeCH$_2$)$_2$. $^{13}$C-NMR: 13.8, 14.6 (2 MeS); 16.4, 16.5, 16.6, 16.7 (4 MeCH$_2$); 30.5 (MeO); 31.5, 31.7 (2 CH$_2$S); 45.7 (d, $^1$J$_{C-P}$ ≈ 155.1 Hz, CHP); 63.8, 64.1, 64.4, 64.8 (4 MeCH$_2$).

Anal. Calc. for C$_{17}$H$_{38}$O$_7$P$_2$S$_4$ (544.70): C 37.49, H 7.03, S 23.55. Found: C 37.60, H 7.16, S 23.29.

In an analogous reaction with 15a, a catalytic amount of TFA (ca. 0.1 vol.%) was added to the solution. After evaporation of the solvent in vacuo, the crude residue forming a thick colorless oil was analysed by $^1$H-NMR spectroscopy. Along with signals of the known 21a, the presence of characteristic signals at 2.40 (s, MeS), 2.90 (m, S-CH$_2$-O), and 3.48 (d, $^2$J$_{H-P}$ ≈ 0.7 Hz, MeO), respectively, revealed the formation of a new product, which was identified as 22a. The comparison of the intensities of MeS-signals for 21a (2.23 ppm) and 22a (2.40 ppm) confirmed the ratio of both compounds as ca. 3:2. Attempted separations of 21a and 22a on silica were unsuccessful, and complete decomposition of 22a was observed.

6. Interception of the “dimeric” thiocarbonyl ylide 20 with S- and N-nucleophiles. The reactions were performed according to the general procedure. Abs. THF (1 ml) was used as a solvent for all experiments, which were carried out with 1 mmol of 14a. After decolorization of the dithioester at –65ºC, 1 mmol of corresponding nucleophile was added and the mixture was slowly warmed up to room temperature. Then, the solvent was evaporated, the crude residue was separated on preparative TLC plates coated with silica gel. The isolated solid products were additionally purified by crystallisation.

Reaction with thiophenol. A mixture of CH$_2$Cl$_2$ and diethyl ether (9:1) was used as eluent. Diisopropyl (2-[(diisoproxyphosphoryl)(methylsulfanyl)(methylsulfanyl)-ethylsulfanyl](methylsulfanyl)(phenylsulfanyl)methane phosphonate (27). Yield: 160 mg (49%), thick, colorless oil. IR (neat): 2980s, 2931m, 2922m, 1645w, 1468m, 1452m, 1439m, 1385s, 1375s, 1248s, 1178m, 1142m, 1109s, 989vs, 889m, 750s. $^1$H-NMR: 1.29–1.37 (m, 4 Me$_2$CH); 2.26, 2.28 (2 s, 2 MeS); 2.95–3.26 (m, 2 CH$_2$S); 3.75 (d, $^2$J$_{H-P}$ ≈ 17.3
Hz, CHP); 4.72–4.88 (m, 4 Me₂CH); 7.24–7.37 (m, 3 arom. H); 7.69–7.72 (m, 2 arom. H). ¹³C-NMR: 14.5, 14.8 (2 d, ³J_C-P ≈ 3.3 and ≈ 10.5 Hz, resp., 2 MeS); 23.5, 23.6, 23.8, 23.9, 24.0, 24.1, 24.3 (4 Me₂CH); 31.0, 31.1 (2 CH₂S); 45.9 (d, ¹J_C-P ≈ 157 Hz, CHP); 53.4 (SC₆S); 72.3–74.1 (4 Me₂CH); 128.2, 129.9, 137.7 (5 arom. CH); 130.0 (1 arom. C). ³¹P-NMR: 18.56, 21.42. MS (EI): 651 (12, M⁺), 269 (100), 225 (20), 183 (33). Anal. Calc. for C₂₄H₄₄O₆P₂S₅ (650.89): C 44.29, H 6.81, S 24.63. Found: C 43.14; H 6.82; S 23.82.

Reaction with benzothiazole. A mixture of CH₂Cl₂ and diethyl ether (4:1) was used as the eluent. Diisopropyl [(benzothiazol-2-yl)sulfanyl][2-[(diisoproxyphosphonyl) (methylsulfanyl)ethylsulfanyl]methylanephosphonate (28). Yield: 140 mg (40%), thick, pale yellow oil. IR (neat): 2980 s, 2931 m, 1458 s, 1427 s, 1385 s, 1375 s, 1248 s, 1178 m, 1142 m, 1103 s, 991 s, 756 s, 665 m. ¹H-NMR: 1.28–1.30 (m, 4 Me₂CH); 2.35, 2.40 (2 s, 2 MeS); 2.93–3.04 (m, 2 CH₂S); 3.80 (d, 2J_H-P ≈ 17.5 Hz, CHP); 4.78–4.87 (m, 4 Me₂CH); 7.13–8.02 (m, 4 arom. H). ¹³C-NMR: 14.5, 15.7 (2 MeS); 23.7, 23.8, 23.9, 24.0, 24.1, 24.2 (4 Me₂CH); 31.0, 32.1 (2 CH₂S); 45.9 (d, ¹J_C-P ≈ 157 Hz, CHP); 65.0 (d, ¹J_C-P ≈ 160 Hz, SC₆S); 72.5, 74.1 (4 Me₂CH); 112.7 (NCS); 121.0–141.3 (4 arom. CH, 2 arom. C). ³¹P-NMR: 17.57, 21.45. MS (EI): 269 (100), 255 (40), 167 (76), 123 (35).

Reaction with 1-cyclohexyl-4,5-dimethyl-(3H)-imidazole-2-thione. A mixture of CH₂Cl₂ and diethyl ether (4:1) was used as eluent. Diisopropyl [(1-cyclohexyl-4,5-dimethyl-1H-imidazol-2-yl)sulfanyl][2-[(diisoproxyphosphonyl)(methylsulfanyl)methylsulfanyl]methylanephosphonate (29). Yield: 230 mg (61%), thick, pale yellow oil. IR (neat): 2978 s, 2931 s, 2858 s, 1722 w, 1578 m, 1450 s, 1385 s, 1373 s, 1252 s, 1105 s, 987 s, 733 s. ¹H-NMR: 1.26–1.35 (m, 4 Me₂CH); 1.73–1.99 (m, 5 cyclohexyl-CH₂); 2.05, 2.15 (2 s, 2 MeS); 2.19, 2.20 (2 s, 2 Me); 2.97 (m, 1 cyclohexyl-CH); 4.05 (d, 2J_H-P ≈ 16.5 Hz, CHP); 4.20–4.28 (m, 2 CH₂S); 4.63–4.91 (m, 4 Me₂CH). ¹³C-NMR: 10.7, 12.5 (2 Me); 14.1. 14.2 (2 MeS); 23.4, 23.6, 23.7, 24.0, 24.1, 24.2, 24.8, 25.2, 26.0, 26.1 (4 Me₂CH, 5 cyclohexyl-CH₂); 30.6, 31.9 (2 CH₂S); 45.2 (d, ¹J_C-P ≈ 156 Hz, CHP); 53.3 (SC₆S); 57.2 (cyclohexyl-CH); 72.1, 72.3, 72.4, 72.5 (4 Me₂CH); 126.1, 135.4, 135.8 (3 imidazole-C). ³¹P-NMR: 21.42. MS (EI): 751 (16, M⁺), 481 (72), 255 (100), 209 (65), 142 (35).
Reaction with benzimidazole. A mixture of CH$_2$Cl$_2$ and MeOH (96:4) was used as eluent. Diisopropyl (benzimidazol-2-yl)/2-[(diisoproxyphosphonyl)(methylsulfanyl)-methylsulfanyl]ethylsulfanyl|methylsulfanyl)methanephosphonate (30). Yield: 300 mg (90%), thick, colorless oil. IR (neat): 2981s, 2931m, 1495m, 1450m, 1387s, 1246s, 1103s, 993vs, 750s. $^1$H-NMR: 1.27–1.35 (m, 4 Me$_2$CH); 1.91, 2.24 (2 s, 2 MeS); 2.58–2.69 (m, 2 CH$_2$S); 3.45 (d, $^2$J$_{H-P}$ ≈ 17.6 Hz, CHP); 4.66–4.90 (m, 4 Me$_2$CH); 7.69–8.44 (m, 4 arom. H). $^{13}$C-NMR: 14.3, 14.5 (2 d, $^3$J$_{C-P}$ ≈ 4.3 and ≈ 8.0 Hz, resp., 2 MeS); 23.6, 23.7, 23.8, 24.1, 24.2, 24.3, 24.4 (4 Me$_2$CH); 30.2, 31.5 (2 CH$_2$S); 45.4 (d, $^1$J$_{C-P}$ ≈ 155 Hz, CHP); 69.0 (NC$_4$S); 72.3–72.5 (4 Me$_2$CH); 116.1, 120.4, 123.1, 123.3 (4 arom. CH); 132.4, 143.5, 143.9 (3 arom. C). $^{31}$P-NMR: 14.70, 21.45. MS (EI): 659 (<4, $M^+$), 317 (40), 269 (100), 118 (64), 83 (56), 43 (62).

Acknowledgement

We thank the analytical sections of our institutes for spectra and analyses. Financial support from the Polish State Committee for Scientific Research (Grant No. 3 TO9A 00716), the French CNRS, the “Région Basse-Normandie”, the European Union (FEDER funding), the Swiss National Science Foundation, and F. Hoffmann-La Roche AG, Basel (Switzerland) is gratefully acknowledged.

REFERENCES


