[2+3]-Cycloadditions of Phosphonodithioformate S-Methanides with C=S, N=N, and C=C Dipolarophiles

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Abstract: The reaction of the methyl (dialkoxyphosphinyl)-dithioformates (=methyl dialkoxyphosphinecarbodithioate 1-oxides) 10 with CH2N2 at −65° in THF yielded cycloadducts which eliminated N2 between −40 and −35° to give the corresponding phosphonodithioformate S-methanides (=methylene-sulfonium (dialkoxyoxidophosphino)(methylthiomethyl)oxymethyl) 11 (Scheme 3). These reactive 1,3-dipoles were intercepted by aromatic thietones to yield 1,3-dithiolanes. Whereas the reaction with thiobenzophenone (12b) led to the sterically more congested isomers 15 regioselectively, a mixture of both regioisomers was obtained with 9H-fluorene-9-thione (12a). Trapping of 11 with phosphono- and sulphonodithioformates led exclusively to the sterically less hindered 1,3-dithiolanes 16 and 18, respectively (Scheme 4). In addition, reactive C=DOUBLE BOND C dipolarophiles such as ethenetetracarbonitrile, maleic anhydride, and N-phenylmaleimide as well as the N=DOUBLE BOND N dipolarophile dimethyl diazenedicarboxylate were shown to be efficient interceptors of 11 (Scheme 5).

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[2+3]-Cycloadditions of Phosphonodithioformate S-Methanides

with C=S, N=N, and C=C Dipolarophiles

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The reaction of the methyl dialkylphosphonodithioformates 10 with CH₂N₂ at –65°C in THF yielded cycloadducts, which eliminated N₂ between –40 and –35°C to give the corresponding phosphonodithioformate S-methanides 11 (Scheme 3). These reactive 1,3-dipoles have been intercepted by aromatic thioketones to yield 1,3-dithiolanes. Whereas the reaction with thiobenzophenone led to the sterically more congested isomers 15 regioselectively, a mixture of both regioisomers was obtained with 9H-fluorene-9-thione. Trapping of 11 with phosphono- and sulfonodithioformates, respectively, led to the sterically less hindered 1,3-dithiolanes 16 and 18 exclusively (Scheme 4). In addition, reactive C=C dipolarophiles such as tetracyanoethene, maleic anhydride, and N-phenyl maleimide as well as the N=N dipolarophile dimethyl azodicarboxylate were shown to be efficient interceptors of 11 (Scheme 5).
1. Introduction. – Thiocarbonyl $S$-methanides are versatile sulfur-containing 1,3-dipoles, which have been extensively studied in terms of the reaction mechanism of their $[2+3]$ cycloadditions (concerted vs. stepwise reaction) and their use in the synthesis of diverse $S$-heterocycles [1-3]. Among the few methods of their generation, the reaction of CH$_2$N$_2$ with C=S dipolarophiles and subsequent elimination of N$_2$ is applied most frequently. The reactive 1,3-dipoles formed in situ can be trapped by different electron-deficient dipolarophiles, but aromatic thioketones proved to be the most reactive ones (superdipolarophiles [4]). Less reactive C=S dipolarophiles are non-enolizable aliphatic thioketones, 1,3-thiazole-5($4H$)-thiones, dithioesters, and $O$-alkyl thioesters.

In contrast to thioketones, dithioesters have been less often used as precursors of thiocarbonyl $S$-methanides. In a classical work, the reaction of methyl 1-dithionaphthoate with CH$_2$N$_2$ at room temperature yielded, in a regioselective manner, the sterically more hindered 1,3-dithiolane [5]. Similarly, treatment of methyl dithiobenzoate (1a) with CH$_2$N$_2$ at $-5^\circ$ led to a mixture of cis- and trans-1,3-dithiolanes 3 [6] (Scheme 1), while methyl dithiopropanoate (1b) gave the corresponding thiiranes of type 4 [6]. In both reactions, thiocarbonyl $S$-methanides 2 are proposed as the reactive intermediates.

\[
\text{Scheme 1}
\]

The reaction of CH$_2$N$_2$ with $\alpha$-oxodithioesters of type 5 has been performed of $-80^\circ$, and the evolution of N$_2$ leading to the corresponding $S$-methanide 6 occurred already at $-60^\circ$. The reactivity of the latter compound depends on the type of R$^1$. Whereas, in the case of 5a (R$^1$ = Ph, R$^2$ = PhCH$_2$), the interception of 6 with methyl acrylate gave the $[2+3]$-cycloadduct 7 exclusively, the reaction of 6 derived from 5b (R$^1$ = C$_7$H$_{15}$, R$^2$ = Me) with maleic anhydride led to a mixture of the $[2+3]$-cycloadduct 8 and the 1,3-dithiole 9 [7] (Scheme 2). The latter is the product of a 1,5-dipolar electrocyclization of 6. The generation of 6 (R$^1$ = C$_7$H$_{15}$, R$^2$ = Me)
in the absence of trapping agents yielded 9 as the sole product. This reaction corresponds with the formation of analogous products from thioketones and α-diazo carbonyl derivatives [8].

Scheme 2

In the case of O-alkyl thioesters, the analogous reaction with CH₂N₂ in Et₂O results in the formation of 5-alkoxy-4,5-dihydro-1,2,3-thiadiazoles [6], which cannot be used for the generation of thiocarbonyl S-methanides. Instead, they eliminate easily alcohol to yield 1,2,3-thiadiazoles [9,10].

In a previous paper we have described the behaviour of phosphonylated thiocarbonyl S-methanides, which easily undergo a dimerization process to give zwitterionic dimers. The latter could either cyclize or be trapped by nucleophiles [11] (see also [12]). In the present paper, reactions of phosphonylated thiocarbonyl S-methanides with C=S, C=C, and N=N dipolarophiles are described.

2. Results and Discussion. – In all experiments described below, the reaction of CH₂N₂ with dithioesters 10a and 10b was carried out in THF at –65°, and an equimolar amount of the respective dipolarophile was added at ca. –60°. The evolution of N₂, indicating the formation of the thiocarbonyl S-methanides of type 11, was observed between –40 and –35°. The crude mixtures were analyzed by ¹H-NMR spectroscopy.

The first experiment was carried out using the most efficient thiocarbonyl compound for [2+3]-cycloadditions with thiocarbonyl S-methanides, i.e., 9H-fluorene-9-thione (12a) [13]. The reactions of the latter with thiobenzophenone S-methanide yields regioselectively the 4,4,5,5-tetrasubstituted 1,3-dithiolane (‘2-CH₂-1,3-dithiolane’) [14], whereas the analysis of the crude mixture of the reaction of 11a with 12a showed that two regioisomeric 1,3-
Dithiolanes have been formed in comparable amounts along with some minor by-products\(^2\). Chromatographic separation led to the pure isomers 13a and 14a in ca. 32% yield each (Scheme 3). The product 13a of the more polar fraction was identical with the cycloadduct obtained earlier from the reverse reaction, \textit{i.e.} from 10a and 9\textit{H}-fluorene-9-thione S-methanide [15]. In agreement with the expected value, the 2-CH\(_2\) absorption in the \(^{13}\text{C}\)-NMR spectrum appeared at 32.2 ppm. The second isomer, 14a, showed the signal of the 5-CH\(_2\) group at 51.1 ppm, which is a typical value for ('5-CH\(_2\)-1,3-dithiolanes') [16]. Comparable results were obtained with 11b and 12a, but in this case, the products 13b and 14b were formed in a ratio of ca. 3:2.

\textit{Scheme 3}

In a second series of experiments, thiobenzophenone (12b), which is another reactive dipolarophile, was used to intercept thiocarbonyl S-methanides 11. Only the sterically more hindered cycloadducts 15a and 15b [15] were obtained in modest yields (Scheme 3). The \(^1\text{H}\)-NMR spectrum of the crude mixture indicated the presence of substantial amounts of by-products, which result from the competitive dimerization of 11\(^3\). Apparently, in this system 12b is not reactive enough to suppress the formation of dimers of 11 (see [11]), which decompose during chromatographic workup. All attempts to intercept 11 with cycloaliphatic thioketones such as adamantanethione or 2,2,4,4-tetramethyl-3-thioxocyclobutanone, which are known to be significantly less reactive than aromatic thioketones, were unsuccessful. Only products resulting from the dimerization of 11 were detected in the \(^1\text{H}\)-NMR spectrum.

\(^2\) According to the \(^1\text{H}\)-NMR spectrum, these compounds are the products of the dimerization of 11 also formed in the absence of a trapping reagent [11].

\(^3\) An additional experiment with 12b was carried out in MeOH. In this case, the crude mixture consisted of 15a and the MeOH adduct of the dimer of 11a (see [11]).
In a previous paper, reactions of 10a with aromatic and cycloaliphatic S-methanides, which lead to phosphonylated 1,3-dithiolanes, were described [15]. The results show that the electron-withdrawing phosphonyl group increases the dipolarphilicity of the C=S group in reactions with thiocarbonyl S-methanides. Therefore, the thiocarbonyl S-methanide 11a, generated from 10a and CH2N2, was treated with 10a at ca. –40°, and after warming to room temperature, a single 1,3-dithiolane 16 was obtained. The absorption of CH2 in the 13C-NMR spectrum appeared at 46.3 ppm, indicating that the sterically less crowded ‘5-CH2’ isomer was formed (Scheme 4). A similar result was obtained when the thiocarbonyl S-methanide 11b was trapped with C-sulfonylated dithioformate 17. Again, a single ‘5-CH2’ isomer 18 was formed (δ(CH2) = 43.9 ppm). No attempts were made to determine the relative configuration of the products.

Scheme 4

In contrast to the activated ‘dithioesters’ 10 and 17, methyl dithiobenzoate was not able to intercept transient S-methanides 11.

In general, thiocarbonyl S-methanides, being electron-rich 1,3-dipoles, react smoothly with electron-poor C=C-dipolarophiles. According to Huisgen et al., tetracyanoethylene (TCNE) is the most reactive C=C interceptor of thiobenzophenone S-methanide [13]. As expected, TCNE undergoes an efficient [2+3]-cycloaddition with 11a to give the tetrahydrothiophene derivative 19 in 75% yield (Scheme 5).

Scheme 5

The reactions with fumaronitrile and dimethyl acetylenedicarboxylate, respectively, were not successful, and again only products of the dimerization of 11 were detected.
However, in the case of maleic anhydride, the cycloaddition competes with the dimerization and the expected [2+3]-cycloadducts 20 were isolated in ca. 60% yield. Similarly, the reactions of 11a and 11b with N-phenylmaleimide led smoothly to the bicyclic products 21a and 21b, respectively. In these cases, no dimerization of 11 was observed. The molecular structures of 20a and 21b were established by X-ray crystallography (Figure). In both cases, the two five-membered rings are *cis*-fused and the phosphono group is *exo* oriented, while the methylsulfanyl group occupies the *endo* position. Both of the Et groups of 21b are disordered over two conformations. In both compounds, 20a and 21b, both five-membered rings have half-chair conformations. The S-containing ring of 20a is twisted on C(5)–S(1), while the O-containing ring is twisted on C(3)–C(4). In 21b, the S-containing ring is twisted on C(2)–S(1), while the O-containing ring is quite flat, but twisted slightly on C(3)–C(4).

Figure. *ORTEP Plots* [17] of the molecular structures of a) 20a and b) of one of the two conformations of 21b (50% probability ellipsoids; arbitrary numbering of atoms)

Similarly to electron-deficient C=C-dipolarophiles, azodicarboxylates are superior reaction partners for thiocarbonyl S-methanides [18]. Also in the reaction with 11a, dimethyl azodicarboxylate showed a comparable reactivity to TCNE, and the 1,3,4-thiadiazolidine 22 was obtained in 72% yield (*Scheme 5*).

In conclusion, the presented results show that phosphonylated dithioformates 10 can be used as precursors of phosphonylated thiocarbonyl S-methanides, which are versatile building blocks for the preparation of phosphonylated S-heterocycles. Moreover, compounds 10 were shown to act as dipolarophiles in reactions with thiocarbonyl S-methanides, to give phosphonylated 1,3-dithiolanes (see also [15]). It is noteworthy that thiocarbonyl S-methanides 11 lead to [2+3]-cycloadducts only with very reactive dipolarophiles. In these
systems, dimerization of the dipolar species always competes with the cycloaddition and, therefore, in the case of less reactive dipolarophiles, no cycloaddition is observed. Unlike aromatic and aliphatic thiocarbonyl S-methanides, no 1,3-dipolar electrocyclization to give thiiranes occurs in the case of 11.

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**Experimental Part**

1. *General.* For general information on instruments and methods see [15]. The $^{31}$P{1H} NMR spectra were recorded on a Bruker DRX 400 spectrometer, in CDCl$_3$; chemical shifts (δ) in ppm relative to H$_3$PO$_4$ (85%) as an external standard.

2. *Starting materials.* Methyl (Diisopropoxy)phophonodithioformate (10a) and (diethoxy)phophonodithioformate (10b) were prepared from the corresponding phosphites and CS$_2$ following a known protocol [19]. 9H-Fluorene-9-thione (thiofluorenone) (12a) was prepared by treatment of 9H-fluoren-9-one in EtOH soln. either with a mixed stream of H$_2$S and HCl [20] or by heating with Lawesson’s reagent in boiling toluene [21]. Thiobenzophenone (12b) was obtained from benzophenone and Lawesson’s reagent in boiling toluene according to [22]. S-Phenyl C-benzenesulfonyldithioformate (17) was prepared in a two step procedure from S-phenyl C-chlorodithioformate following a protocol of Senning and
coworkers [23]. Tetracyanoethene, dimethyl azodicarboxylate, maleic anhydride and N-phenyl maleimide were purchased from Sigma-Aldrich and used without further purification.

3. Reactions of dithioformates 10a and 10b with CH2N2. A soln. of 10a or 10b (1 mmol) in abs. THF (1 ml) was placed under an atmosphere of N2 in a round-bottom flask equipped with a magnetic stirring bar. The orange-red soln. was cooled to –65º in an acetone/dry ice bath, and while stirring, a freshly prepared soln. of CH2N2 in Et2O was added dropwise until the color of the starting material vanished.

4. Reactions of in situ generated Phosphonlated Thiocarbonyl Ylides 11a and 11b with Dipolarophiles. General Procedure. To a colorless soln. obtained according to the protocol described in Section 3 and stirred at –65º, 1.1 mmol of the corresponding dipolarophile was added in portions. Then, the soln. was slowly warmed to r.t., and between –40º and –35º a rapid evolution of N2 was observed. The mixture was stirred at r.t. for 1 h and evaporated i.v. The crude mixture was analysed by 1H-NMR spectroscopy and, after removal of the solvent, the oily or solid residue was separated chromatographically or by crystallization.

4.1. Reaction of 11a with 12a. The reaction yielded 13a and 14a, which were separated on prep. TLC plates (SiO2, CH2Cl2).

Diisopropyl \( \{5-\text{(Methylsulfanyl)}\text{spiro[1,3-dithiolane-4,9'-[9' \text{H}]fluoren]-5-yl}\}\text{phosphonate} \) (13a). More polar fraction. Yield: 150 mg (32%). Colorless crystals. M.p. 117–119º (hexane/CH2Cl2). IR (KBr): 2978s, 2919m, 1447s, 1384m, 1373m, 1241vs (P=O), 1104s, 1009vs (P–O–C), 992vs, 741s, 562s. \(^1\)H-NMR: 0.64, 0.78, 0.99, 1.04 (4d, J_H-H = 6.2, 2 Me2CH); 2.46 (d, \(^4\)J_H-P = 0.5, MeS); 4.22, 4.42 (AB, J_H-H = 8.7, CH2); 4.30–4.53 (m, 2 Me2CH); 7.18–7.61 (m, 6 arom. H); 8.16–8.19 (m, 2 arom. H). \(^{13}\)C-NMR: 17.0 (MeS); 22.2, 23.1, 23.5, 24.0 (4d, \(^3\)J_C-P = 3.5, 2 (Me)2CH); 32.2 (d, \(^3\)J_C-P = 10.6, CH2); 71.1, 73.2 (2d, \(^2\)J_C-P =
8.3, 2 Me₂CH); 72.0 (C₉); 74.5 (d, Jₐₜₜ = 85.0, C₉); 118.8, 119.4, 126.1, 126.8, 128.5, 128.9, 129.0, 129.6 (8 arom. CH); 139.3, 141.4, 142.4, 149.0 (4 arom. C). CI-MS (i-C₄H₁₀): 467 (3, [M+1]⁺), 419 (100, [M-MeS]⁻), 389 (5), 377 (6). Anal. calc. for C₂₂H₂₇O₃PS₃ (466.61): C 56.63, H 5.83, S 20.62; found: C 56.75, H 5.92, S 20.36.

Diisopropyl {2-(Methylsulfanyl)spiro[1,3-dithiolane-4,9’-[9’H]fluoren]-2-yl}phosphonate (14a). Less polar fraction. Yield 150 mg (32%). Thick, pale yellow oil. IR (neat): 2981 vs, 2922 s, 1738 m, 1448 vs, 1385 s, 1244 vs (P=O), 1103 vs, 1010 vs (P–O–C), 989 vs, 897 s, 750 vs, 560 s. ¹H-NMR: 1.41 (d, Jₜₜ = 7.0, Me₂CH); 2.52 (s, MeS); 3.60, 4.03 (AB, Jₜₜ ≈ 14, 4Jₜₜ ≈ 1.3, CH₂); 4.71–5.20 (m, 2 Me₂CH); 7.20–8.29 (m, 8 arom. H). ¹³C-NMR: 16.9 (d, 3Jₜₜ = 0.7, MeS); 23.7, 24.0, 24.6 (2 Me₂CH); 51.1 (d, 3Jₜₜ ≈ 2.4, CH₂); 69.5 (d, 1Jₜₜ ≈ 140, C₉); 73.7, 74.2 (2d, 2Jₜₜ ≈ 4.5, 2 Me₂CH); 73.8 (C₉); 119.9, 120.2, 125.5, 126.5, 128.4, 128.6, 129.1 (8 arom. CH); 139.2, 139.6, 147.9, 148.6 (4 arom. C). ³¹P-NMR: 15.50. Anal. calc. for C₂₂H₂₇O₃PS₃ (466.61): C 56.63, H 5.83, S 20.62; found C 56.56, H 5.81, S 20.58.

4.2. Reaction of 11b with 12a. The reaction yielded products 13b and 14b, which were separated on prep. TLC plates (SiO₂, hexane/AcOEt (7:3)).

Diethyl {5-(Methylsulfanyl)spiro[1,3-dithiolane-4,9’-[9’H]fluoren]-4-yl}phosphonate (13b). More polar fraction. Yield: 220 mg (49%). Colorless crystals. M.p. 83–85° (hexane/Et₂O). IR (KBr): 2977m, 1447s, 1243vs (P=O), 1055vs, 1023vs (P–O–C), 981s, 746s, 556s. ¹H-NMR: 0.86 (td, Jₜₜ = 7.0, 4Jₜₜ = 0.5, MeCH₂); 0.92 (t, Jₜₜ = 7.0, MeCH₂); 2.47 (s, MeS); 3.41–3.87 (m, 2 MeCH₂); 4.23, 4.44 (AB, Jₜₜ = 8.7, CH₂); 7.19–7.39 (m, 4 arom. H); 7.59–7.64 (m, 2 arom. H); 8.14–8.19 (m, 2 arom. H). ¹³C-NMR: 15.8, 15.9 (2d, 3Jₜₜ ≈ 5.5, 2 MeCH₂); 16.9 (MeS); 32.4 (d, 3Jₜₜ = 10.8, CH₂); 63.0, 64.9 (2d, 2Jₜₜ ≈ 7.6, 2 MeCH₂); 72.3 (C₉); 74.9 (d, 1Jₜₜ ≈ 85.0, C₉); 118.9, 119.4, 126.1, 126.8, 128.6, 128.9, 129.2 (8 arom. CH); 139.2, 140.9, 142.2, 149.1 (4 arom. C). CI-MS (NH₃): 456 (9, [M+NH₄]⁺), 439

**Diethyl {2-(Methylsulfanyl)spiro[1,3-dithiolane-4,9'-[9'H]fluoren]-2-yl}phosphonate (14b).** Less polar fraction. Yield: 120 mg (27%). Colorless crystals. M.p. 56–58º (Et_{2}O, –76º). IR (KBr): 2981s, 2917m, 1447s (P=O), 1247vs (P–O–C), 747vs, 738vs, 560vs. \(^1\)H-NMR: 1.31 (t, \(J_{H-H} = 7.0, 2\) MeCH\(_2\)); 2.56 (s, MeS); 3.70, 3.98 (AB, \(J_{H-H} \approx 14, 4\) \(J_{H-P} \approx 1.3\) only for the low-field H), CH\(_2\)); 4.20–4.60 (m, 2 MeCH\(_2\)); 7.20– 8.20 (m, 8 arom. H). \(^13\)C-NMR: 16.5, 16.7 (d, \(3J_{C-P} \approx 5.5, 2\) MeCH\(_2\)); 17.3 (MeS); 51.0 (d, \(3J_{C-P} \approx 3,\) CH\(_2\)); 65.2, 65.5 (2d, \(2J_{C-P} \approx 7.5 \) and 6.7, resp., 2 MeCH\(_2\)); 73.8 (d, \(3J_{C-P} = 5.0, C_q(4))\); 120.0, 120.2, 125.5, 126.2, 128.5, 128.6, 129.2 (8 arom. CH); 139.2, 139.6, 147.9, 148.1 (4 arom. C); \(C_q(2)\) not found. CI-MS (NH\(_3\)): 456 (12, [M+NH\(_4\)]^+), 439 (11, [M+1]^+), 391 (100, [M-MeS]^+). Anal. calc. for C_{20}H_{23}O_{3}PS_{3} (438.55): C 54.77, H 5.27, S 21.93; found: C 54.69, H 5.50, S 21.79.

4.3. **Reaction of 11a with 12b.** The reaction yielded 15a, which was isolated by trituration of the solid residue, obtained after evaporation of the solvent, with hexane. After filtration, the crude material was purified by crystallisation from hexane/Et\(_2\)O.

**Diisopropyl {4-(Methylsulfanyl)-5,5-diphenyl-1,3-dithiolan-4-yl}phosphonate (15a).** Yield: 150 mg (32%). Colorless crystals. M.p. 170–172º (hexane/Et\(_2\)O). IR (KBr): 2980m, 2920w, 1244s (P=O), 1105m, 1005vs (P–O–C), 699m, 559m. \(^1\)H-NMR: 1.05, 1.13, 1.19, 1.21 (4d, \(J_{H-H} = 6.2, 2\) Me\(_2\)CH); 2.45 (d, \(4J_{H-P} = 0.50,\) MeS); 3.86, 3.94 (AB, \(J_{H-H} = 16.0,\) CH\(_2\)); 4.46–4.56, 4.59-4.69 (2m, 2 Me\(_2\)CH); 7.01–7.76 (m, 10 arom. H). \(^13\)C-NMR: 18.9 (MeS); 23.3, 23.5 (2d, \(3J_{C-P} = 6.8 \) and 6.0, resp., Me\(_2\)CH); 24.2 (Me\(_2\)CH); 31.8 (d, \(3J_{P-C} = 5.6,\) CH\(_2\)); 72.7 (d, \(2J_{C-P} = 8.5, 2\) Me\(_2\)CH); 126.7, 126.8 (2d, \(4J_{C-P} = 3.8, 4\) arom. CH); 127.4 (2 arom. CH); 130.7, 131.1 (4 arom. CH); 143.0 (d, \(3J_{C-P} = 6.0,\) arom. C); 145.0 (d, \(3J_{C-P} = 1.6,\) arom.
C; C\text{q}(4), C\text{q}(5) not found. $^{31}$P-NMR: 15.7. CI-MS (NH$_3$): 469 (43, [M+1]$^+$), 421 (100, [M-MeS]$^+$), 391 (57), 377 (98), 199 (33).

4.4. Reaction of 11b with 12b. The reaction yielded 15b, which was isolated by trituration of the semi-solid residue, obtained after evaporation of the solvent, with hexane. After filtration, the crude material was purified by crystallisation from hexane/CH$_2$Cl$_2$.

Diethyl {4-(Methylsulfanyl)-5,5-diphenyl-1,3-dithiolan-4-yl}phosphonate (15b). Yield: 140 mg (32%). Colorless crystals. M.p. 189–191° (hexane/CH$_2$Cl$_2$). IR (KBr): 2985\text{w}, 1443\text{w}, 1249\text{s} (P=O), 1055\text{vs}, 1023\text{vs} (P–O–C), 971\text{s}, 700\text{s}, 560\text{s}. $^1$H-NMR: 0.97, 1.23 (2t, $J$\text{H-H} = 6.9, 2 MeCH$_2$); 2.49 (d, $J$\text{H-P} = 0.55, MeS); 3.62–4.22 (m, 2 MeC$_2$H$_2$); 3.88, 3.97 (AB, $J$\text{H-H} = 9.3, CH$_2$); 7.17–7.27, 7.60–7.66, 7.76–7.79 (3m, 10 arom. H). $^{13}$C-NMR: 15.9, 16.3 (2d, $^3$J\text{C-P} = 5.6, 2 MeCH$_2$); 18.5 (MeS); 31.7 (d, $^3$J\text{C-P} = 5.7, CH$_2$); 63.7, 64.1 (2d, $^2$J\text{C-P} = 8.2, 2 MeCH$_2$); 126.8, 127.6, 130.4, 131.0 (10 arom. CH); 141.6, 142.9 (2 arom. C); C\text{q}(4), C\text{q}(5) not found. CI-MS (NH$_3$): 441 (30, [M+1]$^+$), 393 (100, [M-MeS]$^+$). Anal. calc. for C$_{20}$H$_{25}$O$_3$PS$_3$ (440.57): C 54.52, H 5.72, S 21.83; found: C 54.11, H 5.84, S 21.39.

4.5. Reaction of 11a with 10a. The reaction yielded 16, which was purified by prep. TLC (SiO$_2$, Et$_2$O). An analytically pure sample was obtained by crystallisation from pentane at –76°.

Tetraisopropyl [2,4-Bis(methylsulfanyl)-1,3-dithiolane]-1,4-diphosphonate (16). Yield: 260 mg (51%). Colorless crystals. M.p. 47–49° (pentane). IR (KBr): 2978\text{s}, 2923\text{m}, 1467\text{m}, 1383\text{s}, 1244\text{vs} (P=O), 1142\text{m}, 1104\text{s}, 1012\text{vs} (P–O–C), 982\text{vs} (P–O–C), 894\text{m}, 553\text{s}. $^1$H-NMR: 1.35 (d, $J$\text{H-H} = 7.0, 4 Me$_2$CH); 2.41 (br.s, 2 MeS); 3.30, 4.10 (AB-like m, $J$\text{H-H} = 13.0, CH$_2$); 4.61–5.10 (m, 4 Me$_2$CH). $^{13}$C-NMR (C$_6$D$_6$): 16.1, 19.1 (2 MeS); 23.7, 23.8, 24.0, 24.1, 24.6, 24.7, 24.8 (4 Me$_2$CH); 46.3 (d, $^3$J\text{C-P} $\approx$ 6.7, CH$_2$); 72.8 (dd, $^1$J\text{C-P} = 147.0, $^3$J\text{C-P} = 5.2, \text{...}
C\(_q\)(4)); 73.7, 73.9, 74.1, 74.3 (4 Me\(_2\)CH); \(C\_q\)(2) not found. Anal. calc. for C\(_{17}\)H\(_{36}\)O\(_6\)P\(_2\)S\(_4\) (526.64): C 38.77, H 6.89, S 24.35; found: C 38.98, H 6.99, S 24.53.

4.6. Reaction of 11b with 17. The reaction yielded 18, which was purified by prep. TLC (SiO\(_2\), hexane/AcOEt (3:2)).

**Diethyl (4-Benzensulfonyl-2-methylsulfanyl-4-phenylsulfanyl-1,3-dithiolan-2-yl)phosphonate** (18). Yield: 350 mg (65%). Thick, pale yellow oil. IR (neat): 2985 \(\text{m}\), 1446 \(\text{m}\), 1325 \(\text{s}\), 1252 \(\text{s}\) (P=O), 1147s, 1049vs, 1020vs (P–O–C), 974s, 754s. \(^1\)H-NMR: 1.37, 1.38 (2 \(\text{td}\), \(J\) \(\text{H-H} = 7, 4\) \(J\) \(\text{H-P} = 0.62\) and 0.66, resp., MeCH\(_2\)); 2.18 (\(d\), \(J\) \(\text{H-P} = 0.75\), MeS); 3.47, 4.10 (\(AB\)-like, \(J\) \(\text{H-H} = 13, 3\) \(J\) \(\text{H-P} = 1.6\) and 1.1, resp., CH\(_2\)); 4.21–4.35 (\(m\), 2 Me\(_2\)C\(_\text{H}\)); 7.33–7.48, 7.54–7.59, 7.66–7.72, 7.81–7.85, 8.04–8.08 (5\(m\), 10 arom. H). \(^{13}\)C-NMR: 16.3, 16.4 (2 Me\(_2\)CH); 18.0 (MeS); 43.9 (\(d\), \(J\) \(\text{C-P} = 5.5\), CH\(_2\)); 65.3, 65.5 (2\(d\), \(J\) \(\text{C-P} = 7.3\), 2 Me\(_2\)CH); 71.5 (\(d\), \(J\) \(\text{C-P} = 160, C\_q\)); 97.3 (\(d\), \(J\) \(\text{C-P} = 7, C\_q\)); 128.6, 128.7, 130.5, 131.7, 134.3, 138.0 (10 arom. CH); 129.8, 135.0 (2 arom. C). ESI-MS (NaI+KI): 559 ([\(M+\text{Na}\]^+)\), 417 ([\(M+1–\text{PhS}\]^+)\).

4.7. Reaction of 11a with tetracyanoethylene (TCNE). The mixture was separated chromatographically on a SiO\(_2\) column using hexane with increasing amounts of CH\(_2\)Cl\(_2\) as the eluent. An analytically pure sample was obtained by crystallisation from MeOH at –76\(^\circ\).

**Diisopropyl [3,3,4,4-Tetracyano-2-(methylsulfanyl)tetrahydrothiophen-2-yl]phosphonate** (19). Yield: 300 mg (75%). Colorless crystals. M.p. 26–27\(^\circ\) (MeOH). IR (KBr): 2985s, 2937m, 2254w (C≡N), 1452m, 1389s, 1259s (P=O), 1099s, 1001vs (P–O–C), 758vs. \(^1\)H-NMR: 1.44–1.51 (\(m\), 2 Me\(_2\)CH); 2.58 (\(d\), \(J\) \(\text{H-P} = 0.5\), MeS); 3.92 (s, CH\(_2\)); 4.88–5.05 (\(m\), 2 Me\(_2\)CH). \(^{13}\)C-NMR: 17.8 (MeS); 23.4, 23.9 (2 Me\(_2\)CH); 40.4 (CH\(_2\)); 76.1, 76.5 (2 Me\(_2\)CH); 107.1, 109.6 (4 CN); 3 C\(_q\) not found. Cl-MS (NH\(_3\)): 416 (100, [\(M+\text{NH}_4\]^+)\), 417(19), 418(11), 306(16). Anal. calc. for C\(_{15}\)H\(_{19}\)N\(_4\)O\(_3\)S\(_2\) (398.44): C 45.22, H 4.81, N 14.06, S 16.09; found: C 45.24, H 4.84, N 14.15, S 15.62.
4.8. Reactions of 11a with maleic anhydride and N-phenyl maleimide. Products 20a and 21a were isolated by trituration of the semi-solid residues obtained, after evaporation of the solvent, with hexane/CH₂Cl₂. Analytically pure samples were obtained by crystallization from hexane/CH₂Cl₂.

**Diisopropyl exo-(6-endo-Methylsulfanyl-2,4-dioxo-3-oxa-7-thiabicyclo[3.3.0]octan-6-yl)phosphonate (20a).** Yield: 300 mg (81%). Colorless crystals. M.p. 121–123° (hexane/CH₂Cl₂). IR KBr): 2983m, 2976m, 2929m, 1856m, 1782vs, 1388m, 1376m, 1243vs (P=O), 1218s, 1012vs (P–O–C), 997s, 986s, 934m, 558s. ¹H-NMR: 1.41, 1.42 (2dd, 4J_H-P ≈ 4.0 and ≈ 5.0, resp., 2 Me₂CH); 2.38 (s, MeS); 3.44–3.56 (m, CH₂); 4.03–4.19 (m, 2 CH); 4.77–4.99 (m, 2 Me₂CH). ¹³C-NMR: 16.0 (MeS); 23.4, 23.7, 23.9 (3d, 3J_C-P ≈ 6.7, 5.4, and 3.6, resp., 3 Me of 2 Me₂CH); 24.5 (s, 1 Me of 2 Me₂CH); 33.5 (d, 2J_C-P ≈ 4.7, CH); 56.6 (d, 3J_C-P ≈ 3.5, CH); 73.3, 75.1 (2 Me₂CH); 171.1 (CO). CI-MS (NH₃): 386 (100, [M+NH₄]⁺), 369 (27, [M+1]⁺), 344 (10), 277 (6). Anal. calc. for C₁₃H₂₁O₆PS₂ (368.41): C 42.38, H 5.75, S 17.41; found: C 42.40, H 5.69, S 17.18.

**Diisopropyl exo-(2-endo-Methylsulfanyl-7-phenyl-6,8-dioxo-3-thia-7-azabicyclo[3.3.0]octan-2-yl)phosphonate (21a).** Yield: 240 mg (54%). Colorless crystals. M.p. 99–100° (hexane/CH₂Cl₂). IR (KBr): 2981m, 2925w, 1776w, 1713vs, 1498s, 1387s, 1241s (P=O), 1193m, 1011vs (P–O–C), 984vs, 565m. ¹H-NMR: 1.40, 1.42 (2d, J = 7.8 and 5.9, resp., 2 Me₂CH); 2.41 (s, MeS); 3.51 (d, 4J_H,P ≈ 5.5, CH₂); 3.88–3.94 (m, CH); 4.07 (dd, J_H,H = 14.6, 4J_H,P ≈ 8.5, CH); 4.83–4.98 (2m, 2 Me₂CH); 7.26–7.49 (m, 5 arom. CH). ¹³C-NMR: 16.2 (MeS); 23.5, 23.6, 24.2, 24.3 (4d, 3J_C,P ≈ 4.0, 2 Me₂CH); 33.2 (d, 3J_C,P ≈ 2.5, CH₂); 52.9 (d, 2J_C,P ≈ 4.8, CH); 55.5 (d, 3J_C,P ≈ 3.4, CH); 62.1 (d, 1J_C,P = 163.0, C(2)); 72.6, 74.4 (2d, 2J_C,P ≈ 7.9 and 7.6, resp., Me₂CH); 126.4, 128.7, 129.1 (5 arom. CH); 131.8 (1 arom. C); 171.5 (d, 3J_C,P ≈ 6.8, CO); 175.8 (CO). CI-MS (NH₃): 461 (64 [M+NH₄]⁺), 444 (100,
4.9. Reactions of 11b with maleic anhydride and N-phenyl maleimide. Products 20b and 21b were isolated by trituration of the solid residues, obtained after evaporation of the solvent, with hexane/Et₂O and hexane/CH₂Cl₂, respectively. Analytically pure products were obtained by crystallization from the same solvents.

**Diethyl exo-(6-endo-Methylsulfanyl-2,4-dioxo-3-oxa-7-thiabicyclo[3.3.0]octan-6-yl)phosphonate (20b).** Yield: 143 mg (42%). Colorless crystals. M.p. 104–106º (hexane/Et₂O). IR (KBr): 2981 m, 2964 m, 2928 w, 1861 vs (C=O), 1254m, 1233 s (P=O), 1086 s, 1060 s, 1020 s (P–O–C), 973 m, 957 m, 555 s. ¹H-NMR: 1.40, 1.41 (2 t, J H-H = 2 MeCH₂); 2.38 (s, MeS); 3.49 (d, 4 J H-P ≈ 4.4, CH₂); 4.07–4.42 (m, 2 MeCH₂, 2 CH). ¹³C-NMR: 15.9 (MeS); 16.3, 16.4 (2d, 3 J C-P ≈ 6.0, 2 MeCH₂); 33.3 (d, 3 J C-P ≈ 3.0, CH₂); 52.9 (d, 2 J C-P ≈ 5.5, CH); 56.8 (d, 3 J C-P ≈ 3.7, CH); 61.5 (d, 1 J C-P ≈ 150.0, C₉); 64.2 (d, 2 J C-P ≈ 7.7, MeCH₂); 65.9 (d, 2 J C-P ≈ 7.4, MeCH₂); 165.8, 170.9 (2 C=O). CI-MS (NH₃): 358 (100, [M+NH₄]⁺), 341 (18, [M+1]⁺), 312 (7). Anal. calc. for C₁₁H₁₇O₆PS₂ (340.36): C 38.82, H 5.03, S 18.84; found: C 38.55, H 5.07, S 18.97.

**Diethyl exo-(2-endo-methylsulfanyl-7-phenyl-6,8-dioxo-3-thia-7-azabicyclo[3.3.0]octan-2-yl)phosphonate (21b).** Yield: 255 mg (61%). Colorless crystals. M.p. 141–143º (hexane/CH₂Cl₂). IR KBr: 2981 w, 2923 w, 1775 w, 1713 vs (C=O), 1497 m, 1389 s, 1241 s (P=O), 1196 s, 1048 s, 1017 s (P–O–C), 564 m. ¹H-NMR: 1.40, 1.41 (2t, J H-H = 2 MeCH₂); 2.40 (d, 4 J H-P ≈ 0.5, MeS); 3.43–3.55 (m, CH₂); 3.91–3.98 (m, CH); 4.15 (dd, J H-H = 14.0, 3 J H-P ≈ 8.8, CH); 4.26–4.43 (m, 2 MeCH₂); 7.27–7.49 (m, 5 arom. CH). ¹³C-NMR: 16.0 (MeS); 16.3, 16.4 (2d, 3 J C-P ≈ 5.4, 2 MeCH₂); 32.9 (d, 3 J C-P ≈ 3.2, CH₂); 52.5 (d, 2 J C-P ≈ 6.3, CH); 55.9 (d, 3 J C-P ≈ 2.6, CH); 62.5 (d, 1 J C-P ≈ 160.0, C₉); 63.9, 65.4 (2d, 2 J C-P ≈ 7.5 and 7.4, resp., 2 MeCH₂); 126.4, 128.7, 129.1 (5 arom. CH); 131.7 (1 arom. C); 171.2 (d, 3 J C-P ≈ 5.4, C=O); 175.6 (C=O). CI-MS (NH₃): 433 (69,
4.10. Reaction of 11a with dimethyl azodicarboxylate. Product 22 was purified by prep. TLC (SiO₂, CH₂Cl₂/Et₂O 1:4). The isolated material was purified by crystallisation from hexane/CH₂Cl₂.

Dimethyl 2-(Diisopropoxy)phosphonyl-2-methylsulfonyl-1,3,4-thiadiazolidine-3,4-dicarboxylate (22). Yield: 300 mg (72%). Colorless crystals. M.p. 97–99º (hexane/CH₂Cl₂). IR (KBr): 2981 m, 1736 vs (C=O), 1735 s (C=O), 1448 s, 1352 vs, 1254 vs (P=O), 1238, 1200 s, 1024 s, 995 vs (P–O–C), 565 s. ¹H-NMR: 1.25–1.40 (m, 2 Me₂CH); 2.40 (s, MeS); 3.80, 3.81 (2 s, 2 MeO); 4.36, 5.25 (AB, Jₜₜ ≈ 9.6, CH₂); 4.70–5.17 (m, 2 Me₂CH). ¹³C-NMR: 17.1 (MeS); 23.3, 23.7, 24.0, 24.3 (2 Me₂CH); 49.4 (d, ³JC-P ≈ 2.4, CH₂); 53.8, 54.2 (2 MeO); 73.7, 74.7 (2d, ²JC-P ≈ 8, 2 Me₂CH); 83.6 (C₆); 153.4, 157.5 (2 C=O). ³¹P-NMR: 9.08. Anal. calc. for C₁₃H₂₅N₂O₇PS₂ (416.46): C 37.49, H 6.05, N 6.73, S 15.40; found: C 37.58, H 6.10, N 6.95, S 15.28.

5. X-Ray Crystal-Structure Determination of 20a and 21b (Table and Fig.)⁴. All measurements were performed on a Nonius KappaCCD diffractometer [24] using graphite-monochromated MoKα radiation (λ 0.71073 Å) and an Oxford Cryosystems Cryostream 700 cooler. The data collection and refinement parameters are given in the Table, and views of the molecules are shown in the Figure. Data reduction was performed with HKL Denzo and Scalepack [25]. The intensities were corrected for Lorentz and polarization effects, and an

⁴) CCDC-265652–265653 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/conts/retrieving.html (or from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, U.K. (fax: + 44-(0)1223-336033; e-mail: deposit@ccdc.cam.ac.uk).
absorption correction based on the multi-scan method [26] was applied. The structures were solved by direct methods using SIR92 [27], which revealed the positions of all non-H-atoms. In the case of 21b, both Et groups are disordered over two conformations. Two sets of overlapping positions were defined for the atoms of each Et group and the site occupation factors of the major conformations of these groups refined to 0.69(3) and 0.746(9) for the Et groups attached to O(1) and O(3), respectively. Similar restraints were applied to the chemically equivalent C–O and C–C bond lengths within each disordered conformation. Neighboring atoms within and between each conformation were also restraint to have similar atomic displacement parameters. The non-H-atoms of 20a and 21b were refined anisotropically. All of the H-atoms were placed in geometrically calculated positions and refined using a riding model where each H-atom was assigned a fixed isotropic displacement parameter with a value equal to 1.2 $U_{eq}$ of its parent C-atom (1.5 $U_{eq}$ for the Me groups). The refinement of each structure was carried out on $F^2$ using full-matrix least-squares procedures, which minimized the function $\sum w(F_o^2 - F_c^2)^2$. A correction for secondary extinction was not applied. In 21b, one reflection, whose intensitiy was considered to be an extreme outlier, was omitted from the final refinement. Neutral atom scattering factors for non-H-atoms were taken from [28a], and the scattering factors for H-atoms were taken from [29]. Anomalous dispersion effects were included in $F_c$ [30]; the values for $f'$ and $f''$ were those of [28b]. The values of the mass attenuation coefficients are those of [28c]. All calculations were performed using the SHELXL97 [31] program.

Table. Crystallographic Data for Compounds 20a and 21b
REFERENCES


**Legends**

Figure. *ORTEP Plots* [17] *of the molecular structures of a) 20a and b) of one of the two conformations of 21b* (50% probability ellipsoids; arbitrary numbering of atoms)
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<th>21b</th>
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a) \(w^{-1} = σ^2(F_o^2) + (aP)^2 + bP\) where \(P = (F_o^2 + 2F_c^2)/3\)
Scheme 1

1a R = Ph
b R = Et

Scheme 2

5a R^1 = Ph, R^2 = PhCH_2
b R^1 = C_7H_15, R^2 = Me
Scheme 3

\[
\begin{align*}
\text{ROP-SMe} + \text{CH}_2\text{N}_2 & \rightleftharpoons \text{ROP-S=CH}_2 + \text{N}_2 \\
10a & \quad \text{R = i-Pr} \\
\text{b} & \quad \text{R = Et} \\
11a & \quad \text{R = i-Pr} \\
\text{b} & \quad \text{R = Et} \\
\end{align*}
\]

\[
\begin{align*}
\text{Ph}_2\text{C}=\text{S} & \rightarrow \text{12a} \\
\text{12b} & \rightarrow \text{15a} \\
\text{a} & \quad \text{R = i-Pr} \\
\text{b} & \quad \text{R = Et} \\
\end{align*}
\]

Scheme 4

\[
\begin{align*}
\text{ROP-SMe} + 10a & \rightarrow \text{16} \\
11a & \quad \text{R = i-Pr} \\
\text{b} & \quad \text{R = Et} \\
\end{align*}
\]

\[
\begin{align*}
\text{PhSO}_2\text{S} & \rightarrow \text{17} \\
\text{17} & \rightarrow \text{18} \\
\end{align*}
\]
Scheme 5
Figure