

DDQ-mediated synthesis of functionalized unsymmetrical disulfanes  
Supporting Information

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Contents :

General Information	S1
Improved synthesis of 5,5-dimethyl-2-sulfanyl-2-thioxo-1,3,2-dioxaphosphorinane and bis-(5,5-dimethyl-2-thioxo-1,3,2-dioxaphosphorinan-2-yl) disulfane <b>2a</b>	S2
General procedure for the preparation of disulfanyl derivatives <b>1</b> and representative analytical data	S3
References	S10

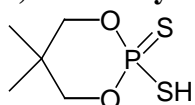
### General Information

All thiols (**3a-n**) required for preparation **1** were purchased from ProChimia ([www.prochimia.com](http://www.prochimia.com)). DDQ is available from Aldrich. 5,5-Dimethyl-2-thioxo-1,3,2-dioxaphosphorinan-2-yl)disulfanyl derivatives **1a**,<sup>1</sup> **1b-c**,<sup>2</sup> **1d-e**,<sup>3</sup> **1g-i**,<sup>4</sup> **1m**<sup>3</sup> were described previously and the analytical data of the obtained compounds were identical with authentic samples. Dichloromethane and acetonitrile were used without drying or further purification. Column chromatography was performed using silica gel 60 (230–400 mesh, Merck). TLC was performed with silica gel Polygram SIL G/UV254 (Macherey-Nagel). Melting points were measured with a Gallenkamp 7936B apparatus and are uncorrected. NMR spectra were recorded on Varian Gemini 500 MHz or 200 MHz spectrometers. The residual solvent peak was used as the internal reference (CDCl<sub>3</sub> :  $\delta = 7.26$  ppm for <sup>1</sup>H,  $\delta = 77.0$  ppm for <sup>13</sup>C). An external standard (85% H<sub>3</sub>PO<sub>4</sub> :  $\delta = 0$  ppm) was used as the reference for recording the <sup>31</sup>P NMR spectra. ESI-MS spectra were recorded on a Mariner PerSeptive Biosystem.

## Improved synthesis of 5,5-dimethyl-2-sulfanyl-2-thioxo-1,3,2-dioxaphosphorinane and bis-(5,5-dimethyl-2-thioxo-1,3,2-dioxaphosphorinanyl) disulfane **2a**

The purification of 5,5-dimethyl-2-sulfanyl-2-thioxo-1,3,2-dioxaphosphorinane has been accomplished previously by vacuum distillation.<sup>5</sup> The vacuum must be kept below 1.5 mmHg upon heating, otherwise content of the flask can decompose and sometimes explode. We have found that crude phosphorodithioic acid can be also purified by crystallization from carbon tetrachloride with 60% yield. Moreover, filtrate after crystallization can be used for preparation of ammonium salt required for preparation of phosphorodithioic acid disulfane **2a** (bis-(5,5-dimethyl-2-thioxo-1,3,2-dioxaphosphorinanyl) disulfane). The modified procedures for preparation of phosphorodithioic acid and its disulfane make developed method more common and versatile.

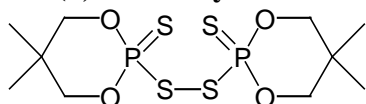
### 5,5-Dimethyl-2-sulfanyl-2-thioxo-1,3,2-dioxaphosphorinane<sup>5</sup>



To a suspension of  $P_4S_{10}$  44.8 g (0.1 mol) in dry toluene (260 mL), a 2,2-dimethylpropane-1,3-diol 41.6 g (0.4 mol) was added. The reaction mixture was stirred at 60-80 °C for 15 h under nitrogen, then traces amount of unreacted  $P_4S_{10}$  were filtered off. Solvent was evaporated under reduced pressure and residue was kept under vacuum at room temperature for 30 minutes. The obtained sticky solid was dissolved in hot  $CCl_4$  (25 mL for each 10 g of crude product) and placed in the freezer (-15 °C) for 6 h. Product was filtered off and dried under vacuum at room temperature to yield 47.6 g (0.24 mol, 60%), the residue from filtrate after evaporation of  $CCl_4$  under reduced pressure can be used for preparation of phosphorodithioic acid ammonium salt.

mp 81-82 °C (Lit.<sup>5c</sup> 81-82 °C),  $^{31}P$  NMR ( $CDCl_3$ ) = 77.68

### Bis-(5,5-dimethyl-2-thioxo-1,3,2-dioxaphosphorinan-2-yl) disulfane **2a**<sup>5</sup>



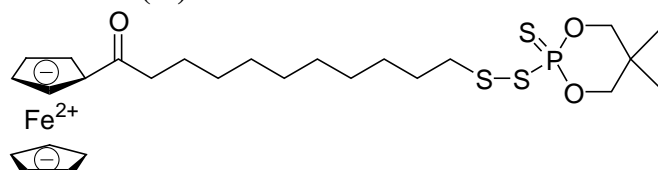
A dry ammonia gas was passed through the solution of 5,5-dimethyl-2-sulfanyl-2-thioxo-1,3,2-dioxaphosphorinane 47.6 g (0.24 mol) (or residue from filtrate after evaporation of  $CCl_4$ , 32 g (0.16 mol)) in mixture of toluene (350 mL) and diethyl ether (50 mL) (ether is required to produce precipitate that is easier to filtered off) cooled in an ice bath for 30 minutes. White precipitate was filtered off and washed with toluene (50 mL) and ether (50 mL). After filtration ammonium salt was dried under vacuum to yield 49.5 g (0.23 mol, 96%) (or 28 g 0.13 mol, 81% from residue after evaporation filtrate) of white powder ( $^{31}P$  NMR ( $D_2O$ ) = 110.22).

A solution of the ammonium salt of phosphorodithioic acid 43 g (0.2 mol) in water (300 mL) was stirred at r.t. and a solution of  $I_2$  25.4 g (0.1 mol) and KI 50 g (0.31 mol) in water (200 mL) was added dropwise. The brown solid was filtered off, washed with water (400 mL) and dissolved in ethyl acetate (500 mL). Solution was washed with 10%  $Na_2S_2O_3$  aqueous solution (50 mL), dried over anhydrous  $Na_2SO_4$  and evaporated under reduced pressure. The residue was recrystallized from ethanol to yield bis-(5,5-dimethyl-2-thioxo-1,3,2-dioxaphosphorinanyl) disulfane **2a** (33.5 g 0.085 mol, 85 %), mp 133-134 °C (Lit.<sup>5c</sup> 133.5-134 °C),  $^{31}P$  NMR ( $CDCl_3$ ) = 80.87

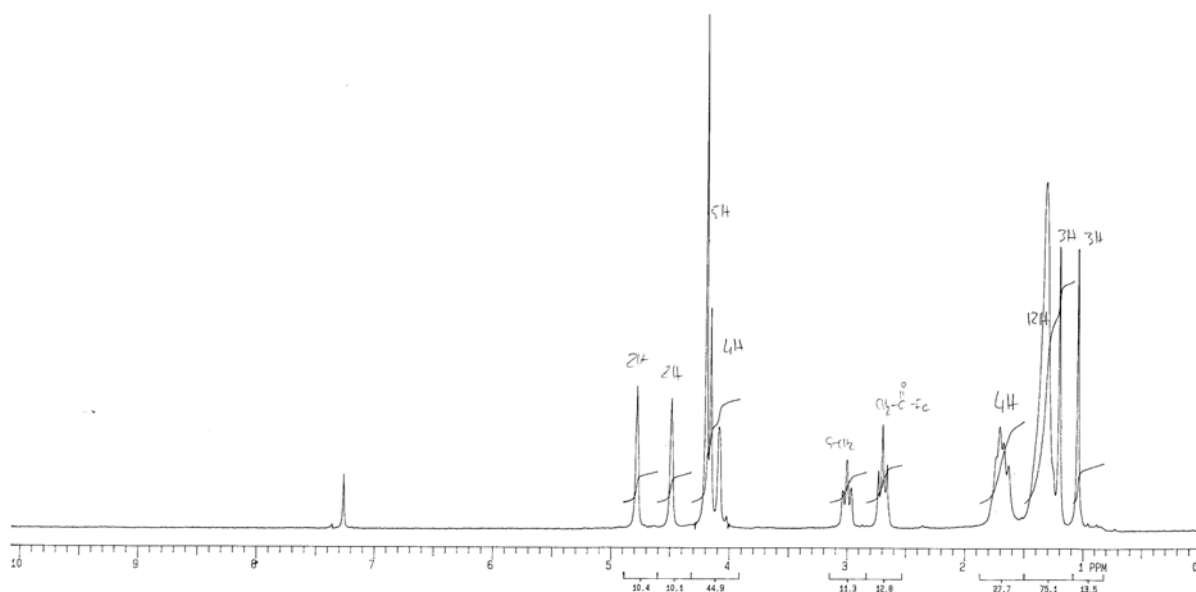
## General procedure for the preparation of disulfanyl derivatives **1** and representative analytical data

A thiol **3** (1.0 mmol) and bis-(5,5-dimethyl-2-thioxo-1,3,2-dioxaphosphorinan-2-yl) disulfane **2a** 394 mg (1.0 mmol) were dissolved in solvent (2.0 mL, dichloromethane or acetonitrile) and cooled to 0 °C in the ice bath. Then a solution of DDQ 114 mg (0.5 mmol) in solvent (2.0 mL, dichloromethane or acetonitrile) was added slowly to the reaction mixture and stirred for 5 min at 0 °C. The reaction was monitored by TLC analysis. Solvent was removed under reduced pressure and the residue was directly purified by column chromatography (SiO<sub>2</sub>).

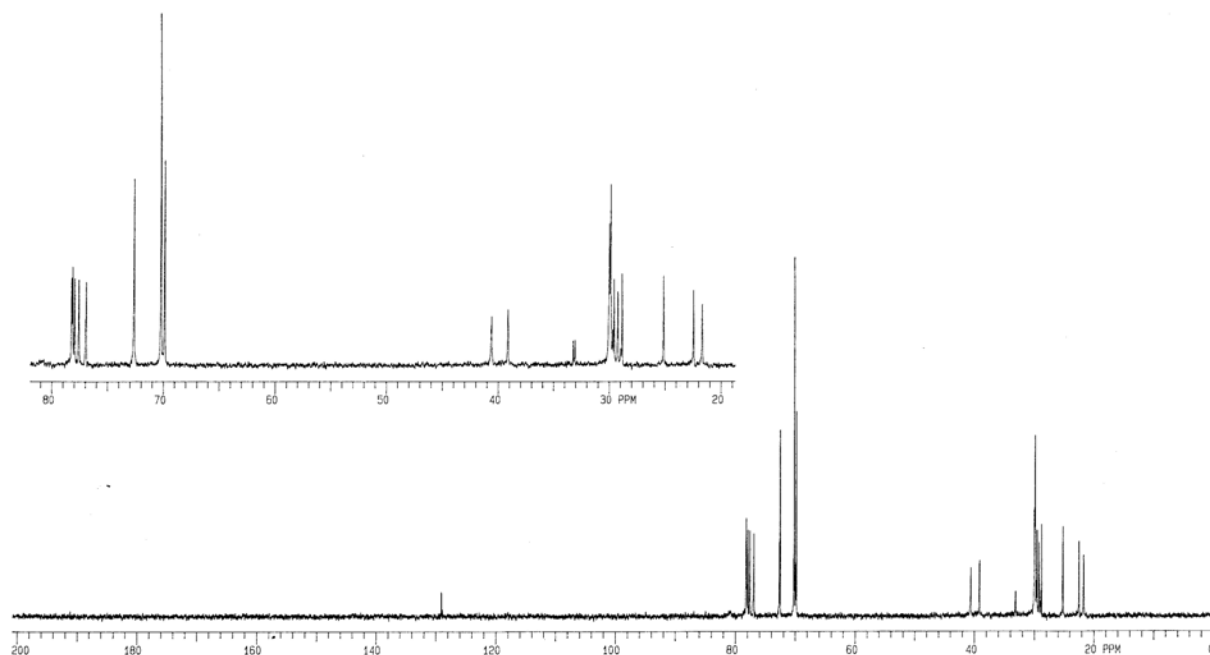
### 11-[(5,5-Dimethyl-2-thioxo-1,3,2-dioxaphosphorinan-2-yl)disulfanyl]undecanoyl-ferrocene (**1f**)



chromatography: CH<sub>2</sub>Cl<sub>2</sub> : EtOAc, 25:1, R<sub>f</sub> = 0.2, red dens oil;  
yield: 478 mg, 0.82 mmol, (82%, reaction in CH<sub>2</sub>Cl<sub>2</sub>);  
yield: 495 mg, 0.85 mmol (85%, reaction in CH<sub>3</sub>CN);

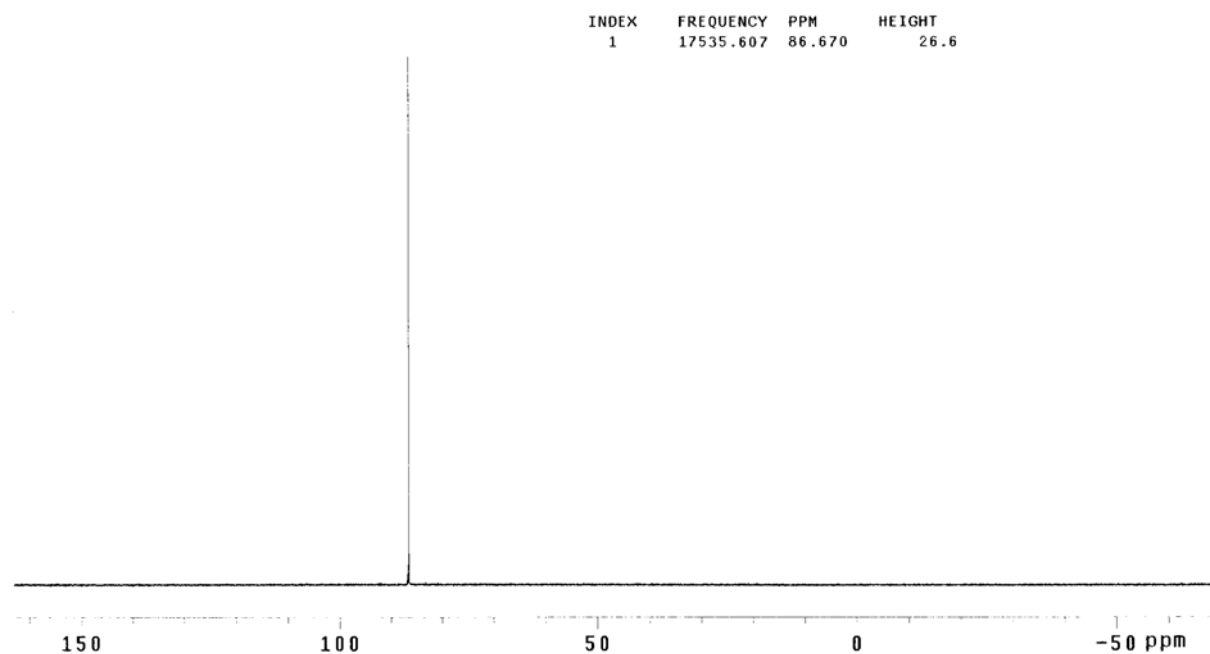


<sup>1</sup>H NMR (200 MHz, CDCl<sub>3</sub>): δ = 1.05 (s, CH<sub>3</sub>, 3 H), 1.20 (s, CH<sub>3</sub>, 3 H), 1.21–1.50 (m, CH<sub>2</sub>, 12 H), 1.55–1.85 (m, CH<sub>2</sub>, 4 H), 2.69 (t, *J* = 7.3 Hz, CH<sub>2</sub>CO, 2 H), 3.00 (t, *J* = 6.9 Hz, PSSCH<sub>2</sub>, 2 H), 4.05–4.15 (m, POCH<sub>2</sub>, 4 H), 4.19 (s, Fc, 5 H), 4.48 (brs, Fc, 2 H), 4.78 (brs, Fc, 2 H).



$^{13}\text{C}$  NMR (50 MHz,  $\text{CDCl}_3$ ):  $\delta$ = 129.2, 77.5 (d,  $^2J_{\text{P-C}}$ = 8.9 Hz), 72.0, 69.6, 69.3, 40.0, 38.5, 32.5 (d,  $^3J_{\text{P-C}}$ = 7.2 Hz), 29.4, 29.3, 29.2, 29.0, 28.6, 28.2, 24.5, 21.9, 21.1.

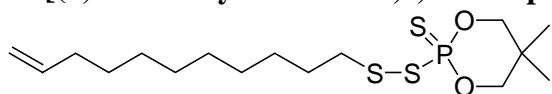
Expected 19, observed 17 signals.



$^{31}\text{P}$  NMR (202 MHz,  $\text{CDCl}_3$ ):  $\delta$ = 86.67.

HRMS (ESI):  $m/z$   $[\text{M} + \text{H}]^+$  calcd for  $\text{C}_{26}\text{H}_{40}\text{FeO}_3\text{PS}_3$ : 583.1227; found: 583.1231.

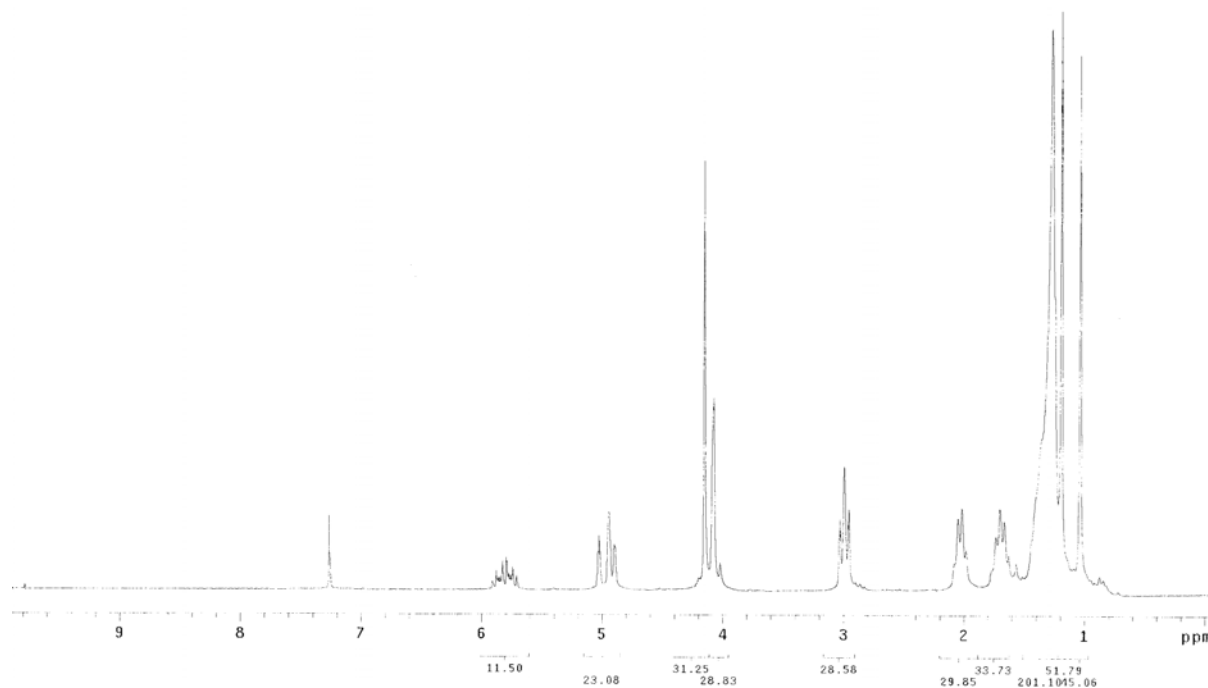
11-[(5,5-Dimethyl-2-thioxo-1,3,2-dioxaphosphorinan-2-yl)disulfanyl]undec-1-ene (1j)



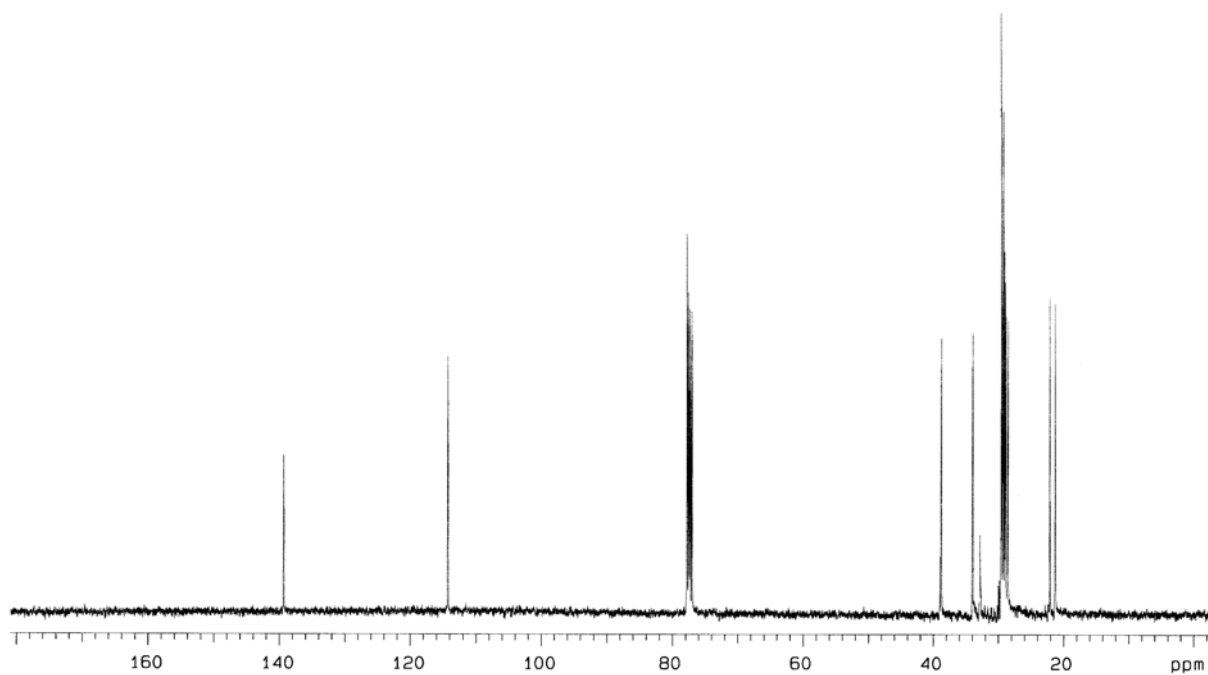
chromatography: CH<sub>2</sub>Cl<sub>2</sub> : EtOAc, 25:1, R<sub>f</sub> = 0.2, colorless oil;

yield: 333 mg, 0.87 mmol, (87%, reaction in CH<sub>2</sub>Cl<sub>2</sub>);

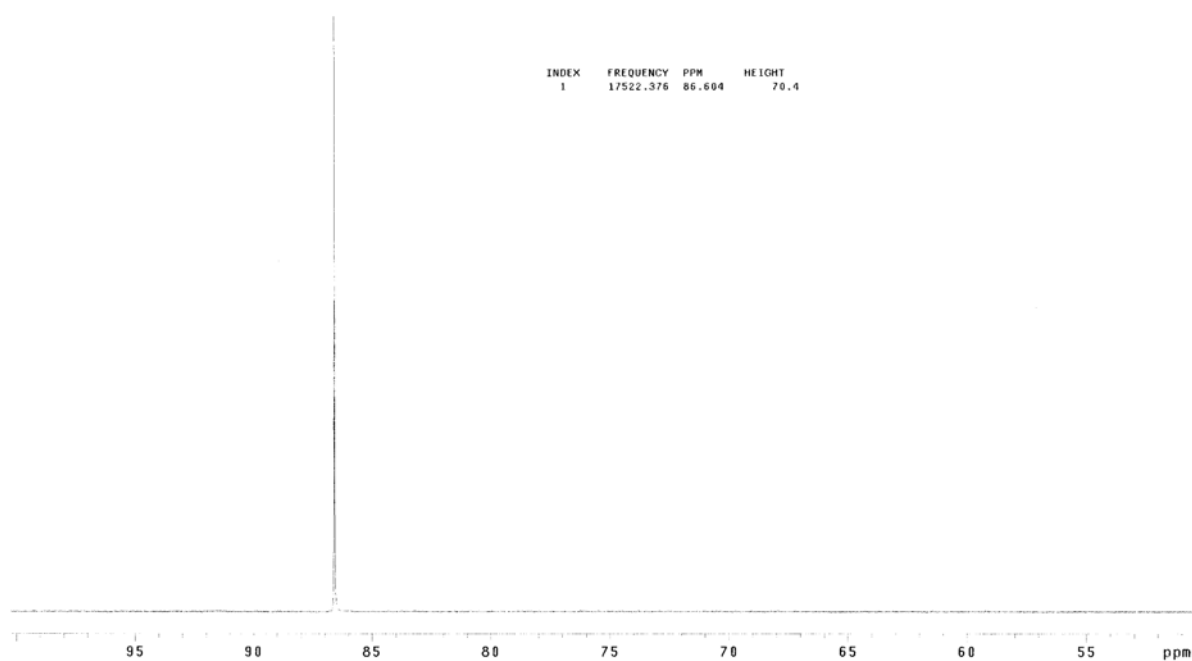
yield: 352 mg, 0.92 mmol (92%, reaction in CH<sub>3</sub>CN);



<sup>1</sup>H NMR (200 MHz, CDCl<sub>3</sub>): δ = 1.05 (s, CH<sub>3</sub>, 3 H), 1.20 (s, CH<sub>3</sub>, 3 H), 1.21–1.50 (m, CH<sub>2</sub>, 12 H), 1.55–1.80 (m, CH<sub>2</sub>, 2 H), 1.90–2.10 (m, CH<sub>2</sub>, 2 H), 3.00 (dt, *J* = 7.3, *J* = 1.7 Hz, PSSCH<sub>2</sub>, 2 H), 4.00–4.20 (m, POCH<sub>2</sub>, 4 H), 4.85–5.05 (m, C=CH<sub>2</sub>, 2 H), 5.70–5.95 (m, C=CH, 1 H).



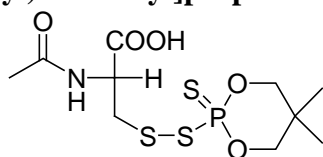
<sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>): δ = 139.1, 114.1, 77.5 (d, <sup>2</sup>J<sub>P-C</sub> = 8.8 Hz), 38.5, 33.7, 32.6 (d, <sup>3</sup>J<sub>P-C</sub> = 7.0 Hz), 29.3, 29.0, 28.8, 28.7, 28.3, 21.9, 21.1.  
Expected 15, observed 13 signals.



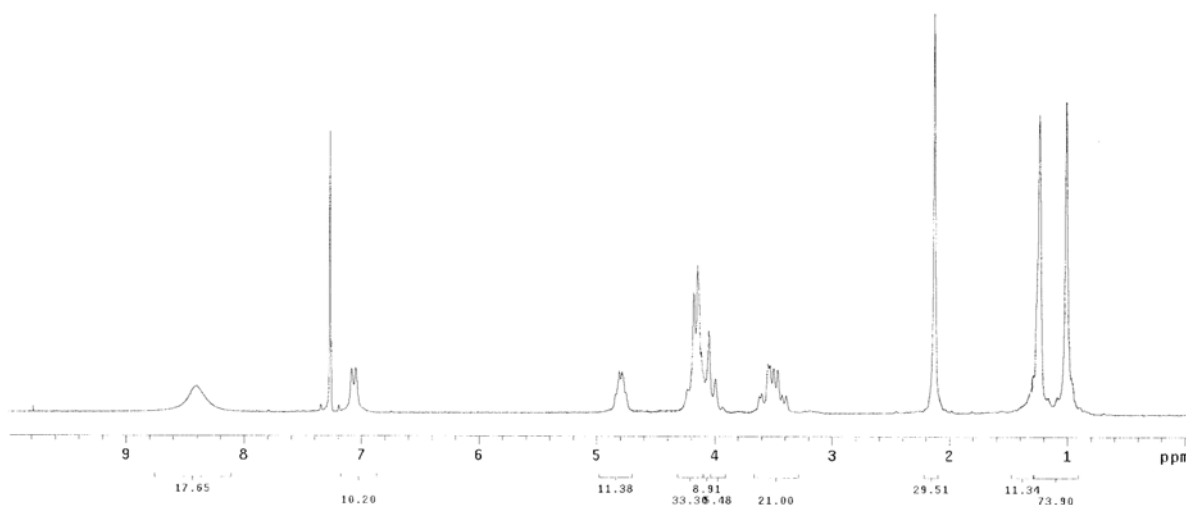
<sup>31</sup>P NMR (202 MHz, CDCl<sub>3</sub>): δ = 86.60.

HRMS (ESI): m/z [M + H]<sup>+</sup> calcd for C<sub>16</sub>H<sub>32</sub>O<sub>2</sub>PS<sub>3</sub>: 383.1302; found: 383.1321.

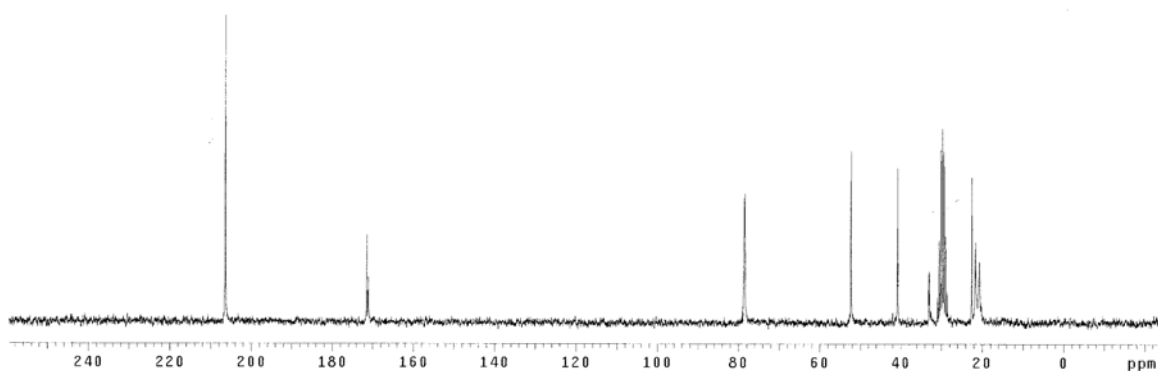
**(R)-2-(N-Acetylamino)-3-[(5,5-dimethyl-2-thioxo-1,3,2-dioxaphosphorinan-2-yl)disulfanyl]propanoic acid (1k)**



chromatography: CH<sub>2</sub>Cl<sub>2</sub> : EtOAc, 25:1, R<sub>f</sub> = 0.2, white solid mp 78-79 °C;  
yield: 320 mg, 0.89 mmol (89%, reaction in CH<sub>3</sub>CN);

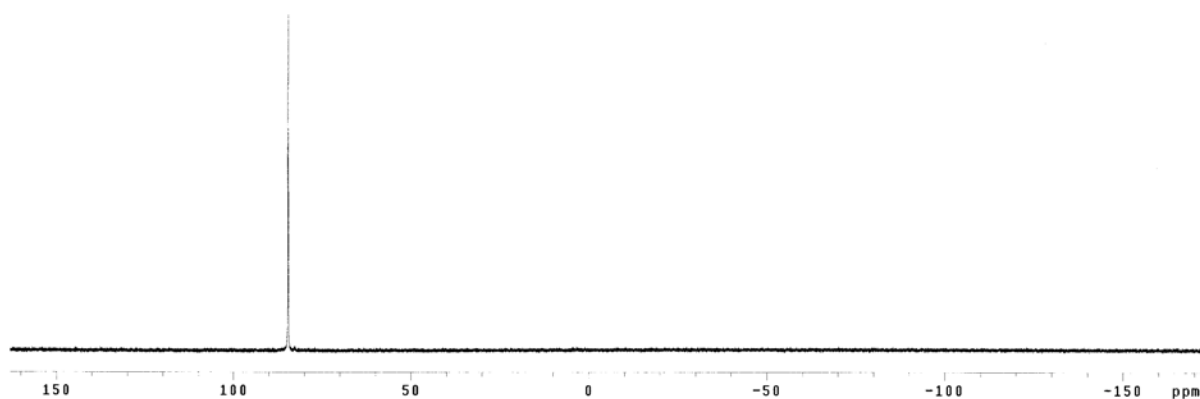


<sup>1</sup>H NMR (200 MHz, CDCl<sub>3</sub>): δ = 1.05 (s, CH<sub>3</sub>, 3 H), 1.25 (s, CH<sub>3</sub>, 3 H), 2.10 (s, Ac, 3 H), 3.37–3.65 (m, SCH<sub>2</sub>, 2 H), 3.95–4.30 (m, POCH<sub>2</sub>, 4 H), 4.70–4.90 (m, NCH, 1 H), 7.07 (d, *J* = 7.0 Hz, NH, 1 H), 8.40 (brs, COOH, 1 H).



<sup>13</sup>C NMR (50 MHz, acetone-d<sub>6</sub>): δ = 171.5, 171.1, 78.5 (d, <sup>2</sup>*J*<sub>P-C</sub> = 8.7 Hz), 52.4, 40.8, 33.1 (d, <sup>3</sup>*J*<sub>P-C</sub> = 7.0 Hz), 22.6, 21.7, 20.7.  
Expected 9, observed 9 signals.

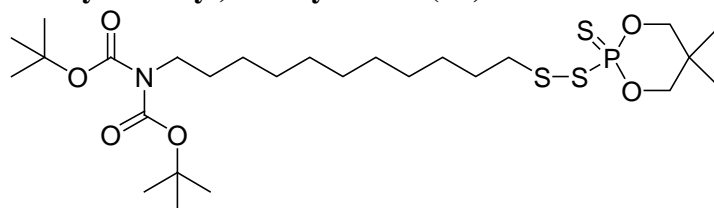
INDEX	FREQUENCY	PPM	HEIGHT
1	17117.573	84.603	12.9



$^{31}\text{P}$  NMR (202 MHz, acetone- $d_6$ ):  $\delta = 84.60$ .

HRMS (ESI):  $m/z$   $[\text{M} + \text{H}]^+$  calcd for  $\text{C}_{10}\text{H}_{19}\text{NO}_5\text{PS}_3$ : 360.0163; found: 360.0171.

**11-[(5,5-Dimethyl-2-thioxo-1,3,2-dioxaphosphorinan-2-yl)disulfanyl]-*N,N*-di-(*tert*-butoxycarbonyl)undecylamine (1n)**

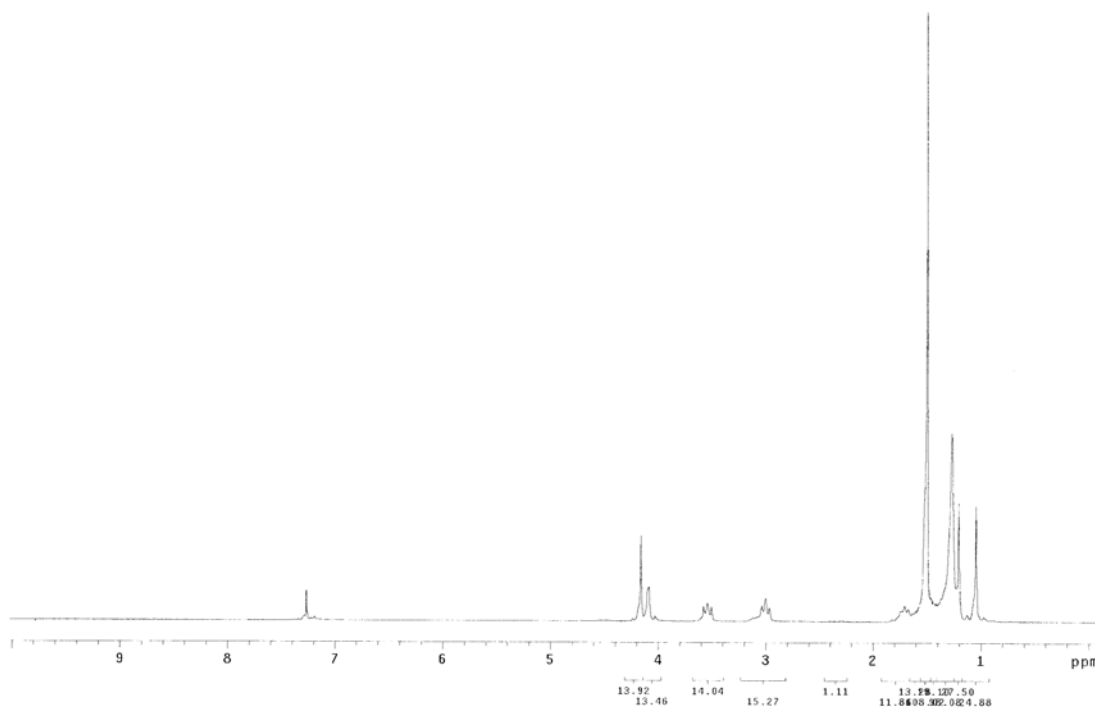


chromatography:  $\text{CH}_2\text{Cl}_2$  then  $\text{CH}_2\text{Cl}_2$  : EtOAc, 25:1,  $R_f = 0.2$ , colorless oil;

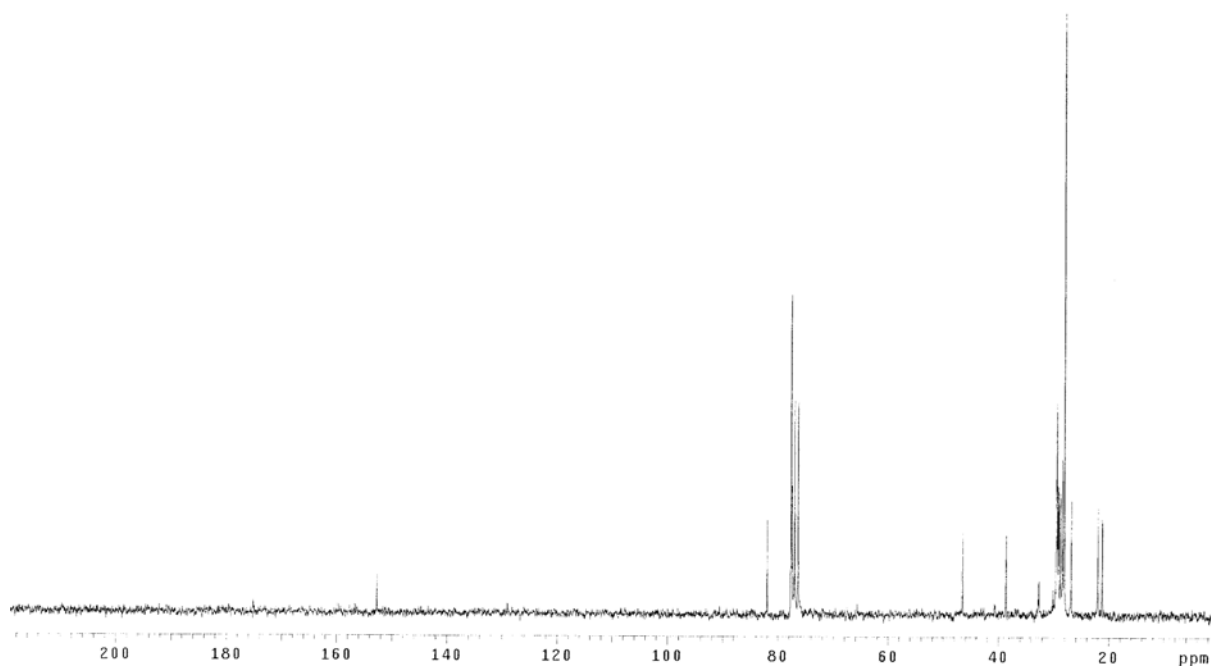
yield: 564 mg, 0.94 mmol, (94%, reaction in  $\text{CH}_2\text{Cl}_2$ );

yield: 576 mg, 0.96 mmol (96%, reaction in  $\text{CH}_3\text{CN}$ );

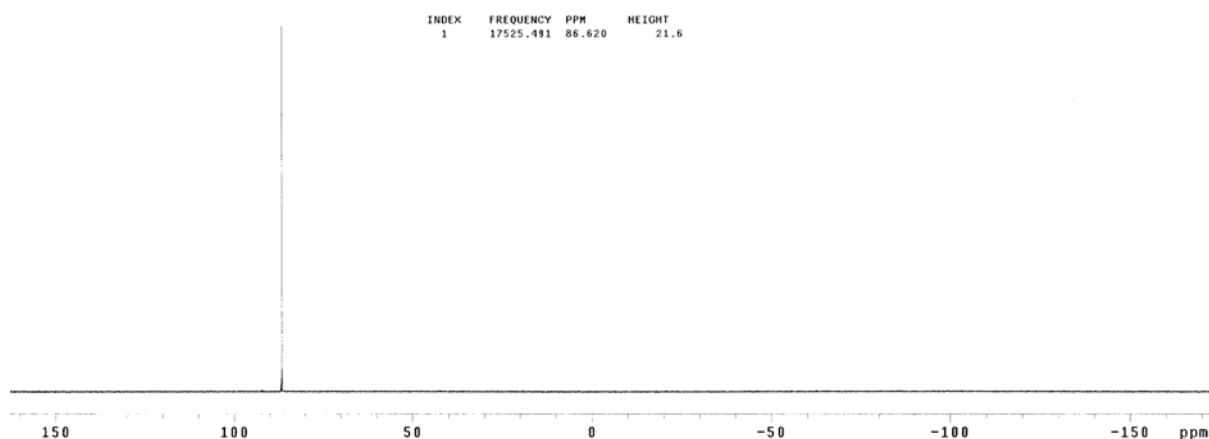




<sup>1</sup>H NMR (200 MHz, CDCl<sub>3</sub>): δ= 1.05 (s, CH<sub>3</sub>, 3 H), 1.21 (s, CH<sub>3</sub>, 3 H), 1.20–1.45 (m, CH<sub>2</sub>, 16 H), 1.51 (s, Boc, 18 H), 1.62–1.80 (m, CH<sub>2</sub>, 2 H), 3.00 (dt, *J*= 7.3, *J*= 1.7 Hz, PSSCH<sub>2</sub>, 2 H), 3.54 (t, *J*= 7.4, NCH<sub>2</sub>, 2 H), 4.05–4.20 (m, POCH<sub>2</sub>, 4 H).



<sup>13</sup>C NMR (50 MHz, CDCl<sub>3</sub>): δ= 152.7, 81.9, 77.5 (d, <sup>2</sup>*J*<sub>P-C</sub>= 9.1 Hz), 46.5, 38.6, 32.6 (d, <sup>3</sup>*J*<sub>P-C</sub>= 7.4 Hz), 30.0, 29.5, 29.4, 29.3, 29.1, 29.0, 28.7, 28.4, 28.1, 26.8, 22.0, 21.2.  
Signals: expected and observed, 18.



$^{31}\text{P}$  NMR (202 MHz,  $\text{CDCl}_3$ ):  $\delta = 86.62$ .

HRMS (ESI):  $m/z$   $[\text{M} + \text{H}]^+$  calcd for  $\text{C}_{26}\text{H}_{51}\text{NO}_6\text{PS}_3$ : 600.2616; found: 600.2621.

5,5-Dimethyl-2-thioxo-1,3,2-dioxaphosphorinan-2-yl)disulfanyl derivatives **1a**,<sup>1</sup> **1b-c**,<sup>2</sup> **1d-e**,<sup>3</sup> **1g-i**,<sup>4</sup> **1m**<sup>3</sup> were described previously and the analytical data of the obtained compounds were identical with authentic samples.

## References

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- [2] Kertmen, A.; Lach, S.; Rachon, J. Witt, D. *Synthesis* **2009**, 1459.
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- [4] Demkowicz, S.; Rachon, J.; Witt, D. *Synthesis* **2008**, 2033.
- [5] (a) Doszczak, L.; Rachon, J.; *J. Chem. Soc. Perkin Trans. 1*, **2002**, 1271. (b) Chauhan, H. P. S.; Bhasin, C. P.; Srivastava, G.; Mehrotra, R. C.; *Phosphorus Sulfur*, **1983**, *15*; 99. (c) Edmundson, R. S. *Tetrahedron*, **1965**, *21*, 2379.