

# A Convenient synthesis of 1-(diethoxyphosphoryl)cyclopropanecarboxylates

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DOI: <http://dx.doi.org/10.3998/ark.5550190.0011.913>

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## Abstract

An efficient synthesis of a series of 1-(diethoxyphosphoryl)cyclopropanecarboxylates was accomplished by the reaction of terminal 1,2-diols cyclic sulfates with triethylphosphonoacetate. The stereochemistry of 2-benzyloxymethyl-1-(diethoxyphosphoryl)cyclopropanecarboxylic acid was determined by the single crystal X-ray structure analysis.

**Keywords:** Cyclopropanation, cyclopropanecarboxylates, 2,2-dioxo-1,3,2-dioxathiolanes, 1-(diethoxyphosphoryl)cyclopropanecarboxylates, X-ray analysis

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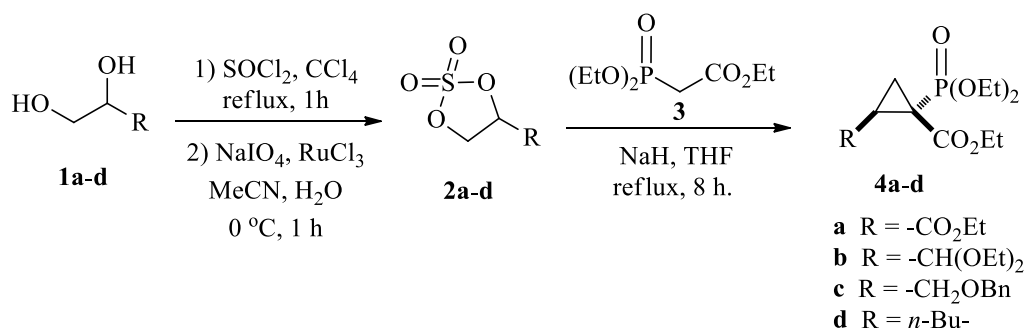
## Introduction

During the last several years cyclopropanation of dialkyl malonates with 4-alkyl-2,2-dioxo-1,3,2-dioxathiolanes has emerged as a versatile method for construction of cyclopropane carboxylic acid derivatives - the attractive synthons of aminocyclopropanecarboxylic acids and various carbo- and heterocyclic compounds.<sup>1-8</sup> It is well documented that succeeding steps of this reaction consist in fully regioselective dioxathiolane ring opening with the malonate anion and intramolecular S<sub>N</sub>2 type substitution of a sulfate residue in the resulting intermediate. Surprisingly, similar cyclopropanation of acetates activated by other electron withdrawing groups remains almost unexplored. To the best of our knowledge the literature contains only one example of such a reaction. It has been demonstrated that the base promoted cyclopropanation of *t*-butyl dimethoxyphosphorylacetate with (*S*)-4-methyl-2,2-dioxo-1,3,2-dioxathiolane proceeds highly regio- and stereoselective, affording *t*-butyl *trans*-(1*R*,2*R*)-1-dimethoxyphosphoryl-2-methylcyclopropanecarboxylate with *ee*>99% and *de* 94%.<sup>9</sup>

## Results and Discussion

In the search of an effective approach to C-2 functionalized *trans*-1-aminocyclopropanephosphonic acids as potential biologically active compounds, we envisaged that the corresponding *trans*-2-alkyl-1-(dialkoxyphosphoryl)cyclopropanecarboxylates **4** might be their useful precursors.

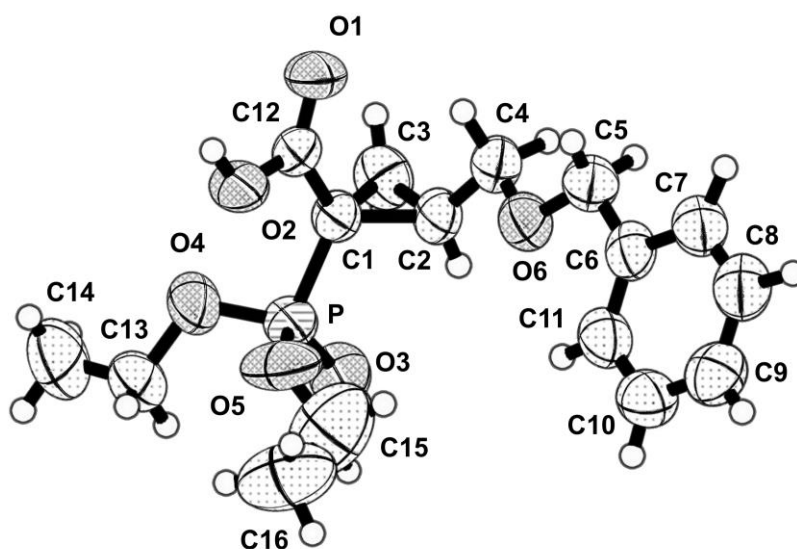
In this paper, we demonstrate that the cyclopropanation reaction of alkyl dialkoxyphosphorylacetates with 2,2-dioxo-1,3,2-dioxathiolanes **2** has general applicability and that it can serve successfully as a source of different carboxylates **4**. We selected commercial triethylphosphonoacetate **3** as a model substrate and structurally various 2,2-dioxo-1,3,2-dioxathiolanes **2a-d** as representative cyclopropanating reagents. The thiolanes **2a-d** were readily synthesized from the appropriate terminal 1,2-diols **1a-d** following the routine one pot Sharpless procedure.<sup>1</sup> The acylation of diols **1a-d** with thionyl chloride followed by oxidation, with sodium periodinate in the presence of catalytic ruthenium chloride, afforded **2a-d** in high yields (Scheme 1). The crude thiolanes **2a-d** did not required purification to be used in subsequent reaction step.



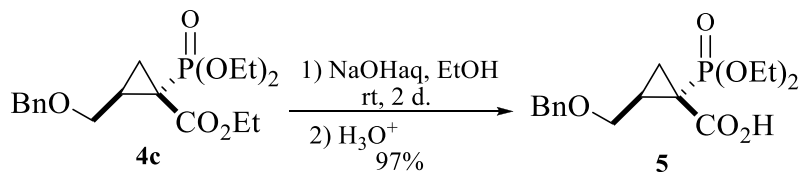
### Scheme 1

Treatment of the thiolanes **2a-d** with triethylphosphonoacetate **3** in the presence of two equivalents of NaH in THF at reflux for 8h provided the corresponding cyclopropanes **4a-d** as single diastereoisomers in all cases (Scheme 1). Spectroscopic studies were not sufficient in determining the stereochemistry of the cyclopropanecarboxylates **4a-d**. The single crystal X-ray structure analysis of the 2-benzyloxymethyl-1-(diethoxyphosphoryl)-cyclopropanecarboxylic acid **5**, which was prepared by base promoted hydrolysis of the cyclopropanecarboxylate **4c**, (Scheme 2) showed that the phosphoryl and benzyloxymethyl groups are in mutual *trans* relationship (Figure 1). The cyclopropane endocyclic C-C bonds show a characteristic bond-length asymmetry which follows from the interactions of ring orbitals with  $\pi$  system of a substituent.<sup>14,15</sup> The shortest bond (C2-C3) is located opposite the diethoxyphosphoryl and carboxylate substituents while the longest (C1-C2) is placed in front of the unsubstituted endocyclic C3 atom. The C1-C3 is a distal bond for the benzyloxymethyl substituent. In the crystal, molecules are linked by strong hydrogen bonds involving the phosphoryl O2 and

carboxylate O3 atoms [O2-H2 0.85(6), O2 $\cdots$ O3\* 2.634(4), H2 $\cdots$ O3\* 1.80(6) (Å), O2-H2 $\cdots$ O3\* 170(3) (°); atom indicated with an asterisk is related by the (x, y-1, z) symmetry operator] resulting in a ladder type arrangement extending along the [010] crystallographic axis. The crystal packing is additionally stabilized by the C-H $\cdots$  $\pi$  interactions<sup>16</sup> between the phenyl rings and hydrogen atoms of the methylene groups. Therefore, taking into account the method of preparation and structural similarity, we by analogy assigned the *trans* configuration to the obtained products **4a-d**. In this context, it is also worth nothing that the values of coupling constant  $^3J_{\text{PH}} = 16.0$  Hz and  $^3J_{\text{PH}} = 16.5$  Hz observed in  $^1\text{H}$  NMR spectra of **4a** and **5** respectively, were consistent with the synperiplanar arrangement of the phosphorus and H-2 atoms.



**Figure 1.** The molecular structure and numbering scheme of the cyclopropane carboxylic acid **5**. Displacement ellipsoids are drawn at the 50% probability level. Hydrogen atoms are represented by circles of an arbitrary radius. Selected bond lengths [Å]: P-O3 1.466(2); P-C1 1.787(3); O1-C12 1.197(3); O2-C12 1.312(4); O6-C4 1.417(4); C1-C3 1.521(4); C1-C2 1.554(3); C2-C3 1.472(5); C1-C12 1.492(4); C2-C4 1.493(4). Selected valency angles [°]: P-C1-C2 112.6(2); P-C1-C3 116.1(2); P-C1-C12 121.5(2); C1-C2-C3 60.3(2); C1-C3-C2 62.5(2); C2-C1-C3 57.2(2); C1-C2-C4 122.9(2); C3-C2-C4 123.9(3); C2-C1-C12 117.7(2) C3-C1-C12 115.2(2);. Selected torsion angles [°]: P-C1-C2-C3 107.4(2); P-C1-C2-C4 -139.3(3); P-C1-C12-O2 13.9(3); O1-C12-C1-C3 -17.7(4); O3-P-C1-C2 -32.7(2) ; O3-P-C1-C3 30.6(3); O3-P-C2-C12 179.6(2); O6-C4-C3-C1 170.3(3); C4-C3-C2-C12 9.8(4).



Scheme 2

## Conclusions

In summary, our studies have clearly demonstrated general applicability of synthetic strategy based on cyclopropanation of triethylphosphonoacetate **3** with cyclic sulfates **2** of terminal 1,2-diols for diastereoselective synthesis of substituted 1-(diethoxyphosphoryl) cyclopropanecarboxylates.

## Experimental Section

**General.** Reagents were purchased from commercial sources and used as received without purification. Solvents were dried by standard procedures. Diols **1a**,<sup>10</sup> **1b**<sup>11</sup> and **1c**<sup>12</sup> were obtained according to the literature procedures. NMR spectra were recorded on a Bruker DPX 250 instrument at 250.13 MHz for <sup>1</sup>H and 62.9 MHz for <sup>13</sup>C and 101.3 MHz for <sup>31</sup>P NMR, respectively, using tetramethylsilane as internal and 85% H<sub>3</sub>PO<sub>4</sub> as external standard. The multiplicities of carbons were determined by DEPT experiments. IR spectra were measured on Specord M80 (Zeiss) instrument. Elemental analyses were performed on Perkin-Elmer PE 2400 analyzer. Melting points were determined in open capillaries and were uncorrected.

### X-ray crystal structure analysis

A colourless single crystal of **5** (0.1 × 0.2 × 0.6 mm) was obtained by a slow evaporation from the chloroform-acetone mixture. X-ray data were collected on the Bruker Smart APEX diffractometer at room temperature with a graphite monochromatized MoK $\alpha$  radiation. Crystal structure was solved with direct methods and further refined using full matrix least squares technique. Crystal data and structure analysis parameters are summarized in Table 1. The following computer programs were applied during the analysis: data collection SMART,<sup>17</sup> data reduction SAINT-PLUS,<sup>18</sup> absorption correction SADABS,<sup>19</sup> structure solution, refinement, and molecular graphics SHELXTL.<sup>20</sup>

Crystallographic data (excluding structure factors) for the structure reported in this article have been deposited with the Cambridge Crystallographic Data Center as supplementary publication no. CCDC 764399. Copies of the data can be obtained free of charge on application

to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK. Any request should be accompanied by a full literature citation.

**Table 1.** Crystal data and structural refinement details for **5**

Parameters	<b>5</b>
Empirical formula	C <sub>16</sub> H <sub>23</sub> O <sub>6</sub> P
Formula weight	356.32
Temperature	293 (2) K
Wavelength	0.71073 Å
Crystal system, space group	monoclinic, <i>P</i> 2 <sub>1</sub>
Unit cell dimensions	<i>a</i> = 10.7927(9), <i>b</i> = 7.0051(5), <i>c</i> = 12.4943(10) Å, $\beta$ = 113.107(3) °
<i>Z</i>	2
Unit cell volume	<i>V</i> = 868.83(12) Å <sup>3</sup>
Density (calculated)	1.362 g cm <sup>-3</sup>
Absorption coefficient	0.19 mm <sup>-1</sup>
F(000)	378.0
Crystal size	0.1 × 0.2 × 0.6 mm
Max. theta for the data collection	25.0°
Index ranges	-12 ≤ <i>h</i> ≤ 12, -8 ≤ <i>k</i> ≤ 8, -14 ≤ <i>l</i> ≤ 14
Number of collected reflections	20942
Number of independent reflections	3069 ( <i>R</i> <sub>int</sub> = 0.023)
Absorption correction	multi-scan (Sadabs)
Refinement method	Full-matrix least-squares on <i>F</i> <sup>2</sup>
Data/restraints/parameters	3069/0/258
Goodness of fit on <i>F</i> <sup>2</sup>	1.071
Final <i>R</i> indices [ <i>I</i> > 2 σ ( <i>I</i> )]	<i>R</i> <sub>1</sub> = 0.0542, <i>wR</i> <sup>2</sup> = 0.1490
<i>R</i> indices (all data)	<i>R</i> <sub>1</sub> = 0.0547, <i>wR</i> <sup>2</sup> = 0.1504
Max. and min. on a difference Fourier map	0.474 and -0.302 eÅ <sup>-3</sup>

**General procedure for preparation 2,2-Dioxo-1,3,2-dioxathiolanes (2a-d)**

(Dioxathiolanes **2a-d** were obtained by general procedure)<sup>1</sup>

**2,2-Dioxo-1,3,2-dioxathiolane-4-carboxylic acid ethyl ester (2a).** Yield: (90%); yellowish oil.

<sup>1</sup>H NMR (CDCl<sub>3</sub>): δ 1.36 (t, <sup>3</sup>*J* = 7.2 Hz, 3H, CH<sub>3</sub>CH<sub>2</sub>O); 4.37 (q, <sup>3</sup>*J* = 7.2 Hz, 2H, CH<sub>2</sub>O); 4.84 (dd, <sup>2</sup>*J* = 9.0 Hz, <sup>3</sup>*J* = 5.7 Hz, 1H, CHCHH); 4.92 (dd, <sup>2</sup>*J* = 9.0 Hz, <sup>3</sup>*J* = 7.2 Hz, 1H, CHCHH); 5.27 (dd, <sup>3</sup>*J* = 7.2 Hz, <sup>3</sup>*J* = 5.7 Hz, 1H, CHCH<sub>2</sub>). <sup>13</sup>C NMR (CDCl<sub>3</sub>): δ 13.62 (s, CH<sub>3</sub>CH<sub>2</sub>O); 63.21 (s, CH<sub>2</sub>O); 69.77 (s, CHCH<sub>2</sub>); 75.80 (s, CHCH<sub>2</sub>); 164.95 (s, C=O). IR (film) ν(C=O) 1752.

**4-Diethoxymethyl-2,2-dioxo-1,3,2-dioxathiolane (2b).** Yield: (70%); yellow oil. <sup>1</sup>H NMR (CDCl<sub>3</sub>): δ 1.24 (t, <sup>3</sup>*J* = 7.0 Hz, 3H, CH<sub>3</sub>CH<sub>2</sub>O); 1.26 (t, <sup>3</sup>*J* = 7.0 Hz, 3H, CH<sub>3</sub>CH<sub>2</sub>O); 3.58 ÷ 3.82

(m, 5H,  $\text{CH}_2\text{O}$ ,  $\text{CH}_2\text{CHCH}$ ,  $\text{CH}_2\text{CH}$ ); 3.98 ÷ 4.05 (m, 2H,  $\text{CH}_2\text{O}$ ); 4.67 (d,  $^3J = 5.0$  Hz, 1H,  $\text{CH}_2\text{CHCH}$ ).  $^{13}\text{C}$  NMR (MHz,  $\text{CDCl}_3$ ):  $\delta$  14.82 (s,  $\text{CH}_3\text{CH}_2\text{O}$ ); 14.86 (s,  $\text{CH}_3\text{CH}_2\text{O}$ ); 64.22 (s,  $\text{CH}_2\text{O}$ ); 65.18 (s,  $\text{CH}_2\text{O}$ ); 68.17 (s,  $\text{CH}_2\text{CHCH}$ ); 79.57 (s,  $\text{CH}_2\text{CHCH}$ ); 99.92 (s,  $\text{CH}_2\text{CHCH}$ ).

**4-Benzylloxymethyl-2,2-dioxo-1,3,2-dioxathiolane (2c).**<sup>2</sup> Yield: (85%); yellowish oil.  $^1\text{H}$  NMR ( $\text{CDCl}_3$ ):  $\delta$  3.78 (d,  $^3J = 5.2$  Hz, 2H,  $\text{CHCH}_2\text{OBn}$ ); 4.50 ÷ 4.76 (m, 4H,  $\text{CH}_2\text{Ph}$ ,  $\text{CHCH}_2\text{O}$ ); 4.99 ÷ 5.10 (m, 1H,  $\text{CHO}$ ); 7.33 ÷ 7.41 (m, 5H,  $\text{CH}_{\text{Ar}}$ ).

**4-Butyl-2,2-dioxo-1,3,2-dioxathiolane (2d).**<sup>13</sup> Yield: (95%); yellowish oil.  $^1\text{H}$  NMR ( $\text{CDCl}_3$ ):  $\delta$  0.94 (t,  $^3J = 6.5$  Hz, 3H,  $\text{CH}_3\text{CH}_2$ ); 1.35 ÷ 1.54 (m, 4H,  $(\text{CH}_2)_2$ ); 1.70 ÷ 1.81 (m, 1H,  $\text{CH}_2\text{CHHCHO}$ ); 1.89 ÷ 2.02 (m, 1H,  $\text{CH}_2\text{CHHCHO}$ ); 4.34 (dd,  $^2J = 8.5$  Hz,  $^3J = 8.2$  Hz, 1H,  $\text{CHCHHO}$ ); 4.71 (dd,  $^2J = 8.5$  Hz,  $^3J = 6.0$  Hz, 1H,  $\text{CHCHHO}$ ); 4.92 ÷ 5.03 (m, 1H,  $\text{CHO}$ ).

### General procedure for preparation 1-(diethoxyphosphoryl)cyclopropanecarboxylates (4a-d)

To a stirred suspension of NaH (0.15g, 6.0mmol) in THF (25mL) triethylphosphonoacetate **3** (0.60mL, 3.0mmol) was added at room temperature. After stirring for 0.5h a solution of corresponding sulfate **2** (3.0mmol) in THF (10mL) was added and the resulting mixture was stirred at room temperature for 0.5h and then at reflux for 8h. After that time, the reaction mixture was poured into water (5mL), extracted with DCM (3x10mL) and organic layer was dried over  $\text{MgSO}_4$ . Removal of the solvent gave the crude products **4**, which were purified by column chromatography (silica gel, eluent: chloroform/acetone 80:20).

**trans-Diethyl 1-(diethoxyphosphoryl)cyclopropane-1,2-dicarboxylate (4a).** Yield: 0.62 g (64%); colorless oil.  $R_f = 0.30$ .  $^{31}\text{P}$  NMR ( $\text{C}_6\text{D}_6$ ):  $\delta$  17.58.  $^1\text{H}$  NMR ( $\text{C}_6\text{D}_6$ ):  $\delta$  1.26 (t,  $^3J_{\text{HH}} = 7.0$  Hz, 3H,  $\text{CH}_3\text{CH}_2\text{O}$ ); 1.27 (t,  $^3J_{\text{HH}} = 7.0$  Hz, 3H,  $\text{CH}_3\text{CH}_2\text{O}$ ); 1.35 (td,  $^3J_{\text{HH}} = 7.0$  Hz,  $^4J_{\text{PH}} = 0.7$  Hz, 3H,  $\text{CH}_3\text{CH}_2\text{OP}$ ); 1.37 (td,  $^3J_{\text{HH}} = 7.0$  Hz,  $^4J_{\text{PH}} = 0.7$  Hz, 3H,  $\text{CH}_3\text{CH}_2\text{OP}$ ); 1.70 (ddd,  $^3J_{\text{PH}} = 16.2$  Hz,  $^3J_{\text{HH}} = 8.5$  Hz,  $^2J_{\text{HH}} = 4.5$  Hz, 1H,  $\text{PCCHH}$ ); 1.92 (ddd,  $^3J_{\text{PH}} = 13.0$  Hz,  $^3J_{\text{HH}} = 6.2$  Hz,  $^2J_{\text{HH}} = 4.0$  Hz, 1H,  $\text{PCCHH}$ ); 2.45 (ddd,  $^3J_{\text{PH}} = 16.0$  Hz,  $^3J_{\text{HH}} = 8.5$  Hz,  $^3J_{\text{HH}} = 6.2$  Hz, 1H,  $\text{PCCH}$ ); 4.10 ÷ 4.25 (m, 8H,  $2 \times \text{CH}_2\text{OP}$ ,  $2 \times \text{CH}_2\text{O}$ ).  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ ):  $\delta$  13.49 (s,  $\text{CH}_3\text{CH}_2\text{O}$ ); 13.64 (s,  $\text{CH}_3\text{CH}_2\text{O}$ ); 15.78 (d,  $^3J_{\text{PC}} = 6.0$  Hz,  $\text{CH}_3\text{CH}_2\text{OP}$ ); 15.83 (s,  $\text{PCCH}_2$ ); 24.17 (s,  $\text{PCCH}$ ); 28.70 (d,  $^1J_{\text{PC}} = 177.95$  Hz,  $\text{PC}$ ); 60.95 (s,  $\text{CH}_2\text{O}$ ); 61.42 (s,  $\text{CH}_2\text{O}$ ); 62.88 (s,  $\text{CH}_2\text{OP}$ ); 62.90 (d,  $^2J_{\text{PC}} = 5.60$  Hz,  $\text{CH}_2\text{OP}$ ); 165.70 (d,  $^2J_{\text{PC}} = 4.9$  Hz,  $\text{C}=\text{O}$ ); 168.81 (d,  $^3J_{\text{PC}} = 4.0$  Hz,  $\text{C}=\text{O}$ ). IR (film)  $\nu_{(\text{C}=\text{O})}$  1740,  $\nu_{(\text{P}=\text{O})}$  1220,  $\nu_{(\text{P}-\text{O})}$  1024. Anal. Calcd. for  $\text{C}_{13}\text{H}_{23}\text{O}_7\text{P}$ : C 48.45, H 7.19. Found: C 48.36, H 7.21.

**trans-Ethyl 2-(diethoxymethyl)-1-(diethoxyphosphoryl)cyclopropanecarboxylate (4b).** Yield: 0.64 g (60%); colorless oil.  $R_f = 0.32$ .  $^{31}\text{P}$  NMR ( $\text{C}_6\text{D}_6$ ):  $\delta$  23.08.  $^1\text{H}$  NMR ( $\text{C}_6\text{D}_6$ ):  $\delta$  1.22 ÷ 1.33 (m, 6H,  $2 \times \text{CH}_3\text{CH}_2\text{O}$ ); 1.34 (t,  $^3J_{\text{HH}} = 7.0$  Hz, 6H,  $2 \times \text{CH}_3\text{CH}_2\text{OP}$ ); 1.43 (t,  $^3J_{\text{HH}} = 7.0$  Hz, 3H,  $\text{CH}_3\text{CH}_2\text{O}$ ); 1.80 ÷ 1.90 (m, 3H,  $\text{PCCH}_2$ ,  $\text{PCCH}$ ); 3.67 ÷ 3.84 (m, 4H,  $2 \times \text{CH}_2\text{O}$ ); 4.00 ÷ 4.25 (m, 4H,  $2 \times \text{CH}_2\text{OP}$ ); 4.34 (q,  $^3J_{\text{HH}} = 7.0$  Hz, 2H,  $\text{CH}_2\text{O}$ ); 4.68 (d,  $^3J_{\text{HH}} = 7.0$  Hz,  $\text{OCHO}$ ).  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ ):  $\delta$  13.72 (s,  $\text{CH}_3\text{CH}_2\text{O}$ ); 14.77 (s,  $\text{CH}_3\text{CH}_2\text{O}$ ); 14.80 (s,  $\text{CH}_3\text{CH}_2\text{O}$ ); 15.91 (s,  $\text{CH}_3\text{CH}_2\text{OP}$ ); 15.99 (s,  $\text{CH}_3\text{CH}_2\text{OP}$ ); 20.26 (d,  $^2J_{\text{PC}} = 4.9$  Hz,  $\text{PCCH}$ ); 21.71 (d,  $^1J_{\text{PC}} = 178.4$  Hz,  $\text{PC}$ ); 27.38 (s,  $\text{PCCH}_2$ ); 61.35 (s,  $\text{CH}_2\text{O}$ ); 62.22 (2d,  $^2J_{\text{PC}} = 5.8$  Hz,  $\text{CH}_2\text{OP}$ ); 63.56 (s,  $\text{CH}_2\text{O}$ );

64.89 (s, CH<sub>2</sub>O); 79.34 (s, OCHO); 168.73 (d, <sup>2</sup>J<sub>PC</sub> = 4.5 Hz, C=O). IR (film) ν<sub>(C=O)</sub> 1748, ν<sub>(P=O)</sub> 1264, ν<sub>(P-O)</sub> 1024. Anal. Calcd. for C<sub>15</sub>H<sub>29</sub>O<sub>7</sub>P: C 51.13, H 8.30. Found: C 51.26, H 8.34.

***trans*-Ethyl 2-(benzyloxymethyl)-1-(diethoxyphosphoryl)cyclopropanecarboxylate (4c).**

Yield: 0.70 g (63%); colorless oil. R<sub>f</sub> = 0.38. <sup>31</sup>P NMR (C<sub>6</sub>D<sub>6</sub>): δ 23.14. <sup>1</sup>H NMR (C<sub>6</sub>D<sub>6</sub>): δ 1.23 (t, <sup>3</sup>J<sub>HH</sub> = 7.2 Hz, 3H, CH<sub>3</sub>CH<sub>2</sub>O); 1.31 (t, <sup>3</sup>J<sub>HH</sub> = 7.0 Hz, 6H, 2xCH<sub>3</sub>CH<sub>2</sub>OP); 1.54 ÷ 1.68 (m, 2H, PCCH<sub>2</sub>); 2.12 ÷ 2.27 (m, 1H, PCCH); 3.48 (dd, <sup>2</sup>J<sub>HH</sub> = 10.5 Hz, <sup>3</sup>J<sub>HH</sub> = 8.7 Hz, 1H, CHHOCH<sub>2</sub>Ph); 3.78 (dd, <sup>2</sup>J<sub>HH</sub> = 10.5 Hz, <sup>3</sup>J<sub>HH</sub> = 5.5 Hz, 1H, CHHOCH<sub>2</sub>Ph); 4.11 ÷ 4.23 (m, 6H, 2xCH<sub>2</sub>OP, CH<sub>2</sub>O); 4.40 (s, 2H, OCH<sub>2</sub>Ph); 7.27 ÷ 7.35 (m, 5H, CH<sub>Ar</sub>). <sup>13</sup>C NMR (CDCl<sub>3</sub>): δ 13.87 (s, CH<sub>3</sub>CH<sub>2</sub>O); 16.10 (d, <sup>3</sup>J<sub>PC</sub> = 6.7 Hz, CH<sub>3</sub>CH<sub>2</sub>OP); 16.20 (d, <sup>3</sup>J<sub>PC</sub> = 6.1 Hz, CH<sub>3</sub>CH<sub>2</sub>OP); 16.58 (s, PCCH<sub>2</sub>); 23.77 (d, <sup>1</sup>J<sub>PC</sub> = 188.5 Hz, PC); 26.31 (d, <sup>2</sup>J<sub>PC</sub> = 2.8 Hz, PCCH); 61.43 (s, CH<sub>2</sub>O); 62.47 (d, <sup>2</sup>J<sub>PC</sub> = 6.2 Hz, CH<sub>2</sub>OP); 62.57 (d, <sup>2</sup>J<sub>PC</sub> = 6.5 Hz, CH<sub>2</sub>OP); 67.40 (s, CHCH<sub>2</sub>O); 72.42 (s, OCH<sub>2</sub>Ph); 127.20 (s, 2xCH<sub>Ar</sub>); 127.37 (s, CH<sub>Ar</sub>); 128.10 (s, 2xCH<sub>Ar</sub>); 136.40 (s, C<sub>Ar</sub>); 166.27 (s, C=O). IR (film) ν<sub>(C=O)</sub> 1724, ν<sub>(P=O)</sub> 1270, ν<sub>(P-O)</sub> 1028. Anal. Calcd. for C<sub>18</sub>H<sub>27</sub>O<sub>6</sub>P: C 58.37, H 7.35. Found: C, 58.49; H, 7.31.

***trans*-Ethyl 2-(butyl)-1-(diethoxyphosphoryl)cyclopropanecarboxylate (4d).**

Yield: 0.58 g (63%); colorless oil. R<sub>f</sub> = 0.48. <sup>31</sup>P NMR (C<sub>6</sub>D<sub>6</sub>): δ 24.30. <sup>1</sup>H NMR (C<sub>6</sub>D<sub>6</sub>): δ 0.89 (t, <sup>3</sup>J<sub>HH</sub> = 7.0 Hz, 3H, CH<sub>3</sub>CH<sub>2</sub>); 1.29 (t, <sup>3</sup>J<sub>HH</sub> = 7.2 Hz, 3H, CH<sub>3</sub>CH<sub>2</sub>O); 1.34 (t, <sup>3</sup>J<sub>HH</sub> = 7.0 Hz, 3H, CH<sub>3</sub>CH<sub>2</sub>OP); 1.35 (t, <sup>3</sup>J<sub>HH</sub> = 7.0 Hz, 3H, CH<sub>3</sub>CH<sub>2</sub>OP); 1.23 ÷ 1.60 (m, 9H, (CH<sub>2</sub>)<sub>3</sub>, PCCH<sub>2</sub>, PCCH); 4.14 (dq, <sup>3</sup>J<sub>PH</sub> = 7.0 Hz, <sup>3</sup>J<sub>HH</sub> = 7.0 Hz, 2H, CH<sub>2</sub>OP); 4.15 (dq, <sup>3</sup>J<sub>PH</sub> = 7.0 Hz, <sup>3</sup>J<sub>HH</sub> = 7.0 Hz, 2H, CH<sub>2</sub>OP); 4.16 (q, <sup>3</sup>J<sub>HH</sub> = 7.2 Hz, 1H, CHHO); 4.21 (q, <sup>3</sup>J<sub>HH</sub> = 7.2 Hz, 1H, CHHO). <sup>13</sup>C NMR (CDCl<sub>3</sub>): δ 13.62 (s, CH<sub>3</sub>CH<sub>2</sub>); 13.90 (s, CH<sub>3</sub>CH<sub>2</sub>O); 16.09 (d, <sup>3</sup>J<sub>PC</sub> = 6.1 Hz, CH<sub>3</sub>CH<sub>2</sub>O)P); 18.17 (d, <sup>2</sup>J<sub>PC</sub> = 2.8 Hz, PCCH<sub>2</sub>); 21.93 (s, CH<sub>3</sub>CH<sub>2</sub>); 24.96 (d, <sup>1</sup>J<sub>PC</sub> = 189.5 Hz, PC); 26.96 (s, CH<sub>3</sub>CH<sub>2</sub>CH<sub>2</sub>); 27.03 (s, PCCH); 30.87 (s, CH<sub>2</sub>CH<sub>2</sub>CH); 61.05 (s, CH<sub>2</sub>O); 62.08 (d, <sup>2</sup>J<sub>PC</sub> = 6.2 Hz, CH<sub>2</sub>OP); 62.18 (d, <sup>2</sup>J<sub>PC</sub> = 6.3 Hz, CH<sub>2</sub>OP); 168.04 (d, <sup>2</sup>J<sub>PC</sub> = 7.2 Hz, C=O). IR (film) ν<sub>(C=O)</sub> 1724, ν<sub>(P=O)</sub> 1252, ν<sub>(P-O)</sub> 1028. Anal. Calcd. for C<sub>14</sub>H<sub>27</sub>O<sub>5</sub>P: C 54.89, H 8.88. Found C 55.00, H 8.84.

**Procedure for preparation *trans*-2-Benzyloxymethyl-1-(diethoxyphosphoryl)cyclopropanecarboxylic acid (5)**

To a solution of cyclopropanecarboxylate **4c** (0.37 g, 1.00 mmol) in ethyl alcohol (5 mL) a solution of NaOH (0.08 g ; 2.00 mmol) in water (0.5 mL) was added and the reaction mixture was stirred at room temperature for 2 days. Then the solvent was evaporated and residue was dissolved in water (10 mL) and extracted with diethyl ether (3x10 mL). Then the water layer was acidified to pH 1 with 3N HCl and extracted with dichloromethane (3x10 mL). The combined organic layers were dried (MgSO<sub>4</sub>) and evaporated under reduced pressure. The residue crystallized on standby to give acid **5** as white solid, which was collected by filtration from diethyl ether.

***trans*-2-(Benzyloxymethyl)-1-(diethoxyphosphoryl)cyclopropanecarboxylic acid (5).**

Yield: 0.33 g (97%); white crystal; m.p. = 102-104 °C. <sup>31</sup>P NMR (CDCl<sub>3</sub>): δ 27.42. <sup>1</sup>H NMR (CDCl<sub>3</sub>): δ 1.30 (td, <sup>3</sup>J<sub>HH</sub> = 7.0 Hz, <sup>4</sup>J<sub>PH</sub> = 0.7 Hz, 6H, 2xCH<sub>3</sub>CH<sub>2</sub>OP); 1.61 (dd, <sup>3</sup>J<sub>PH</sub> = 12.2 Hz, <sup>3</sup>J<sub>HH</sub> = 8.5

Hz, 2H, PCCH<sub>2</sub>); 2.23 (dddd, <sup>3</sup>J<sub>PH</sub> = 16.5 Hz, <sup>3</sup>J<sub>HH</sub> = 10.0 Hz, <sup>3</sup>J<sub>HH</sub> = 8.5 Hz, <sup>3</sup>J<sub>HH</sub> = 8.5 Hz, <sup>3</sup>J<sub>HH</sub> = 5.7 Hz 1H, PCCH); 3.55 (dd, <sup>2</sup>J<sub>HH</sub> = 10.7 Hz, <sup>3</sup>J<sub>HH</sub> = 8.5 Hz, 1H, CHHOCH<sub>2</sub>Ph); 3.78 (dd, <sup>2</sup>J<sub>HH</sub> = 10.7 Hz, <sup>3</sup>J<sub>HH</sub> = 5.7 Hz, 1H, CHHOCH<sub>2</sub>Ph); 4.16 (dq, <sup>3</sup>J<sub>PH</sub> = <sup>3</sup>J<sub>HH</sub> = 7.0 Hz, 1H, CHHOP); 4.17 (dq, <sup>3</sup>J<sub>PH</sub> = <sup>3</sup>J<sub>HH</sub> = 7.0 Hz, 1H, CHHOP); 4.18 (dq, <sup>3</sup>J<sub>PH</sub> = <sup>3</sup>J<sub>HH</sub> = 7.00 Hz, 2H, CH<sub>2</sub>OP); 4.47 (s, 2H, OCH<sub>2</sub>Ph); 7.25 ÷ 7.32 (m, 5H, CH<sub>Ar</sub>). <sup>13</sup>C NMR (CDCl<sub>3</sub>): δ 16.04 (d, <sup>3</sup>J<sub>PC</sub> = 6.1 Hz, CH<sub>3</sub>CH<sub>2</sub>OP); 16.13 (d, <sup>3</sup>J<sub>PC</sub> = 5.0 Hz, CH<sub>3</sub>CH<sub>2</sub>OP); 17.24 (s, PCCH<sub>2</sub>); 23.38 (d, <sup>1</sup>J<sub>PC</sub> = 190.9 Hz, PC); 26.95 (s, PCCH); 63.01 (d, <sup>2</sup>J<sub>PC</sub> = 6.5 Hz, CH<sub>2</sub>OP); 63.11 (d, <sup>2</sup>J<sub>PC</sub> = 6.5 Hz, CH<sub>2</sub>OP); 67.22 (s, CH<sub>2</sub>OCH<sub>2</sub>Ph); 72.43 (s, OCH<sub>2</sub>Ph); 127.36 (s, 2×CH<sub>Ar</sub>); 128.13 (s, CH<sub>Ar</sub>); 128.14 (s, 2×CH<sub>Ar</sub>); 137.94 (s, C<sub>Ar</sub>); 170.34 (d, <sup>2</sup>J<sub>PC</sub> = 8.5 Hz, C=O). IR (film) ν<sub>(C=O)</sub> 1764, ν<sub>(P=O)</sub> 1264, ν<sub>(P-O)</sub> 1020. Anal. Calcd. for C<sub>16</sub>H<sub>23</sub>O<sub>6</sub>P: C 56.14, H 6.77. Found C, 56.23; H, 6.80.

## Acknowledgements

The authors thank Professor Ryszard Bodalski (Technical University of Lodz) for stimulating discussions.

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