

## CHEMISTRY

### Two Useful Synthons Produced from: 5,5-(Dimethylenedioxy) Hex-2-enal and 6,6-(Trimethylenedithio) Hex-3-ene-2-one, Synthesis and Examples of Their Efficacy

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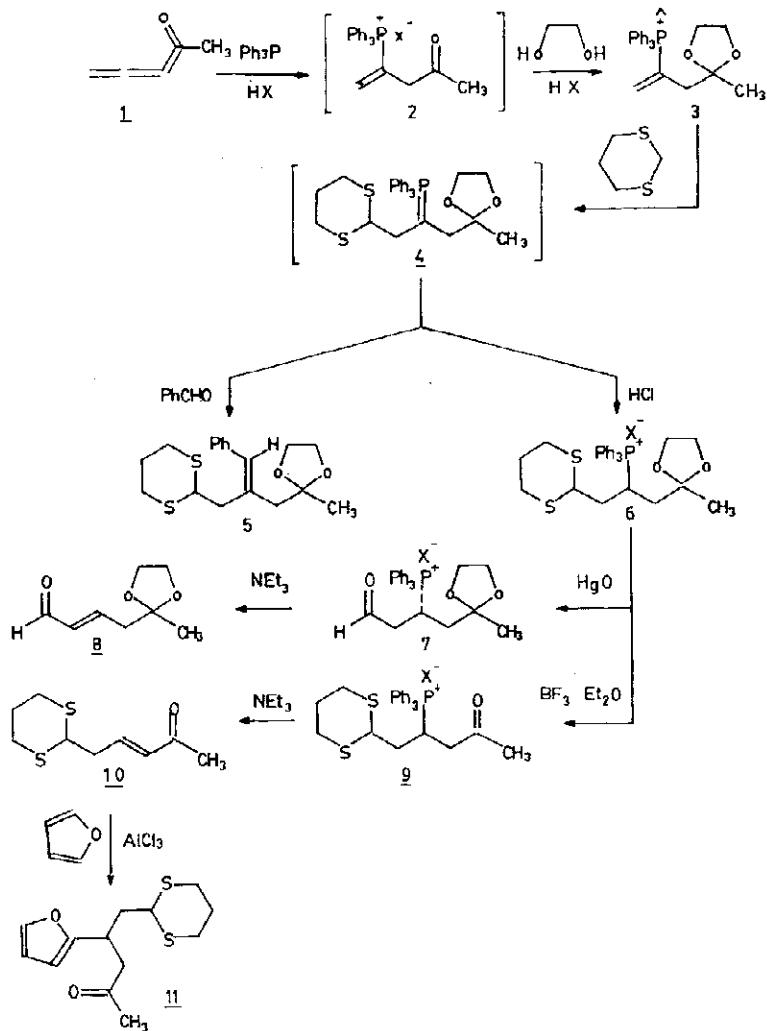
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**Abstract.** The vinylphosphonium salt **3** owing to the presence of the charged phosphonium group, acting as polarity inverter, and as protecting group, allowed us to obtain useful organic synthons from an allenic ketone.

#### Introduction

We recently demonstrated that polarity inversion of the C $\gamma$  carbon atom by a phosphonio group in an allenic structure **1** is a versatile method for the preparation of different synthetically attractive synthons [1,2]. We previously reported that a facile synthesis of the vinyl phosphonium salt **2**, could be accomplished by adding triphenylphosphine to the methyl allenyl ketone (**1**) when (Z=CO-CH $_3$ ) in Scheme 1.

In this paper, we report the extension of the reactivity of this molecule involving the synthesis of 2,2-(dimethylenedioxy)-propyl, 2,2-(trimethylenedithio)-ethyl styrene (**5**), 5,5-(Dimethylenedioxy) Hex-2-enal (**8**) and 6,6-(Trimethylenedithio) Hex-3-ene-2-one (**10**), allowing interesting developments.



Scheme 1.

The methyl allenyl ketone (1) was first converted into triphenyl-2-(4-ethyl 1,2-dioxolane pentenyl) phosphonium salt 3, via unprotected ketonyl vinyl phosphonium homologue 2, by Michael-type addition of triphenyl phosphine catalysed with one equivalent of p-toluenesulfonic acid followed by one pot addition of acetone [1]. The reaction of unsaturated phosphonium salt 3 with one equivalent of 2-lithium 1,3-propyldithiane in tetrahydrofuran (THF) at  $-80^{\circ}\text{C}$  yielded the 2,2-(dimethylenedioxy)-propyl, 2,2-(trimethylenedithio)-ethyl triphenyl phosphine-ylide (4).

Under these conditions this ylide 4 provides an interesting preparation of a bifunctionalized styrene derivative 5, and also, offering easy access to the corresponding phosphonium salt 6. We also report procedures involving treatment of one or the other protected carbonyl functions of phosphonium salt 6 affording the corresponding unsaturated aldehyde 7 or ketone 9.

We found that subsequent reaction of the ylide 4 with benzaldehyde gave rise to Wittig olefination, and with a relatively modest yield due to steric hindrance this led to the formation of the compound 5 (Table 1).

**Table 1. Compounds 5 to 11 prepared**

Product	M.P $^{\circ}\text{C}$	Yield <sup>3</sup> (%)	Molecular <sup>a</sup> Formula	<sup>1</sup> H-NMR(CDCl <sub>3</sub> /TMS) <sup>c</sup> $\delta$ ppm, J (Hz)	<sup>31</sup> P-NMR <sup>d</sup> $\delta$ ppm,
5	Oil	51	C <sub>18</sub> H <sub>24</sub> O <sub>2</sub> S <sub>2</sub> (336)	1.30 (s, 3H, CH <sub>3</sub> ), 1.81-3.00 (m, 10H, 5CH <sub>2</sub> ), 4.0-4.05 (s <sub>2</sub> , 4H, OCH <sub>2</sub> CH <sub>2</sub> O), 4.03 (t, 1H, <div style="display: inline-block; vertical-align: middle; margin-left: 10px;"> <math>\begin{array}{c} \text{S} \\ \diagup \quad \diagdown \\ \text{H-C} \end{array}</math> </div> J=7.8), 6.50 (s, 1H, CH=C), 7.24- 7.39 (m, 5H, C <sub>6</sub> H <sub>5</sub> ).	
6	147.3	87	C <sub>29</sub> H <sub>34</sub> IO <sub>2</sub> PS <sub>2</sub> (636)	1.54 (s, 3H, CH <sub>3</sub> ), 1.58 (dd, 2H, CH <sub>2</sub> - <div style="display: inline-block; vertical-align: middle; margin-left: 10px;"> <math>\begin{array}{c} \text{O} \\ \diagup \quad \diagdown \\ \text{C} \\ \diagdown \quad \diagup \\ \text{O} \end{array}</math> </div> J = 20, 7.3), 1.68-2.10 (m, 4H, 2CH <sub>2</sub> ), 2.37-2.56 (m, 4H, CH <sub>2</sub> -S), 3.9-4.1 (m, 1H, H- C-P), 4.18-4.20 (s <sub>2</sub> , 4H, OCH <sub>2</sub> CH <sub>2</sub> O), 4.59- 4.61 (m, 1H, H-C <div style="display: inline-block; vertical-align: middle; margin-left: 10px;"> <math>\begin{array}{c} \text{S} \\ \diagup \quad \diagdown \\ \text{H-C} \\ \diagdown \quad \diagup \\ \text{S} \end{array}</math> </div> ), 7.50-7.88 (m, 15H, 3C <sub>6</sub> H <sub>5</sub> ).	
7	112		C <sub>26</sub> H <sub>32</sub> IO <sub>2</sub> P (546)	1.28 (s, 3H, CH <sub>3</sub> ), 2.10-2.29 (m, 2H, CH <sub>2</sub> -	31.50

Table 1. Compounds 5 to 11 prepared (Continued)

Product	M.P. °C	Yield <sup>2</sup> (%)	Molecular <sup>3</sup> formula	<sup>1</sup> H-NMR(CDCl <sub>3</sub> /TMS) <sup>4</sup> δ ppm, J (Hz)	<sup>31</sup> P-NMR <sup>4</sup> δ ppm,
				$\text{C} \begin{array}{l} \diagup \text{O} \\ \diagdown \text{O} \end{array} \text{), } 3.42\text{-}3.58(\text{m}, 2\text{H}, \text{CH}_2\text{-C-O}), 3.91\text{-}$	
				4.10(m, 5H, OCH <sub>2</sub> CH <sub>2</sub> O, H-C-P), 7.58-8.29 (m, 5H, 3C <sub>6</sub> H <sub>5</sub> ), 9.3(t, 1H, II-C=O, J=2.0).	
8	Oil	93	C <sub>4</sub> H <sub>12</sub> O <sub>3</sub> (156)	1.38 (s, 3H, CH <sub>3</sub> ), 2.60(d, 2H, CH <sub>2</sub> -	
				$\text{C} \begin{array}{l} \diagup \text{O} \\ \diagdown \text{O} \end{array} \text{, } J=7), 4.02\text{-}4.07 (\text{S}, 4\text{H}, \text{OCH}_2\text{CH}_2\text{O}),$	
				6.90(dd, 1H, =CH-CO, J=16.0, 8.0), 6.15 (td, 1H -CH-CH <sub>2</sub> , J= 16.0, 7.0), 9.7(d, 1H, II-C=O, J=8.0).	
9	136	95	C <sub>27</sub> H <sub>36</sub> IOPS <sub>2</sub> (592)	2.10 (s, 3H, CH <sub>3</sub> ), 1.75-2.20 (m, 4H, 2CH <sub>2</sub> ), 2.70-2.85 (m, 4H, 2CH <sub>2</sub> S), 3.10-3.88(m, 3H, CH <sub>2</sub> -CO, H-C-P) 4.58-4.64 (m, 1H, H-C	30.6
				$\begin{array}{l} \diagup \text{S} \\ \diagdown \text{S} \end{array} \text{),}$	
				7.58-7.89(m, 15H, 3C <sub>6</sub> H <sub>5</sub> ).	
10	Oil	91	C <sub>9</sub> H <sub>14</sub> OS <sub>2</sub> (202)	1.68-2.10 (m, 2H, CH <sub>2</sub> ), 2.20 (s, 3H, CH <sub>3</sub> ), 2.60 (ddd, 2H, CH <sub>2</sub> -C	
				$\begin{array}{l} \diagup \text{S} \\ \diagdown \text{S} \end{array} \text{, } J= 7.1, 6.9, 1.4),$	
				2.75-2.81(m, 4H, 2CH <sub>2</sub> S), 4.10 (td, 1H, H-C	
				$\begin{array}{l} \diagup \text{S} \\ \diagdown \text{S} \end{array} \text{ } J= 6.9, 2.1), 6.05(\text{dd}, 1\text{H}, =\text{CH-CO},$	
				J=15.9, 1.4), 6.70(ddd, 1H, =CH-CH <sub>2</sub> J=15.9, 7.1, 2.1).	
11	Oil	70	C <sub>13</sub> H <sub>18</sub> O <sub>2</sub> S <sub>2</sub>	1.90-2.10 (m, 4H, 2CH <sub>2</sub> ), 2.14 (s, 3H, CH <sub>3</sub> ), 2.62-2.91 (m, 6H, 3CH <sub>2</sub> ), 3.60-3.72 (m, 1H, CH) 3.77 (dd, 1H, CH, J=9.3, 5.4), 6.09 (d, 1H, H, J=3.2), 6.28 (dd, 1H, J=3.2, 1.9), 7.31 (dd, 1H, CH, J=1.9, 0.7).	

a) Yield of recrystallized products, except oils.

b) Satisfactory microanalysis obtained: C +/- 0.17, H +/- 0.06, P - +/- 0.13, S +/- 0.19.

c) Recorded at 250 MHz on a Bruker A C 250 spectrometer, (m, l, s, sc means multiplet, triplet, singlet, broad singlet respectively).

d) Recorded at 80 MHz on a Bruker WP 80 DS.

In order to obtain the phosphonium salt **6**, the ylide **4** was protonated by neutralization of the reaction medium, by adding HCl at 0°C. Starting from this phosphonium salt **6**, deacetalisation was completely performed by acetone transesterification, catalysed by the Lewis acid (Et<sub>2</sub>O·BF<sub>3</sub>). Thus, the resulting compound, a ketonic phosphonium salt **9**, was formed exclusively with a high yield. Using H<sub>2</sub>SO<sub>4</sub> instead of BF<sub>3</sub>, the reaction was not complete, and a mixture of salts **6**, and **9** were obtained.

On the other hand, selective dethioacetalisation of phosphonium salt **6** was completely performed using the mercury oxide reactive [2]. The aldehydic phosphonium salt **7** was cleanly synthesized.

In an improved laboratory procedure [1] the β-elimination of the charged phosphonium groups using triethylamine was performed on salts **7** and **9**. In both cases, the olefination was highly regio- and stereo-selective. 5,5-(Dimethylenedioxy) Hex-2-enal (**8**) and 6,6-(Trimethylenedithio) Hex-3-ene-2-one (**10**) were prepared respectively, and had an E configuration around the newly formed double bond. All structural assignments were made on the basis of <sup>1</sup>H-NMR.

Investigations on the potential of the three functionalized compounds **8** and **10** are in progress. We decided to illustrate the utility of such compounds by the selective preparation furan derivative **11** the α, β unsaturated ketone **10** behaved as a good dienophile but instead of the expected cyclic derivative resulting of a Diels-Alder addition between the compound **10** and furan, the compound **11** was obtained. It was identified by Mass spectroscopy, its purity was confirmed by gaschromatography, and its structure was determined from the spectral data.

This convenient cyclization procedure also proved useful for the synthesis of other derivatives.

### General Experimental Procedure

#### **The 2,2-(dimethylenedioxy)-propyl, 2,2-(trimethylenedithio)-ethyl triphenyl phosphine -ylide (**4**)**

In a round-bottomed flask fitted with a magnetic stirrer, reflux condenser with an N<sub>2</sub>-inlet, and septum, a THF (100mL) solution of 2-lithium 1,3-propyldithiane (930 mg, 7.7 mmol) is prepared as described [3]. Then the vinyl phosphonium salt **3** (4.0g, 7.7 mmol, 1 equiv.) is added, minimizing air-contact, and the resulting solution stirred at r.t. for 90 min.

#### **The 2,2-(dimethylenedioxy)-propyl, 2,2-(trimethylenedithio)-ethyl styrene (**5**)**

The THF solution of the ylide **4**, prepared as above [4] is cooled to -80°C and benzaldehyde (1.2mL, 10 mmol, 1 equiv.) added dropwise with a syringe. The reaction is left to come to r. t. while stirring is continued overnight. The mixture is partitioned between

$\text{CHCl}_3$  (150 mL) and  $\text{H}_2\text{O}$  (150 mL). The organic layer is dried ( $\text{Na}_2\text{SO}_4$ ), and reduced to ca. 30 mL. In a rotary evaporator. The remaining solution is added dropwise to  $\text{Et}_2\text{O}$  (500 mL). The resulting organic layer is collected by filtration. The filtrate is evaporated to dryness in a rotary evaporator and the crude product is chromatographed on silica gel column eluting with  $\text{CH}_2\text{Cl}_2$  to give pure **5** (Table 1).

**The 3-(1,1-(trimethylenedithio), 5,5-(dimethylenedioxy)-hexyl triphenyl phosphonium Iodide (6):**

The THF solution of the ylide **4** prepared as above, is neutralized by adding a solution of 0.1 N HCl. The mixture is partitioned between  $\text{CHCl}_3$  (150 mL) and  $\text{H}_2\text{O}$  (150 mL). The organic layer is dried ( $\text{Na}_2\text{SO}_4$ ) and reduced to ca. 30 mL in a rotary evaporator. The remaining solution is added dropwise to  $\text{Et}_2\text{O}$  (500 mL). The precipitated product **6** is isolated by suction and purified by recrystallization from  $\text{CH}_2\text{Cl}_2$  (40 mL)/ $\text{CH}_3\text{CO}_2\text{CH}_2\text{CH}_3$  (100 mL).

**The 3-(5,5-(dimethylenedioxy)-hex-1-oxo-yl) triphenyl phosphonium Iodide (7):**

Under stirring [5] at r.t., HgO (600 mg, 1.5 equiv.) is added to a solution of salt **6** (2.0 g, 3.1 mmol) in acetonitrile (80 mL)/ $\text{H}_2\text{O}$  (20 mL). The stirring at r.t. is continued for 48 h. The mixture is filtered and the filtrate is diluted by  $\text{CHCl}_3$  (100 mL) and the organic phase is separated. The aqueous phase extracted with  $\text{CHCl}_3$  (2 x 50 mL). The combined organic layers are washed with  $\text{H}_2\text{O}$  (1 x 25 mL), dried ( $\text{Na}_2\text{SO}_4$ ), and reduced to ca. 30 mL in a rotary evaporator. The remaining solution is added dropwise to  $\text{Et}_2\text{O}$  (500 mL). The precipitated product **7** is isolated by suction and is purified by recrystallization from  $\text{CH}_2\text{Cl}_2$  (20 mL)/ $\text{MeCO}_2\text{Et}$  (50 mL).

**The 5,5-(dimethylenedioxy)-hex-2-enal (8):**

To a solution of the salt **7** (1.0 g, 1.8 mmol) in anhyd. MeOH (40 mL) cooled at 0°C, triethylamine (0.5 mL, 2 equiv.) is added. The reaction is left to come to r.t. under stirring which is continued over 24 h at r.t. The mixture is neutralized (pH=7) by adding a solution of 0.1 N HCl. Adding  $\text{H}_2\text{O}$  most of the formed  $\text{Ph}_3\text{P}$  precipitates and it is eliminated by filtration. The obtained filtrate is extracted by  $\text{CHCl}_3$  (200 mL). The organic phase is separated, washed with  $\text{H}_2\text{O}$  (2 x 25 mL), dried ( $\text{Na}_2\text{SO}_4$ ), and reduced to ca. 30 mL in a rotary evaporator. The remaining solution is added dropwise to  $\text{Et}_2\text{O}$  (500 mL). The resulting organic layer is collected by filtration. The filtrate is evaporated to dryness in a rotary evaporator and the crude product is chromatographed on silica gel column eluting with  $\text{CH}_2\text{Cl}_2$  to give pure **8** of E configuration (Table 1).

**The 3-(6,6-(trimethylenedithio)-hex-2-oxo-yl) triphenyl phosphonium Iodide (9):**

Under stirring [6] at r.t.,  $\text{BF}_3 \cdot \text{Et}_2\text{O}$  (3.5 mL, 2 equiv.) is added to a solution of salt **6** (4.0 g, 6.2 mmol) in acetone (40 mL), the stirring at r.t. is continued for 48 h. Adding a solution 0.1N  $\text{NaHCO}_3$ , the mixture is neutralized (pH=7) and diluted by  $\text{CHCl}_3$  (200 mL). The organic phase is separated, washed with  $\text{H}_2\text{O}$  (2 x 25 mL), dried ( $\text{Na}_2\text{SO}_4$ ), and

reduced to ca. 30 mL in a rotary evaporator. The remaining solution is added dropwise to Et<sub>2</sub>O (500 mL). The precipitated product **9** is isolated by suction and purified by recrystallization from CH<sub>2</sub>Cl<sub>2</sub> (40 mL)/MeCO<sub>2</sub>Et (100 mL).

#### The 6,6-(trimethylenedithio)-hex-3-ene-2-one (**10**)

To a solution of the salt **9** (3.6 g, 6.0 mmol) in anhyd. MeOH (100 mL) cooled at 0°C, triethylamine (1.6 mL, 2 equiv.) is added. The reaction is left to come to r.t. under stirring which is continued over 24h at r.t. The mixture is neutralized (pH=7) by adding a solution of 0.1 N HCl. Adding H<sub>2</sub>O most of the formed Ph<sub>3</sub>P precipitates and it is eliminated by filtration. The obtained filtrate is extracted by CHCl<sub>3</sub> (200 mL). The organic phase is separated, washed with H<sub>2</sub>O (2 x 25 mL), dried (Na<sub>2</sub>SO<sub>4</sub>), and reduced to ca. 30 mL in a rotary evaporator. The remaining solution is added dropwise to Et<sub>2</sub>O (500 mL). The resulting organic layer is collected by filtration. The filtrate is evaporated to dryness in a rotary evaporator and the crude product is chromatographed on silica gel column eluting with CH<sub>2</sub>Cl<sub>2</sub> to give pure **10** of E configuration (Table 1).

#### The 4-(2-furyl), 5-(1,3 dithiacyclohexan - 2yl) pentan - 2-one ketone (**11**)

A catalytic amount [7,8] of AlCl<sub>3</sub> (13 mg, 0.1 equiv.) is added to a mixture of hexenone **10** (200 mg, 1 mmol, 1 equiv.), and furan (200 mg, 3 mmol, 3 equiv), in solution in Et<sub>2</sub>O. After stirring during 10 d. at r.t., H<sub>2</sub>O (25 mL) and CHCl<sub>3</sub> (60 mL) are added and the organic layer is separated, washed with H<sub>2</sub>O (25 mL), and dried (Na<sub>2</sub>SO<sub>4</sub>). The solvent is evaporated and the crude material is chromatographed on a silica gel column. Using CH<sub>2</sub>Cl<sub>2</sub> as eluent the pure **11** is isolated (Table 1).

### References

- [1] Cristau, H.J., Viala, J and Cristol, H. "Inversion de polarité par les group phosphores." *Bull. Soc. Chem.*, FR 5 (1985), 980-988.
- [2] Cristau, H.J., Fonte, M and Torrelles, E. "Umpolung Using a Phosphorus Group. A Novel Method for the Chemoselective Synthesis of 2-acetyl or 3-acetyl Morpholines." *Synthesis*, 14 (1989), 301-303.
- [3] Seebach, D. "Methods of Reactivity Umpolung." *Angew. Chem. Int. Ed. Engl.* 16 (1979), 239-259.
- [4] Buono, G. and Pfeiffer, G. "Synthesis and Use in the Willce Reaction of the ylides of β-acylprop-2-enylidene-triphenyl phosphines." *Tetrahedron Letters*, 149 (1972), 108-112.
- [5] Gompper, R. and Wolf, U. "An Improved Aldelyde Synthesis from 1-3 Dithianes." *Liebigs Ann. Chem.* 132 (1979), 1406-1411.
- [6] Hamlet, Z. and Barker, W.D. "An Efficient and Practical Method for the β-Functionalization of Enones." *Synthesis*, 90 (1970), 543-551.
- [7] Schweizer, E.E. "Reactions of α-reingylideno-γ-Butyral Acetones." *J. Am. Chem. Soc.*, 86 (1964), 2744-2749.
- [8] Bestmann, H.J. "Phosphinalkylene und Halogenverbindungen." *Angew. Chem. Int. Ed. Engl.*, 4 (1965), 645-650.

تصنيع المركبان 5.5 - (ثنائي ميثيلين - ثنائي أوكسي) - هكس - 2 - 2 - انال - والمركب 6.6 - (ثلاثي ميثيلين - ثنائي ثيو) - هكس - 3 - 3 - 2 - ون وأمثلة عن أهمية هذه المركبات

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ملخص البحث . الملح فينيل فوسفونيوم (3)، ولوجود مجموعة الفسفونيوم ذات الشحنة والتي تعمل كعاكس للقريبة وكمجموعة حماية، أدى إلى الحصول على كواشف عضوية مفيدة من الكيئونات الأينية.