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ORGANOSULPHUR COMPOUNDS - LXXI[1]

Diverse Reactivity of α-Carbanions Derived from α-Phosphoryl Dithioacetals and α-Phosphoryl Sulphides Towards α,β-Unsaturated Carbonyl Compounds. A General Synthesis of Conjugated Ketene Dithioacetals

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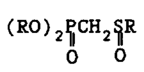
Key Words: α-phosphoryl sulphides, α-phosphoryl dithioacetals, ketene dithioacetals, 1,2 / 1,4-adducts, rearrangement, NMR.

Abstract: α-Lithio-α-phosphoryl dithioacetals **2** react with aldehydes and ketones to give conjugated ketene dithioacetals in moderate to good yields. Monitoring the reaction course by ^{31}P NMR spectra revealed that the reaction with aldehydes involves a 1,2-addition followed by decomposition to the Horner-Wittig reaction products. Ketones react in a different way forming at first the 1,4-adducts that undergo isomerization to the 1,2-adducts and the latter decompose to conjugated ketene dithioacetals. The reaction of α-lithio α-phosphorylmethyl metyl sulphide **6** with ketone (chalcone) has been shown by ^{31}P NMR spectra to give the 1,2-addition product as an intermediate that does not decompose to the Horner-Wittig reaction products but rearranges to the corresponding 1,4-adduct.

INTRODUCTION

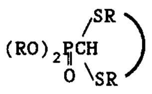
α-Heterosubstituted carbanions are valuable synthetic intermediates that react with electrophiles to form new carbon-carbon or carbon-heteroatom bond. Particularly useful in this regard are the α-phosphonate carbanions stabilized additionally by sulphur.[2] In the course of our studies in this area we have prepared a great number of phosphonates containing various organosulphur substituents in the α-position that readily undergo deprotonation to form the corresponding carbanions. The best examples of such phosphonates, which have been obtained in our laboratory and found synthetic application, are α-phosphoryl sulphoxides **1**,[3] dithioacetals of formylphosphonates **2**,[4] diethyl α-methylthiovinylphosphonate **3**,[5] diethyl α-methylthio-α-trimethylsilylmethanephosphonate **4**[5c] and diethyl α-methylthiophosphonoacetic acid **5**,[6] a recently published bifunctional reagent.

Dithioacetals of formylphosphonates **2** deserve special attention since they are key reagents in the synthesis of ketene dithioacetals (eq.1)[7] which, in turn, have found numerous applications in organic synthesis as $^{+}C-CO^{-}$ equivalents.[8] Recently, cyclic phosphonates **2**, namely 2-phosphoryl-1,3-dithianes and their phosphinoyl analogues, are



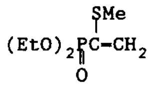
$(RO)_2\underset{O}{\underset{\|}{P}}CH_2\underset{O}{\underset{\|}{S}}R$

1



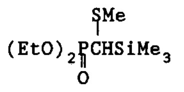
$(RO)_2\underset{O}{\underset{\|}{P}}CH(SR)_2$

2



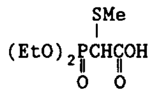
$(EtO)_2\underset{O}{\underset{\|}{P}}\overset{SMe}{C}-CH_2$

3



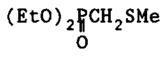
$(EtO)_2\underset{O}{\underset{\|}{P}}\overset{SMe}{CH}SiMe_3$

4



$(EtO)_2\underset{O}{\underset{\|}{P}}\overset{SMe}{CH}\underset{O}{\underset{\|}{C}}OH$

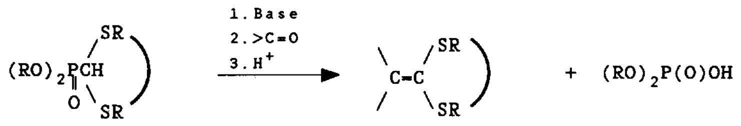
5



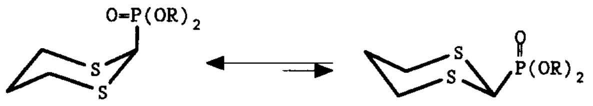
$(EtO)_2\underset{O}{\underset{\|}{P}}CH_2SMe$

6

the subject of intensive conformational studies in connection with a strong axial preference of the phosphoryl group found in the 1,3-dithiane ring and the anomeric effect operating in this system (eq.2).[9]



(eq.1)



(eq.2)

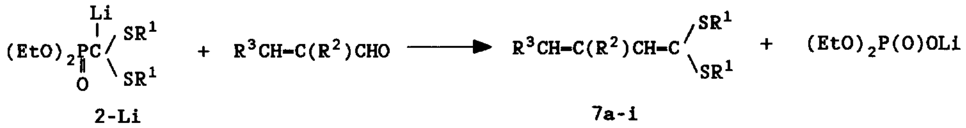
This paper reports the results of our further studies on the reactions of the α-phosphonate carbanions derived from **2** with α,β-unsaturated carbonyl compounds which leads to the formation of conjugated ketene dithioacetals.[10] The latter are the $^{+}C-C-C-CO^{-}$ equivalents. In contrast to simple carbonyl compounds, addition of the metallated **2** to enones may occur in 1,2- or 1,4-fashion leading to the corresponding adducts. Their formation and interconversion was confirmed by isolation and/or detection by means of the low temperature ^{31}P NMR spectroscopy. For comparison purposes we report also chemical behaviour of the α-phosphonate carbanion derived from α-phosphoryl sulphide **6** towards α,β-unsaturated ketone.

RESULTS

Reaction of Lithium Derivatives of α-Phosphoryl Dithioacetals 2 with α,β-Unsaturated Aldehydes

We found that treatment of the lithiated α-phosphoryl dithioacetals **2** with α,β-unsaturated aldehydes results in a clean formation of the Horner-Wittig reaction products i.e. conjugated ketene dithioacetals **7** (eq.3).

Generally, the reaction was performed by addition of a carbonyl compound to the freshly prepared THF solution of the lithium derivative of **2** at -78 °C under argon atmosphere. The reaction was complete in 20-40 minutes at temperatures from -78 to -20 °C as evidenced by ^{31}P NMR spectroscopy. To demonstrate a general character of the



$$(EtO)_2P(O)C(Li)(SR^1)_2 + R^3CH{=}C(R^2)CHO \longrightarrow R^3CH{=}C(R^2)CH{=}C(SR^1)_2 + (EtO)_2P(O)OLi$$

2-Li 7a-i

(eq.3)

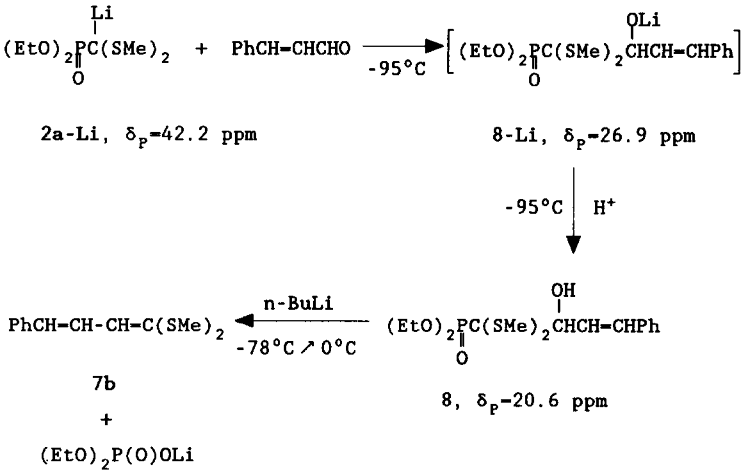
2a, R^1=Me

2b, $R^1+R^1=(CH_2)_3$

2c, $R^1+R^1=CH_2SCH_2$

synthesis of conjugated ketene dithioacetals **7**, the reaction was carried out with three different dithioacetals **2** shown above and five aldehydes: crotonaldehyde, cinnamaldehyde, α-ethyl cinnamaldehyde, cytral and myrtenal. In each case ketene dithioacetals **7** were formed in yields exceeding 90% and isolated in 50-80% yield (see Table).

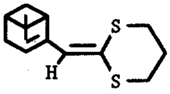
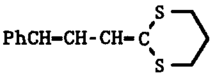
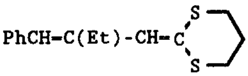
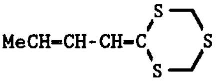
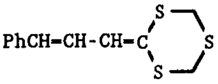
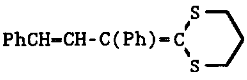
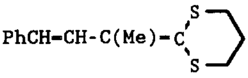
According to the low temperature ^{31}P NMR spectra 1,4-adducts were not detected as intermediates. Therefore, the title reaction should involve the transient formation of 1,2-adducts which decompose to **7**. Indeed, in the case of the reaction of **2a-Li** with cinnamaldehyde, the 1,2-adduct **8** was observed by ^{31}P NMR at -95 °C and successfully trapped by careful acidification of the reaction mixture at this temperature. It was isolated in a pure state in 46-80% yield by column chromatography on silica gel. The adduct **8** was then converted into the ketene dithioacetal **7b** by treatment with n-butyllithium at -78 °C and raising temperature to 0 °C in order to complete the reaction (Scheme 1).



Scheme 1

To the best of our knowledge this is the first successful trap of a 1,2-adduct in the reaction of α-phosphoryl thioacetals with carbonyl compounds. It should be noted, however, that in other reactions of **2-Li** with saturated or unsaturated carbonyl compounds investigated by us using ^{31}P NMR technique at -78 °C we were not able to detect

Table. Synthesis of conjugated ketene dithioacetals

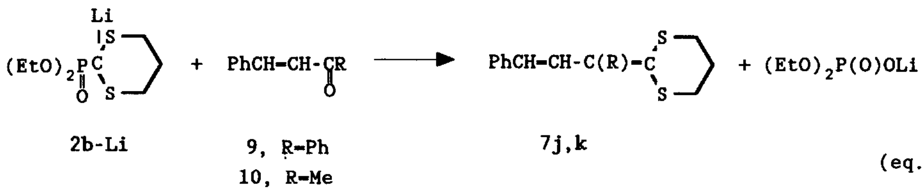
No	Ketene dithioacetals	Time (min)/temperature (°C) of completion of reaction	Yield [b] [%]
7a	MeCH=CH-CH=C(SMe)$_2$	20/-70	80
7b	PhCH=CH-CH=C(SMe)$_2$	40/-20	75
7c	PhCH=C(Et)-CH=C(SMe)$_2$	20/-70	70
7d	RC(Me)=CH-CH=C(SMe)$_2$[a]	20/-78	69
7e		20/-78	64
7f		20/-60	70
7g		40/-60	65
7h		40/-40	50
7i		30/-40	60
7j		146 hrs/25	52
7k		315 hrs/25	33

[a] R=Me$_2$C=CH(CH$_2$)$_2$- [b] yield of isolated product

the formation of 1,2-adducts. We observed only disappearance of a signal due to 2-Li and formation of a new signal characteristic of phosphoric acid anion. These observations indicate that the 1,2-adducts formed in the reaction under discussion are very unstable reaction intermediate that are formed in low concetrations and that their decomposition is comparable or faster than their formation.

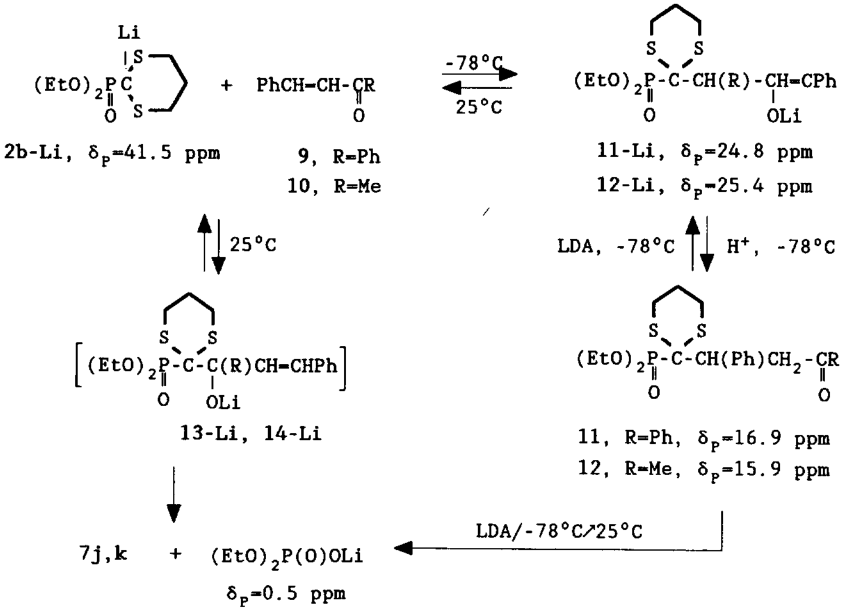
Reaction of Lithium Derivatives of α-Phosphoryl Dithioacetals 2 with α,β-Unsaturated Ketones

To study the reactivity of the α-phosphonate carbanions derived from **2** with ketones we chose **2b-Li** to react with chalcone **9** and benzylideneacetone **10** as carbonyl components of the reaction(eq.4).



(eq.4)

It was found that, in contrast to the reaction of **2-Li** with α,β-unsaturated aldehydes, the reaction with ketones required much longer reaction time and should be carried out at room temperature under strictly moisture and oxygen free conditions. Thus, after treatment of **2b-Li** with benzylideneacetone **10** for 6 days and with chalcone **9** for 13 days, the corresponding ketene dithioacetals **7k** and **7j** were formed in 50-77% yield (^{31}P NMR assay), and isolated in 33-52% yield. However, when the above reactions were carried out and quenched by acidification at -78°C neither ketene dithioacetals **7j** and **7k** nor the corresponding 1,2-adducts **13** and **14** were formed. Instead of them, the 1,4-adduct **11** and **12** (identified by spectral and chemical methods) were separated in 75-90% yield together with a small amount (10-25%) of the starting thioacetal **2b**. More interestingly, when the reaction mixtures were acidified at -20°C, two products were



Scheme 2

isolated: the starting phosphonate **2b** in 70-80% yield and ketene dithioacetals **7j** and **7k** in 20-30% yield. Formation of the latter indicates that at this temperature the 1,2-adducts **11** and **12** should be transiently formed and converted to the Horner-Wittig reaction products **7**.

These observations as well as monitoring the reaction by ^{31}P NMR spectra allow us to propose the following course of the reaction of α,β-unsaturated ketones with **2-Li** (Scheme 2).

In the first step the lithium derivative **2b-Li** undergoes a 1,4-addition to α,β,-unsaturated ketones. Then, the 1,4-adducts primarily formed rearrange to 1,2-adducts via reversible formation of the starting **2b-Li** and ketone and their reiterated reaction in a 1,2-fashion. Finally, the 1,2-adducts undergo fast decomposition to **7** according to the mechanism of the Horner-Wittig reaction. In an independent experiment the 1,4-adduct **11** was transformed into ketene dithioacetal **7j** after treatment with LDA at -78 °C and prolonged standing at 25 °C.

Reaction of Lithium Derivative of α-Diethoxyphosphorylmethyl Methyl Sulphide 6 with Chalcone 9

The investigation of the above reaction was interesting for two reasons. The first is that the α-phosphonate carbanion derived from **6** is less stabilized than those generated from dithioacetals **2**. Secondly, the eventual 1,4-addition of **6-Li** to **9** would afford a potential precursor of 1,4-diketones and cyclopentanones.[11]

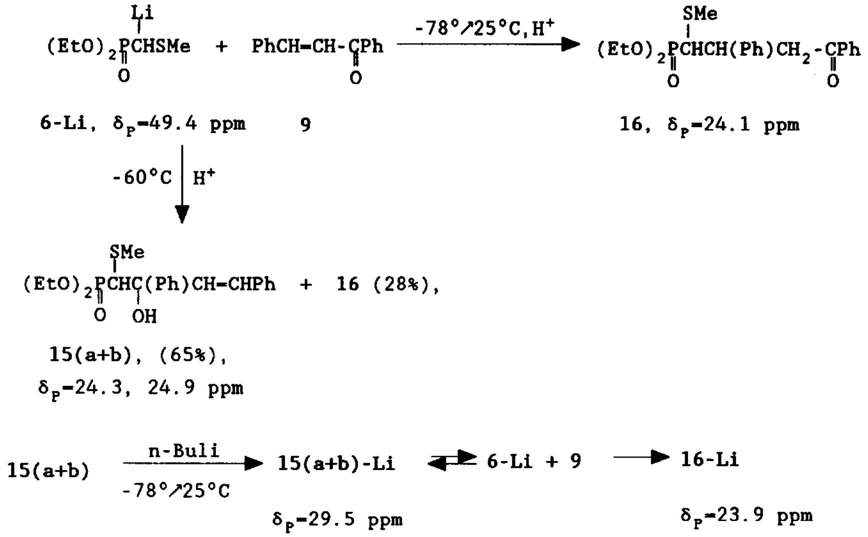
In view of a strong temperature dependence of the 1,2/1,4-addition ratio observed for the reactions of **2-Li** with enones, the addition of **6-Li** to chalcone **9** was carried out and quenched at low temperature (-78°÷-60 °C) and at room temperature. Moreover, in both cases the course of the reaction was followed by ^{31}P NMR spectra. It was found that at low temperature the reaction affords two diastereomeric 1,2-adducts **15(a+b)** (65%) and the 1,4-adduct **16** as a single diastereomer (28%) which were separated by column chromatography.

At 25 °C, however the addition of **6-Li** to **9** resulted in the formation of one diastereomeric 1,4-adduct **16** only isolated in 76% yield. Therefore, it is quite reasonable to assume that the 1,2-adducts **15** are kinetically controlled products that undergo isomerization to the thermodynamically more stable 1,4-adduct **16**. This was confirmed by an independent experiment in which a mixture of the 1,2-adducts **15(a+b)** (1:1 ratio) was treated with stoichiometric amounts of n-butyllithium to give the 1,4-adduct **16** as a main product after 20h at 25 °C. It was accompanied only by the starting lithiophosphonate **6-Li** and chalcone **9**, formation of which was an evidence for a decomposition of **15** back to substrates and for a reiterated attack of **6-Li** on **9** in a 1,4-manner.

It is interesting to point out that, in contrast to the 1,2-adducts formed from dithioacetals **2** with enones, the adducts **15** do not decompose to the corresponding conjugated vinyl sulphides i.e. Horner-Wittig reaction products. Most probably the energy of decomposition of **15** to give the Horner-Wittig products is much higher than that for its rearrangement to **16**.

DISCUSSION

Addition of carbanions to α,β-unsaturated carbonyl compounds represents one of the most important reactions used to lengthen a carbon chain of organic molecules. In



Scheme 3

addition to its great synthetic value, this reaction has been a subject of wide mechanistic studies.[12] Especially interesting was a question of 1,2- versus 1,4-addition, its reversibility and the interconversion of the 1,2- and 1,4-adducts formed. Although some general rules are known which allow to predict the regioselectivity of the addition, in many cases small structural changes both in a nucleophile and enone lead to unpredictable reaction pathway. For instance, 2-lithio 1,3-dithianes and 1,3,5-trithianes react with enones in a 1,2-fashion.[13] However, the lithium derivatives of 2-aryl-1,3-dithianes undergo addition to α,β-unsaturated carbonyl compounds preferentialy in a 1,4-manner or show a tendency towards 1,2→1,4 isomerisations.[14] Similarly behave carbanions derived from acyclic dithioacetals.[15] Furthermore, while addition of 1-lithio-isobutyl phenyl sulphide to cyclohexenone gives 1,2-adduct,[16] the replacement of the isopropyl group in this sulphide by the carbomethoxy group, which does better stabilise negative charge, causes a dramatic change of reactivity and the formation of 1,4-adduct is observed.[17]

The presence of the α-phosphoryl group in the dithioacetal and sulphide structures **2** and **6** should also influence reactivity of the corresponding α-carbanion towards enones. A well-know property of the phosphoryl group to stabilize adjacent carbanion and its bulkiness should favour 1,4-addition. For the same reason, the α-phosphonate carbanions derived from **2** should show better tendency to add to enones in a 1,4-fashion than the corresponding carbanion derived from **6**. On the other hand, due to the presence of the α-phosphoryl group, the formation of the 1,2-adducts may be accompanied by their decomposition to give the Horner-Wittig reaction products.

Indeed, it has been found that α-lithio-α-phosphoryl dithioacetals **2** react both with aldehydes and ketones to give conjugated ketene dithioacetals as the final reaction products. However, aldehydes give the corresponding Horner-Wittig reaction products **7** via the hydroxy-adducts **8** (1,2-addition) as detected by ^{31}P NMR spectroscopy. The reaction course with α,β-unsaturated ketones is different. All the experimental data support the formation of the 1,4-adducts (**11** and **12**) as the first reaction intermediates that undergo isomerization to the 1,2-adducts (**13** and **14**) and the latter decompose to the Horner-Wittig products i.e. conjugated ketene dithioacetals **7**. The 1,4→1,2 adduct rearrangement observed in this case is, to the best of our knowledge, a very rare example of such process[18] and the only one demonstrated in organosulphur compounds.

As it was pointed out above, the α-phosphonate carbanion derived from the sulphide **6** is sterically less crowded and possesses a harder nucleophilic centre (due the presence of only one sulphur atom) than the corresponding carbanions derived from **2**. Therefore, it reacts with chalcone to give predominantly 1,2-adduct **15** at low temperatures. The latter, however, does not decompose to olefine but rearranges to the 1,4-adduct **16** as a more thermodynamically stable product.

$$1^\circ.\quad (RO)_2P(O)C(Li)(SR)_2 \xrightarrow{>C{=}C{-}CHO} [1,2\text{-adduct}]Li \longrightarrow \text{the Horner-Wittig reaction products}$$

$$2^\circ.\quad (RO)_2P(O)C(Li)(SR)_2 \xrightarrow[-78^\circ C]{>C{=}C{-}C(O)R} [1,4\text{-adduct}]Li \xrightarrow[25^\circ C]{}$$

$$[1,2\text{-adduct}]Li \longrightarrow \text{the Horner-Wittig reaction products}$$

$$3^\circ.\quad (RO)_2P(O)CH(Li)SMe \xrightarrow[-78^\circ C]{>C{=}C{-}C(O)R} [1,2\text{-adduct}]Li \xrightarrow[25^\circ C]{}$$

$$[1,4\text{-adduct}]Li \xrightarrow{H^+} 1,4\text{-adduct}$$

Scheme 4

In summary, in this paper we report a general synthesis of conjugated ketene dithioacetals and present a diverse reactivity of α-phpsphonate carbanions towards α,β-unsaturated carbonyl compounds.

EXPERIMENTAL SECTION

Melting points are uncorected. ^{1}H-NMR spectra were recorded with a Perkin Elmer R12 B (60 MHz), a Tesla 35487C (80 MHz) and a Bruker HFX-72 (90 MHz) spectrometers. Tetramethylsilane was used as internal standard. ^{13}C-NMR spectra were recorded using the Bruker HFX-72 spectrometer. Hexamethyldisiloxane (HMDSO) and tetramethylsilane (TMS) were used as internal standards for these spectra. Column chromatography was performed with 40 Merck silica gel (70-230 mesh). Tetrahydrofuran (THF) and diethyl ether were dried over lithium aluminium hydride before use. n-Butyllithium was titrated not longer than 3-4 days before use with an acidimetric method[19]. Results of combustion analysis for compounds **8** and **7a-d** were not satisfactory despite several attempts including the low pressure sample handling at room temperature.

A. *A General Procedure for Synthesis of Conjugated Ketene Dithioacetals 7 from Aldehydes and Ketones.*

A solution of n-butyllithium (0.011 mol) in n-hexane was added dropwise under nitrogen, at -78 °C to a stirred solution of α-phosphoryl dithioacetal **2a**, **2b** or **2c** (0.01 mol) in dry THF (30 ml). The solution was stirred at this temperature for 10 minutes and a solution of α,β-unsaturated aldehyde or ketone (0.01 mol) in dry THF (15 ml) was added dropwise within 15 minutes. The reaction was slowly warmed to room temperature (45 min.). In case of aldehydes the reaction was completed at room temperature. With ketones stirring at 25 °C was continued for a longer time (see Table) under nitrogen and moisture free atmosphere. After evaporation of the solvents, the residue was dissolved in chloroform and washed with saturated aqueous ammonium chloride (2x) and water. The combined chloroform solutions were dried over $MgSO_4$, filtrated and evaporated to give a crude product which was purified by column chromatography over silica using a gradient of n-hexane/acetone as eluent.

1,1-Bis(methylthio)pentadiene-1,3 (7a): 50%; isomer ratio not established; $n_D(20)$ 1.5914; MSEI (m/z,%) 160 (2, $M^{+\cdot}$), ^1H-NMR (60 MHz, CCl_4) δ 1.79 (brd, 3H, ^3J 6.5, CH_3CH), 2.25 (s, 6H, SCH_3), 5.75 (m, 1H, CH_3CH), 6.24-6.86 (m, 2H, vinyl protons);

1,1-Bis(methylthio)-4-phenylbutadiene-1,3 (7b): 75%; one isomer, $n_D(20)$ 1.5977; MSEI (m/z,%) 222 (37); ^1H-NMR (80 MHz, CCl_4) δ 2.30 (s, 6H, SCH_3), 6.32-7.52 (m, 8H, C_6H_5, vinyl protons);

1,1-Bis(methylthio)-3-benzylidenepentene-1 (7c): 70%; isomer ratio 7/1; $n_D(20)$ 1.6115; MSEI (m/z,%) 250 (3, $M^{+\cdot}$) ^1H-NMR (60 MHz, CCl_4) δ 1.08 (t, 3H, ^3J, 7.7, CH_2CH_3), 2.00-2.80 (m, 8H, SCH_3, $C\underline{H}_2CH_3$), 6.22-6.60 (m, 2H, vinyl protons); 7.20 (s, 5H, C_6H_5);

1,1-Bis(methylthio)-4,8-dimethylnonantriene-1,3,7 (7d): 69%; isomer ratio 3/1; $n_D(20)$ 1.5750; MSEI (m/z,%) 242 (11, $M^{+\cdot}$); ^1H-NMR (60 MHz, CCl_4) δ 1.61-1.81 (m, 9H, $(C\underline{H}_3)_2C$, $CH_2(CH_3)C$), 2.08 (m, 4H, $(CH_2)_2$, 2.24 (s, 6H, SCH_3) 4.79-5.25 (m, 1H,=CH, $(CH_2)_2$), 6.35-6.67 (m, 2H, vinyl protons);

2-(α-Pinenylidene)-1,3-dithiane (7e): 64%; isomer ratio not established; $n_D(20)$, 1.6058; MSEI (m/z,%) 252 (62, $M^{+\cdot}$); ^1H-NMR (60 MHz, CCl_4) δ 1.30, 1.87 (2s, 6H, CH_3), 1.96, (m,2H, $CHC\underline{H}_2CH$); 1.82-2.59 (m, 6H; $SCH_2C\underline{H}_2$, $CH_2C\underline{H}$=C, $HCC\underline{H}_2C\underline{H}CH_2$), 2.88 (brd, 4H, $^3J_{H-H}$, 6.3, SCH_2), 5.61 (m, 1H, $=\underline{H}CCH_2$), 6.06 (m, 1H, HC=CS); Anal.Calcd/Found for $C_{14}H_{20}S_2$: C, 66.61/66.80; H, 7.98/7.67;

2-(3-Phenyl-2-propenylidene)-1,3-dithiane (7f):[20] 70%; isomer ratio 1/1, m.p. 83.5-84 °C; MSEI (m/z,%) 234 (71, $M^{+\cdot}$), ^1H-NMR (60 MHz, $CDCl_3$) δ 96-2.40 (m, 2H, $SCH_2C\underline{H}_2$), 2.96 (brt, 4H, $^3J_{H-H}$ 6.5, SCH_2), 6.38-7.60 (m, 8H, C_6H_5, vinyl protons); Anal.Calcd./Found for $C_{13}H_{14}S_2$: C, 66.61/66.40; H, 6.03/6.08; S, 27.36/27.36;

2-(2-Benzylidenebutylene)-1,3-dithiane (7g): 65%; isomer ratio not established; $n_D(20)$, 1.6453; MSEI (m/z,%) 262 (64, $M^{+\cdot}$); ^1H-NMR (60 MHz, CCl_4) δ 1.10 (brt, 3H, $^3J_{H-H}$ 8.0, $CH_2C\underline{H}_3$), 2.20-3.16 (m. 8.0, $SC\underline{H}_2C\underline{H}_2$, $C\underline{H}_2CH_3$), 6.30-6.45 (m, 2H, vinyl protons), 7.2 (s, 5H, C_6H_5); Anal.Calcd./Found for $C_{15}H_{18}S_2$: C, 68.65/68.70; H, 6.91/6.90; S, 24.44/24.38;

2-(2-Butenylidene)-1,3,5-trithiane (7h): 50%; isomer ratio 37/1; $n_D(20)$, 1.6730; MSEI (m/z,%) 190 (11, $M^{+\cdot}$); ^{1}H-NMR (60 MHz, CCl_4) δ 1.78 (d, 3H, $^3J_{H-H}$ 7.0: CH_3CH), 4.02 (s, 4H, CH_2SCH_2), 5.70 (m, 1H, $CH_3CH=$), 6.05-6.60 (m, 2H, vinyl protons); Anal.Calcd./Found for $C_7H_{10}S_3$: C, 44.17/44.35; H, 5.29/5.40;

2-(3-Phenyl-2-propenylidene)-1,3,5--trithiane (7i): 60%; isomer ratio 35/10; m.p. 101.5 °C: MSEI (m/z,%) 252 (25, $M^{+\cdot}$); ^{1}H-NMR (60 MHz, $CDCl_3$) δ 4.05 (s, 4H, CH_2SCH_2), 6.37-7.60 (m, 8H; C_6H_5, vinyl protons); Anal.Calcd./Found for $C_{12}H_{12}S_3$: C, 57.12/57.40; H, 4.76/4.90;

2-(1,3-diphenyl-2-propenylidene)-1,3-dithiane (7j): 53%; isomers ratio 63/1; m.p. 106 °C; MSEI (m/z,%) 310 (100, $M^{+\cdot}$); ^{1}H-NMR (80 MHz, $CDCl_3$) δ 1.98 (m, 2H, $SCH_2\underline{CH_2}$), 2.80 (m, 4H, SCH_2), 6.88 (AB, 2H, J_{AB} 16.5, vinyl protons); Anal.Calcd./Found for $C_{19}H_{18}S_2$: C, 73.50/73.72; H, 5.84/5.80;

2-(1-Methyl-3-phenyl-2-propenylidene)-1,3-dithiane (7k): 33%; isomer ratio not established; m.p. 64-66 °C; MSEI (m/z,%), 248 (12, $M^{+\cdot}$); ^{1}H-NMR (60 MHz, CCl_4) δ 1.72-2.30 (m, 2H, $SCH_2\underline{CH_2}$), 2.02 (s, 3H, CH_3), 2.89 (m, 4H, SCH_2), 7.0 (AB, 2H, J_{AB} 15.9, vinyl protons), 7.05-7.60 (m, 10H, C_6H_5); Anal.Calcd./Found for $C_{14}H_{16}S_2$: C, 67.69/67.90; H, 6.49/6.61.

Synthesis of Diethyl 1,1-Bis(methylthio)-2-hydroxy-4-phenyl-3-butenephosphonate (8):

A solution of n-butyllithium (0.011 mol) in n-hexane was added dropwise to a stirred solution of diethyl bis(methylthio)methanephosphonate **2a** (0.01 mol, 2.44 g) in dry tetrahydrofuran (50 ml) under nitrogen at -78 °C. Vigorous stirring at this temperature was continued for 10 minutes and the temperature of the reaction mixture was carefully lowered to -95 °C. Then, a solution of cinnamaldehyde (0.01 mol, 1.32 g) in a cold, dry tetrahydrofuran (20 ml) was poured into the reaction mixture. The temperature was maintained between -95 °C÷-85 °C. Next, a precooled (-70 °C) solution of sulfuric acid in tetrahydrofuran was added at this temperature until the reaction mixture became colourless. The reaction mixture was warmed to room temperature, water was added solvents were evaporated and the residue was dissolved in chloroform. The chloroform layer after separation from an aqueous one was washed with water, dried over $MgSO_4$, filtered and evaporated to give a liquid which was purified using chromatography over silica (eluent: a gradient of benzene/acetone), to afford pure **8** (2.78 g, 74%); the compound decomposed during distillation. Its purity was checked by the HPLC technique; $n_D(20)$ 1.5629; ^{31}P-NMR ($CHCl_3$) δ 20.9 ppm; ^{1}H-NMR (60 MHz, $CDCl_3$) δ 1.27, 1.31 (2t, 6H, $^3J_{H-H}$7.5, $\underline{H}_3CH_2O$), 2.20 (s, 6H, SCH_3), 3.80-4.80 (m, 6H; $CH_3C\underline{H}_2O$, $C\underline{H}$-$O\underline{H}$) 6.50-7.50 (m, 7H, C_6H_5, vinyl protons); ^{13}C-NMR ($CDCl_3$/HMDSO) δ 10.8 (s, SCH_3); 14.5 (d, J_{POCC} 5.9, $\underline{C}H_3CH_2O$), 59.8 (d, J_{PC} 151.5, PC); 62.3 (m, $CH_3\underline{C}H_2O$, $\underline{C}H(OH)$), 124.8, 125.3, 125.7, 126.6, 130.5, 134.9 (m, phenyl and olefin protons not discerned),

Nucleophilic Addition of 2b-Li to α,β-Unsaturated Ketones. Synthesis of 11 and 12

A solution of n-butyllithium (0.011 mol) in n-hexane was added dropwise under nitrogen at -78 °C to a stirred solution of 2-(diethoxyphosphoryl)-1,3-dithiane (0.01 mol, 2.50 g) in dry THF (70 ml). The resulting solution was stirred at this temperature for 10 minutes and a solution of α,β-unsaturated ketone (0.01 mol) in dry THF (20 ml) was added dropwise within 15 minutes. After stirring for additional 15 minutes the reaction mixture was neutralised with a solution of p-toluenesulfonic acid in THF. The mixture was warmed to room temperature, evaporated and the residue dissolved in chloroform. The chloroform solution was washed with water (2x), dried over $MgSO_4$, filtered and evaporated to give the crude products **11**, **12** which were purified using column chromatography over silica and a gradient of benzene/acetone as eluent.

Diethyl 1,1-(1,3-Propylenedithio)-2,4-diphenyl-4-oxo-butanephosphonate (11): 83%; m.p. 87-89°C, MSEI (m/z,%) 464 (0.4, $M^{+\cdot}$); ^{31}P-NMR (CCl_4) δ 16.7 ppm; ^{1}H-NMR (90 MHz, $CDCl_3$) δ 1.02, 1.36 (2t; 6H, $^3J_{H-H}$ 7.0, $C\underline{H}_3CH_2O$), 1.75-2.16 (m, 2H, $C\underline{H}_2CH_2S$), 2.45-2.63 (m, 2H, $CH_{2(eq)}S$), 3.45-4.40 (m, 5H, $CH_2C\underline{H}$, $CH_{2(ax)}S$), 3.97; 4.24 (2 dq, 4H, $^3J_{POC}$ 7.0, Hz, CH_3CH_2O), 7.15-7.90 (m, 10H, C_6H_5); ^{13}C-NMR ($CDCl_3$/TMS) δ 16.4 (m, $\underline{C}H_3CH_2O$), 23.9 (s, $\underline{C}H_2CH_2S$), 27,2, 28.0 (s, CH_2S), 42.2 (d, J_{PCC} 4.4, P-C-$\underline{C}$), 46.9, (s, C(O)$\underline{C}H_2$), 51.3 (d, J_{PC} 157.4 Hz, P-C); 63.8 (m, $CH_3\underline{C}H_2O$); 127.1, 127.3, 128.0, 128.4, 130.7, 132.4, 137.4, 139.4 (m, C_6H_5), 197.5, (s, C=O); Anal.Calcd./Found for $C_{23}H_{29}O_4PS_2$: C,59.46/59.21; H, 6.28/6.40; P, 6.68/6.67; S, 13.80/13.59.
The structure **11** was confirmed by conversion to 2,4-dinitrophenylhydrazone (orange crystals, m.p. 139-141°C; Anal.Calcd./Found for $C_{29}H_{36}N_4O_7PS_2$: C, 53.78/53.70; H, 5.60/5.76; P, 4.78/5.04).

Diethyl 1,1-(1,3-Propylenedithio)2-phenyl-4-oxo-pentanephosphonate 12: 65%; m.p. 84-86°C, MSEI (m/z,%) 402 (0.2, $M^{+\cdot}$); IR (C=O) 1708 cm^{-1} (Nujol); ^{31}p-NMR (CCl_4) δ 16.9; ^{1}H-NMR (90 MHz, $CDCl_3$) δ 0.99, 1.37 (2t, 6H, $^3J_{H-H}$ 7.0, $C\underline{H}_3CH_2O$), 1.61-2.38 (m, 2H, $C\underline{H}_2CH_2S$), 1.99 (s, 3H, CH_3), 2.42-2.62 (m, 2H, $CH_{2(eq)}S$), 2.98-4.38 (m, 5H, CH_2CH, $CH_{2(ax)}S$); 3.94, 4.22, (2 dq, 4H, $^3J_{H-H}$ 7.0 Hz, $CH_3C\underline{H}_2O$), 7.17-7.41 (m, 5H, C_6H_5); ^{13}C-NMR ($CDCl_3$/HMDSO) δ 16.0 (m, $\underline{C}H_3CH_2O$); 23.9 (s, $\underline{C}H_2CH_2S$); 27.2, 28.0, (2s, $S\underline{C}H_2CH_2\underline{C}H_2S$); 30.3 (s, C(=O)$\underline{C}H_3$); 46.8 (d, $^2J_{PCC}$ 7.4, P-C-$\underline{C}H$); 46.9 (s, C(=O) $\underline{C}H_2$); 51.1 (d, $^1J_{PC}$ 158.8, P-C); 63.9 (m, $CH_3\underline{C}H_2O$); 127.1, 127.4, 130.7, 139.7 (m, C_6H_5); 205.7 (s, C=O); Anal.Calcd./Found for $C_{18}H_{27}O_4PS_2$: C, 53.72/53.35; H, 6.76/6.68; P, 7.70/7.80; S, 15.93/15.64.

Nucleophilic Addition of 1-Lithio-1-(diethoxyphosphoryl)methyl Methyl Sulphide 6-Li to 1,3-Diphenyl-2-propen-1-one (Chalcone).

A solution of n-butyllithium (0.021 mol) in hexane was dropped under argon to a stirred solution of 1-(diethoxyphosphoryl)methyl methyl sulphide **6** (3.96 g, 0.02 mol) in dry tetrahydrofuran (200 ml) cooled to -78°C. After 15 minutes, a solution of chalcone (4.16 g, 0.02 mol) in tetrahydrofuran (50 ml) was added dropwise at this temperature. After additional 15 minutes of stirring, a reaction mixture was neutralised at -78°C÷-60°C and then warmed up to room temperature,

After evaporation of solvents, a residue was dissolved in CH_2Cl_2 (250 ml), washed with saturated aqueous solution of NH_4Cl (100 ml) then with water (2x100 ml) and dried over anhydrous $MgSO_4$. Filtration and evaporation of CH_2Cl_2 afforded a mixture of three products which were separated using column chromatography (Merek silica gel 40, 70-230 mesh, eluent: a gradient of CCl_4/acetone).

Diethyl 1-methylthio-2-hydroxy-2,4-diphenyl-3-butenephosphonate (15a) (one diastereomer) 32%; m.p.=117-119°C ^{31}P-NMR (CCl_4) δ 24.9 ppm; ^{1}H-NMR (90 MHz, $CDCl_3$) δ 1.15, 1.25 (2t, 6H, $^3J_{H-H}$ 7.0, $C\underline{H}_3CH_2O$); 2.15 (s, 3H; SCH_3) 3.22 (d, 1H, $^2J_{P-H}$ 18.0, P-CH); 4.01, 3.98 (2 dq, 4H, $^3J_{P-H}$ 7.0 Hz, CH_3CH_2O), 5.12 (s, 1H, CH), 6.88-7.95 (m, 12H: C_6H_5, vinyl protons); MSEI (m/z,%) 406 ($M^{+\cdot}$, 0.34).

Diethyl 1-methylthio-2-hydroxy-2,4-diphenyl-3-butenephosphonate (15a) (second diastereomers): 33%; m.p. 82-83.5°C (ether/n-hexane), ^{31}P-NMR (CCl_4) δ 24.3 ppm; ^{1}H-NMR (90 MHz, $CDCl_3$) δ 1.28, 1.17 (2t, 6H, $^{3}J_{H-H}$, 7.0, CH_3CH_2O), 1.55 (s, 3H, SCH_3), 3.05 (d, 1H, $^{2}J_{P-H}$ 19.0, PCH), 4.03, 4.06, (2 dq, 4H, $^{3}J_{P-H}$ 7.0 Hz, $CH_3C\underline{H}_2O$), 5.78 (s, 1H, CH), 7.06-7.85 (m, 12H, C_6H_5, vinyl protons); MSEI (m/z,%) 406 ($M^{+\cdot}$, 0.34). Anal. Calcd/Found for C_{21}, $H_{27}O_4PS$: C, 62.05/61,96; H, 6.69/6.69: P, 7.62/7.79; S, 7.90/8.32; O, 15.74/15.42.

Diethyl 1-methylthio-2,4-diphenyl-4-oxobutanephosphonate (16) 28%; m.p. 59-61°C; ^{31}P-NMR (CCl_4) δ 24.1 ppm; ^{1}H-NMR (90 MHz, $CDCl_3$) δ 1.28 (*t*, 6H, $^{3}J_{H-H}$ 7.0, CH_3CH_2O), 1.95 (m, 3H, SCH_3), 2.86 (dd, 1H, $^{2}J_{P-H}$ 19.0, $^{3}J_{H-H}$, 7.0, P-C$\underline{H}$-CH), 3.60-4.50 (m, 7H: $CH_3C\underline{H}_2O$, $C\underline{H}$-$C\underline{H}_2$), 7.02-8.12 (m, 10, C_6H_5), MSEI (m/z,%) 406 ($M^{+\cdot}$, 1.4). Anal.Calcd/Found for $C_{21}H_{27}O_4PS$: C, 62.05/62.25; H, 6.69/6.78; P, 7.62/7.64; S, 7.89/7.92.

Rearrangement (15a-Li/15b-Li→16-Li) - [(1,2)$^-$→(1,4)$^-$]

a) A mixture of diastereomeric 1,2-adducts **14a/14b** (52/48) (60 mg, 0.15 mmol) was dissolved in dry THF (15 ml) and treated dropwise with stoichiometric amount of n-butyllithium at -78°C. The reaction mixture was gradually warmed up to room temperature, left overnight at this temperature and worked up as above. After purification using column chromatography over silica gel the 1,4-adduct **16** was isolated in 70-80% yield.

b) The reaction of **6**-Li with chalcone was performed as described above. Then, the reaction mixture was allowed to warm up to room temperature, left overnight, neutralised, worked up and purified as above. The 1,4-adduct **16** was isolated in 76.5% yield (80-100% based on ^{31}P-NMR spectrum).

B. *^{31}P-NMR studies at low temperatures*

All measurements were done with Jeol JNM-FX 60 (24,3 MHz) and Bruker HFX-72 (36,4 MHz) spectrometers using 85% solution of phosphoric acid as an external standard.

Samples were prepared in the following manner. α-Phosphoryl dithioacetals **2** (0.5 mmol) were preweighted in 10 mm NMR tubes. Before addition of stoichiometric amount of n-butyllithium, 1 ml of dry tetrahydrofuran was added to each sample and the resulting solution was precooled in the dry-ice/acetone bath. All measurements were performed in the range of -78°C÷25°C with continuous change of temperature in the probe.

Reaction of 2a-Li with cinnamaldehyde

A precooled solution of cinnamaldehyde in dry tetrahydrofuran was quickly poured to a solution of **2a**-Li in THF at -95°C. A narrow signal at δ=42.2 ppm disappeared and a broad signal at δ=26.9 ppm attributed to the lithium derivative of the 1,2-adduct **8**-Li appeared in the spectrum. Subsequent quick neutralisation by means of precooled aqueous solution of sulfuric acid afforded three signals at δ=20.6 (46-80%), 18.1 and 0.7 ppm due to the 1,2-adduct **8**, starting material **2a** and phosphoric acid, respectively.

Reaction of 2b-Li with Chalcone and Benzylideneacetone. Rearrangement of 11-Li→13-Li→7j - [(1,4)$^-$→(1,2)$^-$]→ the Horner-Wittig product

Addition of a tetrahydrofuran solution of chalcone to a solution of **2b**-Li in tetrahydrofuran caused disappearance of a signal at δ=41.4 ppm and observation of a new broad signal at δ=24.8 ppm which corresponded to **11**-Li. The latter signal disappeared upon acidification to yield a new one at δ=16.9 ppm attributed to **11**. Similar δ values were obtained for benzylideneacetone.

When the lithiated adduct **11-Li** remained on standing under argon at 25°C, (315 hrs for chalcone and 146 hrs for benzylideneacetone) a signal at δ=24.8 ppm gradually disappeared and two signals at δ=17.4 ppm (10%) and δ=0.5 ppm (77%) due to the protonated **2b** and lithium salt of phosphoric acid, respectively, gradually appeared in the spectrum.

When a pure 1,4-adduct **11** was treated in a THF solution with LDA at -78°C, the signal at δ=16.9 ppm disappeared and a broad signal at δ=24.8 ppm which was attributed to the 1,4-adduct appeared in the spectrum. After a prolonged standing at 25°C only two signals remained in the spectrum at δ=17.4 ppm (60%) and δ=0.5 ppm (40%).

Reaction of 6-Li with Chalcone **9**. *Rearrangement of 15a-Li/15b-Li→16-Li* $[(1,2)^- \rightarrow (1,4)^-]$

After addition of n-BuLi to a solution of **6** in THF at -60°C, a signal at δ=24.5 ppm due to **6** disappeared and a signal at δ=49.4 ppm due to its lithium derivatives **6-Li** appeared in the spectrum. Subsequent addition of stoichiometric amount of the THF solution of chalcone caused disappearance of the latter signal and appearance of two new signals at δ=29.5 ppm (65%, broad, due to **15a/15b-Li**) and δ=23.9 ppm (28%, narrow, due to **16-Li**). Intensity of the former signal gradually decreased while the latter one increased to 93% upon rising temperature from -60°C to 25°C.

Acidification of the reaction at -60°C caused appearance of three signals at δ=24.1 ppm (28%) due to the 1,4-adduct **16**, δ=24.3 ppm and δ=24.9 ppm (33%, all values after work-up, in CCl_4) due to the diastereomeric mixture of **15a/15b**. Acidification at 25°C gave only one signal at δ=24.1 ppm (CCl_4).

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