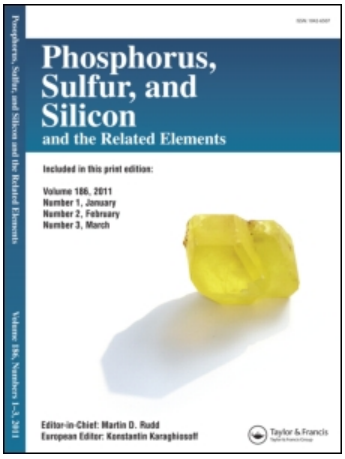


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# FREE RADICAL DESULFENYLATION AND DESELENYLATION OF α-SULFUR AND α-SELENO SUBSTITUTED PHOSPHONATES WITH THE *n*- $Bu_3SnH$/AIBN REAGENTS SYSTEM[1]

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# FREE RADICAL DESULFENYLATION AND DESELENYLATION OF α-SULFUR AND α-SELENO SUBSTITUTED PHOSPHONATES WITH THE *n*-$Bu_3SnH$/AIBN REAGENTS SYSTEM[1]

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Selective desulfenylation and deselenylation of α-sulfur- and α-seleno-substituted phosphonates under free radical conditions are described. Chemoselectivity and scope of the title reactions were studied using phosphonates additionally functionalized in the α-position by alkyl, phenyl, ethoxy, chloro, carbonyl and sulfenyl groups. It was found that reduction of a halogen tolerates the presence of the sulfenyl group and the latter could be reduced in the presence of the sulfinyl and sulfonyl moieties. Moreover, one sulfenyl group was selectively removed from α-phosphoryl dithioacetals and the phenylsulfenyl group was reduced preferentially in the presence of the methylsulfenyl one.

*Key words:* Desulfenylation, deselenylation, α-phosphoryl sulfides, α-phosphoryl selenides, tri-n-butyltin hydride, α,α'-azaisobutyronitrile.

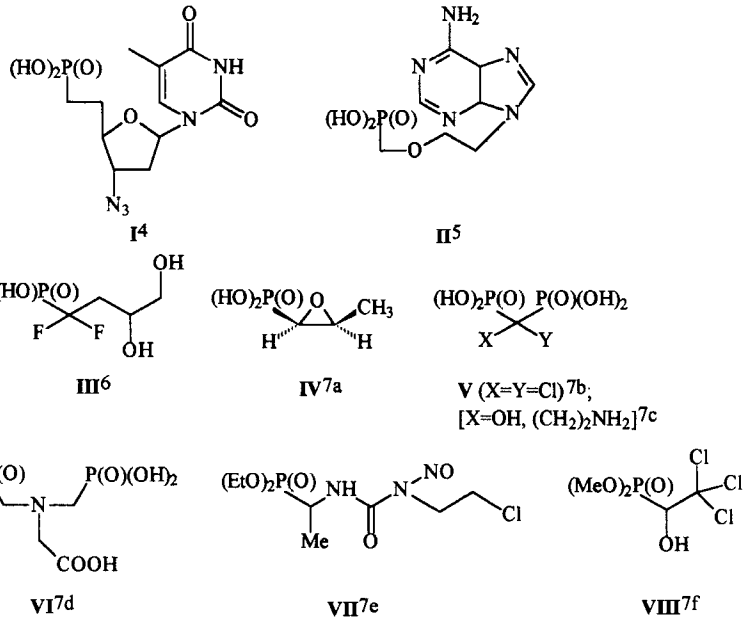


## INTRODUCTION

Organosulfur and organoselenium compounds constitute versatile reagents enabling a series of interesting transformations after which sulfur and selenium atoms are removed from the molecules, usually through the elimination, hydrolysis or reduction processes. Among these reagents particularly interesting are the phosphonates containing sulfur and selenium in the α position to phosphorus.[2] Although numerous methods exist for the preparation of these α-heterosubstituted phosphonates, there is a lack of the reverse and selective processes for removing the sulfur or selenium containing groups from the α position of these phosphonates.[3]

Recently Barton *et al.* showed a nice application of the *n*-$Bu_3SnH$/AIBN reagent system for removal of the α-pyridinesulfenyl residue from a phosphonate molecule to give the phosphonate isostere I which mimics AZT-5'-monophosphate. This compound and many other phosphonates II–VIII, examples of which are shown in Scheme I, constitute a rich family of phosphonates useful in medicine and agriculture.[5–7a–f]

Having this in mind, in a continuation of our interest in the synthesis of natural products and other compounds exhibiting biological activity using organosulfur and organophosphorus compounds,[8] in this paper we describe a general method for α-desulfenylation and α-deselenylation of phosphonates harnessing the *n*-$Bu_3SnH$/AIBN system.



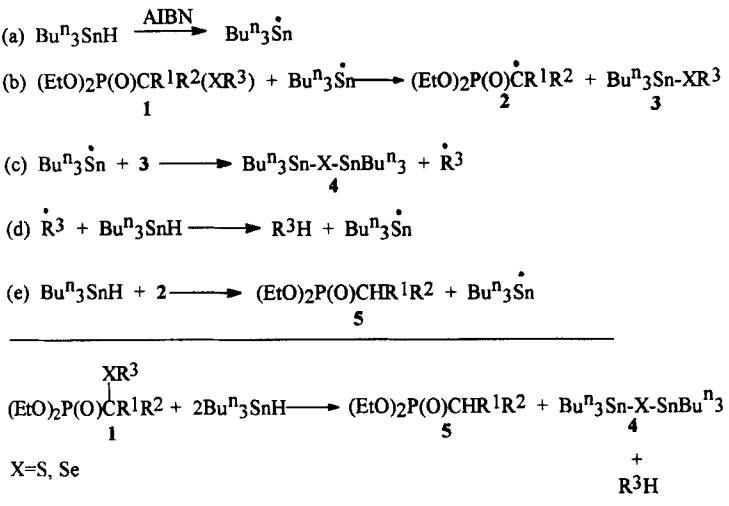

SCHEME I

## RESULTS AND DISCUSSION

It was found that the *n*-$Bu_3SnH$/AIBN reagent system in refluxing toluene cleaves selectively the $\alpha$-carbon-sulfur and $\alpha$-carbon-selenium bonds in the phosphonates **1** according to Scheme II.

In accord with the summary equation, the reaction requires two equivalents of tri-n-butyltin hydride with the exception of the reduction of the C—Cl and C—S bonds in **1n** and **1o** for which 1.6 eq of the hydride was used. In order to study the scope and limitations of this reaction, various $\alpha$-heterosubstituted phosphonates like $\alpha$-phosphoryl sulfides, sulfoxides and sulfones, $\alpha$-phosphoryl selenides, $\alpha$-phosphoryl O,S- and S,S-acetals were synthesized and caused to react under the above reaction conditions. These substrates were both unsubstituted and substituted at the $\alpha$-position by the alkyl, phenyl, chloro and carbonyl groups. The $SR^3$ and $SeR^3$ residues to be removed were also differentiated: $R^3$ = Me, $C_6H_5$, p-$CH_3$-$C_6H_4$ and cyclic.

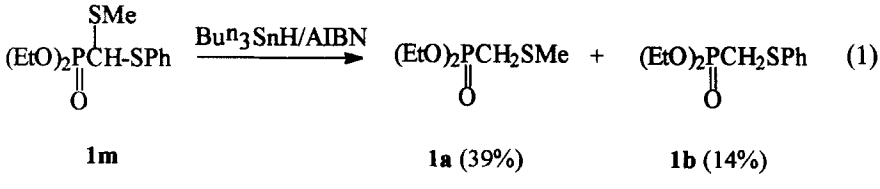
In the course of these investigations, it turned out that $\alpha$-phosphoryl sulfides and $\alpha$-phosphoryl selenides were reduced smoothly through attack of the tin radical at sulfur or selenium atoms. The steric hindrance at the $\alpha$-phosphonate carbon atom did not affect the reaction yield which remained high and comparable to other substrates (**1h**, 86% versus 80% average, Table I). On the other hand, reduction of $\alpha$-hetero [O,S,Cl,$(EtO)_2P(O)$] substituted $\alpha$-phosphoryl sulfides requires a separate discussion due to the electronic diversity borne by these heterogroups and a possibility of their selective reduction. Thus, reduction of the C—Cl bond in **1n**



SCHEME II



tolerates a sulfenyl group unlike the reduction of the α-phosphoryl O,S-acetal **1j** wherein the sulfenyl group was reduced completely. Considering **1j** as the Pummerer reaction product of the corresponding sulfoxide **1p**, the latter reduction constitutes a key step in the conversion of α-phosphoryl sulfides via sulfoxides to α-phosphoryl ethers such as **5g**—a simple, structural analogue of II (Scheme I). Reduction of the α-phosphoryl S,S-dimethyl acetal **1k** and its diphenyl analogue **1l** was accomplished selectively without any preference to a particular sulfenyl group and gave the corresponding α-phosphoryl sulfides **1a** and **1b** in good yields. However, further reduction of the latter sulfides using the same synthetic procedure showed that the tributylstannyl radical prefers to react with the PhS group rather than with the MeS one.[10] Thus, **1b** was reduced almost completely (7% of **1b** left in the reaction mixture) whereas under the same conditions 42% of **1a** was recovered. The same bias was observed for the reduction of the α-phosphoryl S-methyl S-phenyl-acetal **1m**, however, the selection was not complete in this case two different α-phosphoryl sulfides **1a** and **1b** were found in the reaction mixture (Equation 1).

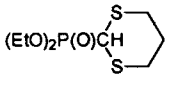


**1m** **1a** (39%) **1b** (14%) (1)

Further demonstration of different reactivity of the tributylstannyl radical towards the PhS and MeS groups was the formation of two different products **5a** and **5f** upon treatment of the structurally similar **1c** and **1i** with the *n*-$Bu_3SnH$/AIBN reagent system. Formation of the β-ketophosphonates **5f** as the major product of the reduction of **1i** and as the minor one of the reduction of **1c** may be explained

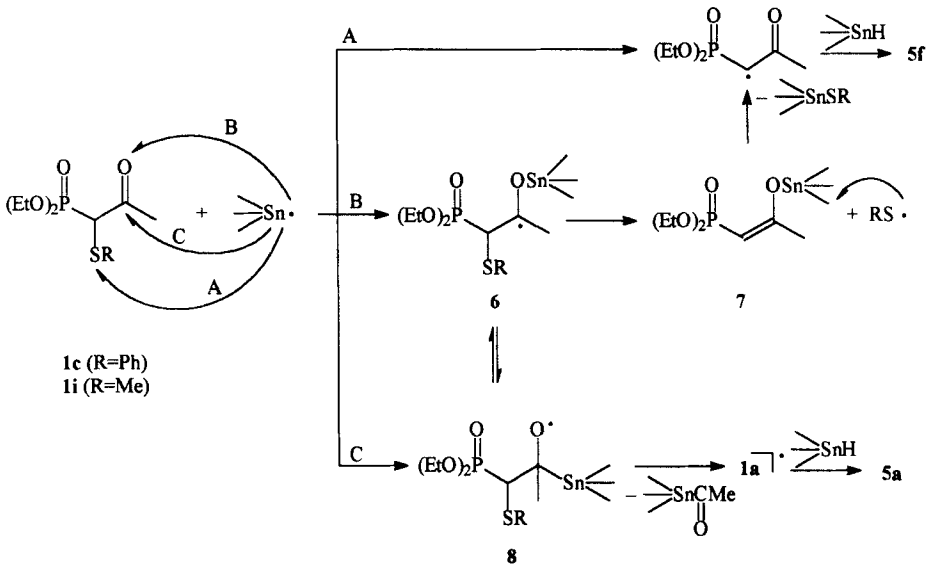
TABLE I

Desulfenylation and deselenylation of $\alpha$-sulfur- and $\alpha$-seleno-substituted phosphonates with the $n$-$Bu_3SnH$/AIBN system

| Substrate (1) | Product (5) | $\delta_{31P}(CDCl_3)$ 1/5 | Yield[a] [%] |
|---|---|---|---|
| $(EtO)_2P(O)CH_2SMe$ (1a) | $(EtO)_2P(O)Me$ (5a) | 24.8/30.8 | 55 |
| $(EtO)_2P(O)CH_2SPh$ (1b) | 5a | 23.4/30.8 | 80 |
| $(EtO)_2P(O)CH(SPh)C(=O)Me$ (1c) | 5a | 23.6(enol);16.2 (ketone)/30.8 | 66 |
| $(EtO)_2P(O)CH(SPh)Me$ (1d) | $(EtO)_2P(O)CH_2Me$ (5b) | 26.7/34.0 | 76 |
| $(EtO)_2P(O)CH(Sp\text{-}Tol)Me$ (1e) | 5b | 26.8/34.0 | 80 |
| $(EtO)_2P(O)CH(SPh)n\text{-}C_6H_{13}$ (1f) | $(EtO)_2P(O)CH_2n\text{-}C_6H_{13}$ (5c) | 26.4/33.1 | 78 |
| $(EtO)_2P(O)CH(SPh)Ph$ (1g) | $(EtO)_2P(O)CH_2Ph$ (5d) | 21.8/27.0 | 89 |
| $(EtO)_2P(O)C(SPh)Me_2$ (1h) | $(EtO)_2P(O)CHMe_2$ (5e) | 29.3/35.7 | 86 |
| $(EtO)_2P(O)CH(SMe)C(=O)Me$ (1i) | $(EtO)_2P(O)CH_2C(=O)Me$ (5f) | 26.0(enol);17.8(keto-ne)/20.2 | 81 |
| $(EtO)_2P(O)CH(SMe)(OEt)$ (1j) | $(EtO)_2P(O)CH_2OEt$ (5g) | 16.6/21.9 | 82 |
| $(EtO)_2P(O)CH(SMe)_2$ (1k) | 1a | 19.1/24.8 | 85 |
| $(EtO)_2P(O)CH(SPh)_2$ (1l) | 1b | 19.5/23.4 | 86 |
| $(EtO)_2P(O)CH(SMe)(SPh)$ (1m) | 1a+1b | 19.3/24.8+23.4 | 39+14 |
| $(EtO)_2P(O)CH(SPh)Cl$ (1n) | 1b | 14.4/23.4 | 95[b] |
|  (1o) | $(EtO)_2P(O)CH_2S(CH_2)_3SSnBu_3^n$ (5h) | 25.0 | 85[b] |
| $(EtO)_2P(O)CH_2S(O)Me$ (1p) | 1p | 16.6 | 100 |
| $(EtO)_2P(O)CH_2S(O)Ph$ (1r) | 1r | 16.8 | 100 |
| $(EtO)_2P(O)CH_2SO_2Me$ (1s) | 1s | 12.5 | 100 |
| $(EtO)_2P(O)CH_2SO_2Ph$ (1t) | 1t | 11.8 | 100 |
| $(EtO)_2P(O)CH(SeMe)Me$ (1u) | 5b | 28.5/34.0 | 88 |
| $(EtO)_2P(O)CH(SePh)n\text{-}C_5H_{11}$ (1w) | $(EtO)_2P(O)CH_2n\text{-}C_5H_{11}$ (5i) | 27.5/33.2 | 70 |
| $(EtO)_2P(O)CH(SePh)Ph$ (1z) | 5d | 23.2/27.0 | 76 |
| $[(EtO)_2P(O)]_2CHS(C=S)NMe_2$ (1x) | $(EtO)_2P(O)CH_2P(O)(OEt)_2$ (5j) | 17.8/19.9 | 75 |

[a] The starting material (%) was recovered for 1a (42); 1b (7), 1c (4) + 5f (7); 1d (12); 1e (20); 1j (18); 1p-1t as given; 1u (7), 1w (7); 1z (5), 1x (20). In the case of 1i, 8% of 5a was formed.
[b] 1.6eq of n-$Bu_3SnH$ was used.

in terms of the thiophilic (pathway A) or oxophilic (pathway B) attack of the tributylstannyl radical **1** (Scheme III). In the latter case the adduct radical **6** undergoes desulfenylation followed by the destannylation of the stannyl enol ether **7** to give the $\beta$-ketophosphonate radical derived from **5f** which also constitutes a product of the thiophilic attack according to the pathway A. On the other hand, the unexpected formation of **5a** as the major product of the reduction of **1c** and as the

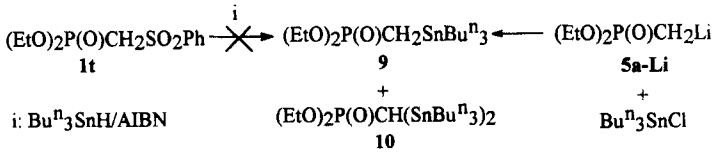



SCHEME III

minor one of the reduction of **1i** may be explained in terms of the carbophilic attack (pathway C) of the tributylstannyl radical at the carbonyl carbon to give the adduct radical **8** remaining in the equilibrium with the radical **6**. This carbophilic attack is favoured most probably due to a possibility of the elimination of the phenylthiomethylphosphonyl radical which constitutes a better leaving group than the methylthiomethylphosphonyl one expected for the reduction of **1i**. It is important to mention in this place that the formation of **5a** cannot be interpreted as a consequence of the further reduction of **5f** by the tin radical because such an attempted reduction brought a quantitative recovery of the starting material **5f**. Other mechanisms involving a transient formation of $\alpha$-stannyl phosphonates were also rejected because of the lack of such species in the $^{31}$P-NMR spectra of the crude reaction mixtures.

An interesting structure of the $\alpha$-bisphosphorylmethyl sulfide **1x** possessing the dithiocarbonyl moiety, affords the bisphosphonate **5j**, both having the P—C skeleton of the Clodronic and Pamidronic acids V (Scheme I). In this case there is a possibility for a bidirectional attack of the tin radical at the thiocarbonyl sulfur atom as in xanthates[11] or at the sulfenyl sulfur as in sulfides; both lead to the same product **5j**.

An attempted reduction of the $\alpha$-phosphoryl sulfoxides **1p** and **1r** resulted in a full recovery of the starting materials. Similarly, reduction of the $\alpha$-phosphoryl sulfones **1s** and **1t** performed in refluxing toluene or *o*-xylene solutions did not bring the anticipated tri-*n*-butylstannylphosphonate **9**,[12] which was prepared independently[13] according to the Scheme IV, but again resulted in a recovery of the starting materials. Treatment of a mixture of the $\alpha$-phosphoryl sulfide **1b**, sulfoxide **1r** and sulfone **1t** with the *n*-$Bu_3SnH$/AIBN reagent system brought the




SCHEME IV

reduction of the former to **5a** (16% of **1b** left) leaving the two latter unchanged. These results show that the presence of the diethoxyphosphoryl group facilitates the reduction of neither the sulfinyl nor the sulfonyl groups.

It is interesting to point out that attempted reduction of the β-sulfenylated phosphonate, i.e. diethyl 1-methylthiomethyl-2-oxobutanephosphonate showed a drastic difference in reactivity in comparison with the reduction of α-sulfenylated phosphonates and did not bring the expected reduction product but a mixture of 13 non-separable phosphorus compounds instead.

In conclusion, we described herein an efficient and selective method of desulfenylation and deselenylation of α-sulfenylated and α-selenylated phosphonates under free radical conditions. From these investigations one can further conclude that 1) reduction of halogen tolerates the presence of a sulfenyl group 2) sulfenyl group can be reduced in the presence of sulfinyl and sulfonyl ones 3) one sulfenyl group can be removed selectively from α-phosphoryl dithioacetals and 4) the phenylsulfenyl group is reduced preferentially in the presence of the methylthio one. The results obtained, especially those concerning the selective transformations, provide an approach to a variety of new α-alkyl, α-aryl and α-heterosubstituted phosphonyl radicals and in consequence lead to the synthesis of modified phosphonates of potential biological interest.



## EXPERIMENTAL

### *General*

The $^1$H- and $^{31}$P-NMR spectra were recorded at 200 and 81 MHz, respectively, using a Bruker AC200 spectrometer. The mass spectra at high resolution were obtained using a Finnigan Mat 95 spectrometer. The MS-GC spectrum of **5h** was obtained using a LKB 2091 spectrometer. The Merck silica gel (60, 230–400 mesh) was used for column chromatography.

### *Materials*

The compounds **1c** and **1i** were prepared by acylation of **1b–Li** and **1a–Li** (from **1b**/**1a** and n-BuLi at −78°C), respectively, with methyl acetate.[14] (−78°C ↗ 25°C/THF, 50–70%). The compounds **1d** and **1f** were synthesized by alkylation of **1b–Li** with methyl and *n*-hexyl iodides, respectively (−78°C ↗ 25°C/THF, **1d**-81%, **1f**-88%).[15] The compound **1h** was obtained by alkylation of **1d–Li** (from **1d** and *n*-BuLi in THF at −78°C) with methyl iodide (−78°C ↗ 25°C/2 hr, 50°C/20 min, THF, 70%).[15] The compounds **1e**, **1g** and **1m** were prepared by sulfenylation of the corresponding α-phosphonate carbanions with di-*p*-tolyl and diphenyl disulfides, respectively.[16] The compounds **1k**, **1l** and **1o** were synthesized by the Arbuzov reaction of the corresponding α-chlorodithioacetals with triethyl phosphite.[17] The compound **1n** was obtained by chlorination of **1b** with N-chlorosuccinimide (10°C ↗ 25°C, benzene, 24 hr, >90%). The compound **1p** was obtained from **1a** by modification of our procedure[18] ($H_2O_2$/MeOH, without $H_2SO_4$/2-propanol as the catalyst, 30 hrs/25°C, 80%). The compound **1r** was prepared by oxidation of **1b**[18] ($H_2O_2$/MeOH, with the catalyst, 30 hr, 91%). α-Phosphoryl sulfones **1s** and **1t** were synthesized by oxidation of **1a** and **1b** with the $SeO_2/H_2O_2$ reagent system[19] (**1s**, 82%, **1a**/$SeO_2$/$H_2O_2$ = 1/1/6; **1t**-100%; **1b**/$SeO_2/H_2O_2$ = 1/2/10, 24 hr). The compound **1u** was obtained from **5b–Li**

by addition of elemental selenium followed by alkylation with methyl iodide (yield: 90–95%).[20] α-Phosphoryl selenides **1w** and **1z** were prepared by selenylation of the corresponding α-phosphonate carbanions with phenylselenyl bromide (−78°C ↗ 25°C, THF).

*General procedure for reduction of α-sulfur-substituted phosphonates* **1a–1o, 1x** *and α-seleno-substituted phosphonates* **1u–1z**: To a refluxing solution of the appropriate α-sulfur- or α-seleno-substituted phosphonate (1 mmol) in the degassed toluene (16 ml), a solution of *n*-$Bu_3SnH$ (582 mg, 538 μl, 2 mmol; for the compounds **1n** and **1o**, 1.6 mmol of *n*-$Bu_3SnH$ was used) and AIBN (57 mg, 0.35 mmol) in toluene (8 ml) was added dropwise under argon using the syringe pump within 2 hours. The resulting solution was refluxed for additional 1 hour and after cooling to room temperature evaporated. The residue was distilled using the Kugelrohr apparatus (with exception of **5e**) and then further separated from the tin salts using a combination of column chromatography over silica gel (*n*-hexane and then a gradient of toluene/acetone) and the preparative TLC.

Spectral properties of the compounds obtained were compared with original samples and/or with the literature data.[13,21,22] The spectral properties of all compounds including the new H-P long range and Sn-P coupling constants and diastereotopy of the diethoxyphosphoryl groups are given below.

*Diethyl Methylthiomethylphosphonate* (**1a**)[22]: $n_D^{20}$ = 1.4667; $^1$H-NMR ($CDCl_3$), δ = 1.33 (dt, 6H, $^3J_{HH}$ = 7.1 Hz, $^4J_{HP}$ = 0.4 Hz, $POCH_2\underline{CH_3}$); 2.27 (d, 3H, $^4J_{HP}$ = 1.2 Hz, $SCH_3$); 2.67 (d, 2H, $^2J_{HP}$ = 12.8, $PCH_2$); 4.15, 4.16 (2xdq, 4H, $^3J_{HH}$ = 7.1 Hz, $^3J_{HP}$ = 8.1 Hz, $PO\underline{CH_2}CH_3$).

*Diethyl Phenylthiomethylphosphonate* (**1b**)[21,22]: $n_D^{20}$ = 1.5349; $^1$H-NMR ($CDCl_3$), δ = 1.29 (dt, 6H, $^3J_{HH}$ = 7.1 Hz, $^4J_{HP}$ = 0.3 Hz, $POCH_2\underline{CH_3}$); 3.19 (d, 2H, $^2J_{HP}$ = 14.1 Hz, $PCH_2$), 4.12, 4.13 (2xdq, 4H, $^3J_{HH}$ = 7.1 Hz, $^3J_{HP}$ = 8.0 Hz, $PO\underline{CH_2}CH_3$); 7.16–7.45 (m, 5H, $C_6H_5$).

*Diethyl Methylphosphonate* (**5a**)[21]: $n_D^{20}$ = 1.4123; $^1$H-NMR ($CDCl_3$); δ = 1.3 (dt, 6H, $^3J_{HH}$ = 7.0 Hz, $^4J_{HP}$ = 0.2 Hz; $POCH_2\underline{CH_3}$); 1.44 (d, 3H, $^2J_{HP}$ = 17.5 Hz, $PCH_3$); 4.06, 4.07 (2xdq, $^3J_{HH}$ = 7.0 Hz, $^3J_{HP}$ = 8.0 Hz).

*Diethyl Ethylphosphonate* (**5b**)[21]: $n_D^{20}$ = 1.4175; $^1$H-NMR ($CDCl_3$); δ = 1.14 (dt, 3H, $^3J_{HP}$ = 20.0 Hz, $^3J_{HH}$ = 7.7 Hz, $PCH_2\underline{CH_3}$); 1.31 (t, 3H, $^3J_{HH}$ = 7.1 Hz, P $OCH_2\underline{CH_3}$); 1.78 (dq, 2H, $^2J_{HP}$ = 18.2 Hz, $^3J_{HH}$ = 7.7 Hz, $P\underline{CH_2}CH_3$); 4.07, 4.08 (2xdq, 4H, $^3J_{HH}$ = 7.1 Hz, $^3J_{HP}$ = 8.1 Hz, $PO\underline{CH_2}CH_3$).

*Diethyl n-Heptylphosphonate* (**5c**): oil; $^1$H-NMR ($CDCl_3$); δ = 0.87 (t, 3H, $^3J_{HH}$ = 7.1 Hz, $(CH_2)_6\underline{CH_3}$); 1.31 (t, 6H, $^3J_{HH}$ = 7.1 Hz, $POCH_2\underline{CH_3}$); 1.19–1.79 (m, 12H, $(CH_2)_6$); 4.07, 4.08 (2xdq, 4H, $^3J_{HH}$ = 7.1 Hz, $^3J_{HP}$ = 8.1 Hz, $PO\underline{CH_2}CH_3$). Anal. Calcd. for $C_{11}H_{25}O_3P$ = 236.29; C-55.91; H-10.66; Found. C-55.81; H-10.70.

*Diethyl Benzylphosphonate* (**5d**)[21]: $n_D^{20}$ = 1.4958; $^1$H-NMR ($CDCl_3$); δ = 1.23 (t, 6H, $^3J_{HH}$ = 7.1 Hz; $POCH_2\underline{CH_3}$); 3.1 (d, 2H, $^2J_{HP}$ = 21.4 Hz; $PCH_2$); 4.00 (dq, 4H, $^3J_{HH}$ = $^3J_{HP}$ = 7.1 Hz, $PO\underline{CH_2}CH_3$), 7.15–7.47 (m, 5H, $C_6H_5$).

*Diethyl i-Propylphosphonate* (**5e**)[21]: oil; $^1$H-NMR ($CDCl_3$); δ = 1.15 (dd, 6H, $^3J_{HP}$ = 11.3 Hz, $^3J_{HH}$ = 7.1 Hz, $PCH(\underline{CH_3})_2$); 1.29 (t, 6H, $^3J_{HH}$ = 7.1 Hz, $POCH(\underline{CH_3})_2$); 1.29 (t, 6H, $^3J_{HH}$ = 7.1 Hz; $POCH_2\underline{CH_3}$); 1.91 (dsept, $^2J_{HP}$ = 18.6 Hz, 1H, $P\underline{CH}$); 4.06, 4.07 (2xdq, 4H, $^3J_{HH}$ = 7.1 Hz, $^3J_{HP}$ = 8.1 Hz, $PO\underline{CH_2}CH_3$).

*Diethyl 2-Oxo-n-propylphosphonate* (**5f**)[21]: $n_D^{20}$ = 1.4364; $^1$H-NMR ($CDCl_3$), δ = 1.32 (dt, 6H, $^3J_{HH}$ = 7.1 Hz, $^4J_{HP}$ = 0.5 Hz, $POCH_2\underline{CH_3}$); 2.30 (s, 3H, C(O)Me); 3.06 (2xd, 2H, $^2J_{HP}$ = 22.9 Hz, $PCH_2$); 4.12, 4.13 (2xdq, 4H, $^3J_{HH}$ = 7.1 Hz, $^3J_{HP}$ = 7.7 Hz, $PO\underline{CH_2}CH_3$).

*Diethyl Ethoxymethylphosphonate* (**5g**): oil; $^1$H-NMR ($CDCl_3$); δ = 1.20 (t, 3H, $^3J_{HH}$ = 7.0 Hz, $CH_2OCH_2\underline{CH_3}$), 1.33 (t, 6H, $^3J_{HH}$ = 7.1 Hz, $POCH_2\underline{CH_3}$); 3.60 (q, 2H, $^3J_{HH}$ = 7.0 Hz, $CH_2O\underline{CH_2}CH_3$); 3.75 (d, 2H, $^3J_{HH}$ = 8.6 Hz, $PCH_2$); 4.15 (dq, 4H, $^3J_{HH}$ = 7.1 Hz, $^3J_{HP}$ = 7.9 Hz, $PO\underline{CH_2}CH_3$). Anal. Calcd. for $C_7H_{17}PO_4$ = 196.18; C-42.85; H-8.73; Found: C-42.60; H-8.60.

*Diethyl 1-(3-tri-n-butylstannylsulfenyl-n-propyl)sulfenylmethylphosphonate* (**5h**): This compound is distillable (Kugelrohr, 210°C/0.6 mmHg) but it contains some amounts of tin salts ($^1$H-NMR). The tin salts can be removed from **5h** using column chromatography over silica gel and the preparative TLC at the expense of decomposition of **5h** by 20–30% ($^{31}$P-NMR).

$^1$H-NMR ($CDCl_3$), δ = 0.89 (t, 9H, $^3J_{HH}$ = 7.1 Hz, $CH_3$), 1.08–1.7 (m, 18H, $(\underline{CH_2})_3CH_3$), 1.33 (t, 6H, $^3J_{HH}$ = 7.0 Hz, $POCH_2\underline{CH_3}$), 1.85 (quintet, 2H, $^3J_{HH}$ = 7.1 Hz, $SCH_2\underline{CH_2}CH_2S$), 2.63 (t, 2H, $^3J_{HH}$ = 7.1 Hz, $CH_2S$), 2.71 (d, 2H, $^2J_{HP}$ = 13.4 Hz, $PCH_2$), 2.84 (dt, 2H, $^3J_{HH}$ = 7.1 Hz, $^4J_{HP}$ = 1.0 Hz; $PCH_2S\underline{CH_2}$); 4.15 (dq, 4H, $^3J_{HH}$ = 7.0 Hz, $^3J_{HP}$ = 7.9 Hz, $PO\underline{CH_2}CH_3$)

MSEI (70 eV, m/z, %) = 547 ($M^+$, 1.5 + other stannyl isotopic peaks of a very low intensity); 487 (16), 488 (11), 489 (31), 490 (16, M—$Bu_3Sn$); 491 (43); 492 (9); 493 (10), **5h** is also unstable under the MS-GC conditions.

*Diethyl n-Hexylphosphonate* (**5i**): $n_D^{20}$ = 1.4286; $^1$H-NMR ($CDCl_3$), $\delta$ = 0.86 (t, 3H, $^3J_{HH}$ = 6.5 Hz, $(CH_2)_5\underline{CH_3}$); 1.29 (t, 6H, $^3J_{HH}$ = 7.1 Hz, $POCH_2\underline{CH_3}$); 1.22–1.78 (m, 10H, $(CH_2)_5$); 4.06, 4.07 (2xdq, 4H, $^3J_{HH}$ = 7.1 Hz, $^3J_{HP}$ = 8.1 Hz, $PO\underline{CH_2}CH_3$). MSEI (15 eV, m/z, %)-222 (3, $M^+$); 179 (16, $(EtO)_2P(O)(CH_2)_3$); 165/28, $(EtO)_2P(O)(\underline{CH_2})_2$; 152 (100, $(EtO)_2P(O)CH_3$); 138 (30, $(EtO)_2POH$); 125 (42); 111 (15). MS-HR-CI: Calcd for $C_{10}H_{24}PO_3$ = 223.1463; Found 223.1456.

*Tetraethyl Methylene Bis(phosphonate)* (**5j**)[21]: $n_D^{20}$ = 1.4444; $^1$H-NMR ($CDCl_3$), $\delta$ = 1.26 (t, 12H, $^3J_{HH}$ = 7.1 Hz, $POCH_2\underline{CH_3}$); 2.36 (t, 2H, $^2J_{HP}$ = 21 Hz, P-$CH_2$P); 4.09 (dq, 8H, $^3J_{HH}$ = 7.1 Hz, $^3J_{HP}$ = 7.8 Hz, $PO\underline{CH_2}CH_3$).

*Reaction of Diethyl Methylphosphonate* **5a** *with Tri-n-butyltin Chloride*

To a stirred solution of **5a** (0.5 g, 3.28 mmol) in dry THF (15 ml), a solution of *n*-butyllithium (2.7 ml, 3.28 mmol + 8%, 1.3 M in *n*-hexane) was added dropwise under argon atmosphere at −78°C. After stirring at this temperature for additional 15 min, a solution of tri-*n*-butyltin chloride (0.53–1.07 g, 1.64–3.28 mmol) in THF (5 ml) was added dropwise. The temperature was rised to 25°C and the resulting solution was refluxed for 30 min. Then, the solvents were evaporated, the residue was partitioned between water and chloroform and filtered through the Celite pad. The chloroform solution was dried over $MgSO_4$, evaporated and distilled using the Kugelrohr apparatus to give the starting phosphonate **5a** (32–40%); diethyl tri-*n*-butylstannylmethylphosphonate **9** (42–49%) and diethyl bis(tri-*n*-butylstannyl)methylphosphonate **10** (10–18%).

*Tri-n-butylstannylmethylphosphonate* (**9**): colorless oil; $^{31}$P-NMR ($CDCl_3$); $\delta$ = 38.6 ppm (Lit. [13], $\delta$ = 37.1 ppm, $CDCl_3$), $^2J_{^{31}P,^{119}Sn}$ = 57.3 Hz. $^1$H-NMR ($CDCl_3$); $\delta$ = 0.84–1.62 (m, 29H, $CH_2$, 3x$C_4H_9$); 1.28 (t, 6H, $J$ = 7.1 $POCH_2\underline{CH_3}$); 3.93–4.12 (m, 4H, $PO\underline{CH_2}CH_3$).

*Diethyl Bis(tri-n-butylstannyl)methylphosphonate* (**10**): colorless oil; $^{31}$P-NMR ($CDCl_3$); $\delta$ = 42.9 ppm (Lit. [13], $\delta$ = 41.3 ppm, $CDCl_3$); $^2J_{^{31}P,^{119}Sn}$ = 54.7 Hz. $^1$H-NMR ($CDCl_3$); $\delta$ = 0.86–1.70 (m, 55H, 6x$C_4H_9$, CH); 1.27 (t, 6H, $J$ = 7.1, $POCH_2\underline{CH_3}$); 3.89–4.05 (m, 4H, $PO\underline{CH_2}CH_3$).



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