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A General One-Pot Synthesis of Vinyl-Thiiranes and Conjugated Dienes

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Abstract: The first general synthesis of vinyl-thiiranes **5** and an efficient preparation of conjugated dienes **6** and **7** based on thio- and selenophosphates is described.

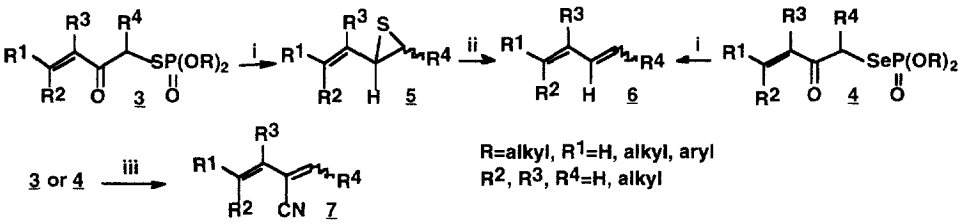
Keywords: vinyl-thiiranes, conjugated dienes, thiophosphates, selenophosphates

Thiiranes are an important class of cyclic sulphides from both a synthetic and a theoretical point of view. Although numerous synthetic routes to thiiranes are known,[1,2] the preparation of only a few examples of vinyl-thiiranes has been published so far.[3] This situation prompted us to develop methodology for a general and efficient synthesis of vinyl-thiiranes.

We have described[4] a strategy for the stereoselective conversion of carbonyl compounds into olefins based on S-(β-oxoalkyl)thiophosphate intermediates **1**[5] and their seleno analogues **2**.[6] We have demonstrated that this methodology is very useful for the synthesis of a variety of unsaturated compounds.[7]

In this communication we report the extension of our methodology to readily available thiophosphates **3** and selenophosphates **4** containing an α,β-unsaturated carbonyl moiety. We recently elaborated the synthesis of **3** and **4**.[6,8] We found that phosphates **3** and **4** are attractive precursors of vinyl-thiiranes **5** and substituted conjugated dienes **6** and **7**.

Selective reduction of thiophosphates **3** using $NaBH_4$ proceeds smoothly at r.t. giving vinyl thiiranes **5** in almost quantitative yield according to NMR. The configuration of the unsaturated bond of the intermediate thiophosphate **3** is preserved in the thiiranes **5**. The reaction is stereoselective in the case of thiophosphate **3** [$(RO)_2$=$OCH_2CMe_2CH_2O$, R^1=Ph, R^4=i-Pr] giving a mixture of cis and trans thiiranes in the ratio 7:3 (entry g).



i: $NaBH_4$, MeOH / Et_2O 1:4 ii: Δ or Ph_3P iii: KCN, 18-crown-6, DME / Et_2O 1:4

Scheme 1

The thiiranes **5** are readily and efficiently converted into the corresponding substituted conjugated dienes **6** (Scheme 1). The thiiranes **5** can be stored in solution at 0°C for

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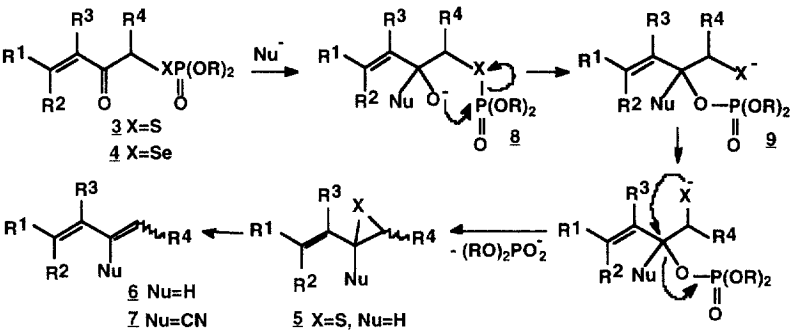
several days. However, they lose sulphur gradually over two days at room temperature to provide conjugated dienes **6** in which the new unsaturated bond has predominantly or even exclusively the E-confi- guration (entry **f**,**h**). Desulphurisation of **5** by the action of triphenylphosphine is stereospecific and proceeds with retention of configuration[9] (entry **g**). The same dienes **6** were obtained by the reduction of selenophosphates **4** using $NaBH_4$. We have also found that thiophosphates **3** and selenophosphates **4** react selectively with cyanide anion (KCN in the presence of 18-crown-6 as catalyst) to give dienes **7** in good yield (Scheme 1).

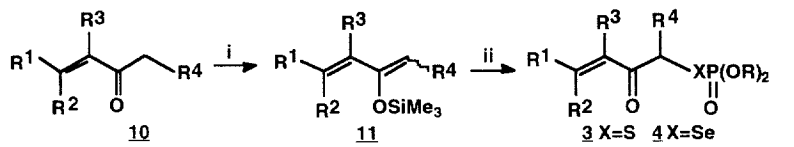
Transformation of thiophosphates **3** and selenophosphates **4** into vinyl-thiiranes **5** and dienes **6** and **7** is presented in Scheme 2.



Scheme 2

The reaction of **3** with nucleophiles results in the formation of diastereoisomeric oxyanions **8** in unequal proportions. The intermediate anions rearrange with migration of a phosphoryl group from sulphur (selenium) to oxygen affording the thiolate (selenolate) anions **9**. Subsequent cyclization via nucleophilic attack at carbon with elimination of phosphate anion gives thiiranes **5** (episelenides) which lose sulphur (selenium) to provide conjugated dienes **6** and **7**.

Phosphates **3** and **4** are readily available from the appropriate α,β-unsaturated ketones **10** via O-silylated dienolates **11** and then thio- and selenophosphorylation of the **11** using $(RO)_2P(O)SCl$ **12** and $(EtO)_3P^+$-SeCl SO_2Cl^- **13** respectively (Scheme 3).[6,8]



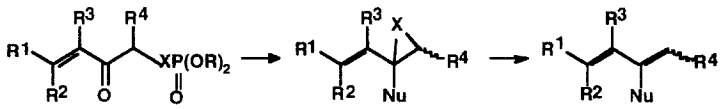
Scheme 3

We obtained best results when conversion of O-silylated dienolates **11** into final vinyl-thiiranes **5** and conjugated dienes **6** and **7** was performed as a "one-pot reaction".

The results of our experiments are shown in the Table. The structures of all compounds prepared described in the Table were confirmed by physical, spectral and analytical data. Configuration of thiiranes **5** and dienes **6** and **7** was assigned on the basis of ^1H and ^{13}C NMR data.

In summary, we have achieved the first general synthesis of vinyl-thiiranes **5** and an attractive alternative preparation of conjugated dienes **6** and **7** based on thio- and selenophosphates.

Table. Vinyl-Thiiranes **5** and Dienes **6** and **7** from Thiophosphates **3** and Selenophosphates **4**



3 X=S 4 X=Se 5 X=S, Nu=H 6 Nu=H 7 Nu=CN

	R	R^1	R^4	X	Nu	Yield[a], % 5	6	7	cis/trans 5[b]	Z/E 6[b]	7[b]
a	Et	Me	H	S	H	63	54[c]				
b	Et	i-Pr	H	S	H	71	70[c]				
c	Et	Me	H	S	H	64					
d	Et	Ph	H	S	H	76	75[c]				
e	Et	Ph	H	Se	H		96[c]				
f	Et	Ph	i-Pr	S	H	93	91[c]		55:45	5:95[c]	
g	$CMe_2(CH_2)_2$[e]	Ph	i-Pr	S	H	91	90[d]		70:30	70:30[d]	
h	Et	H	Me	S	H	62	55[c]		57:43	0:100[c]	
i	Et	$(CH_2)_4$[f]	H	Se	H		84[c]				
j	Et	H	H	S	CN			68[c]			
k	Et	Me	H	S	CN			67[c]			
l	Et	Ph	H	S	CN			58[c]			
m	Et	Ph	H	Se	CN			62[c]			
n	$CMe_2(CH_2)_2$ [e]	Ph	i-Pr	S	CN			83[c]			70:30[c]
o	Et	Ph	i-Pr	S	CN			91[c]			70:30[c]
p	Et	H	Me	S	CN			71[c]			74:26[c]

R^2=R^3=H except **c** R^2 =H, R^3=Me and **i**[f].

[a] No attempts was made to optimise the yields, all yields refer to analytically pure compounds [b] Determined by 500 MHz ^{1}H NMR spectrometry [c] spontaneous desulphurisation or deselenylation [d] desulphurisation using Ph_3P [e] phosphorinane ring [f] R^1, R^3 = $(CH_2)_4$, R^2 =H.

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10. Skowrońska, A.; Dembiński, R.; Gwara, J.; Michalski, J. *Phosphorus, Sulfur and Silicon*, **1988**, *39*, 119 and references therein.
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12. Thiiranes **5** and dienes **6**, typical procedure:

A solution of SO_2Cl_2 (0.05 mol) in CH_2Cl_2 (20 mL) is added dropwise to the O,O,O-triethyl phosphorothioate (0.05 mol) in CH_2Cl_2 (20 mL) at 5°C. Stirring is continued 20 min. at r.t. After removal of about 80% of solvent the crude chlorothiophosphonate **12**[10] is added dropwise to a stirred solution of freshly prepared o-silylated dienolate **11**[11] (0.055 mol) in CH_2Cl_2 (100 mL) at -78°C. Stirring is continued at r.t. for an additional 1 h. The solvent, excess of **11** and trimethylsilyl halide are removed under reduced pressure to give pure thiophosphate **3**. Then **3** (0.05 mol) in Et_2O (10 mL) is added dropwise to a stirred solution of $NaBH_4$ (0.08 mol) in Et_2O/MeOH (40/10 mL) at 10-20°C. Stirring is continued for 2 h and then 50 mL of ice-water is added and the reaction mixture extracted with 3×30 mL pentane, the organic layer washed with water, dried over $MgSO_4$ and pure vinyl-thiirane **5** is separated by distillation. Desulphurisation of **5** afforded the corresponding dienes **6**. A same procedure starting from selenophosphate **4**[6] leads directly to dienes **6**.

Dienes **7**, typical procedure:

Thiophosphate **3** (prepared as above) (0.05 mol) in Et_2O (10 mL) is added to a stirred solution of KCN (dried over P_2O_5) (0.08 mol) and 18-crown-6 (20 mg) in Et_2O/DME (40/10 mL) at r.t. Stirring is continued for 6 h and then 50 mL of water is added and the reaction mixture extracted with 3×30 mL pentane, the organic layer washed with water, dried over $MgSO_4$ and pure **7** is separated from solvent by distillation. A similar procedure starting from selenophosphate **4** also leads to nitriles **7**.

5g ***(trans)-3,4-Epithio-5-methyl-1-phenyl-(E)-1-hexene:*** ^{1}H NMR ($CDCl_3$, 500.13 MHz): 1.09 and 1.12 [d, 3H, J=6.6, $(C\underline{H}_3)_2CH$]; 1.48 [m≡bsext, 1H, J≡7, $(CH_3)_2C\underline{H}$]; 2.74 [dd, 1H, J=8.3 J_2=5.3, $(CH_3)_2CHC\underline{H}S$]; 3.43 (dd, 1H, J=9.2 J_2=5.3, $SC\underline{H}$-CH=); 5.84 (dd, 1H, J=15.7 J_2=9.2, SCH-$C\underline{H}$=); 6.74 (d, 1H, J=15.7, PhC$\underline{H}$=); 7.21-7.39 ($m_{c'}$ $5H_{arom}$). ^{13}C NMR ($CDCl_3$, 50.32 MHz): 21.35 and 21.83 [$(\underline{C}H_3)_2CH$]; 34.90 [$(CH_3)_2\underline{C}H$]; [$(CH_3)_2CH\underline{C}HS$]; 50.59 (=CH$\underline{C}$HS); 126.15, 127.70, 130.35 (Ph); 132.20 and 134.34 (CH=$\underline{C}$H).

5g ***(cis)-3,4-Epithio-5-methyl-1-phenyl-(E)-1-hexene:*** ^{1}H NMR ($CDCl_3$, 500.13 MHz): 1.07 and 1.22 [d, 3H, J=6.6, $(C\underline{H}_3)_2CH$]; 1.64 [m≡dq, 1H, J=10.3 J_2=6.6, $(CH_3)_2C\underline{H}$]; 2.86 [dd, 1H, J=10.3 J_2=6.9, $(CH_3)_2CHC\underline{H}S$]; 3.79 (dd, 1H, J=9.6 J_2=6.9, $SC\underline{H}$-CH=); 6.05 (dd, 1H, J=15.6 J_2=9.6, SCH-$C\underline{H}$=); 6.82 (d, 1H, J=15.7, PhC$\underline{H}$=); 7.21-7.39 ($m_{c'}$ $5H_{arom}$). ^{13}C NMR ($CDCl_3$, 50.32 MHz): 21.34 and 23.05 [$(\underline{C}H_3)_2CH$]; 31.57 [$(C\underline{H}_3)_2\underline{C}H$]; 43.77 [$(CH_3)_2CH\underline{C}HS$]; 49.18 (=CH$\underline{C}$HS); 126.15, 126.31, 127.70, 130.35 (Ph); 126.21 and 128.59 (CH=$\underline{C}$H).

6i ***1-Vinylcyclohexene:*** ^{1}H NMR ($CDCl_3$, 200MHz): 1.61 (m, 4H, $CH_2\underline{C}H_2\underline{C}H_2CH_2$); 2.11 (m, 4H, $\underline{C}H_2CH_2CH_2\underline{C}H_2$); 4.86 (bd, $w_{1/2}$=2.5, 1H, J_{cis}=11.0, =CH_2, H trans to C); 5.04 (bd, $w_{1/2}$=2.5, 1H, J_{trans}=17.2, =$C\underline{H}_2$, H cis to C); 5.73 (bm, $w_{1/2}$=9.5, 1H, >C=$C\underline{H}CH_2$); 6.32 (dd, 1H, J_{trans}=17.2 J_{cis}=11.0, $C\underline{H}$=CH_2). ^{13}C NMR ($CDCl_3$, 50.32 MHz): 22.32 and 22.50 ($CH_2\underline{C}H_2\underline{C}H_2CH_2$); 23.73 and 25.74 ($\underline{C}H_2CH_2CH_2\underline{C}H_2$); 109.51 ($CH_2$=); 129.75 and 140.18 (-CH=); 136.01 (-$\underline{C}$=).

7p ***(Z)-3-Cyano-1,3-pentadiene:*** ^{1}H NMR ($CDCl_3$, 500.13 MHz): 1.88 (d, 3H, J_{vic}=7.7, $C\underline{H}_3CH$=); 5.37 (d, 1H, J_{cis}=10.6, CH$\underline{H}$= trans to C); 5.67 (d, 1H, J_{trans}=17.6, CH$\underline{H}$= cis to C); 6.39 (q quin, 1H, J_{vic}=7.7 J_2=1, $CH_3C\underline{H}$=); 6.50 (ddd, 1H, J_{trans}=17.6 J_{cis}=10.6 J_3=1.5, $C\underline{H}_2$=C$\underline{H}$).

7p ***(E)-3-Cyano-1,3-pentadiene:*** ^{1}H NMR ($CDCl_3$, 500.13 MHz): 2.04 (d, 3H, J_{vic}=7.1, $C\underline{H}_3CH$=); 5.19 (bd, 1H, J_{cis}=10.7, CH$\underline{H}$= trans to C); 5.48 (d, 1H, J_{trans}=17.6, C$\underline{H}$H= cis to C); 6.21 (dd, 1H, J_{trans}=17.6 J_{cis}=10.6, CH_2=C$\underline{H}$); 6.35 (q quin, 1H, J_{vic}=7.1 J_2=1, $CH_3C\underline{H}$=).