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Phosphonates containing sulfur and selenium. Synthesis of vinylphosphonates bearing α-sulfenyl, α-selenenyl, α-sulfinyl and α-seleninyl moieties and studies on nucleophilic addition

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Abstract—The selenenylation of racemic and optically active α-phosphoryl sulfoxides is a key step leading efficiently to α-phosphorylvinyl sulfoxides or α-phosphorylvinyl selenides depending on the reaction conditions. Oxidation of α-phosphorylvinyl selenides and subsequent thermolysis of selenoxides afford alkynylphosphonates. Studies of the stereochemical course of nucleophilic addition to α-phosphoryl sulfoxides show high facial stereoselectivity of the reaction, however, epimerisation at the α-carbon atom leads to mixtures of diastereomers.

1. Introduction

Functionalized vinylphosphonates have attracted much interest in synthetic chemistry and their synthetic applications have been widely investigated in the last two decades.[1,2] In recent years, special attention has been devoted to α-heterosubstituted vinylphosphonates as useful intermediates for the synthesis of natural products.[3–5]

Recently, we have designed[6] and investigated a new type of vinylphosphonate with a sulfinyl substituent as a stereocontrol element. These vinylphosphonates were found to easily undergo Michael reaction, Diels–Alder cycloaddition and cyclopropanation by reaction with sulfur ylides and diazoalkanes. Various types of asymmetric reaction using these α-phosphorylvinyl sulfoxides have been investigated[6b,7] and found to proceed in some cases with considerably high stereoselectivity, which has been attributed to differentiation of the π-faces induced by the sulfinyl group. In this paper, we wish to describe the full account of our studies on the synthesis of our target compounds and investigations into nucleophilic addition.

2. Results and discussion

2.1. Synthesis

One of the best methods to introduce a C–C double bond is the selenenylation and subsequent oxidative selenoxide elimination. In a classical procedure PhSeX (X=Cl, Br, SePh) is used for introduction of the selenenyl moiety. An alternative selenenylation method, developed by Liotta[8] for selenenylation of ketones, involves addition of elemental selenium to enolate anions. This method seems to be a cheaper and easier procedure. In order to find a general methodology for the synthesis of vinylphosphonates, we decided to define the scope and limitations of the selenium addition procedure.

We have found that the α-lithioalkanephosphonates, obtained from the phosphonates **1** and *n*-butyllithium in THF solution at −78 °C, react with elemental selenium, which is simply added to the reaction mixture as a powder.[9] Dissolution of selenium was observed to take place at −30 °C and above affording the corresponding lithium selenoates. The latter, without isolation, were easily converted into the corresponding methyl selenides **2** by treatment with methyl iodide (Scheme 1).

Phosphonates **2a**,**b** possessing β-hydrogen atoms were converted into vinylphosphonates **3a**,**b** by oxidation to the corresponding selenoxides followed by their spontaneous elimination under the reaction conditions. The utility of this

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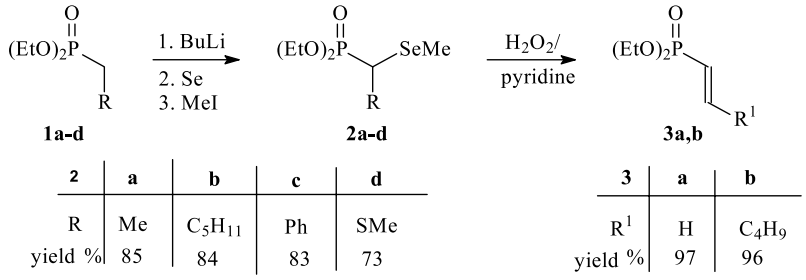
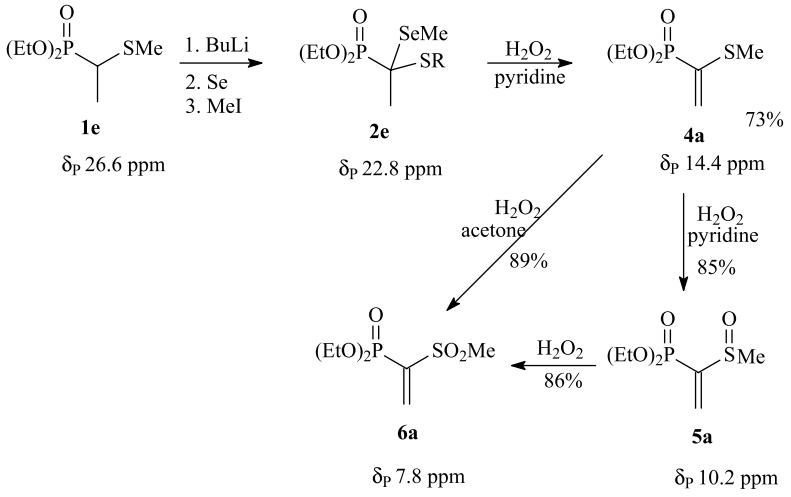


2	a	b	c	d
R	Me	C_5H_{11}	Ph	SMe
yield %	85	84	83	73

3	a	b
R^1	H	C_4H_9
yield %	97	96

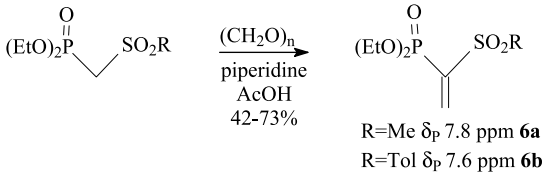
Scheme 1.



Scheme 2.

approach for vinylphosphonate synthesis was demonstrated by the synthesis of diethyl α-methylthiovinylphosphonate **4a** (Scheme 2).

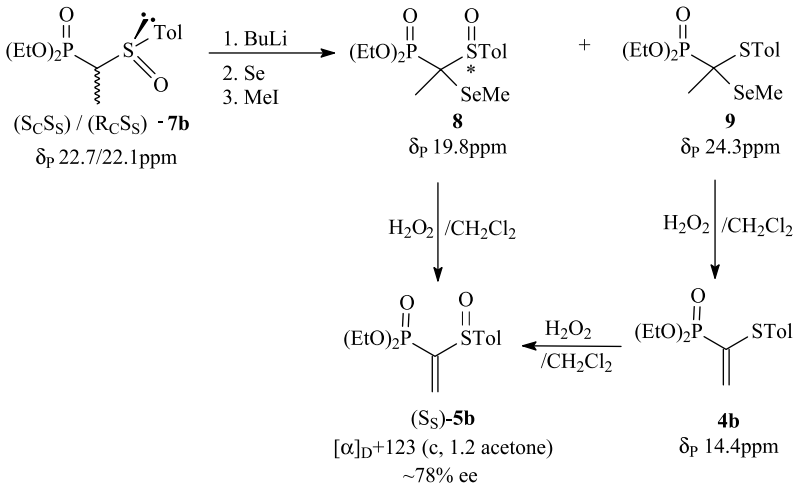
The synthesis of α-phosphorylvinyl sulfides **4** in Scheme 2 is complementary to the earlier syntheses of these compounds, that is, the addition of methanesulfenyl chloride to diethyl vinylphosphonate followed by hydrochloride elimination[10a] and the Peterson reaction of α-silyl α-phosphoryl sulfides.[10b] α-Phosphoryl vinyl sulfides **4** easily undergo oxidation and they can be transformed into the vinyl sulfones **6** using H_2O_2 in acetone solution (Scheme 2). An alternative method for the introduction of the methylene moiety at the carbon atom possessing strongly electron-withdrawing groups is the Mannich reaction. The reaction of α-phosphoryl sulfone with paraformaldehyde in the presence of a catalytic amount of piperidine and acetic acid also afforded the vinyl sulfone **6** in moderate to high yield (42–73%) (Scheme 3).



Scheme 3.

On the other hand, selective oxidation of the vinyl sulfide **4a** by means of H_2O_2 in pyridine solution leads to the corresponding vinyl sulfoxide **5a**, however, this reaction affords the desired compound only in racemic form. Because our interest is focused on the utilization of chiral sulfoxides in asymmetric synthesis we elaborated a new procedure for the synthesis of the optically active sulfoxides **5** starting from the optically active sulfoxides **7**,[11] which are mixtures of two diastereomers $(S_CS_S)/(R_CS_S)$ in a 2:1 ratio (Scheme 4). Thus, the lithium salt of the α-phosphoryl sulfoxide **7b** was found to undergo the reaction with elemental selenium and after methylation and oxygenation afforded the vinyl sulfoxide **5b** in above 50% yield. Unfortunately, it turned out that the addition of selenium does not occur cleanly as in the case of simple phosphonates **1** and in the reaction mixture, in addition to the desired α-phosphorylselenothioketal *S*-oxide **8**, different side products were found. One of them was identified as the corresponding selenothioketal **9**—a sulfoxide reduction product. The latter in the next step undergoes oxidation leading to racemic **5b** (path b). Because oxidative elimination of selenenic acid must be performed on a crude reaction mixture (to avoid sulfenic acid elimination), this reduction–oxidation process decreases the optical purity of the sulfoxide **5b** $[\alpha]_D+123$ (*c*, 1.2 acetone) (Scheme 4). The mechanism of this reduction is not clear.

The efficient and highly stereoselective synthesis of the enantiopure sulfoxide **5b** was accomplished using



Scheme 4.

phenylselenenyl bromide as the selenenylating agent. Thus, the α-carbanion of α-diethoxyphosphorylethyl *p*-tolyl sulfoxide **7b**, formed on treatment with *n*-butyllithium in THF at −78 °C, reacted with PhSeBr and after 3 min the reaction mixture was quenched with cold aqueous solution of $NaHCO_3$. Extraction with ethyl ether afforded the PhSe-substituted sulfoxide **10**, of unknown diastereomeric ratio, since only one broad signal in the ^{31}P NMR spectrum was visible. To complete the synthesis of α-phosphorylvinyl sulfoxide **5b**, oxidation of the selenide moiety was performed using H_2O_2 in CH_2Cl_2 solution at 0 °C which caused benzeneselenenic acid elimination and formation of the desired product (Scheme 5).

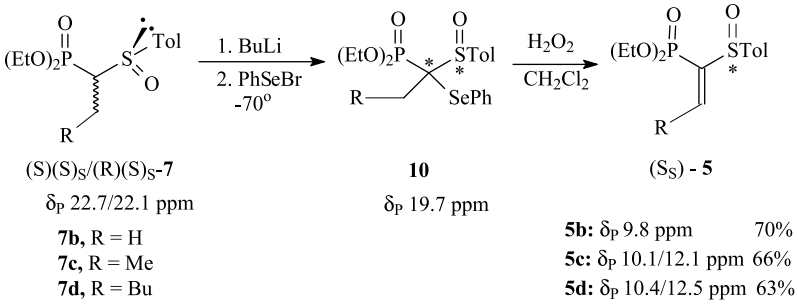
This methodology was extended to the synthesis of β-substituted α-phosphorylvinyl sulfoxides **5c** and **5d.** They were obtained from α-phosphorylpropyl *p*-tolyl sulfoxide **7c** and α-phosphorylhexyl *p*-tolyl sulfoxide **7d** (optically pure at the sulfur atom) according to the procedure described above (Scheme 5).

It is interesting to underline that the oxidative selenoxide elimination affords vinyl sulfoxides **5c**,**d** as mixtures of *E* and *Z* isomers in about 10:1 ratio. After purification by column chromatography both isomers were separated, however, the minor *Z*-isomer was contaminated with a small amount of the starting material. The configuration of the α,β-unsaturated sulfoxides **5c**,**d** was determined[12] based on the $^3J_{P-H}$ coupling constants values which were 41.4 and 42 Hz for *E* and 23.3 and 23.1 Hz for *Z* isomers, respectively.

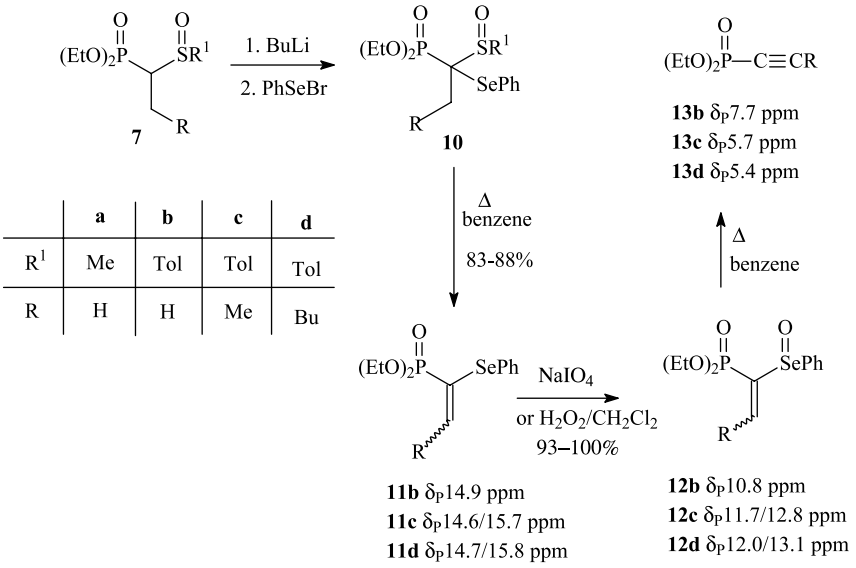
The PhSe-substituted phosphoryl sulfoxides **10**, which upon oxidation undergo transformation to α-phosphorylvinyl sulfoxides **5**, can also afford α,β-unsaturated selenides **11** (Scheme 6). When **10** was heated in a benzene solution, elimination of sulfenic acid took place resulting in the formation of α-phosphorylvinyl selenides **11** in high yields (72–88%). Elimination of *p*-toluenesulfenic acid from **10b**,**c**,**d** occurs quite easily and the full conversion requires heating at 80 °C during the course of a few hours (4–5 h). The conversion of **10a** to **11a**, where the loss of methanesulfenic acid takes place, requires a longer time (ca. 10 h) at the same temperature.

From a preparative point of view, it is worth noting that sulfoxide elimination from **10c**,**d** was found to take place at room temperature when they were subjected to chromatography on a silica gel column. In contrast to stereoselective selenoxide elimination of **10**, the sulfoxide elimination leads to a 1:1 mixture of *E* and *Z* isomers, which were easily separated by column chromatography.

Oxidation of vinyl selenides **11** yields selenoxides **12** in very high yields. It was found that α-phosphorylvinyl selenoxides *E* and *Z*-**12** differ in stability. Whereas the isomer *E* can be stored for a few days, the isomer *Z* easily loses its oxygen (1 day, rt), reverting to starting selenide and



Scheme 5.



	a	b	c	d
R^1	Me	Tol	Tol	Tol
R	H	H	Me	Bu

Scheme 6.

cannot be purified by chromatography. The better stability of the isomer *E*-**12**, where the substituent at the α-carbon atom is on the same side of a double bond as the bulky phosphoryl group, can be attributed to hydrogen bonding between the selenoxide oxygen and the vinyl hydrogen.[13]

Owing to the presence of the selenoxide moiety, the α-phosphoryl vinyl selenoxides **12** were found to undergo further *syn*-elimination. Hence, the thermolysis of **12b**, and *E*-**12c** and *E*-**12d** performed in refluxing (benzene solution affords α-phosphorylalkynes **13** as the only products. In this way a new synthetic approach to this class of compounds was elaborated.[14]

2.2. Nucleophilic addition

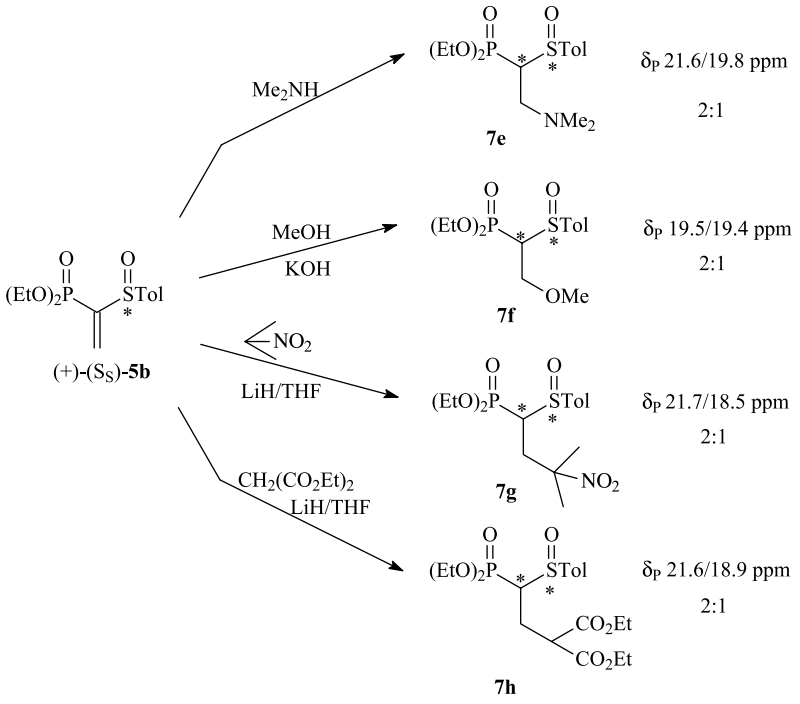
α-Phosphorylvinyl sulfoxides **5** as well as α-phosphoryl-vinyl selenoxides **12** having two electron-withdrawing groups are effective acceptors in conjugate addition of nucleophiles. Taking into account an easy way of elimination of selenenic and sulfenic acid, the sulfoxide **5** and selenoxide **12** can be considered as equivalents of α-phosphoryl alkynes in nucleophilic addition. On the other hand, as we mentioned before, nucleophilic addition to chiral sulfoxides **5** should occur under stereochemical control by the sulfinyl group.

Our first experiments of nucleophilic addition were perfomed using the vinyl sulfoxide **5b** and various heteronucleophiles: dimethylamine, ethyl mercaptan in the presence of Et_3N and methanol in the presence of KOH. In all cases, addition occurred easily at room temperature affording the desired products as a mixture of diastereomers in around 2:1 ratio. This ratio is determined by thermodynamic factors which was established by equilibration using the isolated pure diastereomers. The reaction with the lithium salt of diethyl malonate also affords the corresponding addition product as a mixture of diastereomers in the same ratio (Scheme 7).

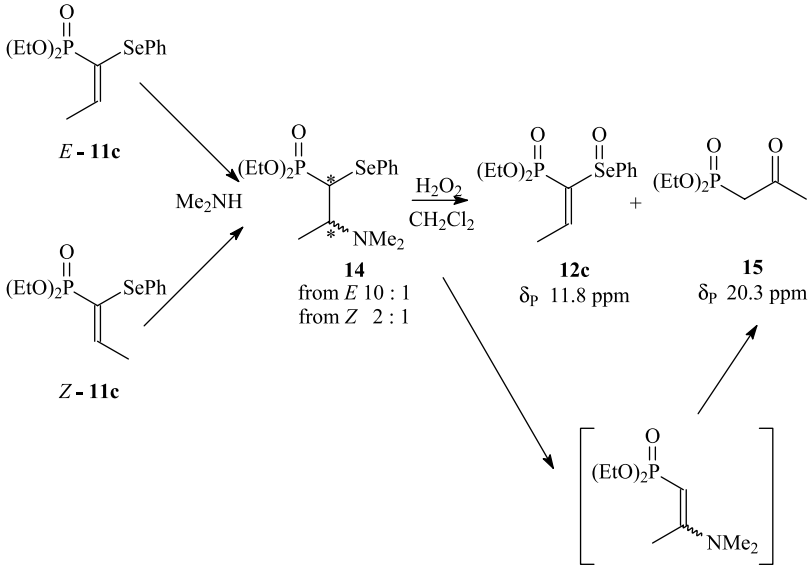
Since the chirality of the α-carbon atom in α-phosphoryl sulfoxide would be destroyed in further transformations (after the Horner reaction or desulfurization), much more interesting from the synthetic point of view is the chirality on the β-carbon atom. In order to establish the stereochemical course of nucleophilic addition to vinylphosphonates with β-substituent, some reactions with different nucleophiles were performed using α-phosphorylvinyl sulfoxides **5c**, **5d** and **5e** and α-phosphorylvinyl selenides and selenoxides **11c** and **12c** as Michael acceptors.

The addition of Me_2NH to *E* and *Z* selenides **11c** afforded the adducts **14** as mixtures of diastereomers in a 10:1 and 2:1 ratio, respectively (Scheme 8). Typical oxidation of **14** with H_2O_2 in CH_2Cl_2 gives two major products, whose ratio depends on the reaction conditions. At room temperature, the only product was the *E*-vinyl selenoxide **12c**. Probably, this temperature favours oxidation of the amine moiety to the corresponding amine oxide, which after elimination, gives rise to a rather stable vinyl selenoxide. With decreasing temperature the selenoxide elimination takes place forming enamine, which, however, undergoes hydrolysis under the reaction and work-up conditions affording β-ketophosphonate **15** as the major product. For this reason no information about the steric course of the reaction can be drawn from these experiments.

Since nucleophilic addition to the selenide **11c** gave no answer concerning the steric course of the addition, the next experiments were performed using the vinyl selenoxide **12c** as starting material. Addition of the malonate anion to α-phosphorylvinyl selenoxide *E*-**12c** occurs easily, but affords the product of isomerization i.e., the β,γ-unsaturated phosphonate **16**. Probably, in this case the equilibrium between α,β and β,γ-isomers is shifted to the latter. To exclude the possibility of this isomerization 2-nitropropane was used in our further studies. The reaction with the potassium salt of 2-nitropropane with *E*-**12c** afforded only the *Z*-isomer of the vinylphosphonate **17** and allylic alcohol **18c** as a side reaction product. The latter was undoubtedly formed as a result of α,β to β,γ-isomerization and allylic



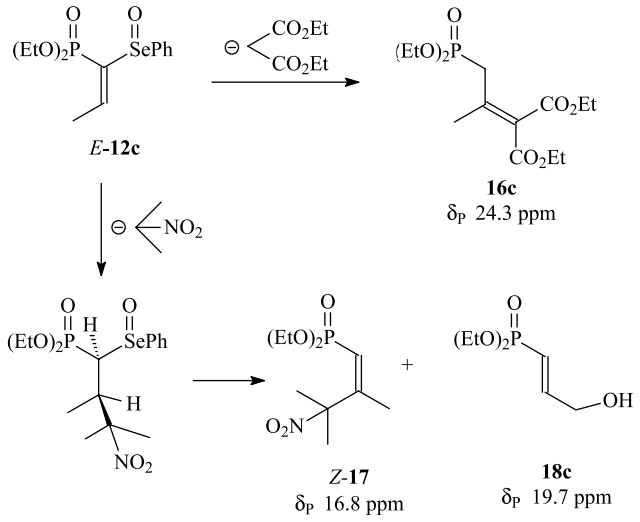
Scheme 7.



Scheme 8.

rearrangement of the starting material **12c** under the reaction conditions (Scheme 9).

The structure of the vinylphosphonate **17** was confirmed by NMR studies using nuclear Overhauser effect. Irradiation of the vinyl proton caused 21% increase of the methyl protons and irradiation of the methyl group of *Z*-**17** (δ_P 16.8) gave a 17% enhancement of the vinyl proton. This indicates that these two moieties are on the same side of the olefinic bond. The *Z*-geometry of the vinylphosphonate **17** obtained as well as the fact of *cis*-geometry of selenoxide elimination, imply *anti*-approach during nucleophilic addition to the α-phosphorylvinyl selenoxides **12**. Unfortunately, the reaction of the *Z*-isomer of **12** with the potassium salt of 2-nitropropane gave a mixture of the same products and additionally some amount of the *E*-isomer of starting material, suggesting the presence of the equilibrium either between *E* and *Z* isomers of starting vinyl selenoxides **12** or *threo* and *erythro* Michael adducts. Taking into account the easy selenoxide elimination (Michael addition product was not detected), the *Z*→*E* isomerization of **12** through allylic selenoxide probably occurs much faster than nucleophilic addition of a bulky nitropropane and only the more stable *trans* isomer undergoes Michael addition selectively affording the product *Z*-**17**.

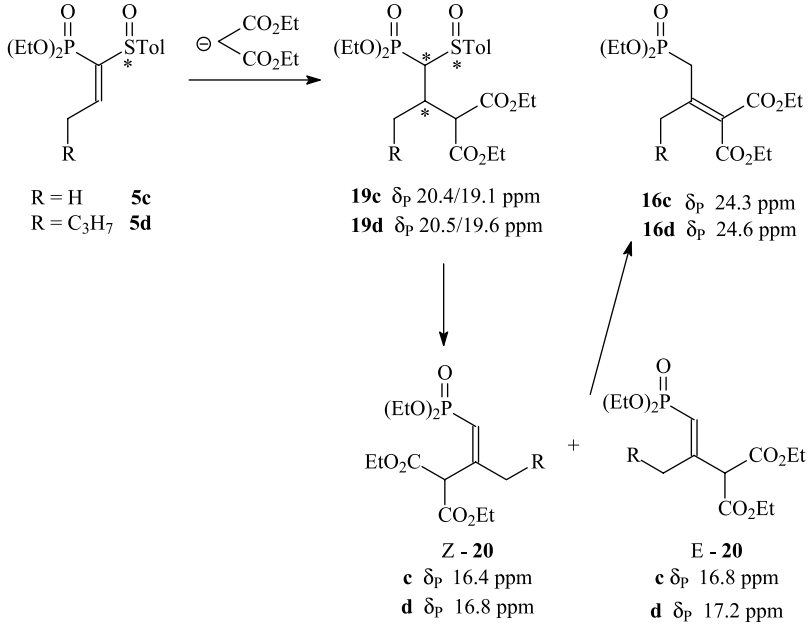


Scheme 9.

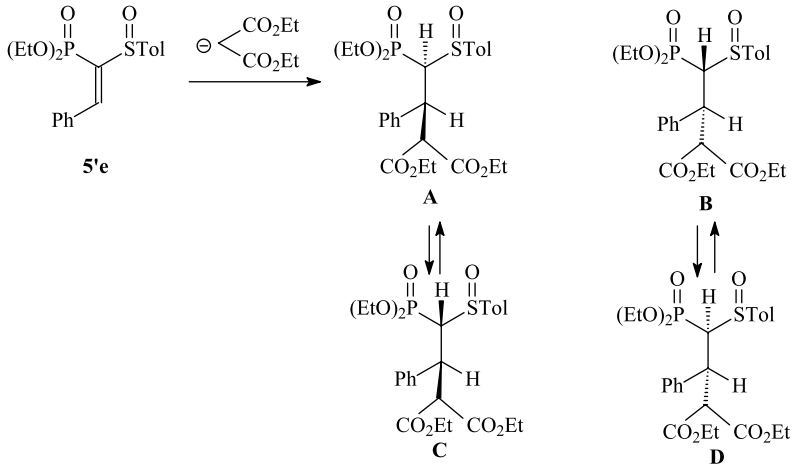
Nucleophilic addition to β-substituted α-phosphorylvinyl sulfoxides is more complex since the reaction should create two centres of chirality under stereochemical control of the sulfinyl group. Having in hand three chiral sulfoxide substrates (**5c**,**d**,**5′e**[15]) we decided to extend the studies on the nucleophilic addition and its stereoselectivity. In the reaction of (*E*)-(*S*)-(1-diethoxyphosphoryl-2-methyl)vinyl *p*-tolyl sulfoxide **5c** with the lithium salt of diethyl malonate, generated by LiH in THF solution, the desired adduct **19c** was formed exclusively as a 5:3 mixture of two (from four) possible diastereomers. The product **19** upon storage at room temperature slowly undergoes sulfoxide elimination yielding the vinylphosphonate **20**. However, in this case the ^{31}P NMR spectra indicated the presence of both *E* and *Z* isomers of **20** formed. Taking into account configurational requirement for *syn*-elimination of sulfenic acid, the presence of two isomers of **20** suggests that they were formed from **19** of *threo* and *erythro* configuration. Those products could be formed when nucleophilic addition to sulfoxide **5** partly occurs in *anti* and partly in *syn*-manner, what is rather unlikely because *anti*-addition was suggested in our model reaction with selenoxide **12c**. Another explanation presumes stereoselective attack of nucleophile leading to only one diastereomer of **19** and partial epimerization on the α-carbon atom under the reaction conditions (Scheme 10).

Addition of the lithium salt of diethyl malonate to *E*-(+)-(1-dimethoxyphosphoryl-2-phenyl)vinyl *p*-tolyl sulfoxide **5′e** affords a mixture of four diastereomers **19′e** δ_P: 21.2/20.9/22.4/21.5 ppm in a 22:15:3:2 ratio. Oxidation of the major pair of diastereomers (21.2/20.9) as well as the minor one (22.4/21.5) separately in order to destroy chirality at sulfur, gave in both cases a mixture of the sulfone **21′e** (18.3/17.9), that is the diastereomers of *threo* and *erythro* configuration. Also in this case we can presume *anti* addition of the malonate nucleophile leading to diastereomers **A** and **B** and then formation of diastereomers **C** and **D** caused by epimerisation on the α-carbon atom. According to our recent studies of asymmetric cyclopropanation of α-phosphorylvinyl sufoxides with sulfur ylides,[13] the major factor controlling the stereoselectivity of this reaction is the conformation of the sulfoxide, where sulfinyl and phosphoryl groups adopt an *anti* orientation, the former being syncoplanar with the carbon–carbon double bond. Nucleophilic addition of the sulfur ylide occurs exclusively from the less-hindered diastereotopic face occupied by the electron lone pair at sulfur. Although we do not have any configurational assignment of addition products **19′e**, it seems likely, that major diastereomer **19′e** (δ_P: 21.2 ppm) has configuration **A**, formed by the same facial nucleophilic attack of the lithium salt of diethyl malonate (Schemes 11 and 12).

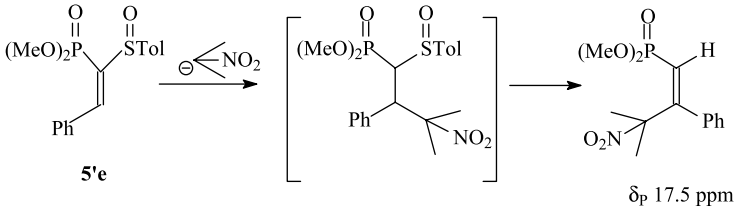
Nucleophilic addition of the sodium salt of 2-nitropropane to *E*-(+)-(1-dimethoxyphosphoryl-2-phenyl)vinyl *p*-tolyl



Scheme 10.



Scheme 11.



Scheme 12.

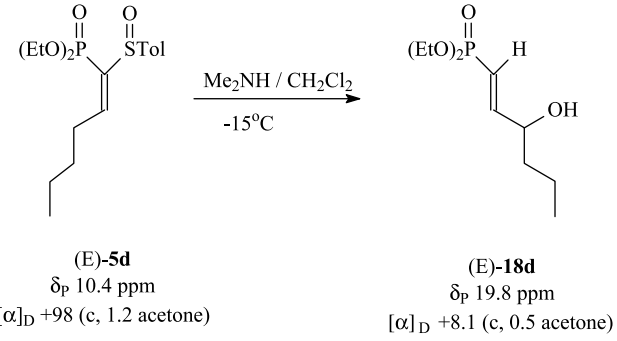
sulfoxide **5′e** was performed in a similar way to selenoxides. It was found that elimination of sulfenic acid from the primary adduct is so fast, that it can not be detected in ^{31}P NMR spectra. Also in this case only one vinylphosphonate was obtained (δ_P 17.5), because instantaneous sulfenic acid elimination from the adduct makes epimerization impossible.

2.3. Allylic alcohol synthesis

The synthesis of different types of γ-hydroxy α,β-unsaturated derivatives from sulfoxides and aldehydes was described as a one step procedure[16] (SPAC reaction, an abbreviation from sulfoxide piperidine aldehyde condensation) based on a sequence of reactions: Knoevenagel condensation, prototropic shift and allylic sulfoxide–sulfenate rearrangement. Usually, the SPAC reaction was carried in CH_3CN in the presence of piperidine at 0 to 60 °C. Using chiral sulfoxides, these reactions gave rise to asymmetric induction ranging from 10–70% ee.[17] In the case of sulfoxides **5c** and **5d**, the presence of a γ-hydrogen in the aliphatic chain creates the possibility of α,β to β,γ isomerization and sigmatropic rearrangement leading to allylic alcohol **18**. This reaction, confirmed already for the analogous vinyl selenoxide **12c**, also occurs in the case of vinyl sulfoxide **5d** affording γ-hydroxyhexenylphosphonate **18d** in excellent yield.

The first experiment leading to allylic alcohol was conducted using optically active α-phosphorylvinyl sulfoxide **5d** by addition of Me_2NH at 0 °C in CH_2Cl_2 solution. γ-Hydroxy- phosphonate **18d**, obtained in this way, exhibited optical rotation $[\alpha]_D+1.5$ (*c*, 0.8 acetone). According to the ^{1}H NMR spectra in the presence of (+)-(*R*)-*t*-butylphenylphosphinothioic acid this value corresponds only to 5% ee. Trying to improve the asymmetric induction, we decreased the temperature to −15 °C. In this case the reaction was complete after 3 days, but we were able to raise the optical purity of the product **18** to 25% $[\alpha]_D+8.1$ (*c*, 0.5 acetone). Because the typical procedure for SPAC reaction applied to α-phosphoryl sulfoxides requires rather vigorous conditions[18] (heating at 40 °C for 12–24 h), our modification using α,β-unsaturated α-phosphoryl sulfoxides seems to give the possibility to obtain optically active γ-hydroxyphosphonates (Scheme 13).

We have developed a general methodology to prepare α-heterosubstituted vinylphosphonates. The crucial step of



Scheme 13.

the synthesis is selenenylation of phosphonates either by phenylselenyl bromide, or elemental selenium, although some limitations of the letter reagent were defined. Applying our procedure we synthesized for the first time, in optically active and racemic form, α,β-unsaturated α-phosphoryl sulfoxides, important reagents in asymmetric synthesis. Our studies on the nucleophilic addition to α-phosphorylvinyl sulfoxides, due to epimerization of addition products, allowed us to present only considerations of the most probable stereochemistry of the process.

3. Experimental

3.1. General

^{1}H, ^{13}C, ^{77}Se and ^{31}P NMR spectra were recorded on a Bruker MSL 300 and Bruker AC 200 Spectrometer, using deuterochloroform as solvent. Mass spectra were recorded on Finnigan MAT95. IR spectra were recorded on Ati Mattson FTIR Spectrometer. The optical rotations were measured on a Perkin–Elmer 241 MC photopolarimeter in acetone solution. The microanalyses were performed on Elemental Analyzer EA 1108.

TLC was carried out on silica gel plates (Merck F_{254}) and silica gel 60 (70-230 ASTM) was used for chromatography. THF was freshly distilled over potassium/benzophenone.

3.2. General procedure for preparation of α-phosphoryl selenides 2

To a stirred solution of phosphonate **1** (20 mmol) in 100 mL of dry THF, a solution of *n*-BuLi (10 mL, 2.2 M in hexane, 22 mmol) was added at −78 °C. After 10 min, selenium powder (20 mmol) was added and the reaction mixture was warmed to appropriate temperature (−30 °C—**2a**; −20 °C—**2b**,**c**; −40 °C—**2d**) and kept at this temperature until the selenium disappeared. Then, the reaction mixture was cooled to −78 °C and methyl iodide (20 mmol) was added. The reaction solution was warmed up and treated with 30 mL of aqueous NH_4Cl. The organic layer was separated and collected with the 50 mL of chloroform extract of the water layer. The combined organic solution was dried over $MgSO_4$ and the solvent was evaporated to give the yellow oil. Purification was performed using column chromatography on silica gel (eluent: benzene–acetone 10:1).

3.2.1. Diethyl (α-methylselenenyl)ethylphosphonate 2a. A pale yellow oil. Yield: 4.42 g (85%); $n_D=1.4860$; IR (neat) 1241, 1028; ^{31}P NMR (81 MHz, $CDCl_3$) δ 28.7 ppm; ^{1}H NMR (200 MHz, $CDCl_3$): δ 1.3 (t, 6H, CH_3CH_2OP, $J=7.1$ Hz); 1.54 (dd, 3H, CH_3CH, $J_{P-H}=17.4$ Hz, $J_{H-H}=7.5$ Hz); 2.15 (s, 3H, $SeCH_3$); 2.76 (dq, 1H, CH_3CH, $J_{P-H}=13.2$ Hz, $J_{H-H}=7.5$ Hz); 4.14 (dq, 4H, CH_3CH_2OP, $J_{P-H}=8.0$ Hz, $J_{H-H}=7.1$ Hz); ^{13}C NMR (50 MHz, $CDCl_3$) δ 4.5; 15.7; 16.3 (d, $J_{P-C}=6$ Hz); 25.5 (d, $J_{P-C}=52.2$ Hz); 62.5 (d, $J_{P-C}=6.9$ Hz); ^{77}Se NMR (57 MHz, $CDCl_3$) δ 536 ppm; HRMS (70 eV) $C_7H_{17}O_3PSe$ requires 260.0087 Found: 260.0075.

3.2.2. Diethyl (α-methylselenenyl)hexylphosphonate 2b. A slightly yellow oil. Yield: 5.30 g (84%); $n_D=1.4732$; IR (neat) 1240, 1024; ^{31}P NMR (81 MHz, $CDCl_3$) δ 28.18 ppm; ^{1}H NMR (200 MHz) δ: 0.84–0.93 (m, 3H, CH_3CH_2); 1.14–1.43 (m,10H: 6H of t, CH_3CH_2OP+4H of m, $(CH_2)_2CH_3$)); 1.45–2.01 (m, 4H, $-(CH_2)_2-$); 2.12 (s, 1H, $SeCH_3$); 2.57 (dt, H, C–*H*, $J_{P-H}=15$ Hz, $J_{H-H}=10$ Hz); 4.16 (dq, 4H, CH_3CH_2OP, $J_{P-H}=8.8$ Hz, $J_{H-H}=7.1$ Hz); ^{13}C NMR (50 MHz, $CDCl_3$) δ 4.5; 13.9; 16.3 (d, $J=6.0$ Hz); 22.3; 27.5 (d, $J=12.0$ Hz); 28.3; 31.1; 33.9; 65.5 (d, $J=13.8$ Hz); ^{77}Se NMR (57 MHz, $CDCl_3$) δ 485 ppm; HRMS (70 eV) $C_{11}H_{25}O_3PSe$ requires 316.0700 Found: 316.0697.

3.2.3. Diethyl (α-methylselenenyl-α-phenyl)methylphosphonate 2c. A pale yellow oil. Yield: 5.35 g (83%); $n_D=1.5380$; ^{31}P NMR (81 MHz, $CDCl_3$) δ 23.98 ppm; ^{1}H NMR (200 MHz, $CDCl_3$) δ: 1.23 ppm (2xt, 6H, CH_3CH_2O, $J=7.1$ Hz); 2.05 (s, 3H, $SeCH_3$); 4.02 (d, 1H, C*H*Ph, $J_{P-H}=17.4$ Hz); 3.23–4.23 (m, 4H, CH_3CH_2OP); 7.27–7.47 (m, 5H, Ar–*H*); ^{13}C NMR (50 MHz, $CDCl_3$) δ 6.2 (d, $J=3.3$ Hz); 16.2 (t, $J=6.9$ Hz); 36.9 (d, $J_{C-P}=149$ Hz); 63.1 (d, $J=16.5$ Hz); 127.5; 128.5; 129.2; 135.7; ^{77}Se NMR ($CDCl_3$, 57 MHz) δ 606 ppm; HRMS (70 eV) $C_{12}H_{19}O_3PSe$ requires 322.0237 Found 322.02369.

3.2.4. Diethyl (α-methylselenenyl-α-methylsulfenyl)-methylphosphonate 2d. A slightly yellow oil. Yield: 4.26 g (73%); $n_D=1.4742$; ^{31}P NMR (81 MHz, $CDCl_3$) δ 21.08 ppm; ^{1}H NMR (200 MHz) δ: 1.34 (t, 6H, CH_3CH_2OP, $J_{H-H}=7.1$ Hz); 2.20 (d, 3H, SCH_3, $J_{P-H}=0.7$ Hz); 2.27 (d, 3H, $SeCH_3$, $J_{P-H}=1.7$ Hz); 3.74 (d, 1H, C*H*, $J_{P-H}=15$ Hz); 4.19 (dq, 4H, OCH_2CH_3, $J_{P-H}=8.8$ Hz, $J_{H-H}=7.1$ Hz); ^{13}C NMR (50 MHz, $CDCl_3$); δ 5.6; 16.0 (d, $J=11.8$ Hz); 16.4 (d, $J_{P-C}=5.6$ Hz); 36.2 (d, $J_{P-C}=154.7$ Hz); 63.5 (d, $J_{P-C}=6.9$ Hz); HRMS (70 eV) $C_7H_{17}O_3PSSe$ requires 291.9801. Found 291.9797.

3.2.5. Diethyl (α-methylselenenyl-α-methylsulfenyl)-ethylphosphonate 2e. A slightly yellow oil. Yield: 4.41 g (72%); $n_D=1.4215$; ^{31}P NMR (81 MHz, $CDCl_3$): δ 23.7 ppm; ^{1}H NMR (200 MHz, $CDCl_3$): δ 1.35 (2×t, 6H, CH_3CH_2OP, $J_{H-H}=7.1$ Hz); 1.77 (3H, d, CH_3, $J_{P-H}=5.3$ Hz); 2.16 (d, 3H, $SeCH_3$, $J_{P-H}=1.5$ Hz); 2.23 (d, 3H, SMe, $J_{P-H}=0.2$ Hz); 4.24 (dq, 4H, CH_3CH_2OP, $J_{P-H}=8.8$ Hz, $J_{H-H}=7.1$ Hz,); ^{13}C NMR (50 MHz, $CDCl_3$): δ 5.2; 13.7 (d, $J=3.3$ Hz); 16.3 (d, $J=5.9$ Hz); 23.3; 43.1 (d, $J=155$ Hz); 63.6 (t, $J=7.2$ Hz); ^{77}Se NMR (57 MHz, $CDCl_3$): δ 636 ppm; HRMS $C_8H_{19}O_3PSSe$ requires 305.9958. Found 305.9965.

3.3. Oxidation of α-phosphoryl selenides

To a solution of α-phosphoryl selenide (15 mmol) in 50 mL of dry pyridine, 30% solution of hydrogen peroxide (15 mmol) was added. The mixture was stirred vigorously at room temperature for 2 h. Then 50 mL of diethyl ether was added and the reaction mixture was washed with water (5×10 mL). The organic layer was dried and solvent evaporated affording vinylphosphonates which were purified by column chromatography (hexane–acetone 15:1).

3.3.1. Diethyl hexen-1-ylphosphonate 3b. A slightly yellow oil. Yield: 3.17 g (96%); $n_D=1.6828$ (isomer *E*); ^{31}P NMR (81 MHz, $CDCl_3$) δ 19.7 ppm (*E*)/18.1 ppm (*Z*)

21:1; ^{1}H NMR (200 MHz, $CDCl_3$): δ 0.89 (t, 3H, CH_3, J_{H-H}=6.8 Hz); 1.31 (t, 6H, OCH_2CH_3, J_{H-H}=7.1 Hz); 1.23–1.45 (m, 4H, CH_2); 2.14–2.24 (m, 2H, CH_2); 4.05 (dq, 4H, CH_3CH_2OP, J_{P-H}=8.0 Hz, J=7.1 Hz); (for isomer *Z*) 5.55 (tdd, 1H, J_{H-H}=1.6, 7.0, 13.0 Hz, J_{P-H}=17.0 Hz); 6.55 (tdd, 1H, J_{H-H}=7.0, 11.0 Hz, J_{P-H}=46.3 Hz); (for the isomer *E*) 5.63 (tdd, 1H, =C–H_2, J_{P-H}=21.2 Hz, J_{H-H}= 1.5, 17.1 Hz,); 6.77 (tdd, 1H, =CH_2, J_{P-H}=22.0 Hz, J_{H-H}=6.6, 17.1 Hz); ^{13}C NMR ($CDCl_3$, 50 MHz); δ 13.6; 16.1 (d, J=6.3 Hz); 21.9, 29.7, 33.6 (d, J=21.6 Hz); 61.3 (d, J=5.4 Hz); 116.5 (d, J=188 Hz); 153.8 (d, J=4.6 Hz); HRMS (70 eV) $C_{10}H_{21}O_3P$ requires 220.1228. Found 220.1214.

3.3.2. Diethyl (α-methylsulfenyl)vinylphosphonate 4a. A slightly yellow oil. Yield: 2.83 g (90%); n_D=1.4868; IR (neat) 1632, 1243, 1026; ^{31}P NMR (81 MHz) δ 14.5 ppm; ^{1}H NMR (200 MHz): δ 1.34 (2×t, 6H, J=7.1 Hz); 2.31 (s, 3H, SCH_3); 4.05 (dq, 4H, J_{H-H}=7.1 Hz, J_{P-H}=8.8 Hz); 5.55 (d, 1H, J_{P-H}=42.9 Hz); 6.18 (d, 1H, J_{P-H}=21.2 Hz); ^{13}C NMR (50 MHz, $CDCl_3$): δ 4.4 (d, J=6.2 Hz); 15.9 (d, J=6.9 Hz); 62.3 (d, J=4.8 Hz); 121.5 (d, J=7.6 Hz); 136.1 (d, J=19.7 Hz); HRMS (70 eV) $C_7H_{15}O_3PS$ requires 210.0479. Found 210.04715.

3.4. Oxidation of α-phosphorylvinyl methyl sulfide 4a to sulfoxide 5a

α-Phosphorylvinyl methyl sulfide **4a** (1 mmol) was dissolved in pyridine (50 mL) and 30% hydrogen peroxide (1 mmol) was added. The mixture was stirred for 6 days at room temperature and then Et_2O (50 mL) was added. The organic solution was washed with water (5×10 mL), dried and evaporated. Sulfoxide **5a** was purified by column chromatography on silica gel (hexane–acetone 20:1).

Yield: 0.266 g (85%); n_D=1.54443. A slightly yellow oil; IR (neat) 1595, 1254, 1027, 1043; ^{31}P NMR (81 MHz, $CDCl_3$): δ 10.22 ppm; ^{1}H NMR (200 MHz, $CDCl_3$): δ 1.34 (2×t, 6H, J=7.1 Hz); 2.79 (s, 3H, SOCH_3); 4.15 (4H, dq, J_{P-H}=8.8 Hz, J_{H-H}=7.1 Hz); 6.69 (d, 1H, J_{H-H}=19.3 Hz, *cis* C=CH); 6.77 (d, 1H, J=40.2 Hz, *trans* C=CH); ^{13}C NMR ($CDCl_3$, 50 MHz): δ 11.1, 15.6 (d, J=6.2 Hz); 63.9 (d, J=89.4 Hz); 125.38 (d, J=100.7 Hz); 133.9 (d, J= 104 Hz); HRMS (70 eV) $C_7H_{15}O_4PS$ requires 226.0428. Found 226.0426.

3.5. Preparation of diethyl α-phosphorylvinyl methylsulfone 6a

Method A (by oxidation of the sulfoxide). The diethyl (α-methylsulfinyl)vinylphosphonate (1 mmol) was dissolved in acetone and two molar excess of hydrogen peroxide was added. The reaction mixture was heated in reflux for 2 h. On the next water (10 mL) was added and acetone was evaporated. The water layer was extracted with chloroform (3×15 mL). The combined organic layers were dried by magnesium sulfate and solvents were evaporated. The colourless oil was separated and purified by column chromatography (hexane–acetone 20:1). Yield 0.2 g (89%).

Method B (by Mannich reaction). Paraformaldehyde (2 mmol) was dissolved in 100 mL of benzene containing a mixture of 5 drops of piperidine and 10 drops of acetic acid and the solution was heated in reflux for 0.5 h. α-Phosphoryl sulfone (1 mmol) was added all at once and the solution was heated in reflux under Dean–Stark water separator for 54 h. The solvent was removed and product was purified by column chromatography (hexane–acetone 20:1).

3.5.1. Diethyl (α-methylsulfonyl)vinylphosphonate 6a. A pale yellow oil. Yield: 0.182 g (42%)—Method B; n_D= 1.5620; IR (neat) 1250, 1019; ^{31}P NMR (81 MHz, $CDCl_3$): δ 7.8 ppm; ^{1}H NMR (200 MHz, $CDCl_3$): δ 1.33 (t, 6H, CH_3CH$_2$OP, J=7.1 Hz); 3.16 (s, 3H, SO_2CH_3); 4.10–4.20 (m, 4H, CH_3CH_2OP); 6.98 (d, 1H, J_{P-H}=17.3 Hz, *cis* C=CH); 7.12 (d, 1H, J_{P-H}=39.3 Hz, *trans* C=CH); ^{13}C NMR ($CDCl_3$, 50 MHz); 16.6 (d, J=7.9 Hz); 18.7; 62.8; 131 (d, J=7.1 Hz); 139 (d, J=171 Hz). Anal. Calcd for $C_7H_{15}O_5PS$: C, 34.71%; H, 6.24%. Found: C, 34.83%; H, 6.32%.

3.5.2. α-Diethyl (1-*p*-tolylsulfonyl)vinylphosphonate 6b. A pale yellow oil. Yield: 0.232 g (73%); n_D=1.5718; IR (neat) 1590, 1261, 1024; ^{31}P NMR (81 MHz, $CDCl_3$): δ 7.6 ppm; ^{1}H NMR (200 MHz, $CDCl_3$): δ 1.25 (t, 6H, CH_3CH$_2$OP, J=7.1 Hz); 2.43 (s, 3H, Ar–CH_3); 4.00–4.23 (m, 4H, CH_3CH_2OP); 6.94 (d, 1H, J_{P-H}=18.4 Hz, *cis* C=CH); 7.18 (d, 1H, J_{P-H}=37.5 Hz, *trans* C=CH); 7.32 and 7.81 (4H, aromatic); ^{13}C NMR ($CDCl_3$, 50 MHz); δ 16.0; 21.4; 63.1 (d, J=5.3 Hz); 126.3; 127.8; 128.6; 128.9; 132.9, (d, J=9.0 Hz); 143.2 (d, J=106 Hz). Anal. Calcd for $C_{13}H_{19}O_5PS$: C, 49.05%; H, 6.02%. Found: C, 49.11%; H, 6.13%.

3.6. Synthesis of optically active α-phosphorylvinyl sufoxides 5

Method A. To a stirred solution of optically active α-(diethylphosphoryl)-ethyl *p*-tolyl sulfoxide **7b** (1.52 g, 5 mmol) in 100 mL of dry THF a 2.2 M solution of *n*-butyllithium (5.5 mmol) in hexane was added dropwise at −78 °C. After 5 min, powder of selenium (0.4 g, 5 mmol) was added. The mixture was warmed slowly to −10 °C when dissolution of selenium was observed. A clear dark brown solution was treated then with methyl iodide (0.61 g, 5 mmol) and after 5 min the solution was quenched with 50 mL of aqueous solution of NH_4Cl. Organic solvents were evaporated and the remaining aqueous solution was extracted with chloroform (2×30 mL). The $CHCl_3$ extract was dried over anhydrous $MgSO_4$ and evaporated giving mixture of products ^{31}P NMR: 19.8 ppm (**8** major product), 24.3 ppm (9–10%). The mixture was dissolved in 50 mL of CH_2Cl_2 and 2 mL of H_2O_2/water (1:1) was added at 0 °C and the reaction was stirred vigorously at this temperature for 2 h. Then 30 mL of water was added. The extraction with CH_2Cl_2 afforded the crude product **5b** which was purified by column chromatography (hexane–acetone 10:1).

Method B. To a stirred THF solution (100 mL) of optically active α-phosphoryl sulfoxide **7** (10 mmol) 5 mL of 2.2 M *n*-BuLi in hexane solution (11 mmol) was added at −78 °C. After 5 min solution of phenylselenyl bromide (0.011 mol), prepared by addition of equimolar amount of bromine to 10 mL of THF solution of diphenyldiselenide, was added all

at once. The reaction mixture was stirred for 2–3 min and then poured to the cooled to 0 °C mixture of 20 mL of diethyl ether and 20 mL of aqueous solution of sodium carbonate. The organic layer was separated, dried over $MgSO_4$ and the solvent evaporated affording compound **10**. α-Phenylselenyl substituted α-phosphoryl sulfoxide **10** was then oxidized in CH_2Cl_2 solution (100 mL) using 3 mL of H_2O_2/water mixture in 1:1 ratio. α-Phosphorylvinyl sulfoxide **5** prepared in this way was purified by column chromatography.

3.6.1. α-Diethyl (1-*p*-tolylsulfinyl)vinylphosphonate 5b. A colourless oil. Yield: 2.11 g (70%); $[\alpha]_D=+157$ (*c*, 2.1, acetone); IR (neat) 1243,1021; ^{31}P NMR (81 MHz, $CDCl_3$) δ 9.8 ppm; ^1H NMR (200 MHz, $CDCl_3$): δ 1.18 (t, 1H, $J=7.2$ Hz); 2.39 (s, 3H, C*H*$_3$Ar); 3.89–4.22 (m, 4H, CH_3CH_2-OP); 6.72 (d, 1H, $J_{P-H}=18.8$ Hz, *cis* C=CH); 6.96 (d, 1H, $J_{P-H}=39.8$ Hz, *trans* C=CH); 7.28–7.57 (4H, aromatic). ^{13}C NMR (50 MHz, $CDCl_3$); δ 15.5 (2×d, $J=7.7$ Hz); 21.1; 62.3 (d, $J=5.7$ Hz); 126.0; 129.4; 132.1(d, $J=5.5$ Hz); 138.8; 142.3; 146.5 (d, $J=177.4$ Hz). Anal. Calcd for $C_{13}H_{19}O_4PS$: C, 51.65%; H, 6.33%. Found C, 51.78; H, 6.52%.

3.6.2. α-Diethyl (1-*p*-tolylsulfinyl)-propen-1-ylphosphonate 5c. A colourless oil. Yield (*E*+*Z*): 2.08 g (66%). Isomer *Z*: ^{31}P NMR (81 MHz, $CDCl_3$): δ 12.1 ppm; ^1H NMR (200 MHz, $CDCl_3$):δ 1.21 (t, 3H, $J=7.2$ Hz, C*H*$_3$CH$_2$O); 1.32 (t, 3H, $J=7.2$ Hz, C*H*$_3$CH$_2$O,); 2.29 (dd, 3H, $J=7.3$; 2.9 Hz, CH_3-=); 2.41 (s, 3H, C*H*$_3$Ar); 4.0–4.23 (m, 4H, CH_3CH_2O); 7.43 (dq, 1H, $J_{H-H}=7.4$ Hz, $J_{P-H}=23.3$ Hz); 7.25–7.68 (4H, aromatic). Isomer *E*: ^{31}P NMR (81 MHz, $CDCl_3$): δ 10.1 ppm; ^1H NMR (200 MHz, $CDCl_3$): δ 1.12; 1.16 (2×t, 6H, C*H*$_3$CH$_2$O); 2.22 (dd, 3H, $J_{P-H}=3.1$ Hz, $J_{H-H}=7.3$ Hz); 2.35 (s, 3H, CH_3Ar); 3.6–4.2 (m, 4H, CH_3CH_2O); 7.35 (dq, 1H, $J_{P-H}=41.3$ Hz); 7.20–7.58 (4H, aromatic). Anal. Calcd for $C_{14}H_{21}O_4PS$: C, 53.15%, H, 6.69%. Found C, 53.37%; H, 6.75%.

3.6.3. α-Diethyl (1-*p*-tolylsulfinyl)-1-hexen-1-ylphosphonate 5d. A colourless oil. Yield (*E*+*Z*): 2.28 g (63%). Isomer *E*: $[\alpha]_D=+98$ (*c*, 1.2 acetone); ^{31}P NMR (81 MHz, $CDCl_3$): δ 10.4 ppm; ^1H NMR (200 MHz, $CDCl_3$): δ 0.93 (t, 3H, $J_{H-H}=7.1$ Hz); 1.12; 1.16 (2×t, 6H, $J_{H-H}=7.1$ Hz); 1.20–1.57 (m, 4H,); 2.37 (s, 3H, CH_3Ar); 2.53 (m, 2H); 3.56–3.99 (m, 4H, CH_3CH_2O); 7.29 (dt, 1H, $J_{P-H}=41.4$ Hz, $J_{H-H}=7.9$ Hz); 7.22–7.57 (4H, aromatic) ^{13}C (50 MHz, $CDCl_3$): δ 13.4; 15.7; 21.0; 21.9; 29.6 (d, $J=6.2$ Hz); 30.3; 61.7 (d, $J=5.0$ Hz); 126.1; 129.2; 134.8(d, $J=181.3$ Hz); 140.5; 146.6; 150.5(d, $J=7.5$ Hz).

3.7. Preparation of α-phosphorylvinyl selenides 11

α-Phosphoryl α-phenylselenenyl sulfoxide **10** (1 mmol) obtained from α-phosphoryl sulfoxide according to the procedure described for preparation of α-phosphorylvinyl sulfoxides was dissolved in 10 mL of benzene and heated under reflux for 2 h. Evaporation of benzene afforded the crude product **11**.

3.7.1. α-Diethyl (1-phenylselenenyl)vinylphosphonate 11b. A yellow pale oil. Yield: 0.281 g (88%); IR (neat) 1610, 1245, 1024; ^{31}P NMR (81 MHz, $CDCl_3$): δ 14.9 ppm; ^1H NMR (200 MHz, $CDCl_3$): δ 1.32 (td, 6H, $J_{H-H}=7.0$ Hz, $J_{P-H}=0.6$ Hz, C*H*$_3$CH$_2$OP); 3.95–4.25 (m, 4H, CH_3CH_2-OP); 5.73 (d, 1H, $J_{P-H}=44$ Hz); 6.61 (d, 1H, $J_{P-H}=20.4$ Hz); 7.3–7.65 (m, 5H aromatic). ^{13}C (50 MHz, $CDCl_3$); δ 15.6 (d, $J=7.3$ Hz); 61.2 (d, $J=5.5$ Hz); 118.23 (d, $J=8.1$ Hz); 134.1 (d, $J=181.2$ Hz); 126.2; 127.3; 130.3; 131.7. Anal. Calcd for $C_{12}H_{17}O_3PSe$: C, 45.15%; H, 5.37%. Found C, 45.31%; H, 5.48%.

3.7.2. α-Diethyl (1-phenylselenenyl)propenylphosphonate 11c. A yellow pale oil. Yield: 0.276 g (83%); ratio of *E*/*Z* isomers 1:1 separated by column chromatography hexane–acetone 30:1. Isomer *E*: IR (neat) 1610, 1245, 1027; ^{31}P NMR (81 MHz, $CDCl_3$): δ 14.6 ppm; ^1H NMR (200 MHz, $CDCl_3$): δ 1.25 (t, 6H, $J_{H-H}=7.1$ Hz, C*H*$_3$CH$_2$OP); 2.12 (dd, 3H, $J_{H-H}=7.3$ Hz, $J_{P-H}=3.2$ Hz, C*H*$_3$C=); 3.8–4.2 (m, 4H, CH_3CH_2OP); 6.66 (dq, 1H, $J_{P-H}=46$ Hz, $J_{H-H}=7.3$, *H*C=); 7.2–7.6 (m, 5H, aromatic); ^{13}C NMR (50 MHz, $CDCl_3$) 15.8 (d, $J=6.5$ Hz); 18.5 (d, $J=17.0$ Hz); 62.0 (d, $J=5.8$ Hz); 120.5 (d, $J=17.0$ Hz); 126.4; 130.2; 130.6; 154.2 (d, $J=13.8$ Hz); ^{77}Se NMR (57 MHz, $CDCl_3$) δ 283.6, $J=19.2$ Hz. Isomer *Z*: ^{31}P NMR (81 MHz, $CDCl_3$) δ 15.7 ppm; ^1H NMR (200 MHz, $CDCl_3$): δ 1.26 (dt, 6H, $J_{H-H}=7.1$ Hz, $J_{P-H}=0.5$ Hz, C*H*$_3$CH$_2$O); 2.10 (dd, 3H, $J_{P-H}=3.0$ Hz, $J_{H-H}=6.9$ Hz, C*H*$_3$C=); 3.9–4.25 (m, 4H, CH_3CH_2OP); 7.52 (dq, 1H, $J_{P-H}=19.1$ Hz, $J_{H-H}=6.9$ Hz, *H*C=); 7.2–7.5 (m, 5H, aromatic). ^{13}C NMR (50 MHz, $CDCl_3$): δ 16.1 (d, $J=6.7$ Hz); 18.4 (d, $J=6.4$ Hz); 62.1 (d, $J=5.4$ Hz); 120.5 (d, $J=189.5$ Hz); 126.4; 128.6; 130.2; 130.6; 154.2 (d, $J=13.8$ Hz). Anal. Calcd for $C_{13}H_{19}O_3PSe$: C, 46.86%; H, 5.75%. Found: C, 46.93%; H, 5.91%.

3.7.3. α-Diethyl (1-phenylselenenyl)hexenylphosphonate 11d. A yellow pale oil. Yield: 0.322 g (86%); ratio of *E*/*Z* isomers 1:1. Separated isomer *E*: ^{31}P NMR (81 MHz, $CDCl_3$): δ 14.7 ppm; ^1H NMR (200 MHz, $CDCl_3$): δ 0.8–1.6 (m, 7H); 1.25 (6H, t, $J_{H-H}=7.0$ Hz, C*H*$_3$CH$_2$OP); 2.57 (tdd, 2H, $J_{H-H}=7.8$, 7.2 Hz, $J_{P-H}=2.6$ Hz, C*H*$_2$C=); 4.0 (4H, m, CH_3CH_2OP); 6.58 (dt, 1H, $J_{P-H}=46$ Hz, $J_{H-H}=7.8$ Hz, *H*C=); 7.25–7.56 (5H, aromatic). ^{13}C NMR (50 MHz, $CDCl_3$): 13.2; 15.8 (d, $J=6.1$ Hz); 21.8; 30.2; 34.4 (d, $J=22.1$ Hz); 62.1 (d, $J=5.7$ Hz); 117.1 (d, $J=185$ Hz); 147.2 (d, $J=5.7$ Hz); 126.1; 126.9; 130.7; 131.2. Anal. Calcd for $C_{16}H_{25}O_3PSe$: C, 51.21%; H, 6.71%. Found: C, 51.45%, H, 6.95%.

3.8. Oxidation of selenides 11 to selenoxides 12

Method A. 2 mmol of the selenide **11** was dissolved in acetone (10 mL) and aqueous solution of sodium metaperiodate (2 mmol) was added dropwise at 0 °C. The reaction mixture was kept overnight in refrigerator and on the next day 20 mL of water added and extracted with $CHCl_3$ (3×15 mL).

Method B. To a solution of 2 mmol of the selenide **11** in CH_2Cl_2 0.25 mL of 30% H_2O_2 was added and reaction mixture was stirred vigorously for 15 min. After then 10 mL of water was added and reaction was extracted with (3×10 mL) CH_2Cl_2.

3.8.1. 1-(Diethoxyphosphoryl)vinyl phenyl selenoxide

12b. A slightly yellow oil. Yield: 0.67 g (~100%); IR (neat) 1243, 1025, 843; ^{31}P NMR (81 MHz, $CDCl_3$) δ 10.8 ppm; ^{1}H NMR (200 MHz, $CDCl_3$) δ: 1.15 (t, 6H, J_{H-H}=7.1 Hz, CH_3CH$_2$OP); 3.7–4.2 (m, 4H, CH$_3$CH_2OP); 6.77 (dd, 1H, J_{P-H}=18.4 Hz, J_{H-H}=1 Hz, *cis* C=CH); 7.12 (dd, 1H, J_{H-H}=1 Hz, J_{P-H}=41.1 Hz, *trans* C=CH); 7.4–7.82 (m, 5H, aromatic).

3.8.2. 1-(Diethylphosphoryl)propenyl phenyl selenoxide *E*-12c. A slightly yellow oil. Yield: 0.649 g (93%); IR (neat) 1247, 1021, 845; ^{31}P NMR (81 MHz, $CDCl_3$): δ 11.7 ppm; ^{1}H NMR (200 MHz, $CDCl_3$): δ 1.22 (t, 6H, J_{H-H}=7.1 Hz, CH_3CH$_2$OP); 2.15 (dd, 3H, J_{H-H}=7.3 Hz, J_{P-H}=3.0 Hz, CH_3C=); 3.4–4.2 (m, 4H, CH$_3$CH_2OP); 7.45 (dq, 1H, J_{P-H}=41.9 Hz, J_{H-H}=7.3 Hz, *trans* C=CH); 7.37–7.85 (m, 5H, aromatic).

Compound **Z-12c**. Yield: 0.677 g (97%); ^{31}P NMR (81 MHz, $CDCl_3$) δ 12.8 ppm; ^{1}H NMR (200 MHz, $CDCl_3$): δ 1.04 (td, 6H, J_{H-H}=7.0 Hz, J_{P-H}=0.5 Hz, CH_3CH$_2$OP); 2.22 (dd, 3H, J_{P-H}=2.8 Hz, J_{H-H}=7.3 Hz, CH_3C=); 4.15 (dq, 4H, J_{P-H}=8.5 Hz, J_{H-H}=7.0 Hz, CH$_3$CH_2OP); 7.46 (dq, 1H, J_{H-H}=7.3 Hz, J_{P-H}=21.2 Hz, C=CH); 7.22–7.61 (m, 5H, aromatic).

3.8.3. 1-(Diethylphosphoryl)hexenyl phenyl selenoxide *E*-12d. A slightly yellow oil. Yield: 0.75 g (96%); ^{31}P NMR (81 MHz, $CDCl_3$) 12.0 ppm ^{1}H NMR (200 MHz, $CDCl_3$): δ 0.78–1.62 (m, 7H); 1.24 (t, 3H, J_{H-H}=7.0 Hz, CH_3CH$_2$OP); 2.55 (m, 2H, CH_2C=); 3.4–4.25 (m, 4H, CH$_3$CH_2OP); 7.38 (dt, J_{P-H}=42 Hz, J_{H-H}=7.9 Hz, CH=); 7.4–7.8 (m, 5H).

3.9. Preparation of alkynylphosphonates 13

The benzene solution (10 mL) of 1 mmol of the selenoxide **12** was heated under reflux for 3 h. After evaporation of solvent, alkynylphosphonate **13** was purified by distillation on Kugel Rohr.

3.9.1. Diethylphosphorylacetylene 13b. A slightly yellow oil. Yield: 0.15 g (93%); bp 80–85 °C/10 mm Hg. ^{31}P NMR (81 MHz, $CDCl_3$): δ 7.7 ppm; ^{1}H NMR (200 MHz, $CDCl_3$)): δ 1.38 (td, 6H, J_{H-H}=7.1 Hz, J_{P-H}=0.7 Hz, CH_3CH$_2$OP); 2.89 (d, 1H, J_{P-H}=13.2 Hz), 4.09 (dq, 4H, J_{P-H}=8.1 Hz, J_{H-H}=7.1 Hz CH$_3$CH_2OP ^{13}C NMR (50 MHz, $CDCl_3$): 15.8 (d, ^3J=6.9 Hz); 62.1 (d, ^2J=6.3 Hz); 70.2 (d, ^1J=307 Hz); 101.0 (d, ^2J=57.1 Hz). HRMS (70 eV) $C_6H_{11}O_3P$ requires 162.04458. Found: 162.0459.

3.9.2. Diethyl phosphorylpropyne 13c. A slightly yellow oil. Yield: 0.142 g (81%); bp 88–92 °C/10 mm Hg ^{31}P NMR (81 MHz, $CDCl_3$) δ 5.7 ppm; ^{1}H NMR (200 MHz, $CDCl_3$): δ 1.35 (td, 6H, J_{H-H}=7.1 Hz, J_{P-H}=0.8 Hz, CH_3CH$_2$OP); 2.00 (d, 3H, J_{P-H}=4.7 Hz, CH_3C), 4.13 (dq, 4H, J_{P-H}=7.8 Hz, J_{H-H}=7.1 Hz, CH$_3$CH_2OP). ^{13}C NMR (50 MHz, $CDCl_3$): 4.4 (d, ^3J=4.7 Hz); 16.0 (d, ^3J=7.1 Hz); 61.7 (^2J=5.9 Hz); 69.9 (d, ^1J=305 Hz); 98.9 (d, ^2J=54.7 Hz). HRMS (70 eV) $C_7H_{13}O_3P$ requires 176.06023. Found 176.0592.

3.9.3. Diethyl phosphorylhexyne 13d. A slightly yellow oil. Yield: 0.207 g (95%); bp 50–55 °C/2 mm Hg ^{31}P NMR (81 MHz, $CDCl_3$): δ 5.4 ppm; ^{1}H NMR (200 MHz, $CDCl_3$): δ 0.92 (t, 3H, J=7.1 Hz); 1.22–1.60 (m, 2H); 1.37 (dt, 6H, J_{H-H}=7.0 Hz, J_{P-H}=0.7 Hz, CH_3CH$_2$OP); 2.35 (dt, 2H, J_{H-H}=7.0 Hz, J_{P-H}=4.4 Hz); 4.15 (dq, 4H, J_{P-H}=8.6 Hz, J_{H-H}=7.0 Hz, CH$_3$CH_2OP). HRMS (70 eV) $C_{10}H_{19}O_3P$ requires 218.1072. Found 218.1032.

3.10. Nucleophilic addition to α-phosphorylvinyl *p*-tolyl sulfoxide 5c

3.10.1. α-Diethyl (1-*p*-tolylsulfinyl)-(2-dimethylamino)-ethylphosphonate 7e. Cooled dimethylamine (0.5 mL) was added to 0.3 g (1 mmol) of α-phosphorylvinyl sulfoxide at 0 °C. The reaction mixture was stirred overnight. An excess of Me_2NH was removed affording **7e** as a mixture of diastereomers 2:1 obtained in quantitative yield. ^{31}P NMR (81 MHz, $CDCl_3$) 21.6/19.8 ppm ^{1}H NMR (200 MHz, $CDCl_3$): δ 1.30 (t, 3H, J=7.1 Hz, CH_3CH$_2$OP); 2.20 (s, 3H, CH_3N); 2.22 (s, 3H, CH_3N); 2.40 (s, 3H, CH_3Ar); 2.74–2.87 (m, 2H, NCH$_2$); 3.08 (td, 1H, J_{P-H}=17.5 Hz, J_{H-H}=6.0 Hz—major); 3.35 (td, 1H, J_{P-H}=17.9 Hz, J_{H-H}=6.2 Hz—minor); 3.97–4.22 (m, 4H, CH$_3$CH_2OP); 7.26–7.34 and 7.51–7.62 (m, 4H, aromatic).

3.10.2. α-Diethyl (1-*p*-tolylsulfinyl)-(2-methoxy)-ethylphosphonate 7f. To a stirred methanol solution (25 mL) of 0.3 g (1 mmol) of (*S*)-(1-diethoxyphosphoryl)vinyl *p*-tolyl sulfoxide 0.057 g (1.2 mmol) of NaH (50%) was added at room temperature. After 2 h of stirring the reaction was quenched with aqueous solution of NH_4Cl, solution was extracted with chloroform (3×30 mL). The $CHCl_3$ extract was dried over anhydrous $MgSO_4$ and after evaporation afforded mixture of diastereomers: ^{31}P NMR (81 MHz, $CDCl_3$) 19.5/19.4 ppm in 2:1 ratio. Purification by column chromatography (hexane–acetone 10:1). Yield: 0.25 g (75%); ^{1}H NMR (200 MHz, $CDCl_3$): δ 1.24 (t, 6H, J=7.1 Hz, CH_3CH$_2$OP); 2.40 (s, 3H, CH_3Ar); 3.20 (td, 1H, J_{P-H}=17.2 Hz, J_{H-H}=3.6 Hz); 3.34 (s, 3H, CH_3O); 3.87–4.25 (6H, m, CH$_3$CH_2OP+CH$_3$OCH_2); 7.23–7.36 and 7.57–7.69 (4H, aromatic). ^{13}C NMR (50 MHz, $CDCl_3$): 16.0 (d, ^3J=4.8 Hz); 21.3; 58.9; 62.6 (d, J=6.4 Hz); 64.5 (d, J=138.4 Hz); 65.1 Hz; 125.4; 126.0; 129.4; 141.9. Anal. Calcd for $C_{14}H_{23}O_5PS$: C, 49.93%; H, 6.91%. Found: C, 49.82%, H, 6.95%.

3.10.3. α-Diethyl (1-*p*-tolylsulfinyl)-(2,2-dimethyl)-(2-nitro)-ethylphosphonate 7g. To a stirred THF solution (50 mL) of 0.3 g (1 mmol) of (*S*)-(1-diethoxyphosphoryl)-vinyl *p*-tolyl sulfoxide **5c** sodium salt of 2-nitropropane, generated by addition 0.057 g (1.2 mmol) of NaH (50%) to 0.12 g of 2-nitropropane in THF solution (15 mL), was added at 0 °C. The reaction mixture was stirred for 2 h (0 °C to room temperature) and was quenched with aqueous solution of NH_4Cl. Organic solvents were evaporated and the remaining aqueous solution was extracted with chloroform (2×30 mL). The $CHCl_3$ extract was dried over anhydrous $MgSO_4$ and evaporated giving mixture of diastereomers ^{31}P NMR (81 MHz, $CDCl_3$) 21.7/18.5 ppm in 2:1 ratio. ^{1}H NMR (200 MHz, $CDCl_3$): δ 1.22 (s, 3H); 1.32 (t, 6H, J=7.0 Hz, CH_3CH$_2$OP); 1.47 (s, 3H); 2.40 (s, 3H, CH_3Ar); 2.32–2.6 (m, 2H); 3.03 (major) (ddd, 1H, J_{P-H}=17.2 Hz, J_{H-H}=5.8, 3.4 Hz, PC*H*S); 3.35 (minor) (ddd, 1H, J_{P-H}=20.3 Hz, J_{H-H}=6.9, 3.6 Hz); 3.95–4.15

(4H, m, CH_3CH_2OP); 7.27–7.36 and 7.47–7.64 (4H, aromatic).

3.10.4. α-Diethyl (1-*p*-tolylsulfinyl)-(2,2-dicarboethoxy)-ethylphosphonate 7h. To a stirred THF solution (50 mL) of 0.3 g (1 mmol) of (*S*)-(1-diethoxyphosphoryl)vinyl *p*-tolyl sulfoxide **5c** lithium salt of diethyl malonate, generated by addition 0.016 g (2 mmol) of LiH to 0.19 g of diethyl malonate in THF solution, was added at 0 °C. The reaction mixture was stirred for 2 h (0 °C to room temperature) and was quenched with aqueous solution of NH_4Cl. Organic solvents were evaporated and the remaining aqueous solution was extracted with chloroform (2×30 mL). The $CHCl_3$ extract was dried over anhydrous $MgSO_4$ and evaporated giving mixture of diastereomers: ^{31}P NMR (81 MHz, $CDCl_3$) 21.6/18.9 ppm in 2:1 ratio, purified by column chromatography (hexane–acetone 10:1). Yield: 0.41 g (88%); ^1H NMR (200 MHz, $CDCl_3$): δ 1.1–1.38 (m, 12H, $CH_3CH_2OP+CH_3CH_2OC$); 1.38–1.79 (m, 2H); 2.37 (s, 3H, CH_3Ar); 3.16 (major) (td, 1H, $J_{P-H}=17.4$ Hz, $J_{H-H}=7.2$ Hz); 3.47 (minor) (td, 1H, $J_{H-H}=7.4$ Hz, $J_{P-H}=14.4$ Hz); 3.63 (major) (t, 1H, $J_{H-H}=7.1$ Hz); 3.87 (minor) (t, 1H, $J_{H-H}=7.1$ Hz); 3.87–4.21 (m, 8H, $CH_3CH_2OP+CH_3CH_2OC$); 7.25–7.36 (m, 2H, aromatic) and 7.47 (major) and 7.64 (minor) (4H, aromatic). Anal. Calcd for $C_{14}H_{31}O_8PS$: C, 51.94%; H, 6.76%. Found: C, 51.79.%, H, 6.95%.

3.11. Reaction of vinyl selenide 11c with Me_2NH

Cooled dimethylamine was added to α-phosphorylvinyl selenide **11c** (0.23 g, 1 mmol) at 0 °C. The reaction mixture was stirred overnight. An excess of Me_2NH was removed and residue was a mixture of diastereomers of **14** obtained in quantitative yield, ^{31}P NMR (81 MHz, $CDCl_3$) 26.6/26.7 ppm.

From *Z*-**11**—ratio 2:1 from *E*-**11**—ratio 10:1. ^1H NMR (200 MHz, $CDCl_3$): δ 1.25–1.34 (9H, m, $CH_3CH_2OP+CH_3C$); 2.22 and 2.25 (2×s, 6H, CH_3N); 3.07–3.17 (m, 1H, CHN); 3.22 (dd, 1H, $J_{P-H}=17.9$ Hz, $J_{H-H}=3.8$ Hz, PCHSe); 4.02–4.29 (m, 4H, CH_3CH_2OP); 7.23–7.69 (m, 5H, aromatic).

3.12. Oxidation of phosphonate 14

To a solution of adduct **14** (mixture of diastereomers) in CH_2Cl_2 mixture of 30% H_2O_2 and water (1:1) was added at (a) −20 °C, (b) room temperature. The reaction was stirred for 0.5–1 h at appropriate temperature yielding mixture of products where β-ketophosphonate **15** (a) or α-phosphorylvinyl selenoxide *E*-**12** (b) as major ones. In both cases *E*-**12** and **15** were separated by chromatography.

3.13. Nucleophilic addition to α-phosphorylpropenyl phenyl selenoxide 12c

3.13.1. Diethyl malonate. To a solution of 3 mmol of diethyl malonate in 20 mL THF, 0.16 g (3.3 mmol) of sodium hydride 50% in oil was added at room temperature. After 30 min the reaction mixture was cooled down to −78 °C and vinyl selenoxide *E*-**12c** (3 mmol) was added. The stirred reaction mixture was warmed up to room temperature, quenched with aqueous NH_4Cl (20 mL) and the product extracted with $CHCl_3$ (3×10 mL). The organic solution was dried over $MgSO_4$, solvent evaporated and the product **16** purified by column chromatography (hexane–acetone 18:1). Yield: 0.628 g (65%); IR(neat) 1729, 1252, 1044; ^{31}P NMR (81 MHz, $CDCl_3$) δ 24.3 ppm; ^1H NMR (200 MHz, $CDCl_3$): δ 1.26 (t, 6H, $J=7.1$ Hz, CH_3CH_2OP); 1.29 (t, 3H, $J_{H-H}=7.0$ Hz, CH_3); 1.31 (t, 3H, $J_{H-H}=7.0$ Hz; 2.36 (s, 3H, $CH_3C=$); 3.37 (d, 2H, $J=24.9$ Hz, $PCH_2C=$); 3.93–4.32 (m, 4H, CH_3CH_2OP).

2-Nitropropane. To a solution of 2-nitropropane (1 mmol) in 30 mL THF potassium *t*-butoxide (1 mmol) was added at room temperature and the mixture was stirred for 30 min. Then the phosphoryl selenoxide *E*-**12c** (1 mmol) was added and this mixture was stirred at room temperature for the next 0.5 h. The reaction was quenched with aqueous NH_4Cl (10 mL) and the product extracted with $CHCl_3$ (3×10 mL). The organic solution was dried over $MgSO_4$, solvent evaporated giving mixture of two products **17** and **18** in about 1:1 ratio, defined by ^{31}P NMR spectra. Both products were separated by column chromatography (benzene/acetone).

3.13.2. Diethyl (2,3-dimethyl)(3-nitro) buten-1 phosphonate 17. A pale yellow oil. Yield: 0.11 g (42%); IR (neat) 1241, 1050, 1025; ^{31}P NMR (81 MHz, $CDCl_3$): δ 16.8 ppm; ^1H NMR (200 MHz, $CDCl_3$): δ 1.33 (t, 6H, $J_{H-H}=7.0$ Hz, CH_3CH_2OP); 1.74 (s, 6H, CH_3CN); 2.08 (dd, 3H, $J_{H-H}=1$ Hz, $J_{P-H}=3.3$ Hz, $CH_3C=$); 4.10 (dq, 4H, $J_{P-H}=8.1$ Hz, $J_{H-H}=7.0$ Hz, CH_3CH_2OP); 5.73 (dq, 1H, $J_{P-H}=13.4$, $J_{H-H}=1$ Hz).

3.13.3. Diethyl 1-propen-3-ol phosphonate 18c. Yield: 0.087 g (45%); ^{31}P NMR (81 MHz $CDCl_3$) δ 19.5 ppm; ^1H NMR (200 MHz $CDCl_3$): δ 1.28 (t, 6H, $J_{H-H}=7.1$ Hz, CH_3CH_2OP); 2.93 (m, 1H, OH); 4.03 (dq, 4H, $J_{H-H}=7.1$ Hz, $J_{P-H}=7.7$ Hz CH_3CH_2OP); 4.22 (m, 2H, CH_2OH); 5.95 (tdd, 1H, $J_{H-H}=2.1$, 17.2 Hz, $J_{P-H}=21.3$ Hz, PCH=); 6.8 (tdd, 1H, $J_{H-H}=3.6$, 17.2 Hz, $J_{P-H}=22.6$ Hz, CH=).

Overhauser effect of **17**. Irradiation of the vinyl proton (δ 5.73 ppm) caused 21% increasing of signal 2.08 (dd, CH_3). Irradiation of the methyl protons (δ 2.08 ppm) caused a 17% enhancement of signal 5.73 (dq, =CH).

3.13.4. Diethyl 1-hexen-3-ol phopsphonate 18d. Yield: 0.18 g (76%); $[\alpha]_D=+8.1$ (*c* 0.5, acetone), ^{31}P NMR (81 MHz, $CDCl_3$); δ 19.8 ppm; ^1H NMR (200 MHz, $CDCl_3$): δ 0.91 (t, 3H, $J=7.2$ Hz, CH_3CH_2); 1.30 (t, 6H, $J=7.0$ Hz, CH_3CH_2OP); 1.2–1.6 (m, 4H); 2.63 (m, 1H, OH); 4.05 (dq, 4H, $J_{H-H}=7.0$ Hz, $J_{P-H}=8.2$ Hz, CH_3CH_2-OP); 4.25 (m, 1H, CHOH); 5.90 (ddd, 1H, $J_{H-H}=17.1$, 1.7 Hz, $J_{P-H}=21.0$ Hz, PCH); 6.77 (ddd, 1H, $J_{H-H}=17.1$, 4.2 Hz, $J_{P-H}=22.4$ Hz, CH=).

References and notes

1. Minami, T.; Motoyoshiya, J. *Synthesis* **1992**, 333–349.
2. Mikołajczyk, M.; Bałczewski, P. *Top. Curr. Chem.* **2003**, *223*, 161–214.

3. Mastalerz, P. In *Handbook of Organophosphorus Chemistry*; Engel, R., Ed.; Marcel Dekker: New York, 1992; Chapter 7, p 277.
4. Venugopalan, B.; Hamlet, A. B.; Durst, T. *Tetrahedron Lett.* **1981**, *22*, 191–194.
5. Gulea, M.; Masson, S. *Top. Curr. Chem.* **2003**, *229*, 161–198.
6. Midura, W. H.; Krysiak, J. A.; Wieczorek, M. W.; Majzner, W. R.; Mikołajczyk, M. *Chem. Commun.* **1998**, 1109–1110. Midura, W. H.; Krysiak, J. A.; Mikołajczyk, M. *Tetrahedron* **1999**, *55*, 14791–14802.
7. Mikołajczyk, M.; Midura, W. H. *Tetrahedron: Asymmetry* **1992**, *3*, 1515–1518. Midura, W. H.; Krysiak, J. A.; Mikołajczyk, M. *Tetrahedron: Asymmetry* **2003**, *14*, 1245–1249.
8. Liotta, D.; Zima, G.; Barnum, Ch.; Saindane, M. *Tetrahedron Lett.* **1980**, *21*, 3643–3646.
9. Mikołajczyk, M.; Grzejszczak, S.; Korbacz, K. *Tetrahedron Lett.* **1981**, *22*, 3097–3100.
10. (a) Mikołajczyk, M.; Kiełbasiński, P.; Grzejszczak, S. *Synthesis* **1983**, 332–334. (b) Mikołajczyk, M.; Bałczewski, P. *Synthesis* **1989**, 101–106.
11. Mikołajczyk, M.; Midura, W.; Grzejszczak, S.; Zatorski, A.; Chefczyńska, A. *J. Org. Chem.* **1978**, *43*, 473–478. Mikołajczyk, M.; Midura, W.; Miller, A.; Wieczorek, M. W. *Tetrahedron* **1987**, *43*, 2967–2976.
12. Reetz, M. T.; Peter, R.; Von Itzstein, M. *Chem. Ber.* **1987**, *120*, 121–124.
13. This hypothesis was recently supported by X-ray analysis of 1-diphenylphosphinoylvinyl *p*-tolyl sulfoxide, where a hydrogen bond between vinyl proton and sulfinyl oxygen with the distance 2.305 (30) Å was found. Midura, W. H.; Krysiak, J. A.; Cypryk, M.; Mikołajczyk, M.; Wieczorek, M. W.; Filipczak, A. D. *Eur.J. Org. Chem.*, in press.
14. Midura, W. H.; Mikołajczyk, M. *Tetrahedron Lett.* **1995**, *36*, 2871–2874.
15. Sulfoxide **5′e** was prepared from (+)-(*S*)-dimethoxyphosphorylmethyl *p*-tolyl sulfoxide according to the procedure described in our recent paper: Midura, W. H.; Mikołajczyk, M. *Tetrahedron Lett.* **2002**, *43*, 3061–3065.
16. Annunziata, R.; Cinquini, M.; Cozzi, F.; Raimondi, L.; Rastelli, A. *Gazz. Chim. Ital.* **1985**, *115*, 637–641. Nokami, J.; Mandai, T.; Nishimura, A.; Takeda, T.; Wakabayashi, S.; Kunieda, N. *Tetrahedron Lett.* **1986**, *27*, 5109–5112. Kosugi, H.; Kitaoka, A.; Takahashi, A.; Uda, H. *Chem. Commun.* **1986**, *56*, 1268–1270.
17. Dominguez, E.; Carretero, J. C. *Tetrahedron* **1990**, *46*, 7197–7206. Trost, B. M.; Mallart, S. *Tetrahedron Lett.* **1993**, *34*, 8025–8028. Guerrero-de la Rosa, V.; Ordonez, M.; Alcudia, F.; Llera, J. M. *Tetrahedron Lett.* **1995**, *36*, 4889–4892.
18. Nokami, J.; Taniguchi, A.; Honda, M.; Fukutake, S. *Chem. Lett.* **1995**, 1025–1026.