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α-Phosphoryl Sulfoxides. XI. Sulfenylation of α-Phosphoryl Sulfoxides and a General Synthesis of Optically Active Ketene Dithioacetal Mono-S-oxides[1-3].

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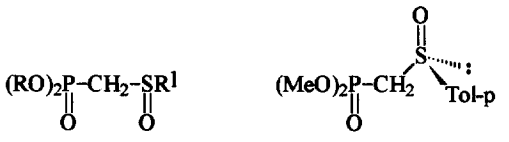
Abstract: Sulfenylation and selenenylation of α-phosphoryl sulfoxides **1** with S-methyl methanethiosulfonate and phenylselenenyl bromide, respectively, affording α-methylsulfenyl- and α-phenylselenenyl-α-phosphoryl sulfoxides **8** and **9** are described. Sulfenylation of (+)-(S)-dimethoxyphosphorylmethyl p-tolyl sulfoxide **2** gave a mixture of optically active diastereoisomers of the sulfoxide **8a** which is a key substrate in the Horner-Wittig synthesis of enantiomeric ketene dithioacetal mono-S-oxides **10**. The **E/Z** ratio of geometrical isomers of **10** was determined and briefly discussed. The crystal and molecular structure of **E**-1-p-tolylsulfinyl-1-methylsulfenyl-2-phenyl-ethene **10a** is reported.

INTRODUCTION

Among α-phosphoryl substituted organosulfur compounds[4], α-phosphoryl sulfoxides **1**, first prepared in racemic and enantiomeric forms in our laboratory[5,6], deserve special attention as useful synthetic reagents and model compounds in stereochemical studies. The most important application of α-phosphoryl sulfoxides **1** is their use in the synthesis of α,β-unsaturated sulfoxides[7], in particular of optically active ones[6].

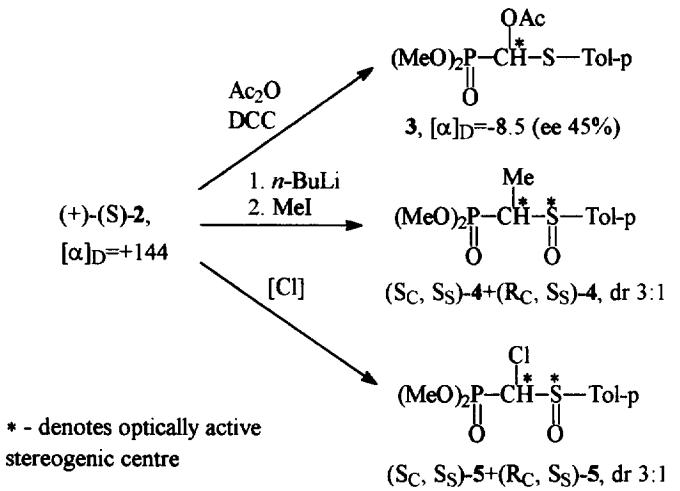
The structure of α-phosphoryl sulfoxides **1** offers also many possibilities for studies of asymmetric induction, especially on the α-methylene carbon atom. In fact, the Pummerer reaction of (+)-(S)-dimethoxyphosphorylmethyl p-tolyl sulfoxide **2**[8] as well as its methylation[9] and chlorination[10] were



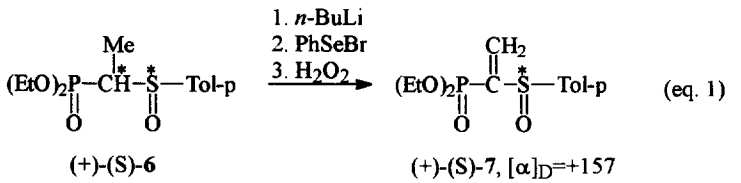
1 (+)-(S)-**2**

found to occur in an asymmetric way to give the corresponding optically active enantiomeric (**3**) and diastereoisomeric (**4** and **5**) products in unequal ratio (see Scheme 1).

Scheme 1. Asymmetric Reactions of α-Phosphoryl Sulfoxide **2**.



Recently, a mixture of the diastereoisomeric sulfoxides **6** obtained by methylation of the α-unsubstituted sulfoxide has been used as a substrate in the synthesis of (+)-(S)-α-diethoxyphosphorylvinyl p-tolyl sulfoxide **7** which is a new chiral Michael acceptor and dienophile[11].



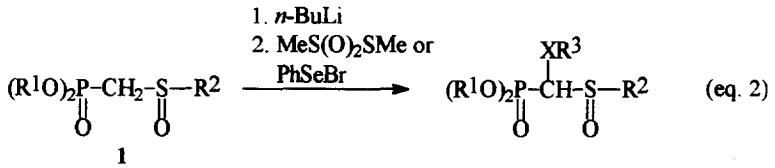
(eq. 1)

In a search for other synthetic applications of α-phosphoryl sulfoxides **1** we turned our attention to the sulfenylation reaction of **1**. The products of this reaction should be key substrates in the synthesis of ketene

dithioacetal mono-S-oxides utilizing the Horner-Wittig olefination raction. The results obtained are described in this paper.

RESULTS AND DISCUSSION

The sulfenylation reaction of α-phosphoryl sulfoxides **1** was carried out in a tetrahydrofuran solution at -78°C using *n*-butyllithium for the α-phosphonate carbanion generation and S-methyl methanethiosulfonate as a sulfenylating agent[12]. When phenylselenenyl bromide was used for the reaction with the α-phosphoryl sulfoxide **1** carbanion, the corresponding selenenylation product was obtained. The analytically pure α-methylsulfenyl- and α-phenylselenenyl sulfoxides **8** and **9** were isolated from the reaction mixture by column chromatography on silica gel. Their structure was confirmed by the ^{1}H and ^{31}P NMR spectra and elemental analysis. Analysis of the NMR spectra of the crude reaction products revealed that the reaction investigated resulted in the formation of two diastereoisomers. The ratios of the diastereoisomers of **8** and **9** and other experimental details are given in Table 1.



8a, R^1=Me, R^2=Tol-p, XR^3=SMe
8b, R^1=Me, R^2=Ph, XR^3=SMe
8c, R^1=Et, R^2=Ph, XR^3=SMe
8d, R^1=Et, R^2=Me, XR^3=SMe
9, R^1=Me, R^2=Tol-p, XR^3=SePh

Table 1. Selected Experimental and Spectroscopic Data of Sulfenylated and Selenenylated α-Phosphoryl Sulfoxides **8** and **9**.

Compound No	Yield %	Diast. ratio	^{31}P NMR ppm
8a	70	1.6:1	18.7/18.0
8b	65	1.4:1	-
8c	80	1.4:1	16.0/14.9
8d	50[a]	1.4:1	14.7/14.6
9	73	1.8:1	20.2/18.9

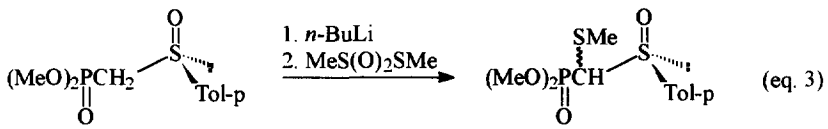
a - yield from ^{31}P NMR spectra of crude reaction mixture [13]

To verify whether the observed ratio of the diastereoisomeric sulfoxides **8** and **9** is a result of a kinetic or thermodynamic control, α-methylsulfenyl-α-phosphorylmethyl p-tolyl sulfoxide **8a** (dr 1.6:1) was treated with sodium hydride in THF overnight. After quenching the above mixture, the same ratio of the

diastereoisomeric sulfoxides **8a** was detected by NMR spectra. This observation indicates that the ratio of the diastereoisomeric sulfoxides **8** and **9** is thermodynamically controlled. Obviously, it is due to a high acidity of the α-methine hydrogen in both structures **8** and **9** and fast epimerization at the α-stereogenic carbon centre under basic reaction condition.

Since the sulfenylation products **8** contain α-hydrogen, proton elimination may readily occur on treatment with a base yielding the appropriate α-phosphonate carbanion. This anion may be used in the Horner-Wittig olefination to afford ketene dithiocetal mono-S-oxides **10**. The latter are in themselves useful synthetic intermediates which can be converted to carboxylic acids by hydrolysis, to homologated aldehydes by reduction followed by hydrolysis, or to ketones on reaction with alkyllithiums followed by alkylation. In terms of the Umpolung concept, ketene dithioacetal mono-S-oxides **10** are $^{+}CC(O)^{-}$ synthons[14].

Our intention to develop the synthesis of optically active synthons of this type, which would be of great interest for asymmetric synthesis, led us to explore the sulfenylation reaction of (+)-(S)- and (-)-(R)-dimethoxyphosphorylmethyl p-tolyl sulfoxide **2** and the Horner-Wittig reaction of the sulfenylation products.



(eq. 3)

(+)-(S)-**2**
$[\alpha]_D$=+144

(-)-**8a**, $[\alpha]_D$=-168
[from (-)-(R)-**2**, $[\alpha]_D$=-137.8
(+)-**8a**, $[\alpha]_D$=+152.6 was obtained]

As expected, the sulfenylation of both enantiomers of **2** with S-methyl methanethiosulfonate gave the corresponding mixtures of the optically active, diastereoisomeric sulfoxides **8a** in 75% yield. Without separation of diastereoisomers the sulfenylated sulfoxide (-)-**8a** was subjected to the Horner-Wittig reaction with benzaldehyde under standard conditions (Procedure A). Thus, a solution of (-)-**8a** in tetrahydrofuran was treated with *n*-butyllithium at -78°C and after a short time with benzaldehyde. The corresponding ketene dithioacetal mono-S-oxide **10a** was formed in 80% yield as a mixture of geometrical isomers **E** and **Z** in a 2.2:1 ratio. The **E/Z** ratio of **10a** was found to be dependent on the Horner-Wittig reaction conditions. For instance, the reaction of (-)-**8a** with benzaldehyde carried out under phase-transfer catalytic conditions (50% KOH/CH_2Cl_2/TEBAB) (Procedure C) gave **10a** in 75% yield and with the **E/Z** ratio equal to 3:1[15]. However, when sodium hydride was used as a base (Procedure B), the prevailing isomer was **Z-10a** (**E/Z**=1:1.8)[16].

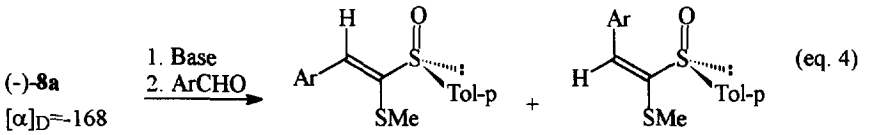
Similar results were obtained with two other aromatic aldehydes: p-methoxybenzaldehyde and p-bromobenzaldehyde (see Scheme 2).

In the case of **10a** and **10b** we were able to separate by column chromatography the obtained **E/Z** mixtures into pure isomers. Likewise from **10c** the major **E**-isomer was isolated in a pure state. It is interesting

to point out that the less polar **E**-isomers of **10** turned out to be the solids while the more polar **Z**-isomers were liquids.

Assignment of the **E** and **Z** configuration to geometrical isomers of **10a** was based in the first instance on the additive increments method[17] which was extended by us to vinylic sulfoxides[18]. Althoug there are some differences between the calculated and observed δ_H-values, the relative positions of the chemical shift for the β-vinyl proton in **E-10a and Z-10a** were predicted correctly.

Scheme 2. Synthesis of Ketene Dithioacetal Mono-S-oxides **10**.



(eq. 4)

E-10 **Z-10**

Comp. No	Procedure	Yield of (E+Z)-10 %	E-10		Z-10	
			$[\alpha]_D$	δ vinyl Found/Calcd.	$[\alpha]_D$	δ vinyl Found/Calcd.
10a, Ar=Ph	A, B, C	72-80	+212	7.81/7.17	-398	7.09/6.75
10b, Ar=p-MeOPh	A	65	+196	a/7.12	-310	a/6.70
10c, Ar=p-BrPh	B	73	+188	7.74/7.20	b	6.93/6.78

a-Vinyl proton of **10b** is covered by aromatic protons; b-the **Z** isomer of **10c** was not isolated in a pure state.

To prove unequivocally the above tentative assignments, the crystal and molecular structure of the sulfoxide (+)-**10a**, $[\alpha]_D$=+212, m.p. 107-108°C, was determined by X-ray diffractometric technique. Its molecular structure with the atom numbering system is shown in Fig. 1. The most important result of the X-ray analysis is that the investigated geometrical isomer of the sulfoxide **10a** has the **E**-geometry. Moreover, the absolute configuration S at the stereogenic sulfur atom was additonally confirmed by three methods: the Rogers η-test[19], the Hamilton test[20], and calculation of the Flack parameter x[21].

Fig. 2 shows the Newman projection around the C1-S2 bond which clearly reveals that the lone electron pair at the sulfur atom S2 is located synclinally with respect to the sulfur atom S1.

The crystal packing of the molecule of (+)-**E-10a** in the unit cell is presented in Fig. 3 in which intra- and intermolecular short contacts are depicted. In the solid state conformation of this sulfoxide there are two short intramolecular hydrogen contacts. The first is between the sulfinyl oxygen atom 01 and the β-vinyl hydrogen at C2 of 2.257Å. The second short contact is observed between 01 and the aromatic hydrogen at C11 of 2.818Å. The molecules of the sulfoxide investigated are held together by two intermolecular hydrogen bonds

between the hydrogen at C14 and the sulfinyl oxygen atom 01 of 2.394Å and the hydrogen at C16 and 01 of 2.461Å.

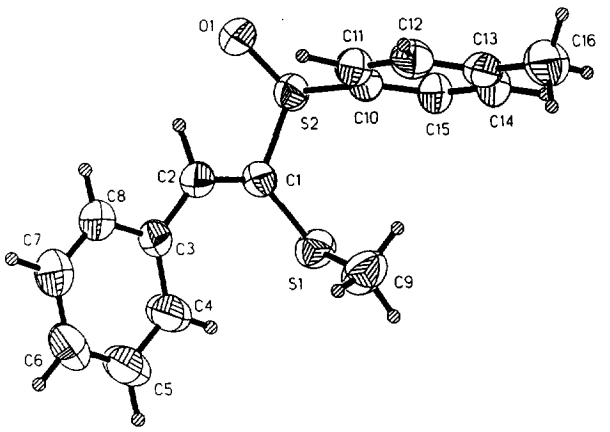


Fig.1. Thermal ellipsoidal view of **10a** with atom numbering scheme.

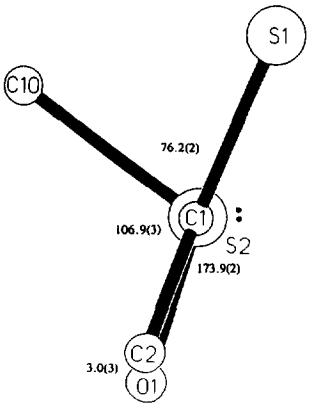


Fig. 2. The Newman projection perpendicular to the C1-S2 bond.

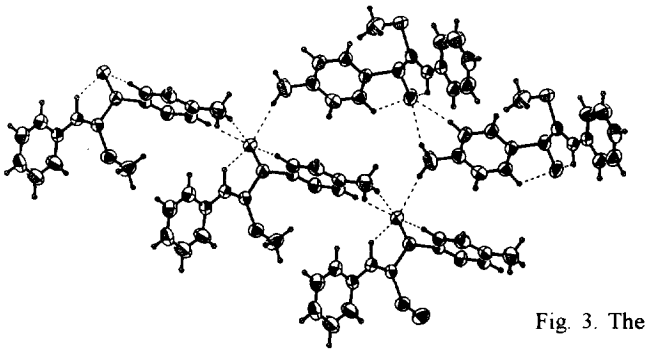


Fig. 3. The crystal packing of **10a** in the unit cell.

The bond distances and angles are listed in Table 2 and 3, respectively. They do not show significant deviations from the expected values. The geometry at phosphorus and sulfur is close to tetrahedral.

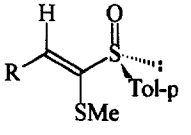
Table 2. Bond lengths (Å).

S1-C1	1.755 (3)	C7-C8	1.378 (5)	C7-H71	1.009 (10)
S1-C9	1.807 (4)	C10-C11	1.386 (5)	C8-H81	0.985 (10)
S2-01	1.484 (3)	C10-C15	1.380 (4)	C9-H91	0.963 (10)
S2-C1	1.811 (3)	C11-C12	1.368 (50	C9-H92	1.023 (10)
S2-C10	1.798 (3)	C12-C13	1.398 (50	C9-H93	0.988 (10)
C1-C2	1.331 (5)	C13-C14	1.391 (50	C11-H111	1.059 (10)
C2-C3	1.458 (5)	C13-C16	1.522 (5)	C12-H121	0.985 (10)
C3-C4	1.400 (5)	C14-C15	1.386 (5)	C14-H141	1.030 (10)
C3-C8	1.385 (5)	C2-H21	1.092 (10)	C15-H151	1.019 (10)
C4-C5	1.382 (6)	C4-H41	1.009 (10)	C16-H161	1.003 (10)
C5-C6	1.370 (6)	C5-H51	1.000 (10)	C16-H162	1.027 (10)
C6-C7	1.378 (5)	C6-H61	0.978 (10)	C16-H163	1.004 (10)

Table 3. Bond lengths (Å).

C1-S1-C9	101.7 (2)	C11-C12-C13	121.7 (3)	S1-C9-H93	106.7 (10)
01-S2-C1	107.8 (2)	C12-C13-C14	118.2 (3)	H91-C9-H92	115.1 (10)
01-S2-C10	106.7 (2)	C12-C13-C16	121.0 (3)	H91-C9-H93	99.4 (10)
C1-S2-C10	96.5 (1)	C14-C13-C16	120.8 (30	H92-C9-H93	110.8 (10)
S1-C1-S2	110.9 (2)	C13-C14-C15	120.4 (3)	C10-C11-H111	125.0 (10)
S1-C1-C2	131.4 (3)	C10-C15-C14	120.0 (3)	H111-C11-C12	115.7 (10)
S2-C1-C2	117.5 (3)	C1-C2-H21	111.0 (10)	C11-C12-H121	119.1 (10)
C1-C2-C3	131.8 (3)	H21-C2-C3	116.8 (10)	H121-C12-C13	119.2 (10)
C2-C3-C4	125.0 (3)	C3-C4-H41	119.0 (10)	C13-C14-H141	121.7 (10)
C2-C3-C8	117.7 (3)	H41-C4-C5	120.4 (10)	H141-C14-C15	118.0 (10)
C4-C3-C8	117.3 (3)	C4-C5-H51	119.0 (10)	C10-C15-H151	119.5 (10)
C3-C4-C5	120.6 (4)	H51-C5-C6	119.9 (10)	C14-C15-H151	120.5 (10)
C4-C5-C6	121.1 (4)	C5-C6-H61	120.5 (10)	C13-C16-H161	121.3 (10)
C5-C6-C7	119.2 (4)	H61-C6-C7	120.3 (10)	C13-C16-H162	113.0 (10)
C6-C7-C8	120.1 (3)	C6-C7-H71	118.9 (10)	C13-C16-H163	99.6 (10)
C3-C8-C7	121.8 (3)	H71-C7-C8	121.0 (10)	H161-C16-H162	116.7 (10)
S2-C10-C11	120.9 (2)	C3-C8-H81	118.4 (10)	H161-C16-H163	100.3 (10)
C2-C10-C15	118.7 (2)	C7-C8-H81	119.9 (10)	H162-C16-H163	100.3 (10)
C11-C10-C15	120 4 (3)	S1-C9-H91	119.2 (10)		
C10-C11-C12	119.2 (3)	S1-C9-H92	105.2 (10)		

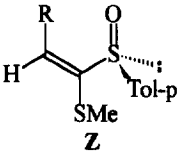
An inspection of the specific rotation values of the isolated **E** and **Z** isomers of **10a-c** reveals an intreresting relationship. Whereas the **E** isomers are dextrorotatory, the corresponding **Z** isomers have a very high negative rotation. The same regularity is observed for other α-unsubstituted and α-substituted vinylic sulfoxides having the same absolute configuration at sulfur and the same relationship between the sulfinyl oxygen atom and β-vinyl proton (see below). Therefore, it seems reasonable to propose that the sign of optical rotation may be used with caution for a rapid assignment of the double bond geometry in enantiomeric vinylic sulfoxides.



E

$[\alpha]_D$=+212

$[\alpha]_D$=+196



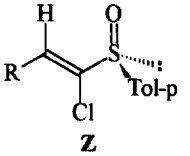
Z

$[\alpha]_D$=-398

$[\alpha]_D$=-310

R=Ph

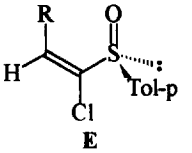
Rp-MeOPh



Z

$[\alpha]_D$=+35

$[\alpha]_D$=+39



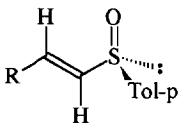
E

$[\alpha]_D$=-336[1]

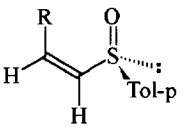
$[\alpha]_D$=-578[1]

R=Ph

R= 



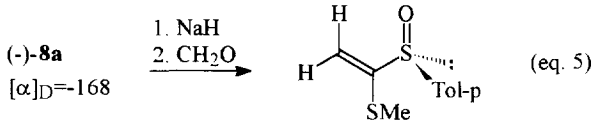
E



Z

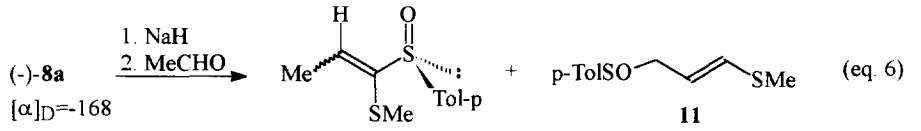
$[\alpha]_D$=+176	R=Ph	$[\alpha]_D$=-736[22]
$[\alpha]_D$=+148	R=n-C_5H_{11}	$[\alpha]_D$=-357[23]
$[\alpha]_D$=+33	R=t-Bu	$[\alpha]_D$=-240[23]
$[\alpha]_D$=+421	R=CO_2Me	$[\alpha]_D$=-438[24]
$[\alpha]_D$=+504	R=CF_3	$[\alpha]_D$=-191[25]

As expected, the Horner-Wittig reaction with formaldehyde using sodium hydride as a base (Procedure B) gave in 90% yield (+)-1-p-tolylsulfinyl-1-methylsulfenyl-ethene **10d** which is a parent compound for the family of optically active ketene dithioacetal mono-S-oxides **10** reported here.



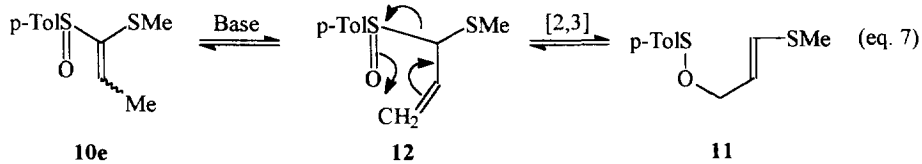
(-)-**8a** $[\alpha]_D$=-168 — 1. NaH, 2. CH_2O — (+)-**10d**, $[\alpha]_D$=+121 (eq. 5)

However, with acetaldehyde as the carbonyl reaction partner the corresponding ketene sulfoxide **10e** was isolated in a much lower yield (52%) and the ^{1}H NMR spectrum of the reaction mixture revealed the presence of a substantial amount of the sulfenate ester **11**.



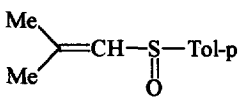
(-)-**8a** $[\alpha]_D$=-168 — 1. NaH, 2. MeCHO — (-)-**10e** $[\alpha]_D$=-24 (ee 33%) + **11** (eq. 6)

The formation of **11** as well as the fact that the sulfoxide (-)-**10e** obtained as above is partially racemized[26] is best explained by assuming that the vinyl sulfoxide **10e** undergoes reversible base-catalyzed isomerization to the corresponding allyl sulfoxide **12** and [2,3]-sigmatropic rearrangement of the latter to the achiral sulfenate **11**[27].

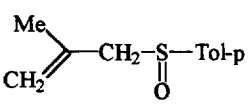


10e — Base — **12** — [2,3] — **11** (eq. 7)

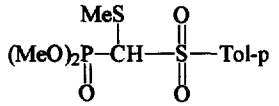
In contrast to aldehydes, the reaction of (-)-**8a** with ketones does not give the expected products. For instance, when acetone was subjected to the Horner-Wittig reaction with the lithium derivative of (-)-**8a**, the vinyl and allyl sulfoxides **13** and **14** were formed and isolated. Most probably they arise from the reaction of the α-phosphoryl sulfoxide **2** with acetone suggesting that under the reaction conditions desulfenylation of **8a** takes place.



13



14



15

Cyclopentenone was found to be unreactive towards sodium salt of (-)-**8a**. After refluxing the reaction components for a few hours in THF, the corresponding α-phosphoryl sulfone **15** was detected in the reaction mixture.

EXPERIMENTAL

NMR spectra were recorded on Bruker MSL 300 and Bruker AC 200 spectrometers in $CDCl_3$ solution. The microanalyses were performed on Elemental Analyzer EA 1108. Column chromatography was performed using Merck 60 (70-230 mesh) silica gel. The optical rotations were measured on a Perkin-Elmer 241H polarimeter. THF was freshly distilled over potassium/benzophenone.

Sulfenylation of α-Phosphoryl Sulfoxides - General Procedure: α-Phosphoryl sulfoxide **1** (8.0 mmol) was dissolved in anhydrous THF (100 ml). The temperature was lowered to -78°C under nitrogen atmosphere and *n*-butyllithium (5.2 ml 1.6M) was added. The mixture was stirred for 15 min. and a solution of methyl methanethiosulfonate (8,1mmol) in THF (30 ml) was added. The reaction was stirred at -78°C for 1 hour and after this time the cold bath was removed. After two hours, the reaction was quenched with a saturated ammonium chloride solution and extracted with dichloromethane (4x50 ml). The organic layer was dried over anhydrous magnesium sulfate. After removal of the solvent the residue was subjected to silica gel chromatography, yielding monosulfenylated sulfoxide **8**.

α-Dimethoxyphosphoryl-α-methylsulfenyl-methyl p-Tolyl Sulfoxide 8a: ^1H NMR ($CDCl_3$): major diastereoisomer δ 2.0 (d, 3H, J_{PH}0.9Hz C$\underline{H}_3$S); 2.40 (s, 3H, C$\underline{H}_3$Ar); 3.70 (d, 1H, C$\underline{H}$P, J=18.4Hz); 3.81 and 3.86 (2xd, 6H, C$\underline{H}_3$OP, J=11.1Hz); 7.31 and 7.62 (A_2B_2, 4H, Ar); minor diastereoisomer δ 2.13 (d, 3H, C$\underline{H}_3$S, J_{PH}0.9Hz); 2.40 (s, 3H, C$\underline{H}_3$Ar); 3.97 (d, 1H, C$\underline{H}$P, J=18.0Hz); 3.77 and 3.83 (2xd, 6H, C$\underline{H}_3$OP J=11.1Hz); 7.31 and 7,73 (A_2B_2, 4H, Ar); ^{13}C NMR ($CDCl_3$): 17.2 (major) 17.7 (minor) (d, J_{PC}5.1Hz); 21.3 (s, CH_3Ar) 53.8 (d); 68.1 (major J=144.7Hz) 66.2 (minor J=143.3Hz) 124.9; 126.3; 129.0; 129.5 Ar. Anal. Calcd. for $C_{11}H_{17}O_4PS_2$ C, 42.86; H, 5.52; Found C, 42.75; H, 5.64

α-Dimethoxyphosphoryl-α-methylsulfenyl-methyl Phenyl Sulfoxide 8b: ^1H NMR ($CDCl_3$): major diastereoisomer δ 1.92 (s, 3H, C$\underline{H}_3$S); 3.70 (d, 1H, C$\underline{H}$P, J=18.8Hz); 3.75 and 3.81 (2xd, 3H, C$\underline{H}_3$OP,

J=11.2Hz); 7.47 (m, 3H, Ar); 7.69 (m, 2H, Ar); minor diastereoisomer δ 2.07 (s, 3H, C<u>H</u>$_3$S); 3.96 (d, 1H, C<u>H</u>P, J=18.0Hz); 3.69 and 3.77 (2xd, 3H, CH$_3$OP, J=11.2Hz); 7.47 (m, 3H, Ar); 7.80 (m, 2H, Ar). Anal. Calcd. for $C_{10}H_{15}O_4PS_2$ C, 40.80; H, 5.10. Found C, 40.43; H, 5.13

α-Diethoxyphosphoryl-α-methylsulfenyl-methyl Phenyl Sulfoxide 8c: ^{1}H NMR ($CDCl_3$): major diastereoisomer δ 1.25 (2t, 6H, C<u>H</u>$_3$CH$_2$O, J=7.2Hz); 1.98 (d, 3H, C<u>H</u>$_3$S, J=0.8Hz); 3.70 (d, 1H, PC<u>H</u>S, J=18.3Hz); 4.16 (m, 4H, C<u>H</u>$_2$O); 7.50 (m, 3H, Ar); 7.72 (m, 2H, Ar).

^{1}H NMR ($CDCl_3$): minor diastereoisomer δ 1.34 (2xt, 6H, C<u>H</u>$_3$CH$_2$O, J=7.1Hz); 2.16 (d, 3H, C<u>H</u>$_3$S, J=0.9Hz); 4.04 (d, 1H, PC<u>H</u>S, J=18.5Hz); 4.16 (m, 4H, C<u>H</u>$_2$O); 7.50 (m, 3H, Ar); 7.81 (m, 2H, Ar); ^{13}C NMR ($CDCl_3$): 16.2; 17.4; 18.4; 63.9; 67.1 (minor J=142.5Hz); 69.0 (major J=144.8Hz); 125.0; 126.6; 128.3; 128.5; 129.9; 131.5; 132.0 Ar. Anal. Calcd. for $C_{13}H_{21}O_4PS_2$: C, 46.98; H, 5.16; S, 19.29. Found C, 47.02; H, 5.05; S, 19.53.

α-Dimethoxyphosphoryl-α-phenylselenenyl-methyl p-Tolyl Sulfoxide 9: ^{1}H NMR ($CDCl_3$): major diastereoisomer δ 2.39 (s, 3H, C<u>H</u>$_3$Ar); 3.87 and 3.92 (2xd, 6H, C<u>H</u>$_3$OP, J_{PH}11.1Hz); 3.98 (d, 1H, C<u>H</u>P, J=16.2Hz); 7.01-7.96 (9H, Ar); minor diastereoisomer δ 2.40 (s, 3H, C<u>H</u>$_3$Ar); 3.78 and 3.81 (2xd, 6H, C<u>H</u>$_3$OP, J=11.1Hz); 4.32 (d, 1H, C<u>H</u>P, J=16.4Hz).^{13}C NMR ($CDCl_3$): 21.0 (CH_3Ar); 54.0 (d, J=5.5Hz); 76.3 (d, J=172.5Hz); 127.6; 129.0; 129.7; 131.4; 132.5; 133.7; 135.5. Anal. Calcd. for $C_{16}H_{19}O_4PSSe$: C, 46.05; H, 4.59. Found C, 46.01; H, 4.63

Horner-Wittig Reaction of Sulfenylated α-Phosphoryl Sulfoxide 8a

Procedure A

To a solution of 0.65 mmol of the sulfoxide **8a** in anhydrous THF, *n*-butyllithium (0.5 ml 1.4M) was added at -78°C. After 5 min. of stirring at this low temperature, aldehyde (0.66 mmol) in anhydrous THF (2 ml) was added. The mixture was stirred at this temperature for 1 h and then at room temperature overnight. The reaction mixture was quenched with aq NH_4Cl and, after removal of organic solvent and extraction with CH_2Cl_2, the crude sulfoxide was obtained. Purification by chromatography gave the analytically pure product **10**.

Procedure B

In a 25 ml flask sodium hydride (50% in mineral oil, 2.57 mmol) was placed. Sulfenylated α-phosphoryl sulfoxide **8a** (2.14 mmol) dissolved in THF was added. Then, the mixture was stirred for 20 min. at room temperature and after this time aldehyde (2.14 mmol) dissolved in anhydrous THF was added. The mixture was stirred for 5 hours and then quenched with a saturated ammonium chloride solution. The organic solvent was evaporated and the aqueous residue was extracted with dichloromethane (3x20 ml). The organic extract was dried over anhydrous sodium sulfate and after removal of the solvent the crude product **10** was obtained. It was purified by silica gel chromatography.

Procedure C

To a solution (5 ml) of sulfenylated α-phosphoryl sulfoxide **8a** (0.65 mmol) in methylene chloride triethylbenzylammonium bromide (TEBAB) (0.06 mmol) and aldehyde (0.66 mmol) were added. Then, 5 ml

of 50% KOH was poured and the mixture was stirred vigorously for 2 hours. After dilution of the reaction mixture with aq. NH_4Cl, the aqueous phase was separated and the organic layer dried over sodium sulphate. Evaporation afforded the crude product **10** which was purified by column chromatography.

1-p-Tolylsulfinyl-1-methylsulfenyl-2-phenyl-ethene 10a

E-10a: m.p. 107-108°; $[\alpha]_D$+212 (c, 1.14 acetone); ^1H NMR ($CDCl_3$): δ 2.02 (s, 3H, $C\underline{H}_3S$); 2.38 (s, 3H, $C\underline{H}_3Ar$); 7.26 and 7.86 (A_2B_2, 4H, $C\underline{H}_3Ar$); 7.38 and 7.90 (m, 5H, Ph); 7.81 (s, 1H, vinyl); ^{13}C NMR ($CDCl_3$): 17.8; 21.4; 126.4; 128.5; 129.5; 129.6; 129.9; 133.6; 135.8; 140.1; 140.6; 142.0. Anal. Calcd. for $C_{16}H_{16}OS_2$ C, 66.67; H, 5.56; S, 22.22. Found C, 66.96; H, 5.83; S, 22.07.

Z-10a: liquid; $[\alpha]_D$-398 (c, 2.55 acetone) ^1H NMR ($CDCl_3$): δ 2.35 (s, 3H, $C\underline{H}_3S$); 2.38 (s, 3H, $C\underline{H}_3Ar$); 7.09 (s, 1H, vinyl); 7.22-7.53 (m, 9H, Ar);

1-p-Tolylsulfinyl-1-methylsulfenyl-2-(p-methoxyphenyl)-ethene 10b

Procedure A, **E-10b**: m.p. 144-145°; $[\alpha]_D$+188 (c, 1.0, acetone); ^1H NMR ($CDCl_3$): δ 2.01 (s, 3H, $C\underline{H}_3S$); 2.38 (s, 3H, $C\underline{H}_3Ar$); 3.83 (s, 3H, $C\underline{H}_3OAr$); 6.9-7.9 (m, 9H, Ar);

Z-10b: liquid; $[\alpha]_D$-310 (c, 2.2 acetone); ^1H NMR ($CDCl_3$): δ 2.32 (s, 3, $C\underline{H}_3S$); 2.38 (s, 3H, $C\underline{H}_3Ar$); 3.83 (s, 3H, $C\underline{H}_3OAr$); 6.9-7.9 (m, 9H, Ar);

^{13}C NMR ($CDCl_3$): 10.3 (major); 13.3 (minor); 17.8 (major); 18.9 (minor); 21.4 (MeAr); 125.0; 126.3; 129.6; 130.6; 131.7; 132.0; 135.9; 136.4; 139.5; 141.8. Anal. Calcd. for $C_{17}H_{18}O_2S_2$ C, 64.15; H, 5.66; S, 20.13. Found C, 64.09; H, 5.76; S, 20.24.

1-p-Tolylsulfinyl-1-methylsulfenyl-2-(p-bromophenyl)-ethene 10c

Procedure C, **E-10c**: m.p. 168-169°; $[\alpha]_D$+223 (c, 1.3 acetone); ^1H NMR ($CDCl_3$): δ 2.03 (s, 3H, $C\underline{H}_3S$); 2.40 (s, 3H, $C\underline{H}_3Ar$); 7.28 and 7.65 (A_2B_2, 4H, MeAr); 7.74 (s, 1H, vinyl); 7.53 and 7.79 (A_2B_2, 4H, BrAr); ^{13}C NMR ($CDCl_3$): 17.7; 21.3; 124.5; 126.3; 129.6; 131.2; 131.7; 132.4; 134.1; 139.7; 141.6; 142.1. Anal. Calcd. for $C_{16}H_{15}OS_2Br$ C, 52.32 H; 4.12 S 17.46. Found C, 51.12 H; 4.13 S; 17.42.

Z-10c: ^1H NMR ($CDCl_3$): δ 2.35 (s, 3H, $C\underline{H}_3S$); 2.40 (s, 3H, $C\underline{H}_3Ar$); 6.93 (s, 1H, vinyl); 7.3-7.8 (m, Ar).

1-p-Tolylsulfinyl-1-methylsulfenyl-ethene 10d

Liquid; $[\alpha]_D$+121 (c, 1.3 acetone); ^1H NMR ($CDCl_3$): δ 2.23 (s, 3H, $C\underline{H}_3S$); 2.39 (s, 3H, $C\underline{H}_3Ar$); 5.66 (d, 1H, vinyl, J=2.0Hz); 6.37 (d, 1H, vinyl, J=2.0Hz); 7.28 and 7.58 (A_2B_2, 4H, Ar) ^{13}C NMR ($CDCl_3$): 16.5; 21.1; 115.1; 125.2; 129.4; 139.2; 141.8; 153.2. Anal. Calcd. for $C_{10}H_{12}OS_2$ C, 56.57; H, 5.70. Found C, 56.46; H, 5.57

1-p-Tolylsulfinyl-1-methylsulfenyl-propene 10e

Liquid; $[\alpha]_D$-24 (c, 1.4 acetone) ^1H NMR ($CDCl_3$): δ 1.94 (s, 3H, $C\underline{H}_3S$); 2.06 (d, 3H, $C\underline{H}_3$=C, J=7.0Hz); 2.37 (s, 3H, $C\underline{H}_3Ar$); 7.11 (q, 1H, vinyl, J=7.0Hz); 7.24 and 7.56 (A_2B_2, 4H, Ar); ^{13}C NMR ($CDCl_3$): 15.2; 19.6; 21.4; 125.9; 138.5; 140.1; 141.7; 142.2. Anal. Calcd. for: $C_{11}H_{14}OS_2$ C, 58.37; H, 6.23. Found C, 58.40; H, 6.06

E-3-Methylsulfenyl-propen-2-yl p-Toluenesulfenate 11

^1H NMR ($CDCl_3$): δ 2.05 (s, 3H, $C\underline{H}_3S$); 2.39 (s, 3H, $C\underline{H}_3Ar$); 4.12 (dd, 2H, J=1.3; 6.1Hz); 5.54 (dt, 3H,

J=6.1; 15.0Hz, vinyl); 6.29 (dt, 3H, vinyl, J=1.3; 15.0Hz); 7.24 and 7.56 (A_2B_2, 4H, Ar)

α-Dimethoxyphosphoryl-α-methylsulfenylmethyl p-Tolyl Sulphone 15

^{31}P NMR ($CDCl_3$) 14.6, ^1H NMR ($CDCl_3$): δ 2.29 (s, 3H, $C\underline{H}_3S$); 2.44 (s, 3H, $C\underline{H}_3Ar$); 3.84 and 3.86 (2xd, 6H, $C\underline{H}_3OP$, J=11.2Hz); 4.12 (d, 1H, $PC\underline{H}$, J=20.1Hz); 7.35 and 7.90 (A_2B_2, Ar). Anal. Calcd. for: $C_{11}H_{17}O_5PS_2$ C, 40.73 H, 5.28. Found C, 40.83; H, 5.28.

Table 4. Crystal data and experimental details for **E-(+)-10a**.

Molecular formula	$C_{16}H_{16}OS_2$
F (000)	608
M_r	288.41
Crystallographic system	orthorhombic
Space group	$P2_12_12_1$
a (Å)	5.3277 (13)
b (Å)	8.1884 (15)
c (Å)	33.745 (7)
V (Å^3)	1472.1 (5)
Z	4
D_c (g/cm^3)	1.301 (20
μ (cm^{-1})	31.3
Crystal dimensions (mm)	0.15. 0.35, 0.55
Radiation, λ (Å)	CuKα, 1.45184
Diffractometer	Enraf-Nonius CAD4
Scan mode	ω/2θ
Scan width (°)	0.72+0.14 tanθ
Absorption correction min, max, av	0.9406, 0.9990, 0.9707
Transmission min, max, av (%)	88.47, 99.80, 94.22
Measured reflections	3362
Independent reflections	2893
Observed reflections [I≥3σ(I)]	2664
R_{int}	0.0307
Maximum 2θ (°)	150
Ranges *h, k, l*	0 to 6,0 to 10, -42 to 42
Parameters refined	190
Weighting scheme	$w=[\sigma^2(F) + 0.00055\ F^2]^{-1}$
$(\Delta/\sigma)_{max}$	0.001
Residual density max, min (eÅ^{-3})	0.266, -0.337
S	1.4230
R_w	0.0473
r	0.0419

Crystal Structure Determination of E-1-p-Tolylsulfinyl-1-methylsulfenyl-2-phenyl-ethene 10a

Crystal and molecular structure of **10a** was determined using data collected at room temperature on a CAD4 diffractometer with graphite monochromatized CuKα radiation[28]. Compound crystallizes in orthorhombic system, in space group $P2_12_12_1$. Crystal data and experimental details are shown in Table 4. Lattice constants were refined by least-squares fit of 25 reflections in θ range 17.7-28.7°. During 55.8 hours

of exposure no decay in intensities of three standard reflections (2, -3, 1; -1, -2, 16; 2, -2, -2) was observed (intensity variation -0.01%). An empirical absorption correction was applied using the ψ-scan method[29,30]. A total of 2664 observed reflections (with $I \geq 3\sigma(I)$), were used to solve the structure by direct methods and to refine it by full matrix least-squares using F's[31,32]. Hydrogen atoms were found in a difference Fourier map and set as riding. Thermal isotropic parameters for H atoms were refined. For all nonhydrogen atoms the anisotropic thermal parameters were applied. The final refinement converged to R=0.0419 (for details see Table 4). The absolute structure of **10a** was determined by three methods: the Rogers η-test, the Hamilton test and calculation of the Flack parameter x. Results: Rogers' method :η=1.09(5), η_{inv}=-1.10(5); Hamilton test: R_{ratio}=1.211, N=2474, then probability of opposite (inv) configuration $\alpha < 10^{-6}$; Flack x parameter: x=-0.01(3), unequivocally confirm the configuration shown in Figure 1. Further details of the crystal structure investigation are available on request from the Cambridge Crystallographic Data Centre[33].

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REFERENCES AND NOTES

1. For part X on α-phosphoryl sulfoxides see: Mikołajczyk, M., Krysiak, J.A., Midura, W.H., Wieczorek, M.W., Błaszczyk, J. *Tetrahedron: Asymmetry*, in press.
2. This paper belongs to a Brazilian series of papers on sulfenylation of organic compounds; for a previous paper see: Wladislaw, B., Marzorati, L., Di Vitta, C. and Claro, N.F. Junior, *Synth. Comm.*, **1996**, *26*, 3485.
3. The main part of the results reported here was presented at the XIIIth International Conference on Phosphorus Chemistry, Jerusalem, **1995** (Abstract Book, p. 177).
4. Mikołajczyk, M., Bałczewski, P. *Advances in Sulfur Chemistry*, Ed. Block, E., JAI Press, Inc., Greenwich, **1994**, Vol. 1, pp 41-96.
5. Mikołajczyk, M., Zatorski, A. *Synthesis*, **1973**, 669.
6. Mikołajczyk, M., Midura, W.H., Grzejszczak, S., Zatorski, A., Chefczyńska, A. *J.Org.Chem.*, **1978**, *43*, 473.
7. Mikołajczyk, M., Grzejszczak, S., Zatorski, A. *J.Org.Chem.*, **1975**, *40*, 1979.
8. Mikołajczyk, M., Zatorski, A., Grzejszczak, S., Costisella, B., Midura, W.H. *J.Org.Chem.*, **1978**, *43*, 2518.
9. Mikołajczyk, M., Midura, W.H., Miller, A., Wieczorek, M.W. *Tetrahedron*, **1987**, *43*, 2967.
10. Mikołajczyk, M., Midura, W.H., Grzejszczak, S., Montanari, F., Cinquini, M., Wieczorek, M.W., Karolak-Wojcichowska, J. *Tetrahedron*, **1994**, *50*, 8053.
11. Mikołajczyk, M., Midura, W.H. *Tetrahedron: Asymmetry*, **1992**, *3*, 1515.
12. For a successful use of this reagent in the sulfenylation reactions of various organic sulfur compounds see: Wladislaw, B., Marzorati, L. *Rev.Heteroatom Chem.*, Ed. Oae, S., Myu, Tokyo, **1993**, *9*, 49-60. See also:
    Wladislaw, B., Marzorati, L. and Biaggio, F.C. *J.Org.Chem.*, **1993**, *58*, 6132;
    Wladislaw, B., Marzorati, L. and Donnici, C.L. *J.Chem.Soc.Perkin Trans I*, **1993**, 3167;
    Wladislaw, B., Marzorati, L., and Zaim, M.H. *Phosphorus Sulfur and Silicon*, **1994**, *92*, 11.
13. In the case of sulfenylation of α-phosphorylmethyl methyl sulfoxide **8d** the reaction does not have synthetic value since the mixture of different products including α-phosphoryldithioacetal is obtained. Moreover, during purification by chromatography unstable products undergo decomposition affording among others S-methyl α-phosphorylthioformate.

14. Hase, T.A. and Jorma Koskimies, K. in *Umpoled Synthons* Ed by Hase, T.A., J.Wiley and Sons, **1987**, p. 34.
15. The Horner reaction performed under PTC conditions using K_2CO_3/CH_2Cl_2 gave **10a** with a 1.5:1 diastereoisomeric ratio, but in 21% yield.
16. The use of LiH as a base afforded **10a** as a mixture of diastereoisomers in a 1:3 ratio, however, in 17% yield.
17. Pasqual, C., Meier, J., Simon, W. *Helv. Chim. Acta*, **1966**, *49*, 164; Matter, U.E., Pasqual, C., Pretsch, E., Simon, W., Sternhell, S. *Tetrahedron*, **1969**, *25*, 691.
18. Mikołajczyk, M., Grzejszczak, S., Zatorski, A. *Tetrahedron*, **1976**, *32*, 969; **1979**, *35*, 1091.
19. Rogers, D. *Acta Cryst.*, **1981**, A37, 734.
20. Hamilton, W.C. *Acta Cryst.*, **1965**, *18*, 502.
21. Flack, H.D. *Acta Cryst.*, **1983**, A39, 876.
22. Mikołajczyk, M., Midura, W.H., Grzejszczak, S., Zatorski, A., Chefczyńska, A. *J.Org.Chem.*, **1978**, *43*, 473.
23. Chaigne, F., Gotteland, J.-P., Malacria, M. *Tetrahedron Lett.*, **1989**, *30*, 1803.
24. Cardellicchio, C., Iacuone, A., Naso, F. *Tetrahedron Lett.*, **1995**, *36*, 6563.
25. Yamazaki, T., Ishikawa, N., Iwatsubo, H., Kitazume, T. *Chem. Commun.*, **1987**, 1340.
26. Enantiomeric excess was determined by ^1H NMR using (+)-R-*t*-butylphenylphosphinothioic acid as a chiral solvating agent; Drabowicz, J., Dudziński, B., Mikołajczyk, M. *Tetrahedron Asymmetry*, **1992**, *3*, 1231.
27. For a more extensive discussion of this problem see: Braverman S. in *Chemistry of Sulphones and Sulphoxides*, Ed. Patai, S., Rappoport, Z., Stirling, C.J.M., J.Wiley and Sons, **1988**., pp. 717-757.
28. Schagen, J.D., Straver, L., van Meurs, F., Williams, G. *CAD4 Manual. Version 5.0.* Enraf-Nonius, Delft, The Netherlands, **1989**.
29. Frenz, B.A. *Enraf-Nonius Structure Determination Package; SDP User's Guide. Version of 17 December 1986.* Enraf-Nonius, Delft, The Netherlands, **1986**.
30. North, A.C.T., Phillips, D.C., Mathews, F.S. *Acta Cryst.* **1968**, *A24*, 351.
31. Sheldrick, G.M. *SHELXTL/PC, Release 4.1.* Siemens Analytical X-Ray Instruments, Inc., Madison, Wisconsin, USA **1991**.
32. *International Tables for X-ray Crystallography, Vol. IV*. The Kynoch Press, Birmingham, England, 1974.
33. Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, England.

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