

## (+)-(S)- $\alpha$ -Diethoxyphosphorylvinyl p-Tolyl Sulfoxide: a New Chiral Michael Acceptor and Dienophile

Marian Mikołajczyk\* and Wanda H. Midura

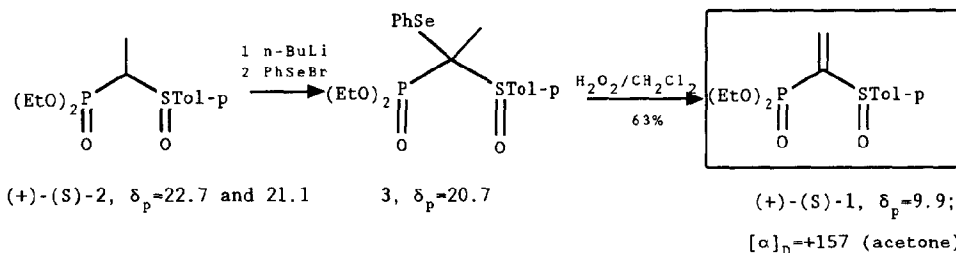
Centre of Molecular and Macromolecular Studies, Polish Academy of Sciences, Department  
of Organic Sulfur Compounds, 90-363 Łódź, Sienkiewicza 112, Poland

(Received in UK 6 October 1992)

**Abstract:** The title reagent, (+)-(S)-1, was prepared from (+)-(S)- $\alpha$ -diethoxyphosphorylethyl p-tolyl sulfoxide 2 by phenylselenylation-deselenylation procedure. Its reactivity was demonstrated by diastereoselective Michael addition of ethanethiol giving rise to 3, tandem Michael addition/intramolecular Horner-Wittig reaction with 2-formyl pyrrole leading to the corresponding pyrrolizine sulfoxide 5 and cycloaddition with cyclopentadiene affording the diastereomeric adducts 6. The steric course of the Diels-Alder reaction is briefly discussed.

Chiral sulfoxides have found a wide application as powerful chiral auxiliaries in asymmetric synthesis and as chiral synthons.<sup>1</sup> Recently, chiral vinyl sulfoxides have been used as dienophiles in asymmetric Diels-Alder reactions.<sup>2</sup> However, because of a very low reactivity of simple vinyl sulfoxides in Diels-Alder reactions, it was necessary to activate the carbon-carbon double bond by introduction of an additional electron-withdrawing group. Usually, the alkoxy carbonyl group is used for such a purpose.<sup>3</sup>

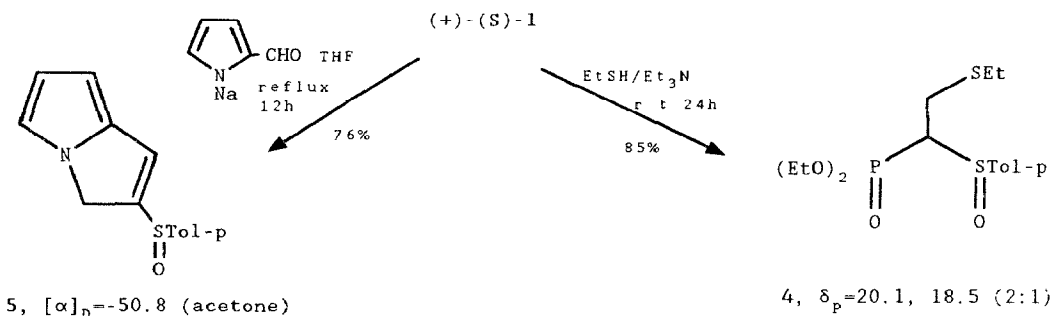
In this paper we would like to report the synthesis of (+)-(S)- $\alpha$ -diethoxyphosphorylvinyl p-tolyl sulfoxide (1) and exemplify its reactivity as a new type of chiral Michael acceptor and dienophile.<sup>4</sup> In contrast to other  $\alpha$ - or  $\beta$ -substituted vinyl sulfoxides reported in the literature, the phosphoryl moiety in 1 functions not only as a double bond activating substituent but also allows the Horner-Wittig reaction to be carried out following the Michael addition. Moreover, the phosphoryl group, like the sulfinyl one, may be chiral thus allowing double asymmetric induction in the Michael and Diels-Alder reactions to be studied.



Scheme 1

A two-step synthesis of the chiral sulfoxide **1** is shown in Scheme 1. The first step involves selenylation of (+)-(S<sub>s</sub>)-α-diethylphosphorylethyl p-tolyl sulfoxide **2** (a mixture of two diastereomers)<sup>5</sup> with phenylselenenyl bromide to give the corresponding PhSe-substituted sulfoxide **3** which, after subsequent oxidative benzeneselenenic acid elimination, affords the desired sulfoxide **1** which is obtained in a pure form by column chromatography.

Preliminary experiments revealed that the chiral vinyl sulfoxide **1** undergoes nucleophilic addition easily. For example, the reaction of **1** with ethanethiol in the presence of triethylamine gave the adduct **4** as a 2:1 mixture of diastereomers.



Scheme 2

The synthetic utility of **1** as a key reagent for the construction of mono- or condensed hetero- or carbocycles containing the chiral vinyl sulfoxide moiety is illustrated by the synthesis of tolyl 3H-pyrrolizine-2-sulfoxide **5**<sup>6</sup> resulting from the tandem Michael addition/intramolecular Horner-Wittig reaction of **1** with the sodium salt of 2-formyl pyrrole. Of interest is that the chiral vinyl sulfoxide moiety in **5** may be used for further asymmetric reactions or converted into the carbonyl group.

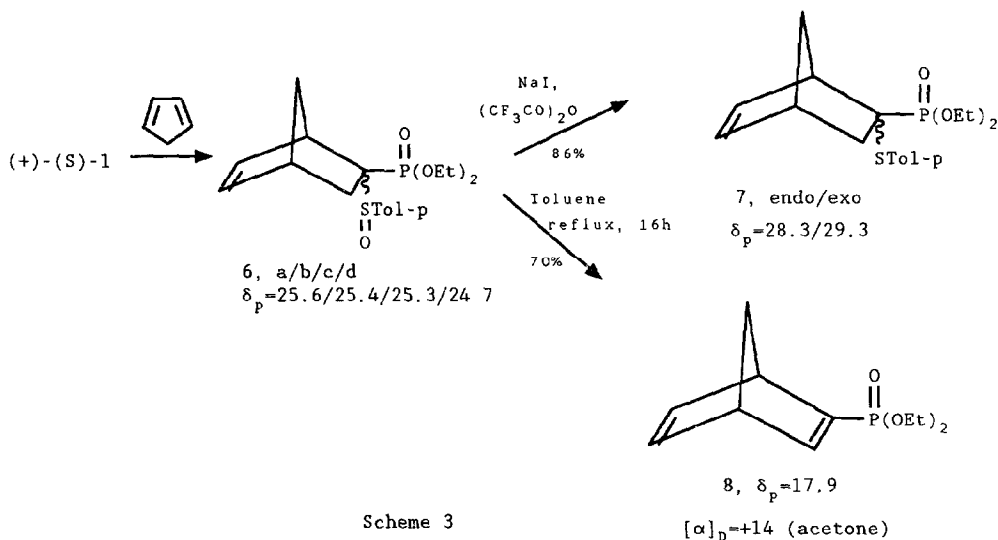
As expected, the presence of the phosphoryl group in **1** considerably enhanced its dienophilic reactivity and cycloaddition with cyclopentadiene was found to occur easily. The results obtained are collected in Table 1. The ratio of the diastereomeric

Table 1 Diels-Alder reaction of **1** with cyclopentadiene

Entry	Reaction conditions			Sulfoxide (%)				Sulfide (%)	
	Catalyst	Solvent	Temp. Time	a	b	c	d	exo-P	endo-P
1.	-	CH <sub>2</sub> Cl <sub>2</sub>	r.t. 10d.	9.8	54.4	30.1	5.7	84.5	15.5
2	-	H <sub>2</sub> O/Me <sub>2</sub> CO	r.t. 2d.	13.2	53.6	27.5	5.7	85.3	14.7
3.	ZnCl <sub>2</sub>	CH <sub>2</sub> Cl <sub>2</sub>	-20° 24h	25.5	74.5	-	-	74.5	25.5
4.	BF <sub>3</sub> ·OEt <sub>2</sub>	CH <sub>2</sub> Cl <sub>2</sub>	-20° 1h	46.4	10.7	24.5	18.4	31.5	68.5

cycloadducts **6** was determined by <sup>31</sup>P NMR spectroscopy and the two diastereomers ( $\delta_P = 25.6$  and  $25.4$  ppm)<sup>7</sup> obtained in the ZnCl<sub>2</sub>-catalyzed reaction (entry 3) were separated by column chromatography (hexane: acetone, 15:1). The endo/exo configuration (with respect

to P) of **6** was assigned utilizing the quin's criterion<sup>8</sup> i.e. the presence (endo) or absence (exo) of the coupling constant between P and C(7) in <sup>13</sup>C NMR spectra. Additionally, the endo/exo ratio in all experiments was confirmed by reduction of the cycloadducts **6** to the corresponding sulfides **7**. Thermal elimination of *p*-toluenesulfenic acid from **6** was also carried out and gave the chiral phosphonate **8**.



Scheme 3

An inspection of the results in Table 1 reveals that the non-catalyzed reaction (entry 1) performed in methylene chloride is very slow. Although the preponderance of exo-selectivity for the phosphoryl group is observed, the  $\pi$ -facial selectivity is rather moderate. An increase of the solvent polarity (entry 2) accelerates cycloaddition which may suggest a non-synchronous transition state with the advanced  $\sigma$ -bond formation at the  $\beta$ -carbon atom in **1**. The addition of zinc chloride (entry 3) substantially increases the dienophilic reactivity of **1** and also improves  $\pi$ -facial selectivity. In this case the reaction occurs also with the predominant exo-selectivity for the P(O)-group and only two diastereomers are formed (<sup>31</sup>P NMR assay). On the contrary, the presence of a strong Lewis acid such as BF<sub>3</sub>·OEt<sub>2</sub> (entry 4) considerably decreases stereoselectivity and favours the endo phosphonate moiety approach.

The above preliminary observations on the steric course of the Diels-Alder reaction investigated may reasonably be explained in terms of steric factors and conformational changes induced by Lewis acids. Thus, zinc chloride as a chelating agent links together both polar phosphoryl and sulfinyl groups in **1** what results in a rigid *s-trans* conformation of the complexed dienophile.<sup>9</sup> On the other hand, since one molecule of boron trifluoride can coordinate only one polar group, the *s-cis* conformation of **1** is more favoured for steric reasons. Therefore, a high diastereoselectivity in the ZnCl<sub>2</sub>-catalyzed reaction is observed, whereas in uncatalyzed reaction and in the presence of BF<sub>3</sub> the ratio of the diastereomeric **6** reflects population of both conformers.

**Acknowledgement.** Financial support of this work by the State Committee for Scientific Research (Grant number 226709203) is gratefully acknowledged.

## References and Notes

- Mikołajczyk, M.; Drabowicz, J. *Topics in Stereochemistry*, 1982, 13, 333.  
Posner, G., in "The Chemistry of Sulfoxes and Sulfoxides", Patai, S.; Rappoport, Z.; Stirling, C.J.M.; Eds., John Wiley and Sons. Chichester, 1988, pp.823-849.
- Koizumi, T., *Phosphorus, Sulfur and Silicon*, 1991, 58, 111 and references cited therein; Lopez, R. and Carretero, J.C., *Tetrahedron Asymmetry*, 1991, 2, 93.
- Recently, vinyl p-tolyl sulfoxide has been efficiently activated for Diels-Alder reactions by its conversion into the corresponding ethoxy sulfonium salt; Ronan, B. and Kagan, H.B.; *Tetrahedron Asymmetry*, 1991, 2, 75.
- $\alpha$ -Diethoxyphosphorylvinyl methyl sulfoxide was obtained in a racemic form in our laboratory (Mikołajczyk, M., Grzejszczak, S and Korbacz, K. *Tetrahedron Lett.*, 1981, 22, 3097), and its  $\beta$ -phenyl analog by Durst and coworkers (Venugopalan, B., Hamlet, A.B. and Durst, T., *Tetrahedron Lett.* 1981, 22, 191) by oxidation of the corresponding vinylic sulfide.
- Mikołajczyk M., Midura W., Miller A., Wieczorek M. *Tetrahedron*, 1987, 43, 2967.
- 5:  $^1\text{H}$  NMR  $\delta$ : 2.39 (s, 3H); 4.45 (m, 2H); 5.93 (s, 1H); 6.25 (dt J=2.0 Hz, 1H); 6.49 (dt J=2.1 Hz, 6.1 Hz, 1H); 7.29 (s, 1H), 7.29 and 7.56 (AA'BB' 4H aromatic).
- Data for exo-6 (less polar):  $^{31}\text{P}$  25.6 ppm,  $[\alpha]_D^{25} = +36.5$  (acetone c=0.8),  $^{13}\text{C}$  NMR 16.3 ( $\text{CH}_3\text{CH}_2\text{O}$ , d J=7 Hz); 21.4 (s,  $\text{CH}_3$ ); 31.3 (s,  $\text{CH}_2$ , C3) 42.5 (d, J=5.2 Hz,  $\text{CH}$ , C4); 45.9 (d,  $\text{CH}_2$ ,  $J_{\text{PC}} = 11.5$  Hz C7); 49.6 (s,  $\text{CH}$ , C1); 62.3 (d, J=6 Hz,  $\text{CH}_3\text{CH}_2\text{O}$ ); 62.5 (d, J=7 Hz,  $\text{CH}_3\text{CH}_2\text{O}$ ); 126.6, 129.1, 135.0 (d, J=3.8 Hz), 137.5, 141.5, 142.2 (aromatic + vinyl).  
 $^1\text{H}$  NMR,  $\delta$ : 1.23 (dt, 6H,  $\text{CH}_3\text{CH}_2\text{O}$ ); 1.5-2.2 (m, 3H); 2.32 (s, 3H); 2.68 (m, 1H); 2.9 (m, 1H); 4.08 (m, 4H,  $\text{CH}_3\text{CH}_2\text{O}$ ); 5.93 (m, 1H, vinyl); 6.28 (m, 1H, vinyl); 7.35 and 7.72 (AA'BB' 4H aromatic).  
Data for endo-6 (more polar):  $^{31}\text{P}$  25.4 ppm,  $[\alpha]_D^{25} = +151.5$  (acetone c=2.6);  $^{13}\text{C}$  NMR 15.7 (C3,  $\text{CH}_3$ , C3); 42.0 (s,  $\text{CH}_3$ , C4); 48.6 (s,  $\text{CH}_2$ , C7); 49.9 (s,  $\text{CH}$ , C1); 61.6 (d, J=7.2 Hz,  $\text{CH}_3\text{CH}_2\text{O}$ ); 63.1 (d, J=6.7 Hz,  $\text{CH}_3\text{CH}_2\text{O}$ ); 70.1 (d, J=137.6 Hz, C2); 126.4, 128.3, 128.7, 129.3 (d, J=11.2 Hz); 139.0 (aromatic + vinyl).  
 $^1\text{H}$  NMR  $\delta$ : 1.21 (dt, 6H); 1.45-2.4 (m, 4H); 2.29 (s, 3H), 2.97 (m, 1H); 3.45 (m, 1H); 4.05 (m, 4H); 6.28 (m, 2H vinyl), 7.15 and 7.5 (AA'BB' 4H aromatic).
- Quin, L.D., Gallagher, M.J., Cunkle, G.T. and Chesnut, D.B., *J. Am. Chem. Soc.*, 1980, 102, 3136.
- Zinc salts were used as chelating agents for  $\alpha$ -substituted vinyl sulfoxides not only in the Diels-Alder reaction but also in conjugate additions. A high stereoselectivity observed in the latter case was rationalized by Posner and coworkers; Posner, G.H. "Asymmetric Synthesis"; Morrison, J.D., Ed.; Academic Press: New York, 1983; vol.2, Part A, Ch.8, p.225.