

2-PHENYLSULFONYL 1,3-DIENES IN ASYMMETRIC DIELS-ALDER REACTIONS WITH CHIRAL ENAMINES AND ENOL ETHERS

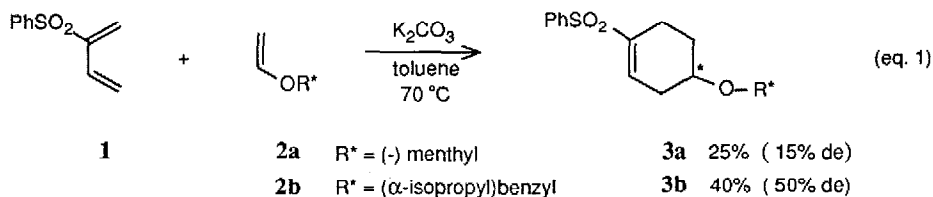
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Summary: 2-Phenylsulfonyl 1,3-dienes underwent diastereoselective inverse electron demand Diels-Alder reactions with enamines (up to 73% de) and enol ethers (up to 50% de).

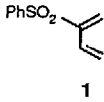
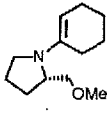
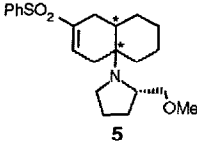
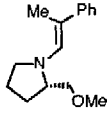
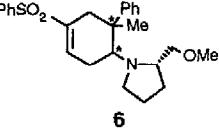
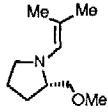
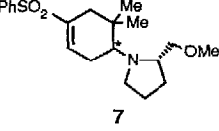
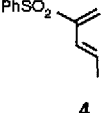
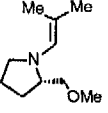
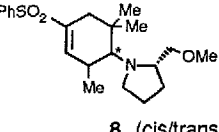
2-Phenylsulfonyl 1,3-dienes are useful building blocks in organic synthesis,¹⁻⁴ and several methods for their preparation have recently been reported.^{1,2,4-6} One important property of these dienes is that they show a dual electron demand in Diels-Alder reactions and thus undergo cycloaddition with both electron deficient and electron rich olefins. Electron rich olefins such as enol ethers, enamines and also indole magnesium salts give highly regioselective cycloadditions with these dienes.^{2a,3} With the aim of obtaining diastereoselective cycloadditions we have now studied the reaction of 2-phenylsulfonyl 1,3-dienes with chiral enamines and enol ethers.

We previously reported that enol ethers undergo [4+2] cycloaddition with 2-phenylsulfonyl-1,3-butadiene. However, the reaction proceeds only slowly and in order to depress the competing Diels-Alder dimerization of the sulfonyldiene a large excess of the enol ether was utilized. With a chiral enol ether this procedure is obviously unattractive. To overcome the problem with its dimerization the sulfonyldiene was added slowly as a dilute solution in methylene chloride to a solution of an equimolar amount of the chiral enol ether in toluene at 70 °C. The halogenated solvent was removed continuously by distillation. Two chiral enol ethers **2a** and **2b** were tried. Dimerization of the diene is still competing and the yields were moderate. The diastereomeric excesses of the products **3a** and **3b** were 15 and 50% respectively (eq. 1).



Because of the low reactivity of the enol ethers in the cycloaddition reaction we focused our attention on chiral enamines. The amine used for the preparation of the different enamines was (*S*)-2-methoxymethylpyrrolidine.⁷ The results of the reaction of a few chiral enamines with sulfonyldienes **1** and **4** are given in Table 1. Reaction of **1** with the chiral enamine from cyclohexanone afforded cycloadduct **5** in 50% yield and 59% de. The ¹H and ¹³C NMR spectra are consistent with only one relative configuration at the bridgehead (presumably *cis*⁸). Acyclic chiral enamines from 2-phenyl- and 2-methylpropanal gave products (**6** - **8**) with a higher diastereomeric excess (71-73% de). In the case of sulfonyldiene **4** a mixture of *cis*- and *trans*-**8** was obtained in a ratio of 1.9:1.

Table 1. Cycloaddition of Chiral Enamines to 2-(Phenylsulfonyl)-1,3-dienes.^a

entry	diene	enamine	product	% yield ^b	% de ^c
1				50	59
2		 E/Z = 9/1		51	73
3				53	72
4				92	71 (cis-8) 71 (trans-8)

a. The reactions were performed in toluene at 70 °C in the presence of K₂CO₃. b. Isolated yield after column chromatography, after careful elution of both diastereoisomers. A control measurement showed that the de of the crude product was the same as in the purified product. c. The diastereomeric excess was determined by ¹H NMR spectroscopy by integration over the vinylic resonances and/or the methoxy signals

The detailed mechanism of these cycloadditions must await further experiments. It is possible that the enamine reactions occur in two steps, the first step being a Michael addition followed by cyclization.⁹

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References and Notes

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- Reaction of the related enamine 1-morpholino-1-cyclohexene with **1** afforded one single isomer.^{2a} Cycloaddition of enamine-type indolylmagnesium iodide to **1** resulted in cis stereochemistry at the bridgehead.³
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