

Asymmetric Induction in [4+2] Cycloadditions of Chiral Enamines to 2-Phenylsulfonyl 1,3-Dienes

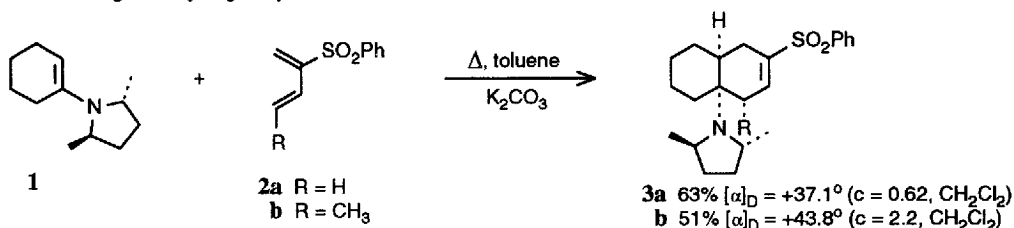
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Abstract. Chiral enamine **1** reacts with 2-phenylsulfonyl 1,3-dienes **2** in a [4+2] cycloaddition to give adducts **3** with high asymmetric induction

Conjugated dienes with electron-withdrawing groups within the diene unit have recently attracted considerable attention.¹⁻⁶ One interesting feature of these dienes is their ability to participate in cycloadditions with both electron-rich and electron-deficient olefins and in this respect arylsulfonyl-substituted dienes have proven synthetically useful.^{1,3-6} Chiral enol ethers and enamines have been used in inverse electron demand Diels-Alder reactions with such dienes to obtain asymmetric induction.^{1c,5,7} We now report on [4+2] cycloadditions of chiral enamine **1** to 2-phenylsulfonyl 1,3-dienes, the use of an enamine with a C₂-symmetric amine unit leading to very high asymmetric induction.



Sulfonyl dienes **2a**^{1d} and **2b**^{1d} were allowed to react with enamine **1**⁸ at 95 °C and 60 °C, respectively. To avoid competing dimerization^{1d} of the sulfonyldiene it was necessary to keep the concentration of the latter low by slow addition.⁹ The cycloadducts **3a** and **3b** formed were isolated and characterized and in each case only one diastereoisomer could be detected according to NMR (¹H, ¹³C) and HPLC analyses. If we assume that an endo transition state is favored, two approaches (A and B) would be possible as shown in Figure 1. Since the lone pair on the nitrogen and the π -system of the enamine double bond should be parallel and the enamine is C₂ symmetric there would be only one conformation of **1**.^{8a} In this conformation one face of the double bond is shielded by one of the methyl groups. For steric reasons approach A is obviously favored over B.

Fig. 1

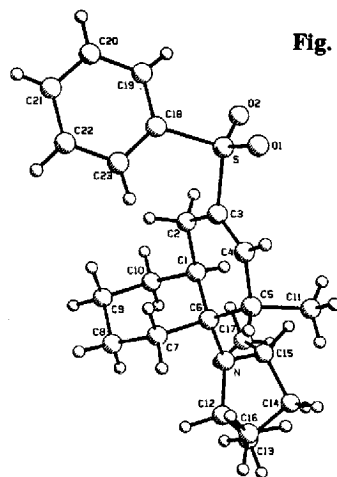
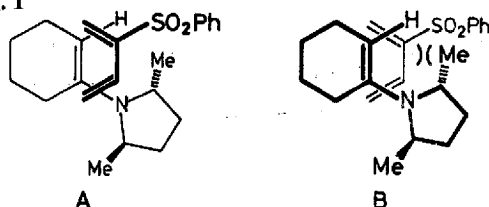
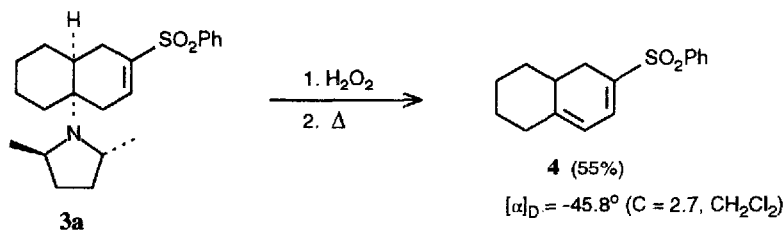


Fig. 2

The structure of **3b** as determined by X-ray crystallography¹⁰ (Figure 2) confirmed the structure assigned.

We previously showed^{1c} that the use of 2-(methoxymethyl)pyrrolidine in the enamine corresponding to **1** gave only 59% de in the cycloaddition to **2a**. The change to a C₂ symmetric amine¹¹ in the enamine thus dramatically improves the stereoselectivity as is also predicted by the transition state model. With 180° rotation of the mono-substituted pyrrolidine two conformations will be present of which one has only moderate face differentiation. With **1** such a rotation around the carbon-nitrogen bond does not change the molecule.^{8a}



For synthetic purposes it is also of interest to recover the chiral auxiliary. This was demonstrated on **3a** where the chiral pyrrolidine was removed via a Cope elimination¹² to give optically active **4**.

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References and Notes

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- A slight excess of the diene (1.3-1.5 equiv.) as a dilute solution (14-25 mM, dried over CaH₂) in Et₂O was added over 24h to a heated solution of the enamine in toluene (0.2ml/mmol enamine), containing K₂CO₃ (100 mg/mmol enamine). The added ether was continuously distilled off.
- Crystal data for 3b*: C₂₃H₃₃O₂NS, *M* = 387.58, monoclinic space group P2₁ (#4) with extra symmetry 1/2-x, 1/2+y, 1/2-z and 1/2+x, y, 1/2+z, a = (8.391(1), b = 11.117(2), c = 22.058(4) Å, β = 90.06(1)°. V = 2058(1) Å³. Z = 4, D_{calc} = 1.251 g/cm³, R = 0.032; crystal size 0.4 x 0.25 x 0.4 mm. Data were measured on a Rigaku AFC6R diffractometer with graphite monochromated Mo-Kα radiation and a 12 KW rotating anode generator using the ω - θ scan technique to a maximum 2θ value of 50.0°. The weak reflections (I < 10.0σ(I)) were rescanned (maximum of 3 rescans) and the counts were accumulated to assure good counting statistics. The intensities of three reflections measured after every 150 reflections remained constant throughout the data collection, indicating crystal and electronic stability. An empirical absorption correction, based on azimuthal scans of several reflections, was applied. The data were corrected for Lorentz and polarization effects.
- (a) The use of enamines with C₂ symmetric *trans*-2,5-bis-(methoxymethyl)pyrrolidine^{11b} in the cycloaddition to 2-phenylsulfonyl 1,3-dienes gave poor chemical yields. (b) Kawanami, Y.; Ito, Y.; Kitagawa, T. Taniguchi, Y. Katsuki, T.; Yamaguchi, M. *Tetrahedron Lett.* **1984**, *25*, 857; Chen, L.Y.; Ghosez, L. *Tetrahedron Lett.* **1990**, *31*, 4467.
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