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CHIRAL KETONE-CATALYZED ASYMMETRIC EPOXIDATION OF STILBENE WITH OXONE®[1]

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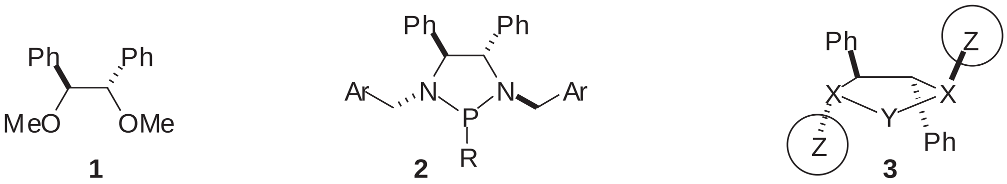
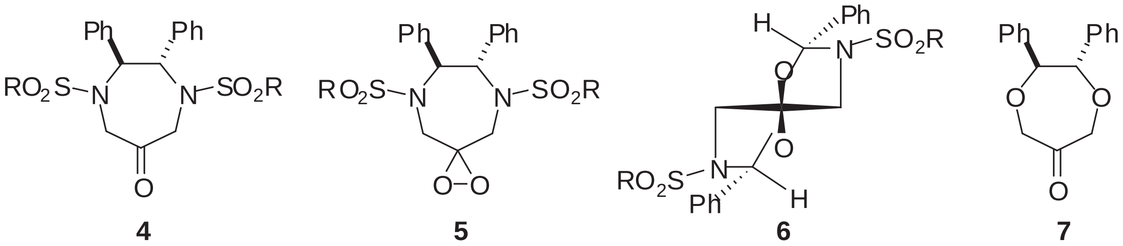
Abstract - Chiral 7-membered ketones bearing a 1,2-ethylenediamine backbone were synthesized and examined their catalytic behaviors in an asymmetric epoxidation of stilbene with Oxone®.

We have been involved in the development of external chiral ligands applicable in a catalytic asymmetric reaction.[2,3] The chiral backbone of our ligands relies on a 1,2-diphenylethane unit bearing ether oxygen or amine nitrogen at both ends as shown in **1** or **2**.[4] The idea being involved in **1** and **2** is postulated by the formation of chiral environment around Y due to the conformation fix of the substituents Z on the heteroatoms X as shown in **3** (Figure 1). In connection with our studies directed towards development of asymmetric oxidation reaction of olefins,[5] we designed a chiral ketone (**4**) as a precursor for a dioxirane (**5**), which has been an established good reagent for epoxidation of an olefin.[6,7] The dioxirane (**5**) is anticipated to take a rigid conformation (**6**) due to steric reason, of which chiral environment is expected to be equivalent to **3** (Figure 2). Since the electron-withdrawing sulfonylamide could enhance the reactivity of **5**, trifluoromethyl, pentafluorophenyl, and 3,5-bistrifluoromethylphenyl groups were chosen as the fluorine substituted R groups. The asymmetric epoxidation of olefins with Oxone® using a related ketone (**7**) as a chiral precursor has been reported.[8] We describe herein an asymmetric epoxidation of *trans*-stilbene using Oxone®-chiral ketones (**4**).



1 **2** **3**

Figure 1. Chiral ligands (**1**, **2**) bearing a 1,2-diphenylethane unit and chiral environment (**3**)



4 **5** **6** **7**

Figure 2. Chiral ketones (**4**, **7**) and dioxirane (**5** (**6**))

The ketones (**4a-d**) were readly prepared in three steps starting from commercially available (*S*,*S*)-**8** (Figure 3). According to the reported procedure, **8** was sulfonated with the corresponding sulfonyl chlorides in methylene chloride to give **9**.[9] Cyclization of **9** was carried out with **10** in DMF by the procedure reported for **7**[8] to afford **11**, which were then oxidized with ozone to **4**.

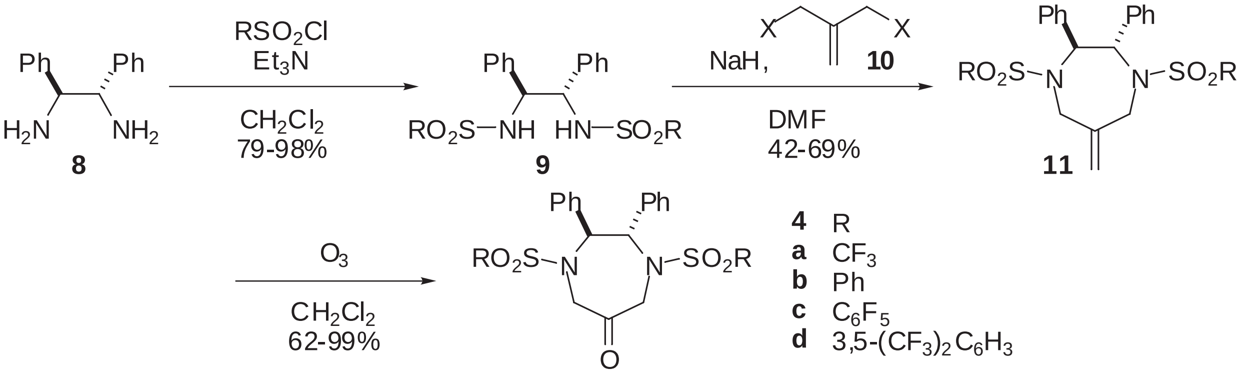
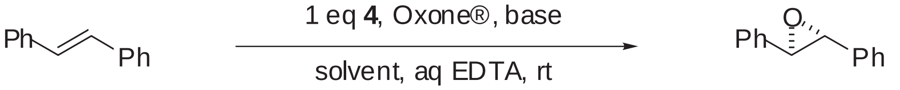


Figure 3. Three step synthesis of **4** from (*S*,*S*)-**8**

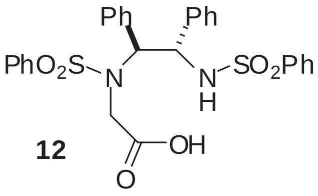
Table 1. Asymmetric epoxidation of stilbene with Oxone®-**4**



entry	4	R	Oxone/eq	Solvent	Base	eq	Addtn time/h[a)]	Time/h	Yield/%	Ee/%
1	**a**	CF_3	5.0	MeCN	$NaHCO_3$	16	1	1	56	11
2	**a**	CF_3	5.0	Dioxane	$NaHCO_3$	16	1	1	71	20
3	**a**	CF_3	1.4	Dioxane	K_2CO_3	6	1	1	trace	
4	**b**	Ph	5.0	Dioxane	$NaHCO_3$	16	3	5	17	17
5	**b**	Ph	1.4	Dioxane	K_2CO_3	6	1	9	27	30
6	**c**	C_6F_5	5.0	Dioxane	$NaHCO_3$	16	1	0	28	26
7	**d**	$(CF_3)_2C_6H_3$	5.0	Dioxane	$NaHCO_3$	16	1	0	42	27

a) Oxone® and a base were added over a period of the indicated time using a syringe drive.

The ketones (**4a-d**) were evaluated as the precursor of **5** in the asymmetric epoxidation reaction of stilbene. According to the previously reported results,[7,8] we first examined the reactions using one equivalent of **4a** in acetonitrile and 1,4-dioxane as the solvents and found that dioxane was superior to acetonitrile with respect to both chemical yield and enantioselectivity (Table 1, entries 1, 2). Sodium bicarbonate was a better base for higher chemical yield than potassium carbonate (entries 2, 3), however, the best ee of 30% was achieved using **4b** in the presence of potassium carbonate (entry 5). The occurrence of Baeyer-Villiger oxidation of the ketone to a lactone and its carboxylic acid is responsible for the poor chemical yield. In fact, a carboxylic acid **12** was isolated in 78% yield as the oxidation product of **4b** (Table 1, entry 4). The trifluoromethanesulfonamide (**4a**) gave the better yield than **4b-d**. A powerful electron withdrawing trifluoromethanesulfonyl group retards



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the Baeyer-Villiger oxidation. An enantioselectivity was determined by HPLC using a chiral stationary phase column (Daicel Chiralcel OD-H). The (*R*,*R*)-absolute configuration of the epoxide was determined by the specific rotation. The sense of enantiofacial differentiation was the same for **4a-d** giving (*R*,*R*)-stilbene oxide in up to 30% ee.

The sense of enantioselectivity is predictable based on the difference in the steric interaction between the sulfonyl moiety of **6** (**5**) derived from **4** and the phenyl group of stilbene as shown in Figure 4. The unexpectedly low ee is also due to the less effective steric repulsion between sulfonyl moiety and phenyl group of stilbene.

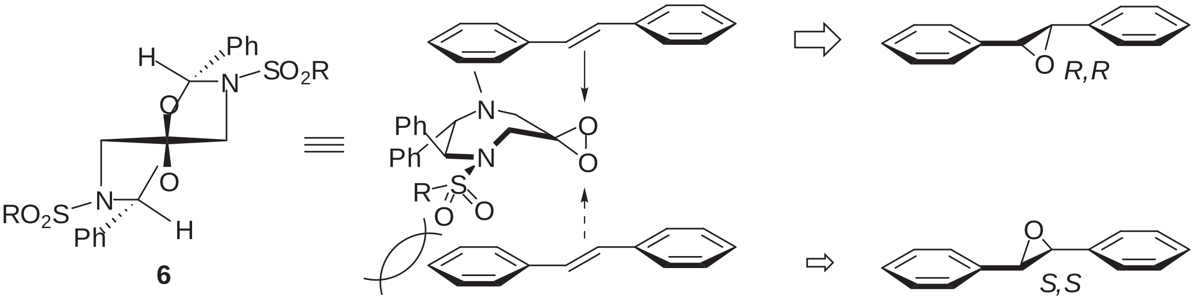

Figure 4. Approaches of dioxirane (**6**) to stilbene giving (*R*,*R*)-epoxide

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