



Scope and Limitations in the Jacobsen Epoxidation of Dienyl Sulfones¹

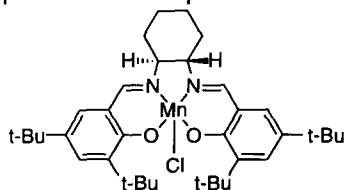
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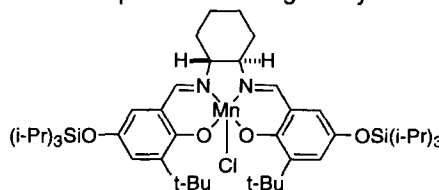
Abstract: Symchiral (salen)Mn(III)Cl complexes catalyze the epoxidation of 2-sulfonyl, 1,3 cyclic dienes with exceptional enantioselectivity. The incorporation of the sulfone moiety increases the enantioselectivity by up to 30%, relative to the unsubstituted cyclic 1,3-diene. © 1997 Elsevier Science Ltd.

Manganese salen complexes have been shown to be effective catalysts for the mild epoxidation of simple alkenes,² and both the Jacobsen and Katsuki catalysts have yielded very high enantioselectivities with a variety of tri and *cis*-disubstituted olefins.³

In the course of our synthetic studies we had occasion to employ the Jacobsen methodology for the epoxidation of 2-phenylsulfonyl-1,3-cyclohexadienes. Jacobsen has shown that while oxidation of the parent 1,3 cyclohexadiene provided a 33% yield of cyclohexadiene monoepoxide of 61%ee using his Manganese salen catalyst **1**, repeating the reaction with 2-acetoxy-1,3-cyclohexadiene resulted in a 30% yield of an 85%ee product. Replacing catalyst **1** with the sterically and electronically optimized salen catalyst **2** typically yielded 5% increases in enantioselectivity.⁴ With these observations in mind, we speculated that cross-conjugated dienyl sulfones might prove to be exceptional substrates for Jacobsen epoxidation using catalyst **2**.



(S,S)-1



(R,R)-2

The initial epoxidation of **3** was carried out at 0°C with a buffered NaOCl solution, using 15 mol% of catalyst **2** and 15 mol% of the additive, 4-phenyl pyridine *N*-oxide (PPNO).⁵ It was subsequently discovered that nearly identical results were obtained by using the commercially available catalyst **16** in 15 mol% without the use of additives, and this method was adopted as the standard procedure for the epoxidation of sulfones **3-12** shown in Table 1.⁷ Encouraged by the success with compounds **3** and **4**, we examined the regiochemical and steric effects of the sulfone moiety via reaction of compounds **5** and **9**. Epoxidation of the fully-conjugated sulfone

5 (entry 3) yielded practically the same enantioselectivity as unsubstituted 1,3-cyclohexadiene, suggesting that sulfone location is critical to catalyst approach, while switching from the bulky phenyl sulfone to the smaller methyl sulfone **9** (entry 7) still afforded an excellent enantioselectivity with almost no formation of the competing aromatization product, methyl phenyl sulfone. Furthermore, the isolated yield of the desired product in each case was substantially higher than that for the parent cyclohexadiene monoepoxide reported by Jacobsen, although competitive aromatization was still observed.⁴

Epoxidation of the 7-membered ring dienyl sulfone occurred in equally high enantioselectivity and with a modest increase in yield, as the troublesome aromatization by-product was avoided. A limitation was observed in the epoxidation of 2-Phenylsulfonyl-1,3-cyclooctadiene **7**. Although the enantioselectivity was still quite high, the reaction was exceptionally sluggish; a feature also evident in the simple epoxidation of **7** with mCPBA. Reverting back to catalyst **2** gave no improvement, but the addition of 15 mol% of PPNO with catalyst **1** did increase the yield to 35%. Increases of PPNO to 30 and 50 mol% and longer reaction times provided no further benefit. Compound **8** also showed no significant reactivity under these same conditions, leading us to speculate that the conformation of these octadienyl sulfones was not appropriate for epoxidation.

Similar to an earlier observation by Jacobsen regarding the epoxidation of 1,3-dienes, asymmetric epoxidation of acyclic dienyl sulfones also proved to be problematic.⁸ Compounds **9** and **10** yielded no oxidation products under either "Jacobsen" conditions, or after treatment with mCPBA. A small amount of the undesired Diels-Alder type products (**22** and **23**) were also formed in the course of these reactions; a problem previously documented by Bäckvall.⁹ We then synthesized sulfone **12**, a substrate we reasoned should be very effective with the Jacobsen catalyst since it possessed both a conjugated system, and cis-geometry, but again, the material proved to be unreactive.⁵

The extraordinarily high enantioselectivity and synthetically useful yields displayed in the epoxidation of cyclic dienyl sulfones such as **4** demonstrates the great potential for these compounds as useful synchiral intermediates.¹⁰ These substrates are easily prepared in good yield and can be readily transformed to useful intermediates as shown earlier by Bäckvall¹¹, and in the following example from our laboratory.¹²

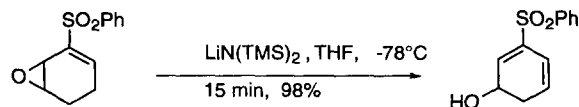
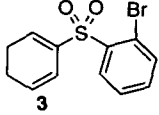
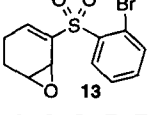
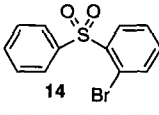
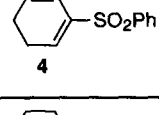
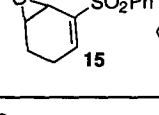
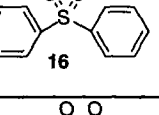
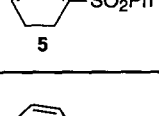
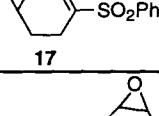
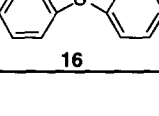
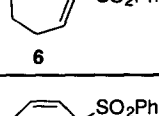
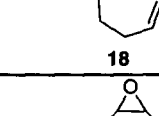
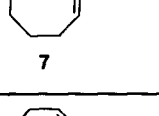
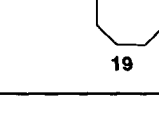
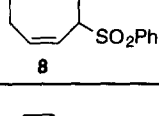
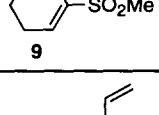
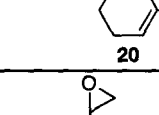
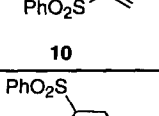
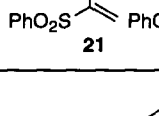
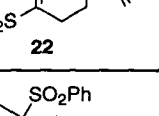
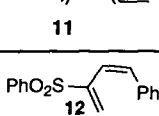
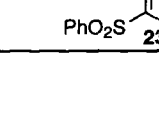
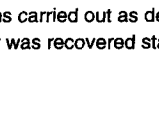


Table 1. Asymmetric Epoxidation of Sulfonylated Dienes^a

Run	Olefin	Product(s)	% Yield	% ee ^b	$[\alpha]_D^{25}$ (CHCl ₃)
1		 	13: 71 14: 25	98	-73.7
2		 	15: 72 16: 25	≥99	-88.7
3		 	17: 69 54 ^e 16: 23	65 68 ^e	-98.7
4			80	≥99	-9.4
5			10 ^c 35 ^{c,d}	90	-
6		-	NR	-	-
7			75	≥99	-98.0
8		 	21: 35 ^c 22: 15	20 ^c	-
9			15 ^c	-	-
10		-	NR	-	-

^aAll reactions carried out as described in footnote 6. ^bee's determined by HPLC using a Daicel Chiralcel OD column. ^cRemainder was recovered starting material. ^dUsing 15 mol% 4-Phenyl Pyridine N-Oxide. ^e Reaction run in Et₂O.

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References and Notes

¹ Synthesis Via Vinyl Sulfones **74**.

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⁶ Purchased from the Aldrich Chemical Company.

⁷ The following experimental procedure is representative: To a solution of **3** (25 mg, .084 mmol) , catalyst **1** (11 mg, .017mmol) in 5 mL of CH₂Cl₂ was added 1.5 mL of buffered NaOCl solution. The reaction mixture was stirred at 4°C until TLC showed the disappearance of starting material (2-4 hrs, except in case of **7**, which required 5h at 25°C). The reaction was diluted with diethyl ether and washed with brine, dried over Na₂SO₄, and concentrated. Flash chromatography afforded pure monoepoxide **13**.

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