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A Ferrocenylsulfide-mediated Sulfur Ylide Epoxidation Reaction

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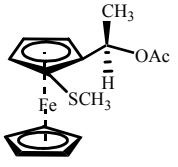
Abstract: A ferrocenylsulfides **1-2** mediated sulfur ylide epoxidation reaction was found to stereoselectively afford *trans*-oxiranes in excellent yields with recoverable starting material.

Keywords: Ferrocenylsulfide, epoxidation, stereoselectivity, oxiranes, sulfur ylide.

Since Wilkinson and Woodward characterized ferrocene as sandwich structure[1] in 1952 , there has been long-standing interest in the extensive application of ferrocenyl compounds[2]. Our aim is to design and synthesize ferrocene-based sulfides, which could find utilization in stereo-and/or enantioselective epoxidation reactions. It is well known that ferrocenyl compounds are widely used as ligands[3] in transition metal-catalyzed asymmetric synthesis. However, to the best of our knowledge, the ferrocenylsulfide mediated sulfur ylide epoxidation reaction has not appeared in the literature until now. Here we wish to report our preliminary results *via* racemic sulfides **1** or **2** to form diaryl oxiranes stereoselectively.

The ferrocenyl sulfides **1** or **2** were synthesized according to literature methods[4]. Our initial attempt to employ **1** or **2** with benzyl bromide to form the sulfonium salt was failed. It might be due to the bulky vicinal group and the weak nucleophilicity of the sulfur atom. Then we treated **2,** in the presence of silver tetrafluoroborate, reacting with benzylbromide to furbish the sulfonium salt **3** (**Scheme 1**) in excellent yield. We observed that the salt **3**, after deprontonation by LDA *in situ*, could react with *para*-nitrobenzaldehyde to afford 2-(4-nitrophenyl)-3-phenyl oxirane **4** with >98% *trans*-isomer in 92% yield **(Scheme 1)**. 95% of sulfide **2** could be recovered.

Figure 1 Racemic ferrocenyl sulfides used in sulfur ylide epoxidation reactions



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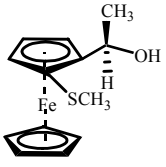

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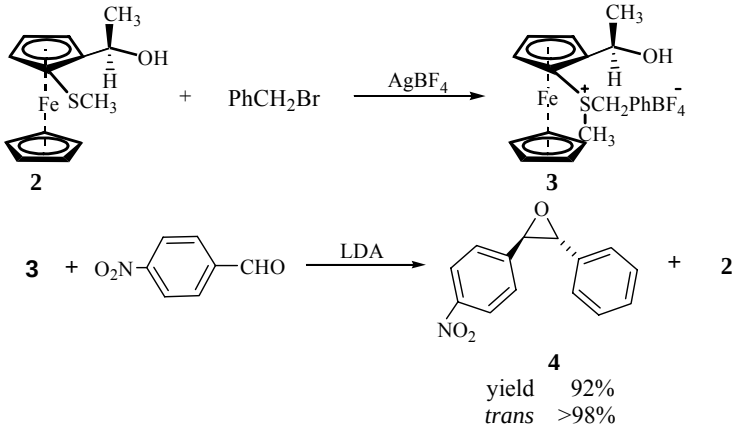
Scheme 1 Two steps for the synthesis of oxirane **4**: formation of the sulfonium salt and sulfur ylide epoxidation *in situ***.**



Encouraged by the above result we tried to simplify the procedure. A one-pot reaction was designed involving all the reagents mixing together. Sulfide **2** (1.0 equiv)**,** benzyl bromide(1.2 equiv) and *para*-nitrobenzaldehyde (1.0 equiv) were mixed with sodium hydroxide(1.2 equiv) at room temperature. The reaction proceeded completely (entry 1, **Table 1**) with exclusive *trans*-isomer. Using the optimized condition we investigated the scope of the reaction by utilizing a series of structurally different aldehydes (**Table 1**). It was found that the aromatic aldehydes worked well with high stereoselectivity in excellent yields. A heteroatomatic aldehyde (entry 6, **Table 1**) also reacted smoothly to give moderate yield. All the cases in **Table 1** afforded nearly unique *trans*-isomer. Another attractive feature of the reaction was that the initial sulfide **2** could be recovered after the reaction in almost quantitative amounts (entry 1—5). Only in one case, for furfural (entry 6), the sulfide was recovered 92% due to longer reaction time.

Table 1 Results of epoxidation studies[a] using sulfide **2** and a range of aldehydes

Entry	Aldehyde	Time(days)	*Trans*/*cis*[b]	Yield(%)[c]	Sulfide Recovered(%)
1	*p*-$NO_2C_6H_4CHO$	0.5	>99:1	99(**4a**)	98
2	*p*-ClC_6H_4CHO	1.5	>99:1	99(**4b**)	98
3	*p*-BrC_6H_4CHO	2	>99:1	96(**4c**)	98
4	C_6H_4CHO	2	>99:1	85(**4d**)	97
5	*p*-MeC_6H_4CHO	2.5	>98:2	87(**4e**)	98
6	Furfural	3.5	>98:2	68(**4f**)	92[d]

a. In this table, benzyl bromide, aldehydes were employed in 1.0 equiv, and NaOH in 1.2 equiv.

b. The ratio of *trans/cis* was determined by ^{1}HNMR according to its coupling constant.

c. Isolated yields after column chromatography.

d. Longer reaction time decreased the recovered amount.

In summary, a ferrocenylsulfide mediated sulfur ylide epoxidation reaction was developed, which offered a novel approach for the stereoselective synthesis of oxiranes. The reaction has high stereoselectivity, excellent yields and simple procedure with mild reaction conditions. The asymmetric version *via* optically pure **1** or **2** will be reported in due communications.

Acknowledgments

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References and Notes

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5. Compound **1**. ^{1}HNMR ($CDCl_3$, δ ppm): 6.12-6.10(q, 1H, J=8.0Hz, FcCH), 4.41(s, 1H, Fc-H-1), 4.38(s, 1H, Fc-H-2), 4.25(s, 1H, Fc-H-3), 4.15(s, 5H, Fc-5H), 2.19(s, 3H, SCH_3), 1.99(s, 3H, $COCH_3$), 1.66-1.65(d, 3H, J=6.5Hz, $FcCHCH_3$). **2**. ^{1}HNMR ($CDCl_3$, δ ppm): 4.98-4.96(q, 1H, J=8.0Hz, FcCH), 4.36(s, 1H, Fc-H-1), 4.27(s, 1H, Fc-H-2), 4.19(s, 1H, Fc-H-3), 4.15(s, 5H, Fc-5H), 4.10(s, 1H, OH), 2.28(s, 3H, SCH_3), 1.58-1.57(d, 3H, J=8.1Hz, $FcCHCH_3$). **3**. Mp. 122-123℃. ^{1}HNMR ($CDCl_3$, δ ppm): 7.49(d, 2H, J=8.0Hz, ArH), 7.38-7.30(m, 3H, ArH), 4.99-4.95(q, 1H, J=8.4Hz, FcCH), 4.36(s, 1H, Fc-H), 4.27(s, 1H, Fc-H), 4.19(s, 1H, Fc-H), 4.15(s, 5H, Fc-H), 4.10(s, 1H, OH), 3.58(s, 2H, SCH_2), 2.28(s, 3H, SCH_3), 1.57(d, 3H, J=8.0Hz, $CHCH_3$). Anal. Calcd for $C_{20}H_{23}BF_4FeS$: C, 54.79; H, 5.25. Found: C, 55.01; H, 5.31. **4a**. ^{1}HNMR ($CDCl_3$, δ ppm): 8.25-8.23(d, 2H, J=8.0Hz, ArH), 7.52-7.50(d, 2H, J=8.0Hz, ArH), 7.43-7.34(m, 5H, ArH), 3.97(s, 1H, CH), 3.85(s, 1H, CH). **4b**. ^{1}HNMR ($CDCl_3$, δ ppm): 7.52-7.45 (m, 6H, ArH), 7.40-7.34(m, 3H, ArH), 3.95(s, 1H, CH), 3.93(s, 1H, CH). **4c**. ^{1}HNMR ($CDCl_3$, δ ppm): 7.52-7.49(d, 2H, J=8.8Hz, ArH), 7.39-7.33(m, 5H, ArH), 7.23-7.21 (d, 2H, J=8.4Hz, ArH), 3.83(s, 1H, CH), 3.82(s, 1H, CH). **4d**. ^{1}HNMR ($CDCl_3$, δppm): 7.40-7.29(m, 10H, ArH), 3.86(s, 2H, CH). **4e**. ^{1}HNMR ($CDCl_3$, δ ppm): 7.38-7.33(m, 5H, ArH), 7.26-7.24(d, 2H, J=8.0Hz, ArH), 7.21-7.19(d, 2H, J=8.0Hz, ArH), 3.865-3.862 (d, 1H, J=1.2Hz, CH), 3.843-3.839(d, 1H, J=1.6Hz, CH), 2.38(s, 3H, CH_3). **4f**. ^{1}HNMR ($CDCl_3$, δ ppm): 7.60(s, 1H, Furyl-H), 7.46-7.44(d, 2H, J=8.0Hz, ArH), 7.41-7.37(m, 3H, ArH), 7.23-7.21(d, 1H, J=4Hz, Furyl-H), 6.53-6.51(q, 1H, J=1.6Hz, Furyl-H), 5.36(s, 2H, CH).

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