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# Asymmetric Sulfenylation of Tin(II) Enolates of Ketones and 3-Acyl-2-oxazolidones. Application to the Synthesis of Optically Active Epoxides

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In the presence of chiral diamines, the reaction between tin(II) enolates of ketones or 3-acyl-2-oxazolidones and thiosulfonates proceeds smoothly to give the corresponding β-keto sulfides with high enantioselectivity. Further, optically active epoxides are prepared from these β-keto sulfides.

In recent years, extensive studies have been carried out on asymmetric reactions employing various enolates as one of the reactants.[1] Among these reactions, the ones in which the chiral auxiliaries are not covalently bonded to the reactants are of special synthetic utility, as tedious procedures for the attachment and removal of the chiral sources are not required.

In a previous communication,[2] we have already reported a highly enantioselective aldol reaction of tin(II) enolates employing a chiral diamine as a ligand. In this reaction, where both the reactants, the ketone and the aldehyde, are achiral, a high degree of enantioselectivity is induced by the effective coordination of the chiral diamine with the stannous ion of the intermediate tin(II) enolate.

To further expand the range of the asymmetric reaction of tin(II) enolates, we subsequently examined the reaction of divalent tin enolates with various electrophiles and in this communication we wish to report the reaction of sulfur electrophiles with tin(II) enolates in the presence of chiral diamine ligands to give chiral β-keto sulfides. As β-keto sulfides can be easily converted into epoxides via β-hydroxy sulfides,[3] a route to chiral epoxides, which are useful synthetic intermediates, is thus established.

In the first place, the tin(II) enolate of propiophenone, generated in situ from propiophenone and stannous triflate with N-ethylpiperidine as base, was treated with phenylsulfenyl chloride in the presence of chiral diamine 1, and the corresponding β-keto sulfide 2 was obtained in good yield. The optical purity of this product was shown to be 54%e.e. based on $^1$H NMR measurements using chiral shift reagent Eu(hfc)$_3$. Having thus successfully attained a moderate amount of asymmetric induction in this reaction, a screening of the sulfenylation reagent was tried in order to increase the optical purity of the product (Table 1). As shown in Table 1, high optical purities were attained when thiosulfonates were employed as the sulfenylation reagent. Especially when the bulky thiosulfonate

(entry 4) was used with two equivalents of tin(II) triflate, the desired keto sulfide was obtained in 78% yield with the high optical purity of 85%e.e. Several diamines were also screened for this reaction, however, the initial diamine 1 gave the best results.

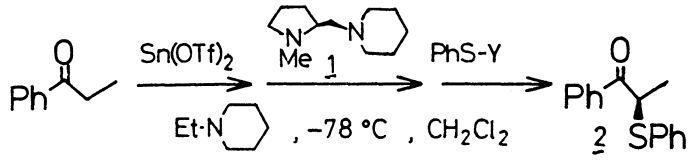
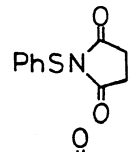
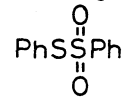
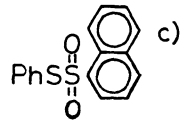



Table 1.[a)]

| PhS-Y | Yield/% | Optical yield/%e.e.[b)] |
|---|---|---|
| 1) PhSCl | 63 | 54 |
| 2)  | 27 | 60 |
| 3)  | 58 | 75 |
| 4)  c) | 78 | 85 |

a) Molar ratio of $Sn(OTf)_2$ : N-ethylpiperidine : substrate : chiral diamine : sulfenylation reagent = 1.0 : 1.2 : 0.8 : 1.2 : 1.2.
b) Determined by using chiral shift reagent $Eu(hfc)_3$.
c) Molar ratio of $Sn(OTf)_2$ : N-ethylpiperidine : substrate : chiral diamine : sulfenylation reagent = 2.0 : 2.4 : 0.8 : 2.4 : 1.2.

Having attained the best conditions for this reaction, the asymmetric sulfenylation of various ketones and 3-acyl-2-oxazolidones was examined (Table 2).

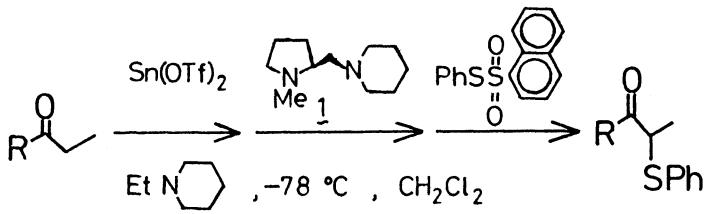
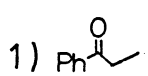
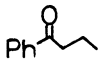
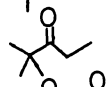
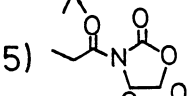
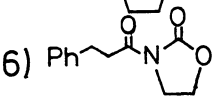



Table 2.[a)]

| Substrate | Yield/% | Optical yield/%e.e. |
|---|---|---|
| 1)  | 78 | 85[b)] |

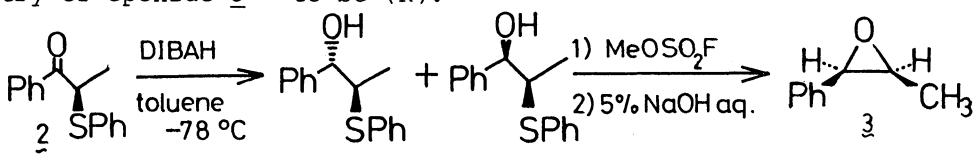
| | | |
|---|---|---|
| 2)  | 80 | 75[c] |
| 3)  | 72 | 50[b] |
| 4)  | 52 | 70[d] |
| 5)  | 93[e] | 81[b] |
| 6)  | 91[e] | 82[f] |

a) Molar ratio of $Sn(OTf)_2$ : N-ethylpiperidine : substrate : chiral diamine : sulfenylation reagent = 2.0 : 2.4 : 0.8 : 2.4 : 1.2.
b) Determined by using chiral shift reagent $Eu(hfc)_3$.
c) The product was reduced to a β-hydroxy sulfide by DIBAH. The major isomer was converted to its MTPA ester and the optical purity was determined by $^{19}F$ NMR.
d) The product was reduced to a β-hydroxy sulfide by DIBAH. The major isomer was isolated and the optical purity was determined by using chiral shift reagent $Eu(tfc)_3$.
e) Molar ratio of $Sn(OTf)_2$ : N-ethylpiperidine : substrate : chiral diamine : sulfenylation reagent = 1.0 : 1.2 : 0.6 : 1.2 : 1.2. In this case $PhSSO_2Ph$ was used as the sulfenylation reagent.
f) The product was reduced to β-hydroxy sulfide by LAH, and then converted to its MTPA ester. Then the optical purity was determined by use of shift reagent $Eu(fod)_3$.

As shown in Table 2, moderate to high enantioselectivity was achieved in all cases. It is noted that particularly high enantioselectivity is realized when 3-acyl-2-oxazolidone derivatives are employed as the tin(II) enolate components.

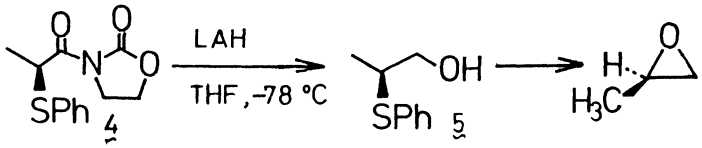
Several asymmetric sulfenylation reactions of enolates have already been reported.[4,5] However, in these reactions, the optical purity of the products obtained are generally low, or either a chiral carbonyl compound or chiral sulfenylation reagent is employed as one of the components (i.e. the chiral source is attached covalently to the substrate). On the other hand, the present reaction is the first example in which a moderate to high degree of enantioselectivity is achieved by employing a chiral ligand with achiral substrates.

Next we examined the derivation of the β-keto sulfides obtained in this reaction to chiral epoxides.[6] When β-keto sulfide 2 was treated with DIBAH, the corresponding β-hydroxy sulfide was obtained in 86% yield with syn : anti ratio of 8 : 1. The optical purity of the major isomer was determined by conversion to its MTPA ester and it was ascertained that no racemization had occurred during the reduction procedure. The β-hydroxy sulfide was subsequently converted to a chiral epoxide by a known method which produces epoxides without racemization.[3] The absolute configuration of the β-keto sulfide was determined from the known absolute stereochemistry of epoxide 3[7] to be (R).




86% anti : syn = 1 : 8

Similarly, the sulfenylated 3-acyl-2-oxazolidone 4, when treated with LAH at -78 °C, was reduced to the corresponding hydroxy sulfide. The optical purity of this β-hydroxy sulfide was determined by comparison with an authentic sample prepared from optically pure S-(+)-1,2-propanediol. In this case, too, it was confirmed that reduction proceeded with no racemization. Furthermore, the absolute configuration of 5 was determined to be (S).




Thus, a route to chiral epoxides from carbonyl compounds via the asymmetric sulfenylation reaction was established. In particular, the sulfenylation of the 3-acyl-2-oxazolidones is noteworthy as a route to the preparation of chiral terminal epoxides of high optical purity.

A typical procedure for the asymmetric sulfenylation reaction is as follows; to a suspension of stannous triflate (458 mg, 1.1 mmol) and N-ethylpiperidine (138 mg, 1.2 mmol) in 2 ml of dichloromethane was added dropwise propiophenone (62 mg, 0.5 mmol) in 1.5 ml of dichloromethane at -78 °C under argon with stirring. After stirring for 30 minutes, (S)-1-methyl-2-[(piperidin-1-yl)methyl]pyrrolidine (237 mg, 1.3 mmol) in 1.5 ml of dichloromethane was added, and the mixture was stirred for 5 minutes. Then benzenethiosulfonate (175 mg, 0.7 mmol) in 1.5 ml of dichloromethane was added. The reaction was further stirred for 2 hours at -78 °C, then quenched with 10% aqueous citric acid solution. The organic layer was extracted with dichloromethane three times and the combined extracts were dried over anhydrous $MgSO_4$. After evaporation of the solvent, the crude product was purified by silica gel column chromatography to afford 1-phenyl-2-thiophenyl-1-propanone in 82% yield.

Thus, the reaction of tin(II) enolates of ketones or 3-acyl-2-oxazolidones with thiosulfonates in the presence of chiral diamines proceeds smoothly to give the corresponding sulfenylated products in good yield with high enantioselectivity. Furthermore, the β-keto sulfides thus obtained are easily converted to chiral epoxides, which are useful intermediates in the synthesis of optically active compounds.

References

1) "Asymmetric Synthesis," ed by J. D. Morrison, Academic Press, Inc., New York (1984), Vol.3.
2) N. Iwasawa and T. Mukaiyama, Chem. Lett., 1982, 1441.
3) W. H. Pirkle and P. L. Rinaldi, J. Org. Chem., 43, 3803 (1978).
4) K. Hiroi, M. Nishida, A. Nakayama, K. Nakazawa, E. Fujii, and S. Sato, Chem. Lett., 1979, 969.
5) R. P. Alexander and I. Paterson, Tetrahedron Lett., 1985, 5339.
6) The reduction of β-keto sulfides has been examined by Oishi and coworkers; M. Shimagaki, T. Maeda, Y. Matsuzaki, I. Hori, T. Nakata, and T. Oishi, Tetrahedron Lett., 1984, 4775.
7) E. Chiellini, M. Marchetti, and F. Ceccarelli, Internat. J. Sulfur Chem. A, 1, 73 (1971).

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