*Communications*

# Microbial reduction of sulfur-containing ketones by *Geotrichum* sp.

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**Bioreduction of some β-carbonyl phenyl sulfides, sulfoxides and sulfones (1, 3, 5, 8, 11 and 13) by *Geotrichum* sp. was studied. Reduction of β-carbonyl phenyl sulfoxides (5 and 8) gave *anti*-Prelog sulfoxide alcohols. ($S, S_S$)-3-Chloro-1-phenylsulfinylpropan-2-ol (9) was obtained in high yield with 95% *e. e.* after recrystallization from methylene chloride-petroleum ether.**

**Keywords** Bioreduction, sulfur-containing ketones, *Geotrichum* sp.

Sulfides, sulfoxide and sulfones are functionalities which possess great synthetic utility for their possible transformation to a variety of functional groups. There has been great interest in the bioreduction of ketones bearing an α-sulfur containing functionality, as this could provide useful synthetic intermediates in asymmetric synthesis of natural products, medicines, and other useful materials.[1] However, the bioreduction of these ketones is critically dependent on both the substituents on the sulfur-containing group and the substitutes on the carbonyl group. Most of the bioreduction afford one isomer of the enantiomeric alcohols following the Prelog's rule.[2] The other isomer is often prepared by tedious chemical transformation. In our previous paper,[3] we reported the reduction of α-ketone esters, β-ketone esters, and α-halomethyl aryl ketones afforded the homo chiral secondary alcohols using *Geotrichum* sp., a reducing fungus isolated from the soil samples, to give products with *anti*-Prelog specificity. Here, we wish to report the reduction of some substituted β-carbonyl phenyl sulfides, sulfoxides and sulfones by *Geotrichum* sp. (Scheme 1).[4]

**Scheme 1** Reagents: i. *Geotrichum* sp., 5% glucose, 30℃; ii. $LiAlH_4$, THF

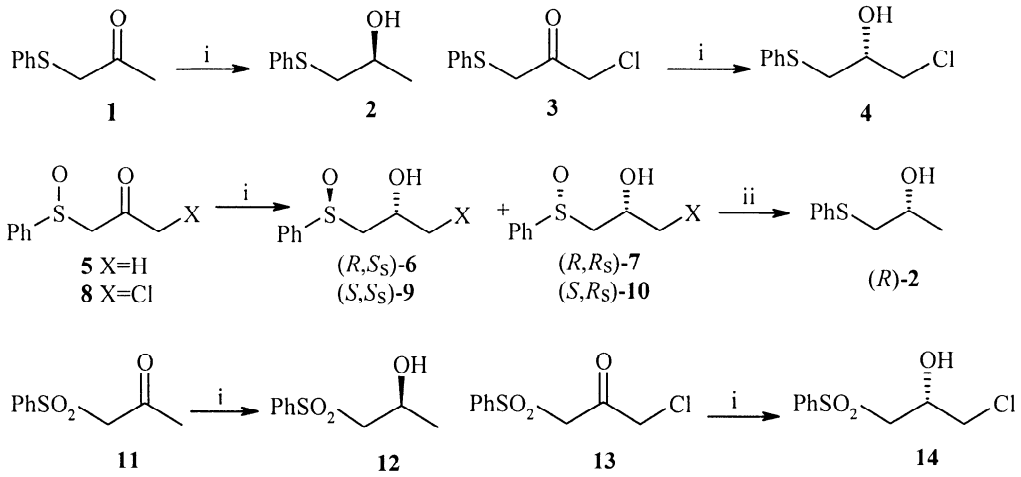


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**Table 1** Bioreduction of ketones **1**, **3**, **5**, **8**, **11**, **13** using *Geotrichum* sp.

| Entry | Substrate | Time (h) | Product | Yield (%)[a] | *e.e.* (%)[b] | Config. |
|---|---|---|---|---|---|---|
| 1 | **1** | 7 | **2** | 82 | 14 | *S* |
| 2 | **3** | 10 | **4** | 15 | 2 | *S* |
| 3 | **5** | 7 | **6**:**7** | 76 | **6**:63 | $R, S_S$ |
| | | | (27:73) | | **7**:16 | $R, R_S$ |
| 4 | **8** | 20 | **9**:**10** | 66(9)[c] | **9**:81(95)[d] | $S, S_S$ |
| | | | (81:19) | | **10**:88 | $S, R_S$ |
| 5 | **11** | 7 | **12** | 96 | 10 | *S* |
| 6 | **13** | 24 | **14** | 85 | 8 | *S* |

[a] Isolated yield. [b] Determined by chiral HPLC analysis. [c] Figure in the parentheses is the yield of unreacted sulfoxide ketone mainly in (*R*)-configuration. [d] Figure in the parentheses indicates the optical purity after recrystallization.

As shown in Table 1, the sulfide **1** and **3** were converted readily to 1-phenylthiopropan-2-ol (**2**) and 3-chloro-1-phenylthiopropan-2-ol (**4**) with *Geotrichum* sp. in 82% and 15% yield, respectively (Entries 1 and 2). However, the optical purity of the products is very low. Similarly, the sulfones **11** and **13** were reduced to 1-phenylsulfonylpropan-2-ol (**12**) and 3-chloro-1-phenylsulfonylpropan-2-ol (**14**) in 96% yield with 10% *e.e.* and 85% yield with 8% *e.e.*, respectively (Entries 5 and 6). Reduction of the racemic 1-phenylsulfinylpropan-2-one (**5**) afforded a 27:73 mixture of ($R, S_S$)-**6** and ($R, R_S$)-**7** with 63% *e.e.* and 16% *e.e.*, respectively. Reduction of the racemic 3-chloro-1-phenylsulfinylpropan-2-one (**8**) gave an 81:19 mixture of ($S, S_S$)-**9** and ($S, R_S$)-**10** with 81% *e.e.* and 88% *e.e.*,[5] respectively. The *e.e.* values were determined by chiral HPLC analysis. The optical purity of ($S, S_S$)-**9** could be improved to 95% by recrystallization from methylene chloride-petroleum ether. The stereochemistry on the carbon atom of **6**/**7** and **9**/**10** can be determined as reduced to (*R*)-**2** with lithium aluminium hydride (Scheme 1).[6] By determination of the Cotton effect in the CD spectra of the optically active sulfoxides and using the rule[7] that a negative Cotton effect for the primary band corresponds to the (*S*)-configuration as sulfur in phenyl alkyl sulfoxides, the absolute configuration on the sulfur atom was assigned, as the major isomer **7** showed a positive Cotton effect while **9** showed a negative Cotton effect (Fig. 1).

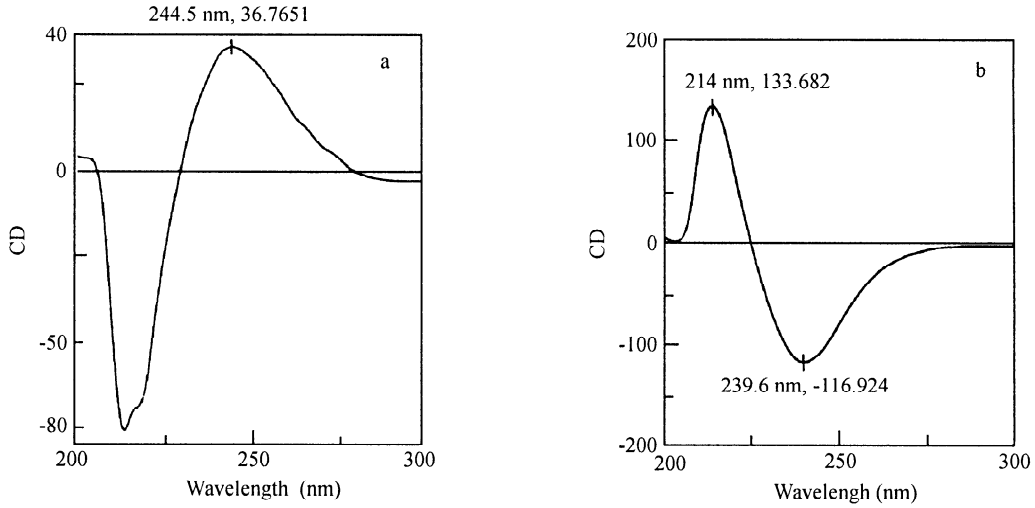


**Fig. 1** CD spectra of the optically active sulfoxides: a, **7**; b, **9**.

In conclusion, we have studied the reduction of some β-carbonyl phenyl sulfides, sulfoxides and sulfones mediated by *Geotrichum* sp. which exhibits *anti*-Prelog specificity in reducing β-carbonyl phenyl sulfoxides **5**

and **8**, and particularly, ($S$, $S_S$)-3-chloro-1-phenylsulfinypropan-2-ol ($S$, $S_S$)-**9** was obtained in good results. However, the corresponding sulfides and sulfones alcohols were obtained with low optical purity, which could be due to either the activity of a single enzyme with low enantioselectivity or the presence of various dehydrogenases which, having different selectivity, would catalyze unwanted redox equilibria causing low optical purity of the formed product. As these compounds are useful chiral building blocks for the construction of various important compounds,[8] the study of methods to improve the enantioselectivity of the microbial reduction is required and this is in progress.

## References and notes


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4. General procedure for the biotransformation: Wet mycelium[3] (15 g) was suspended in 5% glucose solution (50 mL). The substrate (1 mmol) (dissolved in 0.5 mL of DMSO if it is solid) was added slowly. The mixture was shaken at 150 rpm at 30℃ and monitored by TLC.
5. The spectra are: $\nu_{max}$: 3350, 1640, 1450, 1090, 1050, 750 $cm^{-1}$. $\delta_H$ ($CDCl_3$): 7.70—7.50(m, 5H), 4.48—4.41(m, 1H), 3.8(br s, 1H), 3.75—3.53(m, 2H), 3.10—3.06 and 2.95—2.90(m, 2H). *m/z*(%): 218 ($M^+$, 2.7), 126(100), 125(64.4), 78(73.8), 77(33.3), 51(20.4). HRMS: ($C_9H_{11}ClO_2S$)$^+$ Calcd: 218.0168. Found 218.0168.
6. The procedure is as follows. To a solution of **6**/**7** or **9**/**10** (55 mg) in THF (10 mL) was added $LiAlH_4$ (25 mg) and the mixture was stirred at room temperature for 3 h. Usual work-up to give ($R$)-**2** with physical and chemical characteristics corresponding to those of an authentic sample. From **6**/**7**: $[\alpha]_D^{25}$ − 17(*c* 0.8, $CHCl_3$); from **9**/**10**: $[\alpha]_D^{25}$ − 47(*c* 0.8, $CHCl_3$). (Lit.[9] $[\alpha]_D^{25}$ 54.7(*c* 1.0, $CHCl_3$) *S*-).
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