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A SIMPLE ENANTIOSELECTIVE SYNTHESIS OF BOTH ENANTIOMERS OF SULCATOL USING A SINGLE CHIRAL PRECURSOR

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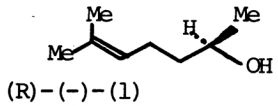
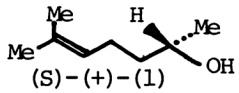
A simple synthesis of (R)-(-)- and (S)-(+)-sulcatol(1), both the aggregation pheromone of Gnathotrichus sulcatus, has been developed using a single chiral precursor.

Sulcatol (1), the aggregation pheromone produced by males of Gnathotrichus sulcatus[1], is a peculiarly interesting substance from the biological point of view as its racemate exhibits more pheromone activity than both (+)- and (-)-enantiomers[2]. However, this does not mean dispensability of enantioselective synthesis of both enantiomers, since it was revealed that the natural pheromone is a 35 : 65 mixture of (R)-(-)- and (S)-(+)-enantiomers. Although racemic[1] and enantioselective[3] syntheses have been developed, we report here an alternative enantioselective synthetic entry which is capable of producing the both enantiomers of sulcatol (1) using a single chiral precursor.



(R)-(-)-(1)
$[\alpha]_D$-14.4° (EtOH)



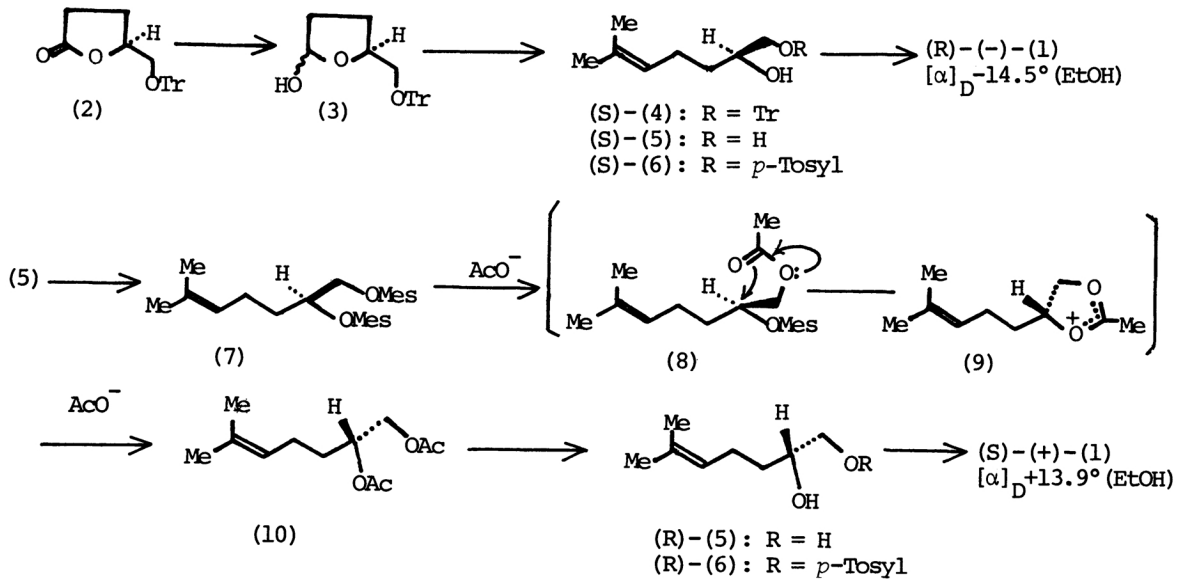
(S)-(+)-(1)
$[\alpha]_D$+14.5° (EtOH)

Reduction of the known chiral lactone (2), easily accessible from L-glutamic acid[4] or D-mannitol[5], using DIBAL gave the lactol (3) which was converted into the olefin ((S)-4) by Wittig reaction. Detritylation of (4) afforded the (S)-1,2-glycol (5), $[\alpha]_D$-17.8° (c = 4.47, EtOH), in 58 % overall yield.

The (S)-glycol (5) was treated with one equiv of p-toluenesulfonyl chloride in the presence of pyridine to give the mono-tosylate ((S)-6) which on reduction with $LiAlH_4$ in THF furnished (R)-(-)-sulcatol (1), $[\alpha]_D$-14.5° (c = 1.95, EtOH) (lit[3]. $[\alpha]_D$-14.5° (c = 0.74, EtOH)), in 49 % overall yield from (S-5).

On the other hand, the (S-5) was treated with methanesulfonyl chloride in the presence of pyridine to give the dimesylate (7). Upon reflux with potassium acetate in acetic anhydride, the

(7) was cleanly converted into the diacetate (10) with complete inversion at the chiral center presumably via the intermolecular substition at the primary center by acetate, followed by spontaneous intramolecular substitution of the secondary center by the introduced neighboring acetoxy group as shown in Scheme[6,7]. Methanolysis of (10) in the presence of potassium carbonate furnished the enantiomeric (R)-glycol (5) $[\alpha]_D$+16.0° (c = 1.84, EtOH), in 74 % overall yield from (S)-counterpart (5). Conversion of the (R)-glycol (5) into (S)-(+)-sulcatol (1), $[\alpha]_D$+13.9° (c = 2.70, EtOH) could be carried out as for its enantiomer in a comparable yield.



References

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2) (a) K. Mori, "The Total Synthesis of Natural Products," Vol. 4, ed. by J. ApSimon, J. Wiley & Sons, New York, 1981, pp. 119-120. (b) J. H. Borden, L. Chong, J. A. McLean, K. N. Slessor, and K. Mori, Science, 192, 894 (1976).

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6) Such an inversion reaction has been recognized in the carbohydrate field, see: (a) R. C. Chalk, D. H. Ball, M. A. Lintner, and L. Long, Jr., J. C. S., Chem. Comm., 1970, 245. (b) K. Kakinuma, Tetrahedron Lett., 1978, 768.

7) Recently, we have developed an efficient inversion reaction of a chiral glycerol derivative using these conditions: S. Takano, K. Seya, E. Goto, M. Hirama, and K. Ogasawara, to be published.

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