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A Short Synthesis of (+)-endo-Brevicomin

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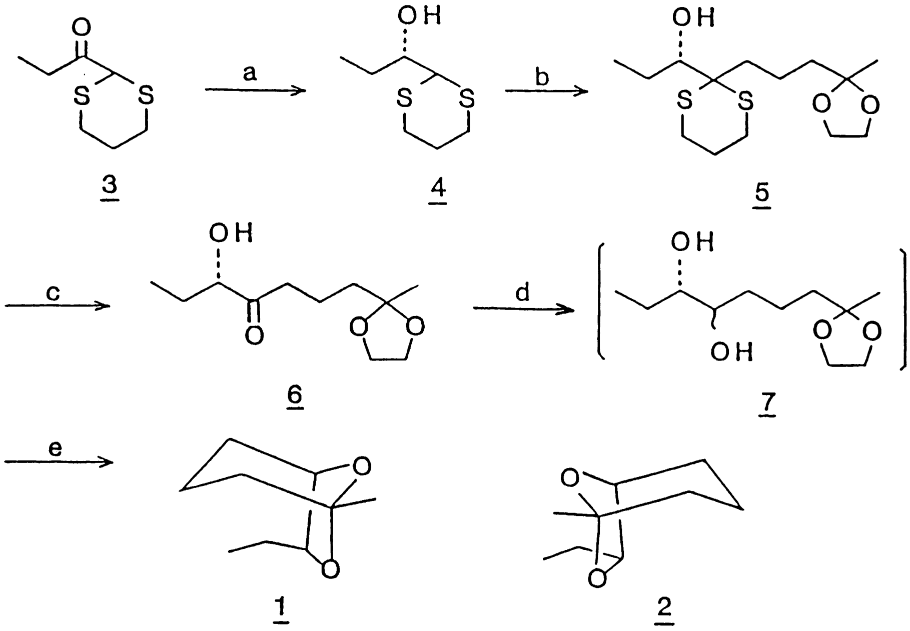
(+)-endo-Brevicomin was synthesized in a few-step-sequence starting from (S)-(-)-1-(1,3-dithian-2-yl)-1-propanol, which was obtained by the baker's yeast reduction of 1-(1,3-dithian-2-yl)-1-propanone.

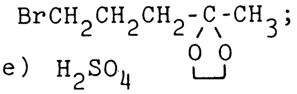
Fujisawa and co-workers$^{1)}$ demonstrated that (S)-α-hydroxythioacetals with high optical purity (>96% ee) were obtained by baker's yeast reduction of various kinds of α-ketothioacetals. These chiral α-hydroxythioacetals are expected to serve as chiral building blocks in the synthesis of variuos natural products. We now report the synthesis of optically active (+)-endo-brevicomin (1) from (S)-(-)-1-(1,3-dithian-2-yl)-1-propanol (4). endo-Brevicomin is one of the attractant pheromones of several pine beetle species belonging to the genera *Dendroctonus* and *Dryocetes*. A number of syntheses of endo-brevicomin have been reported.$^{2)}$

The straightforward synthesis of (+)-endo-brevicomin 1 is illustrated in Scheme 1. Baker's yeast reduction of the 1-(1,3-dithian-2-yl)-1-propanone (3) employed the method of Fujisawa,$^{1)}$ thus (S)-(-)-4 was obtained in good yield. Alkylation of 4 with 5-bromopentan-2-one ethyleneketal$^{3)}$ (2 equiv. of n-BuLi, THF, -18–0 °C) gave ketal (5), $[\alpha]_D^{22}$ -18.3°(c 9.74 $CHCl_3$), in 65% yield. The ketal 5 thus obtained was converted into ketone (6), $[\alpha]_D^{22.5}$ +61.3°(c 5.51 $CHCl_3$), in 70% yield upon treatment with HgO(4 equiv.) and $BF_3 \cdot Et_2O$(2.5 equiv.) in aqueous THF.$^{4)}$ Reduction of ketone 6 with $Zn(BH_4)_2$ in THF$^{5)}$ at -78 °C, and then treatment of 1 mol dm^{-3} sulfuric acid afforded a mixture of 1 and 2 (9:1 ratio) in 56% yield, bp 120 °C/35 mmHg (Kugelrohr). 1 was isolated by preparative gas chromatography, $[\alpha]_D^{21}$ +74.6°(c 1.02 Et_2O), lit$^{2a)}$$[\alpha]_D^{21}$ +78.8° (c 0.5 Et_2O),$^{2b)}$$[\alpha]_D^{25}$ +96.6°(c 0.98

Et_2O),[2c)] $[\alpha]_D^{21}$ +74.6°(c 1.06 Et_2O). The ^1H-NMR spectrum of the synthetic 1 completely coincided with that of the natural one.



Reagents: a) baker's yeast; b) n-BuLi, $BrCH_2CH_2CH_2\text{-}\underset{O\ \ O}{C}\text{-}CH_3$; c) HgO, $BF_3 \cdot Et_2O$, THF, H_2O; d) $Zn(BH_4)_2$, THF; e) H_2SO_4



Scheme 1.

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