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# (R)-S-Benzyl Thioglycerate, a New $C_3$ Bifunctional Chiral Material Obtained in Fermenting Baker's Yeast from Benzyl Mercaptan

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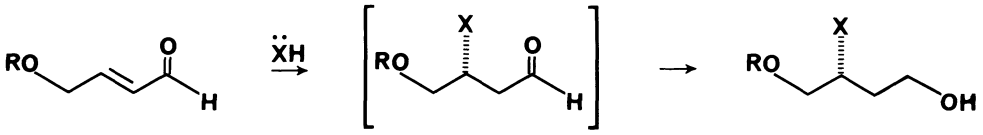
Baker's yeast fermenting on D-glucose, produces from benzyl mercaptan (R)-S-benzyl-thioglycerate, converted into (S)-2,2-dimethyl-1,3-dioxolane-4-methanol of 98.6-99% ee.

The capacity of baker's yeast to catalyze transformations of unnatural substrates other than reduction of products containing carbonyl and (carbonyl activated) double bonds, has been recognized for a long time and is being exploited in preparative organic chemistry.[1] Among baker's yeast ability, the activity of enzymes of the group of Lyases has been encountered, and we have recently reported on the addition of water (XH= $H_2O$) onto α,β -unsaturated aldehydes 1 and 2.[2] In this context, saturated alcohols 3 and 4 of high enantiomeric purity were obtained, as the result of the reduction of the intermediate β-hydroxy aldehyde. Whereas this reaction seemed to be restricted to aldehydes like 1 and 2,[3] no attempt was made on the same substrates with other nucleophiles.

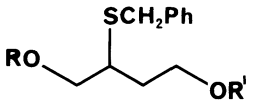



1 R = $CH_2Ph$
2 R = COPh

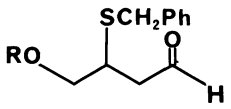
3 R = $CH_2Ph$
4 R = COPh

Therefore we have investigated the possibility of adding benzyl mercaptan to the above mentioned aldehydes, but as a result of a rapid chemical addition followed by reduction, only compounds 5 and 6 deprived of optical rotation were obtained when aldehydes 1 and 2 were incubated in the presence of benzyl mercaptan in

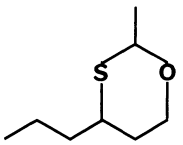
fermenting baker's yeast. However, when aldehydes 7 and 8 were reduced in fermenting yeast at low conversions, optically active 5 and 6 were obtained, following (partial) kinetic resolution. The acetyl derivatives 9 and 10 showed $[\alpha]_D^{20}$ + 22° and +13.5° (c 1, MeOH), respectively. $^1$H NMR experiments on product 9 in the presence of shift reagents and comparison with racemic material showed the presence of 70-75% of a single enantiomer. Determination of optical purity and absolute configuration of these materials requires transformation into known compounds. The conversion of 5 and 6 obtained in baker's yeast reduction of 7 and 8 into 2-methyl-4-propyl-1,3-oxathiane 11 of known absolute configuration is in progress.[4)]




5 R = $CH_2Ph$ R' = H
6 R = COPh R' = H
9 R = $CH_2Ph$ R' = OAc
10 R = COPh R' = OAc




7 R = $CH_2Ph$
8 R = COPh

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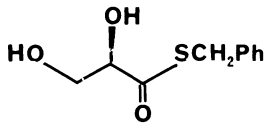
Following those experiments, we became aware of the formation of another product, whose structure, absolute configuration and optical purity, was assigned from spectral evidence and correlation with compounds of known properties. Thus, (R)-S-benzylthioglycerate 12, obtained simply by incubation of $PhCH_2SH$ and baker's yeast in the presence of glucose[5)] $[\alpha]_D^{20}$+69.5 (c 1, MeOH) was transformed into the ketal 13 from which, after LAH reduction, isopropylidene glycerol 14 of (S) absolute configuration was obtained. This was proved to be of 98.6-99% ee from $^1$H NMR and GLC studies of the corresponding esters with (+)MTPA. The obtainment of (R)-13 with an ee which is intermediate between the 99.4% of (S)-13 from D-mannitol and the 94.4% of (R)-13 from L-serine[6)] is significant from a preparative point of view, since it is almost exclusively based on an extractive process from a natural source.

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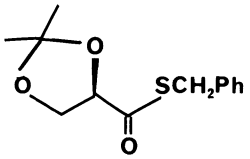


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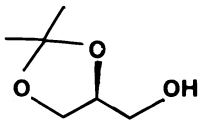


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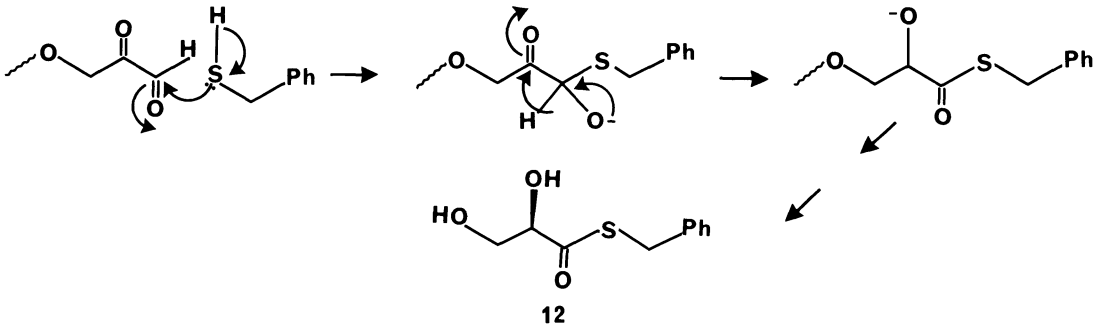
Furthermore, product 12 is a bifunctional starting material, seemingly convertible into (R)-13 by simple manipulation of protective groups. About the origin of the glyceric acid derivative thus obtained, this might arise from thiolysis of an activated ester in the glycolytic pathway from glucose to pyruvate (1,3-diphosphoglycerate for instance),[7] or from a glyoxalase I mediated incorporation of benzyl mercaptan into a hydroxypyruvaldehyde equivalent.[7,8] In fact hydroxypyruvaldehyde is a good substrate in the reaction catalyzed by glyoxalase I from yeast, with glutathione (GSH). On the other hand thioesters so obtained from thiols other than GSH are not further transformed (hydrolyzed).[9] The obtainment of 12 according to the following scheme would then be in agreement with those observations.

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Formation of 12 through pathways observed in the generation of other naturally occuring S-thioesters can also be considered.[10] Results on further investigation to establish the origin of the product observed, will be reported in due course.

References

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3) G. Fronza, C. Fuganti, P. Grasselli, G. Poli, and S. Servi, Biocatalysis, in press.
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5) Conditions of fermentation: in a open jar 20 L of water at 35 °C were mixed with 1.5 kg of commercially available baker's yeast (Distillerie Italiane) and 0.5 kg of anhydrous D-glucose. When the fermentation starts 20 g of benzyl mercaptan diluted in 20 mL of EtOH were added dropwise and the fermentation mixture left under vigorous stirring at 25 °C for 18 h. 2 L of ethyl acetate were added and the organic phase was decanted and filtered over a pad of Celite. The extraction procedure was repeated three times. The organic

phase, dried over $Na_2SO_4$, concentrated in vacuum and purified on silica gel column chromatography gave first 14 g of unreacted benzyl mercaptan and then 1.6 g of pure 12. Although no product was formed in the absence of glucose, we were not able to find a relationship between amount of glucose and yield of 12.

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