CHEMISTRY LETTERS, pp. 1191-1192, 1988.

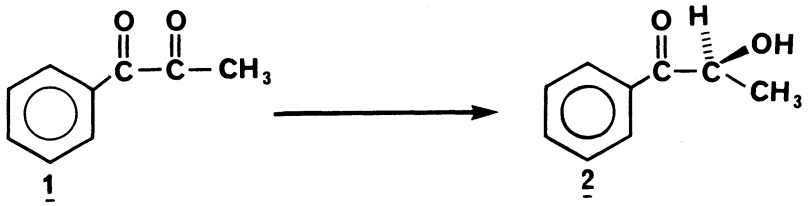
Baker's Yeast Reduction of 1,2-Diketones. Preparation of Pure (S)-(-)-2-Hydroxy-1-phenyl-1-propanone

Robert CHÊNEVERT* and Sonia THIBOUTOT
Département de Chimie, Faculté des Sciences et de Génie,
Université Laval, Québec (Québec), Canada G1K 7P4

1,2-Diketones are readily reduced by fermenting baker's yeast but the reactions proceed with little selectivity. One notable exception is the reduction of 1-phenyl-1,2-propanedione which affords pure (S)-(-)-2-hydroxy-1-phenyl-1-propanone in good yield.

Asymmetric reduction of ketones by microorganisms is a useful preparative method to obtain chiral alcohols.[1] Baker's yeast is the most frequently used microorganism for this purpose. Reduction of β-ketoesters and β-diketones by baker's yeast is well documented and provides useful chiral building blocks for organic synthesis.[2] We herein describe a study of the reduction of 1,2-diketones by baker's yeast.

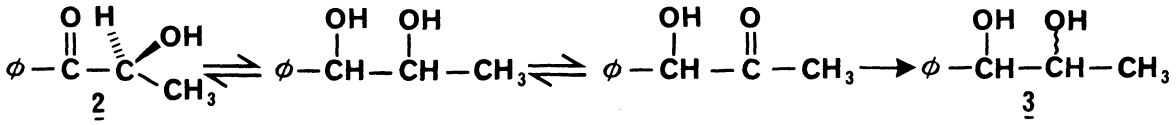
The yeast mediated reductions were performed according to the general procedure described by Seebach et al.[2a] with the following modification: the products were extracted from the fermentation mixture by ethyl acetate. Commercially available 1-phenyl-1,2-propanedione 1 is a good substrate for yeast[3] mediated reduction and by this method pure (S)-(-)-2-hydroxy-1-phenyl-1-propanone 2 was prepared in 80% yield after purification by column chromatography. The reaction is highly regio and enantioselective provided the medium is a phosphate buffer at pH 5. The absolute configuration and optical purity (> 95%) were determined by comparison of the measured optical rotation ($[\alpha]_D$ -84.9°, c 2.0, $CHCl_3$) with the literature value.[4d]



1 2

The enantiomeric composition was further confirmed by NMR analysis using $Eu(hfc)_3$ as a chiral shift reagent. The racemic sample of compound 2 required for this NMR study was prepared by double reduction of dione 1 by sodium borohydride, followed by selective oxidation of the benzylic position with pyridinium dichromate. It should be noted that the bioreduction performed at higher pH gave a mixture of compound 2 and 1-phenyl-1,2-propanediol 3. The most probable explanation for this reaction involves the formation of an enediol followed by further bioreduction

to the diol 3. Compound 2 is also slowly racemized in basic aqueous solution.



Several methods for the synthesis of compound 2 have been recently developed[4] and the above bioreduction route can be favorably compared to other syntheses of this chiral synthon. Chiral α-hydroxy carbonyl compounds are important reagents in asymmetric synthesis.[4d]

In general, 1,2-diketones are good substrates for baker's yeast but the selectivity of the reduction is low. The reduction of benzil gave racemic benzoin in 40% yield. 1,2-Cyclohexanedione was reduced to racemic trans-1,2-cyclohexanediol in 65% yield after recrystallization. Reduction of 2,3-pentanedione gave a mixture of 3-hydroxy-2-pentanone (51%), 2-hydroxy-3-pentanone (36%) and 2,3-pentanediol (13%) in 92% yield; the products are optically inactive. 2,3-Hexanedione gave similar results. (±)-Camphorquinone, (-)-camphorquinone and (+)-camphorquinone were treated with baker's yeast and the composition of the reduction products was determined by NMR analysis.[5] The reduction is not enantioselective but shows regioselectivity. For instance, reduction of (+)-camphorquinone yielded 3-hydroxycamphor (61% exo, 36% endo) as the major product and 2-hydroxy epicamphor (3% exo, 0% endo) as the minor product.

In conclusion, fermenting baker's yeast reduces 1,2-diketones usually with little selectivity. One remarkable exception is the reduction of 1-phenyl-1,2-propanedione to yield pure (S)-(-)-2-hydroxy-1-phenyl-1-propanone, and the reduction of 1,2-diketones by baker's yeast should not be discarded as an easy route to the preparation of other chiral synthons derived from 1,2-diketones. Finally, the reaction medium should be chosen in order to minimize enolization of α-hydroxy carbonyl product.

This work was supported by research grants from the Natural Sciences and Engineering Research Council of Canada and by the Ministère de l'éducation du Québec.

References

1) C.J. Sih and C.S. Chen, Angew. Chem., Int. Ed. Engl., 23, 570 (1984).
2) a) D. Seebach, M.A. Sutter, R.H. Weber, and M.F. Zuger, Org. Synth., 63, 1 (1984); b) S. Tsuboi, E. Nishiyama, H. Furutani, M. Utaka, and A. Takeda, J. Org. Chem., 52, 1359 (1987); c) W. Brooks, P.G. Grothaus, and W.L. Irwin, ibid., 47, 2820 (1982).
3) Saccharomyces cerevisiae, type I, purchased from Sigma Chemical Co.
4) a) D. Enders, H. Lotter, N. Maigrot, J.P. Mazaleyrat, and Z. Welvart, Nouv. J. Chim., 8, 747 (1984); b) N. Maigrot, J.P. Mazaleyrat, and Z. Welvart, J. Org. Chem., 50, 3916 (1985); c) F.A. Davis and A.C. Sheppard, ibid., 52, 954 (1987); d) F.A. Davis and M.S. Haque, ibid., 51, 4083 (1986); e) H. Ohta, M. Ikemoto, M. II, Y. Okamoto, and G. Tsuchihashi, Chem. Lett., 1986, 1169; H. Ohta, H. Yamada, and G. Tsuchihashi, ibid., 1987, 2325.
5) A. Ohno, T. Goto, J. Nakai, and S. Oka, Bull. Chem. Soc. Jpn., 54, 3478 (1981).

(Received April 1, 1988)