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Kinetic Resolution of 2-Formyl-1,1'-binaphthyls by Bakers'-Yeast Reduction of the Formyl Function

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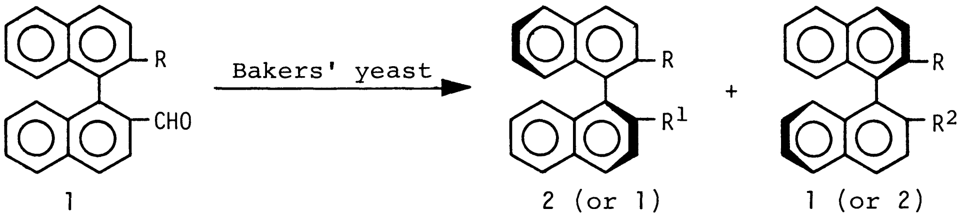
Bakers'-yeast reduction of 2-formyl-1,1'-binaphthyls gave the corresponding optically active 2-hydroxymethyl-1,1'-binaphthyls with the enantiomeric excess reaching up to 70% at 39% conversion in the case of 2-formyl-2'-methoxy-1,1'-binaphthyl.

The use of bakers' yeast as "asymmetric reducing agent" has been well documented.[1] Although many optically active alcohols have been prepared by the reduction of various carbonyl compounds, attention has been centered mostly on the enantio-face differentiation to create C-centro-chirality:[2] To our knowledge, discrimination of axial chirality of biaryls by bakers' yeast has been unprecedented.[3] Herein, we wish to report the obtention of optically active 2-hydroxymethyl-1,1'-binaphthyls via kinetic resolution of 2-formyl-1,1'-binaphthyls by bakers'-yeast reduction of the formyl function (Scheme 1 and Table 1).

In a typical run, a mixture of dry yeast[4] (75 g) and sucrose (150 g) in 1 l of water was stirred mechanically for 1.5 h at 37 °C.[5] To the well stirred, fermenting bakers' yeast was added dropwise a solution of 1.00 g (3.21 mmol) of (±)-2-formyl-2'-methoxy-1,1'-binaphthyl (**1a**) in ethanol (100 ml), and the stirring was continued for 12 h at 37 °C. The reaction was terminated by adding acetone (1 l),



Scheme 1.

Table 1. Bakers'-Yeast Reduction of 2-Formyl-1,1'-binaphthyls

Binaph-CHO (1)	Conversion/% (by HPLC)	Binaph-CH_2OH (2)	R^1	R^2	ee/%
1a; R = OCH_3	39	(S)-**2a**[6]	CH_2OH	CHO	70
1b; R = CH_3	35	(R)-**2b**[7]	CH_2OH	CHO	65
1c; R = H	70	(S)-**2c**[8]	CHO	CH_2OH	10

the mixture was filtered, and the solids were washed with ethanol (500 ml). The combined filtrates were reduced to ca. 300-ml volume in vacuo, and extracted with ethyl acetate. After the usual workup, silica-gel column chromatography eluting with hexane-ethyl acetate (10/1) gave 0.38 g of (S)-(+)-**2a**$^{6)}$ (38% yield based on (±)-**1a**) and 0.55 g of (R)-**1a** (55% yield). The enantiomeric composition of the (S)-**2a** was determined by HPLC equipped with Pirkle type 1-A column (3% i-PrOH-Hexane).

Similar reaction of (±)-**1b** and (±)-**1c** gave (R)-(-)-**2b**$^{7)}$ and (S)-(-)-**2c**,$^{8)}$ respectively, the absolute configurations of which were determined by chemically correlating to axially chiral binaphthyls of known configurations. It should be noted that both diastereo- and enantio-face selection regarding to the formyl function determine the enantiomeric bias of the product alcohol. Although the stereochemical course of the reduction of **1** by bakers' yeast is not clear at present, it is interesting that the helicity of the binaphthyl residue of the prevailing alcohol is reversed in case of **2c**, as compared to **2a** and **2b**.

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References

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2) Cf., For example, M. F. Züger, F. Giovannini, and D. Seebach, Angew. Chem., Int. Ed. Engl., 22, 1012 (1983); K. Nakamura, T. Miyai, K. Nozaki, K. Ushio, S. Oka, and A. Ohno, Tetrahedron Lett., 27, 3155 (1986).
3) Cf., Biochemical preparation of optically active 2,2'-dihydroxy-1,1'-binaphthyl: S. Miyano, K. Kawahara, Y. Inoue, and H. Hashimoto, Chem. Lett., 1987, 355, and literatures cited therein.
4) Oriental Yeast Co., Ltd.
5) The experimental conditions were not optimized; the amount of the yeast may be reduced to up to 1/3 of the weight without substantial effects.
6) $[\alpha]_D^{25}$ +32.1° (c 1.09, $CHCl_3$). The observed optical rotation indicates that the maximum rotation should be +45.9° for (S)-**2a**, while that calculated from the data by Wilson and Cram seemingly amounts to +38.6°.$^{9)}$
7) $[\alpha]_D^{25}$ -9.4° (c 1.92, MeOH). A small sample of the (-)-**2b** was converted to the diastereomeric mixture of (R)-MTPA esters, and the methoxy protons were differentiated on ^{1}H NMR in C_6D_6 by addition of $Eu(fod)_3$. The (-)-**2b** was correlated to (S)-2-methoxy-1,1'-binaphthyl-2'-carboxylic acid ((S)-3).$^{9)}$
8) $[\alpha]_D^{25}$ -3.8° (c 1.83, MeOH). The diastereomeric Mosher esters prepared from (R)-MTPA and partially active **2c** were not differentiated by ^{1}H NMR on addition of $Eu(fod)_3$, while (S)-3$^{10)}$ worked well as the chiral derivatizing agent for **2c**. The (-)-**2c** was correlated to (S)-2-hydroxy-1,1'-binaphthyl.$^{11)}$
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