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Asymmetric Hydrogenation of 2-Aryl-1-nitropropenes by Fermenting Bakers' Yeast

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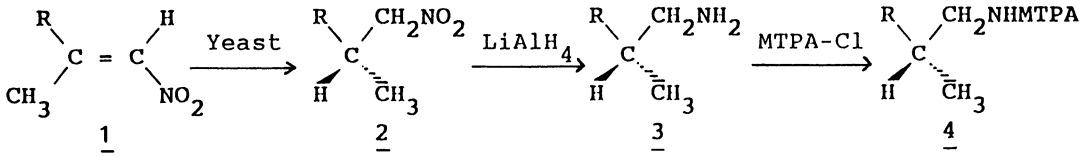
2-Aryl-1-nitropropenes were enantioselectively hydrogenated on C=C double bonds by incubation with fermenting bakers' yeast to afford optically active 2-aryl-1-nitropropanes.

Organic nitro compounds are very important synthetic intermediates, because they can be easily converted to amines, carbonyls, or hydrocabons.[1] Thus, optically active nitro compounds can be expected as useful chiral building blocks for asymmetric synthesis. While the enzymatic method has become increasingly important in organic synthesis,[2] this method has seldom be applied to nitro compounds, because of their antibiotic activities.[3] Recently, it has been demonstrated that some microorganisms are effective to asymmetric hydrogenation of nitroolefins.[4] Together with this, the fact that bakers' yeast has an ability to hydrogenate electron-deficient C=C double bonds conjugated with carbonyl groups[5] has encouraged us to apply the yeast to the hydrogenation of nitroolefins. The substrates should be a nitro olefin bearing a hydrogen atom at its α-position because the cabon bearing a nitro group in the resulting saturated nitro compound often suffers from racemization even under mild conditions.[4] Thus, we first selected 1-nitro-2-phenylpropene 1a as the model substrate.

A mixture of 10 g of dry yeast, 5 g of glucose and 50 ml of tap water was stirred at room temperature for 10 min. About 0.1 g of 1a was added and the stirring was continued at the same temperature for 2 d. The broth was extracted with ethyl acetate. Removal of the solvent gave a residue, which was purified by column chromatography on silica gel. Elution with hexane/diethyl ether afforded 1-nitro-2-phenylpropane 2a, as identified by IR and NMR.[6]

To determine the optical purity, 2a was reduced to amine 3a by $LiAlH_4$[7] followed by conversion to the R-(+)-MTPA amide 4a.[8] HPLC analysis of 4a proved its high optical purity (Table 1). The absolute configuration of 2a was determined by converting 2a to 2-phenylpropanal (5a), $[\alpha]_D^{25}$ -10° (c 2.0, CH_3OH), by $TiCl_3$ in alkaline medium.[9] Since the optical rotation of authentic (S)-5a has been reported to be +120° (c 2.6, CH_3OH),[10] it is concluded that 2a resulting from yeast reduction has (R) configuration. The low optical rotation of 5a is deduced to racemization of 5a in basic medium.

This reaction can be applied to other 2-aryl-1-nitropropenes which have a substituent on the aromatic rings. As listed in Table 1, p-halo- and p-nitroderivatives underwent smooth microbial reduction to give the corresponding saturated optically active nitro compounds (Table 1).



1 2 3 4

Table 1. Hydrogenation of 2-Aryl-1-nitropropenes by Bakers' Yeast

compound	R	Yield of 2/%	$[\alpha]_D^{a)}$	e.e./%
a	C_6H_5	50	+44.3	97.9
b	p-ClC_6H_4	48	+47.1	89.0
c	p-BrC_6H_4	57	+40.8	94.4
d	p-$NO_2C_6H_4$	50	+43.6	nd[b)]

a) Measured in $CHCl_3$ at room temperature (c 1.7-3.4).
b) Not determined.

The starting nitroolefins were prepared from 2-arylpropenes via acetoxynitration and subsequent deacetoxylation.[11] The E-configuration of 1 was confirmed from the long range coupling between methyl's and olefinic protons (1.48 Hz). It is not clear at present whether the fact that the optical purities of the products are lower than 100% depends on the slight contamination of the Z-isomer or not.

In any event, introduction of a chiral center by hydrogenation of nitroolefins is, to our knowledge, a new type of reduction mediated by bakers' yeast, and the investigation on substrate specificities are now under way.

References

1) N. Ono and A. Kaji, Yuki Gosei Kagaku Kyokai Shi, 38, 115 (1980).
2) "Enzymes in Organic Synthesis. Ciba Found. Symp. 111," ed by R. Porter and S. Clark, Pitman, London (1985); "Kousokinou to Seimitsu Yuhkigousei," ed by M. Ohno, C.M.C., Japan (1984).
3) O. Schales and H. G. Graebe, J. Am. Chem. Soc., 74, 4486 (1952).
4) K. Sakai, A. Nakazawa, K. Kondo, and H. Ohta, Agric. Biol. Chem., 49, 2331 (1985).
5) C. Fuganti and P. Grasselli, J. Chem. Soc., Chem. Commun., 1979, 995; T. Kitazume and N. Ishikawa, Chem. Lett., 1983, 237.
6) IR ν_{max}^{NaCl} cm^{-1} 2960, 2920, 1740, 1540, 1490, 1450, 1410, 1380, 1200, 1120, 1020, 770, 700; ^{1}H-NMR $\delta(CDCl_3)$ 1.35 (d, J=7.5 Hz, 3H), 3.55 (sext, J=7.5 Hz, 1H), 4.36 (d, J=7.5 Hz, 2H), 7.03-7.47 (m, 5H).
7) N. Kornblum and L. Fishbein, J. Am. Chem. Soc., 77, 6266 (1955).
8) J. A. Dale, D. L. Dull, and H. S. Mosher, J. Org. Chem., 34, 2543 (1969).
9) J. E. McMurry and J. Melton, J. Org. Chem., 38, 4367 (1973).
10) T. D. Inch, R. V. Ley, and P. Pich, J. Chem. Soc., C, 1968, 1963.
11) F. G. Bordwell and E. W. Garbisch Jr., J. Org. Chem., 27, 2322 (1962); F. G. Bordwell and J. A. Hautala, ibid., 43, 3116 (1979).

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