SYNTHESIS OF CHIRAL LACTONES AND TRIOLS FROM α-ACETYL-γ-BUTYROLACTONES BY USE OF BAKER'S YEAST

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Abstract ——Chiral hydroxyethyllactones prepared from α-acetyl-γ-butyrolactones by fermenting with baker's yeast are reduced to give chiral triols.

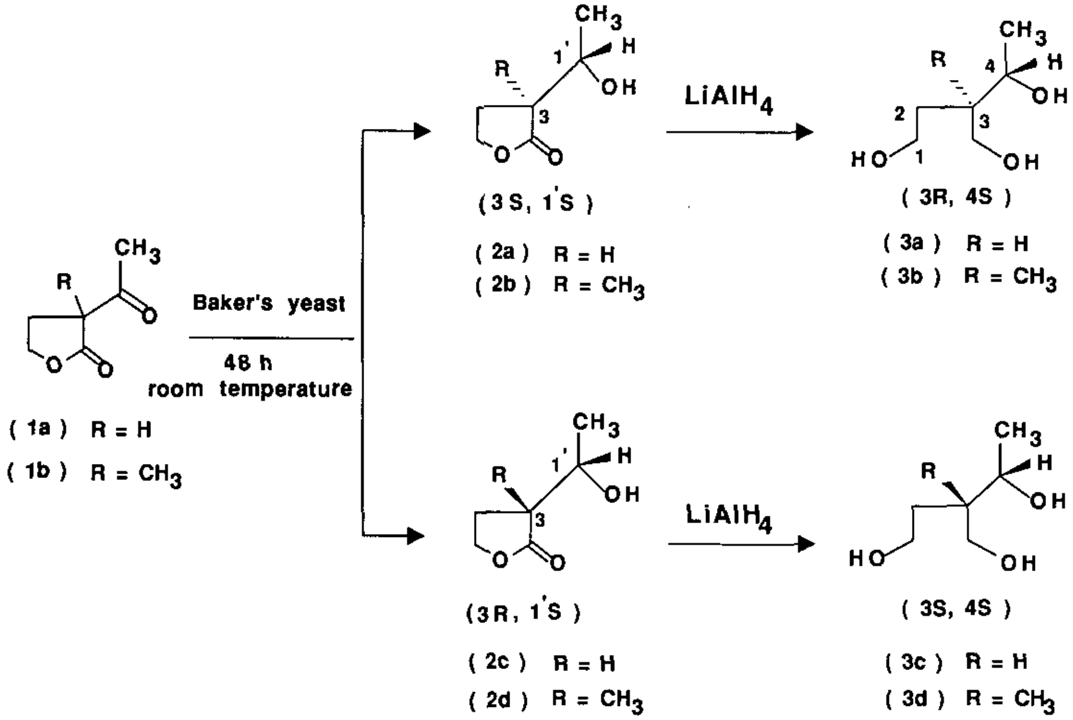
The utilization of emzymes for the synthesis of chiral compounds has been becoming a powerful tool in synthetic organic chemisrty. Asymmetric reduction of carbonyl compounds with baker's yeast (*Saccharomyces cerevisiae*) gave chiral alcohols which have been employed as chiral building blocks for the synthesis of optically active materials.[1] In this paper, we describe a synthesis of chiral lactones and triols, which could be excellent chiral synthons[1,2] for the synthesis of chiral compounds, by reduction of acetyl butyrolactones with baker's yeast.

As shown at Table I, α-acetyl-γ-butyrolactone (1a) and α-acetyl-α-methyl-γ-butyrolactone (1b) were treated with baker's yeast for 48 h at room temperature to afford 3*S*- and 3*R*-(1'*S*-hydroxyethyl)-γ-butyrolactones (2a and 2c), and 3*S*- and 3*R*-methyl-3*S*- and 3*R*-(1'*S*-hydroxyethyl)-γ-butyrolactones (2b and 2d), respectively. The absolute stereochemistry at $C_{1'}$ of 2a-2d was determined as *S*-configuration by Mosher's,[3] modified Mosher's[4] and Horeau methods.[5]

The corresponding chiral triols, (3*R*, 4*S*)- and (3*S*, 4*S*)-3-hydroxymethyl-1,4-pentanediols (3a, 3c), and (3*R*, 4*S*)- and (3*S*, 4*S*)-3-hydroxymethyl-3-methyl-1,4-pentanediols (3b, 3d) were prepared by $LiAlH_4$ reduction of 2a-2d, respectively.

Dedicated to Dr. Masatomo Hamana on the occasion of his 75th birthday.

Table I. Synthesis of Triols (3a-3d)



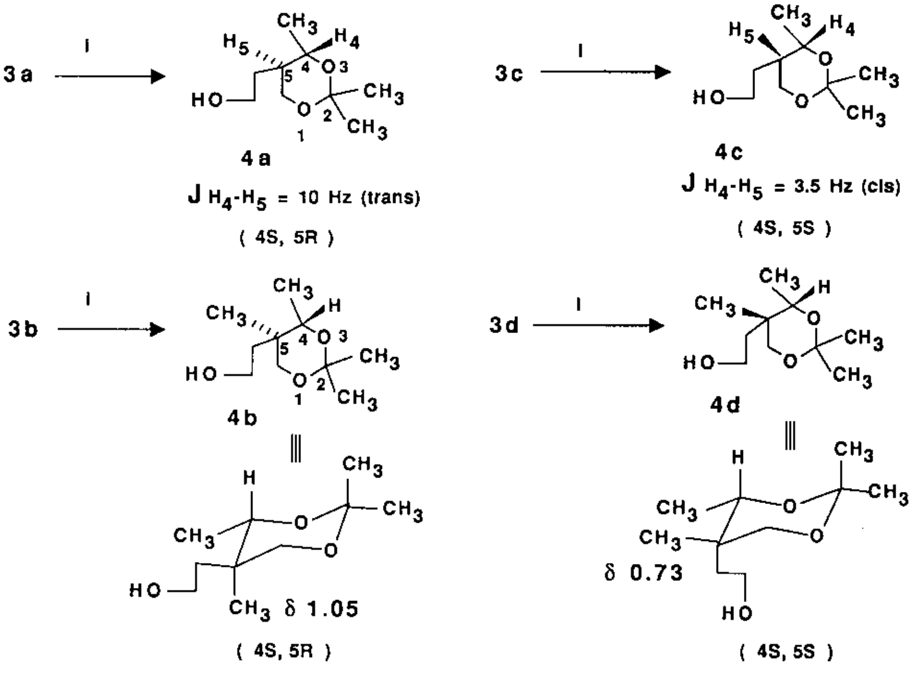
sub-strate	Yields of 2 (%)		$[\alpha]_D$ [a] of 2 (in $CHCl_3$)	%ee [b] of 2	Yields of 3 (%)		$[\alpha]_D$ [a] of 3 (in $CHCl_3$)
1a	2a	40	+ 36.9° (c= 1.3)	84	3a	76	- 6.1° (c= 1.4)
	2c	40	+ 2.9° (c= 1.0)	90	3c	76	+4.4° (c= 1.3)
1b	2b	36	+ 22.3° (c= 1.6)	80	3b	84	+16.4° (c= 1.1)
	2d	40	+ 22.5° (c= 1.6)	90	3d	72	+3.1° (c= 1.5)

a) Temperature: 21-26°. b) Calculated on the ^{1}H-nmr analysis of their (R)- or (S)-MTPA esters.(see ref. 2)

The absolute configuration at C_3 of 3a and 3c was determined by the ^{1}H-nmr spectral analysis of the 1,3-dioxanes (4a and 4c) prepared from 3a and 3c. In the ^{1}H-nmr spectrum of 4a, the coupling constant between H_4 and H_5 was 10 Hz (*trans*), while that of the isomer 4c was 3.5 Hz (*cis*). Thus, the stereochemistry at C_5 of 4a was concluded to be *R*-configuration, and that of 4c was *S*-configuration. Therefore, the absolute stereostructures of 3a and 3c were confirmed as represented in Table I.

The elucidation of the absolute configuration at C_3 of 3b and 3d was achieved by the C_5-methyl resonance[6] (in ^{1}H-nmr spectrum) of 1,3-dioxanes (4b and 4d) .

The C_5-methyl resonance in 4b was observed at δ 1.05 ppm (axial), while that of 4d was at δ 0.73 ppm (equatorial), then the absolute configuration of each C_5 at 4b and 4d was determined as *R* and *S*, respectively (Scheme 1). Consequently, the stereochemistry of 3b and 3d was established as shown in Table I.



I = 2,2-dimethoxypropane / pyridium p-toluenesulfonate
at room temperature for 5 h

Scheme 1

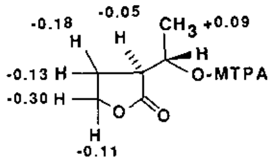
Thus, optically active 3-(1'-hydroxyethyl)-γ-butyrolactones (2a-2d), and 3-hydroxymethyl-1,4-

propanediols (3a-3d) were prepared from α-acetyl-γ-butyrolactones (1a and 1b) by use of baker's yeast.

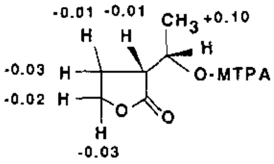
Those lactones and triols are useful for the synthesis of chiral compounds.

REFERENCES AND NOTE

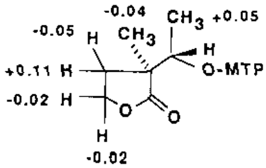
1. R. Csuk and B. I. Glanzer, *Chem. Rev.*,1991, 91, 49; J. B. Jones, *Tetrahedron*, 1986, 42, 3351 and references cited therein.
2. For example, see review: S. Takano and K. Ogasawara, *J. Syn. Org. Chem. Jpn.*, 1989, 47, 813.
3. J. A. Dale , D. L. Dull and H. S. Mosher, *J. Org. Chem.*, 1969, 34, 2543 ; J. A. Dale and H.S. Mosher, *J. Am. Chem. Soc.*, 1973, 95, 512.
4. The Δδ values (ppm) obtained for (*S*) and (*R*)-MTPA esters of 2a-2d (measured by a 400 MHz spectrometer). Δδ(ppm) = δ[(R)-MTPA derivative] – δ[(S)-MTPA derivative]



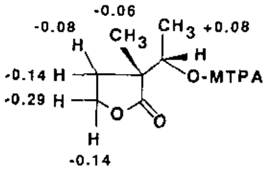
MTPA ester of 2a



MTPA ester of 2c



MTPA ester of 2b



MTPA ester of 2d

See: S. Takano, M. Takahashi, M. Yanase, Y. Sekiguchi, Y. Iwabuchi, and K. Ogasawara, *Chemistry Lett.*, 1988, 1827; T. Kusumi, Y. Fujita, I. Ohtani, and H. Kakisawa, *Tetrahedron Lett.*, 1991, 32, 2923; M. Natsume, K. Yasui, S. Kondo, and S. Marumo, *Tetrahedron Lett.*, 1991, 32, 3087.

5. By esterification of 2a-2d with 2-phenylbutanoic acid anhydride, only (-)-2-phenylbutanoic acid was recovered, thus 1'*S*-configuration was determined. See: A. Horeau, ' Stereochemistry Fundamental and Methods ', Vol. 3, ed. by H. B. Kagan, Georg Thieme Publishers, Stuttgart, 1977, p. 52.
6. A. W. Bogatskij, J. J. Samitow, A. I. Gren, and S. G. Sobolewa, *Tetrahedron*, 1975, 31, 489; M. Anteunis and R. Camerlynck, *Tetrahedron*, 1975, 31, 1841.

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