

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

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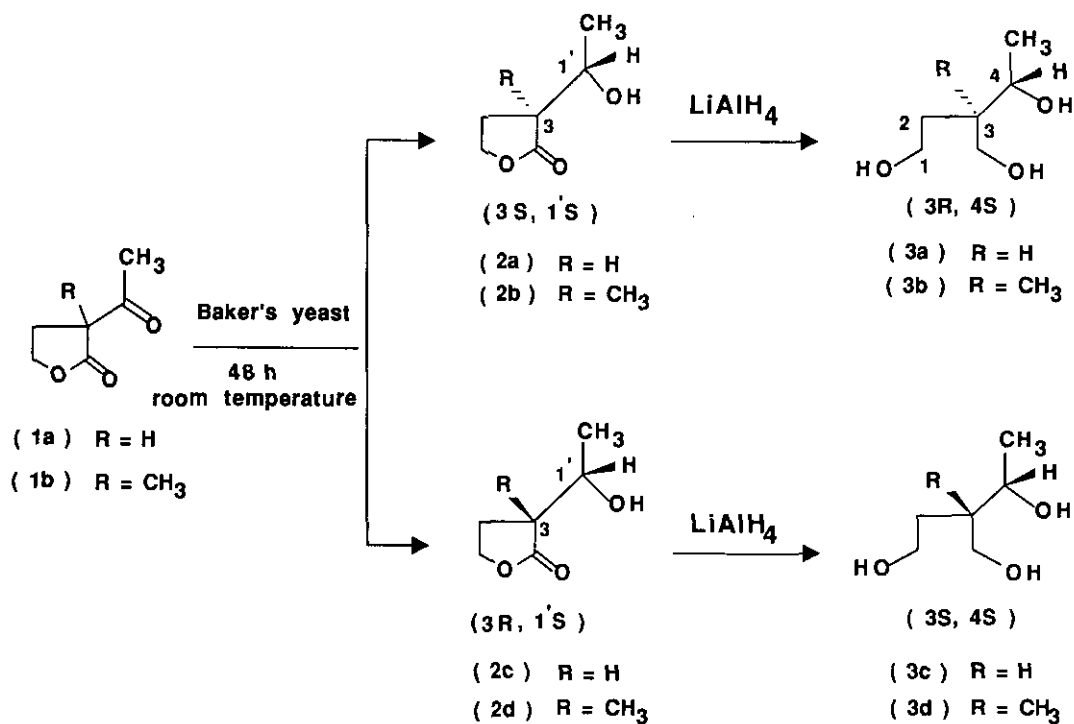
Abstract — Chiral hydroxyethyl lactones prepared from
 α -acetyl- γ -butyrolactones by fermenting with baker's yeast
are reduced to give chiral triols.

The utilization of enzymes for the synthesis of chiral compounds has been becoming a powerful tool in synthetic organic chemistry. 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 C₁ of 2a-2d was determined as *S*-configuration by Mosher's,³ modified Mosher's⁴ 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 LiAlH₄ reduction of 2a-2d, respectively.

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

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



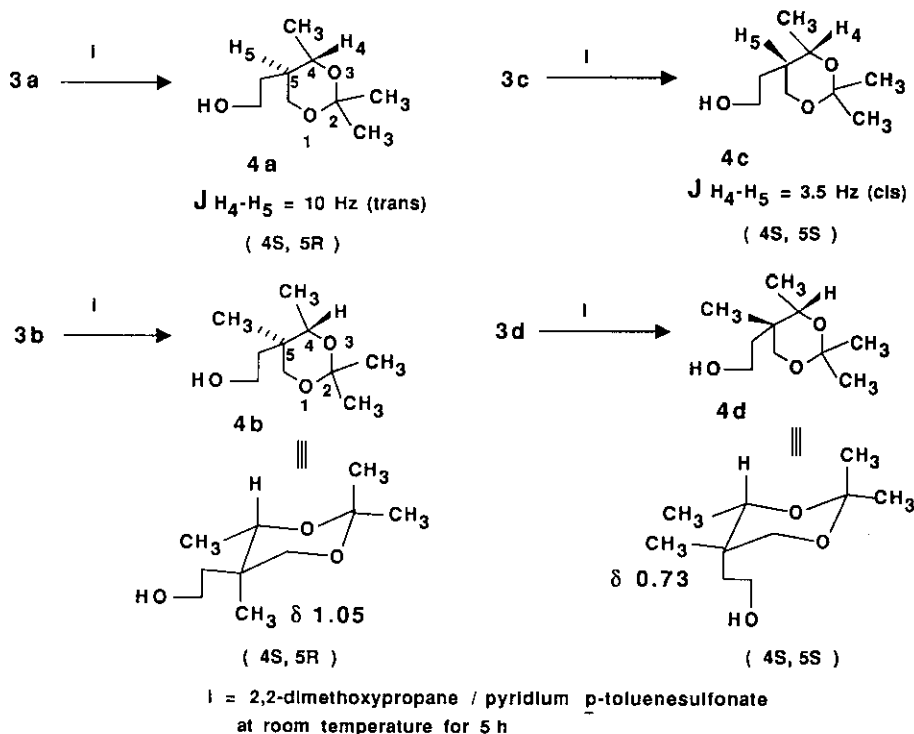
sub- strate	Yields of 2 (%)		$[\alpha]_D^{a)}$ of 2 (in CHCl ₃)	%ee ^{b)} of 2	Yields of 3 (%)		$[\alpha]_D^{a)}$ of 3 (in CHCl ₃)
1 a	2 a	40	+ 36.9° (c= 1.3)	84	3 a	76	- 6.1° (c= 1.4)
	2 c	40	+ 2.9° (c= 1.0)	90	3 c	76	+4.4° (c= 1.3)
1 b	2 b	36	+ 22.3° (c= 1.6)	80	3 b	84	+16.4° (c= 1.1)
	2 d	40	+ 22.5°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

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

The absolute configuration at C₃ of **3a** and **3c** was determined by the ¹H-nmr spectral analysis of the 1,3-dioxanes (**4a** and **4c**) prepared from **3a** and **3c**. In the ¹H-nmr spectrum of **4a**, the coupling constant between H₄ and H₅ was 10 Hz (*trans*), while that of the isomer **4c** was 3.5 Hz (*cis*). Thus, the stereochemistry at C₅ 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 C₃ of **3b** and **3d** was achieved by the C₅-methyl resonance⁶ (in ¹H-nmr spectrum) of 1,3-dioxanes (**4b** and **4d**).

The C₅-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 C₅ 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.



Scheme 1

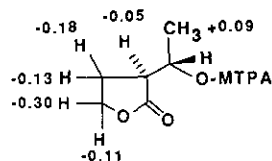
Thus, optically active 3-(1'-hydroxyethyl)- γ -butyrolactones (**2a-2d**), and 3-hydroxymethyl-1,4-

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

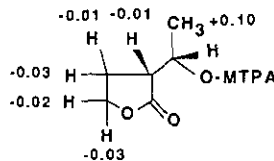
Those lactones and triols are useful for the synthesis of chiral compounds.

REFERENCES AND NOTE

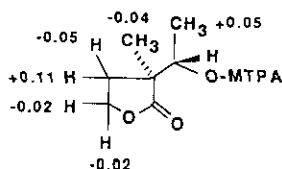
1. R. Csuk and B. I. Glanzer, *Chem. Rev.*, 1991, **91**, 49; J. B. Jones, *Tetrahedron*, 1986, **42**, 3351 and references cited therein.
2. For example, see review: S. Takano and K. Ogasawara, *J. Syn. Org. Chem. Jpn.*, 1989, **47**, 813.
3. J. A. Dale, D. L. Dull and H. S. Mosher, *J. Org. Chem.*,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



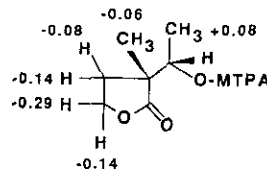
MTPA ester of 2a



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. Samltow, A. I. Gren, and S. G. Sobolewa, *Tetrahedron*, 1975, **31**, 489; M. Anteunis and R. Camerlynck, *Tetrahedron*, 1975, **31**, 1841.

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