Pergamon

Tetrahedron: *Asymmetry* 10 (1999) 403–404

TETRAHEDRON:
ASYMMETRY

Enantioselective synthesis of (+)-3-oxabicyclo[3.2.0]hept-6-en-2-one

Marie-Edith Gourdel-Martin, Corinne Comoy † and François Huet *

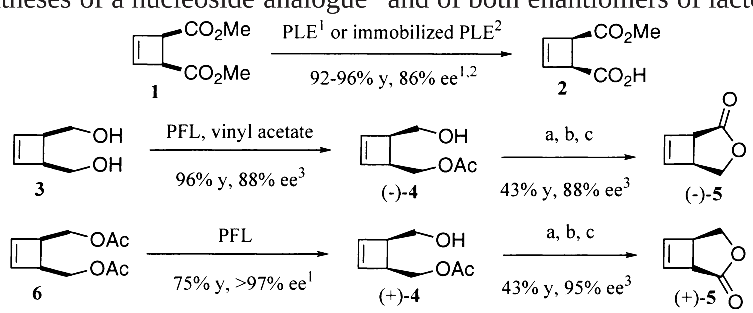
Laboratoire de Synthèse Organique, UPRES A CNRS 6011, Faculté des Sciences, Université du Maine, Avenue Olivier Messiaen, F-72085 Le Mans Cedex 9, France

Received 5 November 1998; accepted 13 January 1999

Abstract

The title compound was obtained in 99.3% ee by enzymatic oxidation of *cis*-2-cyclobutene-1,4-bis(hydroxymethyl) in the presence of horse liver alcohol dehydrogenase. Another route was through desymmetrisation of *cis*-cyclobut-3-ene-1,2-dicarboxylic anhydride with (−)-pantolactone.

Several syntheses of cyclobutene compounds **2** and **4** in an enantiomerically enriched form have been described over the last few years. They involved either pig liver esterase (PLE) catalysed asymmetric hydrolysis of diester **1**[1,2] or enzymatic reactions with diol **3** or the corresponding diacetate **6**, which were carried out in the presence of lipase of *Pseudomonas fluorescens* (PFL).[1,3] These works led to interesting applications for syntheses of a nucleoside analogue[2] and of both enantiomers of lactone **5**.[3]



a: Jones reagent, b: MeOH, MeONa, c: HCl, H_2O

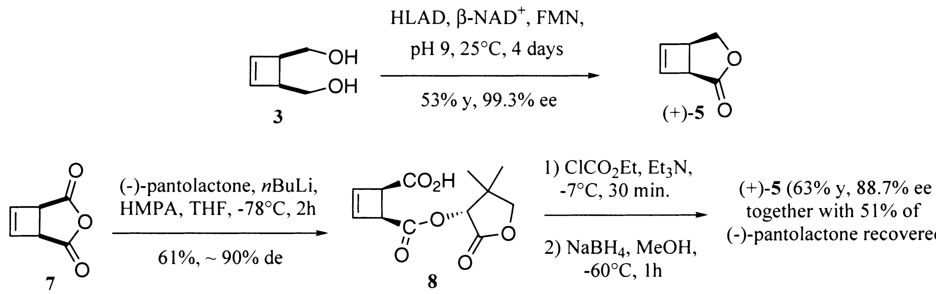
We recently used this lactone, in the racemic form, for the first synthesis of cyclobutene nucleosides unsubstituted at the vinylic position.[4] As we were interested in extending our results to the nonracemic

* Corresponding author. E-mail: fhuet@aviion.univ-lemans.fr

† Present address: Institut Nancéen de Chimie Moléculaire, Université H. Poincaré, Campus Scientifique V. Grignard, BP 239, 54506 Vandoeuvre lès Nancy, France.

0957-4166/99/$ - see front matter
PII: S0957-4166(99)00015-4

series, and despite the satisfying results already published, we envisaged other possibilities to prepare enantiomerically enriched **5**. We were pleased to obtain (+)-**5** in 99.3% ee[5] from diol **3** by horse liver alcohol dehydrogenase (HLAD) mediated oxidation.[6] We also submitted anhydride **7** to desymmetrisation[7] in the presence of (−)-pantolactone and thus prepared hemiester **8**, a potential precursor of both enantiomers of lactone **5**,[8] in fair diastereomeric excess.[9] Reaction of **8** with ethyl chloroformate provided the mixed anhydride. Its reduction gave (+)-**5** together with partial recovery of the chiral auxiliary. In addition, conversion to this isomer of **5** also indicated which was the predominant isomer of **8**.



This work shows new applications of enzymatic reactions with *meso* compounds and leads to alternative preparations of compounds which are interesting from the synthetic point of view.

References

1. Harvey, I.; Crout, H. G. *Tetrahedron: Asymmetry* **1993**, *4*, 807–812.
2. Jung, M. E.; Sledeski, A. W. *J. Chem. Soc., Chem. Commun*. **1993**, 589–591.
3. Binns, F.; Hayes, R.; Hodgetts, K. J.; Saengchantara, S. T.; Wallace, T. W.; Wallis, C. J. *Tetrahedron* **1996**, *52*, 3631–3658.
4. Gourdel-Martin, M.-E.; Huet, F. *J. Org. Chem*. **1997**, *62*, 2166–2172.
5. Enantiomeric excess of (+)-**5** was measured by chiral GPC (30 m Restek β-DEX-sm), $[\alpha]_D^{20}$ +428 ($CHCl_3$, c=1.25). The absolute configuration was deduced from results of Binns et al.[3] and references cited therein.
6. Jones, J. B.; Jakovac, I. J. *Org. Synth.* **1985**, *63*, 10–17.
7. Imado, H.; Ishizuka, T.; Kunieda, T. *Tetrahedron Lett*. **1995**, *36*, 931–934; Albers, T.; Biagini, S. C. G.; Hibbs, D. E.; Hursthouse, M. B.; Abdul Malik, K. M.; North, M.; Uriarte, E.; Zagotto, G. *Synthesis* **1996**, 393–398.
8. It is shown in a scheme of Binns et al.[3] that one enantiomer of the methyl hemiester can provide either of both enantiomers of **5**.
9. Diastereomeric excess of **8** was determined by ^{1}H NMR. Other chiral alcohols [(−)-menthol, (−)-8-phenyl-menthol and (+)-benzyl-mandelate] were tested and led to lower de.