Pergamon

Tetrahedron Letters 39 (1998) 5535–5536

TETRAHEDRON LETTERS

Desymmetrization of *meso*-1,3-Tetrols via Oxazaborolidine-Mediated Enantiotopic Group Selective Ring-Cleavage of Bisacetal Derivatives

Toshiro Harada,* Takayuki Egusa, and Akira Oku

Department of Chemistry Kyoto Institute of Technology, Matsugasaki, Sakyo-ku, Kyoto 606, Japan

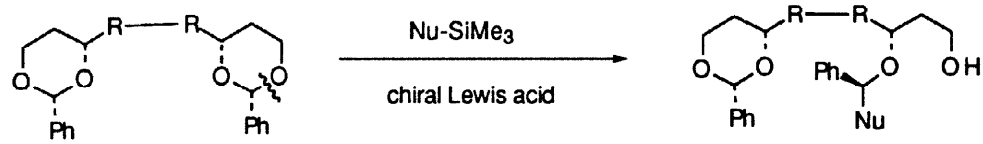
Received 27 April 1998; revised 19 May 1998; accepted 22 May 1998

Abstract: *Meso*-1,3,5,7-heptanetetrol and -1,3,6,8-octanetetrol were desymmetrized via enantiotopic group selective ring-cleavage reaction of their bisacetal derivatives using a chiral oxazaborolidine.

Keywords: acetals; asymmetric induction; cleavage reactions; polyols

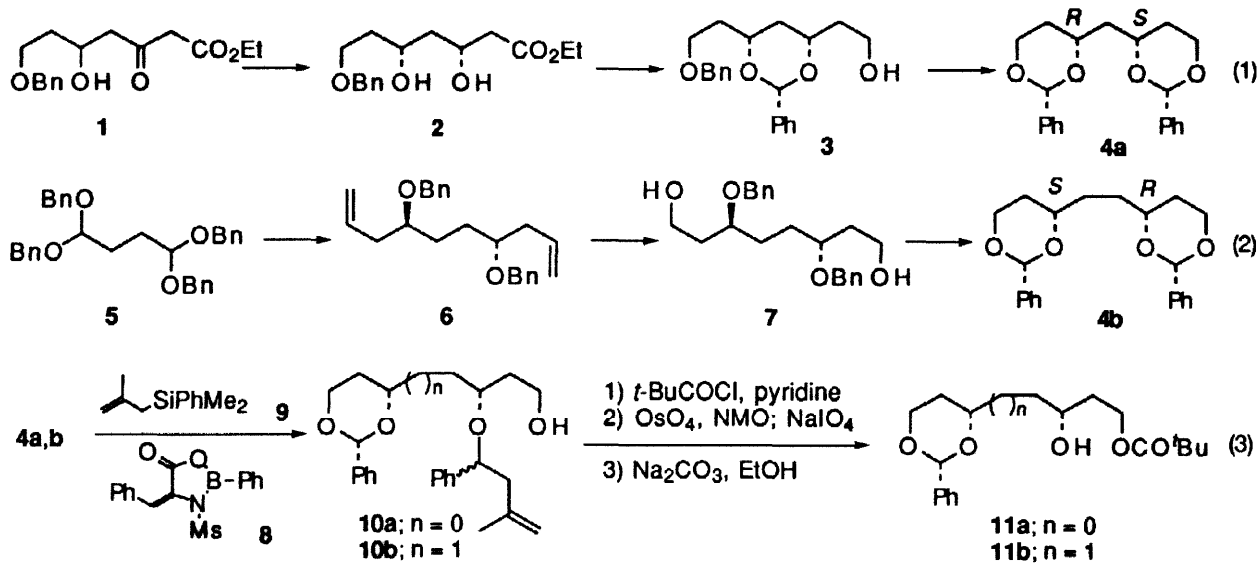
Two-direction chain extension and asymmetric desymmetrization of the resulting *meso* compound have recently emerged as an efficient strategy for the construction of multiple stereogenic centers [1,2]. The approach has been successfully employed in asymmetric syntheses of skipped and propionate-derived 1,3-polyols of potential σ-symmetry [2,3]. Although there is no precedent, enantiodifferentiating ring-cleavage of bisacetal derivatives is a straightforward method for desymmetrization of 1,3-polyols (Scheme 1). In the preceding paper, we reported an intermolecular differentiation of enantiomeric acetals through a chiral oxazaborolidine-mediated ring-cleavage reaction with a methallylsilane as a nucleophile [4]. Herein, we describe an application of the acetal-cleavage reaction to desymmetrization of *meso*-1,3-tetrol derivatives **4a,b**.

Scheme 1



For the synthesis of bisacetal **4a**, hydroxy ester **1** was reduced under chelation-controlled conditions (Et_2BOMe, $NaBH_4$) [5] to give *syn*-diol **2** in 90% yield (eq 1). Protection of the hydroxy groups ($PhCH(OMe)_2$, TsOH) and $LiAlH_4$ reduction transformed **2** into mono-acetal **3** (81%). Deprotection of **3** (H_2, Pd/C) followed by acetalization with benzaldehyde (TsOH, benzene, reflux) furnished a crystalline bisacetal **4a** (mp 91-92 °C) in 63% yield. Bisacetal **4b** was prepared starting from succinaldehyde derivative **5** (eq 2). 1,4-Asymmetric induction developed by Molander et al. [6] was successfully applied to the double allylation of **5** (allyltributyltin, TMSOTf), affording stereoselectively (*meso*:*dl* = 9:1) *meso* product **6** (mp 42-43 °C) in 75% yield. Oxidative cleavage (OsO_4, NMO, $NaIO_4$) and subsequent $NaBH_4$ reduction converted **6** into **7** (69%). After deprotection (H_2, Pd/C) and acetalization of the resulting tetrol with benzaldehyde, bisacetal **4b** (mp 103-103.5 °C) was

0040-4039/98/$19.00
PII: S0040-4039(98)01092-2



isolated in 44% yield.

Ring-cleavage of bisacetal **4a** was examined by using *N*-mesyloxazaborolidine **8** (1.0 equiv) as a chiral Lewis acid and methallylsilane **9** (1.5 equiv) as a nucleophile in anticipation of an enantiodifferentiating reaction on the (*S*)-acetal moiety (eq 3) [4]. When the reaction was carried out in CH_2Cl_2 at -50 °C for 12 h, the mono-cleavage product **10a** was obtained as a mixture of diastereomers in 94% yield together with a small amount of the corresponding bis-cleavage product (< 5%). After protection of the hydroxy group as a pivalate (84%), the 3-methyl-1-phenyl-3-butenyl group was removed in two steps (75%) to give *O*-benzylidene pivalate **11a**. Enantiomeric purity of **11a** was determined to be 88% ee based on the ^1H NMR analysis of the MTPA ester derivative. The absolute configuration of **11a**, established by the modified Mosher's method [7], was in accord with the anticipated reaction on the (*S*)-acetal moiety of **4a**.

Ring-cleavage of **4b** under similar conditions afforded the mono-cleavage product **10b** (82%) together with the bis-cleavage product (15%). Formation of the bis-cleavage product in relatively large amount suggested a higher ee of mono-cleavage product **10b** through the kinetic resolution in the second bond cleavage [8]. Indeed, after conversion into *O*-benzylidene pivalate **11b** (63% overall yield), the ^1H NMR analysis of the MTPA ester derivative established the high ee of 95%[1] as well as the absolute configuration.[2]

References

[1] Schreiber SL. Chem. Scr. 1987;27:563-566

[2] Magnuson SR. Tetrahedron 1995;51:2167-2213.

[3] Harada T, Kagamihara Y, Tanaka S, Oku A. J. Org. Chem. 1992;57:1637.

[4] Harada T, Egusa T, Kinugasa M, Oku A. Tetrahedron Lett. 1998;39: 5531-5534.

[5] Chen K-M, Gunderson KG, Hardtmann GE, Prasad K, Repic O, Shapiro MJ. Chem. Lett. 1987:1923-1926.

[6] Molander GA, Haar JPJr. J. Am. Chem. Soc. 1993;113:40-49.

[7] Ohtani I, Kusumi T, Kashman Y, Kakisawa H. J. Am. Chem. Soc. 1991;113:4092-4096.

[8] Schreiber SL, Schreiber TS, Smith DB. J. Am. Chem. Soc. 1987;109:1525-1529.

1. Ring-cleavage of **4b** using **8** (0.5 equiv) and **9** (0.75 equiv) at -50 °C for 8 h gave **10a** (87% ee) in 58% yield together with the recovery of **4b** (37%).

2. This work was supported partially by a Grant-in-Aid for Scientific Research on Priority Area (09231224) from the Ministry of Education, Science, and Culture, Japan.