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# Diastereoface Differentiating Peracid Oxidation of the Enol Ether Derived from Cyclohexanone and 2,4-Pentanediol: Preparation of Optically Pure 2-Hydroxycyclohexanone Acetal

**Takashi Sugimura,* Norio Nishiyama, Akira Tai,* and**

Faculty of Science, Himeji Institute of Technology, Kanaji, Kamigori, Ako-gun, Hyogo 678-12 Japan

**Tadao Hakushi**

Faculty of Engineering, Himeji Institute of Technology, 2167 Shosha, Himeji, Hyogo 671-22 Japan

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***Abstract:*** Diastereoface differentiating *m*-chloroperbenzoic acid oxidation of the chiral enol ether prepared from cyclohexanone and optically active 2,4-pentanediol proceeded from -72 to 39 °C to give a diastereomeric mixture of the corresponding 2-hydroxycyclohexanone acetal. The diastereomeric excess of the product reached almost 100 % at -72 °C.

Enol ether carrying optically active (2*R*,4*R*)-2,4-pentanediol (PD) moiety as a chiral auxiliary **1**, despite its acyclic structure of the auxiliary, has proved to be a good substrate for diastereoface differentiating Simmons-Smith cyclopropanations.[1] In this reaction, the hydroxyl group of PD moiety clearly plays a role in fixing the flexible auxiliary in the transition state by coordination to zinc. Similar stereocontrol and acceleration of the reaction is also expected for epoxidation with peracid of the same substrate by coordination between the hydroxyl group and peracid.[2] We herein report oxidation of **1** with *m*-chloroperbenzoic acid (MCPBA) and establish the differentiation between the diastereofaces of **1** under the control of the PD moiety.[3]

Oxidation of **1** with MCPBA (1.2 equiv.) in dichloromethane proceeded smoothly at reaction temperatures from -72 to 39 °C giving a mixture of the two diastereomers, **2** and **3** (70-80 % yield after chromatography). The products should be produced via the corresponding epoxide diastereomers as intermediates (Scheme 1).[4,5] The configuration of the major product **2** was determined to be 7*R* by chemical correlation with (2*S*)-(-)-2-hydroxycyclohexanone.[6] The product ratio was determined by capillary GLC analysis (PEG-20M, 50 m) after a part of the reaction mixture had been converted to the trimethylsilyl ethers with trimethylsilylimidazole. As shown in Table 1, the diastereomeric excess (d.e.) of the product increased with decreasing the reaction temperature and reached almost 100 % at -72 °C.

Contribution of the reaction conditions to the product ratio (**2**/**3**) was also studied. The addition of sodium bicarbonate as a acid scavenger and /or the use of the large excess amounts of MCPBA changed neither the product ratio nor the reaction rate.[7] This suggested that the reaction proceeded via the 1 to 1 complex of the reagent and the substrate, and hence the excess reagent and the acid of the side-product did not participate in the differentiation. Thus, the obtained product ratios are considered to be the differentiation ratios of the diasteroface of **1** by the coordinated reagent.[8]

Enantio differentiating α-hydroxylations of various prochiral ketones with chiral oxaziridines[9] or with chiral phase transfer catalysts[10] had been reported, but these process resulted in a synthetically acceptable e.e. only in a case of one particular ketone. The present study opens a secure way to convert prochiral ketones to optically pure α-hydroxyketones, where the carbonyl groups are protected as acetals. Oxidation of an alternative substrate having (3*S*,5*S*)-2,6-dimethyl-3,5-heptanediol instead of (2*R*,4*R*)-PD in **1** also proceeded smoothly and gave one diastereomer predominantly even at 0 °C.

Scheme 1.

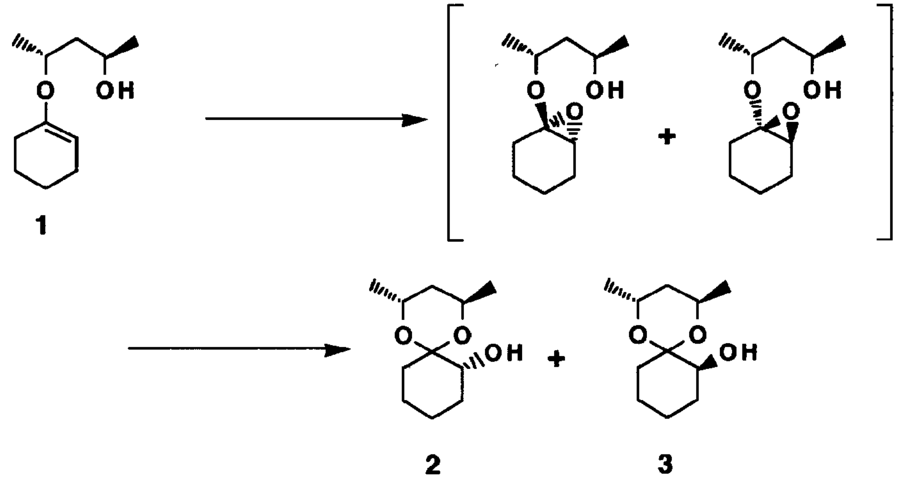

Table 1.

| temp. (°C) | 39 | 27 | 0 | -20 | -45 | -72 |
|---|---|---|---|---|---|---|
| 2/3 | 86/14 | 87/13 | 95/5 | 97/3 | 99/1 | >99.5/>0.5 |
| d.e. (%)$^{a}$ | 72 | 74 | 90 | 94 | 98 | >99 |

a: d.e.= [2-3] / [2+3] x 100

***References and Notes***

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5. Epoxidation of *t*-butyldimethylsilyl ether analog of **1** under the same conditions yielded 2-*t*-butyldimethylsiloxy-4-hydroxypentane and 2-hydroxycyclohexanone.
6. Treatment of **2** with *p*-toluenesulfonic acid monohydrate in diethyl ether afforded (+)-2-hydroxycyclohexanone. $[\alpha]_D^{20}$= 10.4 (c 0.63, $CHCl_3$). litt. for *S* compound of 91 % e.e. $[\alpha]_D$=-13.3 (c 0.53, $CHCl_3$). L. G. Lee; G. M. Whitesides, *J. Org. Chem.*, **1986**, *51*, 25.
7. By the use of the other solvents for this reaction at 0 °C, the products ratios (**2**/**3**) were as follows: hexane 96/4, ether 71/29, THF 51/49.
8. Arrenius plots of the products ratios (**2**/**3**) between -45 to 39 °C were linear (r=0.996), which attribute the reaction isokinetic in this temperature range. The differential activation enthalpy and entropy were $\Delta H^{\ddagger}(R)$-$\Delta H^{\ddagger}(S)$= -4.8 kcal/mol and $\Delta S^{\ddagger}(R)$-$\Delta S^{\ddagger}(S)$= -11.9 cal/mol K.
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