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Highly Stereoselective Formation of Optically Pure 2,4-Oxazolidinedione via Diastereoselective Dihydroxylation of (4*S*)-3-((*E*)-3'-Substituted-2'-Propenoyl)-4-Isopropyl-2-Oxazolidinone

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Abstract: Catalytic asymmetric dihydroxylation (ADH) of (4*S*)-3-((*E*)-3'-substituted-2'-propenoyl)-4-isopropyl -2-oxazolidinone **1a** and **1b** resulted in the in situ rearrangement of the initially produced diols or its osmates to provide 3-((1'*S*)-1'-isopropyl-2'-hydroxyethyl)-5(*S*)-5-((1'*R*)-1'-hydroxybenzyl (**2a**) and -hydroxyethyl (**2b**))-2,4-oxazolidinedione, respectively. The structure of **2a** was determined by X-ray crystal structure analysis.

The Sharpless catalytic asymmetric dihydroxylation[1] of olefins has allowed access to a wide variety of enantiomerically pure vicinal diols. For induction of asymmetry in diol products in the ADH process, cinchona alkaloid derivatives are generally used as chiral ligands. Asymmetric induction could also occur during the dihydroxylation reaction of chiral olefins if the stereogenic center is near the double bond.[2] Thus, we have been interested in use of (4*S*)-4-isopropyl-2-oxazolidinone as a chiral auxiliary for stereoinduction in dihydroxylation reaction.

In order to examine the asymmetric induction effect of the oxazolidinone auxiliary, the dihydroxylation of **1a-b**[3] was carried out in the absence of chiral ligands. However, the reactions of **1a** and **1b** with *N*-methyl-morpholine-*N*-oxide (NMMO) and osmium tetroxide in acetone-H_2O at room temperature gave unexpectedly enantiomerically pure corresponding 2,4-oxazolidinedione **2a-b** in good yields.[4] The other epimer and/or the expected diol were not detected even by TLC. The structure and stereochemistry of **2a** was assigned by X-ray crystal structure analysis (Figure 1).[5]

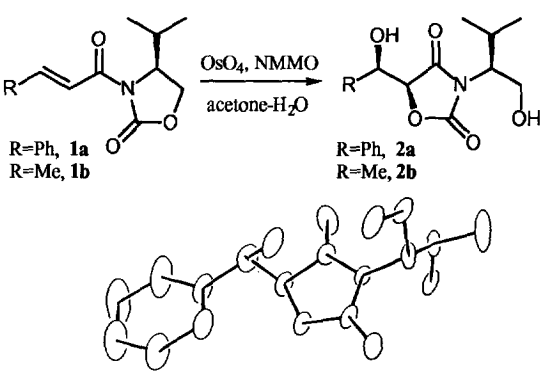

Fig. 1 Molecular structure of **2a**

The stereoselective formation of **2** implies that the dihydroxylation using the oxazolidinone chiral auxiliary has proceeded with extremely high steroselectivity. In the reaction conditions, the initially formed diol or its osmate ester was rapidly rearranged to **2**. At this point, it is not clear why the intramolecular rearrangement occurs so easily.

Nevertheless, formation of **2** is efficient and highly stereoselective and suggest interesting possibilities for the asymmetric synthesis of a variety of chiral 3,5-disubstituted-2,4-oxazolidinedione derivatives. Some of 3,5-disubstituted-2,4-oxazolidinedione derivatives show fungicidal or pharmaceutical activities.[6)]

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4. Typical Procedure: OsO_4 (2 wt.% aqueous solution 6.1 ml, 0.48 mmol) and solid **1** (15.0 mmol) were added successively to a well-stirred solution of NMMO (50 wt.% aqueous solution 5.42 ml, 23.13 mmol) in acetone (60 ml). The reaction was stirred at room temperature until completion (about 8 hr, monitored by TLC; n-hexane : EtOAc = 1 : 1 eluent). Sodium metabisulfite (4.3 g, 15 mmol) was then added and stirred for additinal 20 min. Reaction mixture was diluted with methylene chloride and filtered through celite. After evaporation of the solvent, the residue was purified on silica gel column (n-hexane : EtOAc = 1 : 1 eluent) to give **2**: For **2a**: yield(80%); mp 155-156 °C; $[\alpha]_D^{24}$ -176 (c 1.0, $CHCl_3$); ^{1}H NMR (DMSO-d_6) δ 0.84 (d, J=6.6 Hz, 3H), 0.94 (d, J=6.6 Hz, 3H), 2.10 (m, 1H), 3.60-3.71 (m, 2H), 3.75~3.88 (m, 1H), 4.83 (t, J=5.5 Hz, 1H), 5.09 (dd, J=4.9, 1.6 Hz, 1H), 5.25 (d, J=1.6 Hz, 1H), 6.18 (d, J=4.9 Hz, 1H), 7.2-7.5 (m, 5H); ^{13}C NMR (DMSO-d_6) δ 19.78, 26.85, 58.32, 61.05, 69.87, 82.55, 126.40, 127.50, 128.00, 140.33, 155.09, 172.37. Anal calcd for $C_{15}H_{19}NO_5$: C, 61.42; H, 6.53; N, 4.77. Found: C, 61.4; H, 6.70; N, 4.59. For **2b**: yield(71%); $[\alpha]_D^{24}$-43.5 (c 1.92, $CHCl_3$); ^{1}H NMR (DMSO-d_6) δ 0.79 (d, J=7.1Hz, 3H), 0.92 (d, J=6.6Hz, 3H), 1.23 (d, J=6.6Hz, 3H), 2.09 (m, 1H), 3.55-3.70 (m, 2H), 3.74-3.80 (m, 1H), 4.04 (m, 1H), 4.81 (m, 1H), 4.91 (d, J=1.1Hz, 1H), 5.32 (d, J=5.8Hz, 1H); ^{13}C NMR (DMSO-d_6) δ 19.23, 19.70, 19.81, 26.73, 58.26, 60.85, 64.63, 82.53, 155.25, 172.83.

5. Crystal data for **2a:** $C_{15}H_{19}NO_5$, monoclinic, $P2_1$, a=15.233(3), b=6.314(3), c=16.219(4) Å, β=92.57(4)°, V=1558.3(9) Å^3, Z=2, D_c=1.250 g/cm^3, F(000)=624, λ(MoKα)=0.71073 Å, 1821 Independent reflections with I/σ (I)≥2.0 were used in the analysis. R=0.059. Data for crystallographic analysis were measured on an Enraf-Nonius CAD-4 diffractometer using Mo radiation and ϖ-2 scans in the range of θ; $1.79 < \theta < 24.96$. Structure was solved by direct methods and refined by least squares using the SHEL-X.

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