

- 116.8, 125.2, 126.3, 127.8, 141.3, 143.0, 144.5, 150.9.
15. Preparation of 4-(2-phenyl-isopropyl)-*o*-benzoquinone. 10 g (29 mmol) of 3,6-bis(2-phenylpropyl)catechol and silver oxide 14.72 g (64 mmol) in 50 mL of dichloromethane were stirred for 6 h at 35°C. Evaporation of the solvent gave a brown solid in 90% yield. The crude solid was recrystallized from hexane to obtain brown crystals. mp. 65°C. Anal. found (Calcd. for C<sub>15</sub>H<sub>14</sub>O<sub>2</sub>): C, 79.4 (79.6); H, 6.3 (6.2). IR (KBr, cm<sup>-1</sup>): ν (C-O), 1660. <sup>1</sup>H-NMR (δ, ppm): 1.51 (s), 6.24 (d), 6.40 (d), 6.70 (q), 7.27 (m), 7.35 (d). <sup>13</sup>C-NMR (δ, ppm): 26.9, 43.2, 124.0, 126.6, 128.7, 141.1, 144.8, 159.1, 180.1. All spectroscopic data are available by ordering information.
16. Crystallographic Analysis. All the crystallographic data were obtained on an Enraf-Nonius CAD 4 automatic diffractometer with graphite-monochromated molybdenum radiation at ambient temperature. Preliminary diffractometric investigation indicated triclinic  $P\bar{1}$  (C<sub>1</sub><sup>h</sup>, No. 2). Accurate cell dimensions were obtained from the setting angles of 25 well-centered reflections by using a least-square procedure. The data were corrected for Lorentz-Polarization effect, decay, and absorption with ψ-scan data. The structure was solved by a direct method, followed by successive difference Fourier synthesis. The non-hydrogen atoms were refined anisotropically by using SHELX-76. Hydrogen atoms were placed in calculated positions and refined only for the isotropic thermal factors. *a* = 9.686 (2), *b* = 10.894 (5), *c* = 12.947 (3) Å, α = 74.32 (2), β = 82.68 (2), γ = 68.54 (3), *V* = 1223.5 (7) Å<sup>3</sup>, Scan method = ω/2θ, No. unique data > 3σ (*I*) = 2087, *R* (*R*<sub>w</sub>) = 0.047 (0.055). All crystallographic data (coordinates, anisotropic thermal parameters, bond distances and angles, structure factors) are available from OSJ of authors.

### Diastereoselective Reduction of Chiral 2-(1,3-Oxazinyl) 2-Furylketone: Asymmetric Synthesis of (R)-(+)-2-(1,2-Dihydroxyethyl)furan

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Optically active 2-furylcarbinols serve as useful synthetic intermediates,<sup>1</sup> as they can be converted into 2-alkoxy carboxylic acids<sup>2</sup> or 2*H*-pyran-3-(6*H*)-ones<sup>3</sup> by various oxidative procedures. Therefore, much effort has been directed to the preparation of optically active 2-furylcarbinols.<sup>4</sup>

Recently, the bicyclic 2-(1,3-oxazinyl) ketones **1** derived from (R)-(+)-pulegone have been found to undergo highly stereoselective addition reaction with Grignard, organolithium, and hydride reagents.<sup>5</sup> We reasoned that diastereoselective reduction of oxazinyl 2-furylketone **1a** could give the carbinols (S)-**2a** or (R)-**2a**, from which optically active 2-furyl-

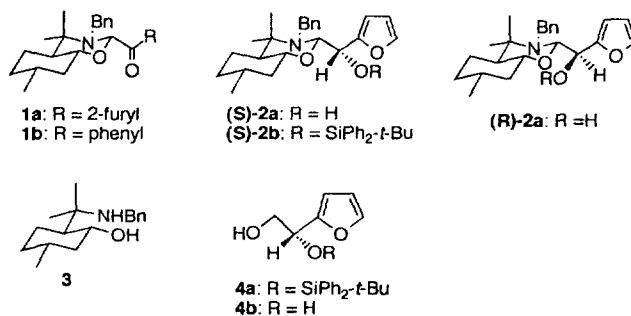
**Table 1.** Diastereoselectivities in the Reduction of Ketone **1a**

Reducing agents	Solvent	Temp. (°C)	(S)- <b>2a</b>	(R)- <b>2a</b>	de% <sup>a</sup>
NaBH <sub>4</sub>	EtOH	0	98	2	96
LiAlH <sub>4</sub>	THF	-78	90	10	80
LiAlH <sub>4</sub>	ether	-78	98	2	96
L-Selectride®	THF	-78	98	2	96
L-Selectride®	ether	-78	98	2	96
<i>n</i> -Bu <sub>4</sub> NBH <sub>4</sub>	CH <sub>2</sub> Cl <sub>2</sub>	20	98	2	96
<i>n</i> -Bu <sub>4</sub> NBH <sub>4</sub>	THF	20	90	10	80
LiAl(O- <i>t</i> -Bu) <sub>3</sub> H	THF	20	90	10	80
LiAl(O- <i>t</i> -Bu) <sub>3</sub> H	ether	20	99	1	98
LiAl(O- <i>t</i> -Bu) <sub>3</sub> H/ 15-crown-5 (2 eq.)	ether	20	99	1	98
LiAl(O- <i>t</i> -Bu) <sub>3</sub> H/ TMEDA (10 eq.)	ether	20	98	2	96
Zn(BH <sub>4</sub> ) <sub>2</sub>	ether	-78	98	2	96
dibal	toluene	-78	55	45	10

<sup>a</sup>The diastereomeric ratios were determined by the integration of C-2 proton signal of the <sup>1</sup>H-NMR spectra.

diol **4b** could be obtained after acidic hydrolysis followed by reduction. Also, ketone **1a** that can be considered as an extension of α-alkoxyketone imposes an interesting question as to the involvement of the furan oxygen in chelation. If the furan oxygen is involved in chelation, the diastereoselectivity in the reduction of **1a** is expected to be lower than in the case of **1b**.<sup>6</sup> In this paper we wish to report on the highly diastereoselective reduction of **1a** and rationalize this result with stereochemical models.

Ketone **1a**<sup>7</sup> was prepared by condensation (CH<sub>2</sub>Cl<sub>2</sub>, molecular sieve 3A, reflux, 2 days) of amino alcohol **3**<sup>5</sup> with 2-furyl glyoxal hydrate<sup>8</sup> in 65% yield as colorless crystal, mp 82-83°C and was reduced to give a mixture of (S)-**2a**<sup>9</sup> and (R)-**2a**, with the results shown in Table 1. The carbinol carbon formed in the LiAl(O-*t*-Bu)<sub>3</sub>H reduction was proven to have the (S)-configuration (*vide infra*). As one can see in Table 1, most reducing agents produced the (S)-isomer in high diastereomeric excess (de). However, diisobutylaluminum hydride (DIBAL) gave an almost equal mixture of two diastereomeric alcohols.

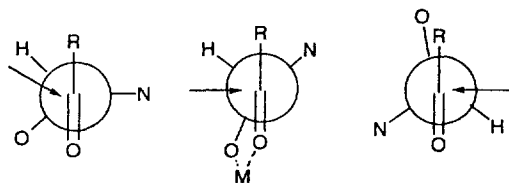


Previously, high stereoselectivity observed in hydride reduction of 2-oxazinyl ketone **1** has been ascribed to the Cram's chelate model involving chelation to the oxygen rather than the nitrogen of the oxazine ring.<sup>5</sup> However, in the present case the reduction with *n*-Bu<sub>4</sub>NBH<sub>4</sub> in CH<sub>2</sub>Cl<sub>2</sub>, which

lacks the chelating ability shows the high stereoselectivity as  $\text{NaBH}_4$ . Furthermore, the presence of crown ether or TMEDA (*M, N, N', N'*-tetramethylenedimine) that may interfere in the chelation of metal ion to the oxygen atoms of ketone and the oxazine ring does not show any detrimental effect in the  $\text{LiAl}(\text{O}-t\text{-Bu})_3\text{H}$  reduction.<sup>10</sup> Also, metal cation can be expected to chelate with the furan ring oxygen as well as the oxazine ring oxygen.<sup>11</sup> Then, the reduction of furylketone **1a** can be less stereoselective than that of phenyl ketone **1b**.<sup>12</sup> However, this is not observed, which implies that the furan ring oxygen does not participate in chelation. Thus, it seems more reasonable to invoke Felkin-Anh model **A** rather than chelate model **B**, even though two models predict the same outcome.<sup>13</sup> However, the reduction in more coordinating solvent (THF) shows lower selectivity than in ether solvent when  $\text{LiAlH}_4$  and  $\text{LiAl}(\text{O}-t\text{-Bu})_3\text{H}$  are used, suggesting the importance of the chelate model here.

DIBAL which is an electrophilic reducing agent has been reported to reduce the oxathianyl ketone (sulfur instead nitrogen in structure **1**) according to the Cornforth's dipolar model **C**.<sup>10</sup> In the present case the reduction of ketone **1b** with DIBAL showed poor selectivity, which may be ascribed to the operation of Felkin's model together with the dipolar model.<sup>14</sup>

R = 2-furyl



A: Felkin's Model B: Cram's Chelate Model C: Dipolar Model

The absolute configuration of the carbinol carbon of **2a** was determined by the following procedures. First, the protection ( $\text{Ph}_2t\text{-BuSiCl}$ , imidazole, DMF, 81% yield) of **2a** (de 98%) obtained by  $\text{LiAl}(\text{O}-t\text{-Bu})_3\text{H}$  reduction, acidic hydrolysis (1 equiv., aq. HCl, MeOH, reflux, 15 min) of the silyl ether **2b** and the  $\text{NaBH}_3\text{CN}$  reduction (pH 4, MeOH) of the resulting aldehyde gave the furan **4a** in 30% yield. Then, deprotection ( $\text{Bu}_4\text{NF}$ , THF, reflux, 5 min) of the silyl group gave the dextrorotatory diol **4b**,<sup>15</sup>  $[\alpha]_D^{20} = +35.8$  ( $\text{CHCl}_3$ ,  $c = 3.75$ ; literature value<sup>16</sup> for (R)-isomer of 100% ee,  $[\alpha]_D^{20} = +36.7$  ( $\text{CHCl}_3$ )), proving the (S)-configuration of carbinol carbon of **2a** obtained by  $\text{LiAl}(\text{O}-t\text{-Bu})_3\text{H}$  reduction. The magnitude of optical rotation of **4b** derived from **2a** of 98% de agreed well with the calculated one, which means that no racemization occurred during the hydrolysis and the subsequent reduction step.

In summary, oxazinyl 2-furyl ketone **1a** can be reduced in high diastereoselectivity and the stereochemistry in this case can be explained more reasonably using Felkin-Anh model rather than Cram's chelate model.

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- <sup>1</sup>H-NMR (200 MHz,  $\text{CDCl}_3$ )  $\delta$  7.46 (d, 1H,  $J = 1.7$  Hz), 7.29 (d, 1H,  $J = 3.7$  Hz), 7.10-6.95 (m, 5H), 6.42 (dd, 1H,  $J = 1.7, 3.7$  Hz), 5.67 (s, 1 H), 4.00, 3.83, (ABq, 2H,  $J = 17$  Hz), 3.64 (dt, 1H,  $J = 3.9, 10$  Hz), 1.41 (s, 3H), 1.09 (s, 3H), 0.98 (d, 3H,  $J = 6.3$  Hz); <sup>13</sup>C-NMR (50.3 MHz,  $\text{CDCl}_3$ )  $\delta$  184.0, 151.0, 146.4, 141.7, 127.4, 125.8, 119.8, 111.8, 88.3, 76.5, 57.9, 47.8, 46.1, 41.2, 35.0, 31.4, 27.1, 25.0, 22.2, 20.2; IR ( $\text{CDCl}_3$ )  $\text{cm}^{-1}$  1730 (C=O).
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- <sup>1</sup>H-NMR (200 MHz,  $\text{CDCl}_3$ )  $\delta$  7.39 (s, 1H), 6.38-6.32 (m, 2H), 4.83 (t, 1H,  $J = 5.4$  Hz), 3.86 (d, 2H,  $J = 5.4$  Hz), 2.98 (br s, 1H, OH), 2.50 (br s, 1H, OH); <sup>13</sup>C-NMR (50.3 MHz,  $\text{CDCl}_3$ )  $\delta$  153.9, 142.6, 110.6, 107.3, 68.3, 66.4.
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