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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 $C_{15}H_{14}O_2$): C, 79.4 (79.6): H, 6.3 (6.2). IR (KBr, cm^{-1}): ν (C-O), 1660. ^{1}H-NMR (δ, ppm): 1.51 (s), 6.24 (d), 6.40 (d), 6.70 (q), 7.27 (m), 7.35 (d). ^{13}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 $P\bar{1}$ (C1^1_i, 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^3, Scan method = ω/2θ, No. unique data > 3σ (I) = 2087, R (Rw) = 0.047 (0.055). All crystallograpic 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,[1] as they can be converted into 2-alkoxy carboxylic acids[2] or 2*H*-pyran-3-(6*H*)-ones[3] by various oxidative procedures. Therefore, much effort has been directed to the preparation of optically active 2-furylcarbinols.[4]

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.[5] 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-
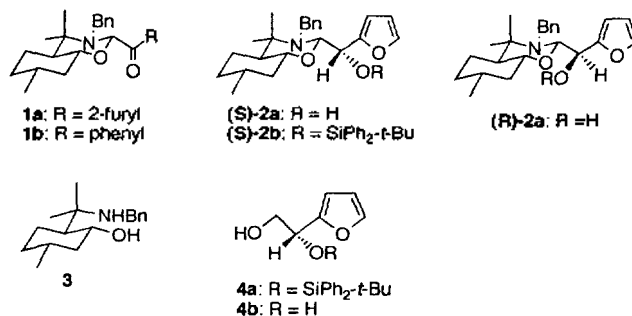
Table 1. Diastereoselectivities in the Reduction of Ketone 1a

Reducing agents	Solvent	Temp. (°C)	(S)-2a	(R)-2a	de%[a]
NaBH$_4$	EtOH	0	98	2	96
LiAlH$_4$	THF	−78	90	10	80
LiAlH$_4$	ether	−78	98	2	96
L-Selectride®	THF	−78	98	2	96
L-Selectride®	ether	−78	98	2	96
n-Bu$_4$NBH$_4$	CH$_2$Cl$_2$	20	98	2	96
n-Bu$_4$NBH$_4$	THF	20	90	10	80
LiAl(O-*t*-Bu)$_3$H	THF	20	90	10	80
LiAl(O-*t*-Bu)$_3$H	ether	20	99	1	98
LiAl(O-*t*-Bu)$_3$H/ 15-crown-5 (2 eq.)	ether	20	99	1	98
LiAl(O-*t*-Bu)$_3$H/ TMEDA (10 eq.)	ether	20	98	2	96
Zn(BH$_4$)$_2$	ether	−78	98	2	96
dibal	toluene	−78	55	45	10

[a] The diastereomeric ratios were determined by the integration of C-2 proton signal of the ^{1}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.[6] In this paper we wish to report on the highly diastereoselective reduction of 1a and rationalize this result with stereochemical models.

Ketone 1a[7] was prepared by condensation (CH$_2$Cl$_2$, molecular sieve 3A, reflux, 2 days) of amino alcohol 3[5] with 2-furylglyoxal hydrate[8] in 65% yield as colorless crystal, mp 82-83°C and was reduced to give a mixture of (S)-2a[9] and (R)-2a, with the results shown in Table 1. The carbinol carbon formed in the LiAl(O-*t*-Bu)$_3$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.


1a: R = 2-furyl
1b: R = phenyl

(S)-2a: R = H
(S)-2b: R = SiPh$_2$-*t*-Bu

(R)-2a: R = H

3

4a: R = SiPh$_2$-*t*-Bu
4b: R = H

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.[5] However, in the present case the reduction with *n*-Bu$_4$NBH$_4$ in CH$_2$Cl$_2$, which

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lacks the chelating ability shows the high stereoselectivity as NaBH₄. 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 LiAl(O-*t*-Bu)₃H reduction.[10] Also, metal cation can be expected to chelate with the furan ring oxygen as well as the oxazine ring oxygen.[11] Then, the reduction of furylketone **1a** can be less stereoselective than that of phenyl ketone **1b**.[12] However, this is not observed, which implies that the furan ring oxygen does not participate in chelation. Thus, it seems more reasonable to invoke FelkinAnh model **A** rather than chelate model **B**, even though two models predict the same outcome.[13] However, the reduction in more coordinating solvent (THF) shows lower selectivity than in ether solvent when LiAlH₄ and LiAl(O-*t*-Bu)₃H 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**.[10] 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.[14]

R = 2-furyl
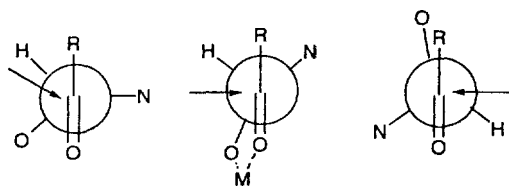
A: Felkin's Model   B: Cram's Chelate Model   C: Dipolar Model

The absolute configuration of the carbinol carbon of **2a** was determined by the following procedures. First, the protection (Ph₂*t*-BuSiCl, imidazole, DMF, 81% yield) of **2a** (de 98%) obtained by LiAl(O-*t*-Bu)₃H reduction, acidic hydrolysis (1 equiv., aq. HCl, MeOH, reflux, 15 min) of the silyl ether **2b** and the NaBH₃CN reduction (pH 4, MeOH) of the resulting aldehyde gave the furan **4a** in 30% yield. Then, deprotection (Bu₄NF, THF, reflux, 5 min) of the silyl group gave the dextrorotatory diol **4b**,[15] [α]_D²⁰ = +35.8 (CHCl₃, c = 3.75; literature value[16] for (R)-isomer of 100% *ee*, [α]_D²⁰ = +36.7 (CHCl₃)), proving the (S)-configuration of carbinol carbon of **2a** obtained by LiAl(O-*t*-Bu)₃H 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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14. However, the reduction of **1b** with DIBAL gives the corresponding (S)-carbinol in high de.[5a]
15. ¹H-NMR (200 MHz, CDCl₃) δ 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); ¹³C-NMR (50.3 MHz, CDCl₃) δ 153.9, 142.6, 110.6, 107.3, 68.3, 66.4.
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