Asymmetric Syntheses of (*S*)-2-Methyl-3,4,5,6-tetrahydro-2*H*-pyran-4-one and (*2S,6S*)-2,6-*trans*-Dimethyl-3,4,5,6-tetrahydro-2*H*-pyran-4-one Which Employ a Common Lactol Intermediate

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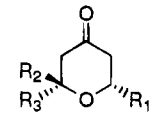
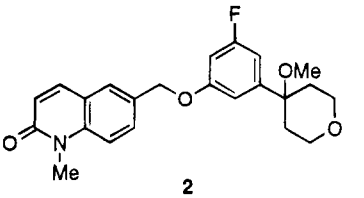
Tetrahydropyran-4-one (**1a**) is an intermediate in the synthesis of the methoxytetrahydropyran series of 5-lipoxygenase inhibitors exemplified by ZD2138 (**2**) (Scheme 1).[1] In order to explore further the biological properties of this series, we chose to investigate the effect of alkyl substitution at the 2- and 6-positions of the tetrahydropyran (THP) ring. The preparation of these compounds required the intermediacy of substituted THP-4-ones. Introduction of 2-methyl into the THP ring introduces chirality and the possibility of diastereomers in target compounds. Preliminary work with racemic compounds in the 2-naphthyl series **3** established that the diastereomers **3a** and **3b** had equivalent potency *in vitro*[2] (IC_{50}s 0.1 μM) but that **3a** showed higher potency *in vivo*.[3] *cis*-2,6-Dimethyl substitution removes chirality, but the diastereomer **3c** was significantly less potent (IC_{50} 0.8 μM) than **3a,b**.

Racemic **1b** used in the synthesis of **3a,b** was prepared through a Prins reaction between homoallylic alcohol and acetaldehyde, followed by oxidation.[4] **1c** was prepared by catalytic reduction of 2,6-dimethyl-4*H*-pyran-4-one.[5] In order to be able to evaluate **3a** and related compounds fully *in vivo*, we required synthetic routes to resolved materials. (*2R,4S*)-**3a**, prepared from (*R*)-**1b**, was much less potent (IC_{50} 1.8 μM) than (±)-**3a**, indicating that the eutomer would be (*2S,4R*) for which (*S*)-**1b** was required. No syntheses of the latter had been reported.[6] The synthesis of (*R*)-**1b** involved a reductive kinetic resolution of **1b** employing horse liver dehydrogenase and reoxidation,[7] but this method was unsuitable for generating (*S*)-**1b** in high enantiomeric excess (ee). Although the *cis*-2,6-dimethyl isomer **3c** had disappointing potency, *trans*-2,6-dimethyl-THP-containing compounds remained of interest. No route to **1d**, either racemic or scalemic, however, has been reported. This report describes our work on the syntheses of (*S*)-**1b** and (*2S,6S*)-**1d** from a common intermediate.

Scheme 1



1a: R_1, R_2, R_3 = H
1b: R_1 = Me; R_2, R_3 = H
1c: R_1, R_3 = Me; R_2 = H
1d: R_1, R_2 = Me; R_3 = H



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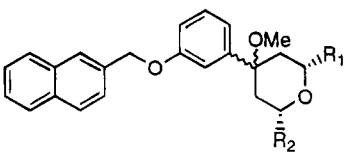
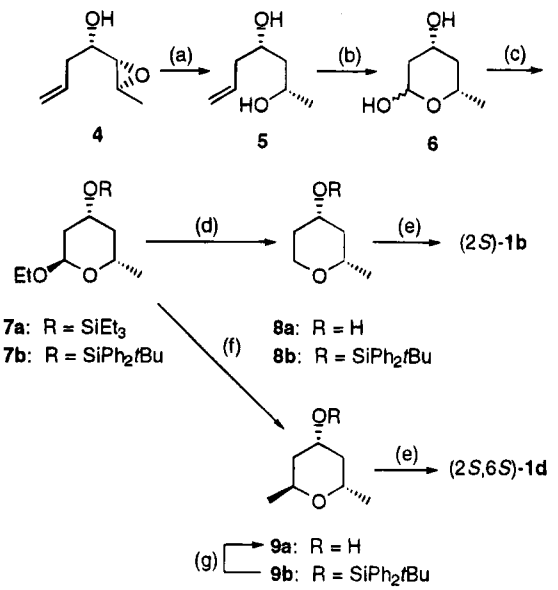


3a: R_1 = Me; R_2 = H; Me/OMe *trans*
3b: R_1 = Me; R_2 = H; Me/OMe *cis*
3c: R_1 = Me; R_2 = Me; Me/OMe *trans*

Scheme 2



[a] Reagents: (a) Red-Al, THF; (b) O_3, EtOH; (c) (1) EtOH, HCl; (2) Et_3SiCl or *t*-$BuPh_2SiCl$, imidazole, DMF; (d) Et_3SiH, TMSOTf, CH_2Cl_2; (e) CrO_3, acetone; (f) Me_3Al, TMSOTf, CH_2Cl_2; (g) n-Bu_4NF, THF.

Results and Discussion

We envisaged that the substituted lactol **6** would provide either 2-methyl- or 2,6-dimethyl-THP derivatives through reduction or nucleophilic substitution of the anomeric substituent, respectively (Scheme 2). Furthermore, in the case of the latter, Lewis acid catalyzed substitution through the intermediacy of a cyclic oxonium ion would lead to introduction of an axial methyl group and thereby generate a *trans*-2,6-geometry, as predicted by stereoelectronic considerations. The lactol **6** would be produced through cleavage of alkene **5** in which the 1,3-diol arrangement was established by hydroxyl-directed reductive opening of epoxide **4**, itself available through asymmetric epoxidation.[8]

(1) Crawley, G. C.; Dowell, R. I.; Edwards, P. N.; Foster, S. J.; McMillan, R. M.; Walker, E. R. H.; Waterson, D.; Bird, T. G. C.; Bruneau, P.; Girodeau, J.-M. *J. Med. Chem.* **1992**, *35*, 2600.
(2) IC_{50} values are for inhibition of LTB_4 biosynthesis in A-23187-stimulated human whole blood (ref 1).
(3) Crawley, G. C. Manuscript in preparation.
(4) Hanschke, E. *Chem. Ber.* **1955**, *88*, 1053.
(5) Eskenazi, C.; Sliwa, H.; Maitte, P. *Bull. Soc. Chim. Fr.* **1971**, 2951–2956.
(6) Part of this work has been reported in preliminary form: Crawley, G. C.; Briggs, M. T.; Dowell, R. I.; Edwards, P. N.; Hamilton, P. M.; Kingston, J. F.; Oldham, K.; Waterson, D.; Whalley, D. P. *J. Med. Chem.* **1993**, *36*, 295.
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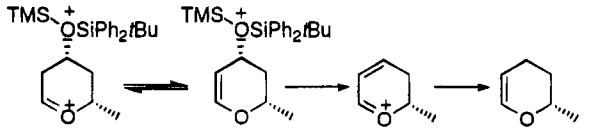
0022-3263/95/1960-4264$09.00/0

Scheme 3



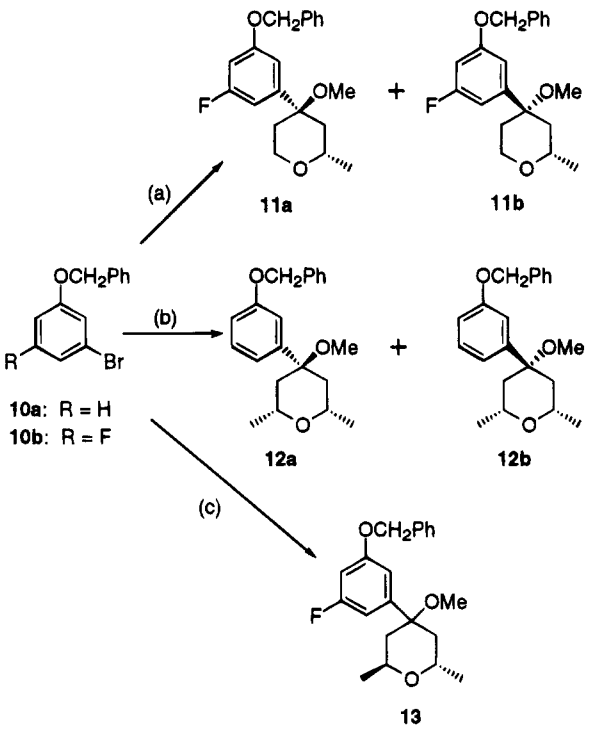
Epoxide **4** was prepared in 35% yield by Sharpless kinetic resolution, using catalytic conditions,[9] of 4-hydroxyhepta-1,5-diene. Slow addition of Red-Al[10,11] at 0 °C to **4** produced diol **5** cleanly in 70% yield and minimized formation of the corresponding 1,2-diol. Ozonolysis in ethanol at −20 °C converted **5** quantitatively to an anomeric mixture of lactols **6** . After triethylsilyl protection of the 4-hydroxyl, the lactol ethyl ether **7a** was reduced to pyranol **8a** with Et_3SiH/trimethylsilyl triflate[12] (TMSOTf) at 5 °C followed by acidic workup. Crude **8a** was always produced cleanly by this procedure and apparently free of significant side products, and yet, despite strenuous efforts to avoid losses due to evaporation or water solubility, the overall yield could never be improved above 40%. We repeated the process substituting *tert*-butyldiphenylsilyl (TBDPS) protection of the 4-hydroxyl group and worked up the final step with aqueous $NaHCO_3$. In this way, not only was the expected protected pyranol **8b** isolated in similar yield, but in addition, TBDPS-O-TMS was detected. The formation of the latter was hypothesized to occur as depicted in Scheme 3 and suggested that material was escaping as volatile methyldihydropyran.

Conducting the reductions of **7a** and **7b** at −40 to −20 °C alleviated the problem to a large extent and raised the yields of **8a** and **8b** to 87 and 70%, respectively. Oxidation of **8a** gave the pyranone (*S*)-**1b** in 81% yield and ≥95% ee.[13] Assignment of the *S*-configuration follows from the Sharpless epoxidation[14] and was confirmed by comparison with (±)-**1b** and (*R*)-**1b** using HPLC on a chiral support. This route has proved reliable and efficient on a large scale, providing (*S*)-**1b** in *ca.* 200 g batches.

For the synthesis of (2*S*,6*S*)-**1d**, **7b** was treated with Me_3Al/TMSOTf[15] at −50 to −30 °C to produce **9b** in 35–41% yield.[16] ^1H NMR decoupling experiments revealed coupling constants of J_{eq-eq} = 3.3 Hz and J_{eq-ax} = 4.8 Hz for one of the methyl-bearing methines, confirming the introduction of an axial methyl. Deprotection (*n*-Bu_4NF, 92%) and oxidation (CrO_3, 75%) gave (2*S*,6*S*)-**1d**, which was clearly distinguishable from the *cis*-isomer **1c** by ^1H NMR and TLC. Furthermore, none of the *cis* isomer could be detected in the ^1H NMR spectrum of the *trans* isomer.

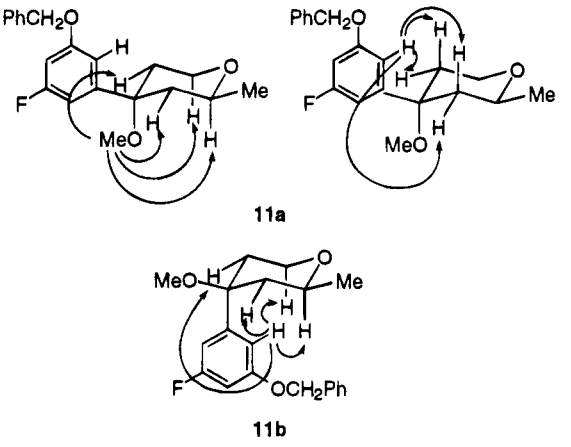
Reaction of the lithio derivative of **10b** with (*S*)-**1b** produced two diastereomeric alcohols (Scheme 4) which were separated readily by chromatography and converted

Scheme 4

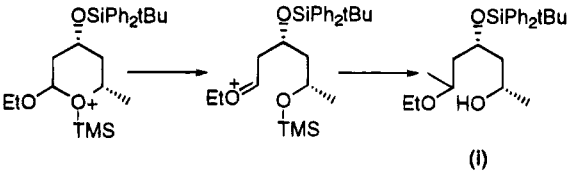


[a] Reagents: (a) (1) Mg, THF, (*S*)-**1b**; (2) NaH, MeI, DMF; (b) as (a) but substituting **1c** for (*S*)-**1b**; (c) as (a) but substituting (2*S*,6*S*)-**1d** for (*S*)-**1b**.

Scheme 5



Scheme 6



to the *O*-methyl ethers **11a,b**, whose configurations were assigned by ^1H NMR. Both diastereomers showed typical ax−ax couplings for the methine protons, establishing that both existed in chair conformations with their methyl groups equatorial (**11a** (C_6D_6), 11.04 Hz; **11b** ($CDCl_3$), 11.2 Hz). Using one-dimensional NOE, the configurations at C-4 were determined as summarized in Scheme 5 in which signal enhancements are indicated by the arrows.

The ratio of **11a,b** produced depended on the reaction conditions. With *n*-BuLi, the ratio **11a**:**11b** was 1:3, and

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(12) Bennek, J. A.; Gray, G. R. *J. Org. Chem.* **1987**, *52*, 892.
(13) (*S*)-**1b** was analyzed for optical purity by chiral HPLC using Chiralcel OB as support and *i*-PrOH/hexanes (2:98) as eluant.
(14) Rossiter, B. E. In *Asymmetric Synthesis*; Morrison, J. D., Ed.; Academic Press, Inc.: New York, 1985; Vol. 5, p 193.
(15) Tomooka, K.; Matsuzawa, K.; Suzuki, K.; Tsuchihashi, G. *Tetrahedron Lett.* **1987**, *28*, 6339.
(16) Similar yields were achieved using BF_3·Et_2O as catalyst. In most experiments, with either catalyst an equivalent amount of **i** was obtained (Scheme 6), arising from an acyclic oxonium ion intermediate.

with Mg, the ratio was 2:1 (combined yields of **11a,b** from **10b** were 69 and 70%, respectively). Similarly, reaction of **10a**–Grignard reactant with **1c** generated, after methylation, the diastereomers **12a,b** in a 2:1 ratio and 60% combined yield.[17] On the other hand, because of its C_2 symmetry, (2*S*,6*S*)-**1d** produced, when reacted with **10b** and Mg, only one stereoisomer which was characterized as the ether **13**.

Thus, in the foregoing studies, effective asymmetric syntheses of (*S*)-**1b** and (2*S*,6*S*)-**1d** have been developed for the first time, and furthermore, these routes are amenable to large-scale laboratory production. Moreover, by employing the opposite chiral auxiliary in the asymmetric epoxidation step, the enantiomers of these tetrahydropyranones are accessible. The compounds **11**–**13** have been elaborated into target 5-lipoxygenase inhibitors, and their biological activities will be reported elsewhere.

Experimental Section

General. All reactions, excluding hydrogenations and ozonolyses, were performed in argon atmospheres. Organic extracts were dried over $MgSO_4$ before evaporation *in vacuo* using rotary evaporators. Volatile materials were evaporated at water pump pressure in a water bath at ≤30 °C. Chromatography refers to flash chromatography and was performed as described.[18] Melting points are uncorrected.

(2*S*,4*S*)-2,4-Dihydroxyhept-6-ene (5). Red-Al (3.36 M in toluene, 170 mL, 0.57 mol) was added dropwise with stirring over 1 h to a solution of **4** (24 g, 0.188 mol) in THF (800 mL) cooled to 0 °C. After warming to rt overnight, the reaction solution was recooled in ice, and 10% H_2SO_4 (500 mL) was added *cautiously*, maintaining the temperature below 10 °C. Solids were removed by filtration, the residue was washed with EtOAc, and the organic phase was washed with a mixture of saturated $NaHCO_3$ and brine. The washings were back-extracted with EtOAc, and the combined extracts were evaporated. Chromatography (EtOAc:hexanes 60:40) gave **5** (17.13 g, 70%) as a colorless oil, contaminated with some 2-methoxyethanol, which was adequate for the next stage: ^{1}H NMR ($CDCl_3$, 200 MHz) δ 5.83 (ddt, 1H, *J* = 17.5, 9.5, 6 Hz), 5.2 (m, 1H), 5.1 (m, 1H), 4.17 (tq, 1H, *J* = 6, 6 Hz), 4.0 (tt, 1H, *J* = 6, 6 Hz), 2.26 (dd, 2H, *J* = 6, 6 Hz), 1.62 (dd, 2H, *J* = 6, 6 Hz), 1.25 (d, 3H, *J* = 6 Hz).

(2*RS*,4*R*,6*S*)-2,4-Dihydroxy-6-methyl-3,4,5,6-tetrahydro-2*H*-pyran (6). Ozonized oxygen (100 L/h) was bubbled through a stirred solution of **5** (34.8 g, 0.27 mol) in EtOH (270 mL) cooled to −20 °C. When TLC (silica gel, EtOAc) indicated disappearance of **5**, the reaction was purged with nitrogen, dimethyl sulfide (30 mL) was added, and the solution was allowed to warm to rt overnight. Evaporation followed by chromatography (EtOAc) gave **6** (34.7 g, 97%), which was converted directly to **8a**.

(2*S*,4*R*,6*S*)-4-((*tert*-Butyldiphenylsilyl)oxy)-2-ethoxy-6-methyl-3,4,5,6-tetrahydro-2*H*-pyran (7b). A few drops of EtOH/HCl were added to **6** (4.14 g, 31 mmol) dissolved in dry EtOH (20 mL) and the solution was stored at 0 °C overnight. After evaporation, the resulting acetal was dissolved in DMF (30 mL) and cooled to 0 °C. Imidazole (3.7 g, 54 mmol) was added, followed by dropwise addition of TBDPS-Cl (7.3 mL, 28 mmol) with stirring. The reaction mixture was kept at 0 °C for 4 h, and ice water (100 mL) was added, and the solution was extracted with Et_2O (2 × 100 mL). The extracts were washed with water (3 × 10 mL) and evaporated to give **7b** as a colorless oil (10.7 g, 86%) which slowly crystallized: mp 73–7 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.67 (m, 4H), 7.4 (m, 6H), 4.85 (d, 1H, *J* = 2.7 Hz), 4.15 (apparent sextet, 1H), 3.65 (dqd, 1H, *J* = 11.4, 6, 2.3 Hz), 3.7 (dq, 1H, *J* = 9.8, 6.8 Hz), 3.28 (dq, 1H, *J* = 9.8, 6.8 Hz), 1.95 (m, 1H), 1.75 (m, 1H), 1.6 (m, 1H), 1.34 (dd, 1H, *J* = 23, 11 Hz), 1.1 (m, 15H). Anal. Calcd for $C_{24}H_{34}O_3Si$: C, 72.31; H, 8.60. Found: C, 72.7; H, 8.4.

(2*S*,4*S*)-4-Hydroxy-2-methyl-3,4,5,6-tetrahydro-2*H*-pyran (8a). Lactol **6** (33.5 g, 0.25 mol) was converted to **7a** (62.6 g, 90%) using the procedure described for the preparation of **7b**. To the stirred product dissolved in dry CH_2Cl_2 (300 mL) and cooled to −40 °C was added Et_3SiH (39.7 mL, 0.25 mol) followed by dropwise addition of TMSOTf (46.3 mL, 0.24 mol). The reaction was maintained at −30 °C for 1 h and −20 °C for 2 h, after which it was added to ice water (300 mL) and adjusted to pH 5–6. Extraction with EtOAc (4 × 100 mL) and evaporation gave an oil which was triturated with EtOAc:hexanes (10:90) and filtered to remove solids. Chromatography (EtOAc:hexanes, 90:10) gave **8a** as a colorless liquid (23 g, 87%): ^{1}H NMR ($CDCl_3$, 250 MHz) δ 4.0 (ddd, 1H, *J* = 11, 4, 2 Hz), 3.78 (tt, 1H, *J* = 10.4, 4 Hz), 3.4 (m, 2H), 1.9 (m, 2H), 1.65 (s, 1H), 1.5 (tdd, 1H, *J* = 12.5, 10.4, 4 Hz), 1.2 (d, 3H, *J* = 6 Hz), 1.2 (m, 1H).

(*S*)-2-Methyl-3,4,5,6-tetrahydro-2*H*-pyran-4-one ((*S*)-1b). (*S*)-**1b** was prepared as a colorless liquid from **8a** according to the literature[7] procedure for the enantiomer: $[\alpha]^{25}_D$ +20° (*c* = 1, CH_2Cl_2); ^{1}H NMR ($CDCl_3$, 250 MHz) δ 4.28 (ddd, 1H, *J* = 11, 4, 2 Hz), 3.7 (m, 2H), 2.7–2.2 (m, 4H), 1.33 (d, 3H, *J* = 6 Hz); ^{13}C NMR (CD_3SOCD_3, 63 MHz) δ 206.5, 73.2, 65.4, 49.2, 41.3, 21.6. Anal. Calcd for $C_6H_{10}O_2 \cdot 0.05H_2O$: C, 62.64; H, 8.85. Found: C, 62.6; H, 9.25.

(2*S*,6*S*)-4-((*tert*-Butyldiphenylsilyl)oxy)-2,6-dimethyl-3,4,5,6-tetrahydro-2*H*-pyran (9b). To a stirred solution of **7b** (2 g, 5 mmol) in CH_2Cl_2 (18 mL) cooled to −50 °C was added Me_3Al (2 M in toluene, 7.5 mL) followed by TMSOTf (1.16 mL, 6 mmol). The reaction was stirred at −30 °C for 2 h, further TMSOTf (1.16 mL, 6 mmol) was added, the mixture was stirred for a further 1 h and then added *cautiously* to a mixture of ice water containing K_2CO_3 and EtOAc. This mixture was filtered through Celite which was washed with EtOAc. The organic solution was separated, the aqueous phase was reextracted with EtOAc, and the combined extracts were evaporated. Chromatography (EtOAc:hexanes, 5:95) gave **9b** as a colorless oil (0.76 g, 41%): ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.65 (m, 4H), 7.4 (m, 6H), 4.17 (m, 6H), 4.0 (tt, 1H, *J* = 9, 4.5 Hz), 3.67 (dqd, 1H, J = 9.1, 6.2, 2.8 Hz), 1.8 (m, 1H), 1.65 (m, 1H), 1.48 (m, 1H), 1.35 (dt, 1H, *J* = 11.3, 10.2), 1.2 (d, 3H, *J* = 6 Hz), 1.1 (s, 9H), 1.0 (d, 3H, *J* = 6 Hz).

(2*S*,6*S*)-2,6-Dimethyl-4-hydroxy-3,4,5,6-tetrahydro-2*H*-pyran (9a). *n*-Bu_4NF (1 M in THF, 23 mL, 23 mmol) was added to a solution of **9b** (6.6 g, 18 mmol) in THF (15 mL), and the mixture was stirred at rt for 4 h. Evaporation and chromatography (EtOAc:hexanes, 60:40) gave **9a** as a colorless oil (2.16 g, 92%): ^{1}H NMR ($CDCl_3$, 200 MHz) δ 4.3 (m, 1H), 4.05 (m, 1H), 3.8 (m, 1H), 1.95 (m, 1H), 1.8 (m, 1H), 1.6 (m, 1H), 1.46 (d, 1H, *J* = 5 Hz), 1.23 (d, 3H, *J* = 6 Hz), 1.2 (d, 3H, *J* = 6 Hz), 1.2 (m, 1H); MS *m*/*z* (CI) 148 [(M + NH_4)$^+$].

(2*S*,6*S*)-2,6-Dimethyl-3,4,5,6-tetrahydro-2*H*-pyran-4-one ((2*S*,6*S*)-1d). We oxidized **9a** by using the same procedure employed for (*S*)-**1b**, giving (2*S*,6*S*)-**1d** as a colorless oil in 75% yield: $[\alpha]^{25}_D$ −29° (*c* = 1, CH_2Cl_2); ^{1}H NMR ($CDCl_3$, 250 MHz) δ 4.3 (m, 2H), 2.55 (ddd, 2H, *J* = 14, 5, 1 Hz), 2.23 (ddd, 2H, *J* = 14, 6, 2 Hz), 1.28 (d, 6H, *J* = 6 Hz); ^{13}C NMR (CD_3SOCD_3, 63 MHz) δ 207.2, 67.3, 47.6, 20.3; MS *m*/*z* (CI) 146 [(M + NH_4)$^+$]. Anal. Calcd for $C_7H_{12}O_2 \cdot 0.13H_2O$: C, 64.42; H, 9.47. Found: C, 64.1; H, 9.6.

(2*S*,4*R*)-4-[3-(Benzyloxy)-5-fluorophenyl]-4-methoxy-2-methyl-3,4,5,6-tetrahydro-2*H*-pyran (11a). (*S*)-**1b** (3.5 g, 30.6 mmol) dissolved in THF (15 mL) was added over 20 min to the Grignard reactant prepared from Mg (0.89 g, 37 mmol), **10b**[1] (10.1 g, 36 mmol), and THF (22 mL). The reaction mixture was heated at 40 °C for 3 h, cooled in ice, added to 10% HCl and extracted with EtOAc. Evaporation followed by chromatography (EtOAc:toluene, 25:75) afforded two alcohols. To the least polar alcohol (3.8 g, 12 mmol) dissolved in DMF (23 mL) and cooled to 0 °C was added NaH (60% suspension in oil, (0.53 g, 13.2 mmol). After 1 h, MeI (0.87 mL, 14 mmol) was added, and the reaction mixture was allowed to warm to rt over 3 h, poured into 10% HCl, and extracted with EtOAc. Evaporation followed by chromatography (EtOAc:toluene, 5:95) gave **11a** (3.24 g, 82%) as an oil: ^{1}H NMR ($CDCl_3$, 200 Hz) δ 7.4 (m, 5H), 6.8 (m, 1H), 6.7 (dt, 1H, *J* = 10, 1 Hz), 6.7 (dt, 1H, *J* = 10, 1 Hz), 5.05 (s, 2H), 3.88 (m, 3H), 2.95 (s, 3H), 1.9 (m, 3H), 1.52 (dd, 1H, *J* =

(17) Diastereomeric assignments for **12a** and **12b** were made on the basis of characteristic ^{1}H NMR ($CDCl_3$) chemical shifts: H_{3eq} δ 2.0 and 2.35, H_{2ax} δ 3.95 and 3.42 for **12a** and **12b**, respectively [cf., ^{1}H NMR ($CDCl_3$) spectra of **11a** and **11b**].

(18) Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923.

13, 10 Hz), 1.2 (d, 3H, J = 6 Hz); MS m/z (EI) 330 (M^+). Anal. Calcd for $C_{20}H_{23}FO_3$: C, 72.70; H, 7.02. Found: C, 72.8; H, 6.7.

(2*S*,4*S*)-4-[3-(Benzyloxy)-5-fluorophenyl]-4-methoxy-2-methyl-3,4,5,6-tetrahydro-2*H*-pyran (11b). **11b** was prepared as an oil in the same way as **11a**, using the more polar alcohol described in that preparation. **11b**: ^1H NMR ($CDCl_3$, 200 MHz) δ 7.4 (m, 5H), 6.8 (m, 1H), 6.7 (dt, 1H, J = 10, 1 Hz), 6.7 (dt, 1H, J = 10, 1 Hz), 5.05 (s, 2H), 3.95 (m, 1H), 3.36 (m, 2H), 2.9 (s, 3H), 2.3 (m, 1H), 1.9 (ddd, 1H, J = 13, 13, 5 Hz), 1.6 (dd, 1H, J = 13, 11 Hz), 1.2 (d, 3H, J = 6 Hz); MS m/z (CI) 348 [$(M + NH_4)^+$]. Anal. Calcd for $C_{20}H_{23}FO_3$: C, 72.70; H, 7.02. Found: C, 72.2; H, 6.8.

(2*S*,6*S*)-4-[3-(Benzyloxy)-5-fluorophenyl]-2,6-dimethyl-4-methoxy-3,4,5,6-tetrahydro-2*H*-pyran (13). Compound **13** was prepared as an oil from (2*S*,6*S*)-**1d**, using the procedure described for **11a**. **13**: ^1H NMR ($CDCl_3$, 200 MHz) δ 7.4 (m, 5H), 6.8 (m, 1H), 6.7 (dt, 1H, J = 10, 2 Hz), 6.6 (dt, 1H, J = 10, 2 Hz), 5.05 (s, 2H), 4.15 (m, 1H), 2.95 (s, 3H), 1.95 (m, 3H), 1.55 (dd, 1H, J = 13.7, 10.4 Hz), 1.47 (d, 3H, J = 6 Hz), 1.2 (d, 3H, J = 6 Hz). Anal. Calcd for $C_{21}H_{25}FO_3$: C, 73.23; H, 7.23. Found: C, 73.5; H, 6.9.

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Supplementary Material Available: Preparative procedures for **3a–c**, (±)-**11a**, (±)-**11b**, **8b**, and **12b**; copies of ^1H NMR spectra of (*S*)-**1b**, **1c**, (2*S*,6*S*)-**1d**, **5**, **7b**, **8a**, **8b**, **9a**, **9b**, **11a**, **11b**, **12a**, and **13** and decoupling experiments for **7b** and **9b**; ^{13}C NMR data for **1c**; chiral HPLC chromatograms for (±)-**1b**, (*R*)-**1b**, and (*S*)-**1b** (24 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from ACS; see any current masthead page for ordering information.

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