Radical $\alpha$-C-H Hydroxyalkylation of Ethers and Acetal

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**General procedures.** $^1$H NMR spectra (400 or 300 MHz) and $^{13}$C NMR spectra (100 or 75 MHz) were measured in CDCl$_3$ or in acetone-$d_6$. Chemical shifts are reported in ppm relative to the internal solvent signal; CHCl$_3$ (7.26 ppm)/acetone-$d_6$ (2.04 ppm) for $^1$H NMR and CDCl$_3$ (77.0 ppm)/acetone-$d_6$ (30.3 ppm) for $^{13}$C NMR. FT-IR spectra were recorded for samples loaded as neat films on NaCl plates. Mass spectra were obtained according to the specified technique.

**2-Butoxy-1-(4-methoxyphenyl)pentan-1-ol (15):** To a solution of 4-methoxybenzaldehyde (408 mg, 3.0 mmol) in dibutyl ether (7) (100 mL, 587 mmol) was added Et$_3$B (2.6 mL, 18 mmol) at room temperature under argon atmosphere. After removal of the argon balloon, the mixture was stirred at the same temperature with continuous bubbling of air through a syringe needle with a balloon [flow rate; ca. 30 mL·h$^{-1}$·mmol$^{-1}$] for 20 h. The reaction mixture was treated with 28% NH$_3$·H$_2$O and extracted with CH$_2$Cl$_2$. The organic extract was dried over MgSO$_4$. Following solvent evaporation in vacuo, the residue was purified by silica gel column chromatography (AcOEt/Hex 1:4) to give alcohol 15 (511 mg, 64%; dr 71:29) as a colorless oil, unreacted aldehyde (29 mg, 7%) as a colorless oil and 1-(4-methoxyphenyl)propan-1-ol (36 mg, 7%) as a colorless oil. Alcohols *threo*-15a and *erythro*-15b were obtained by the following sequence; namely, acetylation of 15 (Ac$_2$O, Et$_3$N, DMAP, CH$_2$Cl$_2$, r.t.; 86% yield), the separation of the acetates by flash chromatography (Et$_2$O/toluene 1:13), and the reductive removal of the acetyl group with LAH (quant.). *threo*-Alcohol 15a: IR (neat) ν 3458 cm$^{-1}$; $^1$H NMR (400 MHz, CDCl$_3$) δ 7.30-7.24 (m, 2H), 6.91-6.85 (m, 2H), 4.47 (d, 1H, J=7.3 Hz), 3.81 (s, 3H), 3.58 (dt, 1H, J=9.1, 6.5 Hz), 3.42 (dt, 1H, J=9.1, 6.5 Hz), 3.33 (m, 1H), 1.62-1.54 (m, 2H), 1.44-1.20 (m, 6H), 0.93 (t, 3H, J=7.3 Hz), 0.84 (t, 3H, J=6.5 Hz); $^{13}$C NMR (100 MHz, CDCl$_3$) δ 159.0, 133.3, 128.0, 113.6, 84.1, 75.6, 70.4, 55.2, 32.7, 32.3, 19.4, 18.3, 14.3, 13.9; MS m/z: 266 (M$^+$), 137 (100%); HRMS (EI) calcd for C$_{16}$H$_{20}$O$_3$ (M$^+$): 266.1882, found: 266.1880. *erythro*-Alcohol 15b: IR (neat) ν 3447 cm$^{-1}$; $^1$H NMR (400 MHz, CDCl$_3$) δ 7.30-7.24 (m, 2H), 6.90-6.85 (m, 2H), 4.83 (d, 1H, J=4.0 Hz), 3.80 (s, 3H), 3.55 (dt, 1H, J=9.1, 6.5 Hz), 3.47 (dt, 1H, J=9.1, 6.5 Hz), 3.37 (dt, 1H, J=8.8, 3.8 Hz), 1.59-1.52 (m, 2H), 1.50-1.33 (m, 4H), 1.27-1.14 (m, 2H), 0.92 (t, 3H, J=7.2 Hz), 0.83 (t, 3H, J=7.1 Hz); $^{13}$C NMR (100 MHz, CDCl$_3$) δ 158.7, 132.9, 127.5, 113.5, 83.6, 73.7, 70.2, 55.2, 32.3, 31.0, 19.4, 19.1, 14.2, 13.9; MS m/z: 266 (M$^+$), 137 (100%); HRMS (EI) calcd for C$_{16}$H$_{20}$O$_3$.
(M⁺): 266.1882, found: 266.1880.

(4-Methoxyphenyl)(oxetan-2-yl)methanol (16): The title compound was obtained according to the above-mentioned procedure from 4-methoxybenzaldehyde (176 mg, 1.29 mmol), oxetane (8) (10 mL, 155 mmol) and Et₃B (1.1 mL, 7.75 mmol). The purification by silica gel column chromatography (AcOEt/Hex 1:2) gave less polar erythro-alcohol 16b (42 mg, 17%) as a colorless solid and more polar threo-alcohol 16a (150 mg, 60%) as a colorless solid (dr 78:22). threo-Alcohol 16a: Mp 51-53°C; IR (neat) ν 3404 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 7.31–7.25 (m, 2H), 6.92–6.85 (m, 2H), 4.84–4.72 (m, 2H), 4.67 (ddd, 1H, J=13.2, 7.3, 5.9 Hz), 4.57 (dt, 1H, J=8.8, 6.1 Hz), 3.80 (s, 3H), 2.62–2.43 (m, 2H); ¹³C NMR (75 MHz, CDCl₃) δ 159.4, 131.1, 128.0, 113.9, 84.9, 76.6, 68.3, 55.2, 23.7; MS m/z: 194 (M⁺), 137 (100%); HRMS (EI) calcd for C₁₁H₁₄O₃ (M⁺): 194.0943, found: 194.0949. erythro-Alcohol 16b: IR (neat) ν 3404 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 7.29–7.26 (m, 2H), 6.90–6.85 (m, 2H), 4.94 (dt, 1H, J=7.5, 3.5 Hz), 4.84 (d, 1H, J=3.3 Hz), 4.67 (dt, 1H, J=8.1, 5.7 Hz), 4.49 (dt, 1H, J=9.4, 5.7 Hz), 3.80 (s, 3H), 2.89–2.77 (m, 2H), 2.31 (m, 1H); ¹³C NMR (75 MHz, CDCl₃) δ 159.2, 130.3, 127.2, 113.8, 85.1, 73.9, 68.8, 55.2, 20.8; MS m/z: 194 (M⁺), 137 (100%); HRMS (EI) calcd for C₁₁H₁₄O₃ (M⁺): 194.0943, found: 194.0937.

(4-Methoxyphenyl)(oxepan-2-yl)methanol (17): The title compound was obtained according to the above-mentioned procedure from 4-methoxybenzaldehyde (255 mg, 1.87 mmol), oxepane (9) (25 mL, 225 mmol) and Et₃B (2.7 mL, 18.7 mmol). The purification by silica gel column chromatography (AcOEt/Hex 1:3) gave less polar erythro-alcohol 17b (33 mg, 7%) as a colorless oil and more polar threo-alcohol 17a (245 mg, 56%) as a colorless oil (dr 88:12). threo-Alcohol 17a: IR (neat) ν 3447 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 7.31–7.24 (m, 2H), 6.90–6.84 (m, 2H), 4.35 (d, 1H, J=8.4 Hz), 4.01 (ddd, 1H, J=11.7, 6.2, 4.6 Hz), 3.80 (s, 3H), 3.67 (ddd, 1H, J=12, 7.2, 4.4 Hz), 3.48 (m, 1H), 1.87–1.32 (m, 8H); ¹³C NMR (75 MHz, CDCl₃) δ 159.3, 132.7, 128.5, 113.7, 84.4, 76.6, 69.3, 55.2, 31.3, 30.9 26.5 25.7; MS m/z: 236 (M⁺), 137 (100%); HRMS (EI) calcd for C₁₃H₂₀O₃ (M⁺): 236.1413, found: 236.1410. erythro-Alcohol 17b: IR (neat) ν 3420 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 7.30–7.25 (m, 2H), 6.90–6.84 (m, 2H), 4.65 (d, 1H, J=4.6 Hz), 3.88 (s, 1H), 3.80 (s, 3H), 3.67 (ddd, 1H, J=9.2, 4.6, 3.1 Hz), 3.56 (ddd, 1H, J=12, 7.2, 4.3 Hz), 2.50 (brs, 1H), 1.88–1.35 (m, 8H); ¹³C
NMR (75 MHz, CDCl₃) δ 158.8, 133.4, 127.8, 113.5, 82.9, 76.3, 70.0, 55.2, 30.8, 29.8, 26.3, 26.2; MS m/z: 236 (M⁺), 137 (100%); HRMS (EI) calcd for C₁₄H₂₀O₃ (M⁺): 236.1413, found: 236.1413.

C2/C4-hydroxyalkylation products 18: (1,3-dioxolan-2-yl)(4-methoxyphenyl)methanol (18a) and (1,3-dioxolan-4-yl)(4-methoxyphenyl)methanol (18b): The title compounds were obtained according to the above-mentioned procedure from 4-methoxybenzaldehyde (408 mg, 3.0 mmol), 1,3-dioxolane (10) (25 mL, 360 mmol) and Et₃B (2.6 mL, 18 mmol). The purification by silica gel column chromatography (AcOEt/Hex 1:2) gave less polar C4-hydroxyalkylation product 18b (70 mg, 11%) as a colorless oil and more polar C2-hydroxyalkylation product 18a (428 mg, 68%) as a colorless oil (C2:C4=86:14). **C2-hydroxyalkylation product 18a:** IR (neat) ν 3458 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 7.38-7.32 (m, 2H), 6.93-6.87 (m, 2H), 4.99 (d, 1H, J=4.4 Hz), 4.62 (d, 1H, J=4.4 Hz), 4.05-3.87 (m, 4H), 3.80 (s, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 159.3, 131.0, 128.0, 113.7, 105.6, 74.0, 65.6, 65.3, 55.2; MS m/z: 210 (M⁺), 137 (100%); HRMS (EI) calcd for C₁₁H₁₄O₄ (M⁺): 210.0892, found: 210.0895. **C4-hydroxyalkylation product 18b:** IR (neat) ν 3458 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.32-7.28 (m, 2H), 6.92-6.87 (m, 2H), 5.10 (s, 1H), 4.94 (s, 1H), 4.53 (d, 1H, J=7.6 Hz), 4.18 (dt, 1H, J=7.0, 6.1 Hz), 3.80 (s, 3H), 3.70 (dd, 1H, J=8.5, 7.0 Hz), 3.62 (dd, 1H, J=8.7, 5.9 Hz), 2.60 (brs, 1H); ¹³C NMR (100 MHz, CDCl₃) δ 159.6, 131.4, 128.1, 114.0, 95.5, 79.9, 74.7, 66.5, 55.3; MS m/z: 210 (M⁺), 137 (100%); HRMS (EI) calcd for C₁₁H₁₄O₄ (M⁺): 210.0892, found: 210.0899.

C₅⁺-hydroxyalkylation product 19a and C₂⁺-hydroxyalkylation product 19b: The title compounds were obtained according to the above-mentioned procedure from 4-methoxybenzaldehyde (408 mg, 3.0 mmol), 2-methyltetrahydrofuran (11) (30 mL, 297 mmol) and Et₃B (2.6 mL, 18 mmol). The purification by silica gel column chromatography (Et₂O/benzene 1:3) gave less polar C2-hydroxyalkylation product 19b (39 mg, 6%) as a colorless oil and a mixture of 19a and 19b (520 mg, 78%) as a colorless oil. Detailed ¹H NMR analysis of the products indicated that 229 mg (34%) of less polar C2-alkylation product 19b (threo/erythro ratio** 71:29) and 291 mg (44%) of more polar C5-alkylation product 19a (threo/erythro 91:9, ** cis/trans ratio** 78:22) were produced in the above-mentioned reaction (See ¹H NMR spectra on page S42). *2-Methyltetrahydrofuran Numbering.

**The stereochemistry of the major compound has yet to be determined.** Shown below are the NMR
data and the analytical data of less polar C2-hydroxalkylation product 19b that was partially separated. **Less polar C2-hydroxalkylation product 19b**: IR (neat) ν 3445 cm\(^{-1}\); \(^1\)H-NMR (300 MHz, CDCl\(_3\)) δ 7.35-7.25 (m, 2H), 6.90-6.82 (m, 2H), 4.51 (s, 1H), 3.95-3.80 (m, 2H), 3.80 (s, 3H), 2.10-1.90 (m, 3H), 1.60-1.48 (m, 1H), 1.08 (s, 3H); \(^1^3\)C NMR (100 MHz, CDCl\(_3\)) δ 158.9, 132.6, 128.4, 113.3, 85.8, 78.4, 68.0, 55.2, 34.5, 26.4, 21.3; MS m/z: 222 (M\(^+\)), 85 (100%); HRMS (EI) calcd for C\(_{13}\)H\(_{16}\)O\(_3\) (M\(^+\)): 222.1256, found: 222.1250.

**2-Butoxy-1-(4-methoxyphenyl)propan-1-ol (20) and 2-Ethoxy-1-(4-methoxyphenyl)pentan-1-ol (21)**: The title compounds were obtained according to the above-mentioned procedure from 4-methoxybenzaldehyde (102 mg, 0.75 mmol), butyl ethyl ether (12) (25 mL, 184 mmol) and Et\(_3\)B (0.65 mL, 4.49 mmol). The purification by silica gel column chromatography (AcOEt/toluene 1:6) gave unreacted aldehyde (31 mg, 30%) as a colorless oil, a mixture of alcohol 20 (52 mg, 29%, dr 71:29) and 21 (37 mg, 21%, dr 72:28) as a colorless oil (50% combined yield), and ethyl adduct (3 mg, 2%) as a colorless oil. Further elution with AcOEt/Hex (1:3) afforded 4-methoxybenzylalcohol (2 mg, 2%) as a colorless oil. The yields and relative ratio of the products 20 and 21 were determined by \(^1\)H NMR analysis (see S51). Alcohols 20a and 21a were obtained by the following sequence; namely, acetylation of a mixture of 20 and 21 (Ac\(_2\)O, Et\(_3\)N, DMAP, CH\(_2\)Cl\(_2\), r.t.; 94% yield), the separation of the acetates by flash chromatography (Et\(_2\)O/Hex 1:14), and the reductive removal of the acetyl group with LAH. The separation of 20b and 21b was found to be unsuccessful, however. Therefore, authentic erythro-alcohols 20b and 21b whose spectroscopic and analytical data are shown below were prepared via the Mitsunobu inversion of each compound of 20a and 21a (4-NO\(_2\)C\(_6\)H\(_4\)CO\(_2\)H, PPh\(_3\); DEAD, toluene, r.t.) followed by ester hydrolysis (20% aq. NaOH, MeOH, r.t.). **threo-Alcohol 20a**: IR (neat) ν 3479 cm\(^{-1}\); \(^1\)H NMR (400 MHz, acetone-\(d_6\)) δ 7.30-7.26 (m, 2H), 6.88-6.84 (m, 2H), 4.40 (dd, 1H, J=6.8, 2.8 Hz), 3.88 (d, 1H, J=2.8 Hz), 3.77 (s, 3H), 3.57 (dt, 1H, J=9.1, 6.5 Hz), 3.47-3.40 (m, 2H), 1.57-1.50 (m, 2H), 1.42-1.33 (m, 2H), 0.90(t, 3H, J=7.4 Hz); MS m/z: 238 (M\(^+\)), 137 (100%); HRMS (EI) calcd for C\(_{14}\)H\(_{22}\)O\(_3\) (M\(^+\)): 238.1569, found: 238.1573. **erythro-Alcohol 20b**: IR (neat) ν 3470 cm\(^{-1}\); \(^1\)H NMR (400 MHz, acetone-\(d_6\)) δ 7.31-7.26 (m, 2H),
6.88-6.84 (m, 2H), 4.60 (t, 1H, J=4.0 Hz), 3.91 (d, 1H, J=4.0 Hz), 3.76 (s, 3H), 3.50-3.42 (m, 2H). 3.30 (dt, 1H, J=9.2, 6.3 Hz), 1.46-1.38 (m, 2H), 1.32-1.23 (m, 2H), 1.02 (d, 3H, J=6.2 Hz), 0.84 (t, 3H, J=7.3 Hz); 13C NMR (100 MHz, acetone-d6) δ 160.0, 136.1, 129.0, 114.3, 81.0, 76.2, 69.7, 55.9, 33.4, 20.4, 15.6, 14.7; MS m/z: 238 (M⁺), 137 (100%); HRMS (EI) calcd for C14H22O3 (M⁺): 238.1569, found: 238.1572. **three-Alcohol 21a:** IR (neat) ν 3447 cm⁻¹; 1H NMR (400 MHz, acetone-d6) δ 7.30-7.26 (m, 2H), 6.88-6.84 (m, 2H), 4.53 (dd, 1H, J=6.1, 3.8 Hz), 3.90 (d, 1H, J=3.8 Hz), 3.76 (s, 3H), 3.64-3.51 (m, 2H), 3.33 (ddd, 1H, J=7.7, 6.2, 3.5 Hz), 1.44-1.14 (m, 4H), 1.12 (t, 3H, J=7.1 Hz), 0.80 (t, 3H, J=7.1 Hz); 13C NMR (100 MHz, acetone-d6) δ 160.2, 135.9, 129.3, 114.4, 85.1, 76.2, 67.1, 55.9, 34.1, 19.9, 16.5, 15.0; MS m/z: 238 (M⁺), 137 (100%); HRMS (EI) calcd for C14H22O3 (M⁺): 238.1569, found: 238.1575. **erythro-Alcohol 21b:** IR (neat) ν 3447 cm⁻¹; 1H NMR (300 MHz, acetone-d6) δ 7.32-7.27 (m, 2H), 6.88-6.83 (m, 2H), 4.64 (t, 1H, J=4.3 Hz), 3.94 (d, 1H, J=4.0 Hz), 3.76 (s, 3H), 3.46-3.35 (m, 2H), 3.30 (m, 1H), 1.52-1.19 (m, 4H), 1.02 (t, 3H, J=7.0 Hz), 0.83 (t, 3H, J=7.1 Hz); 13C NMR (75 MHz, acetone-d6) δ 160.1, 136.4, 129.2, 114.4, 85.1, 75.3, 66.7, 55.9, 33.5, 20.1, 16.4, 15.0; MS m/z: 238 (M⁺), 137 (100%); HRMS (EI) calcd for C14H22O3 (M⁺): 238.1569, found: 238.1571.

**2,3-Dimethoxy-1-(4-methoxyphenyl)propan-1-ol (22) and 2-(2-Methoxyethoxy)-1-(4-methoxyphenyl)ethanol (23):** The title compounds were obtained according to the above-mentioned procedure from 4-methoxybenzaldehyde (408 mg, 3.0 mmol), ethyleneglycol dimethyl ether (13) (50 mL, 480 mmol) and Et3B (2.6 mL, 18 mmol). The purification by silica gel column chromatography (AcOEt/Hex 1:5) gave unreacted aldehyde (70 mg, 17%) and ethyl adduct (40 mg, 8%). Further elution with AcOEt/Hex (1:4 to 1:1) afforded 4-methoxybenzylalcohol (54 mg, 13%) and a mixture of alcohols 22 (dr 51:49) and 23 (376 mg, 55% combined yield, 22:23=62:38). The relative ratio of 22 and 23 was determined by 1H NMR analysis (see S58). Careful purification by silica gel chromatography (AcOEt/Hex 1:1) provided partially separated alcohol 23. Alcohols 22a and 22b were separated by the following sequence; namely, acetylation of 22 with standard protocols (Ac₂O, Et₃N, DMAP, CH₂Cl₂, r.t.; 65% yield), the separation of the acetates by flash chromatography (eluted with Et₂O/Hex 1:5), and reduction with LAH.
**three-Alcohol 22a**: IR (neat) ν 3447 cm⁻¹; ¹H NMR (400 MHz, acetone-d₆) δ 7.32-7.27 (m, 2H), 6.89-6.85 (m, 2H), 4.64 (d, 1H, J=5.9 Hz), 3.98 (brs, 1H), 3.77 (s, 3H), 3.44-3.34 (m, 2H), 3.38 (s, 3H), 3.21 (s, 3H), 3.13 (dd, 1H, J=10.0, 5.6 Hz); ¹³C NMR (100 MHz, acetone-d₆) δ 160.2, 135.4, 129.1, 114.4, 86.2, 73.9, 73.2, 59.5, 59.4, 55.9; MS m/z: 226 (M⁺), 136 (100%); HRMS (EI) calcd for C₁₂H₁₈O₄ (M⁺): 226.1205, found: 226.1201.

**erythro-Alcohol 22b**: IR (neat) ν 3437 cm⁻¹; ¹H NMR (400 MHz, acetone-d₆) δ 7.31-7.27 (m, 2H), 6.88-6.84 (m, 2H), 4.66 (t, 1H, J=4.6 Hz), 4.18 (d, 1H, J=4.4 Hz), 3.76 (s, 3H), 3.49-3.39 (m, 3H), 3.26 (s, 3H), 3.24 (s, 3H); ¹³C NMR (100 MHz, acetone-d₆) δ 160.1, 135.8, 129.2, 114.3, 85.7, 74.0, 73.8, 59.5, 59.1, 55.9; MS m/z: 226 (M⁺), 136 (100%); HRMS (EI) calcd for C₁₂H₁₈O₄ (M⁺): 226.1205, found: 226.1199.

**2-(2-Methoxyethoxy)-1-(4-methoxyphenyl)ethanol (23)**: IR (neat) ν 3447 cm⁻¹; ¹H NMR (300 MHz, acetone-d₆) δ 7.33-7.28 (m, 2H), 6.90-6.84 (m, 2H), 4.75 (dt, 1H, J=7.7, 3.8 Hz), 4.12 (d, 1H, J=3.5 Hz), 3.76 (s, 3H), 3.63-3.41 (m, 6H), 3.28 (s, 3H); ¹³C NMR (75 MHz, acetone-d₆) δ 160.4, 135.7, 128.7, 114.7, 78.5, 73.2, 73.1, 71.6, 59.3, 55.9; MS m/z: 226 (M⁺), 137 (100%); HRMS (EI) calcd for C₁₂H₁₈O₄ (M⁺): 226.1205, found: 226.1206.

**Hydroxyalkylation of ethyl vinyl ether (24)**: The reaction was carried out according to the above-mentioned procedure using 4-methoxybenzaldehyde (408 mg, 3.0 mmol), ethyl vinyl ether (24) (17 mL, 180 mmol) and Et₃B (1.3 mL, 9.0 mmol). The purification by silica gel column chromatography (AcOEt/Hex 1:6) gave a mixture of alcohols 21 (469 mg, 66%, dr 72:28) and 25 (91 mg, 10%). The yields and relative ratio of 21 and 25 were determined by ¹H NMR analysis (see S61). TLC analysis and NMR spectra indicated that compounds 21a and 21b were identical to those obtained by the hydroxyalkylation reaction of butyl ethyl ether (12). Shown below are the NMR data and the analytical data of alcohol 25 which was partially separated by silica gel chromatography (AcOEt/Hex 1:6).

**2,4-Diethoxy-1-(4-methoxyphenyl)heptan-1-ol (25)**: IR (neat) ν 3433 cm⁻¹; ¹H NMR (400 MHz, CDCl₃)* δ 7.33-7.26 (m, 2H), 6.90-6.86 (m, 2H), 4.54 (d, 1H, J=6.5 Hz), 3.81 (s, 3H), 3.66-3.25 (m, 5H), 3.01 (m, 1H), 1.65-1.09 (m, 6H), 1.19 (t, 3H, J=7.0 Hz), 1.17 (t, 3H, J=7.1 Hz), 0.85 (t, 3H, J=7.2 Hz); ¹³C NMR (100 MHz, CDCl₃) δ 159.1, 133.3, 128.2, 113.6, 81.3, 76.0, 75.8, 65.5, 64.1, 55.3, 36.4, 35.8, 18.4, 15.7, 15.6, 14.3; MS m/z: 293 (M⁺-17), 101 (100%); HRMS
(FAB) calc'd for C_{18}H_{31}O_{3} (MH^+): 311.2222, found: 311.2219. *The major signals are shown.

**SI. Scheme 1. Determination of Stereochemistry of Alcohol 14**

**Synthesis of ether 28 (from alcohol 14a):** To a stirred solution of alcohol 14a (30 mg, 0.14 mmol) in DMF (1 mL) at 0°C was added NaNH (60% in oil; 9.0 mg, 0.23 mmol). The mixture was allowed to warm to room temperature and stirred for 20 min. To this mixture was added EtI (21 μL, 0.26 mmol), and the mixture was stirred for 40 min, treated with sat. NH_{4}Cl and extracted with Et_{2}O. The extract was dried over MgSO_{4} and concentrated in vacuo. The residue was purified by silica gel column chromatography (AcOEt/Hex 1:6) to give ether 28 (34 mg, 99%) as a colorless oil. TLC analysis and NMR spectra showed that ether 28 is identical to the authentic material prepared by the following protocol. IR (neat) ν 2974 cm\(^{-1}\); \(^1\)H NMR (300 MHz, CDCl\(_3\)) δ 7.23-7.18 (m, 2H), 6.89-6.84 (m, 2H), 4.15 (d, 1H, J=6.1 Hz), 3.80 (s, 3H), 3.60 (q, 2H, J=7.0 Hz), 3.56 (dq, 1H, J=6.4, 6.2 Hz), 3.42 (dq, 1H, J=9.4, 7.2 Hz), 3.35 (dq, 1H, J=9.4, 7.0 Hz), 1.17 (t, 3H, J=7.2 Hz), 1.16 (t, 3H, J=7.0 Hz), 0.92 (d, 3H, J=6.4 Hz); \(^13\)C NMR (75 MHz, CDCl\(_3\)) δ 159.0, 132.1, 128.6, 113.4, 85.0, 78.5, 65.4, 64.4, 55.2, 16.7, 15.6, 15.3; MS m/z: 238 (M\(^{+}\)), 165 (100%); HRMS (EI) calc'd for C_{13}H_{22}O_{3} (M\(^{+}\)): 238.1569, found: 238.1566.

**Synthesis of diol 30:** To a solution of anethole (29) (530 mg, 3.58 mmol) in aq. t-BuOH (1:1 v/v, 36 mL) at room temperature was added AD-mix-β (5.0 g). After stirring for 24 h, the mixture was treated with sat. Na_{2}S_{2}O_{3} and extracted with AcOEt, and the organic layer was washed with brine. The extract
was dried over MgSO$_4$ and concentrated in vacuo. The residue was purified by silica gel column chromatography (AcOEt/Hex 1:1) to give diol 30 (593 mg, 91%) as a colorless solid. Mp 82-83°C; IR (neat) ν 3425 cm$^{-1}$; $^1$H NMR (300 MHz, CDCl$_3$) δ 7.27-7.22 (m, 2H), 6.90-6.85 (m, 2H), 4.29 (d, 1H, $J$=7.7 Hz), 3.81 (m, 1H), 3.80 (s, 3H), 2.68 (brs, 1H), 2.60 (brs, 1H), 1.02 (d, 3H, $J$=6.2 Hz); $^{13}$C NMR (75 MHz, CDCl$_3$) δ 159.3, 133.2, 128.0, 113.8, 79.0, 72.2, 55.2, 18.6; MS m/z: 182 (M$^+$), 137 (100%); HRMS (EI) calcd for C$_{10}$H$_{14}$O$_3$ (M$^+$): 182.0943, found: 182.0946.

**Synthesis of ether 28 (from diol 30):** To a stirred solution of diol 30 (36 mg, 0.20 mmol) in DMF (1 mL) at 0°C was added NaH (60% in oil; 28 mg, 0.70 mmol). The mixture was allowed to warm to room temperature and stirred for 10 min. To this mixture was added EtI (65 µL, 0.80 mmol), and the mixture was stirred for 2 h, treated with sat. NH$_4$Cl and extracted with Et$_2$O. The extract was dried over MgSO$_4$ and concentrated in vacuo. The residue was purified by silica gel column chromatography (AcOEt/Hex 1:6) to give ether 28 (45 mg, 96%) as a colorless oil.

**Scheme 2. Determination of Stereochemistry of Alcohol 15**

**Synthesis of ether 31 (from alcohol 15a):** To a stirred solution of alcohol 15a (33 mg, 0.12 mmol) in DMF (1 mL) at 0°C was added NaH (60% in oil; 8.0 mg, 0.20 mmol). The mixture was allowed to warm to room temperature and stirred for 10 min. To this mixture was added BuI (25 µL, 0.22 mmol), and the mixture was stirred for 11 h, treated with sat. NH$_4$Cl and extracted with Et$_2$O. The extract was
dried over MgSO₄ and concentrated in vacuo. The residue was purified by silica gel column chromatography (AcOEt/Hex 1:20) to give ether 31 (37 mg, 93%) as a colorless oil. TLC analysis and the NMR spectra showed ether 31 to be identical to the authentic material that was prepared according to the following protocol. IR (neat) ν 2959 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 7.22-7.17 (m, 2H), 6.89-6.83 (m, 2H), 4.18 (d, 1H, J=6.2 Hz), 3.81 (s, 3H), 3.68 (dt, 1H, J=9.0, 6.4 Hz), 3.46 (dt, 1H, J=9.2, 6.6 Hz), 3.37-3.21 (m, 3H), 1.61-1.12 (m, 12H), 0.9 (t, 3H, J=7.2 Hz), 0.88 (t, 3H, J=7.2 Hz), 0.81 (t, 3H, J=7.0 Hz); ¹³C NMR (75 MHz, CDCl₃) δ 158.9, 132.3, 128.6, 113.4, 84.5, 82.9, 71.6, 68.8, 55.1, 33.5, 32.4, 32.0, 29.7, 19.4, 19.0, 14.1, 13.9, 13.87; MS m/z: 322 (M⁺), 193 (100%); HRMS (EI) calcd for C₂₅H₃₄O₃ (M⁺): 322.2508, found: 322.2503.

**Synthesis of olefin 33:** To a stirred solution of alcohol 32 (322 mg, 1.66 mmol) in benzene (7 mL) at room temperature were added TsOH·H₂O (1.0 mg, 0.005 mmol) and Na₂SO₄ (40 mg, 0.28 mmol). After stirring for 1 h at reflux, Na₂SO₄ (40 mg, 0.28 mmol) was added. After 2 h, the mixture was filtered through a celite pad, and the filtrate was extracted with Et₂O and washed with sat. NaHCO₃. The extract was dried over MgSO₄ and concentrated in vacuo. The residue was purified by silica gel column chromatography (AcOEt/Hex 1:80) to give olefin 33 (256 mg, 88%) as a colorless oil. IR (neat) ν 2959 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 7.30-7.25 (m, 2H), 6.86-6.81 (m, 2H), 6.33 (d, 1H, J=16 Hz), 6.08 (dt, 1H, J=16, 6.8 Hz), 3.80 (s, 3H), 2.17 (ddd, 2H, J=15.8, 7.0, 1.3 Hz), 1.48 (dq, 2H, J=14.5, 7.2 Hz), 0.95 (t, 3H, J=7.3 Hz); ¹³C NMR (75 MHz, CDCl₃) δ 158.6, 130.8, 129.2, 128.8, 126.9, 113.9, 55.2, 35.1, 22.6, 13.7; MS m/z: 176 (M⁺), 147 (100%); HRMS (EI) calcd for C₁₂H₁₆O (M⁺): 176.1201, found: 176.1198.

**Synthesis of diol 34:** To a solution of olefin 33 (197 mg, 1.12 mmol) in aq. t-BuOH (1:1 v/v, 12 mL) at room temperature was added AD-mix-β (1.6 g). After stirring for 16 h, the mixture was treated with sat. Na₂S₂O₃ and extracted with AcOEt, and the organic layer was washed with brine. The extract was dried over MgSO₄ and concentrated in vacuo. The residue was purified by silica gel column chromatography (AcOEt/Hex 1:2) to give diol 34 (221 mg, 94%) as a colorless oil. IR (neat) ν 3383 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 7.27-7.21 (m, 2H), 6.91-6.85 (m, 2H), 4.36 (d, 1H, J=7.2 Hz), 3.80 (s, 3H), 3.65 (m, 1H), 2.30 (brs, 2H), 1.57-1.20 (m, 4H), 0.84 (t, 3H, J=7.0 Hz); ¹³C NMR (75
MHz, CDCl₃) δ 159.4, 133.3, 128.0, 113.9, 77.6, 75.8, 55.2, 34.7, 18.8, 13.9; MS m/z: 210 (M⁺), 137 (100%); HRMS (EI) calc for C₁₂H₁₈O₃ (M⁺): 210.1256, found: 210.1258.

**Synthesis of ether 31 (from diol 34):** To a stirred solution of diol 34 (44 mg, 0.21 mmol) in DMF (1 mL) at 0°C was added NaH (60% in oil; 29 mg, 0.73 mmol). The mixture was allowed to warm to room temperature. After stirring for 10 min, Bu₃SnH (95 µL, 0.84 mmol) was added. After 10 min, additional NaH (60% in oil; 29 mg, 0.73 mmol) was added, and stirring was continued for another 3 h. The mixture was treated with sat. NH₄Cl, extracted with Et₂O, dried over MgSO₄ and concentrated under vacuo. The residue was purified by silica gel column chromatography (AcOEt/Hex 1:20) to give ether 31 (64 mg, 95%) as a colorless oil.

**SI. Scheme 3. Determination of Stereochemistry of Alcohol 16**

![Scheme 3](image)

**Erythro-diol 35 (from less polar 16b):** To a solution of alcohol 16b (37 mg, 0.19 mmol) in THF (1.5 mL) at 0°C was added LAH (22 mg, 0.57 mmol). After stirring for 10 min at room temperature, the mixture was heated at reflux for 30 min. The mixture, cooled to 0°C, was treated with 28% NH₄OH and stirred at room temperature for an additional 30 min. Following addition of celite, the mixture was filtered through a celite pad and concentrated in vacuo to provide sufficiently pure diol 35 (37 mg, quant.) as a colorless solid. This compound was recrystallized from Et₂O-hexane to give colorless prisms. Mp 79-80°C; IR (neat) ν 3391 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 7.32-7.26 (m, 2H), 6.93-6.87 (m, 2H), 4.62 (d, 1H, J=4.6 Hz), 3.81 (s, 3H), 3.77-3.68 (m, 1H), 1.85 (brs, 2H), 1.60-1.20 (m, 2H), 0.97 (t, 3H, J=7.3 Hz); ¹³C NMR (100 MHz, CDCl₃) δ 159.1, 132.5, 128.0, 113.7, 76.6, 76.4.
55.3, 24.9, 10.3; MS m/z: 196 (M⁺), 137 (100%); HRMS (EI) calcd for C₁₁H₁₀O₃ (M⁺): 196.1100; found: 196.1103.

**Acetal 36:** To a solution of *erythro* diol 35 (20 mg, 0.10 mmol) in 3,3-dimethoxypropane (3 mL) at room temperature was added PPTS (7.5 mg, 0.03 mmol). After stirring for 1 h, the mixture was extracted with Et₂O, washed with sat. NaHCO₃, dried over MgSO₄ and concentrated in vacuo. The residue was purified by silica gel column chromatography (AcOEt/Hex 1:12) to give acetal 36 (17 mg, 73%) as a colorless oil. NOE analysis of this compound indicated that the ethyl and 4-methoxyphenyl substituents in 36 assumed a *syn*-arrangement. IR (neat) ν 2984 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.4-7.72 (m, 2H), 6.85-6.85 (m, 2H), 5.14 (d, 1H, J=6.6 Hz), 4.22 (ddd, 1H, J=11, 6.6, 4.4 Hz), 3.80 (s, 3H), 1.62 (s, 3H), 1.46 (s, 3H), 1.23-1.13 (m, 1H), 1.03-0.93 (m, 1H), 0.81 (t, 3H, J=7.3 Hz); ¹³C NMR (100 MHz, CDCl₃) δ 159.0, 130.2, 128.2, 113.4, 107.8, 80.6, 79.8, 55.2, 27.6, 25.1, 24.7, 10.6; MS m/z: 236 (M⁺), 178 (100%); HRMS (EI) calcd for C₁₄H₂₀O₃ (M⁺): 236.1413; found: 236.1408

**SI. Scheme 4. Synthesis of Authentic *threo*-Alcohol 17a**

![Chemical Diagram]

**Synthesis of tosylate 39:** To a solution of alcohol 38 (97 mg, 0.442 mmol) in CH₂Cl₂ (3 mL) at room temperature were added Et₃N (245 μL, 1.77 mmol) and TsCl (126 mg, 0.662 mmol). After stirring for 11 h, Et₃N (184 μL, 1.32 mmol) and TsCl (84 mg, 0.44 mmol) were added. After 2.5 h, the mixture
was extracted with Et$_2$O, washed with brine and dried over MgSO$_4$. Following solvent evaporation in vacuo, the residue was purified by silica gel column chromatography (AcOEt/Hex 1:6) to give tosylate 39 (144 mg, 87%, $E/Z$=96:4) as a colorless oil. IR (neat) ν 2934 cm$^{-1}$; $^1$H NMR (300 MHz, CDCl$_3$), an asterisk indicates the minor (Z)-isomer.) δ 7.81-7.76 (m, 2H), 7.34-7.20 (m, 4H), 6.87-6.80 (m, 2H), 6.29 (d, 1H, J=15.8 Hz), 6.00 (dt, 1H, J=15.8, 7.0 Hz), 5.48* (dt, J=11.6, 7.2 Hz), 4.03 (t, 2H, J=6.4 Hz), 3.80 (s, 3H), 2.43 (s, 3H), 2.17-2.10 (m, 2H), 1.72-1.60 (m, 2H), 1.46-1.30 (m, 4H); $^{13}$C NMR (75 MHz, CDCl$_3$) δ 158.7, 144.6, 133.2, 130.6, 129.8, 129.5, 128.2, 127.9, 127.0, 113.9, 70.5, 55.3, 32.7, 28.7, 24.9, 21.6, 14.1; MS m/z: 374 (M$^+$), 147 (100%); HRMS (EI) calcd for C$_{21}$H$_{26}$O$_6$S(M$^+$): 374.1552, found: 374.1549.

**Diol 40:** To a solution of tosylate 39 (119 mg, 0.32 mmol) in aq. t-BuOH (1:1 v/v, 3.2 mL) at room temperature was added AD-mix-β (446 mg). After stirring for 7 h, aq. t-BuOH (1:1 v/v, 3.2 mL) and AD-mix-β (446 mg) were added, and stirring was continued for an additional 12 h. The mixture was treated with sat. Na$_2$S$_2$O$_3$ and extracted with AcOEt, and the organic layer was washed with brine. The extract was dried over MgSO$_4$ and concentrated in vacuo. The residue was purified by silica gel column chromatography (AcOEt/Hex 1:2) to give diol 40 (104 mg, 80%) as a colorless oil. IR (neat) ν 3416 cm$^{-1}$; $^1$H-NMR (300 MHz, CDCl$_3$) δ 7.79-7.74 (m, 2H), 7.32 (d, 2H, J=7.9 Hz), 7.80-7.22 (m, 2H), 6.92-6.86 (m, 2H), 4.35 (d, 1H, J=7.3 Hz), 3.98 (t, 2H, J=6.4 Hz), 3.81 (S, 3H), 3.66-3.57 (m, 1H), 2.44 (s, 3H), 2.00 (brs, 2H), 1.65-1.55 (m, 2H), 1.47-1.18 (m, 6H); $^{13}$C NMR (75 MHz, CDCl$_3$) δ 159.4, 144.6, 133.2, 133.1, 129.8, 128.0, 127.8, 113.9, 77.6, 75.7, 70.5, 55.2, 32.3, 28.6, 25.2, 24.9, 21.6; MS m/z: 408 (M$^+$), 137 (100%); HRMS (EI) calcd for C$_{21}$H$_{26}$O$_6$S(M$^+$): 408.1607, found: 408.1599.

**Threeo-alcohol 17a (from diol 40):** To a solution of diol 40 (28 mg, 0.07 mmol) in DMF (1 mL) at 0°C was added NaH (60% in oil; 21 mg, 0.51 mmol), and the mixture was allowed to warm to room temperature. After stirring for 1 h, the mixture was poured into sat. NH$_4$Cl and extracted with AcOEt. The extract was dried over MgSO$_4$ and concentrated in vacuo. The residue was purified by silica gel column chromatography (AcOEt/Hex 1:2) to give threeo alcohol 17a (6.7 mg, 41%) as a colorless oil. TLC analysis and NMR spectra indicated that ether 17a was identical to the major alcohol obtained by
the hydroxyalkylation reaction of oxepane (9).

Synthesis of authentic three-butyl ether 20a (SI. Scheme 5): To a solution of three-diol 30 (100 mg, 0.55 mmol) in benzene (3 mL) at room temperature were added n-PrCHO (100 μL, 1.1 mmol) and PPTS (41 mg, 0.17 mmol). After stirring for 12 h under reflux with the Dean-Stark apparatus, the mixture was extracted with Et₂O and washed with sat. NaHCO₃. The extract was dried over Na₂SO₄ and concentrated in vacuo. The residue was purified by silica gel column chromatography (AcOEt/Hex 1:20) to give acetal 41 (109 mg, 84%, dr 1:1) as a colorless oil.

(4R,5R)-4-(4-Methoxyphenyl)-5-methyl-2-propyl-1,3-dioxolane (41): IR (neat) ν 2962 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 7.34-7.24 (m, 2H), 6.93-6.86 (m, 2H), 5.32 (t, 0.5H, J=4.7 Hz), 5.24 (t, 0.5H, J=4.7 Hz), 4.41 (d, 0.5H, J=7.5 Hz), 4.36 (d, 0.5H, J=8.0 Hz), 3.90-3.80 (m, 1H), 3.81 (s, 3H), 1.79-1.69 (m, 2H), 1.60-1.45 (m, 2H), 1.34 (d, 1.5H, J=6.0 Hz), 1.28 (d, 1.5H, J=6.0 Hz), 1.00 (t, 1.5H, J=7.3 Hz), 0.98 (t, 1.5H, J=7.3 Hz); ¹³C NMR (75 MHz, CDCl₃) δ 159.7, 159.5, 131.1, 129.9, 127.6, 127.6, 114.0, 104.8, 103.8, 85.6, 84.1, 80.8, 78.9, 55.3, 36.9, 36.8, 17.2, 17.18, 17.0, 16.2, 14.1, 14.07;
MS m/z: 236 (M⁺), 192 (100%); HRMS (EI) calcd for C₁₄H₂₀O₃ (M⁺): 236.1412, found: 236.1415.

Acetal 41 was subjected to the following reductive acetal cleavage. To a stirred solution of acetal 41 (64 mg, 0.27 mmol) in toluene (2 mL) at room temperature was added DIBAL (0.95 M in hexane, 340 μL, 0.32 mmol). After 30 min, the mixture was treated with additional DIBAL (0.95 M in hexane, 570 μL, 0.54 mmol) and stirred for an additional 1 h. DIBAL (0.95 M in hexane, 570 μL, 0.54 mmol) was again added and then the mixture was stirred for 2 h. The mixture, cooled to 0°C, was treated with 28% NH₄OH and stirred at room temperature for an additional 30 min. Following addition of celite, the mixture was filtered through a celite pad and concentrated in vacuo to give a mixture of alcohols 20a and 42 (64 mg, quant.) as a colorless oil. Acetylation of a mixture of 20a and 42 with standard protocol (Ac₂O, Et₃N, DMAP, CH₂Cl₂, r.t.; 88% yield) followed by the separation of the acetates by flash chromatography (Et₂O/Hex 1:12) and subsequent reduction with LAH afforded pure threo-alcohol 20a. TLC analysis and NMR spectra indicated that alcohol 20a was identical to the major alcohol obtained by the hydroxyalkylation of butyl ethyl ether (12).

**Synthesis of authentic threo-ethyl ether 21a:** To a solution of threo-diol 34 (205 mg, 0.98 mmol) in benzene (5 mL) at room temperature were added acetaldehyde (110 μL, 1.95 mmol) and PPTS (74 mg, 0.29 mmol). After stirring for 50 min under reflux with the Dean-Stark apparatus, additional acetaldehyde (110 μL, 1.95 mmol) was added. After stirring for 50 min, the mixture was extracted with Et₂O, washed with sat. NaHCO₃, dried over Na₂SO₄ and concentrated in vacuo. The residue was purified by silica gel column chromatography (AcOEt/Hex 1:15) to give acetal 43 (188 mg, 81%, dr 3:2) as a colorless oil.

**(4R,5R)-4-(4-methoxyphenyl)-2-methyl-5-propyl-1,3-dioxolane (43):** IR (neat) ν 2959 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 7.34-7.24 (m, 2H), 6.93-6.87 (m, 2H), 5.44 (q, 0.4H, J=5.0 Hz), 5.32 (q, 0.6H, J=4.8 Hz), 4.49 (d, 0.6H, J=7.0 Hz), 4.46 (d, 0.4H, J=8.1 Hz), 3.81 (s, 3H), 3.80 (m, 1H), 1.70-1.25 (m, 4H), 1.49 (d, 1.8H, J=5.0 Hz), 1.45 (d, 1.2H, J=5.0 Hz), 0.90 (t, 3H, J=7.0 Hz); ¹³C NMR (75 MHz, CDCl₃) δ 159.6, 159.4, 131.5, 130.4, 128.0, 127.8, 113.9, 101.8, 100.8, 84.8, 84.4, 83.0, 82.7, 55.2, 34.5, 33.6, 20.6, 20.4, 19.4, 19.3, 13.98, 13.95; MS m/z: 236 (M⁺), 164 (100%); HRMS (EI) calcd for C₁₄H₂₀O₃ (M⁺): 236.1412, found: 236.1408. Acetal 43 was subjected to the
following reductive acetal cleavage. To a solution of acetal 43 (102 mg, 0.43 mmol) in toluene (3 mL) at room temperature was added DIBAL (0.95 M in hexane, 0.91 mL, 0.86 mmol). After stirring for 3 h, additional DIBAL (0.95 M in hexane, 0.91 mL, 0.86 mmol) was added. The mixture was then stirred for 21 h during which time (after 3 h) another equivalent of DIBAL (0.95 M in hexane, 0.91 mL, 0.86 mmol) and (after 7h) additional DIBAL (0.95 M in hexane, 0.45 mL, 0.43 mmol) were added. The mixture, cooled to 0°C, was treated with 28% NH₄OH and stirred at room temperature for an additional 30 min. Following addition of celite, the mixture was filtered through a celite pad and concentrated in vacuo. The residue was purified by silica gel column chromatography (AcOEt/Hex 1:7) to give less polar alcohol 44 (40 mg, 38%) as a colorless oil and more polar alcohol 21a (58 mg, 56%) as a colorless oil. TLC analysis and NMR spectra indicated that alcohol 21a was identical to the major alcohol obtained by the hydroxyalkylation of butyl ethyl ether (12).

**SI. Scheme 6. Determination of Stereochemistry of Alcohol 22**

![Chemical structure](image)

**Synthesis of ether 45 (from 22a):** To a stirred solution of alcohol 22a (11 mg, 0.05 mmol) in DMF (0.5 mL) at 0°C was added NaH (60% in oil; 6 mg, 0.14 mmol). After 10 min, the mixture was allowed to warm to room temperature and stirred for an additional 30 min. Following addition of Mel (10 µL, 0.16 mmol), the mixture was stirred for 20 min. The mixture was treated with sat. NH₄Cl,
extracted with Et₂O, dried over MgSO₄ and concentrated in vacuo. The residue was purified by silica gel column chromatography (AcOEt/Hex 1:3) to give ether 45 (11 mg, 98%) as a colorless oil. TLC analysis and NMR spectra indicated that ether 45 was identical to the compound obtained from 47 by the following protocols. IR (neat) v 2930 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 7.30-7.25 (m, 2H), 6.94-6.89 (m, 2H), 4.30 (d, 1H, J=6.0 Hz), 3.84 (s, 3H), 3.49 (s, 3H), 3.48-3.41 (m, 2H), 3.28 (s, 3H), 3.26 (s, 3H), 3.08 (m, 1H); ¹³C NMR (75 MHz, CDCl₃) δ 159.2, 131.0, 128.6, 113.7, 83.9, 83.3, 71.5, 59.1, 59.07, 56.9, 55.2; MS m/z: 240 (M⁺), 151 (100%); HRMS (EI) calcd for C₁₃H₂₀O₄ (M⁺): 240.1362, found: 240.1363.

**Synthesis of diol 47:** To a solution of ether 46 (129 mg, 0.73 mmol) in aq. t-BuOH (1:1 v/v, 7.2 mL) at room temperature was added AD-mix-β (1.0 g). After stirring for 10.5 h, the mixture was treated with sat. Na₂S₂O₅ and extracted with AcOEt, and the organic layer was washed with brine. The extract was dried over MgSO₄ and concentrated in vacuo. The residue was purified by silica gel column chromatography (AcOEt/Hex 1:1) to give diol 47 (146 mg, 95%) as a colorless solid. Mp 97-98°C; IR (neat) v 3439 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.32-7.28 (m, 2H), 6.92-6.88 (m, 2H), 4.65 (d, 1H, J=6.6 Hz), 3.81 (s, 3H), 3.80-3.77 (m, 1H), 3.39-3.28 (m, 2H), 3.35 (s, 3H), 2.64 (brs, 2H); ¹³C NMR (100 MHz, CDCl₃) δ 159.3, 132.5, 127.8, 113.9, 74.7, 74.6, 73.5, 59.2, 55.3; MS m/z: 212 (M⁺), 137 (100%); HRMS (EI) calcd for C₁₁H₁₆O₄ (M⁺): 212.1049, found: 212.1052.

**Synthesis of ether 45 (from diol 47):** To a stirred solution of diol 47 (27 mg, 0.13 mmol) in DMF (1 mL) at 0°C was added NaN₃ (60% in oil; 13 mg, 0.32 mmol), and the mixture was allowed to warm to room temperature. After 1 h, MeI (24 µL, 0.38 mmol) was added. After 50 min, the mixture was treated with sat. NH₄Cl, extracted with Et₂O, dried over MgSO₄ and concentrated in vacuo. The residue was purified by silica gel column chromatography (AcOEt/Hex 1:3) to give ether 45 (30 mg, 99%) as a colorless oil.