

Supporting Information

Friedel-Crafts Alkylation of Arenes with Epoxides Promoted by Fluorinated Alcohols or Water

*Guo-Xing Li and Jin Qu**

The State Key Laboratory of Elemento - Organic Chemistry,
Nankai University, Tianjin 300071, China
gujin@nankai.edu.cn

Table of Contents

General information.....	S2
Preparations of aryloxymethyloxiranes in table 2.....	S2
Characterization data of aryloxymethyloxiranes in table 2.....	S2–S4
General procedure for reactions in table 2.....	S4
Characterization data of reaction products in table 2.....	S4–S9
General procedure for the intermolecular reactions in table 3.....	S9
Characterization data of reaction products in table 3.....	S9–S12
Reference.....	S12
NMR spectra.....	S13–S32

General information: All reactions were carried out in aerial atmosphere. Water was purchased from Watson's or from Milli-Q® Ultrapure Water Purification System. 2,2,2-trifluoroethanol (TFE) and 1,1,1,3,3,3-hexafluoroisopropanol (HFIP) were used as received from Acros®. Substrates were synthesized according to the known procedures. Flash column chromatography was performed using the indicated solvent system on Qingdao–Haiyang® silica gel (200–300 mesh). All of the compounds were characterized by ¹H NMR and ¹³C NMR. ¹H NMR spectra were recorded at 300 MHz, 400 MHz or 600 MHz NMR machine; ¹³C NMR spectra were recorded at 75 MHz, 100 MHz or 150 MHz NMR machine. Peaks recorded are relative to the internal standards: TMS (δ = 0.00) for ¹H NMR and CDCl₃ (δ = 77.00) for ¹³C NMR spectra. Optical rotations were measured on a Perkin Elmer 341 MC polarimeter. High resolution mass spectral analyses (HRMS) were performed on high resolution ESI–FTICR mass spectrometer (Varian 7.0 T).

General procedure for the preparation of starting materials.

(2*R*,3*R*)-2-((3,5-Dimethoxyphenoxy)methyl)-3-phenyloxirane (Table 2, entry 1, starting material 1a)¹

A solution of 3,5-dimethoxyphenol (0.32 mmol, 49 mg) in DMF (2 mL) was added via syringe to a suspension of sodium hydride (0.53 mmol, 13 mg) in DMF (2 mL) at 0°C under N₂. The mixture was stirred until gas evolution ceased, and a solution of enantiomerically pure (ee > 99%) [(2*R*,3*R*)-3-phenyloxiran-2-yl]methyl 4-methylbenzenesulfonate] (0.35 mmol, 106 mg) in DMF (2 mL) was added via syringe to the mixture. The solution was stirred for ca. 48 h at 0°C. The reaction mixture was suspended in MeOH (2.5 mL) and brine (30 mL) and extracted with Et₂O (4 × 8 mL). The residual oil was purified by column chromatography on silica gel using hexane: EtOAc (95:5) as eluent to afford the product (78 mg, 85%) as colorless oil. $[\alpha]_D^{20} = +54.0$ ($c = 1.0$ in CHCl₃), liter.: $[\alpha]_D^{27} = +52.6$ ($c = 1.2$ in CHCl₃); ¹H NMR (600 MHz, CDCl₃): δ = 3.42 (br s, 1H), 3.80 (s, 6H), 3.94 (d, J = 2.1 Hz, 1H), 4.11 (dd, J = 5.4, 10.8 Hz, 1H), 4.32 (dd, J = 2.4, 10.8 Hz, 1H), 6.16 (br s, 1H), 6.18 (br s, 2H), 7.33–7.39 (m, 5H); ¹³C NMR (150 MHz, CDCl₃): δ = 55.2, 56.2, 60.0, 67.9, 93.4, 93.5, 125.6, 128.3, 128.4, 136.4, 160.2, 161.5; HRMS (ESI): m/z calcd for C₁₇H₁₉O₄: 287.1283; found: 287.1287 [M+H]⁺.

Characterization data of aryloxymethyloxiranes in table 2

(2*R*,3*R*)-2-[(4-Methoxyphenoxy)methyl]-3-phenyloxirane (Table 2, entry 2, starting material 1b)¹

The general procedure was applied to 4-methoxyphenol to afford the product (70 mg, 85%) as a white solid: m.p. = 100–101 °C; $[\alpha]_D^{20} = +47.5$ ($c = 1.0$ in CHCl₃), liter.: $[\alpha]_D^{25} = +48.3$ ($c = 1.0$ in CHCl₃); ¹H NMR (600 MHz, CDCl₃): δ = 3.35–3.39 (m, 1H), 3.76 (s, 3H), 3.88–3.90 (m, 1H), 4.08 (dd, J = 5.1, 11.0 Hz, 1H), 4.26 (dd, J = 3.1, 11.0 Hz, 1H), 6.81–6.91 (m, 4H), 7.26–7.38 (m, 5H); ¹³C NMR (150 MHz, CDCl₃): δ = 55.7, 56.4, 60.4, 68.7, 114.7, 115.8, 125.7, 128.4, 128.6, 136.6, 152.7, 154.3; HRMS (ESI): m/z calcd for C₁₆H₁₆NaO₃: 279.0997; found: 279.0994 [M+Na]⁺.

(2R,3R)-2-[(4-tert-butylphenoxy)methyl]-3-phenyloxirane (Table 2, entry 3, starting material 1c)¹

The general procedure was applied to 4-tert-butylphenol to afford the product (72 mg, 80%) as a white solid: m.p. = 126–127 °C; $[\alpha]_D^{20} = +53.3$ ($c = 1.0$ in CHCl_3), liter.: $[\alpha]_D^{27} = +54.2$ ($c = 0.8$ in CHCl_3); ^1H NMR (600 MHz, CDCl_3): $\delta = 1.30$ (s, 9H), 3.39–3.41 (m, 1H), 3.91 (d, $J = 2.4$ Hz, 1H), 4.14 (dd, $J = 5.1, 11.1$ Hz, 1H), 4.31 (dd, $J = 3.3, 11.1$ Hz, 1H), 6.88–6.90 (m, 2H) 7.29–7.37 (m, 7H); ^{13}C NMR (150 MHz, CDCl_3): $\delta = 31.5, 34.1, 56.4, 60.3, 68.0, 114.2, 125.7, 126.3, 128.4, 128.5, 136.6, 144.0, 156.2$; HRMS (ESI): m/z calcd for $\text{C}_{19}\text{H}_{22}\text{NaO}_2$: 305.1517; found: 305.1520 [M+Na]⁺.

(2R,3R)-2-(phenoxyethyl)-3-phenyloxirane (Table 2, entry 4, starting material 1d)¹

The general procedure was applied to phenol to afford the product (58 mg, 80%) as a white solid: m.p. = 100–101 °C; $[\alpha]_D^{20} = +44.5$ ($c = 1.0$ in CHCl_3), liter.: $[\alpha]_D^{24} = +45.6$ ($c = 1.0$ in CHCl_3); ^1H NMR (400 MHz, CDCl_3): $\delta = 3.39$ –3.42 (m, 1H), 3.91 (d, $J = 2.1$ Hz, 1H), 4.14 (dd, $J = 5.0, 11.1$ Hz, 1H), 4.32 (dd, $J = 3.3, 11.1$ Hz, 1H), 6.94–7.0 (m, 3H), 7.27–7.38 (m, 7H); ^{13}C NMR (150 MHz, CDCl_3): $\delta = 56.4, 60.3, 67.9, 114.7, 121.3, 125.7, 128.4, 128.6, 129.6, 136.5, 158.5$; HRMS (ESI): m/z calcd for $\text{C}_{15}\text{H}_{14}\text{NaO}_2$: 249.0891; found: 249.0887 [M+Na]⁺.

(2R,3R)-2-((4-bromophenoxy)methyl)-3-phenyloxirane (Table 2, entry 5, starting material 1e)

The general procedure was applied to 4-bromophenol to afford the product (86 mg, 89%) as a white solid: m.p. = 117–118 °C; $[\alpha]_D^{20} = +46.0$ ($c = 1.0$ in CHCl_3); ^1H NMR (600 MHz, CDCl_3): $\delta = 3.39$ –3.41 (m, 1H), 3.92 (d, $J = 2.4$ Hz, 1H), 4.10 (dd, $J = 5.4, 10.8$ Hz, 1H), 4.32 (dd, $J = 3.0, 10.8$ Hz, 1H), 6.83–6.86 (m, 2H), 7.34–7.40 (m, 5H); ^{13}C NMR (150 MHz, CDCl_3): $\delta = 56.2, 60.0, 68.1, 113.5, 116.5, 125.7, 128.5, 128.6, 132.3, 136.3, 157.6$; HRMS (ESI): m/z calcd for $\text{C}_{15}\text{H}_{13}\text{BrNaO}_2$: 326.9997; found: 326.9991 [M+Na]⁺.

(2R,3R)-2-((4-iodophenoxy)methyl)-3-phenyloxirane (Table 2, entry 6, starting material 1f)¹

The general procedure was applied to 4-iodophenol to afford the product (84 mg, 75%) as a white solid: m.p. = 95–96 °C; $[\alpha]_D^{20} = +42.0$ ($c = 1.0$ in CHCl_3), liter.: $[\alpha]_D^{27} = +41.1$ ($c = 1.1$ in CHCl_3); ^1H NMR (600 MHz, CDCl_3): $\delta = 3.39$ (br s, 1H), 3.91 (br s, 1H), 4.07 (dd, $J = 4.8, 10.8$ Hz, 1H), 4.31 (dd, $J = 1.8, 10.8$ Hz, 1H), 6.74 (d, $J = 8.4$ Hz, 2H), 7.30–7.37 (m, 5H) 7.58 (d, $J = 3.6$ Hz, 2H); ^{13}C NMR (150 MHz, CDCl_3): $\delta = 56.3, 60.0, 68.1, 83.5, 117.1, 125.7, 128.5, 128.6, 136.3, 138.3, 158.3$; HRMS (ESI): m/z calcd for $\text{C}_{15}\text{H}_{13}\text{INaO}_2$: 374.9858; found: 374.9852 [M+Na]⁺.

(2R,3R)-2-[(naphthalen-2-yloxy)methyl]-3-phenyloxirane (Table 2, entry 7, starting material 1g)²

The general procedure was applied naphthalene-2-ol to afford the product (71 mg, 80%) as a white solid: m.p. = 108–109 °C; $[\alpha]_D^{20} = +26.7$ ($c = 1.0$ in CHCl_3); ^1H NMR (400 MHz, CDCl_3): $\delta = 3.48$ (m, 1H), 3.99 (d, $J = 3.0$ Hz, 1H), 4.25 (dd, $J = 7.8, 16.8$ Hz, 1H), 4.46 (dd, $J = 4.5, 16.5$ Hz, 1H), 7.18–7.23 (m, 6H), 7.44–7.47 (m, 1H), 7.45 (m, 1H), 7.7–7.80(m, 3H);

¹³C NMR (150 MHz, CDCl₃): δ = 56.4, 60.2, 67.9, 107.0, 118.8, 123.9, 125.7, 126.5, 126.8, 127.7, 128.4, 128.6, 129.2, 129.6, 134.4, 136.5, 156.4; HRMS (ESI): *m/z* calcd for C₁₉H₁₇O₂: 277.1229; found: 277.1233 [M+H]⁺.

(2R,3R)-2-[(6-bromonaphthalen-2-yloxy)methyl]-3-phenyloxirane (Table 2, entry 8, starting material 1h)

The general procedure was applied to 6-bromonaphthalen-2-ol to afford the product (101 mg, 89%) as a white solid: m.p. = 123–124 °C; [α]_D²⁰ = +31.1 (*c* = 1.0 in CHCl₃); ¹H NMR (600 MHz, CDCl₃): δ = 3.49 (m, 1H), 3.99 (br s, 1H), 4.26 (dd, *J* = 4.8, 11.1 Hz), 4.47 (dd, *J* = 2.4, 10.8 Hz, 1H), 7.17 (s, 1H), 7.25 (dd, *J* = 1.8, 8.7 Hz, 1H), 7.34–7.41 (m, 5H), 7.53 (d, *J* = 9.0 Hz, 1H), 7.62 (d, *J* = 8.4 Hz, 1H), 7.69 (d, *J* = 9.0 Hz, 1H), 7.95 (s, 1H); ¹³C NMR (150 MHz, CDCl₃): δ = 56.4, 60.1, 68.1, 107.1, 117.4, 119.8, 125.7, 128.4, 128.5, 128.6, 128.7, 129.8, 129.7, 130.3, 132.9, 136.4, 156.7; HRMS (ESI): *m/z* calcd for C₁₉H₁₆BrO₂: 355.0334; found: 355.0326 [M+H]⁺.

2-[(3,5-dimethoxyphenoxy)phenylmethyl]oxirane (Table 2, entry 9, starting material 1i)³
¹H NMR (400MHz, CDCl₃): δ = 2.79–2.84 (m, 2H), 3.31–3.34 (m, 1H), 3.70 (s, 6H), 5.10 (d, *J* = 6.0 Hz), 6.10 (d, *J* = 6.0 Hz), 6.03 (t, *J* = 3.0 Hz), 6.06 (d, *J* = 3.6 Hz), 7.30–7.42 (m, 5H); ¹³C NMR (150 MHz, CDCl₃): δ = 45.0, 54.3, 55.2, 79.1, 93.5, 94.9, 126.7, 128.4, 128.7, 137.4, 159.4, 161.3; HRMS (ESI): *m/z* calcd for C₁₇H₁₉O₄: 287.1283; found: 287.1276 [M+H]⁺.

3-[(3,5-dimethoxyphenoxy) methyl]-2,2-dimethyloxirane (Table 2, entry 10, starting material 1j)

The general procedure which using racemic (3,3-dimethyloxiran-2-yl)methyl 4-methylbenzenesulfonate^{4,5} was applied to 3,5-dimethoxyphenol afford the product (65 mg, 85%) as a white solid: ¹H NMR (400MHz, CDCl₃): δ = 1.35 (s, 3H), 1.38 (s, 3H), 3.12 (t, *J* = 1.8 Hz, 1H), 3.76 (s, 6H), 4.00–4.04 (m, 1H), 4.07–4.11 (m, 1H), 6.10–6.12 (m, 3H); ¹³C NMR (100 MHz, CDCl₃): δ = 18.9, 24.6, 55.3, 58.2, 61.1, 67.0, 93.3, 93.5, 160.4, 161.5; HRMS (ESI): *m/z* calcd for C₁₃H₁₉O₄: 239.1283; found: 239.1281 [M+H]⁺.

General procedure for the preparation of product in hexafluoroisopropanol.

(3S,4R)-5,7-dimethoxy-4-phenylchroman-3-ol (Table 2, entry 1, product 2a)¹

The starting material of (2R,3R)-2-((3,5-dimethoxyphenoxy)methyl)-3-phenyloxirane **1a** (43 mg, 0.15 mmol) was dissolved in 5mL of hexafluoroisopropanol and was refluxed under ambient pressure. The solvent of reaction mixture was removed under reduced pressure. The residue was underwent column chromatography on silica gel using hexane: EtOAc (80:20) as eluent to afford **2a** (43 mg, >99%) as a colorless oil. [α]_D²⁰ = +53.0 (*c* = 1.0 in CHCl₃), liter.: [α]_D²⁷ = +52.3 (*c* = 1.1 in CHCl₃); ¹H NMR (600 MHz, CDCl₃): δ = 2.26 (br s, 1H), 3.47 (s, 3H), 3.70 (s, 3H), 3.85–3.93 (m, 3H), 4.15 (br s, 1H), 6.00 (d, *J* = 1.2 Hz, 1H), 6.07 (d, *J* = 1.2 Hz, 1H), 7.00 (d, *J* = 7.2 Hz, 2H), 7.20 (t, *J* = 7.2 Hz, 1H), 7.17 (t, *J* = 7.2 Hz, 2H); ¹³C NMR (150 MHz, CDCl₃): δ = 43.4, 55.2, 55.4, 65.3, 69.3, 92.5, 93.0, 101.9, 126.3, 128.0, 128.3, 143.5, 155.1, 159.7, 160.3; HRMS (ESI): *m/z* calcd for C₁₇H₁₉O₄: 287.1283; found: 287.1287 [M+H]⁺.

(3S,4R)-6-methoxy-4-phenylchroman-3-ol (Table 2, entry 2, product 2b)¹

The general procedure was applied to **1b** to afford **2b** (37 mg, 96%) as a white solid: $[\alpha]_D^{20} = +3.5$ ($c = 1.0$ in CHCl_3), liter.: $[\alpha]_D^{28} = +3.4$ ($c = 1.0$ in CHCl_3); ^1H NMR (600 MHz, CDCl_3): $\delta = 2.15$ (br s, 1H), 3.65 (s, 3H), 3.97 (m, 1H), 4.07–4.10 (m, 2H), 4.15 (dd, $J = 1.2, 10.2$ Hz, 1H), 6.41 (d, $J = 2.4$ Hz, 1H), 6.78 (dd, $J = 3.0, 8.7$ Hz, 1H), 6.88 (d, $J = 9.0$ Hz, 1H), 7.16–7.17 (m, 2H), 7.26–7.29 (m, 1H), 7.33–7.36 (m, 2H); ^{13}C NMR (150 MHz, CDCl_3): $\delta = 50.4, 55.6, 66.6, 69.9, 114.7, 115.4, 117.3, 122.6, 127.1, 128.7, 129.1, 142.5, 148.2, 154.1$; HRMS (ESI): m/z calcd for $\text{C}_{16}\text{H}_{16}\text{NaO}_3$: 279.0997; found: 279.0997 [$\text{M}+\text{Na}]^+$.

(3S,4R)-6-tert-butyl-4-phenylchroman-3-ol (Table 2, entry 3, product 2c)¹

The general procedure was applied to **1c** to afford **2c** (42 mg, 99%) as a white solid: $[\alpha]_D^{20} = +206.0$ ($c = 1.0$ in CHCl_3), liter.: $[\alpha]_D^{26} = +204.2$ ($c = 1.0$ in CHCl_3); ^1H NMR (600 MHz, CDCl_3): $\delta = 1.20$ (s, 9H), 1.85 (br s), 3.99–4.02 (m, 1H), 4.09–4.15 (m, 3H), 6.87 (d, $J = 7.2$ Hz, 1H), 6.88 (s, 1H), 7.12–7.15 (m, 2H), 7.21 (dd, $J = 2.4, 9.0$ Hz, 1H), 7.25–7.27 (m, 1H), 7.32–7.34 (m, 2H); ^{13}C NMR (150 MHz, CDCl_3): $\delta = 31.4, 34.0, 50.2, 66.4, 70.0, 115.9, 120.8, 125.3, 126.9, 128.1, 128.6, 129.1, 142.8, 144.0, 151.8$; HRMS (ESI): m/z calcd for $\text{C}_{19}\text{H}_{22}\text{NaO}_2$: 305.1517; found: 305.1515 [$\text{M}+\text{Na}]^+$.

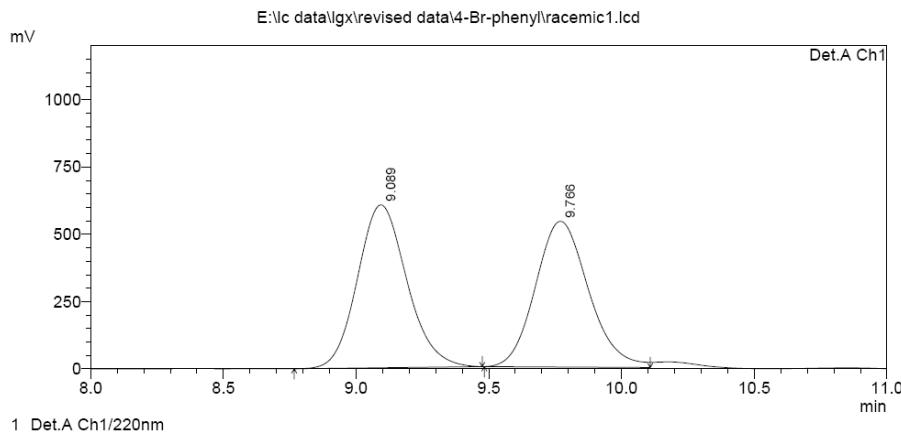
(3S,4R)-4-phenylchroman-3-ol (Table 2, entry 4, product 2d)¹

The general procedure was applied to **1d** to afford **2d** (30 mg, 88%) as a white solid: $[\alpha]_D^{20} = -34.0$ ($c = 1.0$ in CHCl_3), liter.: $[\alpha]_D^{27} = -33.9$ ($c = 1.0$ in CHCl_3); ^1H NMR (600 MHz, CDCl_3): $\delta = 2.12$ (br s, 1H), 4.03–4.06 (m, 1H), 4.12 (br s, 2H), 4.22 (dd, $J = 1.2, 10.8$ Hz, 1H), 6.89 (d, $J = 4.2$ Hz, 2H), 6.96 (d, $J = 8.4$ Hz, 1H), 7.16 (d, $J = 7.2$ Hz, 2H), 7.18–7.21 (m, 1H), 7.28–7.29 (m, 1H), 7.34–7.36 (m, 2H); ^{13}C NMR (150 MHz, CDCl_3): $\delta = 50.2, 66.8, 69.8, 116.6, 121.3, 122.1, 127.1, 128.2, 128.8, 129.1, 131.3, 142.5, 154.1$; HRMS (ESI): m/z calcd for $\text{C}_{15}\text{H}_{14}\text{NaO}_2$: 249.0891; found: 249.0887 [$\text{M}+\text{Na}]^+$.

(3S,4R)-6-bromo-4-phenylchroman-3-ol (Table 2, entry 5, product 2e)

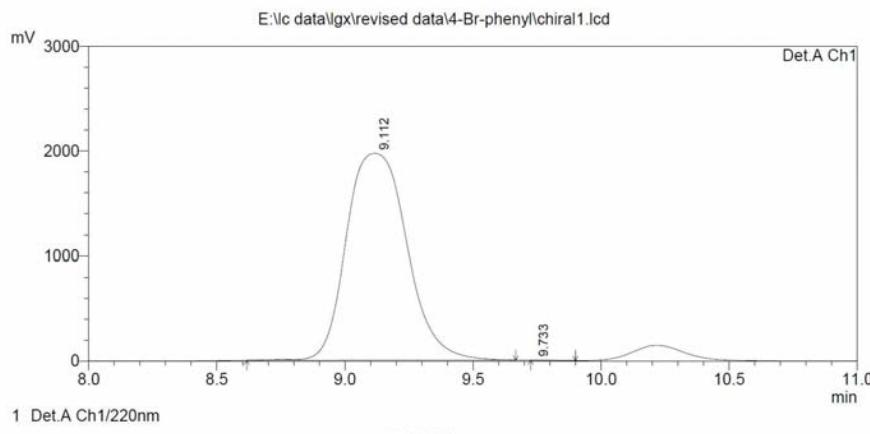
The general procedure was applied to **1e** to afford **2e** (40 mg, 87%) as a white solid: m.p. = 120–121°C; $[\alpha]_D^{20} = +33.9$ ($c = 1.0$ in CHCl_3); ^1H NMR (600 MHz, CDCl_3): $\delta = 1.50$ (br s, 1H), 3.95 (m, 1H), 4.00 (d, $J = 4.8$ Hz, 1H), 4.04 (td, $J = 2.4, 5.4$ Hz, 1H), 4.11 (dd, $J = 2.4, 10.8$ Hz, 1H), 6.76 (d, $J = 9.0$ Hz, 1H), 7.05 (d, $J = 7.2$ Hz, 2H), 7.21–7.30 (m, 4H); ^{13}C NMR (150 MHz, CDCl_3): $\delta = 50.0, 66.8, 69.3, 113.3, 118.5, 124.3, 127.4, 128.9, 129.0, 131.2, 133.6, 141.7, 153.2$; Chiral HPLC: AD-H (heptane/isopropanol = 85/15, 0.8 mL/min⁻¹, UV at 254 nm, t (major) = 9.1 min, t (minor) = 9.7 min, ee > 99%; HRMS (ESI): m/z calcd for $\text{C}_{15}\text{H}_{13}\text{BrNaO}_2$: 326.9997; found: 326.9991 [$\text{M}+\text{H}]^+$.

<Chromatogram>



PeakTable					
Peak#	Ret. Time	Area	Height	Area %	Height %
1	9.089	7835850	605308	51.003	52.815
2	9.766	7527764	540793	48.997	47.185
Total		15363614	1146101	100.000	100.000

<Chromatogram>



PeakTable					
Peak#	Ret. Time	Area	Height	Area %	Height %
1	9.112	32420968	1970998	99.999	99.997
2	9.733	293	56	0.001	0.003
Total		32421261	1971053	100.000	100.000

(3S,4R)-6-iodo-4-phenylchroman-3-ol (Table 2, entry 6, product 2f)¹

The general procedure was applied to **1f** to afford **2f** (46 mg, 88%) as a white solid: $[\alpha]_D^{20} = +14.9$ ($c = 1.0$ in CHCl_3), liter.: $[\alpha]_D^{25} = +15.04$ ($c = 0.9$ in CHCl_3); ^1H NMR (600 MHz, CDCl_3): $\delta = 2.10$ (br s, 1H), 4.01–4.04 (m, 1H), 4.07–4.10 (m, 2H), 4.18 (dd, $J = 1.8, 10.8$ Hz, 1H), 6.73 (d, $J = 8.4$ Hz, 1H), 7.13–7.48 (m, 7H); ^{13}C NMR (150 MHz, CDCl_3): $\delta = 49.8, 66.7, 69.3, 83.3, 119.0, 124.8, 127.4, 128.9, 129.0, 137.1, 139.7, 141.8, 154.1$; HRMS (ESI): m/z calcd for $\text{C}_{15}\text{H}_{13}\text{INaO}_2$: 374.9858; found: 374.9852 $[\text{M}+\text{Na}]^+$.

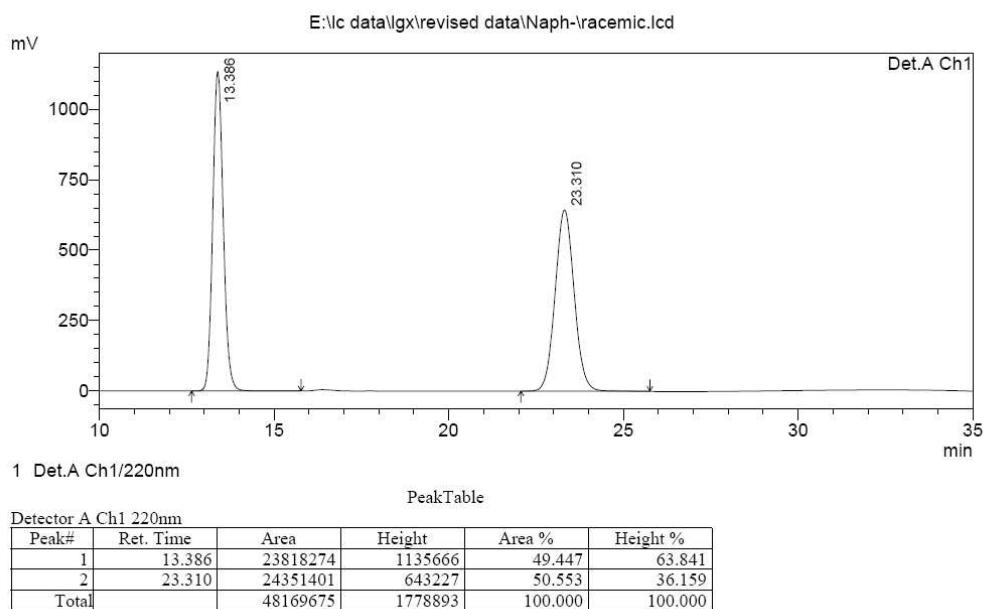
(1R,2S)-1-phenyl-2,3-dihydro-1H-benzo[f]chromen-2-ol (Table 2, entry 7, product 2g)²

The general procedure was applied **1g** to afford **2g** (38 mg, 91%) as a white solid: $[\alpha]_D^{20} = -88.7$ ($c = 1.0$ in CHCl_3); ^1H NMR (600 MHz, CDCl_3): $\delta = 2.00$ (br s, 1H), 4.06–4.07 (m, 2H), 4.14–4.15 (m, 1H), 4.59 (br s, 1H), 7.08–7.14 (m, 4H), 7.18–7.22 (m, 4H), 7.38–7.40 (m, 1H),

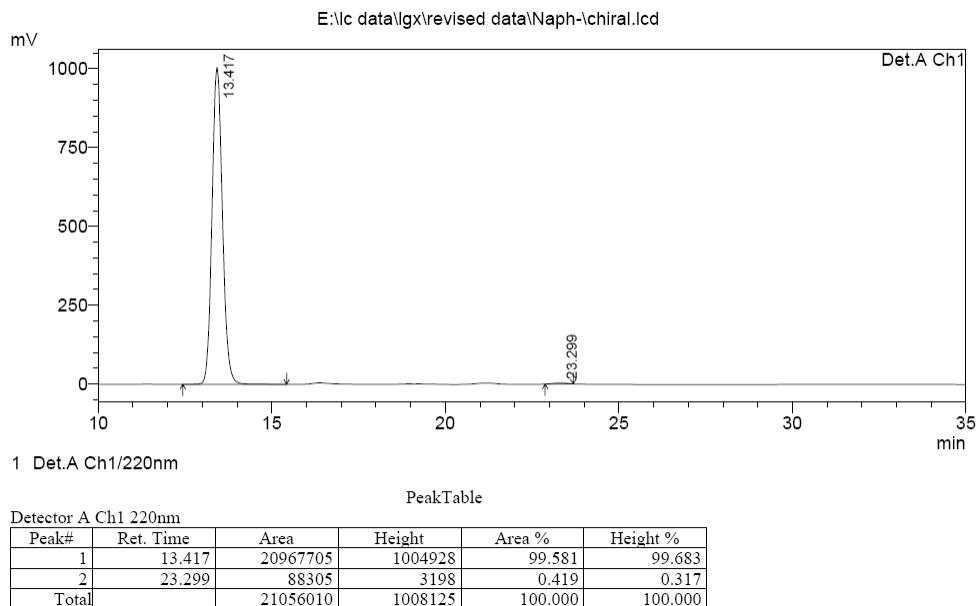
7.66–7.69 (m, 2H); ^{13}C NMR (150 MHz, CDCl_3): δ = 45.9, 64.8, 69.7, 111.7, 118.5, 122.9, 123.5, 126.7, 126.8, 128.5, 129.3, 129.8, 133.4, 143.0, 151.7; HRMS (ESI): m/z calcd for $\text{C}_{19}\text{H}_{17}\text{O}_2$: 277.1229; found: 277.1233 [$\text{M}+\text{H}]^+$.

The observed optical rotation of compound **2g** can not match with the reported value. We performed the chiral HPLC analysis of this sample and the result indicated that the enantiomeric excess value of the product is 99%ee. Chiral HPLC: AD-H (heptane/isopropanol = 85/15, 0.8 mL/min⁻¹, UV at 254 nm, t (major) = 13.4 min, t (minor) = 23.3 min, ee > 99%

<Chromatogram>



<Chromatogram>

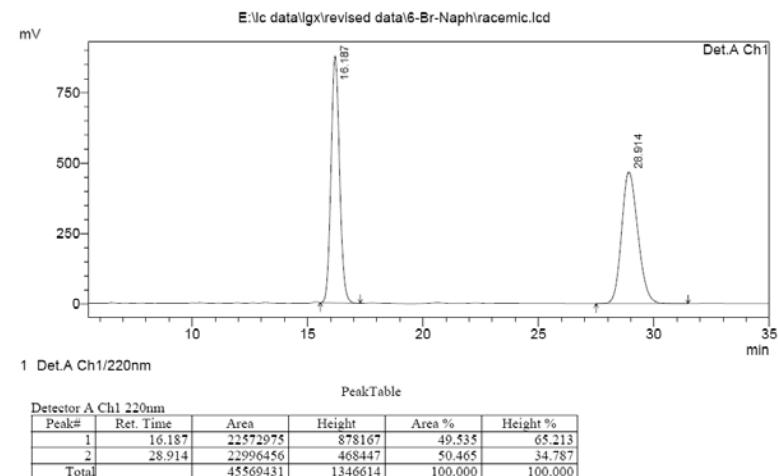


(1R,2S)-8-bromo-1-phenyl-2, 3-dihydro-1H-benzo[f]chromen-2-ol (Table 2, entry 8,

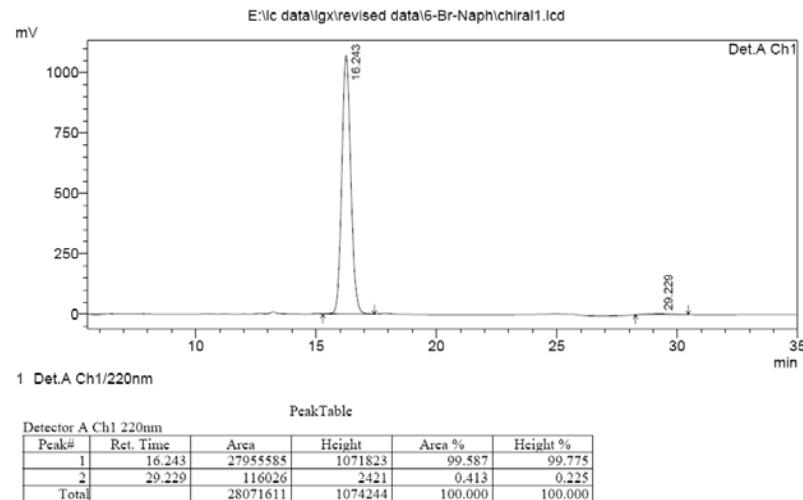
product 2h)

The general procedure was applied **1h** to afford **2h** (51mg, 96%) as a white solid: m.p. = 138–139 °C; $[\alpha]_D^{20} = -49.5$ (c = 1.0 in CHCl_3); ^1H NMR (600 MHz, CDCl_3): δ = 2.30 (br s, 1H), 4.03 (br s, 2H), 4.09 (dd, J = 3.6, 6.6 Hz, 2H), 4.79 (d, J = 1.2, 1H), 7.02 (d, J = 10.8 Hz, 2H), 7.08–7.20 (m, 4H), 7.22 (s, 1H), 7.54 (d, J = 13 Hz, 1H), 7.81 (s, 1H); ^{13}C NMR (150 MHz, CDCl_3): δ = 45.8, 64.8, 69.5, 112.2, 117.2, 119.7, 124.7, 127.0, 128.3, 128.4, 128.9, 129.8, 130.4, 131.0, 131.9, 142.6, 151.9; Chiral HPLC: AD-H (heptane/isopropanol = 85/15, 0.8 mL/min⁻¹, UV at 254 nm, t (major) = 16.2 min, t (minor) = 29.2 min, ee > 99%; HRMS (ESI): m/z calcd for $\text{C}_{19}\text{H}_{16}\text{BrO}_2$: 355.0334; found: 355.0324 [M+H]⁺.

<Chromatogram>



<Chromatogram>



5,7-dimethoxy-2-phenylchroman-3-ol (Table 2, entry 9, product 2i)³

The general procedure was applied to **1i** to afford **2i** (22 mg, 51%) as a colorless oil: ^1H NMR (400 MHz, CDCl_3): δ = 1.73 (br s, 1H), 2.62 (dd, J = 8.4, 16.4 Hz, 1H), 2.99 (dd, J = 5.6, 16.4 Hz, 1H), 3.76 (s, 3H), 3.80 (s, 3H), 4.10 (dd, J = 8.0, 13.6 Hz, 1H), 4.78 (d, J = 8.0 Hz, 1H), 6.13 (dd, J = 2.0, 16.0 Hz, 2H), 7.36–7.44 (m, 5H); ^{13}C NMR (100 MHz, CDCl_3): δ = 27.2,

55.3, 55.4, 68.2, 81.7, 91.8, 93.0, 101.4, 127.0, 128.6, 128.8, 138.1, 155.1, 158.8, 159.7; HRMS (ESI): m/z calcd for C₁₇H₁₉O₄: 287.1283; found: 287.1272 [M+H]⁺.

5,7-dimethoxy-4,4-dimethylchroman-3-ol (Table 2, entry 10, product 2j)

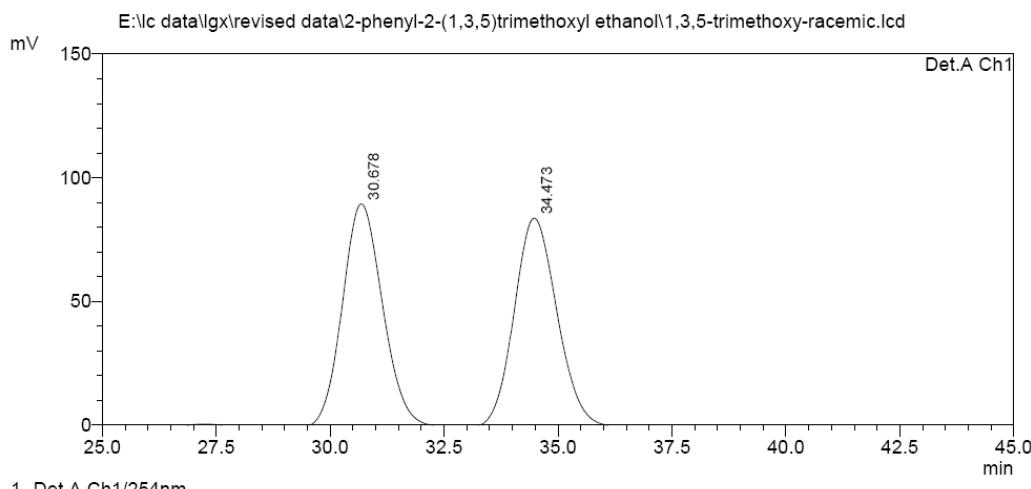
The general procedure was applied to **1j** to afford **2j** (19 mg, 52%) as a white solid: m.p. = 83–84 °C; ¹H NMR (400 MHz, CDCl₃): δ = 1.35 (s, 3H), 1.45 (s, 3H), 1.90 (br s, 1H), 3.56 (dd, *J* = 1.6, 4.4 Hz, 1H), 3.75 (s, 3H), 3.78 (s, 3H), 4.05–4.13 (m, 2H), 6.06 (d, *J* = 2.4 Hz, 1H), 6.10 (d, *J* = 2.4 Hz); ¹³C NMR (100 MHz, CDCl₃): δ = 22.8, 27.5, 35.6, 55.1, 55.2, 66.4, 74.9, 99.4, 99.6, 110.6, 154.7, 159.2, 160.7; HRMS (ESI): m/z calcd for C₁₃H₁₉O₄: 239.1283; found: 239.1273 [M+H]⁺.

General procedure for intermolecular ring-opening of epoxides

(R)-2-(2,4,6-trimethoxyphenyl)-2-phenylethanol (Table 3, product 3a)

1,3,5-Trimethoxybenzene (5 mmol, 840 mg) and (*R*)-styrene oxide (1 mmol, 120 mg) were dissolved in 5 mL of hexafluoroisopropanol and was refluxed at ambient pressure for 30 minutes. Purified the desired product by column chromatography on silica gel using hexane: EtOAc (90:20) as eluent to afford **3a** (176 mg, 61%) as a white solid: m.p. = 80–81 °C; [α]_D²⁰ = +19.3 (c = 1.0 in CHCl₃); ¹H NMR (400 MHz, CDCl₃): δ = 1.94 (br s, 1H), 3.71 (s, 6H), 3.77 (s, 3H), 4.27 (d, *J* = 7.2 Hz, 2H), 4.80 (t, *J* = 7.2 Hz, 1H), 6.13 (s, 2H), 7.11–7.31 (m, 5H); ¹³C NMR (100 MHz, CDCl₃): δ = 43.1, 55.2, 55.6, 64.7, 91.1, 110.4, 125.6, 127.9, 128.0, 142.4, 159.3, 160.0; Chiral HPLC: OD-H (heptane/isopropanol = 90/10, 0.4 mL/min⁻¹, UV at 254 nm, t (minor) = 31.0 min, t (major) = 34.5 min, ee = 95%; HRMS (ESI): m/z calcd for C₁₂H₁₈NaO₄: 249.1103; found: 249.1105 [M+Na]⁺.

<Chromatogram>



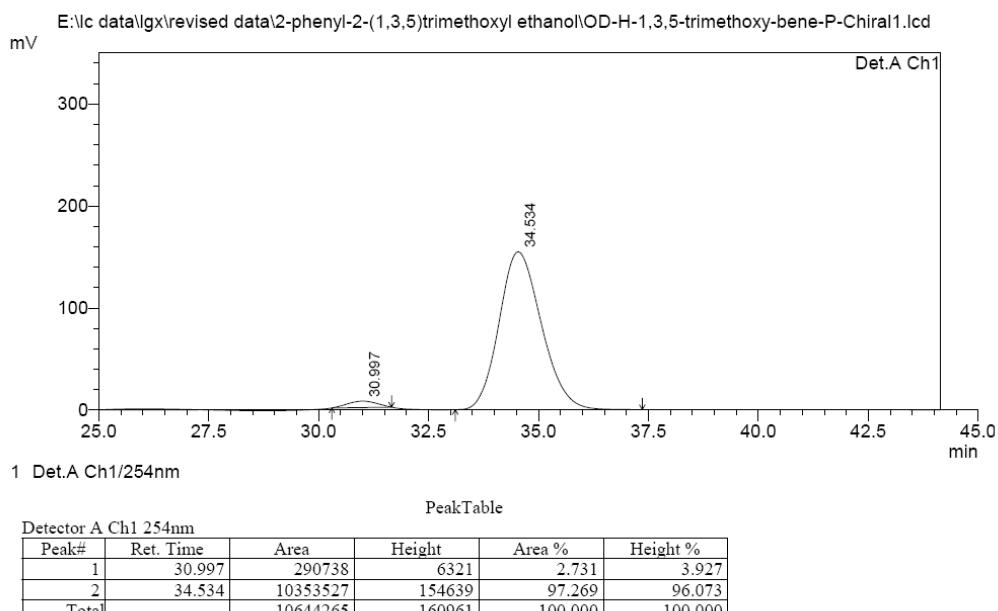
1 Det.A Ch1/254nm

PeakTable

Detector A Ch1 254nm

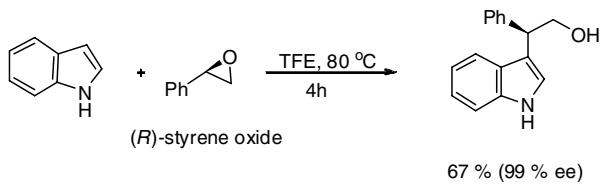
Peak#	Ret. Time	Area	Height	Area %	Height %
1	30.678	5523934	89911	50.001	51.629
2	34.473	5523702	84238	49.999	48.371
Total		11047636	174149	100.000	100.000

<Chromatogram>

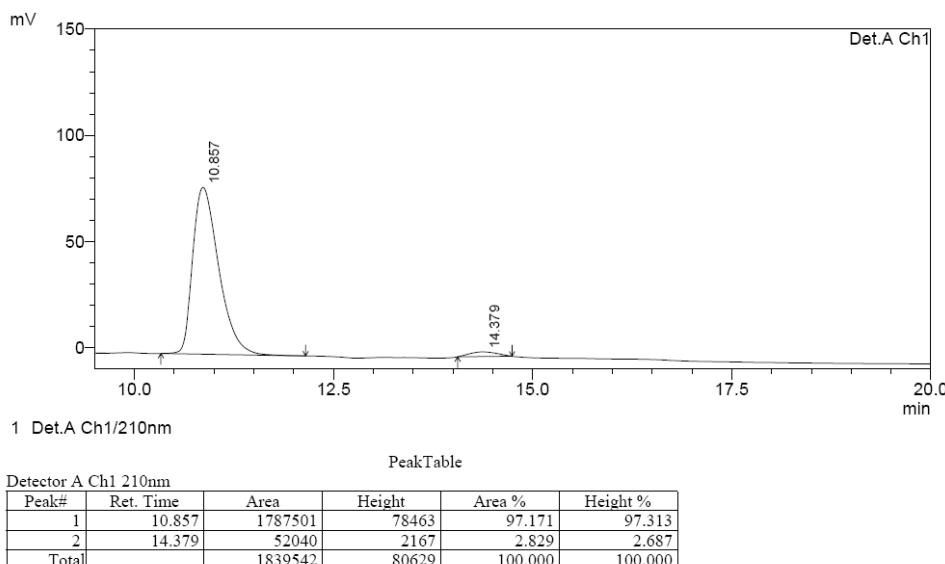


The observed enantiomeric excess value of the product is 94.5%. We think the enantiomeric purity of (*R*)-styrene oxide (purity >98.5%, purchased from Acros Organics Co.) we have could be lower than 98.5%. Because we do not have the special chiral GC column (Chiraldex γ-TA column) which is used to separate (*R*)- and (*S*)- styrene oxide. We did a parallel experiment to establish the real enantiomeric purity of this (*R*)-styrene oxide. The reaction between (*R*)-styrene oxide and indole in refluxing TFE is stereospecific as reported by Professor Mayr's group (Scheme 1). We carried this reaction using the (*R*)-styrene oxide we have at the identical reaction condition. The ee value of the reaction product is 94.3%, similar with our previous observation. This showed that the reaction between 1,3,5-trimethoxybenzene and (*R*)-styrene oxide is stereospecific. The observed 94.5% enantiomeric excess value of the product is because the enantiomeric excess value of (*R*)-styrene oxide we have is 94.5%.

Scheme 1



Westmaier, M.; Mayr, H. *Chem. Eur. J.* **2008**, *14*, 1638.



2-(1,1,1,3,3,3-hexafluoropropan-2-yloxy)-2-phenylethanol⁶

Using hexane: EtOAc (90:10) as eluent to afford the byproduct (86 mg, 30%) as a colorless oil. ¹H NMR (400 MHz, CDCl₃): δ = 2.35 (dd, J = 5.0 Hz, 1H), 3.66–3.72 (m, 1H), 3.89–3.95 (m, 1H), 4.10–4.21 (m, 1H), 4.85 (dd, J = 3.8 Hz, 1H), 7.32–7.35 (m, 2H), 7.39–7.41 (m, 3H); ¹³C NMR (100 MHz, CDCl₃): δ = 66.6, 72.5, 72.9, 73.2, 73.5, 73.8, 86.1, 119.6, 120.59, 122.35, 123.43, 127.7, 128.9, 129.6, 134.8; MS (ESI): *m/z* calcd for C₁₁H₁₀F₆O₂: 288.0; found: 286.8 [M-H]⁺.

2-(2,3,4-trimethoxy-6-methylphenyl)-2-phenylethanol (Table 3, product 3b)

The general procedure was applied to 1,2,3-trimethoxy-5-methylbenzene to afford (76 mg, 50%) the product as a white solid: m.p. = 60–61 °C; ¹H NMR (400 MHz, CDCl₃): δ = 1.18 (br s, 1H), 2.22 (s, 3H), 3.33 (s, 3H), 3.74 (s, 3H), 3.77 (s, 3H), 4.21 (dd, J = 6.4, 10.6 Hz, 1H), 4.28 (dd, J = 6.4, 10.6 Hz, 1H), 4.43 (dd, J = 6.4, 10.6 Hz, 1H), 6.46 (s, 1H), 7.10 (t, J = 6.8 Hz, 1H), 7.16–7.23 (m, 5H); ¹³C NMR (100 MHz, CDCl₃): δ = 21.1, 46.6, 55.8, 60.2, 60.5, 64.6, 109.8, 125.3, 125.9, 126.1, 127.6, 128.2, 129.0, 132.7, 140.6, 142.4, 151.9, 152.6; HRMS (ES+): *m/z* calcd for C₁₈H₂₂NaO₄: 325.1416; found: 325.1415 [M+Na]⁺.

2-(2,5-dimethoxyphenyl)-2-phenylethanol (Table 3, product 3c)

The general procedure was applied to 1,4-dimethoxybenzene to afford the product (45 mg, 35%) as a colorless oil: ¹H NMR (400 MHz, CDCl₃): δ = 1.61 (br s, 1H), 3.66 (s, 3H), 3.67 (s, 3H), 4.05 (d, J = 4.8 Hz, 2H), 4.56 (t, J = 7.2 Hz, 1H), 6.64–6.74 (m, 3H), 7.14–7.23 (m, 5H); ¹³C NMR (100 MHz, CDCl₃): δ = 46.5, 55.6, 56.1, 65.4, 111.2, 111.8, 115.3, 126.6, 128.4, 128.5, 131.2, 141.1, 151.7, 153.6; HRMS (ESI): *m/z* calcd for C₁₆H₁₈NaO₃: 281.1154; found: 281.1156 [M+Na]⁺.

2-(4-methoxyphenyl)-2-phenylethanol (Table 3, product 3d)

The general procedure was applied to anisole to afford the product (17 mg, 15%) as a colorless oil: ¹H NMR (400 MHz, CDCl₃): δ = 1.54 (br s, 1H), 3.70 (s, 3H), 4.04–4.11 (m, 3H), 6.79 (d, J = 8.0 Hz, 2H), 7.11 (d, J = 8.0 Hz, 2H), 7.13–7.18 (m, 3H), 7.23 (d, J = 7.2 Hz,

2H); ^{13}C NMR (100 MHz, CDCl_3): δ = 52.8, 55.2, 66.2, 114.1, 126.7, 128.2, 128.6, 129.2, 133.4, 141.7, 158.4; HRMS (ESI): m/z calcd for $\text{C}_{15}\text{H}_{16}\text{NaO}_2$: 251.1048; found: 251.1036 [M+Na]⁺.

1-(2,4,6-trimethoxyphenyl)propan-2-ol (Table 3, product 3e)²

1,3,5-Trimethoxybenzene (1 mmol, 168 mg) and 2-methyloxirane (2 mmol, 116mg) were dissolved in 5 mL of hexafluoroisopropanol and was refluxed at ambient pressure for 48 hours. The solvent was removed under reduced pressure. The desired product was purified by column chromatography on silica gel using hexane: EtOAc (90: 20) as eluent to afford **4** (65 mg, 29%) as a colorless oil. ^1H NMR (400 MHz, CDCl_3): δ = 1.19 (d, J = 6.0 Hz, 3H), 2.35 (br s, 1H), 2.72–2.84 (2H), 3.81 (s, 6H), 3.82 (s, 3H), 3.93–4.00 (m, 1H), 6.15 (s, 2H); ^{13}C NMR (100 MHz, CDCl_3): δ = 23.0, 32.0, 55.3, 55.6, 68.6, 90.6, 107.6, 159.0, 159.7.

References

- ¹ R. Marcos, C. Rodríguez-Escrich, C. Herrerías, M. A. Pericàs, *J. Am. Chem. Soc.*, 2008, **130**, 16838–16839 (Note: enantiomer was synthesized).
- ² Z.-J. Shi, C. He, *J. Am. Chem. Soc.*, 2004, **126**, 5964–5965.
- ³ Y. X. Liu, X. B. Li, G. Lin, Z. Xiang, J. Xiang, M. Z. Zhao, J. H. Chen, Z. Yang, *J. Org. Chem.*, 2008, **73**, 4625–4629.
- ⁴ F. Fringuelli, R. Germani, F. Pizzo, F. Santinelli, G. Savelli, *J. Org. Chem.*, 1992, **57**, 1198–1202.
- ⁵ C. Lampard, J. A. Murphy, *Tetrahedron*, 1993, **49**, 3841–3848.

