Asymmetric Epoxidation of *cis*-Alkenes Mediated by Iminium Salts:
Highly Enantioselective Synthesis of Levromakalim

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Supplementary information

General Experimental

Infrared spectra were obtained using a Perkin-Elmer Paragon 1000 FT-IR spectrophotometer; solution spectra were obtained in dichloromethane and thin film spectra were acquired using sodium chloride plates, neat or as nujol mulls. ¹H and ¹³C NMR spectra were measured at 250.13 and 62.86 MHz respectively using a Bruker AC 250 MHz instrument or at 400.13 and 100.62 MHz respectively using a Bruker DPX 400 MHz instrument. The solvent used for NMR spectroscopy was CDCl₃ (unless otherwise stated) using tetramethylsilane as the internal reference. Mass spectra were recorded using a Jeol-SX102 instrument, utilizing electron impact (EI) or fast atom bombardment (FAB) techniques, or by the EPSRC national mass spectrometry service at the University of Wales, Swansea, utilizing electrospray (ES) techniques. Analysis by GCMS was carried out using a Fisons AS 800GC 8000 series instrument, using a 15 m x 0.25 mm DB-5 column and an electron impact low resolution mass spectrometer. Melting points were recorded using an Electrothermal-IA 9100 melting point instrument and are uncorrected. Optical rotations were measured with an Optical Activity polAAr 2001 instrument, operating at 589 nm, corresponding to the sodium D line, at the temperatures indicated. Microanalyses were performed on a Perkin Elmer Elemental Analyser 2400 CHN.

Chromatographic manipulations used silica gel as the adsorbent. Reactions were monitored using thin layer chromatography on aluminium-backed plates with Merck Kieselgel 60 F254 silica gel. TLC plates were visualized by UV radiation at a wavelength of 254 nm, or stained by exposure to an ethanolic solution of phosphomolybdic acid (acidified with concentrated sulphuric acid), followed by charring where appropriate. Purification by column chromatography was carried out using Merck Kieselgel 60 H silica gel adsorbent.

Reactions requiring anhydrous conditions were carried out using glassware dried overnight at 150 °C, under a nitrogen atmosphere unless otherwise stated. Light petroleum (b.p. 40-60 °C) was distilled from calcium

chloride prior to use. Ethyl acetate was distilled from calcium sulphate or calcium chloride. Dichloromethane was distilled from calcium hydride. Other reaction solvents were used as obtained.

Enantiomeric excesses were determined either by NMR spectroscopy or by chiral HPLC. Proton NMR spectra were recorded in deuteriated chloroform on a Bruker AC 250 instrument, operating at 250.13 MHz, in the presence of europium (III) tris[3-(hepta-fluoropropylhydroxymethylene)-(+)-camphorate] [(+)-Eu(hfc)₃] as the chiral shift reagent, and tetramethylsilane as the internal standard. A Chiracel OD column was used for the determination of enantiomeric excesses of non-racemic mixtures by chiral HPLC on a TSP Spectra Series P200 instrument, with a TSP Spectra Series UV100 ultraviolet absorption detector set at 254 nm, and a Chromojet integrator.

***N*-Formyl (4*S*,5*S*)-2,2-dimethyl-4-(4-(methylthio)phenyl)-5-amino-1,3-dioxane**

(1*S*,2*S*)-(+)-2-Amino-1-(4-(methylthio)phenyl)-1,3-propanediol (5.0 g, 23.4 mmol) was dissolved in methanol (50 ml), and methyl formate (1.4 ml, 25.7 mmol) added, followed by sodium methoxide (0.5 ml, 2.3 mmol). The reaction was stirred for 3.5 h, and the solvent removed under reduced pressure. The resulting yellow oil was dissolved in acetone (250 ml), and 2,2-dimethoxypropane (30 ml) and camphor sulfonic acid (0.5 g, 2.3 mmol) added. The reaction was stirred for 4 h and monitored by TLC. The solvents were removed under reduced pressure and the residue re-dissolved in ethyl acetate, washed with saturated aqueous sodium hydrogen carbonate, dried (MgSO₄), and the solvents removed under reduced pressure to give the product as a colourless oil (5.5 g, 84%); [α]_D +1.3 (*c* 1.27, CHCl₃); $\nu_{\max}$ (film) /cm⁻¹ 3315, 2988, 2362, 1667, 1494, 1380, 1197, 1084, 947; δ_{H} (250 MHz; CDCl₃) 1.54 (3 H, s) 1.58 (3 H, s), 2.45 (3 H, s), 3.87 (1 H, dd, *J* 7.5, 1.0 Hz), 4.24 (1 H, dd, *J* 7.5, 1.0 Hz), 4.24-4.30 (1 H, m), 5.16 (1 H, d, *J* 1.3 Hz), 6.27 (1 H, d, *J* 5.8 Hz), 7.20 (4 H, s), 7.97 (1 H, s); δ_{C} (100 MHz; CDCl₃) 15.8, 18.5, 29.7, 45.3, 64.6, 71.4, 99.7, 125.8, 126.6, 135.0, 138.8, 160.5; *m/z* (EI) 281.1081; C₁₄H₁₉NO₃S (M⁺) requires 281.1085.

***N*-Formyl (4*S*,5*S*)-2,2-dimethyl-4-(4-(methylsulfonyl)phenyl)-5-amino-1,3-dioxane**

N-Formyl (4*S*,5*S*)-2,2-dimethyl-4-(4-(methylthio)phenyl)-5-amino-1,3-dioxane (4.0 g, 14.2 mmol) was dissolved in dichloromethane (100 ml), and the solution cooled to 0 °C. A solution of *m*-CPBA (2.2 eq, 7.03 g, 31.0 mmol) in chloroform (20 ml) was added dropwise over 10 min. The reaction mixture was stirred for 2 h, transferred to a separating funnel, and washed with saturated aqueous sodium hydrogen carbonate (2 x 40 ml) and brine (2 x 40 ml), and dried (MgSO₄). The solvents were removed under reduced pressure to give a colourless oil, which was crystallized from chloroform/diethyl ether to give the product as colourless crystals (3.8 g, 85%); m.p. 146-147 °C; [α]_D -11.6 (*c* 1.21, CHCl₃); Found C, 52.68; H, 6.12; N, 4.33. C₁₄H₁₉NO₅S requires C, 53.66; H, 6.11; N, 4.47%; $\nu_{\max}$ (film) /cm⁻¹ 3054, 2993, 1675, 1516, 1382, 1300, 1239, 1202, 1149, 1086, 948; δ_{H} (400 MHz; CDCl₃) 1.54 (3 H, s), 1.57 (3 H, s), 3.01 (3 H, s), 3.82 (1 H, dd, *J* 12.0, 2.0 Hz), 4.33 (1 H, dd, *J* 12.0, 1.6 Hz), 4.37 (1 H, dd, *J* 10.0, 1.6 Hz), 5.25 (1 H, s), 6.51 (1 H, d, *J* 9.2 Hz), 7.52 (2 H, d, *J* 8.0 Hz), 7.85 (2 H, d, *J* 8.0 Hz), 7.89 (1H, s); δ_{C} (100 MHz; CDCl₃) 18.9, 29.9, 44.8, 45.4, 64.9, 71.9, 100.4, 127.0, 127.5, 140.0, 145.0, 160.9; *m/z* (EI) 314.1058; C₁₄H₁₉NO₅S (M⁺H) requires 314.1062.

(4*S*,5*S*)-2,2-Dimethyl-4-(4-(methylsulfonyl)phenyl)-5-amino-1,3-dioxane

N-Formyl (4*S*,5*S*)-2,2-dimethyl-4-(4-(methylsulfonyl)phenyl)-5-amino-1,3-dioxane (1.8 g, 5.8 mmol) was dissolved in aqueous hydrazine hydrate (85%) (40 ml) and the solution heated under reflux for 2.5 h. The reaction mixture was allowed to cool to room temperature and extracted with ethyl acetate (3 x 40 ml). The organic layers were washed with water (2 x 40 ml), dried (MgSO₄), and the solvents removed under reduced pressure to give a colourless oil, which was crystallized from ethyl acetate/diethyl ether to give the product as colourless crystals (1.6 g, 96%); m.p. 120-122 °C; [α]_D²⁰ +50.0 (*c* 1.00, CHCl₃); Found: C 54.64, H 6.69, N 4.83. C₁₃H₁₉NO₄S requires C 54.72, H 6.71, N 4.91%; $\nu_{\max}$ (film) /cm⁻¹ 3372, 2991, 1601, 1380, 1198, 1077, 949; δ_{H} (400 MHz; CDCl₃) 1.56 (6 H, s), 2.85 (1 H, m), 3.06 (3 H, s), 3.88 (1 H, dd, *J* 11.6, 2.0 Hz), 3.24 (1 H, dd, *J* 11.6, 2.4 Hz), 5.12-5.21 (1 H, m), 7.55 (2 H, d, *J* 8.0 Hz), 7.95 (2 H, d, *J* 8.0 Hz); δ_{C} (100 MHz; CDCl₃) 19.0, 30.0, 44.9, 49.8, 66.8, 73.9, 99.9, 127.2, 127.9, 139.9, 146.6; *m/z* (EI) 285.1028; C₁₃H₁₉NO₄S (M⁺) requires 285.1035.

(+)-[(4*S*,5*S*)-2,2-dimethyl-4-[4-(methylsulfonyl)-phenyl]-1,3-dioxan-5-yl]-3,4-dihydroisoquinolinium tetraphenylborate

A solution of (4*S*,5*S*)-2,2-dimethyl-4-(4-(methylsulfonyl)phenyl)-5-amino-1,3-dioxane (0.75 g, 3.0 mmol) in ethanol (7.5 ml) was added dropwise to 2-(2-bromoethyl)benzaldehyde (0.69 g, 3.3 mmol). After the addition was complete the reaction flask was stoppered to contain the hydrogen bromide generated, and the reaction mixture stirred overnight while attaining ambient temperature. A solution of sodium tetraphenylborate (1.1 g, 3.3 mmol) in the minimum amount of acetonitrile was added in one portion to the reaction mixture, and, after stirring for 5 minutes, the organic solvents were removed under reduced pressure. Ethanol was added to the residue, followed by water. The resulting yellow solid was collected by filtration and washed with additional ethanol followed by diethyl ether, and recrystallized from dichloromethane/hexane to give the product as yellow plates (1.55 g, 73%); m.p. 199-201 °C (dec.); $[\alpha]_D^{20} +126.7$ (*c* 1.20, acetone); Found: C, 75.62; H, 6.32; N, 1.84. $C_{46}H_{46}BNO_4S \cdot 0.5H_2O$ requires C, 75.79; H, 6.50; N, 1.92%; ν_{max} (film) / cm^{-1} 1636, 1603, 1572, 1478, 1383, 1314, 1266, 1202, 1150, 1076, 1032, 956; δ_H (400 MHz; acetone- d_6), 1.69 (3H, s), 1.72 (3H, s), 2.60-2.69 (1 H, m), 2.85-2.96 (1 H, m), 3.00 (3H, s), 3.65-3.72 (1 H, m), 4.12-4.20 (1 H, m), 4.49 (1 H, d, *J* 13.6 Hz), 4.54-4.59 (1 H, m), 4.77 (1 H, dd, *J* 13.6, 2.8 Hz), 6.05 (1 H, d, *J* 2.8 Hz), 6.80 (4 H, t, *J* 7.2 Hz), 6.92 (8 H, t, *J* 7.2 Hz), 7.30-7.40 (8 H, m), 7.49 (1 H, t, *J* 7.6 Hz), 7.73-7.83 (3 H, m), 7.82 (2 H, d, *J* 8.2 Hz), 7.95 (2 H, d, *J* 8.2 Hz), 9.28 (1 H, s); δ_C (100 MHz; acetone- d_6), 18.8, 25.4, 29.4, 44.3, 52.3, 62.9, 66.1, 71.5, 101.7, 122.3, 125.3, 126.0, 127.6, 128.8, 129.3, 129.4, 135.4, 137.0, 137.0, 137.9, 142.4, 143.2, 165.0, 169.0; *m/z* (ES) 400.1586; $C_{22}H_{26}NO_4S$ (cation) requires 400.1583.

Tetraphenylphosphonium monoperoxysulfate (TPPP)

Oxone^{TM} triple salt (2 KHSO₅:KHSO₄:K₂SO₄) (15.0 g, 48.8 mmol w.r.t. KHSO₅) was dissolved in deionized water (300 ml), and the solution stirred at 10–15 °C (water bath). A solution of tetraphenylphosphonium chloride (15.0 g, 40.0 mmol) in distilled dichloromethane (300 ml) was added over 5 min, and the mixture stirred for an additional 30 min. The organic layer was separated, and the solvent removed under reduced pressure at room temperature. The colourless residue, the crude salt, was transferred to a fritted glass funnel and washed with distilled water (2 x 75 ml). The solid was dissolved in dichloromethane (180 ml), and the solution dried (MgSO₄). Hexane was added until cloudiness developed, and the flask was placed in the freezer (–20 °C) overnight, producing a colourless precipitate of the salt about 85% pure in peroxide (15.4 g, 70%). δ_H (250 MHz; CDCl₃) 7.64 (8 H, m), 7.78 (8 H, m), 7.89 (4 H, m), 8.92 (1 H, s).

General procedure for catalytic asymmetric epoxidation of simple alkenes mediated by iminium salts using tetraphenylphosphonium monoperoxysulfate

Tetraphenylphosphonium monoperoxysulfate (2 eq with respect to the substrate) was dissolved in the chosen solvent (2 ml per 0.1 g oxidant), and cooled to the required temperature. Iminium salt (10 mol%) was dissolved in the chosen solvent (0.5 ml per 0.1 g oxidant). The two solutions were brought to the reaction temperature, and the solution of iminium salt catalyst added dropwise to the solution of oxidant over 15-20 min; the temperature was monitored during the addition, and any increase in temperature minimized. A solution of the alkene substrate in the reaction solvent (0.5 ml per 0.1 g oxidant) was added in the same manner. The mixture was stirred at the reaction temperature until the substrate was completely consumed. Diethyl ether (pre-cooled to the reaction temperature) (20 ml per 0.1 g oxidant) was added to induce precipitation of the remaining oxidant. The mixture was filtered through celite, and the solvent removed under reduced pressure. Diethyl ether (40 ml) was added to the brown residue, and the solution passed through a short pad of silica gel to remove catalyst residues. The solvent was removed under reduced pressure to yield the epoxide.

Indene oxide

Indene (0.116 g, 1.0 mmol) afforded *indene oxide* (0.110 g, 83%)¹ as a colourless oil (0.110 g, 83%); $\nu_{\max}$ (neat)/cm⁻¹ 3027, 2917, 1482, 1464, 1390, 1372, 1232, 1183, 1142, 829, 758, 745, 723; δ_{H} (250 MHz; CDCl₃) 2.97 (1 H, dd, J 2.7 and 18.1 Hz), 3.21 (1 H, d, J 17.6 Hz), 4.13 (1 H, t, J 3.0 Hz), 4.26 (1 H, dd, J 1.1 and 2.8 Hz), 7.14-7.29 (3 H, m), 7.49 (1 H, dd, J 1.7 and 6.6 Hz); δ_{C} (100 MHz; CDCl₃) 34.6, 57.6, 59.1, 125.2, 126.1, 126.3, 128.6, 141.0, 143.6.

1,2-Dihydronaphthalene oxide

1,2-Dihydronaphthalene (0.130 g, 1.0 mmol) afforded *1,2-dihydronaphthalene oxide*² as a colourless oil (0.130 g, 89%); $\nu_{\max}$ (neat)/cm⁻¹ 3059, 3028, 2930, 2850, 1602, 1493, 1316, 1129, 1088, 1030, 964; δ_{H} (400 MHz; CDCl₃) 1.60-1.70 (1 H, m), 2.31-2.39 (1 H, m), 2.45 (1 H, dd, J 15.6 and 5.6 Hz), 2.65-2.70 (1 H, m), 3.65 (1 H, t, J 4.0 Hz), 3.78 (1 H, d, J 4.4 Hz), 7.01 (1 H, d, J 7.2 Hz), 7.14-7.23 (2 H, m), 7.33 (1 H, d, J 7.2 Hz); δ_{C} (100 MHz; CDCl₃) 22.2, 24.8, 55.2, 55.5, 126.5, 128.8, 128.8, 129.9, 132.9, 137.1.

Cis- β -methylstyrene oxide

Cis- β -methylstyrene (0.118 g, 1.0 mmol) afforded *cis*- β -methylstyrene oxide ² as a colourless oil (0.114 g, 85%); $\nu_{\max}$ (neat)/cm⁻¹ 3061, 2994, 1604, 1496, 1450, 1258, 1149, 9563, 853, 742, 700, 619; δ_{H} (250 MHz; CDCl₃) 1.12, (3 H, d, *J* 5.4 Hz), 3.32-3.40 (1 H, m), 4.08 (1 H, d, *J* 4.3 Hz), 7.24-7.39 (5 H, m); δ_{C} (62.5 MHz; CDCl₃) 12.8, 55.4, 57.8, 126.9, 127.7, 128.3, 135.8.

(Z)-Hept-2-ene oxide

(Z)-Hept-2-ene (0.098 g, 1.0 mmol) afforded (*Z*)-hept-2-ene oxide ³ as a colourless oil (0.078 g, 68%); $\nu_{\max}$ (neat)/cm⁻¹ 2959, 2930, 2874, 1390, 1259, 1218, 1151, 1114, 1032, 752; δ_{H} (400 MHz; CDCl₃) 0.93 (3 H, t, *J* 8.0 Hz), 1.20 (3 H, d, *J* 4.0 Hz), 1.32-1.50 (6 H, m), 2.86-2.91 (1 H, m), 2.99-3.06 (1 H, m); δ_{C} (100 MHz; CDCl₃) 12.2, 13.0, 21.6, 26.2, 27.6, 51.6, 56.1.

6-Cyanobenzopyran oxide

6-Cyanobenzopyran (0.185 g, 1.0 mmol) afforded 6-cyanobenzopyran oxide ⁴ as a colourless oil which solidified upon standing (0.119 g, 59%); $\nu_{\max}$ (film)/cm⁻¹ 3089, 3038, 2979, 2934, 2226, 1615, 1579, 1490, 1346, 1279, 1157, 1107, 1046, 955; δ_{H} (400 MHz; CDCl₃) 1.22 (3 H, s), 1.52 (3 H, s), 3.47 (1 H, d, *J* 4.4 Hz), 3.86 (1 H, d, *J* 4.4 Hz), 6.79 (1 H, d, *J* 8.4 Hz), 7.45 (1 H, dd, *J* 2.0, 8.4 Hz), 7.58 (1 H, d, *J* 2.4 Hz); δ_{C} (100 MHz; CDCl₃) 23.4, 25.9, 50.3, 62.7, 75.1, 104.7, 119.0, 119.2, 121.5, 134.2, 134.8, 156.87.

6-Nitrobenzopyran oxide

6-Nitrobenzopyran (0.205 g, 1.0 mmol) afforded 6-nitrobenzopyran oxide ⁴ as a colourless oil which solidified upon standing (0.105 g, 52%); $\nu_{\max}$ (film)/cm⁻¹ 3075, 2926, 2850, 1621, 1590, 1518, 1344, 1281, 1209, 1160, 1088, 955; δ_{H} (400 MHz; CDCl₃) 1.33 (3 H, s), 1.63 (3 H, s), 3.57 (1 H, dd, *J* 4.4 Hz), 4.00 (1 H, d, *J* 4.4 Hz), 6.89 (1 H, d, *J* 9.0 Hz), 8.15 (1 H, dd, *J* 2.8, 9.0 Hz), 8.30 (1 H, d, *J* 2.8 Hz); δ_{C} (100 MHz; CDCl₃) 23.1, 25.5, 50.0, 62.1, 75.2, 118.5, 120.3, 125.8, 126.3, 141.5, 158.3.

6-Chlorobenzopyran oxide

6-Chlorobenzopyran (0.179 g, 1.0 mmol) afforded *6-chlorobenzopyran oxide*⁴ as a colourless oil (0.148 g, 76%); $\nu_{\max}$ (film)/cm⁻¹ 3080, 2985, 2933, 1611, 1579, 1478, 1366, 1339, 1268, 1237, 1202, 1168, 1103, 1087, 1036, 954; δ_{H} (400 MHz; CDCl₃) 1.17 (3 H, s), 1.50 (3 H, s), 3.41 (1 H, dd, *J* 4.4 Hz), 3.77 (1 H, d, *J* 4.4 Hz), 6.67 (1 H, d, *J* 8.6 Hz), 7.11 (1 H, dd, *J* 2.6 and 8.6 Hz), 7.24 (1 H, d, *J* 2.6 Hz); δ_{C} (100 MHz; CDCl₃) 22.5, 25.6, 50.4, 62.6, 73.4, 119.4, 121.6, 125.7, 129.2, 130.2, 151.2.

(-)-(3*S*,4*R*)-3-Hydroxy-2,2-dimethyl-4-(2-oxocyclopentyl)chroman-6-carbonitrile⁴

A solution of pyrrolidin-2-one (2.12 g, 2.49 mmol) and (-)-3*S*,4*S*-2,2-dimethyl-1*a*,7*b*-dihydro-2*H*-1,3-dioxacyclopropa[*a*] naphthalene-6-carbonitrile (0.50 g, 2.49 mmol) in DMSO (20 ml) was treated with NaH (60 %) (0.06 g, 2.49 mmol). The reaction mixture was stirred for 6 h, cautiously quenched with water, and extracted with ethyl acetate (3 x 50 ml). The organic layer was washed with water (2 x 30 ml) and brine (30 ml), and dried (MgSO₄). The solvents were removed under reduced pressure to give a pale yellow oil, which was purified by column chromatography, eluting with hexane/ethyl acetate, and crystallization from ethanol, to give the product as colourless crystals (0.37 g, 52%); m.p. 237-240 °C (lit⁵ 242-244 °C); $[\alpha]_{\text{D}}^{20}$ -53.1 (*c* 1.12, CHCl₃), [lit $[\alpha]_{\text{D}}^{26}$ -52.2 (*c* 1.00, CHCl₃)]; $\nu_{\max}$ (film)/cm⁻¹ 3229, 2975, 2222, 1650; δ_{H} (250 MHz; CDCl₃) 1.28 (3 H, s), 1.55 (3 H, s), 2.07-2.17 (2 H, m), 2.55-2.61 (2 H, m), 3.00-3.09 (1 H, m), 3.36-3.43 (1 H, m), 3.67-3.78 (2 H, m), 5.23 (1 H, d, *J* 10.4 Hz), 6.88 (1 H, d, *J* 8.6 Hz), 7.24 (1 H, t, *J* 1.9 Hz), 7.45 (1 H, dd, *J* 8.5, 2.0 Hz); δ_{C} (62.5 MHz; CDCl₃) 18.4, 18.7, 27.0, 42.4, 52.0, 70.0, 80.8, 104.2, 118.9, 119.3, 121.1, 131.9, 133.3, 157.7, 178.2.

Determination of enantiomeric excess for 1a,2,3,7b-Tetrahydro-1-oxa-cyclopropa[*a*]naphthalene:

^1H -NMR conditions: 8-10 mg substrate
                                     3-5 mg (+)-Eu(hfc)₃

Racemic:

Enantiomerically enriched: Reaction in CHCl_3 :

Enantiomerically enriched: Reaction in CH_3CN :

Determination of enantiomeric excess for (Z)-2-Methyl-3-phenyl-oxirane:

^1H -NMR conditions: 8-10 mg substrate
3-5 mg (+)-Eu(hfc)₃

Racemic:

Enantiomerically enriched: Reaction in CHCl_3 :

Enantiomerically enriched: Reaction in CH_3CN :

Determination of enantiomeric excess for 2,2-Dimethyl-1a,7b-dihydro-2H-1,3-dioxacyclopropa[a]naphthalene-6-carbonitrile:

HPLC conditions: Flow : 1.3
Hex:IPA : 90:10

Racemic: Retention times: (3*R*,4*R*) = 12.98; (3*S*,4*S*) = 15.46.

Enantiomerically enriched: Reaction in CHCl₃ Retention times: (3*R*,4*R*) = 13.28; (3*S*,4*S*) = 15.79.

Enantiomerically enriched: Reaction in CH₃CN Retention times: (3*R*,4*R*) = 12.80; (3*S*,4*S*) = 15.50.

CHANNEL A INJECT 19-02-02 16:02:24 STORED TO BIN # 2

DATA SAVED TO BIN # 2

19-02-02 16:02:24 CH= "A" PS= 1.

FILE 1. METHOD 0. RUN 2 INDEX 2 BIN 2

PEAK# AREA% RT AREA BC

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2	4.229	4.21	1476304	01
3	0.087	4.96	30320	01
4	0.026	5.9	9187	01
5	0.615	8.51	214726	02
6	0.331	9.23	115420	02
7	0.976	9.82	340769	02
8	6.103	11.31	2130305	02
9	8.676	12.8	3028648	08
10	78.004	15.5	27229284	07

TOTAL 100. 34907434

Determination of enantiomeric excess for 6-Chloro-2,2-dimethyl-1a,7b-dihydro-2H-1,3-dioxacyclopropa[a]naphthalene

HPLC conditions: Flow : 0.3
Hex:IPA : 99:1

Racemic: Retention times: (3*R*,4*R*) = 51.50; (3*S*,4*S*) = 60.35.

Enantiomerically enriched: Reaction in CHCl_3 Retention times: (3*R*,4*R*) = 13.28; (3*S*,4*S*) = 15.79.

Determination of enantiomeric excess for 2,2-Dimethyl-6-nitro-1a,7b-dihydro-2*H*-1,3-dioxacyclopropa[*a*]naphthalene:

HPLC conditions: Flow : 1.0
Hex:IPA : 90:10

Racemic: Retention times: (3*R*,4*R*) = 15.50; (3*S*,4*S*) = 17.98.

Enantiomerically enriched: Reaction in CHCl₃ Retention times: (3*R*,4*R*) = 15.90; (3*S*,4*S*) = 18.40.

ppm

ppm

1.607
1.569
1.543

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5.253
4.391
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3.805
3.800

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6.505

7.890
7.867
7.846
7.536
7.516
7.481

pt

BRB-II-178

160.86
144.71
140.00
127.97
127.59
127.29
126.96
100.38
77.84
77.72
77.52
77.21
71.91
64.93
45.43
44.83
29.94
29.77
18.91

24.78
22.19

55.52
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77.76
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77.12

137.07
133.58
132.91
129.94
128.83
128.80
126.51
123.84

ppm

ppm

Levcromakalim

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