Stereoselective Synthesis of Novel β,γ-Epoxy-Hydroxylamines and 4-Hydroxyalkyl-1,2-Oxazetidines

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**General.** Tetrahydrofuran (THF) was freshly distilled under a nitrogen atmosphere over sodium/benzophenone ketyl. *N,N,N',N'*-Tetramethylethylenediamine (TMEDA) was distilled over finely powdered calcium hydride. Nitrones 4a–c\(^1\) and 4g-i\(^2\) were prepared according to the reported procedures. Petroleum ether refers to the 40-60 °C boiling fraction. For the \(^1\)H and \(^13\)C NMR spectra (\(^1\)H NMR 300, 400, 500 MHz; \(^13\)C NMR 75.4, 100 MHz, 125 MHz), CDCl\(_3\) was used as the solvent. MS-ESI analyses were performed on LC/MSD trap system VL. Optical rotation of compounds 5c,d,j and 6c,d,j was measured with a polarimeter using a cell of 1 dm path length at 25 °C; the concentration (c) is expressed in g/100 mL. Enantiomeric purity assay for compound 5c,d,j and 6c,d,j was ascertained by HPLC employing a Daicel Chiralcel OD-H column (250 x 4.6 mm). Melting points were uncorrected. Analytical thin layer chromatography (TLC) was carried out on precoated 0.25 mm thick plates of Kieselgel 60 F254; visualization was accomplished by UV light (254 nm) or by spraying a solution of 5 % (w/v) ammonium molybdate and 0.2 % (w/v) cerium(III) sulfate in 100 ml 17.6 % (w/v) aq. sulphuric acid and heating to 200 °C for some time until blue spots appear. All reactions involving air-sensitive reagents were performed under nitrogen in oven-dried glassware using syringe-septum cap technique.

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\(^1\) Gautheron-Chapouland, V.; Pandya, S. U.; Cividino, P.; Masson, G.; Py, S.; Vallée, Y. *Synlett* **2001**, 8, 1281-1283.

Preparation of β,γ-epoxyhydroxylamines (5a–k). General Procedure. A solution of s-BuLi (1.2 mmol, 0.86 mL of a 1.4 M solution in cyclohexane) [or n-BuLi (1.5 mmol, 0.94 mL of a 1.6 M solution in hexanes) in the case of oxirane 3] was added to a pre-cooled (−98 °C, methanol/liquid nitrogen bath) solution of oxiranes 1-3 (1.0 mmol) and TMEDA (3.0 mmol, 0.45 mL) in THF (9 mL) under N₂ and stirring. After 10 min at this temperature (1 h in the case of oxirane 2 and 30 min in the case of oxirane 3), a solution of the nitrone 4 (1.2 mmol) in THF (2 mL) was added dropwise. The resulting mixture was stirred for 30 min at −98 °C; after this time, it was allowed to warm to rt, quenched with sat. aq. NH₄Cl and extracted with Et₂O (3 × 20 ml); the combined organic layers were dried (Na₂SO₄), filtered and the solvent was removed under reduced pressure. The crude was purified by flash column-chromatography (silica gel; petroleum ether/Et₂O 8-9/2-1) to give compounds 5a–k.

(1R*,2R*)-N-Cumyl-N-hydroxy-1,2-diphenyl-2,3-epoxypropanamine (5a): colourless oil, 60%; ¹H NMR (500 MHz) δ: 1.13 (s, 3 H), 1.18 (s, 3 H), 2.23 (d, J = 5.4 Hz, 1 H), 2.42 (d, J = 5.4 Hz, 1 H), 4.48 (br. s, exchanges with D₂O, 1 H), 4.53 (s, 1 H), 7.08–7.10 (m, 2 H), 7.22–7.49 (m, 13 H); ¹³C NMR (125 MHz) δ: 23.2, 26.2, 49.8, 62.2, 64.4, 66.3, 125.8, 126.0, 126.1, 126.7, 127.10, 127.13, 127.4, 127.5, 130.7, 136.4, 140.1, 146.7; MS (ESI); m/z 382 [M + Na]⁺; FT–IR (film, cm⁻¹): 3486, 1601, 1495, 1447, 1360, 1174, 1076, 1030, 987, 760, 697; HRMS (EI) calcd for C₂₄H₂₅NO₂ (M⁺): 359.4608. Found: 359.4611.

(1R*,2R*)-N-Cumyl-N-hydroxy-2-phenyl-1-p-tolyl-2,3-epoxypropanamine (5b): colourless oil, 42%; ¹H NMR (500 MHz) δ: 1.15 (s, 3 H), 1.19 (s, 3 H), 2.24 (d, J = 5.2 Hz, 1 H), 2.38 (s, 3 H), 2.40 (d, J = 5.2 Hz, 1 H), 4.40 (br. s, exchanges with D₂O, 1 H), 4.51 (s, 1 H), 7.10–7.22 (m, 7 H), 7.36–7.46 (m, 7 H); ¹³C NMR (125 MHz) δ: 20.8, 23.3, 26.2, 49.8, 62.4, 64.3, 66.1, 125.9, 126.1, 126.7, 127.47,
127.53, 127.9, 130.6, 133.3, 136.7, 140.4, 146.9; MS (ESI); m/z 396 [M + Na]+; FT–IR (film, cm⁻¹): 3432, 2979, 1508, 1446, 1356, 1173, 984, 821, 739, 700; HRMS (EI) calcd for C₂₅H₂₇NO₂ (M⁺): 373.2042. Found: 373.2045.

(1R*,2R*)-1-(4-Chlorophenyl)-N-cumyl-N-hydroxy-2-phenyl-2,3-epoxypropanamine (5c): white solid, mp 90–91 °C (hexane), 50%; ¹H NMR (500 MHz) δ: 1.11 (s, 3 H), 1.18 (s, 3 H), 2.17 (d, J = 5.5 Hz, 1 H), 2.40 (d, J = 5.5 Hz, 1 H), 4.41 (br. s, exchanges with D₂O, 1 H), 4.48 (s, 1 H), 7.06–7.08 (m, 2 H), 7.21–7.26 (m, 5 H), 7.36–7.41 (m, 7 H); ¹³C NMR (125 MHz) δ: 23.1, 26.6, 49.7, 62.0, 64.4, 65.7, 125.9, 126.0, 126.3, 126.9, 127.3, 127.55, 127.60, 132.08, 133.13, 135.0, 139.9, 146.3; MS (ESI); m/z 416 [M + Na]+; FT–IR (KBr, cm⁻¹): 3491, 2926, 1594, 1489, 1361, 1090, 1017, 833, 762, 699.

(1S,2S)-(−)-5c: 78%, er: 98/2, (tₘᵣₐᵢⱼ = 13.4 min, tₘᵢᵢᵦ = 14.1 min by HPLC, n-hexane/iPrOH 9/1, flow 0.4 mL/min, 230 nm), [α]₂⁰ˢ = −28 (c 1, CHCl₃).

(1R*,2R*)-N-Cumyl-1-(2-furyl)-N-hydroxy-2-phenyl-2,3-epoxypropanamine (5d): colourless oil, 82%; ¹H NMR (500 MHz) δ: 1.15 (s, 3 H), 1.25 (s, 3 H), 2.46 (d, J = 5.5 Hz, 1 H), 2.52 (d, J = 5.5 Hz, 1 H), 4.62 (br. s, exchanges with D₂O, 1 H), 4.68 (s, 1 H), 6.37 (m, 1 H), 6.44 (d, J = 3.1 Hz, 1 H), 7.12–7.14 (m, 2 H), 7.20–7.22 (m, 3 H), 7.37–7.38 (m, 6 H); ¹³C NMR (125 MHz) δ: 22.6, 25.9, 50.5, 60.5, 61.9, 64.4, 111.0, 111.4, 126.2, 126.4, 126.6, 127.2, 127.8, 127.9, 139.5, 140.8, 146.5, 148.8; MS (ESI); m/z 372 [M + Na]+; FT–IR (film, cm⁻¹): 3454, 3057, 2986, 1494, 1379, 1162, 1012, 930, 740, 700; HRMS (EI) calcd for C₂₂H₂₃NO₃ (M⁺): 349.1678. Found: 349.1675.

(1S,2S)-(−)-5d: 60%, er: 98/2, (tₘᵣᵢⱼ = 7.3 min, tₘᵢᵦ = 7.9 min by HPLC, n-hexane/iPrOH 9/1, flow 0.7 mL/min, 230 nm), [α]₂⁰ˢ = −17 (c 1, CHCl₃).
(1\(R^*,2R^*\))-N-Cumyl-N-hydroxy-1-(4-methoxyphenyl)-2-phenyl-2,3-epoxypropanamine (5e): colourless oil, 54%; \(^1\)H NMR (500 MHz) \(\delta\): 1.13 (s, 3 H), 1.19 (s, 3 H), 2.24 (d, \(J = 4.9\) Hz, 1 H), 2.41 (d, \(J = 4.9\) Hz, 1 H), 3.84 (s, 3 H), 4.46 (br. s, exchanges with D\(_2\)O, 1 H), 4.49 (s, 1 H), 6.84 (d, \(J = 7.9\) Hz, 2 H), 7.08–7.45 (m, 12 H); \(^1^3\)C NMR (125 MHz) \(\delta\): 23.1, 26.1, 49.6, 54.6, 62.3, 64.1, 65.5, 112.4, 125.7, 125.9, 126.5, 127.3, 127.4, 128.2, 131.7, 140.1, 146.7, 158.5; MS (ESI); \(m/z\) 412 [M + Na\(^+\)]; FT–IR (film, cm\(^{-1}\)): 3492, 2933, 1609, 1510, 1360, 1250, 1178, 1031, 834, 750, 700.

(1\(R^*,2R^*\))-N-Cumyl-N-hydroxy-1-[5-(3-trifluoromethylphenyl)-2-furyl]-2-phenyl-2,3-epoxypropanamine (5f): yellow solid, mp 117-118°C (hexane), 82%; \(^1\)H NMR (500 MHz) \(\delta\): 1.19 (s, 3 H), 1.31 (s, 3 H), 2.56 (d, \(J\) = 5.5 Hz, 1 H), 2.60 (d, \(J = 5.5\) Hz, 1 H), 4.70 (s, 1 H), 4.73 (br. s, exchanges with D\(_2\)O, 1 H), 6.56 (d, \(J = 3.0\) Hz, 1 H), 6.69 (d, \(J = 3.0\) Hz, 1 H), 7.15–7.23 (m, 5 H), 7.37–7.41 (m, 5 H), 7.51–7.52 (m, 2 H), 7.77–7.78 (m, 1 H), 7.85 (s, 1 H); \(^1^3\)C NMR (125 MHz) \(\delta\): 23.0, 25.9, 50.7, 61.0, 61.6, 64.5, 107.8, 114.0, 120.2 (q, \(^3\)\(J_{C-F}\) = 4.0 Hz), 123.5 (q, \(^3\)\(J_{C-F}\) = 4.0 Hz), 124.1 (q, \(^1\)\(J_{C-F}\) = 272.0 Hz), 126.4, 126.55, 126.60, 126.7, 127.4, 127.9, 128.0, 129.1, 131.1 (q, \(^2\)\(J_{C-F}\) = 32.0 Hz), 131.4, 139.4, 146.1, 149.5, 150.7; MS (ESI); \(m/z\) 516 [M + Na\(^+\)]; FT–IR (KBr, cm\(^{-1}\)): 3450, 2974, 1619, 1448, 1336, 1170, 1118, 902, 786, 695.

(1\(R^*,2R^*,3S^*\))-1-(4-Chlorophenyl)-N-cumyl-N-hydroxy-2-phenyl-2,3-epoxybutanamine (5g): colourless oil, 60%; \(^1\)H NMR (500 MHz) \(\delta\): 1.11 (s, 3 H), 1.23 (d, \(J = 6.1\) Hz, 3 H), 1.39 (s, 3 H), 3.03 (q, \(J = 5.0\) Hz, 1 H), 4.13 (br. s, exchanges with D\(_2\)O, 1 H), 4.15 (s, 1 H), 7.15 (s, 4 H), 7.26 (s, 6 H), 7.33–7.36 (m, 2 H), 7.47–7.49 (m, 2 H); \(^1^3\)C NMR (125 MHz) \(\delta\): 13.9, 21.2, 29.3, 62.9, 65.9, 66.0, 66.3, 126.0, 126.5,
(1R*,2R*,3R*)-1-(4-Chlorophenyl)-N-cumyl-N-hydroxy-2,3-diphenyl-2,3-epoxypropanamine (5h): white solid, 101–102 °C, 65%; 1H NMR (500 MHz) δ: 1.16 (s, 3 H), 1.20 (s, 3 H), 3.53 (s, 1 H), 4.38 (s, 1 H), 4.46 (br. s, exchanges with D2O, 1 H), 6.89–6.91 (m, 2 H), 7.05–7.10 (m, 5 H), 7.20–7.24 (m, 8 H), 7.31 and 7.45 (2 × d, AB system, J = 8.2 Hz, 4 H); 13C NMR (125 MHz) δ: 22.7, 27.1, 60.3, 64.8, 68.1, 70.2, 125.88, 125.90, 126.3, 126.7, 126.8, 127.07, 127.10, 127.5, 127.8, 132.2, 133.3, 134.6, 135.3, 136.3, 146.5; MS (ESI); m/z 492 [M + Na]+; FT–IR (KBr, cm−1): 3549, 3029, 1598, 1419, 1325, 1165, 1124, 1068, 760, 700.

(1R*,2R*)-N-t-Butyl-1-(4-trifluoromethylphenyl)-N-hydroxy-2-phenyl-2,3-epoxypropanamine (5i): colourless oil, 60%; 1H NMR (300 MHz) δ: 0.87 (s, 9 H), 2.32 (d, J = 5.5 Hz, 1 H), 2.48 (d, J = 5.5 Hz, 1 H), 4.56 (br. s, exchanges with D2O, 1 H), 4.78 (s, 1 H), 7.30–7.73 (m, 9 H); 13C NMR (125 MHz) δ: 26.2, 51.4, 59.3, 61.3, 66.2, 123.8 (q, 1JCF = 272.0 Hz), 124.0 (q, 3JCF = 4.0 Hz), 126.0, 126.8, 127.5, 129.3 (q, 2JCF = 32.0 Hz), 130.8, 139.3, 141.4; MS (ESI); m/z 388 [M + Na]+; FT–IR (film, cm−1): 3500, 2976, 1618, 1419, 1325, 1165, 1124, 1068, 760, 700.

(1R*,2R*)-N-t-Butyl-N-hydroxy-1,2-diphenyl-2,3-epoxypropanamine (5j): white solid, mp 119–121 °C (hexane), 63%; 1H NMR (300 MHz) δ: 0.89 (s, 9 H), 2.40 (d, J = 5.5 Hz, 1 H), 2.47 (d, J = 5.5 Hz, 1 H), 4.51 (br. s, exchanges with D2O, 1 H), 4.76 (s, 1 H), 7.30–7.47 (m, 10 H); 13C NMR (125 MHz) δ: 26.2, 51.3, 59.2, 61.7, 66.5, 126.1, 126.6,
127.1, 127.2, 127.4, 130.6, 137.0, 139.9; MS (ESI); m/z 320 [M + Na]+; FT–IR (KBr, cm⁻¹): 3457, 2978, 1494, 1449, 1385, 1210, 1028, 978, 888, 758, 750, 700.

(1S,2S)-(−)-5j: 63%, er: 98/2, (t_R minor = 10.2 min, t_R major = 11.3 min by HPLC, n-hexane/iPrOH 97/3, flow 0.5 mL/min, 230 nm), [α]^{25}_D = −65 (c 1, CHCl₃).

(1R,2R)-(−)-5j: 60%, er: 98/2, (t_R major = 10.2 min, t_R minor = 11.3 min by HPLC, n-hexane/iPrOH 97/3, flow 0.5 mL/min, 230 nm), [α]^{25}_D = +62 (c 1, CHCl₃).

(1R*,2R*)-N-t-Butyl-1-(4-chlorophenyl)-N-hydroxy-2-phenyl-2,3-epoxypropanamine (5k): colourless oil, 78%; ^1H NMR (300 MHz) δ: 0.88 (s, 9 H), 2.35 (d, J = 5.5 Hz, 1 H), 2.47 (d, J = 5.5 Hz, 1 H), 4.38 (br. s, exchanges with D₂O, 1 H), 4.71 (s, 1 H), 7.25–7.53 (m, 9 H); ^13C NMR (125 MHz) δ: 25.5, 50.5, 58.4, 60.7, 65.1, 125.3, 126.0, 126.6, 126.7, 131.2, 132.2, 134.9, 138.7; MS (ESI); m/z 354 [M + Na]+; FT–IR (film, cm⁻¹): 3433, 2978, 1488, 1361, 1206, 1099, 1017, 955, 763, 704.
Preparation of 4-Hydroxyalkyl-1,2-oxazetidines (6a–k). **General Procedure.** To a solution of \(\beta,\gamma\)-epoxyhydroxylamine 5 (1 mmol) in \(i\)-PrOH (5 mL) an aqueous solution of NaOH (5 mL, 10% w/v) was added. The reaction mixture was then heated to 60 °C (or stirred at rt in the case of \(N\)-t-butylhydroxylamines 5i–k) for 4-6 hours until the substrate 5 disappeared (TLC monitoring: petroleum ether/Et\(_2\)O 8-9/2-1). After this time the resulting reaction mixture was allowed to warm to rt; then it was poured into 10 mL of water and extracted with Et\(_2\)O (3 \(\times\) 10 mL). The combined organic layers were then washed with saturated brine (3 \(\times\) 10 mL), dried (Na\(_2\)SO\(_4\)), and concentrated in vacuo. The crude mixture was flash-chromatographed (silica gel; petroleum ether/Et\(_2\)O 6-8/4-2) to give compounds 6a–k.

\(\text{(3R*},4S*)-(N\text{-Cumyl-3,4-diphenyl-1,2-oxazetidin-4-yl)methanol} \quad (6a):\)
colourless oil, 50%; \(^1\)H NMR (500 MHz) \(\delta\): 1.43 (s, 3 H), 1.49 (br. d, \(J\) = 9.5 Hz, exchanges with D\(_2\)O, 1 H), 1.55 (s, 3 H), 3.43 (d, \(J\) = 13.5 Hz, 1 H), 3.52 (br. dd, \(J\) = 13.5, 9.5 Hz, 1 H), 5.50 (s, 1 H), 7.07–7.2 (m, 10 H), 7.41–7.44 (m, 2 H), 7.51–7.54 (m, 2 H), 7.73–7.74 (m, 2 H); \(^{13}\)C NMR (125 MHz) \(\delta\): 22.1, 26.0, 63.8, 66.4 (2 \(\times\) C), 88.2, 126.0, 127.0, 127.47, 127.50, 127.60, 127.64, 127.7, 128.1, 128.3, 137.2, 138.3, 142.1; MS (ESI); \(m/z\) 382 [M + Na\(^+\)]; FT–IR (film, cm\(^{-1}\)): 3441, 2980, 1638, 1495, 1382, 1258, 1048, 822, 764, 700; HRMS (EI) calcd for C\(_{24}\)H\(_{24}\)ClNO\(_2\) (M\(^+\)): 393.1496. Found: 393.1494.

\(\text{(3R*},4S*)-(N\text{-Cumyl-4-phenyl-3-p-tolyl-1,2-oxazetidin-4-yl)methanol} \quad (6b):\)
white solid, mp 62–63 °C (hexane), 70%; \(^1\)H NMR (500 MHz) \(\delta\): 1.36 (br. s, exchanges with D\(_2\)O, 1 H), 1.38 (s overlapping br. s at \(\delta\) 1.36, 3 H), 1.51 (s, 3 H), 2.25, (s, 3 H), 3.38 (d, \(J\) = 13.5 Hz, 1 H), 3.46 (br. d, 1 H), 5.41 (s, 1 H), 6.91 and 6.98 (2 \(\times\) d, AB system, \(J\) = 8.0 Hz, 4 H), 7.04–7.19 (2 m, 5 H), 7.39–7.52 (2 m, 3 H), 7.68–7.70
(3R*,4S*)-[3-(4-Chlorophenyl)-N-cumyl-4-phenyl-1,2-oxazetidin-4-yl]methanol (6c): colourless oil, 70%; ^1^H NMR (500 MHz) δ: 1.26 (br. s, exchanges with D$_2$O, 1 H), 1.37 (s, 3 H), 1.52 (s, 3 H), 3.38 (d, J = 13.4 Hz, 1 H), 3.47 (br. d, J = 13.4 Hz, 1 H), 5.42 (s, 1 H), 7.02–7.19 (m, 9 H), 7.38–7.51 (m, 3 H), 7.67 (d, J = 7.8 Hz, 2 H); ^1^C NMR (125 MHz) δ: 22.3, 25.8, 63.9, 65.7, 66.4, 88.2, 126.0, 127.3, 127.6, 127.8, 127.9, 128.2, 129.7, 133.5, 135.9, 138.0, 141.8; MS (ESI); m/z 416 [M + Na]$^+$; FT–IR (film, cm$^{-1}$): 3445, 2986, 1600, 1489, 1382, 1259, 1090, 833, 765, 700.

(3S,4R)-(+)6c: 78%, er: 98/2, ($t_R$ minor = 8.7 min, $t_R$ major = 14.2 min by HPLC, n-hexane/iPrOH 9/1, flow 0.7 mL/min, 230 nm), $[\alpha]_{25}^D = +152$ (c 1.7, CHCl$_3$).

(3R*,4S*)-[N-Cumyl-3-(2-furyl)-4-phenyl-1,2-oxazetidin-4-yl]methanol (6d): colourless oil, 62%; ^1^H NMR (500 MHz) δ: 1.25 (br. s exchanges with D$_2$O, 1 H), 1.39 (s, 3 H), 1.56 (s, 3 H), 3.34 (d, J = 13.6 Hz, 1 H), 3.40 (d, J = 13.6 Hz, 1H), 5.43 (s, 1 H), 5.90 (d, J = 3.2 Hz, 1H) 6.12 (dd, J = 3.2, 1.8 Hz, 1H) 7.16–7.27 (m, 6 H), 7.36–7.39 (m, 1 H), 7.45–7.48 (m, 2 H), 7.66 (d, J = 7.8 Hz, 2 H); ^1^C NMR (125 MHz) δ: 22.1, 25.3, 60.3, 63.8, 66.5, 87.6, 110.0, 110.2, 125.5, 127.3, 127.7, 127.8, 127.9, 128.1, 138.8, 141.4, 142.0, 150.9; MS (ESI); m/z 372 [M + Na]$^+$; FT–IR (film, cm$^{-1}$): 3418, 2928, 1495, 1446, 1385, 1259, 1076, 885, 765, 700; HRMS (EI) calcd for C$_{22}$H$_{25}$NO$_3$ (M$^+$): 349.1678. Found: 349.1677.
(3S,4R)-(−)-6d: 62%, er: 98/2, \( t_{R\text{ minor}} = 8.1 \text{ min} \), \( t_{R\text{ major}} = 9.8 \text{ min} \) by HPLC, \( n\)-hexane/iPrOH 9/1, flow 0.7 mL/min, 230 nm), \([\alpha]^{25}_D = +206 \text{ (c 0.9, CHCl}_3\text{)}.\)

\((3R^*,4S^*)\)-[\(N\)-Cumyl-3-(4-methoxyphenyl)-4-phenyl-1,2-oxazetidin-4-yl]methanol (6e): colourless oil, 40%; \(^1\text{H NMR (500 MHz) } \delta: 1.41 \text{ (s, 3 H), 1.46 (br. s, exchanges with D}_2\text{O, 1 H), 1.52 (s, 3 H), 3.40 (d, } J = 13.4 \text{ Hz, 1 H), 3.47 (br d, } J = 13.4 \text{ Hz, 1 H), 3.73 \text{ (s, 3 H), 5.42 (s, 1 H), 6.65 and 7.03 (2} \times d, \text{ AB system, } J = 8.6 \text{ Hz, 4 H), 7.06–7.08 (m overlapping d at } \delta 7.03, 2 \text{ H), 7.16–7.22 (m, 3 H), 7.39–7.52 (2 m, 3 H), 7.70–7.71 (m, 2 H); }^{13}\text{C NMR (125 MHz) } \delta: 22.1, 26.0, 55.0, 63.8, 66.0. 66.5, 88.3, 112.9, 126.1, 127.0, 127.4, 127.6, 127.7, 128.0, 129.5, 129.6, 138.5, 142.2, 159.1; \text{ MS (ESI); } m/z 412 \text{ [M + Na]}^+; \text{ FT–IR (film, cm}^{-1} \text{): 3543, 2979, 1614, 1514, 1446, 1248, 1172, 1033, 834, 765, 700.\)

\((3R^*,4S^*)\)-[\(N\)-Cumyl-3-[5-(3-trifluoromethylphenyl)-2-furyl]-4-phenyl-1,2-oxazetidin-4-yl]methanol (6f): colourless oil, 65%; \(^1\text{H NMR (500 MHz) } \delta: 1.30 \text{ (br. s, exchanges with D}_2\text{O, 1 H), 1.45 (s, 3 H), 1.62 (s, 3 H), 3.44 (d, } J = 13.6 \text{ Hz, 1 H), 3.53 (br. d, } J = 13.6 \text{ Hz, 1 H), 5.50 (s, 1 H), 5.97 (d, } J = 3.4 \text{ Hz, 1 H), 6.45 (d, } J = 3.4 \text{ Hz, 1 H), 7.23–7.69 (m, 14 H); }^{13}\text{C NMR (125 MHz) } \delta: 22.5, 24.9, 60.2, 64.0, 66.3, 87.7, 106.9, 112.6, 120.4 (q, } ^3\text{J}_{C-F} = 4.0 \text{ Hz), 123.6, } (q, } ^3\text{J}_{C-F} = 4.0 \text{ Hz), 123.9 (q, } ^1\text{J}_{C-F} = 270.0 \text{ Hz), 125.7, 126.6, 127.6, 127.7, 127.8, 127.9, 128.1, 128.9, 131.0 (q, } ^2\text{J}_{C-F} = 34.0 \text{ Hz), 131.1, 138.7, 141.4, 151.5, 151.8; \text{ MS (ESI); } m/z 516 \text{ [M + Na]}^+; \text{ FT–IR (film, cm}^{-1} \text{): 3543, 3062, 2925, 1619, 1495, 1335, 1169, 1124, 908, 796, 697; \text{ HRMS (EI) calcd for } C_{29}H_{26}F_3NO_3 (M^+): 493.1865. \text{ Found: 493.1868.} \)}
(3'R*,4'S*,1S*)-1-[3-(4-Chlorophenyl)-N-cumyl-4-phenyl-1,2-oxazetidin-4-yl]ethanol (6g): white solid, mp 138–139 °C (hexane), 80%;

$^1$H NMR (500 MHz) $\delta$: 0.71 (d, $J = 6.7$ Hz, 3 H), 1.04 (br. d, exchanges with D$_2$O, $J = 11.6$ Hz, 1 H), 1.32 (s, 3 H), 1.56 (s, 3 H), 3.62 (dq like sextet, $J = 11.6$, 6.7 Hz, 1 H), 5.56 (s, 1 H), 7.00-7.07 (m, 6 H), 7.16-7.20 (m, 3 H), 7.40-7.43 (m, 1 H), 7.50-7.53 (m, 2 H), 7.68-7.70 (m, 2 H); $^{13}$C NMR (125 MHz) $\delta$: 16.6, 22.4, 25.9, 63.8, 66.2, 70.2, 90.0, 126.1, 126.9, 127.66, 127.70, 127.8, 128.0, 128.1, 129.7, 133.3, 136.4, 138.9, 141.7; MS (ESI); m/z 408 [M + H]$^+$; FT–IR (KBr, cm$^{-1}$): 3529, 2980, 1489, 1279, 1085, 952, 840, 769, 700; Anal. Calcd for C$_{25}$H$_{26}$ClNO$_2$: C 73.61 %; H 6.42 %; N 3.43 %. Found: C 74.00 %; H 6.44, N 3.65 %.

(3'R*,4'S*,1R*)-1-[3-(4-Chlorophenyl)-N-cumyl-4-phenyl-1,2-oxazetidin-4-yl]phenylmethanol (6h): colourless oil, 78%; $^1$H NMR (500 MHz) $\delta$: 1.41 (s, 3 H), 1.46 (s, 3 H), 2.32 (br. s, exchanges with D$_2$O, 1 H), 4.57 (s, 1 H), 5.62 (s, 1 H), 6.67 (br. d, $J = 6.6$ Hz, 2 H), 6.94 (d, $J = 7.3$ Hz, 2 H), 7.01–7.20 (m, 10 H), 7.37–7.39 (m, 1 H), 7.48–7.50 (m, 2 H), 7.70 (d, $J = 7.5$ Hz, 2 H); $^{13}$C NMR (100 MHz) $\delta$: 22.5, 25.8, 64.0, 68.1, 78.9, 88.0, 126.7, 127.0, 127.5, 127.6, 127.65. 127.70, 127.73, 127.8, 128.0, 128.2, 130.5, 133.5, 136.3, 137.1, 137.6, 142.6; MS (ESI); m/z 492 [M + Na]$^+$; FT–IR (KBr, cm$^{-1}$): 3500, 2979, 1600, 1491, 1365, 1090, 909, 844, 733, 702; HRMS (EI) calcd for C$_{30}$H$_{28}$ClNO$_2$ (M$^+$): 469.1809. Found: 469.1806.
(3R*,4S*)-[N-t-Butyl-4-phenyl-3-(4-trifluoromethyl)-1,2-oxazetidin-4-yl]methanol (6i): colourless oil, 50%; ¹H NMR (500 MHz) δ: 1.13 (s, 9 H), 2.31 (br. s, exchanges with D₂O, 1 H), 3.74 (d, J = 13.3 Hz, 1 H), 3.90 (d, J = 13.3 Hz, 1 H), 5.68 (s, 1 H), 7.06–7.07 (m, 2 H), 7.16–7.17 (m, 3 H), 7.23 and 7.34 (2 × d, AB system, J = 8.1 Hz, 4 H); ¹³C NMR (125 MHz) δ: 24.1, 59.4, 65.8, 66.9, 87.1, 124.0 (q, J_C–F = 272.0 Hz), 124.5 (q, J_C–F = 4.0 Hz), 126.0, 127.4, 127.8, 128.5, 129.7 (q, J_C–F = 32.0 Hz), 137.9, 141.5; MS (ESI); m/z 388 [M + Na]⁺; FT–IR (film, cm⁻¹): 3418, 2973, 1621, 1421, 1326, 1165, 1127, 1067, 846, 702; HRMS (EI) calcd for C₂₀H₂₂F₃NO₃ (M⁺): 365.1603. Found: 365.1606.

(3R*,4R*)-[N-t-Butyl-4-phenyl-3-(4-trifluoromethyl)-1,2-oxazetidin-4-yl]methanol (6i): colourless oil, 5%; ¹H NMR (500 MHz) δ: 1.06 (s, 9 H), 1.90 (br. s, exchanges with D₂O, 1 H), 3.54 (d, J = 12.0 Hz, 1 H), 3.97 (d, J = 12.0 Hz, 1 H), 5.22 (s, 1 H), 7.33–7.40 (m, 3 H), 7.43–7.46 (m, 2 H), 7.67 and 7.79 (2 × d, AB system, J = 8.2 Hz, 4 H); ¹³C NMR (100 MHz) δ: 24.0, 59.3, 66.4, 69.5, 83.9, 123.9, 124.0 (q, J_C–F = 272.0 Hz), 125.3 (q, J_C–F = 4.0 Hz), 127.7, 128.1, 128.7, 130.2 (q, J_C–F = 32.0 Hz), 140.7, 142.0; MS (ESI); m/z 388 [M + Na]⁺; FT–IR (film, cm⁻¹): 3418, 2926, 1527, 1364, 1325, 1166, 1127, 852, 701.

(3R*,4S*)-(N-t-Butyl-3,4-diphenyl-1,2-oxazetidin-4-yl)methanol (6j): white solid, mp 82–83 °C (hexane), 70%; ¹H NMR (500 MHz) δ: 1.15 (s, 9 H), 2.39 (br. s, exchanges with D₂O, 1 H), 3.74 (d, J = 13.1 Hz, 1 H), 3.92 (d, J = 13.1 Hz,
1 H), 5.62 (s, 1 H), 7.09–7.17 (m, 10); $^{13}$C NMR (125 MHz) $\delta$: 24.0, 59.1, 66.4, 67.0, 87.0, 126.0, 126.9, 127.40, 127.43, 128.1, 137.3, 138.3; MS (ESI); $m/z$ 320 [M + Na]$^+$; FT–IR (KBr, cm$^{-1}$): 3441, 3029, 2930, 1495, 1455, 1224, 1048, 990, 832, 771, 700; Anal. Calcd for C$_{19}$H$_{23}$NO$_2$: C 76.73 %; H 7.80 %; N 4.71 %. Found: C 76.45 %; H 7.67, N 4.82 %.

(3$S$,4$R$)-(+)–6j: 80%, er: 98/2, ($t_R$ minor = 6.9 min, $t_R$ major = 7.3 min by HPLC, n-hexane/iPrOH 9/1, flow 0.7 mL/min, 230 nm), $[\alpha]^{25}_D = +261$ (c 0.8, CHCl$_3$).

(3$R$,4$S$)-(−)–6j: 75%, er: 98/2, ($t_R$ major = 6.9 min, $t_R$ minor = 11.3 min by HPLC, n-hexane/iPrOH 9/1, flow 0.7 mL/min, 230 nm), $[\alpha]^{25}_D = -256$ (c 0.9, CHCl$_3$).

(3$R^*$,4$S^*$)–[N-$t$-Butyl-3-(4-chlorophenyl)-4-phenyl-1,2-oxazetidin-4-yl]methanol (6k): white solid, mp 105–106 °C (hexane), 95%; $^1$H NMR (500 MHz) $\delta$: 1.10 (s, 9 H), 2.14 (br. s, exchanges with D$_2$O, 1 H), 3.69 (d, $J = 13.4$ Hz, 1 H), 3.85 (br. d, $J = 13.4$ Hz, 1 H), 5.57 (s, 1 H), 7.01–7.06 (m, 6 H), 7.15–7.19 (m, 3 H); $^{13}$C NMR (125 MHz) $\delta$: 24.1, 59.4, 65.8, 67.1, 87.1, 126.1, 127.3, 127.8, 129.7, 133.4, 136.1, 138.1; MS (ESI); $m/z$ 354 [M + Na]$^+$; FT–IR (KBr, cm$^{-1}$): 3419, 2972, 1597, 1490, 1362, 1224, 1090, 1016, 837, 721, 701; Anal. Calcd for C$_{19}$H$_{22}$ClNO$_2$: C 68.77 %; H 6.68 %; N 4.22 %. Found: C 69.16 %; H 6.87, N 4.25 %.
5h
5i-major
6i-minor
NO

\[ \text{Ph} \]

6j

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S57
DPFGSE-NOE experiment

\[ \text{(3R*,4S*)-6i} \]

selective preirradiation
DPFGSE-NOE experiment

selective preirradiation

(3R*,4R*)-6i