Supporting Information for

Highly Enantioselective Darzens Reaction between Diazoacetamides and Aldehydes Catalyzed by A (+)-Pinanediol-Ti(OⁱPr)₄ System

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General Information

All experiments were reacted under an atmosphere of nitrogen unless otherwise indicated. Flasks were all flamed and cooled before use. All solvents were dried before use. ¹H NMR and ¹³C NMR spectra were reported on a Brucker 300 MHz, 400 MHz, 500 MHz spectrometer. HPLC analysis was performed on an Agilent 1260 or Agilent 1220 (UV detection monitored at 254 nm). HRMS spectra were recorded on Agilent Q-TOF 6540. Chiral HPLC data for the epoxidation products could be obtained using a Chiralcel OD-H or Chiralpak AD-H column. These chiral columns were purchased from Daicel Chemical Industries, LTD. IR spectra were recorded on a Nicolet PROTÉGÉ 460 spectrometer. Melting points were determined on a SGW X-4B melting point apparatus. Optical rotations were determined on a Rudolph Autopol IV polarimeter. The low temperature reactions were carried out in EYELA low temp bath (PSL-1810).

Solid and liquid aldehydes were purchased from Aladdin Reagent (Shanghai, China), and they were sublimed or distilled before use.

Preparation of the diazoacetamides^{1, 2}

N-phenylacetamide



A 1 L three-necked round bottom flask fitted with a magnetic stir bar was dried and cooled under nitrogen. A solution of p-toluenesulfonylhydrazone of glyoxylic acid chloride³ (0.332 mmol, 86g) in CH₂Cl₂ was added into the flask and stirred at 0°C for 20 minutes. Then aniline (33.6 mL, 0.365 mol, 1.1 equiv) and DBU (101.0 mL, 0.664 mol, 2 equiv) were added sequentially to the reaction flask at 0°C slowly. After stirring for 2.5 h at 0°C, the reaction mixture was then added sat. NH₄Cl and the layers separated. The aqueous layer was extracted CH₂Cl₂ twice, while the organic layers were combined, washed with brine once, dried over Na₂SO₄ and evaporated in vacuo. The residue was purified by column chromatography on silica gel (eluting with CH₂Cl₂/MeOH = 50:1) to get a brown solid. The solid was washing with ether to give the final compound as a yellow solid (34.6%, 18.5 g).

¹H NMR (500 MHz, DMSO-*d*6): δ (ppm) 9.75 (s, 1H), 7.54-7.52 (d, J = 10 Hz, 2H), 7.30-7.27 (t, J = 7.5 Hz, 2H), 7.02-6.99 (t, J = 7.5 Hz, 1H), 5.50 (s, 1H); ¹³C NMR (500 MHz, DMSO-*d*6): δ 163.6, 139.6, 128.8, 122.7, 118.6, 48.1.

N-(4-Methoxyphenyl)diazoacetamide



N-(4-Methoxyphenyl)diazoacetamide was prepared according to the procedure described above with *p*-toluenesulfonylhydrazone of glyoxylic acid chloride³ (27.6 mmol, 7.2 g) and 4-anisidine (30.4 mmol, 3.75 g) to give the compound as a yellow solid (30%, 1.58 g). ¹H NMR (500 MHz, DMSO-*d*6): δ (ppm) 9.61 (s, 1H), 7.44-7.43 (d, *J* = 5 Hz, 2H), 6.87-6.85 (d, *J* = 10 Hz, 2H), 5.44 (s, 1H), 3.71 (s, 3H); ¹³C NMR (500 MHz, DMSO-*d*6): δ 163.1, 154.9, 132.7, 120.2, 113.9, 55.2, 47.7.

N-(4-Chlorophenyl)diazoacetamide

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N-(4-Chlorophenyl)diazoacetamide was prepared according to the procedure described above with p-toluenesulfonylhydrazone of glyoxylic acid chloride³ (27.6 mmol, 7.2 g) and 4-chloroanisidine (30.4 mmol, 3.88 g) to give the compound as a yellow solid (50%, 2.70 g).

¹H NMR (500 MHz, DMSO-*d*6): δ (ppm) 9.84 (s, 1H), 7.56-7.55 (d, *J* = 5 Hz, 2H), 7.34-7.32 (d, *J* = 10 Hz, 2H), 5.49 (s, 1H); ¹³C NMR (500 MHz, DMSO-*d*6): δ 163.7, 138.5, 128.7, 126.2, 120.1, 48.3.

N-benzyl-2-diazoacetamide



N-benzyl-2-diazoacetamide was prepared according to the procedure described above with *p*-toluenesulfonylhydrazone of glyoxylic acid chloride³ (22.1 mmol, 5.7 g) and benzylamine (24.3 mmol, 2.60 g) to get a pure yellow solid (20%, 0.77 g).

¹H NMR (300 MHz, CDCl₃): δ (ppm) 7.35-7.28 (m, 5H), 5.46 (s, 1H), 4.76 (s, 1H), 4.49-4.47 (d, J = 6 Hz, 1H); ¹³C NMR (300 MHz, CDCl₃): δ 165.4, 138.3, 128.8, 127.7, 127.6, 47.2, 44.1.

General Procedure for the Racemic Darzens Reactions:^a A 25-ml flask containing 4 Å molecular sieves was dried under vacuum. To the flask was added CH_2Cl_2 (10 ml), and the solution was cooled to 0°C. To the mixture were then added the corresponding aldehyde (1.2 mmol) and the diazoacetamide (1 mmol). Then Ti(O-*i*-Pr)₄ (0.1 mmol) was introduced into the system by a syringe. The reaction was stirred at 0°C for about 12 hours. After the completion of the reaction, the solution was poured into H₂O and extracted with CH_2Cl_2 twice. The combined organic layers were dried over Na₂SO₄ and evaporated in vacuo. The residue was purified by column chromatography to give the product.

Table 1 Ti(OⁱPr)₄ catalyzed Darzens reaction of aldehyde with diazoacetamide^a



Entry		Yield
Lindy	Aldenyde	$(\%)^b$
1	CH ₃ CH ₂ CHO	52(8)
2	CH ₃ CH ₂ CH ₂ CHO	58(4)
3	CH ₃ (CH ₂) ₃ CHO	62(6)
4	CH ₃ (CH ₂) ₄ CHO	71(4)
5	PhCH ₂ CHO	54(6)
6	PhCH ₂ CH ₂ CHO	65(11)
7	(CH ₃) ₂ CHCH ₂ CHO	56(3)
8	(CH ₃) ₂ CHCHO	63(3)
9	Cyclohexane-CHO	46(6)
10	PhCHO	67(9)
11	3-NO ₂ -PhCHO	57(10)
12	4-NO ₂ -PhCHO	53(12)
13	3-MeO-PhCHO	48(7)
14	4-CN-PhCHO	52(6)
15	3-F-PhCHO	48(8)
16	2,3-di-Methoxy-PhCHO	63(4)
17	1-naphthaldehyde	56(11)
18	4-Me-PhCHO	65(5)
19	4- ^t Bu-PhCHO	59(9)

^{*a*} Unless otherwise noted, all reactions were carried out with aldehyde (1.2 mmol), diazoacetamide (1 mmol), Ti($O^{i}Pr$)₄ (0.1 mmol) and M.S. 4Å (150 mg) in CH₂Cl₂ (5 mL) at 0°C for 12 hours. ^{*b*}Isolated yield based on diazoacetamide. The ratio of *cis* isomer to *trans* isomer was > 20:1 for all of the cases by H-NMR analysis of crude products. The number in the parenthesis is the percentage of **b** in crude products.

General Procedure for the Asymmetric Darzens Reactions: To a Schlenk tube was added chiral diol (0.12 mmol), Ti(OⁱPr)₄ (0.1 mmol) and CH₂Cl₂ (4 mL) under nitrogen atmosphere. The solution was stirred at room temperature for 1h. Then 4Å M.S was added. After the resulting mixture was cooled to -10° C, aldehyde (1.2 mmol) and diazoacetamide (1 mmol) were added into the mixture subsequently under a nitrogen atmosphere. The resulting mixture was stirred at -10° C for 12 hours. The completion of the reaction was monitored by TLC analysis. The reaction mixture was quenched with H₂O (0.5 mL) and filtered through a pad of celite. The filtrate was dried over anhydrous Na₂SO₄, filtered and concentrated under vacuum. The residue was purified by flash column chromatography (eluted with ethyl acetate/petroleum ether) to give the desired compound. The ee value was determined by chiral HPLC analysis with a Daicel Chiralpak AD-H

or Daicel Chiralcel OD-H column.

(2*R*,3*R*)-3-ethyl-*N*-phenyloxirane-2-carboxamide: Colorless oil (Flash column chromatography eluent: petroleum ether/ethyl acetate = 10/1), yield: 92%; Enantiomeric excess: 98.2%, determined by HPLC (Daicel Chiralcel OD-H, n-hexane/2-propanol = 90/10, flow rate = 1.0 mL/min, λ = 254 nm, T = 30 °C, retention time: 8.74 min (minor), 18.19 min (major); ¹H NMR (300 MHz, CDCl₃): δ (ppm) 7.87 (s, 1H), 7.59-7.55 (m, 2H), 7.39–7.31 (m, 2H), 7.19-7.11 (m, 1H), 3.67-3.66 (d, *J* = 3 Hz, 1H), 3.29-3.23 (m, 1H), 1.69-1.63 (m, 2H), 1.11-1.09 (t, *J* = 7.5 Hz, 3H); ¹³C NMR (300 MHz, CDCl₃): δ 165.5, 136.5, 129.2, 124.9, 119.8, 60.3, 55.7, 21.4, 10.3; $[\alpha]_D^{20}$ = +34.0 (c = 0.60, CH₂Cl₂); IR (KBr): 3296, 2967, 1670, 1596, 1525, 1444, 755, 692; HRMS calcd.for (C₁₁H₁₃NO₂)+ requires m/z 191.0946, found m/z 191.0947.



(2*R*,3*R*)-3-propyl-*N*-phenyloxirane-2-carboxamide: Colorless oil (Flash column chromatography eluent: petroleum ether/ethyl acetate = 10/1), yield: 90%; Enantiomeric excess: 99.1%, determined by HPLC (Daicel Chiralcel OD-H, n-hexane/2-propanol = 90/10, flow rate = 1.0 mL/min, λ = 254 nm, T = 30°C, retention time: 8.03 min (minor), 15.73 min (major); ¹H NMR (300 MHz, CDCl₃): δ (ppm) 7.87 (s, 1H), 7.59-7.55 (m, 2H), 7.39-7.34 (m, 2H), 7 .19-7.14 (m, 1H), 3.66-3.64 (d, *J* = 6 Hz, 1H), 3.32-3.27 (m, 1H), 1.62–1.55 (m, 4H), 1.01-0.96 (m,3H); ¹³C NMR (300 MHz, CDCl₃): δ 165.6, 136.5, 129.2, 124.9, 119.8, 59.1, 55.5, 29.7, 19.5, 13.8; $[\alpha]_D^{20}$ = +40.6 (c = 0.58, CH₂Cl₂); IR (KBr): 3264, 2961, 2872, 1664, 1609, 1552, 1448, 1246, 1051, 757, 691; HRMS calcd.for (C₁₂H₁₅NO₂)⁺ requires m/z 205.1103, found m/z 205.1101.



(*2R*,*3R*)-**3-butyl-***N***-phenyloxirane-2-carboxamide:** Colorless oil (Flash column chromatography eluent: petroleum ether/ethyl acetate = 10/1), yield: 91%; Enantiomeric excess: 97.2%, determined

by HPLC (Daicel Chiralcel OD-H, n-hexane/2-propanol = 90/10, flow rate = 1.0 mL/min, λ = 254 nm, T = 30°C, retention time: 7.55 min (minor), 13.55 min (major); ¹H NMR (300 MHz, CDCl₃): δ (ppm) 7.87 (s, 1H), 7.58–7.55 (m, 2H), 7.39-7.34(m, 2H), 7.19-7.14 (m, 1H), 3.66-3.64 (d, *J* = 6 Hz, 1H), 3.32-3.26 (m, 1H), 1.67-1.60 (m, 2H), 1.55-1.49 (m, 2H), 1.42-1.34 (m, 2H), 0.94-0.89 (t, *J* = 7.5 Hz, 3H); ¹³C NMR (300 MHz, CDCl₃): δ 165.6, 136.5, 129.2, 124.9, 119.8, 59.3, 55.6, 28.2, 27.5, 22.4, 13.9; $[\alpha]_D^{20}$ = +36.7 (c = 0.55, CH₂Cl₂); IR (KBr): 3297, 2955, 2928, 2861, 1671, 1597, 1526, 1444, 1315, 1241, 748, 689; HRMS calcd.for (C₁₃H₁₇NO₂)⁺ requires m/z 219.1259, found m/z 219.1255.



(2*R*,3*R*)-3-isopropyl-*N*-phenyloxirane-2-carboxamide: Colorless oil (Flash column chromatography eluent: petroleum ether/ethyl acetate = 15/1), yield: 83%; Enantiomeric excess : 98.1%, determined by HPLC (Daicel Chiralcel OD-H, n-hexane/2-propanol = 90/10, flow rate = 1.0 mL/min, λ = 254 nm, T = 30°C, retention time: 7.85 min (minor), 10.93 min (major); ¹H NMR (300 MHz, CDCl₃): δ (ppm) 7.86 (s, 1H), 7.59–7.56 (m, 2H), 7.40-7.31 (m, 2H), 7.20-7.11 (m, 1H), 3.69-3.67 (d, *J* = 6 Hz, 1H), 3.00-2.96 (m, 1H), 1.56-1.48 (m, 1H), 1.19-1.16 (d, *J* = 9 Hz, 3H), 1.03-1.01 (d, *J* = 6 Hz, 3H); ¹³C NMR (300 MHz, CDCl₃): δ 165.7, 136.5, 129.2, 124.9, 119.8, 64.6, 56.0, 27.8, 20.2, 18.3; $[\alpha]_D^{20} = +32.0$ (c = 0.60, CH₂Cl₂); IR (KBr): 3274, 2971, 2933, 1668, 1599, 1543, 1443, 754, 692; HRMS calcd.for (C₁₂H₁₅NO₂)⁺ requires m/z 205.1103, found m/z 205.1106.



(2*R*,3*R*)-3-isobutyl-*N*-phenyloxirane-2-carboxamide: Colorless oil (Flash column chromatography eluent: petroleum ether/ethyl acetate = 10/1), yield: 81%; Enantiomeric excess: 97.7%, determined by HPLC (Daicel Chiralpak AD-H, n-hexane/2-propanol = 90/10, flow rate = 1.0 mL/min, $\lambda = 254$ nm, T =30°C, retention time: 7.65 min (major), 8.32 min (minor); ¹H NMR (300MHz, CDCl₃): δ (ppm) 7.88 (s, 1H), 7.58-7.55 (m, 2H), 7.40-7.34 (m, 2H), 7.19-7.14 (m, 1H), 3.64-3.63 (d, *J* = 3 Hz, 1H), 3.35-3.29 (m, 1H), 1.92-1.86 (m, 1H), 1.60-1.45 (m, 2H), 1.03-0.97

(m, 6H); ¹³C NMR (300 MHz, CDCl₃): δ 165.56, 136.5, 129.2, 124.9, 119.8, 58.4, 55.2, 36.4, 26.5, 22.8, 22.5; $[\alpha]_D^{20} = +41.2$ (c = 0.50, CH₂Cl₂); IR (KBr): 3304, 3270, 2959, 2931, 1674, 1603, 1552, 1446, 757, 693; HRMS calcd for (C₁₃H₁₇NO₂)⁺ requires m/z 219.1259, found m/z 219.1262.



(2*R*,3*R*)-3-cyclohexyl-*N*-phenyloxirane-2-carboxamide: Colorless oil (Flash column chromatography eluent: petroleum ether/ethyl acetate = 15/1), yield: 85%; Enantiomeric excess: 96.2%, determined by HPLC (Daicel Chiralpak AD-H, n-hexane/2-propanol = 90/10, flow rate = 1.0 mL/min, λ = 254 nm, T =30°C, retention time: 8.96 min (major), 11.02 min (minor); ¹H NMR (300 MHz, CDCl₃): δ (ppm) 7.90 (s, 1H), 7.58-7.55 (m, 2H), 7.40 – 7.35 (m, 2H), 7.20-7.14 (m, 1H), 3.67-3.65 (d, *J* = 6 Hz, 1H), 3.04-3.00 (m, 1H), 2.02-1.99 (m, 1H), 1.75-1.66 (m, 4H), 1.25-1.15 (m, 6H); ¹³C NMR (300MHz, CDCl₃): δ 165.6, 136.5, 129.2, 124.9, 119.9, 63.4, 55.60, 36.9, 30.5, 28.4, 25.9, 25.1; $[\alpha]_D^{20}$ = +26.7 (c = 0.45, CH₂Cl₂); IR (KBr): 3293, 2931, 2852, 1678, 1600, 1542, 1449, 1313, 1247, 746, 692; HRMS calcd.for (C₁₅H₁₉NO₂)⁺ requires m/z 245.1416, found m/z 245.1417.



(2*R*,3*R*)-3-benzyl-*N*-phenyloxirane-2-carboxamide: White solid (Flash column chromatography eluent: petroleum ether/ethyl acetate = 10/1), mp 85-87 °C, yield: 83%; Enantiomeric excess: 95.4%, determined by HPLC (Daicel Chiralcel OD-H, n-hexane/2-propanol = 90/10, flow rate = 1.0 mL/min, λ = 254 nm, T =30°C, retention time: 16.42 min (minor), 24.53 min (major); ¹H NMR (300 MHz, CDCl₃): δ (ppm) 7.99 (s, 1H), 7.63-7.60 (m, 2H), 7.41-7.34 (m, 4H), 7.30-7.28 (m, 1H), 7.21-7.16 (m, 1H), 3.76-3.74 (d, *J* = 6 Hz, 1H), 3.55-3.49 (m, 1H), 2.99-2.97 (d, *J* = 6 Hz, 2H); ¹³C NMR (300MHz, CDCl₃): δ 165.2, 136.4, 135.9, 129.2, 128.9, 128.8, 127.1, 125.0, 119.9, 59.2, 55.7, 34.3; [α]_D²⁰ = +51.9 (c = 0.52, CH₂Cl₂); IR (KBr): 3277, 3061, 1668, 1597, 1541, 1445, 1315, 1246, 977, 747, 695; HRMS calcd.for (C₁₆H₁₅NO₂)⁺ requires m/z 253.1103, found m/z 253.1099.



(2*R*,3*R*)-3-pentyl-*N*-phenyloxirane-2-carboxamide: Colorless oil (Flash column chromatography eluent: petroleum ether/ethyl acetate = 10/1), yield: 88%; Enantiomeric excess: 96.7%, determined by HPLC (Daicel Chiralpak AD-H, n-hexane/2-propanol = 90/10, flow rate = 1.0 mL/min, $\lambda = 254$ nm, T =30°C, retention time: 6.94 min (major), 7.79 min (minor); ¹H NMR (300 MHz, CDCl₃): δ (ppm) 7.87 (s, 1H), 7.58-7.55 (m, 2H), 7.39-7.34 (m, 2H), 7.19-7.14 (m, 1H), 3.65-3.64 (d, *J* = 3 Hz, 1H), 3.32-3.26 (m, 1H), 1.63-1.54 (m, 4H), 1.35-1.31 (m, 4H), 0.92-0.87 (m, 3H); ¹³C NMR (300 MHz, CDCl₃): δ 165.6, 136.5, 129.1, 124.9, 119.8, 59.3, 55.6, 31.4, 27.7, 25.8, 22.4, 13.9; $[\alpha]_D^{20} = +72.5$ (c = 0.40, CH₂Cl₂); IR (KBr): 3296, 3203, 2956, 2929, 2859, 1681, 1602, 1533, 1445, 1313, 1245, 755, 693; HRMS calcd.for (C₁₄H₁₉NO₂)⁺ requires m/z 233.1416, found m/z 233.1414.



(2*R*,3*R*)-3-phenethyl-*N*-phenyloxirane-2-carboxamide: Colorless oil (Flash column chromatography eluent: petroleum ether/ethyl acetate = 10/1), yield: 84%; Enantiomeric excess: 97.7%, determined by HPLC (Daicel Chiralcel OD-H, n-hexane/2-propanol = 90/10, flow rate = 1.0 mL/min, λ = 254 nm, T =30°C, retention time: 14.24 min (minor), 20.47 min (major); ¹H NMR (300 MHz, CDCl₃): δ (ppm) 7.88 (s, 1H), 7.58-7.55 (m, 2H), 7.40-7.28 (m, 4H), 7.25-7.15 (m, 4H), 3.68-3.66 (d, *J* = 6 Hz, 1H), 3.35-3.29 (m, 1H), 2.90-2.85 (t, *J* = 7.5 Hz, 2H), 2.02-1.92 (m, 2H); ¹³C NMR (300 MHz, CDCl₃): δ 165.3, 140.3, 136.5, 129.2, 128.6, 128.4, 126.4, 124.9, 119.8, 58.5, 55.5, 32.3, 29.6; [α]_D²⁰ = +45.0 (c = 0.28, CH₂Cl₂); IR (KBr): 3302, 1672, 1604, 1522, 1498, 1444, 835, 753, 698; HRMS calcd for (C₁₇H₁₇NO₂)⁺ requires m/z 267.1259, found m/z 267.1262.



(2R,3R)-3-phenyl-N-phenyloxirane-2-carboxamide: White solid (Flash column chromatography eluent: petroleum ether/ethyl acetate = 10/1), mp 105-109 °C, yield: 81%;

Enantiomeric excess: 85.1%, determined by HPLC (Daicel Chiralpak AD-H, n-hexane/2-propanol = 70/30, flow rate = 1.0 mL/min, λ = 254 nm, T = 30°C, retention time: 6.24 min (major), 7.26 min (minor); ¹H NMR (300 MHz, CDCl₃): δ (ppm) 7.55 (s, 1H), 7.44-7.42 (d, 2H), 7.37-7.29 (m, 3H), 7.21-7.16 (m, 3H), 7.10-7.05 (m, 1H), 4.46-4.44 (d, *J* = 10 Hz, 1H), 3.95-3.94 (d, *J* = 5 Hz, 1H); ¹³C NMR (300 MHz, CDCl₃): δ 164.5, 136.0, 132.8, 128.9, 128.8, 128.6, 126.4, 124.9, 120.3, 58.7, 56.6; $[\alpha]_D^{20} = -17.8$ (c = 0.40, CH₂Cl₂); IR (KBr): 3326, 1673, 1530, 1496, 1444, 750, 689; HRMS calcd.for (C₁₅H₁₃NO₂)⁺ requires m/z 239.0946, found m/z 239.0944.



(*2R,3R*)-3-(4-nitrophenyl)-*N*-phenyloxirane-2-carboxamide: White solid (Flash column chromatography eluent: petroleum ether/ ethyl acetate = 7/1), mp 137-139 °C, yield: 88%; Enantiomeric excess: 95.2%, determined by HPLC (Daicel Chiralpak AD-H, n-hexane/2-propanol = 70/30, flow rate = 1.0 mL/min, λ = 254 nm, T = 30°C, retention time: 7.54 min (major), 14.90 min (minor); ¹H NMR (500 MHz, CDCl₃): δ (ppm) 8.21-8.19 (d, *J* = 10 Hz, 2H), 7.61-7.58 (m, 3H), 7.24-7.21 (m,4H), 7.11-7.08 (m,1H), 4.48-4.47 (d, *J* = 5 Hz,1H), 4.02-4.01 (d, *J* = 5 Hz, 1H); ¹³C NMR (500 MHz, CDCl₃): δ 163.3, 148.1, 139.8, 135.6, 129.2, 127.4, 125.3, 123.8, 119.9, 57.8, 56.8; $[\alpha]_D^{20} = -47.5$ (c = 0.40, CH₂Cl₂); IR (KBr): 3392, 3340, 1665, 1598, 1529, 1446, 1347, 1106, 751, 690; HRMS calcd for (C₁₅H₁₂N₂O₄)⁺ requires m/z 284.0797, found m/z 284.0795.



(2R,3R)-3-(4-cyanophenyl)-*N*-phenyloxirane-2-carboxamide: White solid (Flash column chromatography eluent: petroleum ether/ethyl acetate = 10/1), mp 143-145 °C, yield: 84%; Enantiomeric excess: 92.5%, determined by HPLC (Daicel Chiralpak AD-H, n-hexane/2-propanol = 70/30, flow rate = 1.0 mL/min, λ = 254 nm, T = 30°C, retention time: 7.44 min (major), 12.00 min (minor); ¹H NMR (400 MHz, CDCl₃): δ (ppm) 7.63-7.60 (t, *J* = 7.5 Hz, 3H), 7.54-7.53 (d, *J* = 5 Hz, 2H), 7.27-7.24 (t, *J* = 7.5 Hz, 2H), 7.21-7.19 (d, *J* = 10 Hz, 2H), 7.11-7.09 (t, *J* = 5 Hz, 1H),

4.44-4.43 (d, J = 5 Hz, 1H), 3.99-9.88 (d, J = 5 Hz, 1H); ¹³C NMR (500 MHz, CDCl₃): δ 163.4, 138.0, 135.7, 132.4, 129.1, 127.3, 125.3, 120.0, 118.2, 112.8, 57.9, 56.7; $[\alpha]_D^{20} = -45.0$ (c = 0.28, CH₂Cl₂); IR (KBr): 3298, 2234, 1704, 1606, 1551, 1444, 760, 699; HRMS calcd.for (C₁₆H₁₂N₂O₂)⁺ requires m/z 264.0899, found m/z 264.0896.



(2*R*,3*R*)-3-(3-methoxyphenyl)-*N*-phenyloxirane-2-carboxamide: White solid (Flash column chromatography eluent: petroleum ether/ethyl acetate = 10/1), mp 98-100 °C, yield: 83%; Enantiomeric excess: 92.6%, determined by HPLC (Daicel Chiralpak AD-H, n-hexane/2-propanol = 90/10, flow rate = 1.0 mL/min, λ = 254 nm, T = 30°C, retention time: 16.72 min (major), 21.01 min (minor); ¹H NMR (500 MHz, CDCl₃): δ (ppm) 7.55 (s, 1H), 7.25-7.19 (m, 5H), 7.08-7.05 (m, 1H), 7.00-6.99 (d, *J* = 5 Hz, 1H), 6.94 (s, 1H), 6.82-6.80 (m, 1H), 4.41-4.40 (d, *J* = 5 Hz, 1H), 3.92-3.91 (d, *J* = 5 Hz, 1H), 3.74 (s, 3H); ¹³C NMR (500 MHz, CDCl₃): δ 164.4, 159.7, 136.1, 134.2, 129.8, 128.9, 124.9, 120.2, 118.6, 114.6, 111.8, 58.7, 56.6, 55.3; [α]_D²⁰ = -27.5 (c = 0.53, CH₂Cl₂); IR (KBr): 3302, 1664, 1604, 1528, 1444, 1254, 1037, 752, 689; HRMS calcd.for (C₁₆H₁₅NO₃)⁺ requires m/z 269.1052, found m/z 269.1056.



(2*R*,3*R*)-3-(3-fluorophenyl)-*N*-phenyloxirane-2-carboxamide: White solid (Flash column chromatography eluent: petroleum ether/ ethyl acetate = 10/1), mp 99-101 °C, yield: 78%; Enantiomeric excess: 89.2%, determined by HPLC (Daicel Chiralpak AD-H, n-hexane/2-propanol = 70/30, flow rate = 1.0 mL/min, λ = 254 nm, T = 30°C, retention time: 6.09 min (major), 7.07 min (minor); ¹H NMR (500 MHz, CDCl₃): δ (ppm) 7.53 (s, 1H), 7.32-7.28 (m, 1H), 7.24-7.19 (m, 5H), 7.15-7.13 (d, *J* = 10 Hz, 1H), 7.10-7.07 (t, *J* = 7.5 Hz, 1H), 7.00-6.97 (m, 1H), 4.42-4.41 (d, *J* = 5 Hz, 1H), 3.94-3.93 (d, *J* = 5 Hz, 1H); ¹³C NMR (500 MHz, CDCl₃): δ 163.9, 135.8, 135.2,

129.0, 125.1, 122.1, 120.2, 115.9, 115.8, 113.8, 113.6, 58.1, 56.6; $[\alpha]_D^{20} = -18.8$ (c = 0.53, CH₂Cl₂); IR (KBr): 3353, 1666, 1599, 1531, 1446, 755, 690; HRMS calcd.for (C₁₅H₁₂FNO₂)⁺ requires m/z 257.0852, found m/z 257.0848.



(2*R*,3*R*)-3-(p-tolyl)-*N*-phenyloxirane-2-carboxamide: White solid (Flash column chromatography eluent: petroleum ether/ ethyl acetate = 10/1), mp 127-128 °C, yield: 76%; Enantiomeric excess: 84.3%, determined by HPLC (Daicel Chiralpak AD-H, n-hexane/2-propanol = 90/10, flow rate = 1.0 mL/min, λ = 254 nm, T = 30°C, retention time: 12.10 min (major), 17.00 min (minor); ¹H NMR (500 MHz, CDCl₃): δ (ppm) 7.54 (s, 1H), 7.30-7.28 (d, *J* = 10 Hz, 2H), 7.25-7.19 (m, 4H), 7.13-7.11 (d, *J* = 10 Hz, 2H), 7.08-7.05 (t, *J* = 7.5 Hz, 1H), 4.40-4.39 (d, *J* = 5 Hz, 1H), 3.91-3.90 (d, *J* = 5 Hz, 1H), 2.28 (s, 3H); ¹³C NMR (500 MHz, CDCl₃): δ 164.6, 138.5, 136.1, 130.0, 129.3, 128.9, 126.3, 124.8, 120.2, 58.8, 56.7, 21.2; $[\alpha]_D^{20}$ = -15.5 (c = 0.40, CH₂Cl₂); IR (KBr): 3347, 1666, 1599, 1533, 1445, 751, 690; HRMS calcd.for (C₁₆H₁₅NO₂)⁺ requires m/z 253.1103, found m/z 253.1101.



(2*R*,3*R*)-3-(naphthalen-1-yl)-*N*-phenyloxirane-2-carboxamide: White solid (Flash column chromatography eluent: petroleum ether/ ethyl acetate = 10/1), mp 136-137 °C, yield: 67%; Enantiomeric excess: 71.3%, determined by HPLC (Daicel Chiralpak AD-H, n-hexane/2-propanol = 70/30, flow rate = 1.0 mL/min, λ = 254 nm, T = 30°C, retention time: 6.91 min (major), 9.31 min (minor); ¹H NMR (500 MHz, CDCl₃): δ (ppm) 8.16-8.15 (d, *J* = 5 Hz, 1H), 7.85-7.83 (d, *J* = 10 Hz, 1H), 7.80-7.78 (d, *J* = 10 Hz, 1H), 7.61-7.57 (m, 2H), 7.54-7.51 (m, 1H), 7.45-7.39 (m, 2H), 7.15-7.12 (t, *J* = 15 Hz, 2H), 7.03-6.97 (m, 3H), 4.81-4.80 (d, *J* = 5 Hz, 1H), 4.17-4.16 (d, *J* = 5 Hz, 1H); ¹³C NMR (500 MHz, CDCl₃): δ 164.6, 135.9, 133.3, 131.2, 129.3, 129.0, 128.8, 128.7, 127.0, 126.5, 124.8, 124.3, 123.5, 120.2, 58.0, 56.5; [α]_D²⁰ = -41.99 (c = 0.80, CH₂Cl₂); IR

(KBr): 3300, 1669, 1597, 1549, 1496, 1445, 760, 694; HRMS calcd.for $(C_{19}H_{15}NO_2)^+$ requires m/z 289.1103, found m/z 289.1106.



(2*R*,3*R*)-3-(2,3-dimethoxyphenyl)-*N*-phenyloxirane-2-carboxamid: White solid (Flash column chromatography eluent: petroleum ether/ ethyl acetate = 10/1), mp 87-89 °C, yield: 81%; Enantiomeric excess: 73.6%, determined by HPLC (Daicel Chiralpak AD-H, n-hexane/2-propanol = 70/30, flow rate = 1.0 mL/min, λ = 254 nm, T = 30°C, retention time: 6.42 min (major), 7.08 min (minor); ¹H NMR (500 MHz, CDCl₃): δ (ppm) 7.64 (s, 1H), 7.27-7.21 (m, 4H), 7.07-7.04 (m, 2H), 6.95-6.94 (d, *J* = 5 Hz, 1H), 6.85-6.84 (d, *J* = 5 Hz, 1H), 4.50-4.49 (d, *J* = 5 Hz, 1H), 3.96-3.95 (d, *J* = 5 Hz, 1H), 3.89 (s, 3H), 3.82 (s, 3H); ¹³C NMR (500 MHz, CDCl₃): δ 164.5, 152.6, 147.9, 136.3, 128.9, 126.9, 124.7, 123.9, 120.0, 118.3, 113.0, 61.2, 56.7, 55.7; [α]_D²⁰ = -28.8 (c = 0.80, CH₂Cl₂); IR (KBr): 3326, 1669, 1598, 1543, 1444, 1251, 1041, 752, 693; HRMS calcd.for (C₁₇H₁₇NO₄)⁺ requires m/z 299.1158, found m/z 299.1154.



(2*R*,3*R*)-3-(3-nitrophenyl)-*N*-phenyloxirane-2-carboxamide: White solid (Flash column chromatography eluent: petroleum ether/ ethyl acetate = 7/1), mp 146-147 °C, yield: 90%; Enantiomeric excess: 88.5%, determined by HPLC (Daicel Chiralpak AD-H, n-hexane/2-propanol = 70/30, flow rate = 1.0 mL/min, λ = 254 nm, T = 30°C, retention time: 7.39 min (major), 9.57 min (minor); ¹H NMR (500 MHz, CDCl₃): δ (ppm) 8.33 (s, 1H), 8.15-8.13 (m, 1H), 7.75-7.69 (m, 2H), 7.53-7.50 (t, *J* = 7.5 Hz, 1H), 7.25-7.21 (m, 4H), 7.09-7.06 (m, 1H), 4.49-4.48 (d, *J* = 5 Hz, 1H), 4.02-4.01 (d, *J* = 5 Hz, 1H); ¹³C NMR (500 MHz, CDCl₃): δ 163.3, 148.2, 135.6, 135.0, 132.4, 129.8, 129.1, 125.3, 123.8, 121.5, 120.0, 57.6, 56.9; [α]_D²⁰ = -15.7 (c = 0.60, CH₂Cl₂); IR

(KBr): 3299, 1664, 1596, 1531, 1443, 1346, 745, 688; HRMS calcd.for $(C_{15}H_{12}N_2O_4)^+$ requires m/z 284.0797, found m/z 284.0793.



(2*R*,3*R*)-3-(4-(tert-butyl)phenyl)-*N*-phenyloxirane-2-carboxamide: White solid (Flash column chromatography eluent: petroleum ether/ ethyl acetate = 7/1), mp 109-110 °C, yield: 73%; Enantiomeric excess: 82.1%, determined by HPLC (Daicel Chiralpak AD-H, n-hexane/2-propanol = 70/30, flow rate = 1.0 mL/min, λ = 254 nm, T = 30°C, retention time: 5.11 min (major), 5.81 min (minor); ¹H NMR (500 MHZ, CDCl₃): δ (ppm) 7.45 (s, 1H), 7.34 (s, 4H), 7.22-7.19 (t, *J* = 7.5 Hz, 2H), 7.08-7.04 (m, 3H), 4.42-4.41 (d, *J* = 5 Hz, 1H), 3.91 (d, 1H), 1.25 (s, 9H); ¹³C NMR (500 MHz, CDCl₃): δ 165.0, 151.8, 135.9, 130.0, 128.8, 126.3, 125.6, 125.0, 120.6, 58.6, 56.4, 34.6, 31.2; $[\alpha]_D^{20} = -20.5$ (c = 0.85, CH₂Cl₂); IR (KBr): 3374, 3057, 2967, 2867, 1677, 1602, 1533, 1444, 751, 689; HRMS calcd for (C₁₉H₂₁NO₂)⁺ requires m/z 295.1572, found m/z 295.1568.



(*2R,3R*)-3-ethyl-*N*-(4-chlorophenyl)oxirane-2-carboxamide: White solid, mp 98-100 °C; (Flash column chromatography eluent: petroleum ether/ethyl acetate = 15/1); ¹H NMR (300 MHz, CDCl₃): δ (ppm) 7.68 (s, 1H), 7.54-7.51 (m, 2H), 7.33-7.28 (m, 2H), 3.66-3.65 (d, *J* = 3 Hz, 1H), 3.29-3.23 (m, 1H), 1.69-1.61 (m, 2H), 1.13-1.08 (t, *J* = 7.5 Hz, 3H); ¹³C NMR (300 MHz, CDCl₃): δ 165.6, 135.1, 129.9, 129.2, 121.0, 60.4, 55.7, 21.4, 10.3; $[\alpha]_D^{20} = +17.5$ (c = 0.65, CH₂Cl₂); IR (KBr): 3294, 2980, 1676, 1592, 1521, 1457, 776, 693; HRMS calcd.for (C₁₁H₁₂ClNO₂)⁺ requires m/z 225.0557, found m/z 225.0561.



(2R,3R)-3-ethyl-*N*-(4-methoxyphenyl)oxirane-2-carboxamide: White solid, mp 87-89 °C; (Flash column chromatography eluent: petroleum ether/ethyl acetate = 15/1); ¹H NMR (300 MHz, CDCl₃): δ (ppm) 7.77 (s, 1H), 7.49-7.46 (m, 2H), 6.91-6.66 (m, 2H), 3.81 (s, 3H), 3.66-3.65 (d, *J* = 3 Hz, 1H), 3.28-3.22 (m, 1H), 1.68-1.61 (m, 2H), 1.14-1.09 (t, *J* = 7.5 Hz, 3H); ¹³C NMR (300 MHz, CDCl₃) δ 165.2, 156.7, 129.6, 121.5, 114.3, 60.3, 55.7, 55.5, 21.3, 10.3; $[\alpha]_D^{20}$ = +22.8 (c = 0.70, CH₂Cl₂); IR (KBr): 3293, 2969, 1666, 1599, 1526, 1461, 829, 724. HRMS calcd.for (C₁₂H₁₅NO₃)⁺ requires m/z 221.1052, found m/z 221.1050.

References

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- 2. Aman A. Desai.; Wulff, W. D. J. Am. Chem. Soc. 2010, 132, 13100-13103.
- 3. Blankley, C. J.; Stauter, F. J.; House, H. O. Org. Synth. 1969, 49, 22-20.



110 10 f1 (ppm) :10





f1 (ppm)



110 100 f1 (ppm)





f1 (ppm)



110 100 f1 (ppm)



110 100 f1 (ppm)





110 100 f1 (ppm)



100 90 f1 (ppm)



110 100 f1 (ppm)



110 1 f1 (ppm)





f1 (ppm)







fl (ppm)





fl (ppm)



120 110 f1 (ppm)



120 110 f1 (ppm)





f1 (ppm)







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峰	保留时间	类型	峰宽	峰面积	峰高	峰面积
#	[min]		[min]	[mAU*s]	[mAU]	%
	-					
1	8.785	MM R	0.2061	9762.76465	789.51038	48.1800
2	2 18.956	MM R	0.4554	1.05003e4	384.28284	51.8200



峰	保留时间 类型	峰宽	峰面积	峰高	峰面积
#	[min]	[min]	[mAU*s]	[mAU]	%
	-				
1	8.737 VB	0.1971	1218.96179	95.38253	0.9060
2	2 18.190 MM R	0.7364	1.33320e5	3017.33667	99.0940



峰	保留时间	类型	峰宽	峰面积	峰高	峰面积
#	[min]		[min]	[mAU*s]	[mAU]	%
	-					
1	8.276	BB	0.1944	3.23850e4	2545.90649	49.2984
2	2 16.181	BB	0.3938	3.33067e4	1295. 98071	50.7016



峰	保留时间	类型	峰宽	峰面积	峰高	峰面积
#	[min]		[min]	[mAU*s]	[mAU]	%
1	8.027	MM R	0.7744	584.97437	12.58978	0.3596
2	15.732	BB	0.9602	1.62067e5	2500.21362	99.6404





峰	保留时间	类型	峰宽	峰面积	峰高	峰面积
#	[min]		[min]	[mAU*s]	[mAU]	%
	-					
1	7.846	BB	0.1719	888. 55359	79.82246	0.9618
2	2 10.925	MM R	0.4549	9.14916e4	3352.40308	99.0382



峰	保留时间	类型	峰宽	峰面积	峰高	峰面积
#	[min]		[min]	[mAU*s]	[mAU]	%
1	7.543	MM R	0.2010	6350.85107	526.57440	49.3872
2	13.649	MM R	0.3607	6508.45264	300.76416	50.6128



峰	保留时间	类型	峰宽	峰面积	峰高	峰面积
#	[min]		[min]	[mAU*s]	[mAU]	%
1	7.546	MM R	0.2099	340. 53079	27.03893	1.3979
2	13.547	MM R	0.3657	2.40188e4	1094.71106	98.6021



哞	保留时间	尖坚	峰苋	峰囬枳	峰尚	峰曲积
#	[min]		[min]	[mAU*s]	[mAU]	%
	-					
	1 7.681	BV	0.1503	3683.81299	369.44888	50.4217
4	2 8.328	VB	0.1675	3622.19897	326.27832	49.5783



峰	保留时间	类型	峰宽	峰面积	峰高	峰面积
#	[min]		[min]	[mAU*s]	[mAU]	%
	-					
1	7.647	BV	0.1569	2.52929e4	2480.86792	98.8302
2	8.322	VB	0.1789	299.37488	24.43357	1.1698



峰	保留时间	类型	峰宽	峰面积	峰高	峰面积
#	[min]		[min]	[mAU*s]	[mAU]	%
	-					
1	6.955	BB	0.1343	1.17464e4	1339.85754	50.2428
2	2 7.770	BB	0.1587	1.16329e4	1106.37610	49.7572



峰	保留时间	类型	峰宽	峰面积	峰高	峰面积
#	[min]		[min]	[mAU*s]	[mAU]	%
	-					
1	6.939	BB	0.2161	3.32750e4	2454.92041	98.3584
2	2 7.793	MM R	0.1556	555.36938	59.48106	1.6416







峰	保留时间	类型	峰宽	峰面积	峰高	峰面积
#	[min]		[min]	[mAU*s]	[mAU]	%
	-					
1	16.416	MM R	0.9512	4574.26855	80.15108	2.2901
2	2 24. 525	MM	1.6216	1.95166e5	2005.86951	97.7099



峰	保留时间 类型	峰宽	峰面积	峰高	峰面积
#	[min]	[min]	[mAU*s]	[mAU]	%
	-				
1	14.241 BB	0.3384	661.47461	30. 57475	1.1773
2	20.469 MM R	0.6588	5.55257e4	1404.75916	98.8227



峰	保留时间	类型	峰宽	峰面积	峰高	峰面积
#	[min]		[min]	[mAU*s]	[mAU]	olo
1	6.483	MM R	0.1577	1.16029e4	1226.08435	50.2734
2	7.125	VB	0.1597	1.14767e4	1082.61194	49.7266



保留时间	类型	峰宽	峰面积	峰高	峰面积
[min]		[min]	[mAU*s]	[mAU]	0/0
6.422	MM R	0.1717	2.55879e4	2483.47461	86.7708
7.079	MM R	0.2016	3901.16187	322.58728	13.2292
	保留时间 [min] 6.422 - 7.079	保留时间 类型 [min] 6.422 MM R 7.079 MM R	保留时间 类型 峰宽 [min] [min] 6.422 MM R 0.1717 7.079 MM R 0.2016	保留时间 类型 峰宽 峰面积 [min] [min] [mAU*s] 	保留时间 类型 峰宽 峰面积 峰高 [min] [min] [mAU] [min] [min] [mAU*s] [mAU] [6.422 MM R 0.1717 2.55879e4 2483.47461 7.079 MM R 0.2016 3901.16187 322.58728



	峰	保留时间	类型	峰宽	峰面积	峰高	峰面积
_							
	1	15.615	BB	0.4616	3743.90112	123.52816	49.9940
	2	19.942	BB	0.5595	3744.80371	102.42806	50.0060



峰	保留时间	类型	峰宽	峰面积	峰高	峰面积
#	[min]		[min]	[mAU*s]	[mAU]	00
	-					
1	16.719	MM R	0.4349	2.35213e4	901.38867	96.3121
2	21.096	MM R	0.5502	900.67114	27.28159	3.6879



峰	保留时间	类型	峰宽	峰面积	峰高	峰面积
#	[min]		[min]	[mAU*s]	[mAU]	00
	-	-				
1	6.186	BB	0.1309	1.61670e4	1868.82556	49.9907
2	2 7.187	BB	0.1557	1.61730e4	1603.37769	50.0093



峰	保留时间	类型	峰宽	峰面积	峰高	峰面积
#	[min]		[min]	[mAU*s]	[mAU]	010
	-					
1	6.240	MM R	0.1468	1.19163e4	1352.98706	92.5344
2	2 7.255	MM R	0.1800	961.39966	89.01225	7.4656



峰	保留时间	类型	峰宽	峰面积	峰高	峰面积
#	[min]		[min]	[mAU*s]	[mAU]	%
	-					
1	12.074	MM R	0.2943	2.17388e4	1231.07727	49.9388
2	2 16.969	MM R	0.4147	2.17922e4	875.90741	50.0612



峰	保留时间	类型	峰宽	峰面积	峰高	峰面积
#	[min]		[min]	[mAU*s]	[mAU]	%
	-					
1	12.101	MM R	0.4494	6.49088e4	2407.19409	92.1646
2	2 16.999	MM R	0.5675	5518.22705	162.07231	7.8354



峰	保留时间	类型	峰宽	峰面积	峰高	峰面积
#	[min]		[min]	[mAU*s]	[mAU]	00
	-					
1	7.255	BB	0.1788	2.14252e4	1853.80811	49.6935
2	2 11.952	BB	0.3096	2.16894e4	1083.42834	50.3065



峰	保留时间	类型	峰宽	峰面积	峰高	峰面积
#	[min]		[min]	[mAU*s]	[mAU]	%
	-					
1	7.444	MM R	0.1842	1.76481e4	1596.54309	96.2347
2	2 12.005	MM R	0.3070	690.50201	37.48735	3.7653



峰	保留时间	类型	峰宽	峰面积	峰高	峰面积
#	[min]		[min]	[mAU*s]	[mAU]	00
	·					
1	5.113	VB	0.1325	5384.97070	625.00677	49.8598
2	5.806	BB	0.1409	5415.24414	590.83435	50.1402



峰	保留时间	类型	峰宽	峰面积	峰高	峰面积
#	[min]		[min]	[mAU*s]	[mAU]	olo
1	5.109	MM R	0.1479	1.05048e4	1183.52649	91.0625
2	5.807	MM R	0.1554	1031.01672	110.59381	8.9375



峰	保留时间	类型	峰宽	峰面积	峰高	峰面积
#	[min]		[min]	[mAU*s]	[mAU]	%
	-					
1	7.446	MM R	0.1961	7970. 53418	677.37585	49.9398
2	2 15.107	MM R	0.4189	7989.74805	317.90814	50.0602



峰	保留时间	类型	峰宽	峰面积	峰高	峰面积
#	[min]		[min]	[mAU*s]	[mAU]	%
	-					
1	7.542	MM R	0.2027	2.58419e4	2124.65674	97.6208
2	2 14.902	MM R	0.3910	629.81018	26.84662	2.3792





峰	保留时间	类型	峰宽	峰面积	峰高	峰面积
#	[min]		[min]	[mAU*s]	[mAU]	010
	-					
1	5.914	BB	0.1277	7239.83105	864.29602	50.5540
2	6.964	BB	0.1521	7081.14355	711.80042	49.4460



峰	保留时间	类型	峰宽	峰面积	峰高	峰面积
#	[min]		[min]	[mAU*s]	[mAU]	%
	-					
1	6.086	MM R	0.1637	1.39752e4	1423.18799	94. 5959
2	2 7.073	MM R	0.1930	798.37598	68.92690	5.4041





峰	保留时间	类型	峰宽	峰面积	峰高	峰面积
#	[min]		[min]	[mAU*s]	[mAU]	%
1	7.391	MM R	0.1989	2.77730e4	2327.37207	94.2687
2	9.565	MM	0.2327	1688.52551	120.94827	5.7313