Bimorpholine Derivatives as a New Class of Organocatalysts for Asymmetric Conjugate Additions

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Supporting Information

General Remarks. All reactions were carried out under a nitrogen atmosphere with oven dried glassware. Concerning ¹H (400 MHz) and ¹³C (100 MHz) NMR spectra, chemical shift (δ) are given in ppm relative to tetramethylsilane (0 ppm). Multiplicity is indicated as follows : s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet), dd (doublet of doublet), br s (broad singlet). Coupling constants are reported in Hz. GC/MS were recorded with Electronic Impact EI (70 eV) as source; m/z (%). Mass spectra (MS) were obtained by EI (70 eV) and High resolution mass spectra HRMS by Electrospray Ionisation (ESI) or by electronic impact(EI) . Optical rotations were measured at 25°C in a 10 cm cell in the stated solvent ; [α]_D values are given in 10⁻¹ deg.cm² g⁻¹ (concentration c given as g/100 mL). Enantiomeric excesses were determined by chiral Super Fluid Chromatography (SFC), with appropriated program using a gradient of methanol or by chiral Gas Chromatography (GC), with appropriated program using a gradient of temperature. Temperature programs are described as follows: initial temperature (°C) – initial time (min) – temperature gradient (°C/min) – final temperature (°C); retention times (R_T) are given in min. Flash chromatography was performed using florisil® 100-200 mesh or silicagel 32-63 μm, 60 Å.

Evolution of reaction was followed by TLC. Chloroform, used for Michael addition of aldehydes to nitroolefins was purchased from Acros and used as received. Chloroform, extra dry, with molecular sieves, used for Michael addition of aldehydes to 1,1-bis(benzenesulfonyl) ethylene **8** was purchased from Acros and dried by filtration over basic alumina. 1,1-bis(benzenesulfonyl)ethylene **8** was purchased from Fluka or synthesized by known experimental procedures¹ starting from commercially available thiophenol and dichloromethane. Trans-β-nitrostyrene **4**, trans-2-(nitrovinyl)thiophene **6a**, 1-methoxy-4-(2-nitrovinyl)benzene **6c** was respectively purchased from Fluka, Aldrich, and Lancaster. Nitroolefins **6b** and **6d** were synthesized by known experimental procedures.² 3S,3'S-bimorpholine **1** was prepared according to the literature procedure.³

¹ Preparation of bis(phenylthio)methane, see Screttas, C. G.; Micha-Screttas, M. *J. Org. Chem* **1979**, *44*, 713. Preparation of bis(phenylsulfonyl)methane, see Nantz, M. H.; Radisson, X.; Fuchs, P. L. *Synth. Commun.* **1987**, *17*, 55. Preparation of 1,1-bis(benzenesulfonyl)ethylene **2** : for the 1st step Setter, see H.; Steinbeck, K. *Liebigs Ann. Chem.* **1974**, 1315. And for the 2nd step, see Carpino, L. A. *J. Org. Chem.*, **1973**, *38*, 2600.

² For Henry reaction of a nitroalkane and a carbonyl compound, see Baer, H. H.; Urbas, L. *The Chemistry of the Nitro and Nitroso Groups*; Feuer, H., Ed.; Interscience: New York, **1970**, Vol. 2, pp 75-200. For dehydration of the resultant 2-nitro alcohol, see Seebach, D.; Knochel, P. *Helv. Chim. Acta* **1984**, *67*, 261.

³ (a) Kanger, T.; Kriis, K.; Pehk, T.; Müürisepp, A-M.; Lopp, M. *Tetrahedron : Asymmetry* **2002**, *13*, 857. b) Kanger, T.; Laars, M.; Kriis, K.; Kailas, T.; Müürisepp, A-M.; Pehk, T.; Lopp, M. *Synthesis* **2006**, in press.

Aldehydes **3a-d** and **3f** were purchased from Fluka and used as received. 2-cyclohexylacetaldehyde **3e** was prepared according to the literature procedure.⁴

Methanol was used without previous distillation. HCl, TFA and AcOH were purchased from Fluka, NaBH₄, NaBH₃CN, acetone were purchased from Acros and used as received. Et₂O was dried by filtration over activated alumina.

I. Synthesis of Organocatalysts 2a-c

(*S,S*)-*N*-*i*Pr-3,3'-bimorpholine (**2a**) : To a solution of 3*S*,3'*S*-bimorpholine **1** (2.91

mmol) in diethyl ether (12 mL) was added molecular sieves 4Å (~ 0.5 g) and acetone (2.91 mmol). The mixture was stirred overnight, then K₂CO₃ was added and the mixture was stirred 1 hour and then was filtered. Solvent was removed to give the crude aminal (586 mg, 95%). Then, to a solution of aminal (586 mg, 2.76 mmol) in MeOH (10 mL) was added by portion at 0°C NaBH₄ (1.5 eq.) then acetic acid (4eq.). The solution was stirred 3 hours at 0°C and then diluted with diethyl ether (10 mL) and hydrolyzed with NaOH_{aq.} 30% (5 mL) and water (10

mL). The solution was decanted; the aqueous phase was extracted twice with EtOAc. The combined organic phases were washed with brine, dried over K₂CO₃, filtered, concentrated under reduced pressure and purified by Kugelrohr distillation (P= 0.2 mbar, 140°C) to give a white solid (449 mg, 76%, 72% overall yields). $[\alpha]_D^{20} = +53.42$ (c 1.1, CHCl₃).

¹H NMR (400 MHz, CDCl₃) : δ = 4.10-4.02 (m, 2H), 3.73-3.52 (m, 2H), 3.40-3.27 (m, 4H), 3.15-3.09 (m, 1H), 3.07-2.97 (m, 1H), 2.67-2.60 (m, 1H), 2.44-2.29 (m, 3H), 2.20-2.14 (m, 1H), 1.01 (br, 1H), 0.83-0.81 (d, 3H, J= 6.56 Hz), 0.71-0.69 (d, 3H, J= 6.56 Hz).

¹³C NMR (100 MHz, CDCl₃) : δ = 69.12 (CH₂), 67.61 (CH₂), 66.43 (CH₂), 66.14 (CH₂), 58.20 (CH), 53.27 (CH), 48.47 (CH), 46.85 (CH₂), 42.60 (CH₂), 21.70 (CH₃), 16.05 (CH₃).

IR : 3307w, 2963m, 2851m, 1803m, 1448m, 1313m, 1296m, 1266m, 1178m, 1098s, 973m cm⁻¹.

HRMS (ESI) Calcd for C₁₁H₂₂N₂O₂ [M+H]⁺ 215.1681, found 215.1759.

GC/MS (80-1-20-270-3) : R_T = 8.95 min.

(*S,S*)-*N*-Me-3,3'-bimorpholine (**2b**) : To a solution of 3*S*,3'*S*-bimorpholine **1** (2.91 mmol) in diethyl ether (12 mL) was added molecular sieves 4Å (~ 0.5 g) and aqueous formaldehyde 40% (2.91 mmol). The mixture was stirred overnight, then K₂CO₃ was added and the mixture was stirred 1 hour and then was filtered. Solvent was removed to give the crude aminal (535 mg, 100%). Then, to a solution of aminal (535 mg, 2.91 mmol) in MeOH (15 mL) was added by portion at

0°C NaBH₃CN (1.5 eq., 4.12 mmol, 259 mg) then trifluoroacetic acid (4eq., 10.98 mmol, 0.82 mL). The solution was stirred 1h30 at 0°C and then diluted with ether (20 mL) and hydrolyzed with NaOH_{aq.} 30% (5 mL) and water (10 mL). The solution was decanted; the aqueous phase was extracted four times with ether. The combined organic phases were washed with brine, dried over K₂CO₃, filtered, concentrated under reduced pressure. The crude was purified by Kugelrohr distillation (P= 0.2 mbar, 120°C) to give a white solid (449 mg, 83%, 83% overall yields). $[\alpha]_D^{20} = +58.4$ (c 1.0, CHCl₃).

⁴ Rumbolt, G.; Rigbi, G. *J. Org. Chem.*, **1996**, 61, 3557.

^1H NMR (400 MHz, CDCl_3) : δ = 3.96-3.87 (m, 2H), 3.77-3.70 (m, 2H), 3.55-3.42 (m, 2H), 3.37-3.32 (m, 2H), 3.24-3.19 (m, 1H), 2.97-2.86 (m, 2H), 2.74-2.69 (m, 1H), 2.35 (s, 3H), 2.33-2.29 (m, 1H), 2.17-2.12 (m, 1H), 1.89 (br, 1H).

^{13}C NMR (100 MHz, CDCl_3) : δ = 68.34 (CH_2), 67.67 (CH_2), 66.22 (CH_2), 65.87 (CH_2), 64.26 (CH), 54.99 (CH_2), 53.96 (CH), 46.42 (CH_2), 42.83 (CH_3).

IR : 3307m, 2854s, 2792m, 1461m, 1449m, 1315m, 1291m, 1277m, 1155w, 1116s, 1098s, 1052m, 981m cm^{-1} .

MS (ESI): m/z (%) 205 (3), 197 (10), 101 (31), 100 (100), 99 (12), 86 (31), 70 (25), 56 (11).

HRMS (EI) Calcd for $\text{C}_4\text{H}_8\text{NO}^\bullet$ [$m/z=86$] 86.060455, found 86.060589.

(*S,S*)-*N*-iPr-3,3'-bimorpholine hydrochloride **2c** : To a solution of diamine (**2a**) (94.3 mg, 0.44 mmol) in diethylether (3 mL) was added at 0°C a solution of hydrochloric acid 1.25M in MeOH (0.37 mL, 0.46 mmol). After a few minutes the solvent was removed *in vacuo* to give a yellow viscous solid (110 mg, 100%). The product was purified by crystallisation in a mixture of cyclohexane and ethyl acetate to afford a white solid (102 mg, 93%).

^1H NMR (400 MHz, CDCl_3) : δ = 4.11-4.08 (m, 1H), 4.00-3.87 (m, 3H), 3.74-3.336 (m, 5H), 3.30-3.21 (m, 1H), 3.12-3.04 (m, 2H), 3.02-2.96 (m, 2H), 2.75-2.72 (m, 1H), 1.28-1.26 (m, 1H), 1.26-1.24 (d, 3H, $J=6.48$ Hz), 1.19-1.18 (d, 3H, $J=6.34$ Hz), 0.88-0.83 (m, 1H).

II. Addition of unmodified aldehydes to nitroolefins catalyzed by N-iPr-3*S*,3'*S*-bimorpholine derivative (iPBM)

General Procedure 1 : To a solution of **iPBM** (0.05 mmol, 15 mol%) in solvent (3 mL) was added at the appropriate temperature the aldehyde (10 eq. 3.35 mmol) and the nitroolefin (1 eq., 0.335 mmol). The evolution of the reaction was controlled by TLC until completion. The solution was then hydrolyzed with 1N HCl (2 mL). The layers were separated and the aqueous phase was extracted with CH₂Cl₂ (2 x 3 mL). The combined organic phases were dried over MgSO₄, filtered, concentrated and purified by flash column chromatography on silica gel using a mixture of cyclohexane and ethylacetate as eluent.

(2*S*,3*R*)-2-(Methylethyl)-4-nitro-3-phenylbutyraldehyde (**5a**) : From isovaleraldehyde **3a** and nitrostyrene **4** according to the *General Procedure 1* to give a pale yellow oil (67 mg, 85%). The enantiomeric excess was determined by chiral GC (Hydrodex-B-3P, iso 150°C, 45cm/s *R*_t: 38.43 min (2*R*, 3*S*) and 39.52 min (2*S*, 3*R*)). [α]_D²⁰ = -63.2° (*c*=1.03, ee = 88% (2*S*, 3*R*), CHCl₃). ¹H NMR (400.1 MHz, CDCl₃) : δ = 9.93 (d, 1H, *J* = 2.2 Hz), 7.36-7.25 (m, 3H), 7.19-7.17 (m, 2H), 4.68-4.64 (dd, 1H, *J* = 4.28 Hz, *J* = 12.36 Hz), 4.60-4.54 (m, 1H), 3.92-3.86 (m, 1H), 2.79-2.74 (m, 1H), 1.75-1.67 (m, 1H), 1.10-1.08 (d, 3H, *J* = 7.36 Hz), 0.89-0.87 (d, 3H, *J* = 7.08 Hz). Other spectroscopic data are in agreement with published data.⁵

2-(*S*)-(2-nitro-1-(*R*)-phenylethyl)-pentanal (**5d**) : From valeraldehyde **3d** and nitrostyrene **4** according to the *General Procedure 1* to give a pale yellow oil (69.3 mg, 88%). The enantiomeric excess was determined by SFC (Chiralcel OD-H, 2 mL/min, 200 bar, 2% MeOH, 30°C, *R*_t: 8.14 min (1'*S*, 2*R*) and 8.90 min (1'*R*, 2*S*)). [α]_D²⁰ = -39.8° (*c* 1.0, ee = 89% (1'*S*, 2*R*), CHCl₃). ¹H NMR (400.1 MHz, CDCl₃) : δ = 9.70 (d, 1H, *J* = 2.2), 7.36-7.29 (m, 3H), 7.18-7.16 (m, 2H), 4.74-4.61 (m, 2H), 3.82-3.74 (m, 1H), 2.73-2.60 (m, 1H), 1.52-1.44 (m, 1H), 1.40-1.25 (m, 2H), 1.12-0.94 (m, 1H), 0.79 (t, 3H, *J* = 7.32 Hz). Other spectroscopic data are in agreement with published data.⁵

(2*S*,3*R*)-2-cyclohexyl-4-nitro-3-phenylbutanal **5e** : From 2-cyclohexylacetaldehyde **3e** and nitrostyrene **4** according to the *General Procedure 1* to give a white solid (56.6 mg, 88%). The enantiomeric excess was determined by SFC (Chiralcel OJ, 2 mL/min, 200 bar, 2% MeOH, 30°C, *R*_t: 4.92 min (2*S*, 3*R*) and 5.70 min (2*R*, 3*S*)). [α]_D²⁰ = -60.1° (*c* 1.0, ee = 90% (2*S*, 3*R*), CHCl₃). ¹H NMR (400.1 MHz, CDCl₃) : δ = 9.90 (d, 1H, *J* = 2.52 Hz), 7.36-7.27 (m, 3H), 7.18-7.16 (m, 2H), 4.68-4.57 (m, 2H), 3.98-3.91 (m, 1H), 2.74-2.70 (m, 1H), 1.77-1.56 (m, 6H), 1.35-1.28 (m, 2H), 1.08-0.99 (m, 5H). ¹³C NMR (100.6 MHz, CDCl₃) : δ = 204.72 (CHO), 137.42 (C_{quat}), 129.35 (2CH), 128.28 (CH), 128.10 (2CH), 79.07 (CH₂), 59.18 (CH), 41.38 (CH), 38.19 (CH), 32.29 (CH₂), 28.42 (CH₂), 26.87 (CH₂), 26.38 (CH₂), 26.26 (CH₂).

⁵ a) J.M. Betancort, C.F.III Barbas, *Org. Lett.* **2001**, 3, 3737. b) O. Andrey, A. Alexakis, A. Tomassini, G. Bernardinelli, *Adv. Synth. Catal.* **2004**, 346, 1147.

IR : 3029 w, 2922 m, 2849 m, 1703 s, 1559 s, 1547 s, 1494 m, 1445 m, 1431 m, 1396 w, 1380 m, 1258 w, 1225 w, 1195 w, 1170 w, 1096 w, 1070 w, 1031 w, 958 w, 912 w, 861 w cm⁻¹.

MS (ESI) *m/z* (%): 228 (3), 163 (10), 147 (23), 146 (63), 145 (100), 144 (29), 133 (10), 131 (24), 128 (13), 118 (21), 117 (63), 115 (24), 105 (77), 104 (94), 103 (27), 95 (31), 92 (11), 83 (57), 82 (18), 81 (55), 79 (23), 78 (26), 77 (30), 69 (12), 67 (36), 65 (13).

HRMS (EI) Calcd for C₁₀H₁₀O₃•• [*m/z*=146] 146.073165, found 146.073140.

(2*S*,3*R*)-2-Methyl-4-nitro-3-phenylbutyraldehyde (**5f**) : From propionaldehyde **3f** and nitrostyrene **4** at -3°C according to the *General Procedure 1* to give a pale yellow oil (59.6 mg, 86%). The enantiomeric excess was determined by GC (Hydrodex-B-3P, 135-65-1-170-5 °C *R_t* = 85.01 min (2*R*, 3*S*) and 85.53 min (2*S*, 3*R*)). [α]_D²⁰ = -36.3° (*c* 1.0, ee = 80% (2*S*, 3*R*), CHCl₃). ¹H NMR (400.1 MHz, CDCl₃) : δ = 9.72 (d, 1H, *J* = 1.76 Hz), 7.36-7.29 (m, 3H), 7.17-7.15 (m, 2H), 4.82-4.77 (m, 1H), 4.71-4.65 (m, 1H), 3.84-3.78 (m, 1H), 2.81-2.73 (m, 1H), 1.01 (d, 3H, *J* = 7.32 Hz). Other spectroscopic data are in agreement with published data.⁵

(2*S*,3*R*)-2-Methyl-4-nitro-3-(thien-2-yl)butyraldehyde **7a** : From propionaldehyde and nitroolefin **6a** according to the *General Procedure 1* at -3°C to give a pale yellow oil (63.3 mg, 89%). The enantiomeric excess was determined by GC (Hydrodex-B6-TBDBM, 145-30-1-170°C 45 cm/s *R_t*: 36.20 min (2*R*, 3*S*) and 36.75 min (2*S*, 3*R*)). [α]_D²⁰ = -33.3° (*c* 1.0, ee = 79% (2*S*, 3*R*), CHCl₃). ¹H NMR (400 MHz, CDCl₃) : δ = 9.69 (d, 1H, *J* = 1.2 Hz), 7.25-7.23 (m, 1H), 6.96-6.94 (m, 1H), 6.90-6.89 (m, 1H), 4.80-4.75 (dd, 1H, *J*=8.68, *J*= 12.88 Hz), 4.70-4.65 (dd, 1H, *J*=8.84, *J*= 12.60 Hz), 4.26-4.21 (m, 1H), 2.82-2.74 (m, 1H), 1.14-1.12 (d, 3H, *J*= 7.36 Hz). Other spectroscopic data are in agreement with published data.^{5b}

(2*S*,3*R*)-3-(4-chlorophenyl)-2-methyl-4-nitrobutanal **7b** : From propionaldehyde and nitroolefin **6b** according to the *General Procedure 1* at -3°C to give a pale yellow solid (68.0 mg, 84%). The enantiomeric excess was determined by GC (ChiralDEX-B-TA, 145°C isotherm 45 cm/s *R_t*: 128.67 min (2*R*, 3*S*) and 131.56 min (2*S*, 3*R*)). [α]_D²⁰ = -37.7° (*c* 1.0, ee = 75% (2*S*, 3*R*), CHCl₃). ¹H NMR (400 MHz, CDCl₃) : δ = 9.69 (d, 1H, *J* = 1.52 Hz), 7.34-7.30 (d, 2H, *J*= 13.88 Hz), 7.13-7.09 (d, 2H, *J*= 13.64 Hz), 4.81-4.76 (dd, 1H, *J*=5.08, *J*= 12.64 Hz), 4.67-4.61 (dd, 1H, *J*= 9.60, *J*= 12.64 Hz), 3.82-3.76 (m, 1H), 2.82-2.71 (m, 1H), 1.01-0.99 (d, 3H, *J*= 7.32 Hz).

¹³C NMR (100.6 MHz, CDCl₃) : δ = 202.01 (CHO), 135.36 (C_{quat}), 134.31 (C_{quat}), 129.66 (2CH), 129.54 (2CH), 78.12 (CH₂), 48.46 (CH), 43.65 (CH), 12.42 (CH₃).

IR : 2903 w, 2923 w, 2829 w, 2739 w, 1716 s, 1547 s, 1489 m, 1450 w, 1415 w, 1380 s, 1343 w, 1264 w, 1200 w, 1156 w, 1091 m, 1013 m, 913 m, 863 m, 819 m, 793 m cm⁻¹.

MS (ESI) : *m/z* (%) 241 (5), 196 (23), 195 (10), 194 (66), 181 (15), 179 (45), 168 (16), 167 (17), 166 (47), 165 (29), 153 (10), 152 (16), 151 (21), 141 (16), 140 (63), 139 (36), 138 (100), 137 (16), 131 (35), 130 (17), 129 (15), 128 (16), 127 (62), 126 (14), 125 (97), 117 (20), 116 (25), 115 (46), 114 (11), 112 (22), 103 (59), 102 (25), 101 (25), 91 (18), 89 (21), 77 (48), 76 (10), 75 (27), 63 (18).

HRMS (EI) Calcd for C₁₁H₁₂ClNO₃ 241.05057, found 241.050571.

(2*S*,3*R*)-2-Methyl-4-nitro-3-(4-methoxyphenyl)butyraldehyde **7c** : From propionaldehyde **3f** and nitroolefin **6c** according to the *General Procedure 1* at -3°C to give a pale yellow solid (64.5 mg, 81%). The enantiomeric excess was determined by GC (Chiraldex-B-TA, 145°C isotherm 45 cm/s R_t : 91.96 min (2*S*, 3*R*) and 95.25 min (2*R*, 3*S*)). $[\alpha]_D^{20} = -20.5^\circ$ (c 1.05, $ee = 78\%$ (2*S*, 3*R*), $CHCl_3$).

1H NMR (400 MHz, $CDCl_3$) : $\delta = 9.71$ (d, 1H, $J = 1.8$ Hz), 7.08-7.06 (d, 2H, $J = 8.56$ Hz), 6.87-6.85 (d, 2H, $J = 8.56$ Hz), 4.78-4.73 (dd, 1H, $J = 5.52$, $J = 12.64$ Hz), 4.66-4.60 (m, 1H), 3.78 (s, 3H), 2.77-2.69 (m, 1H), 1.27-1.20 (m, 1H), 1.01-0.99 (d, 3H, $J = 7.32$ Hz). Other

spectroscopic data are in agreement with published data.^{5b}

(2*S*,3*S*)-3-Cyclohexyl-2-methyl-4-nitro-butyraldehyde **7d** : From propionaldehyde and nitroolefin **6d** according to the *General Procedure 1* at -3°C to give a pale yellow solid (conversion=25%, 16.5 mg, 23%). The enantiomeric excess was determined by GC (Chiraldex-B-TA, 145°C isotherm 45 cm/s R_t : 91.96 min (2*S*, 3*R*) and 95.25 min (2*R*, 3*S*)). $[\alpha]_D^{20} = -10.5^\circ$ (c 0.35, $ee = 85\%$ (2*S*, 3*S*), $CHCl_3$).

1H NMR (400.1 MHz, $CDCl_3$) : $\delta = 9.75$ (s, 1H), 4.66-4.61 (dd, 1H, $J = 5.32$, 13.16 Hz), 4.46-4.41 (dd, 1H, $J = 6.84$, 13.4 Hz), 2.63-2.62 (m, 2H), 1.87-1.59 (m, 5H), 1.50-1.41 (m, 1H), 1.27-0.90 (m, 5H), 1.20 (d, 3H, $J = 7.0$ Hz). Other spectroscopic data are in agreement with published data.^{5b}

III. Addition of unmodified aldehydes to vinyl sulfones catalyzed by N-*i*Pr-3*S*,3'*S*-bimorpholine derivative (iPBM)

Bis(phenylsulfonyl)ethyl-3-methylbutanal **9** : To a solution of **iPBM 2a** (0.08 mmol, 0.25 eq., 17 mg) in dry chloroform filtered on basic alumina (3 mL) was added 1,1-bis(benzenesulfonyl)ethylene **8** (0.335 mmol, 1 eq., 0.103 g). Then, after cooling at -60°C, isovaleraldehyde **3a** (3.35 mmol, 10 eq., 0.36 mL) was introduced. After 2 hours, the reaction was hydrolysed with NH_4Cl aq. sat. (2 mL). The layers were separated and the aqueous phase was extracted with CH_2Cl_2 (3 x 3 mL). The combined organic phases were dried over Na_2SO_4 , filtered, concentrated and purified by flash column chromatography on Florisil® (c-Hex/AcOEt 2:1) to obtain a pale yellow oil (105 mg, 79%). The enantiomeric excess was determined by chiral SFC (chiralcel OJ column, 2 mL/min, 200 bar, MeOH 10%-2-1-25%, 30°C, R_t : 5.51 (*S*), 7.73 (*R*)). $[\alpha]_D = -28.6^\circ$ (c 0.99, $ee = 55\%$, $CHCl_3$).

1H NMR (400 MHz, $CDCl_3$) : $\delta = 9.58$ (s, 1H), 7.96-7.87 (dd, 4H, $J_1 = 24.1$ Hz, $J_2 = 7.4$ Hz), 7.72-7.66 (m, 2H), 7.59-7.54 (m, 4H), 4.70-4.67 (dd, 1H, $J_1 = 9.12$ Hz, $J_2 = 3.04$ Hz), 2.94-2.89 (m, 1H), 2.53-2.46 (m, 1H), 2.17-2.10 (m, 2H), 0.98 (d, 3H, $J = 7.08$ Hz), 0.93 (d, 3H, $J = 7.04$ Hz). Other spectroscopic data are in agreement with published data.⁶

⁶ Mossé, S.; Alexakis, A. *Org. Lett.* **2005**, 7, 4361.

¹H 2a iPBM (400 MHz, CDCl₃)

¹³C 2a iPBM (100 MHz, CDCl₃)

¹H 2b (400 MHz, CDCl₃)

¹³C 2b (100 MHz, CDCl₃)

¹H NMR (CDCl₃, 400 MHz)

¹H 5f (400 MHz, CDCl₃)

¹H 7a (400 MHz, CDCl₃)

¹H 7b (400 MHz, CDCl₃)

¹³C 7b (100 MHz, CDCl₃)

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Area Percent Report
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Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: FID1 A,

Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	38.431	MM	0.2690	4.32527	2.68023e-1	3.29129
2	39.522	MM	0.3356	119.72359	5.94492	91.10304
3	42.583	MM	0.2661	3.12083	1.95452e-1	2.37478
4	43.006	MM	0.2945	4.24588	2.40328e-1	3.23088

CHIRALCEL OD-H

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 Area Percent Report
 =====

Sorted by Signal

Multiplier : 1.000000

Signal 1: LDAD1 C, Sig=210,8 Ref=360,100

Peak #	RT [min]	Type	Width [min]	Area [mAU*sec]	Height [mAU]	Area %
1	8.140	MM	0.298	33542.97656	1873.20447	82.1933
2	8.906	MM	0.239	2004.82495	139.84015	4.9126
3	9.509	MM	0.242	1767.83276	121.51196	4.3319
4	10.154	MM	0.285	3494.25366	204.22614	8.5623

Area Percent Report

Sorted by Signal

Multiplier : 1.000000

Signal 1: LDAD1 C, Sig=210,8 Ref=360,100

Peak #	RT [min]	Type	Width [min]	Area [mAU*sec]	Height [mAU]	Area %
1	4.970	MM	0.133	9940.98633	1247.41003	36.5600
2	5.655	MM	0.136	10301.83691	1261.37341	37.8871
3	6.112	MM	0.131	3555.91309	451.14575	13.0776
4	7.585	MM	0.129	3392.17749	438.82660	12.4754

CHIRALCEL OJ

Area Percent Report

Sorted by Signal

Multiplier : 1.000000

Signal 1: LDAD1 B, Sig=220,15 Ref=450,40

Peak #	RT [min]	Type	Width [min]	Area [mAU*sec]	Height [mAU]	Area %
1	4.921	MM	0.164	9341.16797	949.74426	95.2767
2	5.704	MM	0.146	463.08890	52.98405	4.7233

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 Area Percent Report
 =====

Sorted By : Signal
 Multiplier : 1.0000
 Dilution : 1.0000
 Use Multiplier & Dilution Factor with ISTDs

Signal 1: FID1 A,

Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	85.012	MM	0.3102	24.62792	1.32341	9.02923
2	85.531	MM	0.3252	221.08931	11.33157	81.05700
3	88.936	MM	0.3565	27.04060	1.26413	9.91378

peak #	R.T. min	Start min	End min	PK TY	peak height	peak area	peak % max.	% of total
1	36.202	35.885	36.447	M	36835	4810592	11.52%	10.329%
2	36.745	36.466	37.348	M	298398	41763663	100.00%	89.671%
Sum of corrected areas:						46574255

Area Percent Report

Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: FID1 A,

Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	129.155	MM	0.9406	97.86758	1.73408	27.80884
2	131.661	MM	0.9465	99.56387	1.75327	28.29084
3	134.445	MM	0.7366	77.60066	1.75586	22.05004
4	136.446	MM	0.7750	76.89763	1.65365	21.85028

Area Percent Report

Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: FID1 A,

Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	128.679	MM	1.0810	229.19563	3.53361	70.25446
2	131.568	MM	0.9035	32.41710	5.97961e-1	9.93669
3	134.496	MM	0.7722	54.44006	1.17507	16.68730
4	136.558	MM	0.5847	10.18361	2.90259e-1	3.12154

Area Percent Report

Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: FID1 A,

Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	91.961	MM	1.1811	311.93246	4.40164	72.40574
2	95.257	MM	1.1520	37.59717	5.43959e-1	8.72705
3	100.008	MM	1.2297	58.62838	7.94591e-1	13.60882
4	103.197	MM	1.1458	22.65377	3.29517e-1	5.25839

Area Percent Report

Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: FID1 A,

Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	58.496	MM	0.1427	4.12935	4.82396e-1	6.39671
2	59.305	MM	0.1636	50.32845	5.12724	77.96295
3	60.296	MM	0.1478	2.61124	2.94536e-1	4.04503
4	61.992	MM	0.1442	7.48527	8.64967e-1	11.59531

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Area Percent Report
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Sorted by Signal

Multiplier : 1.000000

Signal 1: LDAD1 C, Sig=210,8 Ref=360,100

Peak #	RT [min]	Type	Width [min]	Area [mAU*sec]	Height [mAU]	Area %
1	5.519	MM	0.166	9159.06250	922.13611	77.5409
2	7.739	MM	0.196	2652.84497	225.13580	22.4591