SUPPORTING INFORMATION

Orthoacylimines: A New Class of Chiral Auxiliaries for Nucleophilic Addition of Organolithium Reagents to Imines

Alessandro A. Boezio, Geoffrey Solberghe, Caroline Lauzon and André B. Charette*

Département de Chimie, Université de Montréal, P.O. Box 6128, Station Downtown, Québec, Canada H3C 3J7. E-mail: andre.Charette@umontreal.ca

Experimental procedures and characterization data for the new compounds.

General: All non-aqueous reactions were run under an inert atmosphere (nitrogen or argon) with rigid exclusion of moisture from reagents and glassware using standard techniques for manipulating air-sensitive compounds.¹ All glassware was stored in the oven and/or was flame-dried prior to use under an inert atmosphere of gas. Anhydrous solvents were obtained either by filtration through drying columns (THF, ether, CH₂Cl₂, benzene, DMF, CH₃CN, toluene, hexane, methanol) on a GlassContour system (Irvine, CA), by distillation over calcium hydride (Et₃N, ClCH₂CH₂Cl, pyridine, diisopropylamine, isopropanol) or by distillation over sodium/benzophenone (DME). Analytical thin-layer chromatography (TLC) was performed on precoated, glass-backed silica gel (Merck 60 F254). Visualization of the developed chromatogram was performed by UV absorbance, aqueous cerium molybdate, ethanolic phosphomolybdic acid, iodine, aqueous potassium permanganate, or ninhydrine. Flash column chromatography was performed using 230-400 mesh silica (EM Science or Silicycle) of the indicated solvent system according to standard technique.² Melting points were obtained on a Buchi melting point apparatus and are uncorrected. High resolution mass spectra were performed by the Centre régional de spectroscopie de masse de l'Université de Montréal. Combustion analyses were performed by the Laboratoire d'analyse élémentaire de l'Université de Montréal.

Analytical gas chromatography was carried out on a gas chromatograph equipped with a splitless mode capillary injector and a flame ionization detector or with a system equipped with an EI mass detector. Unless otherwise noted, the injector and detector temperatures were set to 250 °C and hydrogen was used as the carrier gas (63 psi). Data are reported as follows: column type, oven temperature, carrier pressure, and retention time (*t_r*).

Analytical Supercritical Fluid Chromatography was performed on an instrument equipped with a diode array UV detector.

Materials: Unless otherwise stated, commercial reagents were used without purification. All aldehydes were purified by distillation. The diol **10a**³, **10b**⁴, **10c**⁵, **10d**⁶, **10e**⁷, **10f**⁸ were prepared according to the literature. The resulting amines hydrochlorides **9a**⁹, **9b**¹⁰, **9c**¹¹, **9d**¹¹, **9e**¹², **9f**⁹, **9g**¹³, **9h**¹⁴, **9i**¹⁵, **9j**¹⁶ and the (S)-t-leucine **14**¹⁷ were compared with literature.

(4*R*,5*R*)-2-Azido-4,5-diphenyl-1,3-dioxolane (11a). Compound **11a** was prepared by the general procedure and the crude material was purified on silica gel (5/5/90 Et₃N/toluene/hexanes) to afford the pure orthoacylazide **11a** as a colorless oil (14.80 g, 60%): *R_f* 0.75 (toluene); [α]_D²⁰ +60.7 (*c* 1.99, CHCl₃); ¹H NMR (400 MHz, CDCl₃) δ 7.48-7.42 (m, 8H), 7.37-7.34 (m, 2H), 6.70 (s, 1H), 5.18 (d, *J* = 8.8 Hz, 1H), 4.97 (d, *J* = 8.8 Hz, 1H); ¹³C NMR (100 MHz, CDCl₃) δ 135.6, 134.7, 128.9, 128.7, 128.6(2), 126.7, 126.6, 108.9, 86.7, 84.5; Anal. Calcd for C₁₅H₁₃N₃O₂: C, 67.40; H, 4.90; N, 15.72. Found: C, 67.72; H, 5.00; N, 15.72.

(4*R,5*R**)-2-Azido-4,5-di-1-naphthyl-1,3-dioxolane (11b).** Compound **11b** was prepared by the general procedure and the crude material was purified on silica gel (5% Et₃N/hexanes) to afford the pure orthoacylazide **11b** as a white solid (632 mg, 65%): mp 64-65 °C; *R_f* 0.35 (5% Et₃N/hexanes); ¹H NMR (400 MHz, CDCl₃) δ 8.03 (d, *J* = 7.2 Hz, 1H), 7.88 (dd, *J* = 8.0, 5.0 Hz, 2H), 7.81 (dd, *J* = 16.0, 8.2 Hz, 2H), 7.70 (d, *J* = 7.1 Hz, 1H), 7.60 (t, *J* = 7.7 Hz, 1H), 7.49 (t, *J* = 7.8 Hz, 2H), 7.37 (t, *J* = 7.5 Hz, 1H), 7.30 (t, *J* = 7.5 Hz, 1H), 7.13 (t, *J* = 8.5 Hz, 2H), 6.97 (td, *J* = 7.7, 1.2 Hz, 1H), 6.89 (s, 1H), 6.06 (d, *J* = 8.4 Hz, 1H), 6.01 (d, *J* = 8.4 Hz, 1H); ¹³C NMR (100 MHz, CDCl₃) δ 133.7, 133.4, 132.0, 130.9(2), 130.8, 129.6, 129.2, 128.6, 128.4, 126.0, 125.7(2), 125.5, 125.4, 125.2, 125.1, 124.3, 122.8, 122.5, 109.3, 82.8, 82.3; Anal. Calcd for C₂₃H₁₇N₃O₂: C, 75.19; H, 4.66; N, 11.44. Found: C, 75.45; H, 4.61; N, 10.99.

(4*R*,5*R*)-2-Azido-4,5-bis-4'-[(4'*R*)-2',2',-dimethyl-1,3-dioxolane]-1,3-dioxolane (11c). Compound **11c** was prepared by the general procedure and the crude material was purified on silica gel (5% Et₃N/hexanes) to afford the pure orthoacylazide **11c** as colorless oil (761.6 mg, 65%): *R_f* 0.35 (5% Et₃N/hexanes); [α]_D²⁰ +12.3 (*c* 6.19, CHCl₃); ¹H NMR (400 MHz, CDCl₃) δ 6.17 (s, 1H), 4.27 (dd, *J* = 5.4, 4.3 Hz, 1H), 4.20-4.17 (m, 2H), 4.13 (dd, *J* = 14.7, 6.32 Hz, 1H), 4.06-3.99 (m, 3H), 3.93 (dd, *J* = 8.7, 4.9 Hz, 1H), 1.41 (d, *J* = 4.4 Hz, 6H), 1.32 (d, *J* = 1.6 Hz, 6H); ¹³C NMR (100 MHz, CDCl₃) δ 109.8(2), 109.0, 80.1, 78.5, 75.5, 75.0, 66.8, 65.4, 26.5, 26.2, 24.9, 24.7; Anal. Calcd for C₁₃H₂₁N₃O₆: C, 49.52; H, 6.71; N, 13.33. Found: C, 49.56; H, 6.96; N, 13.38.

(4*S*,5*S*)-2-Azido-4,5-bis[(benzyloxy)methyl]-1,3-dioxolane (11d). Compound **11d** was prepared by the general procedure and the crude material was purified on silica gel (5% Et₃N/hexanes) to afford the pure orthoacylazide **11d** as colorless oil (460.1 mg, 68%): *R_f* 0.35 (5% Et₃N/hexanes); [α]_D²⁰ -2.0 (*c* 7.09, CHCl₃); ¹H NMR (400 MHz, CDCl₃) δ 7.43-7.34 (m, 10H), 6.28 (s, 1H), 4.63 (d, *J* = 5.2 Hz, 4H), 4.38-4.35 (m, 1H),

4.30-4.27 (m, 1H), 3.78-3.63 (m, 4H); ^{13}C NMR (100 MHz, CDCl_3) δ 137.6(2), 128.4, 127.8, 127.7, 127.6, 108.9, 77.8, 77.7, 73.5, 73.4, 70.3, 69.2; Anal. Calcd for $\text{C}_{19}\text{H}_{21}\text{N}_3\text{O}_4$: C, 64.21; H, 5.96; N, 11.82. Found: C, 64.49; H, 6.06; N, 11.64.

(4R,5R)-2-Azido-N,N,N',N'-tetramethyl-1,3-dioxolane-4,5-dicarboxamide (11e). Compound **11e** was prepared by the general procedure and the crude material was purified on silica gel (5/15/80 Et_3N /hexanes/ EtOAc) to afford the pure orthoacylazide **11e** as a white solid (773.1 mg, 62%): mp 58-59 °C; R_f 0.35 (5/15/80 Et_3N /hexanes/ EtOAc); $[\alpha]_D^{20}$ -18.7 (c 4.61, CHCl_3); ^1H NMR (400 MHz, CDCl_3) δ 6.19 (s, 1H), 5.53 (d, J = 5.7 Hz, 1H), 5.15 (d, J = 5.7 Hz, 1H), 3.06 (s, 6H), 2.87 (d, J = 7.3 Hz, 6H); ^{13}C NMR (100 MHz, CDCl_3) δ 166.4, 166.2, 109.2, 76.16, 74.8, 36.8(2), 35.7, 35.6; Anal. Calcd for $\text{C}_9\text{H}_{15}\text{N}_5\text{O}_4$: C, 42.02; H, 5.88; N, 27.22. Found: C, 42.06; H, 5.98; N, 27.21.

(4R*,6R*)-2-Azido-4,6-diphenyl-1,3-dioxane (11f). Compound **11f** was prepared by the general procedure and the crude material was purified on silica gel (5% Et_3N /hexanes) to afford the pure orthoacylazide **11f** as a colorless oil (645.1 mg, 57%): R_f 0.55 (5% Et_3N /hexanes); ^1H NMR (400 MHz, CDCl_3) δ 7.56-7.36 (m, 10H), 5.79 (s, 1H), 5.51 (dd, J = 5.1, 3.0 Hz, 1H), 5.00 (dd, J = 10.8, 3.4 Hz, 1H), 2.58 (ddd, J = 14.2, 10.9, 5.8 Hz, 1H), 2.50 (dt, J = 14.3, 3.2 Hz, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ 140.1, 138.5, 129.0, 128.6, 128.1, 127.9, 126.3, 125.8, 100.7, 73.7, 72.9, 34.6.

N-[(4R,5R)-4,5-Diphenyl-1,3-dioxolan-2-yl]-N-[(1E)-phenylmethylene]amine (5a). Compound **5a** was prepared by the general procedure and the crude material was purified on silica gel (5% Et_3N /hexanes) to afford the pure imine **5a** as a colorless oil (2.22 g, 89%): R_f 0.20 (5% Et_3N /hexanes); $[\alpha]_D^{20}$ +44.4 (c 2.16, CHCl_3); ^1H NMR (400 MHz, CDCl_3) δ 8.60 (s, 1H), 7.97 (d, J = 6.3 Hz, 2H), 7.55-7.50 (m, 2H), 7.45-7.38 (m, 11H), 6.50 (s, 1H), 5.25 (d, J = 8.4 Hz, 1H), 4.97 (d, J = 8.4 Hz, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ 163.0, 137.5, 136.9, 135.6, 132.3, 129.6, 129.1, 129.0, 128.9, 128.8, 127.7, 127.2, 114.8, 87.1, 85.0; Anal. Calcd for $\text{C}_{22}\text{H}_{19}\text{NO}_2$: C, 80.22; H, 5.81; N, 4.25. Found: C, 79.93; H, 6.17; N, 4.37.

N-[(4R,5R)-4,5-Diphenyl-1,3-dioxolan-2-yl]-N-[(1E,2E)-3-phenylprop-2-enylidene]amine (5b). Compound **5b** was prepared by the general procedure and the crude material was purified on silica gel (5% Et_3N /hexanes) to afford the pure imine **5b** as a white solid (2.42 g, 86%): mp 98-99 °C; R_f 0.20 (5% Et_3N /hexanes); $[\alpha]_D^{20}$ +4.0 (c 2.09, CHCl_3); ^1H NMR (400 MHz, CDCl_3) δ 8.34 (d, J = 6.2 Hz, 1H), 7.58 (d, J = 6.6 Hz, 2H), 7.46-7.39 (m, 13H), 7.17 (d, J = 6.5 Hz, 2H), 6.40 (s, 1H), 5.22 (d, J = 8.4 Hz, 1H), 4.97 (d, J = 8.4 Hz, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ 164.7, 145.8, 137.3, 136.8, 135.8, 130.3, 129.4, 129.0(2), 128.9, 128.1, 127.9, 127.7, 127.3, 114.8, 87.2, 85.0; Anal. Calcd for $\text{C}_{24}\text{H}_{21}\text{NO}_2$: C, 81.10; H, 5.96; N, 3.94. Found: C, 80.99; H, 6.03; N, 3.96.

N-[(1E)-2,2-Dimethylpropylidene]-N-[(4R,5R)-4,5-diphenyl-1,3-dioxolan-2-yl]amine (5c). Compound **5c** was prepared by the general procedure and the crude material was purified on silica gel (3% Et_3N /hexanes) to afford the pure imine **5c** as a colorless oil (2.32 g, 93%): R_f 0.35 (3% Et_3N /hexanes); $[\alpha]_D^{20}$ +37.5 (c 1.98, CHCl_3); ^1H NMR (400 MHz, CDCl_3) δ 7.91 (s, 1H), 7.48-7.46 (m, 2H), 7.42-7.35 (m, 8H), 6.25 (s, 1H), 5.24 (d, J = 8.4 Hz, 1H), 4.91 (d, J = 8.4 Hz, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ 174.8, 138.0, 137.1, 129.0, 128.9, 128.8(2), 127.8, 127.1, 115.3, 87.1, 85.0, 36.8, 27.1; Anal. Calcd for $\text{C}_{20}\text{H}_{23}\text{NO}_2$: C, 77.64; H, 7.49; N, 4.53. Found: C, 77.68; H, 7.79; N, 4.42.

N-[(4R,5R)-4,5-Diphenyl-1,3-dioxolan-2-yl]-N-[(1E)-2-furylmethylene]amine (5d). Compound **5d** was prepared by the general procedure and the crude material was purified on silica gel (5% Et_3N /hexanes) to afford the pure imine **5d** as a yellow oil (1.88 g, 76%): R_f 0.20 (5% Et_3N /hexanes); $[\alpha]_D^{20}$ +30.4 (c 3.59, CHCl_3); ^1H NMR (400 MHz, CDCl_3) δ 8.40 (s, 1H), 7.65 (d, J = 1.1 Hz, 1H), 7.40-7.31 (m, 10H), 7.03 (d, J = 3.4 Hz, 1H), 6.57 (dd, J = 3.4, 1.7 Hz, 1H), 6.44 (s, 1H), 5.16 (d, J = 8.5 Hz, 1H), 4.93 (d, J = 8.5 Hz, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ 151.5, 151.1, 146.4, 137.1, 136.7, 129.0, 128.9, 127.6, 127.2, 117.3, 114.4, 112.5, 87.1, 84.8; Anal. Calcd for $\text{C}_{20}\text{H}_{17}\text{NO}_3$: C, 75.22; H, 5.37; N, 4.39. Found: C, 75.14; H, 5.45; N, 4.47.

N-[(4R,5R)-4,5-Diphenyl-1,3-dioxolan-2-yl]-N-[(1E)-2-methylpropylidene]amine (5e). Compound **5e** was prepared by the general procedure and the crude material was purified on silica gel (5% Et_3N /hexanes) to afford the pure imine **5e** as a colorless oil (399.1 mg, 36%): R_f 0.55 (5% Et_3N /hexanes); $[\alpha]_D^{20}$ +42.0 (c 3.14, CHCl_3); ^1H NMR (400 MHz, CDCl_3) δ 7.89 (d, J = 4.6 Hz, 1H), 7.40-7.29 (m, 10H), 6.16 (s, 1H), 5.14 (d, J = 8.4 Hz, 1H), 4.86 (d, J = 8.4 Hz, 1H), 2.66 (m, 1H), 1.24 (dd, J = 6.9, 1.9 Hz, 6H); ^{13}C NMR (100 MHz,

CDCl₃) d 172.6, 136.9, 136.3, 128.4, 128.3(2), 127.1, 126.6, 114.6, 86.5, 84.4, 33.8, 18.8; Anal. Calcd for C₁₉H₂₁NO₂: C, 77.26; H, 7.17; N, 4.74. Found: C, 77.04; H, 7.38; N, 4.90.

***N*-[(4*R**,5*R**)-4,5-Di-1-naphthyl-1,3-dioxolan-2-yl]-*N*-[(1*E*)-phenylmethylen]amine (5f).** Compound **5f** was prepared by the general procedure and the crude material was purified on silica gel (5% Et₃N/hexanes) to afford the pure imine **5f** as a white solid (620.9 mg, 84%): mp 55-56 °C; R_f 0.25 (5% Et₃N/hexanes); ¹H NMR (400 MHz, CDCl₃) d 8.68 (s, 1H), 8.07-8.01 (m, 3H), 7.91-7.81 (m, 5H), 7.63-7.48 (m, 7H), 7.40-7.31 (m, 2H), 7.14 (t, *J* = 7.8 Hz, 1H), 7.06 (t, *J* = 7.8, 1H), 6.74 (s, 1H), 6.23 (d, *J* = 7.9 Hz, 1H), 6.11 (d, *J* = 7.9 Hz, 1H); ¹³C NMR (100 MHz, CDCl₃) d 163.7, 135.7, 134.4, 134.2, 134.0, 133.2, 132.5, 131.7, 129.9, 129.5, 129.3, 129.2, 129.1, 126.4, 126.3, 126.2, 126.1, 126.0(2), 125.9, 125.6, 124.0, 123.7, 115.3, 83.7, 82.8; Anal. Calcd. for C₃₀H₂₃NO₂: C, 83.89; H, 5.40; N, 3.26. Found: C, 83.78; H, 5.54; N, 3.28.

***N*-[(4*R*,5*R*)-4,5-Bis-4'-[(4'*R*)-2',2',-dimethyl-1,3-dioxolane]-1,3-dioxolan-2-yl]-*N*-[(1*E*)-phenylmethylen]amine (5g).** Compound **5g** was prepared by the general procedure and the crude material was purified on silica gel (5/5/90 Et₃N/AcOEt/hexanes) to afford the pure imine **5g** as a white solid (447.2 mg, 76%): mp 95-96 °C; R_f 0.30 (5/5/90 Et₃N/AcOEt/hexanes): [α]_D²⁰ +19.51 (c 2.16, CHCl₃); ¹H NMR (300 MHz, CDCl₃) d 8.33 (s, 1H), 7.80 (dt, *J* = 4.5, 1.7 Hz, 2H), 7.49-7.40 (m, 3H), 6.06 (s, 1H), 4.44-4.37 (m, 2H), 4.32-4.26 (q, *J* = 5.4 Hz, 1H), 4.16-4.02 (m, 5H), 1.47 (d, *J* = 9.9 Hz, 6H), 1.36 (d, *J* = 6.0 Hz, 6H); ¹³C NMR (100 MHz, CDCl₃) d 163.1, 135.2, 132.4, 129.5, 129.1, 115.2, 110.3, 110.1, 80.3, 79.2, 76.8, 76.0, 67.6, 66.4, 27.3, 27.0, 25.8, 25.5; Anal. Calcd. for C₂₀H₂₇NO₆: C, 63.64; H, 7.21; N, 3.71. Found: C, 63.57; H, 7.31; N, 3.72.

***N*-[(4*S*,5*S*)-4,5-Bis[(benzyloxy)methyl]-1,3-dioxolan-2-yl]-*N*-[(1*E*)-phenylmethylen]amine (5h).** Compound **5h** was prepared by the general procedure and the crude material was purified on silica gel (5/10/85 Et₃N/AcOEt/hexanes) to afford the pure imine **5h** as a colorless oil (1.32 g, 85%): R_f 0.35 (5/10/85 Et₃N/AcOEt/hexanes): [α]_D²⁰ -1.00 (c 5.49, CHCl₃); ¹H NMR (300 MHz, CDCl₃) d 8.41(s, 1H), 7.81 (dt, *J* = 6.4, 1.6 Hz, 2H), 7.50-7.30 (m, 13H), 6.15 (d, *J* = 0.6 Hz, 1H), 4.65 (s, 2H), 4.61 (d, *J* = 1.7 Hz, 2H), 4.41 (q, *J* = 6.1 Hz, 1H), 4.31 (q, *J* = 6.1 Hz, 1H), 3.86-3.68 (m, 4H); ¹³C NMR (75 MHz, CDCl₃) d 163.0, 138.4(2), 135.4, 132.2, 129.6, 129.0, 128.9, 128.8, 128.1, 114.8, 78.2, 78.0, 74.0, 73.9, 71.8, 70.5; Anal. Calcd. for C₂₆H₂₇NO₄: C, 74.80; H, 6.52; N, 3.35. Found: C, 74.51; H, 6.79; N, 3.40.

(4*R*,5*R*)-*N,N,N',N'*-Tetramethyl-2-[(1*E*)-phenylmethylen]amino-1,3-dioxolane-4,5 dicarboxamide (5i). Compound **5i** was prepared by the general procedure and the crude material was purified on silica gel (5/15/80 Et₃N/hexanes/EtOAc) to afford the pure imine **5i** as a white solid (394.6 mg, 87%): mp 150-151 °C; R_f 0.35 (5/15/80 Et₃N/hexanes/EtOAc): [α]_D²⁰ -24.16 (c 1.49, CHCl₃); ¹H NMR (300 MHz, CDCl₃) d 8.41(s, 1H), 7.80 (dt, *J* = 6.5, 1.7 Hz, 2H), 7.48-7.39 (m, 3H), 6.25 (d, *J* = 0.8 Hz, 1H), 5.66 (d, *J* = 5.9 Hz, 1H), 5.28 (d, *J* = 5.9 Hz, 1H), 3.20 (d, *J* = 9.2 Hz, 6H), 2.98 (d, *J* = 12.8 Hz, 6H); ¹³C NMR (100 MHz, CDCl₃) d 168.2, 167.7, 163.7, 135.2, 132.5, 129.7, 129.1, 115.2, 77.1, 74.8, 74.8, 37.7, 37.6, 36.3(2); Anal. Calcd. for C₁₆H₂₁N₃O₄: C, 60.17; H, 6.53; N, 13.16. Found: C, 60.04; H, 6.77; N, 12.96.

***N*-[(4*R**,6*R**)-4,6-Diphenyl-1,3-dioxan-2-yl]-*N*-[(1*E*)-phenylmethylen]amine (5j).** Compound **5j** was prepared by the general procedure and the crude material was purified on silica gel (5% Et₃N/hexanes) to afford the pure imine **5j** as a colorless oil (453.3 mg, 74%): R_f 0.35 (5% Et₃N/hexanes); ¹H NMR (300 MHz, CDCl₃) d 8.65(s, 1H), 7.95 (dd, *J* = 7.6, 1.8 Hz, 2H), 7.65 (d, *J* = 8.0 Hz, 2H), 7.57-7.34 (m, 11H), 6.03 (d, *J* = 1.1 Hz, 1H), 5.61 (d, *J* = 4.6 Hz, 1H), 5.10 (dd, *J* = 11.2, 2.9 Hz, 1H), 2.66 (dq, *J* = 14.1, 5.8 Hz, 1H), 2.55 (dt, *J* = 13.9, 2.8 Hz, 1H); ¹³C NMR (100 MHz, CDCl₃) d 164.4, 141.5, 139.8, 135.7, 132.4, 129.8, 129.5, 129.1, 129.0, 128.5, 128.1, 127.2, 126.7, 105.3, 74.6, 73.6, 35.1; Anal. Calcd. for C₂₃H₂₁NO₂: C, 80.44; H, 6.16; N, 4.08. Found: C, 79.90; H, 6.20; N, 4.05.

(1*R*)-1-Phenylethanaminium chloride (9a). The general procedure was followed and the enantiomeric ratio (91:9) was determined by GC analysis of the trifluoroamide derivative on chiral stationary phase (Chiraldex B-PH, 30 m, 110 °C, H₂, 10 psi, FID): (*S*)-**9a** *t*_r, 15.3 min, (*R*)-**9a** *t*_r, 16.0 min). The crude material was purified on silica gel (15% MeOH/CH₂Cl₂) to afford the pure amine hydrochloride **9a** as a white solid (252.2 mg, 100%): mp 151-152 °C; R_f 0.35 (15% MeOH/CH₂Cl₂); [α]_D¹⁸ +3.3 (c 2.09, MeOH); ¹H NMR (400 MHz, CD₃OD) d 7.53-7.39 (m, 5H), 5.08 (br, 3H), 4.49 (q, *J* = 6.9 Hz, 1H), 1.66 (d, *J* = 6.9 Hz, 3H); ¹³C NMR (100 MHz, CD₃OD) d 138.7, 129.3, 129.2, 126.8, 51.4, 19.9; Anal. Calcd for C₈H₁₂ClN: C, 60.95; H, 7.67; N, 8.89; Found: C, 60.84; H, 7.80; N, 8.77.

(1R)-1-Phenylpentan-1-aminium chloride (9b). The general procedure was followed and the enantiomeric ratio (86:14) was determined by SFC analysis of the benzamide derivative on chiral stationary phase (Chiralcel OD, 40 °C, 200 bar, 5% MeOH in CO₂, 2.0 mL/min, 205.8 nm): (*R*)-**9b** *t_r*, 8.3 min, (*S*)-**9b** *t_r*, 11.9 min). The crude material was purified on silica gel (15% MeOH/CH₂Cl₂) to afford the pure amine hydrochloride **9b** as a white solid (305.0 mg, 95%): mp >250 °C; *R_f* 0.35 (15% MeOH/CH₂Cl₂); [α]_D²⁰ -18.9 (*c* 12.81, MeOH); ¹H NMR (400 MHz, CD₃OD) δ 7.48-7.41 (m, 5H), 4.97 (br, 3 H), 4.24 (dd, *J* = 9.5, 5.8 Hz, 1H), 2.06-1.94 (m, 2H), 1.40-1.27 (m, 3H), 1.18-1.13 (m, 1H), 0.90 (t, *J* = 7.2 Hz, 3H); ¹³C NMR (100 MHz, CD₃OD) δ 137.4, 129.3(2), 127.4, 56.0, 34.3, 27.9, 22.2, 13.1; Anal. Calcd for C₁₁H₁₈ClN: C, 66.15; H, 9.08; N, 7.01; Found: C, 66.35; H, 9.40; N, 6.82.

(2R,3E)-4-Phenylbut-3-en-2-aminium chloride (9c). The general procedure was followed and the enantiomeric ratio (88:12) was determined by SFC analysis of the benzamide derivative on chiral stationary phase (Chiralcel OD, 40 °C, 200 bar, 5% MeOH in CO₂, 2.0 mL/min, 205.8 nm): (*R*)-**9c** *t_r*, 21.7 min, (*S*)-**9c** *t_r*, 26.6 min). The crude material was purified on silica gel (15% MeOH/CH₂Cl₂) to afford the pure amine hydrochloride **9c** as a white solid (260.9 mg, 100%): mp 155-156 °C; *R_f* 0.35 (15% MeOH/CH₂Cl₂); [α]_D²⁰ +18.1 (*c* 8.01, MeOH); ¹H NMR (400 MHz, CD₃OD) δ 7.43 (d, *J* = 7.1 Hz, 2H), 7.29 (t, *J* = 7.5 Hz, 2H), 7.22 (t, *J* = 7.3 Hz, 1H), 6.72 (d, *J* = 16.0 Hz, 1H), 6.27 (dd, *J* = 16.0, 7.5 Hz, 1H), 5.15 (br, 3H), 4.00 (dt, *J* = 13.4, 6.7 Hz, 1H), 1.45 (d, *J* = 6.7 Hz, 3H); ¹³C NMR (100 MHz, CD₃OD) δ 137.3, 135.2, 129.9, 129.6, 127.9, 127.5, 50.8, 19.9; Anal. Calcd for C₁₀H₁₄ClN: C, 65.39; H, 7.68; N, 7.63. Found: C, 65.78; H, 7.94; N, 7.43.

(1E,3R)-1-Phenylhept-1-en-3-aminium chloride (9d). The general procedure was followed and the enantiomeric ratio (85:15) was determined by SFC analysis of the benzamide derivative on chiral stationary phase (Chiralcel OD, 40 °C, 200 bar, 5% MeOH in CO₂, 2.0 mL/min, 254.3 nm): (*S*)-**9d** *t_r*, 22.8 min, (*R*)-**9d** *t_r*, 26.3 min). The crude material was purified on silica gel (15% MeOH/CH₂Cl₂) to afford the pure amine hydrochloride **9d** as a white solid (319.7 mg, 100%): mp 168-169 °C; *R_f* 0.35 (15% MeOH/CH₂Cl₂); [α]_D²⁰ -34.5 (*c* 7.80, MeOH); ¹H NMR (400 MHz, CD₃OD) δ 7.48 (d, *J* = 7.2 Hz, 2H), 7.34 (t, *J* = 7.4 Hz, 2H), 7.28 (t, *J* = 7.3 Hz, 1H), 6.79 (d, *J* = 15.9 Hz, 1H), 6.20 (dd, *J* = 15.9, 8.7 Hz, 1H), 5.07 (br, 3H), 3.86 (td, *J* = 8.8, 5.3 Hz, 1H), 1.87-1.83 (m, 1H), 1.78-1.74 (m, 1H), 1.41-1.36 (m, 4H), 0.93 (t, *J* = 6.9 Hz, 3H); ¹³C NMR (100 MHz, CD₃OD) δ 137.2, 137.0, 129.9, 129.7, 128.0, 126.1, 55.5, 34.4, 28.9, 23.5, 14.4; Anal. Calcd for C₁₃H₂₀ClN: C, 69.16; H, 8.93; N, 6.20. Found: C, 69.25; H, 9.13; N, 6.15.

(1S,2E)-1,3-Diphenylprop-2-en-1-aminium chloride (9e). The general procedure was followed and the enantiomeric ratio (88:12) was determined by SFC analysis of the benzamide derivative on chiral stationary phase (Chiralcel OD, 40 °C, 200 bar, 10% MeOH in CO₂, 2.0 mL/min, 205.8 nm): (*R*)-**9e** *t_r*, 17.7 min, (*S*)-**9e** *t_r*, 19.7 min). The crude material was purified on silica gel (15% MeOH/CH₂Cl₂) to afford the pure amine hydrochloride **9e** as a white solid (218.2 mg, 90%): mp 212-213 °C; *R_f* 0.35 (15% MeOH/CH₂Cl₂); [α]_D²⁰ -15.8 (*c* 5.18, MeOH); ¹H NMR (400 MHz, CD₃OD) δ 7.55 (d, *J* = 7.7 Hz, 2H), 7.47 (t, *J* = 8.0 Hz, 4H), 7.41 (t, *J* = 7.2, 1H), 7.33 (t, *J* = 7.3 Hz, 2H), 7.27 (t, *J* = 7.1 Hz, 1H), 6.78 (d, *J* = 15.9 Hz, 1H), 6.52 (dd, *J* = 15.8, 7.3 Hz, 1H), 5.10 (d, *J* = 7.56 Hz, 1H), 5.03 (br, 3H); ¹³C NMR (100 MHz, CD₃OD) δ 137.6, 136.1, 134.7, 129.4, 129.1, 128.9, 128.7, 127.4, 126.9, 125.5, 57.4.

(2R)-3,3-Dimethylbutan-2-aminium chloride (9f). The general procedure was followed and the enantiomeric ratio (93:7) was determined by SFC analysis of the benzamide derivative on chiral stationary phase (Chiralcel OD, 40 °C, 200 bar, 5% MeOH in CO₂, 2.0 mL/min, 205.8 nm): (*R*)-**9f** *t_r*, 3.1 min, (*S*)-**9f** *t_r*, 4.5 min). The crude material was purified on silica gel (15% MeOH/CH₂Cl₂) to afford the pure amine hydrochloride **9f** as a white solid (111.4 mg, 62%): mp >250 °C; *R_f* 0.35 (15% MeOH/CH₂Cl₂); [α]_D²⁰ -2.47 (*c* 2.84, MeOH); ¹H NMR (400 MHz, CD₃OD) δ 5.60 (br, 3H), 3.13 (q, *J* = 6.8 Hz, 1H), 1.28 (d, *J* = 6.8 Hz, 3H), 1.02 (s, 9H); ¹³C NMR (100 MHz, CD₃OD) δ 56.7, 33.0, 25.1, 13.7; Anal. Calcd for C₆H₁₆ClN: C, 52.35; H, 11.72; N, 10.18. Found: C, 51.95; H, 12.08; N, 10.11.

(3R)-2,2-Dimethylheptan-3-aminium chloride (9g). The general procedure was followed and the enantiomeric ratio (96:4) was determined by SFC analysis of the benzamide derivative on chiral stationary phase (Chiralcel OD, 40 °C, 200 bar, 5% MeOH in CO₂, 2.0 mL/min, 205.8 nm): (*R*)-**9g** *t_r*, 2.9 min, (*S*)-**9g** *t_r*, 3.5 min). The crude material was purified on silica gel (15% MeOH/CH₂Cl₂) to afford the pure amine hydrochloride **9g** as a white solid (166.5 mg, 70%): mp 158-159 °C; *R_f* 0.35 (15% MeOH/CH₂Cl₂); [α]_D²⁰

+35.6 (c 1.96, MeOH); ^1H NMR (400 MHz, CD_3OD) δ 4.91 (br, 3H), 2.88 (dd, $J = 10.0, 2.5$ Hz, 1H), 1.82–1.71 (m, 1H), 1.58–1.30 (m, 5H), 1.03 (s, 9H), 0.98 (t, $J = 7.0$ Hz, 3H); ^{13}C NMR (100 MHz, CD_3OD) δ 61.6, 33.3, 28.9, 28.7, 25.3, 22.6, 13.2.

(1S)-2,2-Dimethyl-1-phenylpropan-1-aminium chloride (9h). The general procedure was followed and the enantiomeric ratio (99:1) was determined by SFC analysis of the benzamide derivative on chiral stationary phase (Chiralcel OJ, 40 °C, 200 bar, 5% MeOH in CO_2 , 2.0 mL/min, 254.3 nm): (*S*)-**9h** t_r , 4.6 min, (*R*)-**9h** t_r , 5.6 min). The crude material was purified on silica gel (15% MeOH/ CH_2Cl_2) to afford the pure amine hydrochloride **9h** as a white solid (141.8 mg, 54%): mp >250 °C; R_f 0.55 (15% MeOH/ CH_2Cl_2); $[\alpha]_D^{20}$ -5.8 (c 7.28, MeOH); ^1H NMR (400 MHz, CD_3OD) δ 7.56–7.40 (m, 5H), 5.13 (br, 3H), 4.18 (s, 1H), 1.05 (s, 9H); ^{13}C NMR (100 MHz, CD_3OD) δ 135.8, 128.9, 128.6, 128.5, 64.8, 34.2, 25.8.

(1R)-1-(2-Furyl)ethanaminium chloride (9i). The general procedure was followed and the enantiomeric ratio (89:11) was determined by SFC analysis of the benzamide derivative on chiral stationary phase (Chiralcel OD, 40 °C, 200 bar, 5% MeOH in CO_2 , 2.0 mL/min, 205.8 nm): (*R*)-**9i** t_r , 5.7 min, (*S*)-**9i** t_r , 6.3 min). The crude material was purified on silica gel (15% MeOH/ CH_2Cl_2) to afford the pure amine hydrochloride **9i** as a yellow gummy solid (149.2 mg, 75%): R_f 0.35 (15% MeOH/ CH_2Cl_2); $[\alpha]_D^{20}$ +5.1 (c 4.28, MeOH); ^1H NMR (300 MHz, CD_3OD) δ 7.58 (dd, $J = 1.9, 0.8$ Hz, 1H), 6.53 (d, $J = 3.3$ Hz, 1H), 6.46 (dd, $J = 3.3, 1.8$ Hz, 1H), 5.07 (br, 3H), 4.55 (q, $J = 6.9$ Hz, 1H), 1.65 (d, $J = 6.9$ Hz, 3H); ^{13}C NMR (100 MHz, CD_3OD) δ 152.8, 144.8, 111.9, 109.4, 45.8, 18.2.

(1R)-1-(2-Furyl)pentan-1-aminium chloride (9j). The general procedure was followed and the enantiomeric ratio (85:15) was determined by SFC analysis of the benzamide derivative on chiral stationary phase (Chiralcel OD, 40 °C, 200 bar, 5% MeOH in CO_2 , 2.0 mL/min, 205.8 nm): (*R*)-**9j** t_r , 5.4 min, (*S*)-**9j** t_r , 6.3 min). The crude material was purified on silica gel (15% MeOH/ CH_2Cl_2) to afford the pure amine hydrochloride **9j** as a yellow solid (77.3 mg, 33%): mp 141–142 °C; R_f 0.35 (15% MeOH/ CH_2Cl_2); $[\alpha]_D^{20}$ -10.6 (c 3.21, MeOH); ^1H NMR (300 MHz, CD_3OD) δ 7.57 (dd, $J = 1.9, 0.8$ Hz, 1H), 6.49 (dq, $J = 3.3, 0.4$ Hz, 1H), 6.45 (dd, $J = 3.3, 1.9$ Hz, 1H), 4.99 (br, 3H), 4.31 (dd, $J = 9.1, 5.9$ Hz, 1H), 2.02–1.84 (m, 2H), 1.46–1.13 (m, 4H), 0.91 (t, $J = 2.5$ Hz, 3H); ^{13}C NMR (100 MHz, CD_3OD) δ 152.4, 144.7, 111.8, 110.2, 50.2, 33.6, 29.0, 23.4, 14.3; Anal. Calcd for $\text{C}_9\text{H}_{16}\text{ClNO}$: C, 56.99; H, 8.50; N, 7.38. Found: C, 57.01; H, 8.63; N, 7.28.

N-[(1R)-2,2-Dimethyl-1-phenylpropyl]-2,2,2-trifluoroacetamide (13). Trifluoroacetic anhydride (2.4 mL, 17.6 mmol, 5.00 equiv) was added to a solution of (*S*)-2,2-dimethyl-1-phenylpropyl-ammonium chloride **9h** (92 % ee, 700.1 mg, 3.05 mmol, 1.00 equiv) and Et_3N (1.23 mL, 8.77 mmol, 2.50 equiv) in DCM (10 mL, 0.35 M) at 0 °C. After 72 h of stirring at 0 °C, the mixture was concentrated under reduced pressure and the crude material was purified on silica gel (10% AcOEt/hexanes) to afford the pure amide **13** as a white solid (830.2 mg, 91%): mp 109–111 °C; R_f 0.30 (10% AcOEt/hexanes); $[\alpha]_D^{20}$ -130.0 (c 1.13, CHCl_3); ^1H NMR (300 MHz, CDCl_3) δ 7.34 (m, 3H), 7.17 (m, 2H), 6.70 (br, 1H), 4.81 (d, $J = 9.5$ Hz, 1H), 0.96 (s, 9H); ^{13}C NMR (75 MHz, CDCl_3) δ 156.9 (q, $J_{\text{CF}} = 36.7$ Hz), 138.3, 128.6, 128.3, 128.2, 116.4 (q, $J_{\text{CF}} = 288.2$ Hz), 62.8, 35.5, 26.6. Anal. Calcd for $\text{C}_{13}\text{H}_{16}\text{F}_3\text{NO}$: C, 60.22; H, 6.22; N, 5.40. Found: C, 60.17; H, 6.00; N, 5.30.

(S)-*t*-Leucine (14). To a solution of the amide **13** (520.0 mg, 2.00 mmol, 1.00 equiv) in a mixture of $\text{CCl}_4/\text{CH}_3\text{CN}/\text{H}_2\text{O}$ (3 mL/3 mL/4.5 mL) was added successively NaIO_4 (647 mg, 30.0 mmol, 15.0 equiv) and $\text{RuCl}_3 \cdot \text{H}_2\text{O}$ (40.0 mg, 0.20 mmol, 0.10 equiv). The resulting mixture was stirred vigorously for 24 h at rt. The black crude mixture was filtered on a pad of celite and the solid residue was washed with MeOH and CH_2Cl_2 . After concentration under reduced pressure of the filtrate, the residue was directly dissolved in 40 mL of MeOH and 20 mL aqueous NaOH (1 M) were added. After 16 h of stirring at rt, the solution was concentrated under reduced pressure. The residue was then dissolved in HCl (1M) and the solution was concentrated under reduced pressure. The amino acid•HCl was neutralized by passing it through an ion exchange resin column (Dowex® 50W40) and by eluting with 5 % (v/v) aqueous ammonia. The positive ninhydrin fraction were combined and evaporated on reduced pressure to afford pure *t*-leucine **14** as a white solid (280.1 mg, 68%). The enantiomeric ratio (96:4) (92 % ee) was determined by SFC analysis of the methyl ester benzamide derivative on chiral stationary phase (Chiralcel OD, 40 °C, 200 bar, 2% MeOH in CO_2 , 0.6 mL/min, 205.8 nm): (*R*)-**14** t_r , 15.7 min, (*S*)-**14** t_r , 16.7 min): mp >250 °C; $[\alpha]_D^{20}$ +37.3 (c 1.05, AcOH), lit: $[\alpha]_D^{20}$ +30.0 (c 1.00, AcOH); ^1H NMR (400 MHz, D_2O) δ 3.24 (s, 1H), 0.93 (s, 9H); ^{13}C NMR (100 MHz, D_2O) δ 176.3, 64.8, 32.5, 26.3.

- ¹ Shriver, D. F.; Drezzdon, M. A. *The manipulation of air-sensitive compounds*; 2nd Edition ed.; Wiley: New York, 1986.
- ² Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923.
- ³ McKee, B. H.; Gilheany, D. G.; Sharpless, K. B. *Org. Synth.* **1992**, *70*, 47-53.
- ⁴ Handa, Y.; Inanaga, J. *Tetrahedron Lett.* **1987**, *28*, 5717-5718.
- ⁵ Schmid, C. R.; Bryant, J. D.; Dowlatzadah, M.; Phillips, J. L.; Prather, D. E.; Schantz, R. D.; Sear, N. L. Vianco, C. S. *J. Org. Chem.* **1991**, *56*, 4056-4058.
- ⁶ Helgeson R. C.; Weisman, G. R.; Toner, J. L.; Tarnowski, T. L.; Chao Y.; Mayer, J. M.; Cram, D. J. *J. Am. Chem. Soc.* **1979**, *101*, 4928-4941.
- ⁷ Seebach, D.; Kalinowski, H.-O.; Bastani, B.; Crass, G.; Daum, H.; Dörr, H.; DuPreez, N. P.; Ehrig, V.; Langer, W.; Nüssler, C.; Oei, H.-A.; Schmidt, M. *Helv. Chim. Acta* **1977**, *60*, 301-325.
- ⁸ Dale, J. J. *Chem. Soc.* **1961**, 910-922.
- ⁹ Rangaishenvi, M. V.; Singaram, B.; Brown, H. C. *J. Org. Chem.* **1991**, *56*, 3286-3294.
- ¹⁰ Eddine, J. J.; Cherqaoui, M. *Tetrahedron: Asymmetry* **1995**, *6*, 1225-1228.
- ¹¹ This amine has been reported by Enders (ref. a) but the correlation is not consistent with the derivatization study done by Larchevèque (ref. b): (a) Enders, D.; Schankat, J. *Helv. Chim. Acta*, **1993**, *76*, 402-406. (b) Imogai, H.; Petit, Y.; Larcheveque, M. *Syn. Lett.* **1997**, *5*, 615-617.
- ¹² (a) Robin, S.; Rousseau, G. *Eur. J. Org. Chem.* **2000**, *17*, 3007-3012. (b) Matt, P.; Loiseleur, O. Koch, G.; Pfaltz, A.; Lefebvre, C.; Feucht, T.; Helmchen, G. *Tetrahedron: Asymmetry* **1994**, *5*, 573-584.
- ¹³ (a) Enders, D.; Schubert, H.; Nübling, C. *Angew. Chem., Int. Ed. Engl.* **1986**, *25*, 1109-1110. (b) Enders, D.; Nübling, C.; Schubert, H. *Liebigs Ann. /Recueil* **1997**, 1089-1100.
- ¹⁴ Smith, H. E.; Warren, Jr. M. E.; Katzin, L. I. *Tetrahedron* **1968**, *24*, 1327-1335.
- ¹⁵ (a) KuoY.-H.; Shih, K.-S. *Chem. Pharm. Bull.* **1991**, *39*, 181-183. (b) Alvaro, G.; Martelli, G.; Savoia, D.; Zoffoli, A. *Synthesis* **1998**, *12*, 1773-1777.
- ¹⁶ (a) Liao, L.-X.; Wang, Z.-M.; Zhou, W.-S. *Tetrahedron: Asymmetry* **1997**, *8*, 1951-1954. (b) Currie, G. S.; Drew, M. G. B.; Harwood, L. M.; David, J.; Luke, R. W. A.; Vickers, R. J. *J. Chem. Soc., Perkin Trans. 1* **2000**, *17*, 2982-2990.
- ¹⁷ Bommarius, A. S.; Schwarm, M.; Stingl, K.; Kottenhahn, M.; Huthmacher, K.; Drauz, K. *Tetrahedron: Asymmetry*, **1995**, *6*, 2851-2888.