Supporting information

Catalytic Enantioselective Amadori-Heyns Rearrangement of Racemic α-Hydroxy Ketones with Arylamines: Synthesis of Optically Active α-Arylamino Ketones

Angelo Frongia,* Francesco Secci, Francesca Capitta, Pier Paolo Piras and Maria Luisa Sanna

Dipartimento di Scienze Chimiche e Geologiche, Università degli studi di Cagliari, Complesso Universitario di Monserrato, S.S. 554, Bivio per Sestu, I-09042, Monserrato, Cagliari, Italy

afrongia@unica.it

Table of Contents

Absolute configuration determination of 3ao 2
Experimental protocols 3
Copies of NMR spectra 11
Copies of HPLC chromatograms of racemic/enantioenriched products 28
**Absolute configuration determination of 3ao**

Absolute configuration of 3ao was assigned by its conversion to the corresponding β-amino alcohols (with either a 1,2-syn and 1,2-anti relationship) 4 and 5 and comparison of the specific rotation with reported value.

![Chemical structure](image)

Comparison of $[\alpha]_D$ value obtained for compounds 4 ($[\alpha]_D^{27} = +37.2$ (c 0.43, CH$_2$Cl$_2$, ee 79%)) and 5 ($[\alpha]_D^{26} = +18.1$ (c 0.66, CH$_2$Cl$_2$, ee 79%)), to that presented in literature for ent-4 (2R,3R)-3-(phenylamino)butan-2-ol ($[\alpha]_D^{20} = -88.0$ (c 1.07, CH$_2$Cl$_2$, ee 90%))$^1$ and ent-5 (2S,3R)-3-(phenylamino)butan-2-ol ($[\alpha]_D^{20} = -31.7$ (c 1.04, CHCl$_3$, ee 96%))$^2$ allowed us to assign a $S$ configuration at the 3 position.

**Synthesis of 3-(phenylamino)butan-2-ol 4 and 5.** To a solution of 3ao (0.074g, 0.456 mmol) in MeOH (3 mL), NaBH$_4$ (0.022 g) was slowly added maintaining the pH = 5-6 by addition of glacial acetic acid. The reaction mixture was stirred at room temperature for 2h, then evaporated. The residue was dissolved in NaOH (1mL) and the solution was extracted with CHCl$_3$. Evaporation of the organic layer gave an oil which was flash-chromatographed (silica gel, mixture of hexane/ether, 5:1→1:1) to give pure products 4 and 5 (0.03 g, 40% yield, diastereoisomeric ratio 40:60). The spectroscopic data are in accordance with those presented in literature.$^{1,2}$
Experimental protocols

**General Methods.** $^1$H NMR spectra were recorded at 500, 400 or 300 MHz at 27°C with CDCl$_3$ as solvent. Data are reported as follows: chemical shifts ($\delta$), multiplicity, integration and coupling constants. $^{13}$C NMR spectra were recorded operating respectively at 124, 100 or 75 MHz at 27°C with CDCl$_3$ as solvent. Infrared spectra were recorded on a FT-IR spectrophotometer. Low resolution mass spectral analyses were recorded in E.I. (70 eV) mode. Relative intensities are given in parentheses. Enantiomeric excesses of $\alpha$-arylamino ketones were determined by HPLC, using a Chiralcel OJ, OD-H and Chiralpak AD-H analytical column with $i$-PrOH/hexane as eluent, using authentic racemic samples for reference comparison. Analytical thin layer chromatography was performed using 0.25 mm silica gel 60-F plates. Flash chromatography was performed using columns of 230-400 mesh silica gel 60 (0.040-0.063 mm). Yields refer to chromatographically pure materials. 3-hydroxy-2-butanone was purchased and used without further purification. 2-hydroxycyclohexanone was obtained by treating its dimer (purchased) with dilute (5%) HCl. The product was extracted with dichloromethane, dried, and stripped of solvent. $^3$ 3-hydroxy-4-phenylbutan-2-one and 2-hydroxypentan-3-one were synthesized by application of acetoacetate chemistry.$^4$

**General Procedure for $\alpha$-Arylamination of $\alpha$-Hydroxy Ketones.**

In an ordinary vial equipped with a magnetic stir bar, $\beta$-isocupreidine (0.122 mmol) was suspended in toluene (0.5 mL) under argon atmosphere. After stirring at room temperature for 30 min, the $\alpha$-hydroxy ketone $\mathbf{1}$ (4.06 mmol) was added, and the mixture was stirred for 30 min before the aniline $\mathbf{2}$ (0.406 mmol) was added. The mixture was allowed to stir at room temperature for 4-44 h. The crude reaction mixture was directly loaded on silica gel column without aqueous work-up and pure products were obtained by flash column chromatography (silica gel, mixture of hexane/ether). The racemates were synthesized using DMAP as catalyst at room temperature.
3-(4-methoxyphenylamino)butan-2-one 3aa: The spectroscopic data are in accordance with those presented in literature.\(^5\) Yield 95\% (74 mg); yellow oil. IR (neat): 3410, 2979, 1715, 1512, 1252 cm\(^{-1}\). \([\alpha]_D^{22} = +4.7 \ (c\ 2.11, \text{CHCl}_3).\) \(^1\)H NMR (500 MHz, CDCl\(_3\)) \(\delta\): 1.37 (d, 3H, \(J = 7.0\) Hz), 2.17 (s, 3H), 3.71 (s, 3H), 3.97 (q, 1H, \(J = 7.0\) Hz), 6.51 (d, 2H, \(J = 9.0\) Hz), 6.75 (2H, \(J = 9.0\) Hz). \(^{13}\)C NMR (125 MHz, CDCl\(_3\)) \(\delta\): 18.0, 25.8, 55.7, 59.5, 114.4, 115.0, 140.7, 152.4, 210.6. MS \(m/z\): 193 (M\(^+\) (8)), 150 (100), 135 (14), 107 (10), 77 (5). Anal. Calcd. for C\(_{11}\)H\(_{15}\)NO\(_2\); C, 68.37; H, 7.82; N, 7.25 Found: C, 68.35; H, 7.80; N, 7.29. The ee was determined to be 71\% ee by HPLC (Chiralcel OD-H column, hexane/i-PrOH = 98:2, flow rate 1.0 mL/min, \(\lambda = 254\) nm) \(t_R\) (major) = 18.53 min, \(t_R\) (minor) = 16.48 min.

3-(p-tolylamino)butan-2-one 3ab: The spectroscopic data are in accordance with those presented in literature.\(^5\) Yield 68\% (49 mg); orange oil. IR (neat): 3386, 2871, 1716, 1618, 1524 cm\(^{-1}\). \([\alpha]_D^{24} = +2.4 \ (c\ 4.82, \text{CHCl}_3).\) \(^1\)H NMR (500 MHz, CDCl\(_3\)) \(\delta\): 1.31 (d, 3H, \(J = 7.0\) Hz), 2.11 (s, 3H), 2.15 (s, 3H), 3.94 (q, 1H, \(J = 7.0\) Hz), 6.40 (d, 2H, \(J = 8.0\) Hz), 6.90 (d, 2H, \(J = 8.0\) Hz). \(^{13}\)C NMR (125 MHz, CDCl\(_3\)) \(\delta\): 17.9, 20.3, 25.7, 58.9, 113.1, 127.1, 129.8, 144.2, 210.5. MS \(m/z\): 177 (M\(^+\) (10)), 134 (100), 119 (13), 91 (15), 65 (9), 43 (7). Anal. Calcd. for C\(_{11}\)H\(_{15}\)NO; C, 74.54; H, 8.53; N, 7.90 Found: C, 74.55; H, 8.50; N, 7.88. The ee was determined to be 74\% ee by HPLC (Chiralcel OJ column, hexane/i-PrOH = 80:20, flow rate 1.0 mL/min, \(\lambda = 254\) nm) \(t_R\) (major) = 13.96 min, \(t_R\) (minor) = 9.80 min.

3-(4-ethylphenylamino)butan-2-one 3ac: Yield 58\% (45 mg); yellow oil. IR (neat): 3399, 2968, 1720, 1622, 1528 cm\(^{-1}\). \([\alpha]_D^{22} = +2.2 \ (c\ 4.45, \text{CHCl}_3).\) \(^1\)H NMR (500 MHz, CDCl\(_3\)) \(\delta\): 1.10 (t, 3H, \(J = 8.0\) Hz), 1.31 (d, 3H, \(J = 7.0\) Hz), 2.10 (s, 3H), 2.45 (q, 2H, \(J = 7.5\) Hz), 3.94 (q, 1H, \(J = 7.0\) Hz), 6.42 (d, 2H, \(J = 8.5\) Hz), 6.92 (d, 2H, \(J = 8.0\) Hz). \(^{13}\)C NMR (125 MHz, CDCl\(_3\)) \(\delta\): 15.7, 17.9, 25.6, 27.8, 58.8, 113.0, 128.6, 133.7, 144.4, 210.4. MS \(m/z\): 191 (M\(^+\) (19)), 148 (100), 119 (19), 77 (11), 43 (8). Anal. Calcd. for C\(_{12}\)H\(_{17}\)NO; C, 75.35; H, 8.96; N, 7.32 Found: C, 75.30; H, 9.00; N, 7.33. 

4}
The ee was determined to be 77% ee by HPLC (Chiralcel OJ column, hexane/i-PrOH = 80:20, flow rate 1.0 mL/min, λ = 254 nm) t_R(major) = 11.66 min, t_R(minor) = 7.84 min.

3-(4-propylphenylamino)butan-2-one 3ad: Yield 60% (50 mg); yellow oil. IR (neat): 3386, 2964, 1712, 1614, 1524 cm\(^{-1}\). \([\alpha]_D^{24} = +2.0 \ (c \ 5.0, \ CHCl_3)\). \(^1\)H NMR (500 MHz, CDCl\(_3\)) δ: 0.94 (t, 3H, J = 7.0 Hz), 1.42 (d, 3H, J = 7.0 Hz), 1.56-1.64 (m, 2H), 2.22 (s, 3H), 2.49 (t, 2H, J = 7.5 Hz), 4.05 (q, 1H, J = 7.0 Hz), 6.52 (d, 2H, J = 8.5 Hz), 7.01 (d, 2H, J = 8.5 Hz). \(^{13}\)C NMR (125 MHz, CDCl\(_3\)) δ: 13.7, 18.0, 24.7, 25.7, 37.0, 58.9, 113.0, 129.2, 132.2, 144.4, 210.5. MS m/z: 205 (M\(^+\) (7)), 162 (100), 133 (13), 120 (13), 118 (13), 43 (6). Anal. Calcd. for C\(_{13}\)H\(_{19}\)NO; C, 76.06; H, 9.33; N, 6.82 Found: C, 76.09; H, 9.35; N, 6.79.

The ee was determined to be 78% ee by HPLC (Chiralcel OJ column, hexane/i-PrOH = 80:20, flow rate 1.0 mL/min, λ = 254 nm) t_R(major) = 10.25 min, t_R(minor) = 7.20 min.

3-(4-butylphenylamino)butan-2-one 3ae: Yield 54% (48 mg); yellow oil. IR (neat): 3395, 2930, 1720, 1622, 1520 cm\(^{-1}\). \([\alpha]_D^{25} = +2.2 \ (c \ 4.51, \ CHCl_3)\). \(^1\)H NMR (500 MHz, CDCl\(_3\)) δ: 0.93 (t, 3H, J = 7.5 Hz), 1.31-1.37 (m, 2H), 1.42 (d, 3H, J = 7.0 Hz), 1.52-1.59 (m, 2H), 2.21 (s, 3H), 2.51 (t, 2H, J = 8.0 Hz), 4.04 (q, 1H, J = 7.0 Hz), 6.51 (d, 2H, J = 8.5 Hz), 7.00 (d, 2H, J = 8.5 Hz). \(^{13}\)C NMR (125 MHz, CDCl\(_3\)) δ: 13.9, 18.0, 22.3, 25.7, 33.9, 34.6, 58.9, 113.0, 129.2, 132.4, 144.4, 210.5. MS m/z: 219 (M\(^+\) (12)), 176 (100), 133 (19), 118 (12), 91 (7). Anal. Calcd. for C\(_{14}\)H\(_{21}\)NO; C, 76.67; H, 9.65; N, 6.39 Found: C, 76.70; H, 9.60; N, 6.41. The ee was determined to be 76% ee by HPLC (Chiralcel OJ column, hexane/i-PrOH = 80:20, flow rate 1.0 mL/min, λ = 254 nm) t_R(major) = 8.34 min, t_R(minor) = 6.02 min.

3-(4-tert-butylphenylamino)butan-2-one 3af: Yield 61% (54 mg); yellow oil. IR (neat): 3399, 2968, 1716, 1618, 1520 cm\(^{-1}\). \([\alpha]_D^{26} = +2.5 \ (c \ 4.76, \ CHCl_3)\). \(^1\)H NMR (500 MHz, CDCl\(_3\)) δ: 1.30 (s, 9H), 1.43 (d, 3H, J = 7.0 Hz), 2.23 (s, 3H), 4.05 (q, 1H, J = 7.0 Hz), 4.29 (brs, 1H), 6.54 (d, 2H, J = 6.5 Hz), 7.22 (d, 2H, J = 8.5 Hz). \(^{13}\)C NMR (125 MHz, CDCl\(_3\)) δ: 18.0, 25.7, 31.4, 33.8, 58.8, 112.6, 126.1, 140.7, 144.1, 210.4. MS m/z: 219 (M\(^+\) (7)), 176 (100), 160 (16), 146 (7), 120 (10), 91
(4). Anal. Calcd. for C_{14}H_{21}NO; C, 76.67; H, 9.65; N, 6.39. Found: C, 76.63; H, 9.67; N, 6.38. The ee was determined to be 81% ee by HPLC (Chiralcel OJ column, hexane/i-PrOH = 80:20, flow rate 1.0 mL/min, \( \lambda = 254 \) nm) \( t_R(\text{major}) = 16.18 \) min, \( t_R(\text{minor}) = 6.86 \) min.

3-(4-phenyl phenylamino)butan-2-one 3ag: Yield 65% (63 mg); yellow solid. M.p. 106-107 °C. IR (nujol): 3390, 3032, 1716, 1618, 1490 cm\(^{-1}\). \([\alpha]_D^{25} = +2.3 \) (c 1.73, CHCl\(_3\)). \(^1\)H NMR (500 MHz, CDCl\(_3\)) \( \delta \): 1.33 (d, 3H, \( J = 7.0 \) Hz), 2.11 (s, 3H), 4.00 (q, 1H, \( J = 7.0 \) Hz), 4.36 (brs, 1H), 6.53 (d, 2H, \( J = 8.5 \) Hz), 7.25-7.41 (m, 7H). \(^{13}\)C NMR (125 MHz, CDCl\(_3\)) \( \delta \): 17.9, 25.8, 58.5, 113.2, 126.1, 126.3, 128.0, 128.6, 130.9, 141.0, 145.8, 209.7. MS \( m/z \): 239 (M\(^+\) (10)), 196 (100), 169 (12), 152 (14), 115 (4). Anal. Calcd. for C_{16}H_{17}NO; C, 80.30; H, 7.16; N, 5.85. Found: C, 80.26; H, 7.19; N, 5.81. The ee was determined to be 67% ee by HPLC (Chiralcel OJ column, hexane/i-PrOH = 80:20, flow rate 1.0 mL/min, \( \lambda = 254 \) nm) \( t_R(\text{major}) = 83.61 \) min, \( t_R(\text{minor}) = 38.36 \) min.

3-(4-phenoxyphenylamino)butan-2-one 3ah: Yield 67% (69 mg); yellow oil. IR (neat): 3386, 2981, 2359, 1720, 1494 cm\(^{-1}\). \([\alpha]_D^{25} = +1.0 \) (c 1.91, CHCl\(_3\)). \(^1\)H NMR (500 MHz, CDCl\(_3\)) \( \delta \): 1.45 (d, 3H, \( J = 7.0 \) Hz), 2.24 (s, 3H), 4.07 (q, 1H, \( J = 7.0 \) Hz), 6.57-6.59 (m, 2H), 6.91-6.95 (m, 4H), 7.01-7.04 (m, 1H), 7.27-7.31 (m, 2H). \(^{13}\)C NMR (125 MHz, CDCl\(_3\)) \( \delta \): 17.9, 25.8, 59.1, 114.1, 121.2, 122.0, 129.4, 143.0, 148.2, 158.8, 209.8. MS \( m/z \): 255 (M\(^+\) (10)), 212 (100), 118 (20), 77 (8). Anal. Calcd. for C_{16}H_{17}NO\(_2\); C, 80.26; H, 7.16; N, 5.85. Found: C, 80.26; H, 7.19; N, 5.48. The ee was determined to be 69% ee by HPLC (Chiralcel OJ column, hexane/i-PrOH = 80:20, flow rate 1.0 mL/min, \( \lambda = 254 \) nm) \( t_R(\text{major}) = 28.37 \) min, \( t_R(\text{minor}) = 24.89 \) min.

3-(4-(methylthio)phenylamino)butan-2-one 3ai: Yield 73% (61 mg); yellow oil. IR (neat): 3386, 2981, 1712, 1605, 1499 cm\(^{-1}\). \([\alpha]_D^{25} = +5.6 \) (c 2.48, CHCl\(_3\)). \(^1\)H NMR (500 MHz, CDCl\(_3\)) \( \delta \): 1.39 (d, 3H, \( J = 7.0 \) Hz), 2.18 (s, 3H), 2.38 (s, 3H), 4.03 (q, 1H, \( J = 7.0 \) Hz), 4.39 (brs, 1H), 6.49 (d, 2H, \( J = 8.5 \) Hz), 7.18 (d, 2H, \( J = 9.0 \) Hz). \(^{13}\)C NMR (125 MHz, CDCl\(_3\)) \( \delta \): 17.8, 18.9, 25.8, 58.5, 113.6, 125.1, 131.4, 145.2, 209.5. MS \( m/z \): 209 (M\(^+\) (18)), 166 (100), 151 (16), 119 (29), 43 (8). Anal. Calcd. for C_{11}H_{15}NOS; C, 63.12; H, 7.22; N, 6.69; S, 15.32. Found: C, 63.10; H, 7.20; N, 6.71; S,
The ee was determined to be 71% ee by HPLC (Chiralcel OJ column, hexane/i-PrOH = 80:20, flow rate 1.0 mL/min, λ = 254 nm) tR(major) = 27.80 min, tR(minor) = 17.43 min.

3-(4-bromophenylamino)butan-2-one 3aj: Yield 44% (43 mg); yellow oil. IR (neat): 3386, 2981, 1716, 1597, 1494 cm\(^{-1}\). \([\alpha]_D^{20} = +5.5.\) (c 1.45, CHCl\(_3\)). \(^1\)H NMR (500 MHz, CDCl\(_3\)) δ: 1.41 (d, 3H, J = 7.0 Hz), 2.21 (s, 3H), 4.03 (q, 1H, J = 7.0 Hz), 6.44 (d, 2H, J = 8.5 Hz), 7.25 (d, 2H, J = 9.0 Hz). \(^1^3\)C NMR (125 MHz, CDCl\(_3\)) δ: 17.6, 25.8, 58.4, 114.5, 116.6, 131.9, 132.0, 145.3, 209.2. MS m/z: 241 (M\(^+\) (8)), 198 (100), 118 (100), 91 (23), 76 (20), 43 (37). Anal. Calcd. for C\(_{10}\)H\(_{12}\)BrNO; C, 49.61; H, 5.00; N, 5.79 Found: C, 49.66; H, 4.97; N, 5.83.

The ee was determined to be 68% ee by HPLC (Chiralcel OD-H column, hexane/i-PrOH = 98:2, flow rate 1.0 mL/min, λ = 254 nm) tR(major) = 14.67 min, tR(minor) = 11.83 min.

3-(m-toly lamino)butan-2-one 3al: Yield 57% (41 mg); yellow oil. IR (neat): 3390, 2981, 1716, 1597, 1494 cm\(^{-1}\). \([\alpha]_D^{20} = +3.9.\) (c 4.09, CHCl\(_3\)). \(^1\)H NMR (500 MHz, CDCl\(_3\)) δ: 1.43 (d, 3H, J = 7.0 Hz), 2.22 (s, 3H), 2.29 (s, 3H), 4.07 (q, 1H, J = 7.0 Hz), 6.38 - 6.41 (m, 2H), 6.57 (d, 1H, J = 7.5 Hz), 7.08 (t, 1H, J = 7.5 Hz). \(^1^3\)C NMR (125 MHz, CDCl\(_3\)) δ: 18.0, 21.5, 25.7, 58.6, 110.0, 113.7, 118.9, 129.2, 132.9, 145.6, 210.2. MS m/z: 177 (M\(^+\) (6)), 134 (100), 119 (12), 91 (19), 65 (10), 43 (14). Anal. Calcd. for C\(_{11}\)H\(_{15}\)NO; C, 74.54; H, 8.53; N, 7.90 Found: C, 74.52; H, 8.51; N, 7.93. The ee was determined to be 73% ee by HPLC (Chiralcel OJ column, hexane/i-PrOH = 80:20, flow rate 1.0 mL/min, λ = 254 nm) tR(major) = 11.76 min, tR(minor) = 8.38 min.

3-(3,4-dimethoxyphenylamino)butan-2-one 3am: Yield 74% (67 mg); yellow oil. IR (neat): 3382, 2832, 1716, 1524, 1235 cm\(^{-1}\). \([\alpha]_D^{22} = +7.9.\) (c 3.27, CHCl\(_3\)). \(^1\)H NMR (500 MHz, CDCl\(_3\)) δ: 1.39 (d, 3H, J = 7.5 Hz), 2.19 (s, 3H), 3.78 (s, 3H), 3.82 (s, 3H), 4.00 (q, 1H, J = 7.0 Hz), 6.04-6.06 (m, 1H), 6.22 (d, 1H, J = 2.5 Hz), 6.71 (d, 1H, J = 8.5 Hz). \(^1^3\)C NMR (100 MHz, CDCl\(_3\)) δ: 17.9, 25.7, 55.6, 56.6, 59.4, 99.3, 103.5, 113.1, 141.2, 141.9, 150.0, 210.5. MS m/z: 223 (M\(^+\) (14)), 180 (100), 164 (18), 149 (8), 79 (7), 43 (6). Anal. Calcd. for C\(_{12}\)H\(_{17}\)NO\(_3\); C, 64.55; H, 7.67; N, 6.27 Found: C, 64.54; H, 7.70; N, 6.25. The ee was determined to be 65% ee by HPLC (Chiralcel OJ column,
hexane/i-PrOH = 80:20, flow rate 1.0 mL/min, λ = 254 nm) t_R(major) = 33.03 min, t_R(minor) = 27.16 min.

3-(o-tolylamino)butan-2-one 3an: The spectroscopic data are in accordance with those presented in literature. Yield 26% (19 mg); yellow oil. IR (neat): 3416, 2981, 1716, 1609, 1511 cm\(^{-1}\). \([\alpha]_D^{22} = +17.8\) (c 1.9, CHCl\(_3\)). \(^1\)H NMR (500 MHz, CDCl\(_3\)) \(\delta\): 1.48 (d, 3H, \(J = 7.0\) Hz); 2.23 (s, 3H), 2.24 (s, 3H), 4.13 (q, 1H, \(J = 7.0\) Hz), 4.36 (brs, 1H), 6.47 (d, 1H, \(J = 8.0\) Hz), 6.70 (t, 1H, \(J = 7.5\) Hz), 7.09-7.11 (m, 2H). \(^1^3\)C NMR (125 MHz, CDCl\(_3\)) \(\delta\): 17.4, 18.1, 25.6, 58.5, 109.7, 117.4, 122.3, 127.1, 130.4, 144.4, 209.9. MS \(m/z\): 177 (M\(^+\) (7)), 134 (100), 118 (17), 91 (19), 65 (11), 43 (13). Anal. Calcd. for C\(_{11}\)H\(_{15}\)NO; C, 74.54; H, 8.53; N, 7.90 Found: C, 74.55; H, 8.55; N, 7.91. The ee was determined to be 11% ee by HPLC (Chiralcel OJ column, hexane/i-PrOH = 80:20, flow rate 1.0 mL/min, λ = 254 nm) t_R(major) = 9.11 min, t_R(minor) = 8.03 min.

3-(phenylamino)butan-2-one 3ao: The spectroscopic data are in accordance with those presented in literature. Yield 37% (24 mg); yellow solid. M.p. 51-52°C. IR (nujol): 3390, 2368, 1716, 1605, 1511 cm\(^{-1}\). \([\alpha]_D^{25} = +4.1\) (c 1.92, CHCl\(_3\)). \(^1\)H NMR (500 MHz, CDCl\(_3\)) \(\delta\): 1.43 (d, 3H, \(J = 7.0\) Hz), 2.22 (s, 3H), 4.08 (q, 1H, \(J = 7.0\) Hz), 6.58 (d, 2H, \(J = 8.0\) Hz), 6.74 (t, 1H, \(J = 7.5\) Hz), 7.17-7.21 (m, 2H). \(^1^3\)C NMR (125 MHz, CDCl\(_3\)) \(\delta\): 17.9, 25.7, 58.6, 113.0, 117.9, 129.4, 146.4, 210.0. MS \(m/z\): 163 (M\(^+\) (7)), 120 (100), 91 (6), 77 (19), 43 (9). Anal. Calcd. for C\(_{10}\)H\(_{13}\)NO; C, 73.59; H, 8.03; N, 8.58 Found: C, 73.53; H, 8.05; N, 8.57. The ee was determined to be 79% ee by HPLC (Chiralcel OJ column, hexane/i-PrOH = 90:10, flow rate 1.0 mL/min, λ = 254 nm) t_R(major) = 13.89 min, t_R(minor) = 10.34 min.

3-(4-methoxyphenylamino)-1-phenylbutan-2-one 3ba: The spectroscopic data are in accordance with those presented in literature. Yield 82% (89 mg); white solid. M.p. 82-84°C. IR (nujol): 3390, 2832, 1720, 1516, 1239 cm\(^{-1}\). \([\alpha]_D^{27} = +2.2\) (c 0.87, CHCl\(_3\)). \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\): 1.38 (d, 3H, \(J = 7.2\) Hz), 3.73 (s, 3H), 3.81 (ABq, 2H, \(J = 15.6\) Hz, \(J = 25.6\) Hz), 4.11 (q, 1H, \(J = 6.8\) Hz), 6.48 (d, 2H, \(J = 8.8\) Hz), 6.74 (d, 2H, \(J = 8.8\) Hz), 7.16 (d, 2H, \(J = 7.6\) Hz), 7.24-7.33 (m, 3H). \(^1^3\)C
NMR (100 MHz, CDCl$_3$) $\delta$: 18.1, 45.6, 55.7, 58.6, 114.6, 114.9, 127.0, 128.6, 129.5, 133.6, 140.4, 152.5, 210.1. MS m/z: 269 (M$^+$ (6)), 150 (100), 135 (5), 91 (10). Anal. Calcd. for C$_{17}$H$_{19}$NO$_2$; C, 75.81; H, 7.11; N, 5.20 Found: C, 75.78; H, 7.13; N, 5.17. The ee was determined to be 61% ee by HPLC (Chiralpak AD-H column, hexane/i-PrOH = 90:10, flow rate 1.0 mL/min, $\lambda = 254$ nm) $t_R$(major) = 17.18 min, $t_R$(minor) = 14.61 min.

3-(4-methoxyphenylamino)pentan-2-one 3ca: Yield 73% (61 mg); yellow oil. IR (neat): 3382, 2973, 1716, 1520, 1239 cm$^{-1}$. $[\alpha]_{D}^{25}$ = -1.3. ($c$ 2.89, CHCl$_3$). $^1$H NMR (400 MHz, CDCl$_3$) $\delta$: 0.93 (t, 3H, $J = 7.6$ Hz), 1.67-1.74 (m, 1H), 1.85-1.92 (m, 1H), 2.15 (s, 3H), 3.72 (s, 3H), 3.88 (t, 1H, $J = 6.0$ Hz), 4.05 (brs, 1H), 6.53 (d, 2H, $J = 8.4$ Hz), 6.75 (d, 2H, $J = 8.4$ Hz). $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$: 9.5, 24.8, 26.3, 55.7, 65.3, 114.4, 114.9, 141.0, 152.3, 210.5. MS m/z: 207 (M$^+$ (12)), 164 (100), 149 (12), 122 (20), 107 (10), 43 (27). Anal. Calcd. for C$_{12}$H$_{17}$NO$_2$; C, 69.54; H, 8.27; N, 6.76 Found: C, 69.50; H, 8.32; N, 6.71. The ee was determined to be 73% ee by HPLC (Chiralcel OJ column, hexane/i-PrOH = 70:30, flow rate 1.0 mL/min, $\lambda = 254$ nm) $t_R$(major) = 12.05 min, $t_R$(minor) = 10.19 min.

2-(4-methoxyphenylamino)cyclohexanone 3da: The spectroscopic data are in accordance with those presented in literature.$^8$ Yield 62% (55 mg); yellow solid. M.p. 100-102 °C. IR (nujol): 2947, 2368, 1716, 1516, 1239 cm$^{-1}$. $[\alpha]_{D}^{28}$ = +19.7 ($c$ 1.92, CHCl$_3$). $^1$H NMR (300 MHz, CDCl$_3$) $\delta$: 1.34-1.42 (m, 1H), 1.58-1.78 (m, 2H), 1.84-1.88 (m, 1H), 2.05-2.10 (m, 1H), 2.30-2.37 (m, 1H), 2.48-2.58 (m, 2H), 3.66 (s, 3H), 3.83-3.86 (m, 1H), 6.51 (d, 2H, $J = 5.4$ Hz), 6.70 (d, 2H, $J = 5.4$ Hz). $^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$: 24.1, 28.0, 35.9, 41.1, 55.8, 62.9, 114.5, 114.9, 140.7, 152.3, 208.7. MS m/z: 219 (M$^+$ (80)), 191 (44), 176 (15), 162 (100), 149 (56), 134 (32). Anal. Calcd. for C$_{13}$H$_{17}$NO$_2$; C, 71.21; H, 7.81; N, 6.39 Found: C, 71.24; H, 7.78; N, 6.37. The ee was determined to be 73% ee by HPLC (Chiralcel OD-H column, hexane/i-PrOH = 98:2, flow rate 1.0 mL/min, $\lambda = 254$ nm) $t_R$(major) = 19.15 min, $t_R$(minor) = 16.56 min.

References


Copies of NMR spectra

3aa
3ab
3ad
3ae
3af
3ai
3am
3ba

**NMR Spectra**

The spectra provide detailed information about the chemical shifts and multiplicities of the protons and carbons in compound 3ba. The top spectrum is the proton NMR (1H NMR), showing the integration and multiplicity of the protons. The bottom spectrum is the carbon-13 NMR (13C NMR), indicating the chemical shifts of the carbons in the molecule.

The proton NMR spectrum shows peaks at various chemical shifts, indicating the presence of different types of protons with different environments.

The carbon-13 NMR spectrum reveals the chemical shifts of the carbons, which are crucial for identifying the structure and confirming the connectivity of the atoms in the molecule.
Electronic Supplementary Material (ESI) for Chemical Communications
This journal is © The Royal Society of Chemistry 2013

3ca

O
N
H
O

Electronic Supplementary Material (ESI) for Chemical Communications
This journal is © The Royal Society of Chemistry 2013
Copies of HPLC chromatograms of racemic/enantioenriched products

3aa: Chiralcel OD-H column, hexane/i-PrOH = 98:2, flow rate 1.0 mL/min, λ = 254 nm
**3ab:** Chiralcel OJ column, hexane/i-PrOH = 80:20, flow rate 1.0 mL/min, $\lambda = 254$ nm
**3ac**: Chiralcel OJ column, hexane/i-PrOH = 80:20, flow rate 1.0 mL/min, $\lambda = 254$ nm
3ad: Chiralcel OJ column, hexane/i-PrOH = 80:20, flow rate 1.0 mL/min, λ = 254 nm
3ae: Chiralcel OJ column, hexane/i-PrOH = 80:20, flow rate 1.0 mL/min, λ = 254 nm
3af: Chiralcel OJ column, hexane/i-PrOH = 80:20, flow rate 1.0 mL/min, λ = 254 nm
3ag: Chiralcel OJ column, hexane/i-PrOH = 80:20, flow rate 1.0 mL/min, λ = 254 nm
3ah: Chiralcel OJ column, hexane/i-PrOH = 80:20, flow rate 1.0 mL/min, λ = 254 nm
3ai: Chiralcel OJ column, hexane/i-PrOH = 80:20, flow rate 1.0 mL/min, $\lambda = 254$ nm
3aj: Chiralcel OD-H column, hexane/i-PrOH = 98:2, flow rate 1.0 mL/min, λ = 254 nm

Quantitation method: Absolute concentration
Standard component: No
Normalization: 100.00

<table>
<thead>
<tr>
<th>No</th>
<th>Retention min</th>
<th>Area mV*sec</th>
<th>Area %</th>
<th>Name</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>11.04</td>
<td>26501.310</td>
<td>51.09</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>13.77</td>
<td>25370.361</td>
<td>48.91</td>
<td></td>
</tr>
</tbody>
</table>

Quantitation method: Absolute concentration
Standard component: No
Normalization: 100.00

<table>
<thead>
<tr>
<th>No</th>
<th>Retention min</th>
<th>Area mV*sec</th>
<th>Area %</th>
<th>Name</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>11.83</td>
<td>8847.744</td>
<td>15.99</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>14.67</td>
<td>46495.990</td>
<td>84.01</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>No</th>
<th>Retention min</th>
<th>Area mV*sec</th>
<th>Area %</th>
<th>Name</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>30.00</td>
<td>55343.734</td>
<td>100.00</td>
<td></td>
</tr>
</tbody>
</table>
3al: Chiralcel OJ column, hexane/i-PrOH = 80:20, flow rate 1.0 mL/min, $\lambda = 254$ nm

Quantitation method: Absolute concentration
Standard component: No
Normalization: 100.00

<table>
<thead>
<tr>
<th>No</th>
<th>Retention (min)</th>
<th>Area (mV*sec)</th>
<th>Area %</th>
<th>Name</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>8.36</td>
<td>5856.876</td>
<td>50.05</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>11.67</td>
<td>5844.443</td>
<td>49.95</td>
<td></td>
</tr>
</tbody>
</table>

Quantitation method: Absolute concentration
Standard component: No
Normalization: 100.00

<table>
<thead>
<tr>
<th>No</th>
<th>Retention (min)</th>
<th>Area (mV*sec)</th>
<th>Area %</th>
<th>Name</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>8.38</td>
<td>73.381</td>
<td>13.61</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>11.76</td>
<td>465.624</td>
<td>86.39</td>
<td></td>
</tr>
</tbody>
</table>

25.00 539.005 100.00
3am: Chiralcel OJ column, hexane/i-PrOH = 80:20, flow rate 1.0 mL/min, λ = 254 nm
3an: Chiralcel OJ column, hexane/i-PrOH = 80:20, flow rate 1.0 mL/min, λ = 254 nm
**3ao:** Chiralcel OJ column, hexane/i-PrOH = 90:10, flow rate 1.0 mL/min, $\lambda = 254$ nm
3ba: Chiralpak AD-H column, hexane/i-PrOH = 90:10, flow rate 1.0 mL/min, \( \lambda = 254 \text{ nm} \)
**3ca**: Chiralcel OJ column, hexane/i-PrOH = 70:30, flow rate 1.0 mL/min, $\lambda = 254$ nm
3da: Chiralcel OD-H column, hexane/i-PrOH = 98:2, flow rate 1.0 mL/min, λ = 254 nm