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Supporting information for

Design of primary amine functionalized polymer containing chiral isosorbide in the main chain for the asymmetric synthesis of isoquinuclidine derivatives

K. Hiba and K. Sreekumar*

Department of Applied Chemistry, Cochin University of Science and Technology, Kochi-682022, India.

E-mail: K. Sreekumar- kskpolymer.cusat@gmail.com



Figure S2 ¹³C NMR spectrum of Chiral-ISO-PECH





Figure S4 ¹H NMR spectrum of Chiral-ISO-PECH-Amine



Figure S5 ¹³C NMR spectrum of Chiral-ISO-PECH-Amine

Analytical data of synthesized Isoquinuclidine derivatives

3-exo-(4-Methoxyphenyl)-2-phenyl-2-azabicyclo[2.2.2]octan-5-one (4a)



Brown waxy solid; GC-MS (M⁺): 307; ¹H NMR (CDCl₃, 400 MHz): δ (ppm) 7.51-7.24 (m, 4H), 7.09-6.78 (m, 1H), 6.63 (d, *J* = 6.7 Hz, 2H), 6.54 (d, *J* = 8.2 Hz, 2H), 4.84-4.65 (m, 1H), 4.60-4.47 (m, 1H), 3.76 (s, 3H), 2.81-2.59 (m, 2H), 2.38-2.31 (m, 2H), 2.19-2.10 (m, 1H), 2.07-1.86 (m, 1H), 1.83-1.65 (m, 1H); ¹³C NMR (CDCl₃, 100 MHz,): δ (ppm) 193.1, 131.5, 129.1, 127.2, 117.7, 114.2, 113.1, 83.3, 61.9, 55.3, 51.2, 48.2, 42.3, 29.7, 26.0, 16.3.

3-endo-(4-Methoxyphenyl)-2-phenyl-2-azabicyclo[2.2.2]octan-5-one (5a)¹



Brown waxy solid; GC-MS (M⁺): 307; ¹H NMR (CDCl₃, 400 MHz): δ (ppm) 7.25-7.10 (m, 5H), 6.84 (d, J = 8.4, 2H), 6.67 (d, J = 8.4, 2H), 4.61-4.59 (m, 1H), 4.55-4.47 (m, 1H), 3.77 (s, 3H), 2.80-1.50 (m, 7H); ¹³C NMR (CDCl₃, 100 MHz,): δ (ppm) 212.1, 158.9, 148.2, 133.7, 131.7, 129.3, 126.7, 117.7, 114.5, 114.3, 113.3, 65.4, 55.2, 52.3, 48.5, 45.9, 29.7, 22.7, 22.5; enantiomeric excess: 73 %, determined by HPLC (Chiralpak IB-3 column, hexane:isopropanol (90:10), flow rate 1.0 mL min⁻¹, 254 nm): major enantiomer R_t = 10.9 min, minor enantiomer R_t = 15.4 min.

3-exo-Phenyl-2-phenyl-2-azabicyclo[2.2.2]octan-5-one (4b)²



Brown solid; m. p. 112-113 °C (lit.² 112-113 °C); GC-MS (M⁺): 277; ¹H NMR (CDCl₃, 400 MHz): δ (ppm) 7.39-7.33 m, 4H), 7.28-7.25 (m, 1H), 7.14-7.10 (m, 2H), 6.68 (t, *J* = 7.2 Hz, 1H), 6.57 (d, *J* = 8.4 Hz, 2H), 4.75 (d, *J* = 2.0 Hz, 1H), 4.53-4.52 (m, 1H), 2.77-2.68 (m, 2H), 2.42-2.37 (m, 1H), 2.29-2.19 (m, 1H), 1.95-1.84 (m, 1H), 1.74-1.60 (m, 2H); ¹³C NMR (CDCl₃, 100 MHz,): δ (ppm) 213.1, 147.9, 139.8, 129.1, 128.6, 127.2, 125.9, 117.5, 112.9, 62.3, 51.0, 48.2, 42.3, 26.0, 16.4.

3-endo-Phenyl-2-phenyl-2-azabicyclo[2.2.2]octan-5-one (5b)²



Brown solid; m. p. 121-122 °C (lit.² 120-121 °C); GC-MS (M⁺): 277; ¹H NMR (CDCl₃, 400 MHz): δ (ppm) 7.27-7.25 (m, 4H), 7.18-7.15 (m, 1H), 7.15-7.08 (m, 2H), 6.69 (t, *J* = 7.4 Hz, 1H), 6.62-6.58 (m, 2H), 4.61 (d, *J* = 2.7 Hz, 1H), 4.47 (m, 1H), 2.75- 2.67 (m, 2H), 2.42-2.37 (m, 1H), 2.27-2.17 (m, 1H), 2.10-2.01 (m, 1H), 1.98-1.92 (m, 1H), 1.70-1.63 (m, 1H); ¹³C NMR (CDCl₃, 100 MHz,): δ (ppm) 211.3, 147.7, 141.4, 128.9, 128.6, 127.1, 125.2, 117.3, 112.9, 65.6, 52.0, 48.3, 45.6, 22.5, 22.4; enantiomeric excess: 22 %, determined by HPLC (Chiralpak IB-3 column, hexane:isopropanol (90:10), flow rate 1.0 mL min⁻¹, 254 nm): major enantiomer R_t = 7.6 min, minor enantiomer R_t = 7.1 min.

3-exo-(4-Chlorophenyl)-2-phenyl-2-azabicyclo[2.2.2]octan-5-one (4c)²



Brown solid; m. p. 138-140 °C (lit.² 138-139 °C); GC-MS (M⁺): 311; ¹H NMR (CDCl₃, 400 MHz): δ (ppm) 7.32 (m, 4H), 7.14-7.10 (m, 2H), 6.70 (t, *J* = 7.4 Hz, 1H), 6.56-6.54 (m, 2H), 4.72 (d, *J* = 2.8 Hz, 1H), 4.52-4.51 (m, 1H), 2.76-2.70 (m, 1H), 2.66-2.64 (m, 1H), 2.39(dd, *J* = 18.8 Hz, 1.7 Hz, 1H), 2.25-2.16 (m, 1H), 1.93-1.85 (m, 1H), 1.70-1.59 (m, 2H); ¹³C NMR (CDCl₃, 100 MHz,): δ (ppm) 212.6, 147.6, 138.4, 132.9, 129.1, 128.8, 127.3, 117.8, 112.9, 61.8, 50.7, 48.1, 42.2, 26.0, 16.3.

3-endo-(4-Chlorophenyl)-2-phenyl-2-azabicyclo[2.2.2]octan-5-one (5c)²



Brown solid; m. p. 154-155 °C (lit.² 156-157 °C); GC-MS (M⁺): 311; ¹H NMR (CDCl₃, 400 MHz): δ (ppm) 7.27-7.22 (m, 4H), 7.20-7.14 (m, 2H), 6.76-6.72 (m, 1H), 6.62-6.60 (m, 2H), 4.61 (d, J = 2.8 Hz, 1H), 4.53-4.52 (m, 1H), 2.76-2.68 (m, 2H), 2.47 (dd, J = 18.8 Hz, 2.6 Hz, 1H), 2.31-2.22 (m, 1H), 2.16-2.00 (m, 2H), 1.78-1.70 (m, 1H); ¹³C NMR (CDCl₃, 100 MHz,): δ (ppm) 210.7, 147.3, 139.8, 132.7, 128.8, 128.7, 126.6, 117.6, 112.9, 64.9, 51.8, 48.3, 45.6, 22.4, 22.2; enantiomeric excess: 92 %, determined by HPLC (Chiralpak IB-3 column, hexane:isopropanol (90:10), flow rate 1.0 mL min⁻¹, 254 nm): major enantiomer R_t = 9.2 min, minor enantiomer R_t = 7.8 min.

3-exo-(4-Bromophenyl)-2-phenyl-2-azabicyclo[2.2.2]octan-5-one (4d)²



Brown solid; m. p. 123-124 °C (lit.² 125-126 °C); GC-MS (M⁺): 356; ¹H NMR (CDCl₃, 400 MHz): δ (ppm) 7.47 (d, *J* = 8.4 Hz, 2H), 7.26 (d, *J* = 8.0 Hz, 2H), 7.14-7.10 (m, 2H), 6.70 (t, *J* = 7.4 Hz, 1H), 6.55 (d, *J* = 8.2 Hz, 2H), 4.70 (d, *J* = 2.6 Hz, 1H), 4.52-4.51 (m, 1H), 2.76-2.70 (m, 1H), 2.66-2.64 (m, 1H), 2.39 (dd, *J* = 18.8 Hz, 1.6 Hz, 1H), 2.24-2.15 (m, 1H), 1.94-1.86 (m, 1H), 1.68-1.60 (m, 2H); ¹³C NMR (CDCl₃, 100 MHz,): δ (ppm) 212.5, 147.6, 139.0, 131.7, 129.1, 127.7, 121.0, 117.8, 112.9, 61.8, 50.7, 48.2, 42.2, 26.0, 16.3.

3-endo-(4-Bromophenyl)-2-phenyl-2-azabicyclo[2.2.2]octan-5-one (5d)²



Brown solid; m. p. 158-159 °C (lit.² 157-158 °C); GC-MS (M⁺): 356; ¹H NMR (CDCl₃, 400 MHz): δ (ppm) 7.41 (d, J = 8.3 Hz, 2H), 7.18-7.14 (m, 4H), 6.74 (t, J = 7.2 Hz, 1H), 6.61 (d, J = 8.2 Hz, 2H), 4.59 (d, J = 2.2 Hz, 1H), 4.53-4.52 (m, 1H), 2.75-2.68 (m, 2H), 2.46 (dd, J = 18.8 Hz, 1.6 Hz, 1H), 2.29-2.24 (m, 1H), 2.15-2.01 (m, 2H), 1.78-1.71 (m, 1H); ¹³C NMR (CDCl₃, 100 MHz,): δ (ppm) 210.9, 147.6, 140.6, 131.9, 129.2, 127.2, 121.2, 117.9, 113.2, 65.3, 52.0, 48.6, 45.9, 22.7, 22.6; enantiomeric excess: 41 %, determined by HPLC (Chiralpak IB-3 column, hexane:isopropanol (90:10), flow rate 1.0 mL min⁻¹, 254 nm): major enantiomer R_t = 9.9 min, minor enantiomer R_t = 9.6 min.

3-endo-(3,4-Dimethoxyphenyl)-2-phenyl-2-azabicyclo[2.2.2]octan-5-one (5e)



Brown waxy solid; GC-MS (M⁺): 337; ¹H NMR (CDCl₃, 400 MHz): δ (ppm) 7.11 (t, *J* = 7.8 Hz, 2H), 6.79-6.60 (m, 6H), 4.52 (m, 1H), 4.47 (m, 1H), 3.77 (s, 3H), 3.76 (s, 3H), 2.71-2.67 (m, 2H), 2.42-2.10 (m, 1H), 1.99-1.94 (m, 1H), 1.69-1.65 (m, 2H), 1.38-1.34 (m, 1H); ¹³C NMR (CDCl₃, 100 MHz,): δ (ppm) 211.0, 148.3, 147.2, 133.3, 128.2, 116.8, 116.6, 112.4, 110.5, 107.6, 64.8, 54.9, 54.8, 51.3, 47.5, 44.9, 30.9, 28.7, 21.6, 21.5, 13.1; enantiomeric excess: 78 %, determined by HPLC (Chiralpak IB-3 column, hexane:isopropanol (90:10), flow rate 1.0 mL min⁻¹, 254 nm): major enantiomer R_t = 10.9 min, minor enantiomer R_t = 15.5 min.

3-endo-(4-Nitrophenyl)-2-phenyl-2-azabicyclo[2.2.2]octan-5-one (5f)³



Yellow liquid; GC-MS (M⁺): 322; ¹H NMR (CDCl₃, 400 MHz): δ (ppm) 8.19 (d, J = 8.4 Hz, 2H), 7.49 (d, J = 8.4 Hz, 2H), 7.20 (t, J = 7.5 Hz, 2H), 6.79 (t, J = 7.5 Hz, 1H), 6.61 (d, J = 7.5 Hz, 2H), 4.75 (d, J = 2.4 Hz, 1H), 4.60 (m, 1H), 2.81-2.70 (m, 2H), 2.52 (d, J = 18.9 Hz, 1H), 2.31-2.05 (m, 3H), 1.86-1.76 (m, 1H); ¹³C NMR (CDCl₃, 100 MHz,): δ (ppm) 210.6, 149.2, 147.3, 129.5, 126.7, 124.4, 123.8, 118.6, 113.5, 65.3, 51.9, 48.8, 45.9, 22.6, 22.4; enantiomeric excess: 34 %, determined by HPLC (Chiralpak IB-3 column, hexane:isopropanol (90:10), flow rate 1.0 mL min⁻¹, 254 nm): major enantiomer R_t = 7.3 min, minor enantiomer R_t = 8.1 min.

3-exo-(Furan-2-yl)-2-phenyl-2-azabicyclo[2.2.2]octan-5-one (4g)



Brown waxy solid; GC-MS (M⁺): 267; ¹H NMR (CDCl₃, 400 MHz): δ (ppm) 7.37-7.33 (m, 1H), 7.19-7.13 (m, 1H), 7.11-6.99 (m, 3H), 6.70-6.61 (m, 1H), 6.60-6.28 (m, 2H), 4.73 (m, 1H), 4.37 (m, 1H), 2.96-2.91 (m, 1H), 2.81-2.63 (m, 1H), 2.35-2.17 (m, 1H), 1.87-1.82 (m, 1H), 1.66-1.64 (m, 1H), 1.77-1.72 (m, 1H), 1.36-1.34 (m, 1H); ¹³C NMR (CDCl₃, 100 MHz,): δ (ppm) 212.8, 153.2, 148.1, 142.3, 129.4, 118.0, 113.0, 110.5, 108.0, 57.7, 48.1, 42.2, 29.7, 26.0, 17.3.

3-endo-(Furan-2-yl)-2-phenyl-2-azabicyclo[2.2.2]octan-5-one (5g)



Brown waxy solid; GC-MS (M⁺): 267; ¹H NMR (CDCl₃, 400 MHz): δ (ppm) 7.28 (s, 1H), 7.19-7.14 (m, 3H), 6.69-6.67 (m, 2H), 6.19 (s, 1H), 6.11 (s, 1H), 4.62 (m, 1H), 4.37 (m, 1H), 2.84-2.73 (m, 2H), 2.53-2.42 (m, 1H), 2.38-1.94 (m, 2H), 1.64-1.34 (m, 2H); ¹³C NMR (CDCl₃, 100 MHz,): δ (ppm) 211.9, 154.7, 148.1, 142.4, 129.3, 118.0, 113.1, 106.8, 60.3, 49.2, 48.4, 45.9, 29.7, 22.4, 21.9; enantiomeric excess: 62 %, determined by HPLC (Chiralpak IB-3 column, hexane:isopropanol (90:10), flow rate 1.0 mL min⁻¹, 254 nm): major enantiomer R_t = 6.1 min, minor enantiomer R_t = 5.6 min.

2-exo-(4-Methoxyphenyl)-3-phenyl-2-azabicyclo[2,2,2]octan-5-one (4h)²



Yellow solid; m. p. 111-112 °C (lit.² 110-111 °C); GC-MS (M⁺): 307; ¹H NMR (CDCl₃, 400 MHz): δ (ppm) 7.41-7.32 (m, 4H), 7.30-7.22 (m, 1H), 6.74-6.66 (m, 2H), 6.56-6.49 (m, 2H), 4.68 (d, *J* = 2.4 Hz, 1H), 4.42-4.40 (m, 1H), 3.67 (s, 3H), 2.77-2.71 (m, 1H), 2.66-2.63 (m, 1H), 2.38-2.33 (m, 1H), 2.30-2.18 (m, 1H), 1.92-1.80 (m, 1H), 1.75-1.67 (m, 1H), 1.65-1.54 (m, 1H); ¹³C NMR (CDCl₃, 100 MHz,): δ (ppm) 236.3, 174.5, 165.2, 163.0, 151.4, 149.9, 148.8, 137.4, 136.9, 85.4, 78.4, 73.8, 71.6, 64.7, 49.1, 39.2.

2-endo-(4-Methoxyphenyl)-3-phenyl-2-azabicyclo[2,2,2]octan-5-one (5h)²



Yellow solid; m. p. 201-202 °C (lit.² 200-201 °C); GC-MS (M⁺): 307; ¹H NMR (CDCl₃, 400 MHz): δ (ppm) 7.26-7.25 (m, 4H), 7.18-7.16 (m, 1H), 6.71 (d, *J* = 8.8 Hz, 2H), 6.58 (d, *J* = 8.8 Hz, 2H), 4.54 (d, *J* = 2.4 Hz, 1H), 4.38-4.36 (m, 1H), 3.65 (s, 3H), 2.74- 2.72 (m, 2H), 2.43- 2.38 (m, 1H), 2.20-2.17 (m, 1H), 2.08-2.00 (m, 1H), 1.99-1.93 (m, 1H), 1.70-1.65 (m, 1H); ¹³C NMR (CDCl₃, 100 MHz,): δ (ppm) 211.4, 151.6, 142.1, 141.9, 128.5, 127.1, 125.3, 114.4, 114.3, 66.0, 55.4, 52.1, 49.2, 45.9, 22.5, 22.2; enantiomeric excess: 70 %, determined by HPLC (Chiralpak IB-3 column, hexane:isopropanol (90:10), flow rate 1.0 mL min⁻¹, 254 nm): major enantiomer R_t = 8.9 min, minor enantiomer R_t = 11.3 min.

2-exo-(4-Bromophenyl)-3-phenyl-2-azabicyclo[2.2.2]octan-5-one (4i)²



Pale yellow solid; m. p. 158-160 °C (lit.² 158-159 °C); GC-MS (M⁺): 356; ¹H NMR (CDCl₃, 400 MHz): δ (ppm) 7.39-7.32 (m, 4H), 7.30-7.28 (m, 1H), 7.18 (d, *J* = 9.0 Hz, 2H), 6.44 (d, *J* = 9.0 Hz, 2H), 4.70 (d, *J* = 2.0 Hz, 1H), 4.48-4.47 (m, 1H), 2.75- 2.65 (m, 2H), 2.43-2.39 (m, 1H), 2.29-2.21 (m, 1H), 1.94-1.86 (m, 1H), 1.70-1.62 (m, 2H); ¹³C NMR (CDCl₃, 100 MHz,):

δ (ppm) 212.7, 146.8, 139.1, 131.8, 128.7, 127.4, 125.8, 114.5, 109.5, 62.2, 50.9, 48.4, 42.3, 25.9, 16.3.

2-endo-(4-Bromophenyl)-3-phenyl-2-azabicyclo[2.2.2]octan-5-one (5i)²



Pale yellow solid; m. p. 119-121 °C (lit.² 120-121 °C); GC-MS (M⁺): 356; ¹H NMR (CDCl₃, 400 MHz): δ (ppm) 7.30-7.26 (m, 2H), 7.23-7.17 (m, 5H), 6.51-6.47 (m, 2H), 4.58 (d, J = 2.4 Hz, 1H), 4.45-4.44 (m, 1H), 2.78-2.70 (m, 2H), 2.46-2.41 (m, 1H), 2.24-2.16 (m, 1H), 2.15-1.97 (m, 2H), 1.75-1.68 (m, 1H); ¹³C NMR (CDCl₃, 100 MHz,): δ (ppm) 210.8, 146.7, 140.8, 131.7, 128.8, 127.5, 125.7, 116.4, 114.8, 65.7, 52.0, 48.8, 45.7, 22.8, 22.5; enantiomeric excess: 21 %, determined by HPLC (Chiralpak IB-3 column, hexane:isopropanol (90:10), flow rate 1.0 mL min⁻¹, 254 nm): major enantiomer R_t = 9.3 min, minor enantiomer R_t = 10.5 min.

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Gas chromatogram of 4a



Mass spectrum of 4a











¹³C NMR spectrum of 4a



¹³C NMR spectrum of 5a





Gas chromatogram of 4b and 5b mixture





Abundance







Gas chromatogram of 5b



Mass spectrum of 5b







¹³C NMR spectrum of 4b



¹³C NMR spectrum of 5b



Gas chromatogram of 4c and 5c mixture







Mass spectrum of 4c



Gas chromatogram of 5c







¹C NMR spectrum of 4c



¹³C NMR spectrum of 5c



Gas chromatogram of 4d and 5d mixture



Gas chromatogram of 4d



Mass spectrum of 4d



Gas chromatogram of 5d

50-

0-

ó





15

HPLC profile of 5d

25

30 min

20

10

5



¹³C NMR spectrum of 4d



¹³C NMR spectrum of 5d







Mass spectrum of 4e



Gas chromatogram of 5e







¹³C NMR spectrum of 5e



Gas chromatogram of 4f and 5f mixture







HPLC profile of 5f





Gas chromatogram of 4g and 5g mixture



Gas chromatogram of 4g



Mass spectrum of 4g



Gas chromatogram of 5g



HPLC profile of 5g



¹³C NMR spectrum of 4g



¹³C NMR spectrum of 5g







Gas chromatogram of 4h



Mass spectrum of 4h



Gas chromatogram of 5h





HPLC profile of 5h



Gas chromatogram of 4i and 5i mixture



Gas chromatogram of 4i



Mass spectrum of 4i



Gas chromatogram of 5i



HPLC profile of 5i



¹³C NMR spectrum of 4i



¹³C NMR spectrum of 5i