Supporting Information

Chiral dendrigraft polymer for asymmetric synthesis of isoquinuclidines

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Experimental

1. Materials

Chloromethyl polystyrene (1% DVB crosslinked, 100–200 mesh) was obtained from Thermax India Ltd. as a gift sample. It was washed with methanol, dioxane and acetone and dried under vacuum. Sodium hydride, Tetrabutyl ammonium bromide, p-toluene sulphonyl chloride, Sodium azide, LiAlH₄, methyl acrylate and ethylene diamine all were purchased from local vendors and were used as received. All solvents were distilled by standard procedures prior to use.

2. Preparation of 3-nitro-4-chloromethylpolystyrene

Chloromethyl polystyrene (5 g) was added slowly in small lots with stirring to fuming nitric acid (50mL) taken in a 250 mL RB flask and cooled to 0 °C. The addition was very slow that the temperature was not allowed to rise above 5 °C. After the completion of addition, the temperature was maintained at 0-5 °C for 1 h with constant stirring. The temperature was slowly brought to 30 °C with in a period of 3 h. The reaction mixture was heated slowly to 50 °C for 1 day. It was poured over crushed ice. The polymer beads were recovered by filtration, washed with water, dioxane and methanol.

Yellow beads; Yield: 5.2 g; IR (cm⁻¹): 3026 cm⁻¹, 2928 cm⁻¹, 1596 cm⁻¹, 1360 cm⁻¹.

3. Preparation of polyepichlorohydrin- PECH

Epichlorohydrin (15.65 mL, 0.2 mol) was added through a dropping funnel to a cooled reaction mixture containing dichloromethane (15 mL), Pentaerythritol (1.36 g, 0.01 mol) and BF₃-etherate (1.256 mL, 0.01 mol) with constant stirring. The reaction mixture was stirred for 24 h at 30 °C. After completion of the reaction, the reaction mixture was taken in a separating funnel and washed with saturated sodium carbonate solution followed by distilled water. The solvent was removed under vacuum. In the case of
glycerol initiated PECH, the amount of various reactants were 11.742 mL (0.15 mol) epichlorohydrin and 0.73 mL (0.01 mol) glycerol. In the case of ethylene glycol initiated PECH, 7.828 mL (0.1 mol) epichlorohydrin and 0.557 mL (0.01 mol) ethylene glycol with the same amount of BF$_3$ etherate were added.

Pale yellow viscous liquid; Mp (GPC): 1037. Polydispersity: 1.27; Yield: 13 g; IR (cm$^{-1}$): 3430, 2925, 1107, 695; $^1$H NMR (400 MHz, CDCl$_3$) δ: 3.2-4.0 (m, CH$_2$, CH & OH), 1.1 (CH), 1.8 (CH$_2$) ppm;

4. Coupling of PECH to the Resin

Sodium hydride (1 g) was added to a stirred solution of PECH (5.0-6.0 g) in dry DMF (50 mL) at 0 °C. After 2 h, Merrifield resin (1.0 g), and tetrabutyl ammonium bromide (216 mg, 0.62 mmol) were added and the mixture was shaken at room temperature for 20 h. The reaction was quenched by addition of water (20 mL) and the resin was filtered followed by washing with DMF/Water (1:1, 3 times), DMF (3 times), THF (3 times) and dichloromethane (3 times) and dried to constant weight under vacuum to yield the PECH loaded resin. The unreacted PECH was removed by soxhlet extraction with dichloromethane and dried under vacuum for 24 h.

Yield: 2.81 g; Chlorine Capacity: 7.17 mmols/g; IR (cm$^{-1}$): 3430, 3026, 2925, 1602, 1528, 1448, 1360, 1107, 695; Solid State $^{13}$C NMR (100M Hz.): 19, 23.8, 38.4, 43.5, 69, 76.5, 125.76, 132.96, 142.22 ppm; Hydroxyl group capacity: 1.86 mmolsg$^{-1}$.

5. Estimation of hydroxyl group

0.5 g of the hydroxyl compound was taken in a RB flask fitted with a condenser. 10 mL of the acetylation mixture (1 volume acetic anhydride + 4 volume anhydrous pyridine) was added. It was heated on a boiling water bath for 60 min. The reaction mixture was removed from water bath, 20 ml distilled water was added, shaken well to ensure complete hydrolysis of the unchanged acetic anhydride, cooled and allowed to stand for 10 min. The solution was titrated with 1 N NaOH using phenolphthalein as indicator.

6. Tosylation of hydroxyl group
The resin supported PECH (1.0 g) was dispersed in pyridine and cooled to -5 °C. A cold solution of p-toluene sulphonyl chloride (0.7 g, 0.004 mol) in 5 mL pyridine was added slowly. Upon complete addition, the temperature was held at -5 °C for 30 min, and allowed to come to 30 °C overnight. The contents of the flask were quenched by pouring ice water. It was filtered and washed with ice water, methanol, ether and acetone.

Yield: 1.08 g; % S-2.44; IR (cm\(^{-1}\)): 3456, 3025, 2935, 1627, 1596, 1482, 1360, 1117, 1010, 700.

7. Synthesis of Polyazide

The resin supported tosylated PECH (1.0 g) was allowed to swell in DMF, sodium azide (0.455 g, 0.007 mol) in 10 ml DMF was added and heated at 85-90 °C for one day. It was filtered and washed with water, methanol, dichloromethane and acetone. The resin obtained was dried under vacuum for 24 h.

Yield: 1.21 g; IR (cm\(^{-1}\)): 3026, 2900, 2100, 1596, 1458, 1360, 1075. Solid State \(^{13}\)C NMR (100 MHz,): 15.6, 19, 23.2, 38.5, 75.0, 125.76, 148.8 ppm;

8. Synthesis of Polyamine (Synthesis of G0 polymer)

The azide substituted resin (1 g) was suspended in dry THF taken in a RB flask and kept at 0 °C in an ice bath. Slurry of LiAlH\(_4\) (0.304 g, 0.008 mol) in dry THF was added drop wise to the reaction mixture with stirring. The reaction mixture was kept at 0 °C for 1 h. The temperature was slowly brought to 50 °C. It was stirred at 50 °C for two days to ensure complete reduction. Excess LiAlH\(_4\) was removed by adding ethyl acetate. It was filtered under vacuum, washed with ethyl acetate, THF, ether, water, methanol and acetone. The resin was dried under vacuum for 24 h.

Yield: 0.82 g; Amine Capacity: 9.13 mmols/g; IR (cm\(^{-1}\)): 3462, 3451, 3026, 2928, 1375, 1006;

9. Estimation of amine capacity

The polystyrene resin bearing the amino groups (100 mg) was suspended in HCl (0.1 M, 40 ml) for 24 h with occasional stirring. The resin was filtered and washed with distilled water. The filtrate and washings were
collected. The unreacted HCl was determined by titration against standard NaOH solution with the use of phenolphthalein indicator. A blank titration was also carried out. From the titre values, the amount of amino groups per gram of the resin was calculated.

10. Michael addition reaction (Synthesis of G 0.5 polymer)

The resin (0.5 g) was added in portions to a RB flask containing excess methyl acrylate (0.68 mol, 8 mL) and methanol (5 mL) at room temperature with stirring. The reaction mixture was stirred at room temperature for 7 days under an atmosphere of nitrogen. The reaction was monitored using Ninhydrin test. After the reaction, excess methyl acrylate was decanted; methanol (10 mL) was added. The solution was filtered, and washed with methanol, ethanol, ether, and acetone. It was dried under vacuum for 24 h.

Yield: 1.4 g; IR (cm\(^{-1}\)); 2900, 1738, 1350, 1245: Solid State\(^{13}\)C NMR (100 MHz); 169, 148.7, 123.8, 65, 38.5, 18 ppm.

11. Procedure for transamination (Synthesis of G1 polymer)

The resin (1.0 g) was added in small portions with stirring to a mixture of excess ethylene diamine (0.135 mol, 10 mL) and methanol (50 mL) taken in a RB flask and cooled to 0 °C in an ice salt bath. The reaction mixture was stirred at 0 °C for 1h and the temperature was allowed to rise to the room temperature and stirred at room temperature for 7 days to ensure complete reaction. After the completion of the reaction, the resin was filtered under vacuum and washed well with DMF, dichloromethane, methanol and ether. It was dried under vacuum for 24 h.

Yield: 1.5 g; Amine Capacity: 16.02 mmolsg\(^{-1}\); IR (cm\(^{-1}\)); 3500, 2915, 1641, 1375, 1041;

12. Michael addition reaction (Synthesis of G1.5 polymer)

The resin (1.0 g) was added in portions to a RB flask containing excess methyl acrylate (0.27 mol, 25 mL) and methanol (30 mL) at room temperature with stirring. The reaction mixture was stirred at room temperature for 10 days under an atmosphere of nitrogen. The reaction was monitored using Ninhydrin test. After the reaction, excess methyl acrylate was decanted; methanol was
added. The solution was filtered and washed with methanol, ethanol, ether, and acetone. It was dried under vacuum for 24 h.

Yield: 2.95 g; IR (cm$^{-1}$); 2980, 1740, 1356, 1086; Solid State $^{13}$C NMR (100M Hz); 169.4, 144.3, 122.2, 38.8, 22 ppm.

13. Procedure for transamination (Synthesis of G2 polymer)

The resin (1.0 g) was added in small portions with stirring to a mixture of excess ethylene diamine (0.27 mol, 20 mL) and methanol (20 mL) taken in a RB flask and cooled to 0°C in an ice salt bath. The reaction mixture was stirred at 0°C for 1h and the temperature was allowed to rise to the room temperature and stirred at room temperature for 7 days to ensure complete reaction. After the completion of the reaction, the resin beads were filtered under vacuum and washed with DMF, dichloromethane, methanol and ether. It was dried under vacuum for 24 h.

Yield: 1.6 g; Amine Capacity: 25.12 mmols/g; IR (cm$^{-1}$); 3500, 2915, 1662, 1385, 1038;

14. Test for Heterogeneity of the Reaction

To examine whether there was any leaching of the metal complex from the polymer-bound dendrigraft catalyst, viz. chiral-PEN-G2-Cu, into the reaction medium during the aza Diels-Alder reaction, separate experiments were conducted under standard conditions. The filtrate obtained by separating the solid catalyst after completion of the reaction was extracted with ethyl acetate. The aqueous layer was subsequently treated with a fresh batch of reactants in a reaction vessel and the reactions were allowed to continue. There was no formation of the product. This suggests that the reaction does not proceed after removal of the catalyst. Moreover, the presence of copper could not be detected when the filtrate, obtained after isolating the solid catalysts by filtration, was subjected to AAS analysis. The possibility of the copper species leaching out of the catalyst can thus be ruled out on the basis of the evidence gathered, which also proves the heterogeneous nature of the catalytic process.

15. Regeneration of the Catalyst
The reusability of the catalyst for subsequent catalytic cycles was examined using cyclohexenone, benzaldehyde and aniline as the substrates. After the completion of the reaction, the solid catalyst was separated from the reaction mixture by filtration, washed with CCl₄, ethyl acetate, methanol and acetone. It was dried in vacuum at 50 °C for about 5h. The dried solid catalyst was weighed and added to a fresh reaction mixture of cyclohexenone (1 mmol), benzaldehyde (1 mmol) and aniline (1 mmol) and CCl₄ (3 mL). The progress of the reaction was monitored by thin layer chromatography (TLC) and GCMS. The procedure for the above mentioned system was repeated for five reaction cycles.

1) GPC Profile of polyepichlorohydrin (PECH)

![Graph showing GPC profile with retention times and molecular weights.]

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2) ¹H NMR spectrum of polyepichlorohydrin (PECH)
3) Scanning electron micrograph of nitrated Merrifield Resin

![Image of nitrated Merrifield Resin](image1.png)

4) Scanning electron micrograph of PECH attached Merrifield Resin

![Image of PECH attached Merrifield Resin](image2.png)

5) EDX spectrum of PECH attached Merrifield Resin

![Image of EDX spectrum](image3.png)
6) IR spectra of nitrated Merrifield resin

7) IR spectra of PECH attached Merrifield resin
8) IR spectra of polyazide resin
9) Solid state $^{13}$C NMR spectrum of polyazide on Merrified resin

10) Solid State $^{13}$C NMR spectrum of PEN G0.5 polymer
11) $^1$H NMR Spectrum of PEN G0 polymer

12) $^1$H NMR Spectrum of PEN G1 polymer

13) MALDI MS Spectrum of PEN-G1 Polymer
14) AFM image of PEN-G1 Polymer

15) $^1$H NMR Spectrum of PEN G2 polymer
16) MALDI MS Spectrum of PEN-G2 Polymer

17) AFM image of PEN-G2 Polymer
18) TEM image of PEN-G2 polymer

19) MALDI-TOF MS spectrum of GLR-G2 polymer
20) UV-Vis-DRS spectrum of Cu complex of proline modified PEN-G2
21) EPR spectrum of PEN-G2 polymer

22) X-ray diffraction (XRD) pattern of PEN-G2 and PEN-G2-Cu

23) XPS spectra of Cu (2p$_{3/2}$) of PEN-G2-Cu
24) Characterization of Aza Diels Alder Products

1) 2,3-Diphenyl-2-azabicyclo[2.2.2]octan-5-one (6a)

Brown solid.

$^1$H NMR (400 MHz, CDCl$_3$): 7.36(t, J=8Hz, 1H); 6.77(d, J=9Hz, 2H); 6.59(d, J=9Hz, 2H); 4.53(d, J=2.5Hz, 1H); 4.41(m, 1H); 3.72(S, 3H); 2.75(m,1H); 2.70(m,1H); 2.47(m, 1H); 2.24(m, 1H); 2.11(m,1H); 2.02(m,1H); 1.73(m,1H).

MS (m/z): 277.15; tR (min) (HPLC) = 3.06 and 5.59.

![Structure of 6a](image)

2) 3-(3-Nitrophenyl)-2-phenyl-2-azabicyclo[2.2.2]octan-5-one (6b)

Brown solid.

$^1$H NMR (400 MHz, CDCl$_3$): 7.24-7.15(m, 5H); 6.86(d, J=8Hz, 1H); 6.77(d, J=9Hz, 2H); 6.63(d, J=9Hz, 2H); 4.53(d, J=2.5Hz, 1H); 4.41(m, 1H); 3.72(S, 3H); 2.75(m,1H); 2.70(m,1H); 2.47(m, 1H); 2.24(m, 1H); 2.11(m,1H); 2.02(m,1H); 1.73(m,1H).

MS (m/z): 389.15; tR (min) (HPLC) = 3.06 and 5.59.
3) 3-(3-Bromophenyl)-2-phenyl-2-azabicyclo[2.2.2]octan-5-one (6c)

Brown solid.

$^1$H NMR (400 MHz, CDCl$_3$): 7.56 (S, 1H); 7.43 (d, J=8Hz, 1H); 7.34 (d, J=8Hz, 1H); 7.26 (d, J=8Hz, 1H); 7.17 (d, J=7.5Hz, 1H); 7.15 (d, J=7.5Hz, 1H); 6.74 (t, J=8Hz, 1H); 6.57 (d, J=8Hz, 2H); 4.72 (d, J=2.5Hz, 1H); 4.54 (m, 1H); 2.72 (dt, J=10Hz, 3Hz, 1H); 2.64 (q, J=3Hz, 1H); 2.41 (dd, J=10Hz, 3Hz, 1H); 2.24 (m, 1H); 1.94 (m, 1H); 1.67 (m, 1H).

MS (m/z): 355.06, 357.06; tR (min) (HPLC) = 5.38 and 6.24.

4) 2-(3-Chlorophenyl)-3-(3-nitrophenyl)-2-azabicyclo[2.2.2]octan-5-one (6d)

Brown solid.

$^1$H NMR (400 MHz, CDCl$_3$): 7.43 (S, 1H); 7.35 (d, J=8Hz, 1H); 7.22 (d, J=8Hz, 1H); 7.16 (t, J=8Hz, 1H); 6.77 (s, J=9Hz, 1H); 6.59 (d, J=9Hz, 2H); 6.43 (d, J=9Hz, 1H); 4.53 (d, J=2.5Hz, 1H); 4.41 (m, 1H); 2.75 (m, 1H); 2.70 (q, 1H); 2.47 (m, 1H); 2.24 (m, 1H); 2.11 (m, 1H); 2.02 (m, 1H); 1.73 (m, 1H).
5) 3-(4-Methoxyphenyl)-2-phenyl-2-azabicyclo[2.2.2]octan-5-one (6e)

Brown solid.

\[ \text{NMR (400 MHz, CDCl}_3\text{): 7.43(S, 1H); 7.35(d, J=8Hz, 1H); 7.22(d, J=8Hz, 1H); 7.16(t, J=8Hz, 1H); 6.77(d, J=9Hz, 2H); 6.59(d, J=9Hz, 1H); 4.53(d, J=2.5Hz, 1H); 4.41 (m, 1H); 3.72(S, 3H); 2.75(m, 1H); 2.70(m, 1H); 2.47(m, 1H); 2.24(m, 1H); 2.11(m, 1H); 2.02(m, 1H); 1.73(m, 1H).} \]

MS (m/z): 307.16; tR (min) (HPLC) = 5.71 and 6.14.

6) 3-(4-Chlorophenyl)-2-phenyl-2-azabicyclo[2.2.2]octan-5-one (6f)

Brown solid.

\[ \text{NMR (400 MHz, CDCl}_3\text{): 1.65–1.85 (m, 1H), 1.95–2.35 (m, 3H), 2.40–2.55 (m, 1H), 2.65–2.85 (m, 2H), 4.55 (br m, 1H), 4.64 (br m, 1H), 6.65 (d, 2H, J = 8.3Hz), 6.76 (t, 1H, J = 7.5Hz), 7.00 (dd, 2H, J = 8.6Hz), 7.19 (dd, 2H, J = 7.5Hz, 8.3Hz), 7.23–7.33 (m, 2H).} \]

MS (m/z): 311.11, 313.12; tR (min) (HPLC) = 4.84 and 5.60.

7) 2-(4-Methoxy-phenyl)-3-phenyl-2-aza-bicyclo[2,2,2]octan-5-one (6g)
Brown solid.

\(^1\)H NMR (400 MHz, CDCl\(_3\)): 1.73(m, 1H), 2.03(m, 1H), 2.15(m, 1H), 2.27(m, 1H), 2.47(dd, \(J = 2.48\)Hz, 1H), 2.74(m, 1H), 2.76(dd, \(J = 2.48\)Hz 1H), 3.72(s, 3H), 4.44(s, 1H), 4.58(d, \(J = 2.51\)Hz, 1H), 6.61-6.65(m, 2H), 6.75-6.79(m, 2H), 7.21-7.31(m, 5H).

MS (m/z): 307.16; tR (min) (HPLC) = 4.80 and 5.10.

8) 3-(3-Bromo-phenyl)-2-(4-methoxy-phenyl)-2-aza-bicyclo [2.2.2] octan-5-one (6h)

Brown solid.

\(^1\)H NMR (400 MHz, CDCl\(_3\)): 7.43(S, 1H); 7.35(d, \(J=8\)Hz, 1H); 7.22(d, \(J=8\)Hz, 1H); 7.16(t, \(J=8\)Hz, 1H); 6.77(d, \(J=9\)Hz, 2H); 6.59(d, \(J=9\)Hz, 2H); 4.53(d, \(J=2.5\)Hz, 1H); 4.41(m,1H); 3.72(S, 3H); 2.75(m,1H); 2.70(q,1H); 2.47(m,1H); 2.24(m,1H); 2.11(m,1H); 2.02(m,1H); 1.73(m,1H).

\(^13\)C NMR (100 MHz, CDCl\(_3\)): 211, 152, 145, 144, 142, 131, 130, 129, 123, 114.5, 66, 56, 52, 50, 46, 23, 22.

MS (m/z): 385.07, 387.07; tR (min) (HPLC) = 4.85 and 6.63.

9) 3-(3-Chlorophenyl)-2-phenyl-2-aza-bicyclo [2.2.2] octan-5-one (6i)

Brown solid.

\(^1\)H NMR (400 MHz, CDCl\(_3\)): 7.28(S, 1H); 7.23(d, \(J=8\)Hz, 1H); 7.21(d, \(J=8\)Hz, 1H); 7.20-7.16(m,3H); 6.76(t, \(J=8\)Hz, 1H); 6.64(d, \(J=9\)Hz, 2H); 4.62(d, \(J=3\)Hz, 1H); 4.54(m,1H); 2.77(q,1H); 2.74(dt
10) 2-(4-Nitrophenyl)-3-phenyl-2-aza-bicyclo[2.2.2]octan-5-one (6j)

Brown solid.

$^1$H NMR (400 MHz, CDCl$_3$): 7.29(d, J=8Hz, 2H); 7.16(d, J=8Hz, 2H); 7.14(d, J=8Hz, 2H); 6.73(t, J=7Hz, 1H); 6.57(d, J=8Hz, 2H); 4.72(d, J=2.5Hz, 1H); 4.52(m,1H); 2.73(dt, J=10Hz, 3Hz, 1H); 2.67(q, J=3Hz, 1H); 2.39(dd, J=10Hz, 3Hz, 1H); 2.23(m, 1H); 1.90(m, 1H); 1.66(m, 2H).

$^{13}$C NMR (100 MHz, CDCl$_3$): 213, 148, 142, 135, 130, 129, 128, 126, 124, 118, 113, 62, 51, 48, 42, 26, 16.

MS (m/z): 322.13; tR (min) (HPLC) = 4.53 and 4.93.
$^1$H NMR spectrum of 2,3-Diphenyl-2-aza-bicyclo[2.2.2]octan-5-one (6a)

$^1$H NMR spectrum of 3-(3-Bromophenyl)-2-phenyl-2-aza-bicyclo[2.2.2]octan-5-one (6c)

$^1$H NMR spectrum of 3-(3-Bromo-phenyl)-2-(4-methoxy-phenyl)-2-aza-bicyclo[2.2.2]octan-5-one (6h)
$^1$H NMR spectrum of 3-(3-Chlorophenyl)-2-phenyl-2-aza-bicyclo[2.2.2]octan-5-one (6i)
$^1$H NMR spectrum of 2-(4-Nitrophenyl)-3-phenyl-2-aza-bicyclo[2.2.2]octan-5-one (6j)

$^{13}$C NMR spectrum of 3-(3-Bromo-phenyl)-2-(4-methoxy-phenyl)-2-aza-bicyclo [2.2.2]octan-5-one (6h)
$^{13}$C NMR spectrum of 2-(4-Nitrophenyl)-3-phenyl-2-aza-bicyclo [2.2.2]octan-5-one (6j)
$^1$H-$^1$H COSY spectrum of 6a
GC-MS spectrum of 2,3-Diphenyl-2-aza-bicyclo[2.2.2]octan-5-one (6a)
GC-MS spectrum of 3-(3-Chlorophenyl)-2-phenyl-2-aza-bicyclo [2.2.2] octan-5-one (6i)
GC-MS spectrum of 3-(3-Chlorophenyl)-2-phenyl-2-aza-bicyclo [2.2.2] octan-5-one (6i-endo)
HPLC traces of Aza Diels Alder products

6a)