Supplementary data

Amino-diol borate complexation for controlling transport phenomena of penetrant molecules into polymeric matrices

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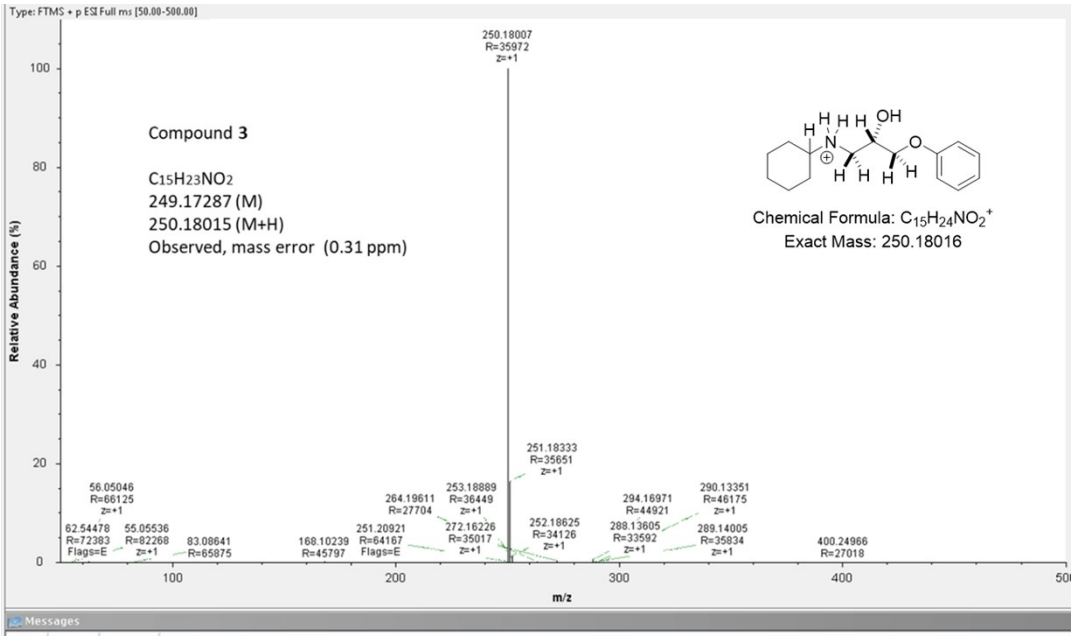
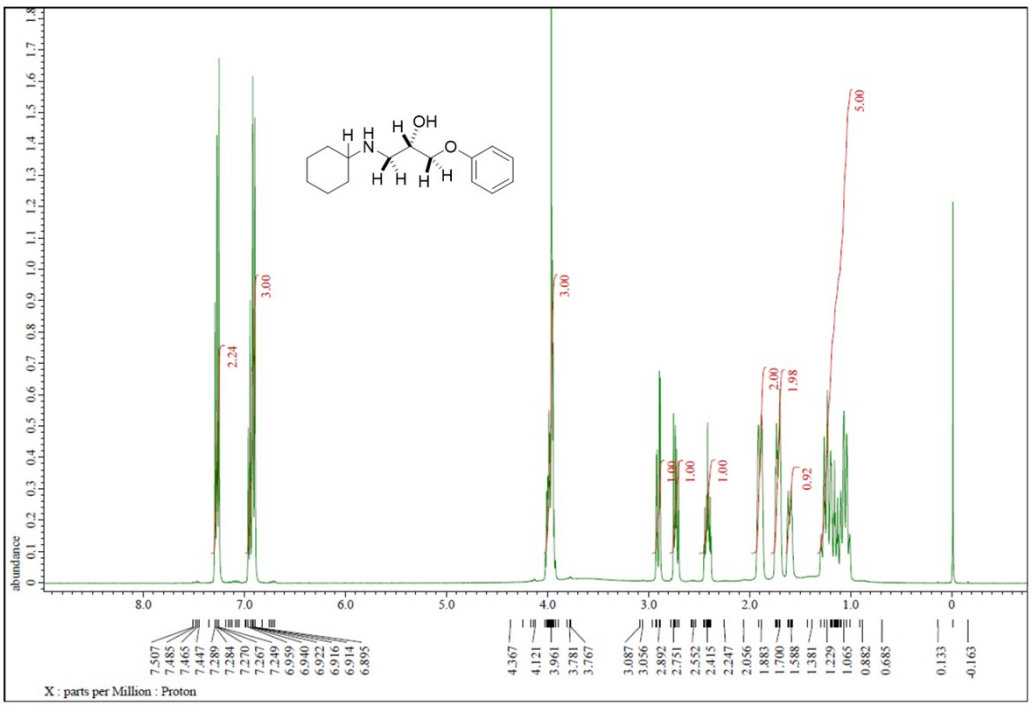
Experimental procedures

1-(cyclohexylamino)-3-phenoxypropan-2-ol (β-amino-alcohol **3**)

Cyclohexylamine (10.00 g, 0.101 moles, 5 equivs.) and phenylglycidyl ether (75.71 g, 0.504 moles) were combined in a round bottomed flask under an inert atmosphere of nitrogen gas with stirring. The reaction mixture was heated to 50 °C for a period of 4 hour before the excess cyclohexylamine was removed under reduced pressure, resulting in the isolation of the crude product as pale yellow crude solid, (24.97 g, 99%). The crude product was then recrystallized from ethyl acetate and petroleum ether to give the desired, known β-amino-alcohol **3** (1-(cyclohexylamino)-3-phenoxypropan-2-ol) as a fine white solid (21.37 g, 85%).[1] ν_{max}/cm^{-1} 3274 (N-H, 2°-amine), 3150br (O-H), 2928 and 2858 (CH_2 & CH) 1245 (C-N); δH(400 MHz; $CDCl_3$; Me_4Si) 0.99-1.31 (5 H, m, CH_2 cyclohex), 1.56-1.64 (1 H, m, CH_2 cyclohex), 1.67-1.77 (2 H, m CH_2 cyclohex), 1.85-1.94 (2 H. app.d, CH_2 cyclohex), 2.37-2.46 (1 H, m, cyclic-C*H*-N), 2.69-2.78 (1 H, dd, J = 12.0, 7.2, CH_2-NH), 2.87-2.93 (1 H, dd, J = 12.0, 3.2, CH_2-NH), 3.91-4.03 (3 H, m, CH_2-OPh + C*H*-OH), 6.87-6.97 (3 H, m, ArH), 7.23-7.30 (2 H, m, ArH); δC(400 MHz; $CDCl_3$; Me_4Si) 25.1 (*C*H_2 ring), 26.1(*C*H_2 ring), 33.6 (*C*H_2 ring), 49.2 (*C*H_2-NH), 56.9 (*C*H-NH), 68.4 (*C*H-OH), 70.7 (*C*H_2-OPh), 114.6 (Ar), 120.9 (Ar), 129.5 (Ar), 158.8 (Ar-O); *m/z* 250.18007 (MH^+, 100% calc. for $C_{15}H_{24}NO_2$ = 250.18015).




abundance
X : parts per Million : Proton
2.24
3.00
3.00
1.00
1.00
1.00
2.00
1.98
0.92
5.00
7.507
7.485
7.465
7.447
7.289
7.284
7.270
7.267
7.249
6.959
6.940
6.922
6.916
6.914
6.895
4.367
4.121
3.961
3.781
3.767
3.087
3.056
2.892
2.751
2.552
2.415
2.247
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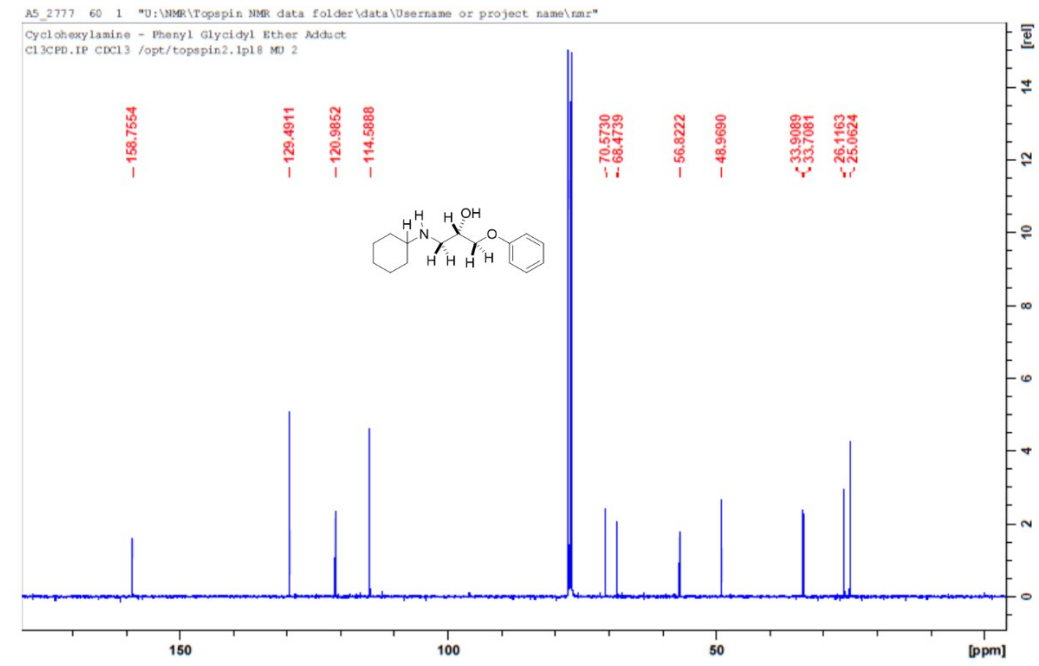
1.700
1.588
1.381
1.229
1.065
0.882
0.685
0.133
-0.163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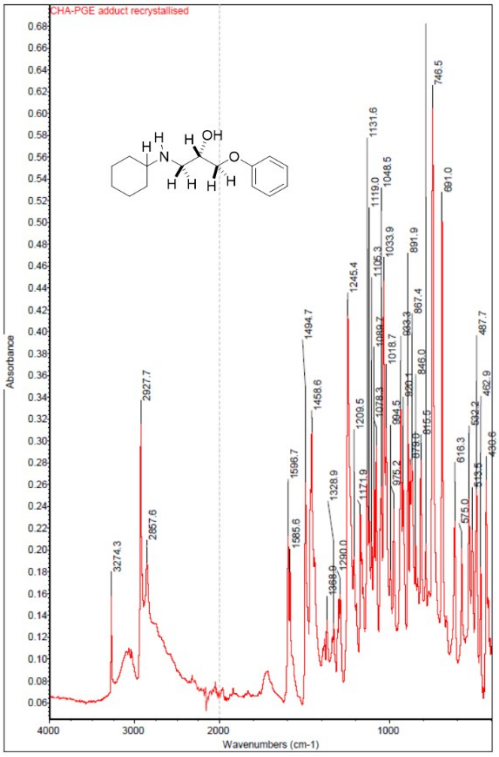
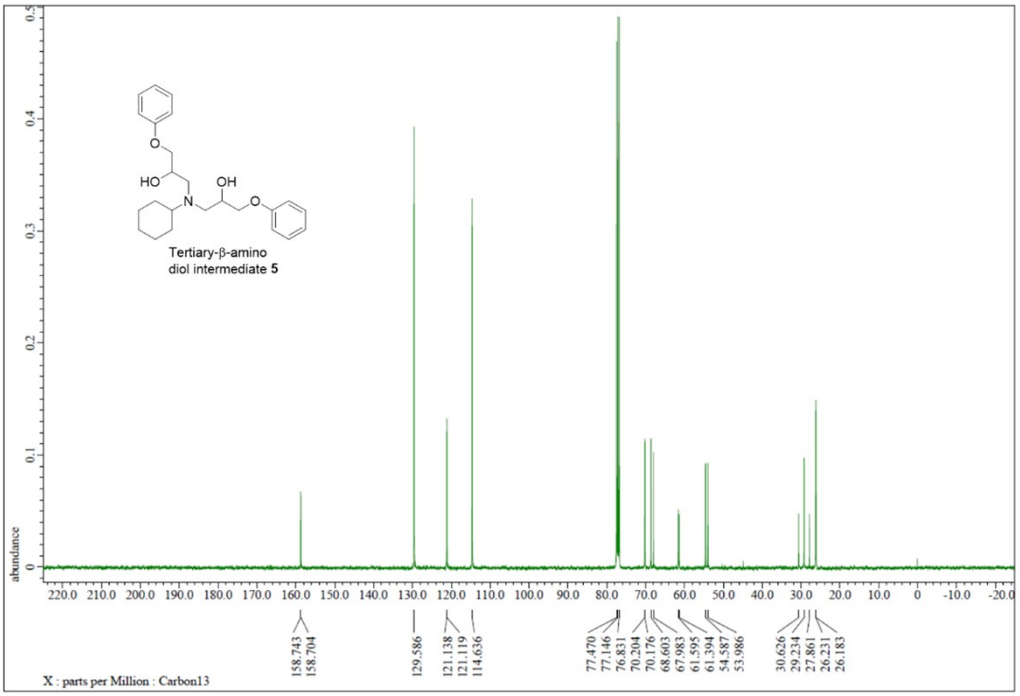
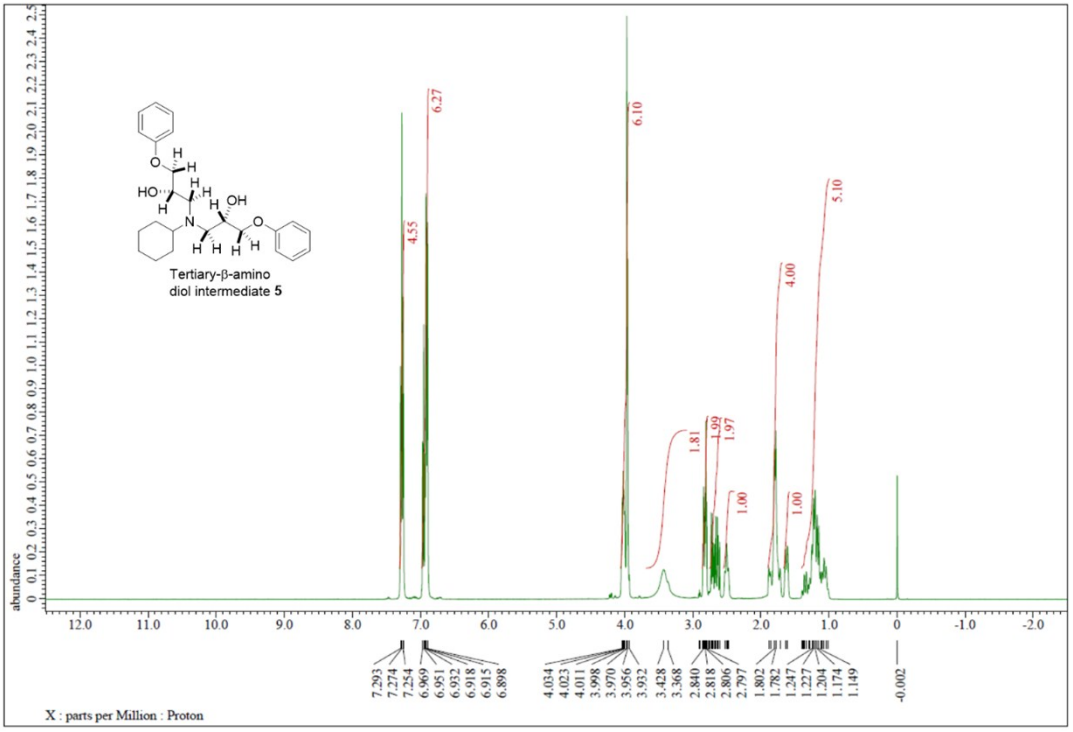
Cyclohexylamine - Phenyl Glycidyl Ether Adduct
C13CPD.IP CDCl3 /opt/topspin2.1pl8 MU 2
158.7554
129.4911
120.9852
114.5888
70.5730
68.4739
56.8222
48.9690
33.9089
33.7081
26.1163
25.0624
[rel]
[ppm]

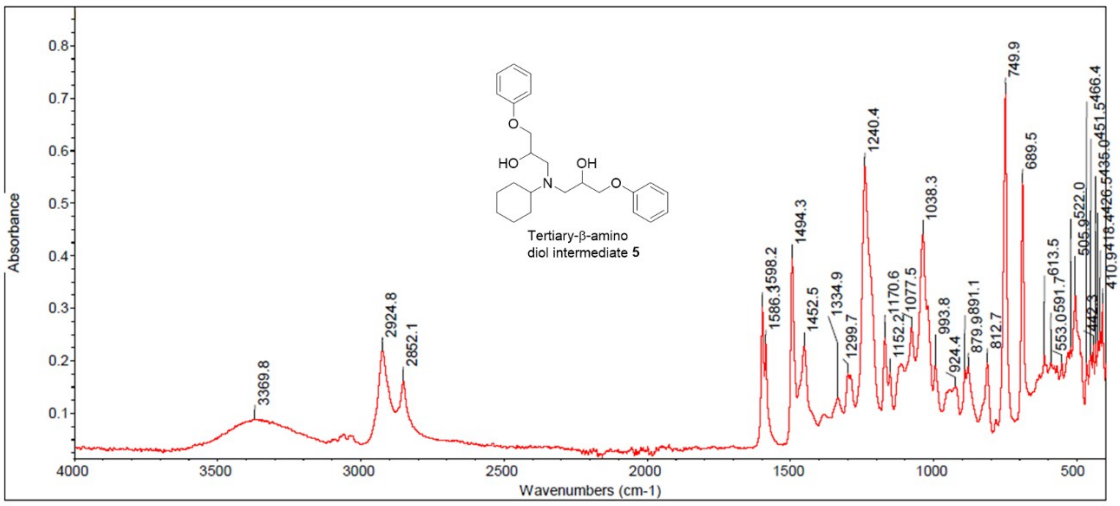


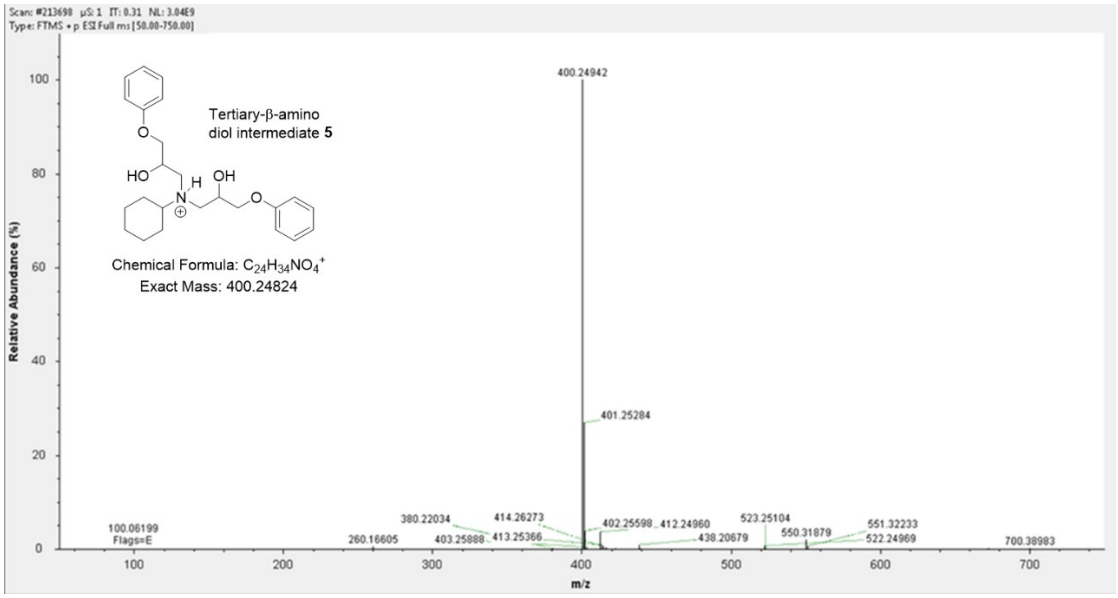
Tertiary-β-amino diol intermediate 5

1-(cyclohexylamino)-3-phenoxypropan-2-ol **3** (10.00 g, 0.0401 mol) and phenylglycidyl ether (6.32 g, 0.0421 moles, 1.05 equivs.) were combined in a round bottomed flask under an inert atmosphere of nitrogen gas with stirring. The reaction mixture was heated to 110 ^{o}C for a period of 3 hour before allowing to cool. The crude tertiary-β-amino diol intermediate **5** was isolated as a pale yellow oil (16.3 g, 99%) which was used immediately in the next stage without further purification. ν_{max}/cm^{-1} 3370br (O-H), 2925 and 2852 (CH_2 & CH) 1240 (C-N); δH(400 MHz; $CDCl_3$; Me_4Si) 1.01-1.40 (5 H, m, CH_2 cyclohex), 1.62 (1 H, app.d, J = 12.0, CH_2 cyclohex), 1.69-1.90 (4 H, m CH_2 cyclohex), 2.44-2.54 (1 H, m, cyclic-C*H*-N), 2.59-2.73 (2 H, dd, J = 13.5, 8.0, CH_2-NH), 2.78-2.85 (2 H, dt, J = 13.5, 5, 5, CH_2-NH), 3.51 (2 H, br.s, 2 x OH), 3.90-4.00 (6 H, m, CH_2-OPh + C*H*-OH), 6.85-6.99 (6 H, m, ArH), 7.23-7.29 (4 H, m, ArH); δC(400 MHz; $CDCl_3$; Me_4Si) 26.1 (*C*H_2 ring), 26.2 (*C*H_2 ring), 27.9 (*C*H_2 ring), 29.2 (*C*H_2 ring), 30.6 (*C*H_2 ring), 54.0 (*C*H_2-NH), 54.6 (*C*H_2-NH), 61.4 (*C*H-NH), 61.6 (*C*H-NH), 68.0 (*C*H-OH), 68.6 (*C*H-OH), 70.18 (*C*H_2-OPh), 70.20 (*C*H_2-OPh), 114.64 (Ar), 121.12 (Ar), 121.14 (Ar), 129.6 (Ar), 158.70(Ar), 158.74 (Ar); *m/z* 400.2494 (MH^+, 100% calc. for $C_{24}H_{34}NO_4$ = 400.2488)


Tertiary-β-amino
diol intermediate 5
abundance
X : parts per Million : Carbon13


Tertiary-β-amino
diol intermediate 5
abundance
X : parts per Million : Proton

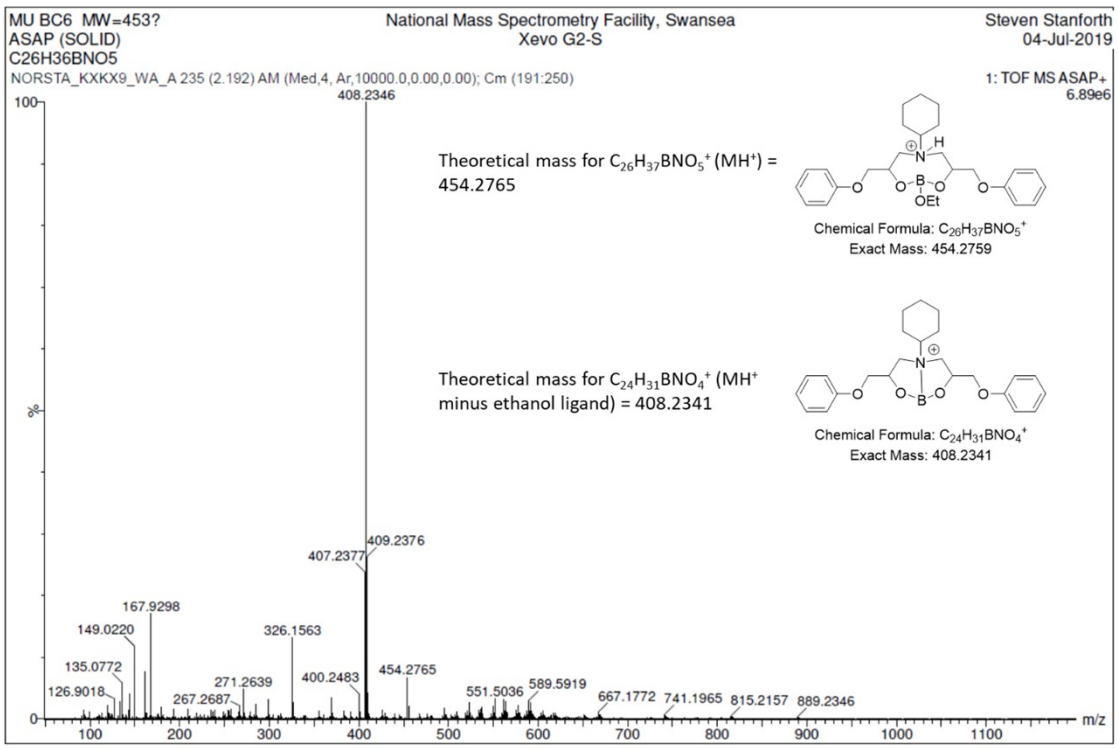


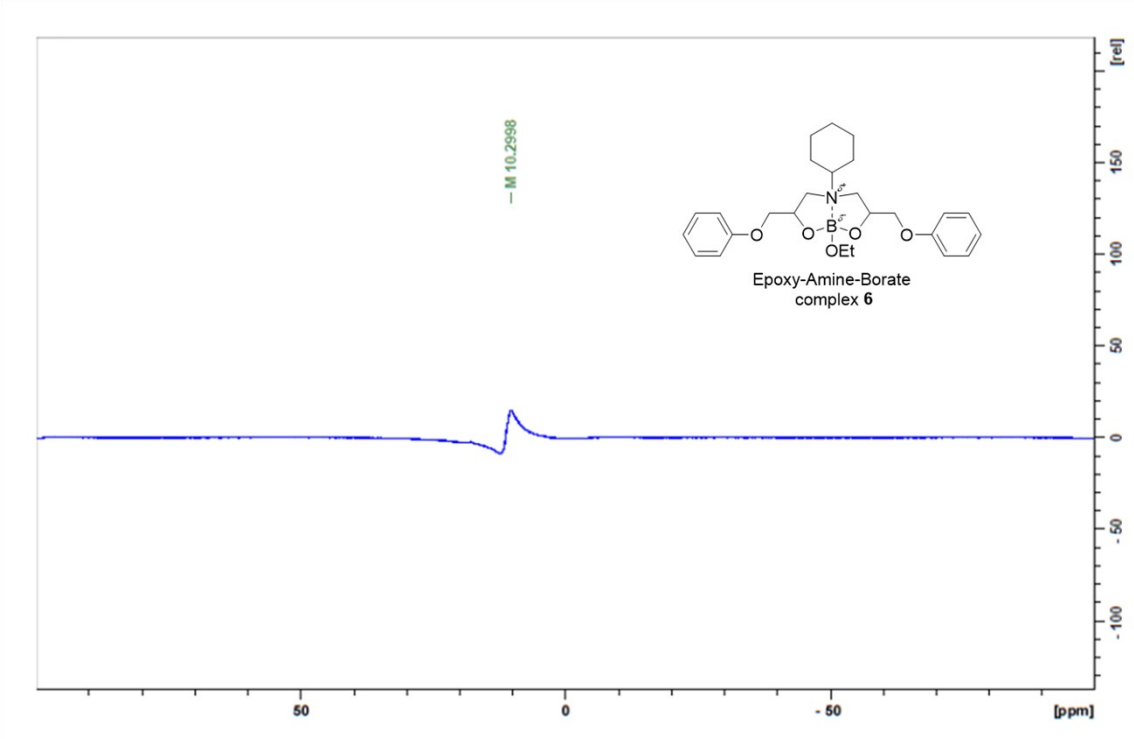


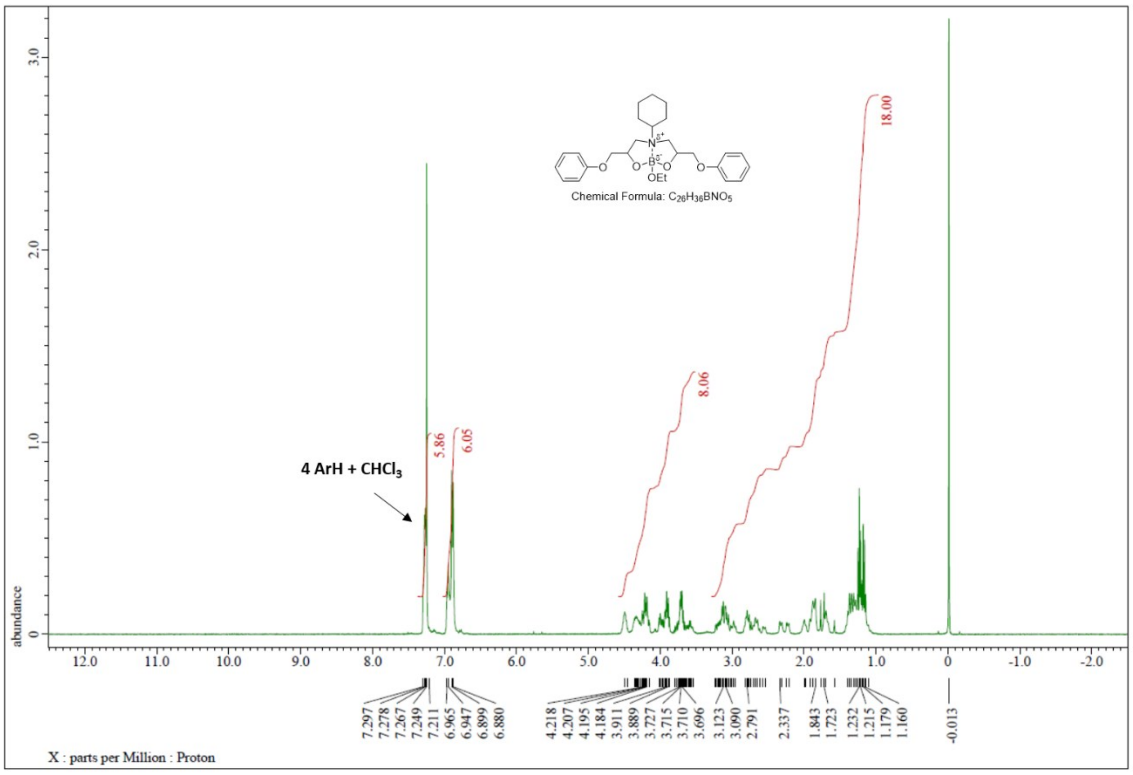
Epoxy-Amine-Borate complex 6

Tertiary-*β*-amino diol intermediate **5** (2.00 g, 5.01 mmol) was dissolved in anhydrous toluene (10.0 mL) in a round bottomed flask under an inert atmosphere of nitrogen gas with stirring. The reaction mixture was treated with triethylborate (0.805 g, 5.51 mmol, 1.1 equivs.) resulting in the immediate precipitation of a fine white solid product which was isolated by filtration, before washing with fresh anhydrous toluene (2 x 1 mL), suction drying and then drying in a vacuum oven at 60 °C under vacuum. The final product was isolated as a fine white solid (1.63 g, 72%) after further recrystallisation from toluene. Crystals for single crystal x-ray diffraction studies were obtained by dissolving the product in the minimal volume of hot acetonitrile then allowed to slowly crystallise over 5 days at ambient temperature in a sealed vial. This resulted in large uniform crystals suitable for single crystal X-ray diffraction. ν_{max}/cm^{-1} 2927 and 2857 (CH_2 & CH) 1246 (C-N) (note: absence of broad OH band around 3000 cm^{-1}); δH(400 MHz; CDCl3; Me_4Si) 1.08-2.04 (13 H, m, 5 x C*H*$_2$ cyclohex, C*H*$_3$CH$_2$OB), 2.18-3.24 (5 H, m, 2 x C*H*$_2$-NH, cyclic-C*H*-N), 3.50-4.55 (8H, m, C*H*$_2$-OPh, C*H*-OH, C*H*$_2$OB), 6.85-6.98 (6 H, m, ArH), 7.22-7.32 (4 H, m, ArH); δC = 18.4 (CH_3), 18.5 (CH_3), 25.5 (*C*H$_2$ ring), 25.6 (*C*H$_2$ ring), 25.7 (*C*H$_2$ ring), 25.7 (*C*H$_2$ ring), 25.8 (*C*H$_2$ ring), 25.9 (*C*H$_2$ ring) 27.5 (*C*H$_2$ ring), 28.4 (*C*H$_2$ ring), 28.5 (*C*H$_2$ ring), 28.7 (*C*H$_2$ ring), 53.2 (*C*H$_2$-NH), 53.8 (*C*H$_2$-NH), 58.2 (*C*H$_2$-NH), 58.2 (*C*H$_2$-NH), 58.3 (*C*H$_2$-NH), 62.1 (*C*H$_2$-NH), 65.7 (*C*H-N/O), 66.1 (*C*H-N/O), 66.8 (*C*H-N/O), 67.2 (*C*H-N/O), 67.8 (*C*H-N/O), 68.0 (*C*H-N/O), 69.1 (*C*H-N/O), 69.4 (*C*H-N/O), 69.8 (*C*H$_2$-O), 70.1 (*C*H-N/O), 70.3 (*C*H$_2$-O), 70.4 (*C*H$_2$-O), 70.9 (*C*H$_2$-O), 71.2 (*C*H$_2$-O), 114.5 (Ar), 114.6 (Ar), 120.8 (Ar), 121.1 (Ar), 129.6 (Ar), 129.6 (Ar), 158.6 (Ar quat), 158.7 (Ar quat) 158.7 (Ar quat); δB(400 MHz; CDCl3) 10.30 (B(NR)(OR)$_3$); X-ray supplementary data: Full crystallographic information available from the deposition to the Cambridge Crystallographic Data Centre (deposition number CCDC 1894132). *m/z* 454.2765 (MH$^+$, 9% calc. for $C_{26}H_{37}BNO_5$ = 454.2759),

m/z 408.2346 ($MH^+ - CH_3CH_2OH$, 100% calc. for $C_{24}H_{31}BNO_4$ = 408.2341); Elemental Analysis calc'd for $C_{26}H_{37}BNO_5$: C, 68.88; H, 8.00; N, 3.09; Found C, 68.74; H, 7.89; N, 3.04.



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5.86
6.05
8.06
18.00
abundance
X : parts per Million : Proton
7.297
7.278
7.267
7.249
7.211
6.965
6.947
6.899
6.880
4.218
4.207
4.195
4.184
3.911
3.889
3.727
3.715
3.710
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1.179
1.160
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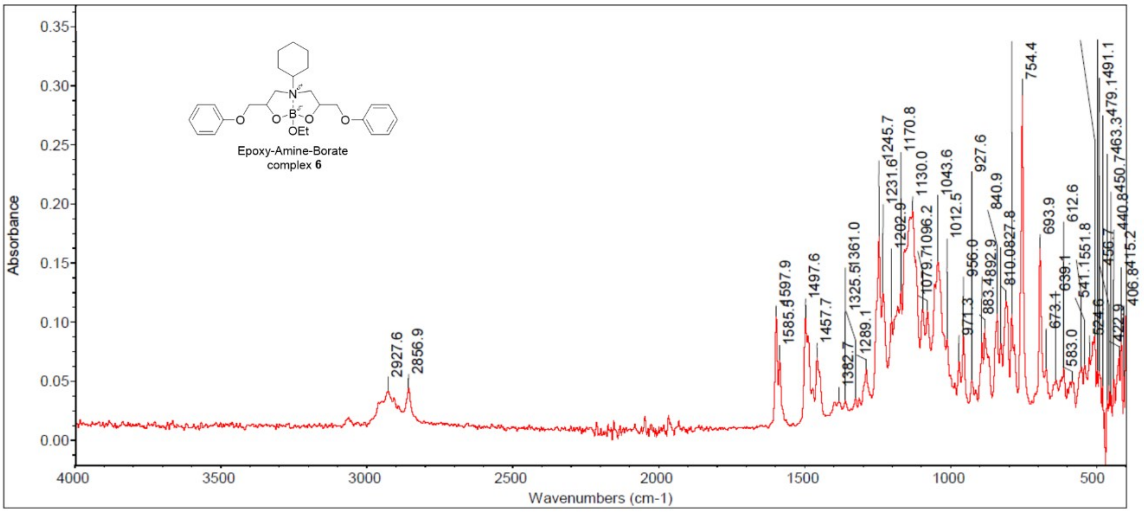
Epoxy-Amine-Borate
complex 6
Absorbance
Wavenumbers (cm-1)
2927.6
2856.9
1585.5
1597.9
1497.6
1457.7
1382.7
1325.5
1361.0
1289.1
1231.6
1245.7
1202.9
1170.8
1130.0
1079.7
1096.2
1043.6
1012.5
971.3
956.0
927.6
883.4
892.9
840.9
810.0
827.8
754.4
693.9
673.1
639.1
612.6
583.0
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456.7
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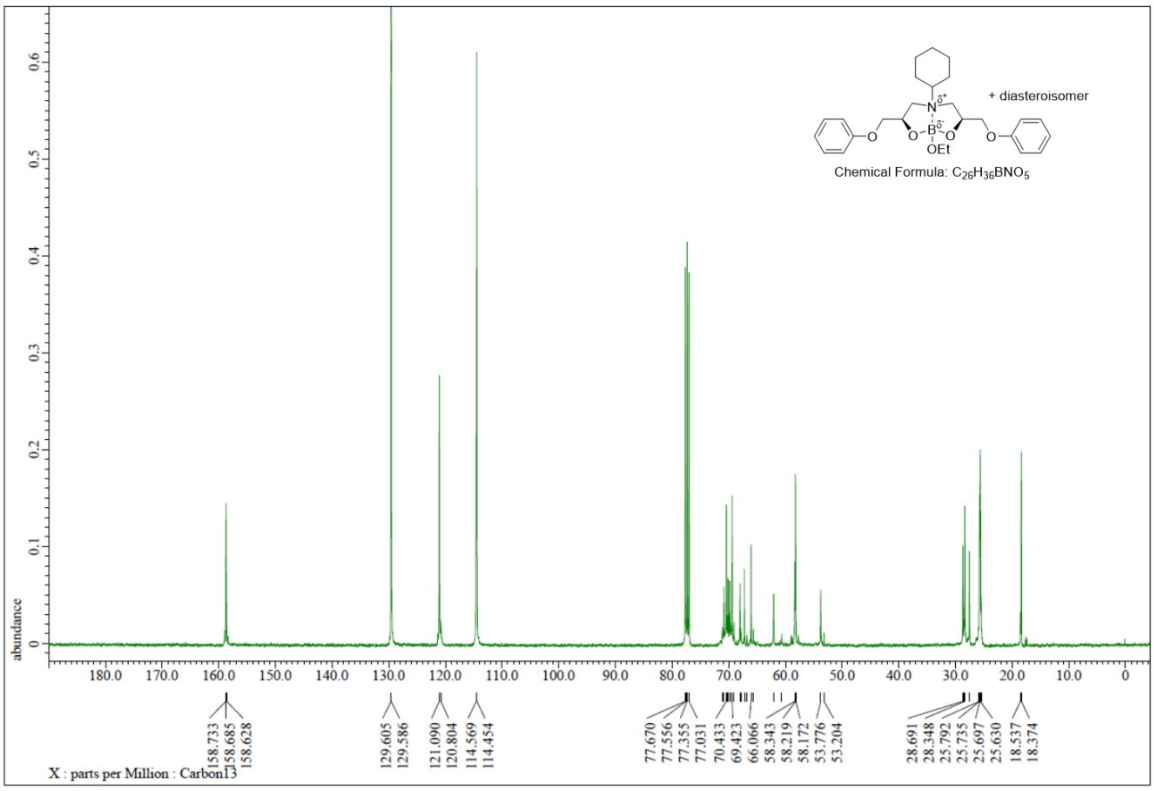
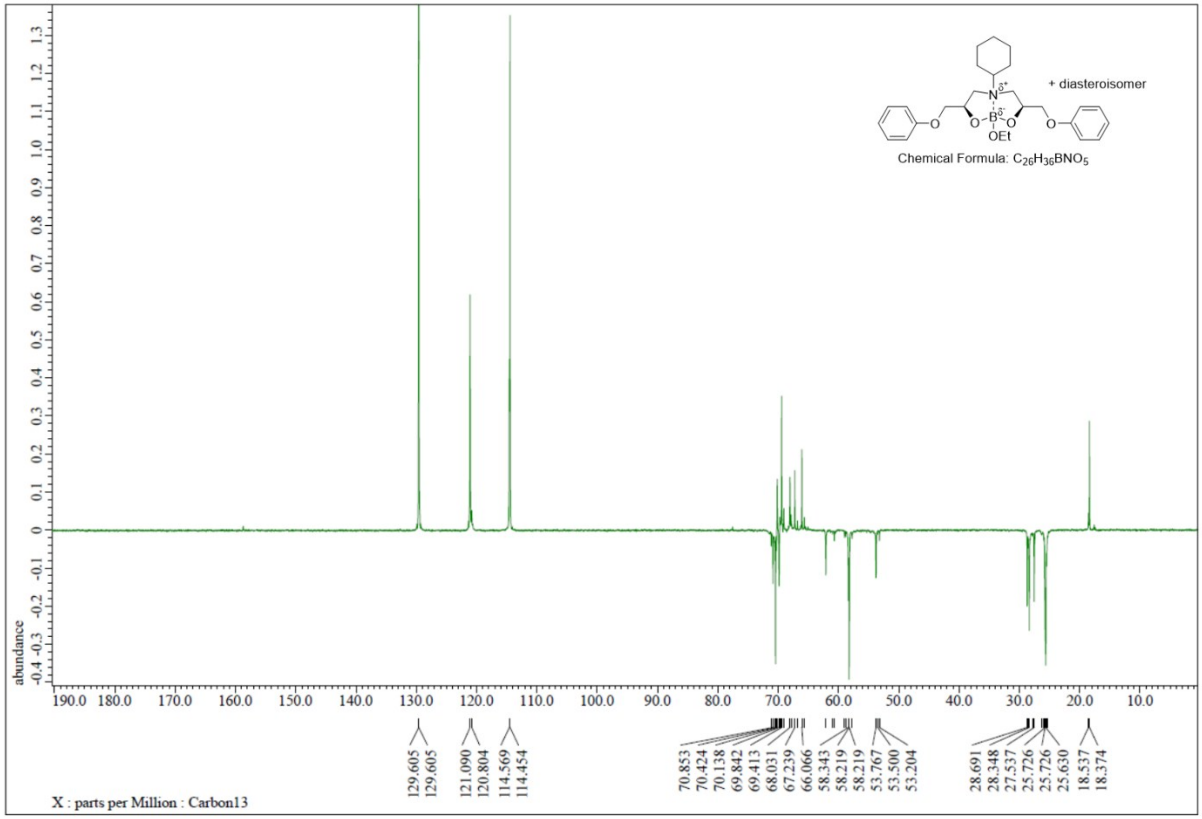
491.1
450.7
440.8
415.2
406.8



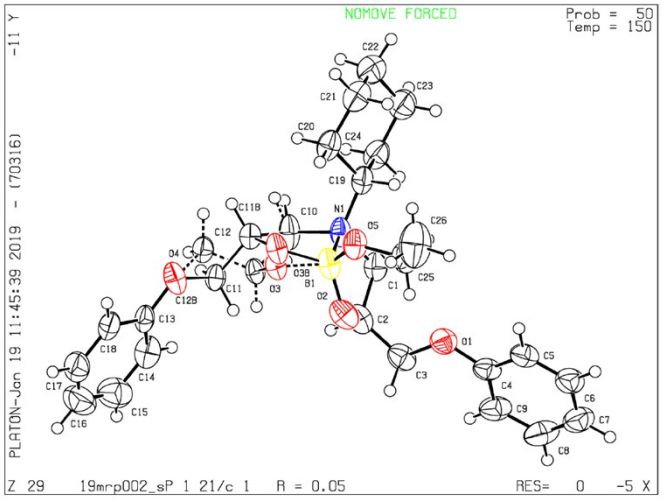


Mass Spectrometry Instrument data

The Direct injection MS analysis was performed on a Thermo scientific Q-Exactive mass spectrometer system (Thermo, Loughborough, UK). The sample introduction was set to 50 microliter/min with a stabilization time of 2 mins. Heated electrospray ionization (HESI) introduction source settings: the capillary temperature and voltage were maintained at 325°C and 3.8 KV (Positive mode) respectively. (N_2) Sheath flow was set to 45, an Auxiliary flow was set to 15 and Sweep gas flow

to 5 (all arbitrary units). The radio frequency of the S-lens was set to 50. For MS^1 profiling the mass spectrometer was operating at 35K mass resolution with a average scan rate of 7.2 $scan/s^{-1}$ with automatic gain control (AGC) at 5e5 and a maximum injection time of 50ms. The samples was dissolved in ACN with 0.1% formic acid at a concentration of approximately 1mg per mL and introduced into the MS as previously mentioned above. ACN/Water (50/50 v/v) solution followed by Isopropanol alcohol (all with 0.1 % formic acid) was flow through the system between samples at 200 microliter/min for 5 mins to clean the system and assess for carry over effect (repeat if required) before moving on to the next sample.

Single crystal X-ray diffraction (deposition number CCDC 1894132).



[1] J. R. Lizza, G. Moura-Letts, *Synthesis* 2017, **49(06)**, 1231.