Electronic Supplementary Material (ESI) for Chemical Communications

Supplementary Information

Assembly-driven synthesis of hybrid molecular capsules controlled by chiral sorting

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Experimental procedures for synthesis of molecular capsules

Synthesis of homochiral capsules

Resorcin[4]arene (0.1 mmol, 75 mg), D- or L-amino acid (0.425 mmol) and $HCHO_{aq}$ (37%, 0.4 mmol, 0.03 ml) were stirred overnight in chloroform (2 ml) at room temperature, then for 24h at 65°C. After cooling, the mixture was dried with anhydrous $MgSO_4$ and filtered. The filtrate was evaporated to dryness. Acetonitrile was added to the residue and it was treated with ultrasound. The precipitate was collected by filtration and vacuum dried.

Synthesis of hydrid capsules –procedure A (Fig. 3a)

Resorcin[4]arene (0.05 mmol, 38mg), D-valine (0.2125 mmol, 25mg), $HCHO_{aq}$ (37%, 0.4 mmol, 0.03 ml) and (L-**2a**)$_2$ capsule (0.05 mmol, 71mg) were stirred overnight at room temperature in $CHCl_3$ and then at 65°C for 24h. It was then dried with anhydrous $MgSO_4$. The solvent was evaporated from the filtrate, acetonitrile was added to the residue and it was treated with ultrasound. The precipitate was collected through filtration and vacuum dried.

Synthesis of hydrid capsules –procedure B (Fig. 3b)

D- and L-amino acids (0.425 mmol) were put in separate Schlenck tubes. Resorcin[4]arene (0.1 mmol, 75 mg) and $HCHO_{aq}$ (37%, 0.4 mmol, 0.03 ml) were added to both of them and the mixtures were stirred in $CHCl_3$ overnight at room temperature and then at 65°C for 24h. The resulting mixtures were poured together in a round bottom flask and allowed to equilibrate at room temperature for 24h. The reaction mixture was then dried with anhydrous $MgSO_4$ and filtered. The filtrate was evaporated to dryness, acetonitrile was added to the residue and it was treated with ultrasound. The precipitate was separated through filtration and vacuum dried.

Analytical data

(L-2b)$_2$

^{1}H NMR (CDCl$_3$/400MHz): δ 7.44 (bd, 4H), 7.23 (bs, 4H), 6.70 (bt, 4H), 4.48 (bm, 4H), 4.15 (bm, 4H), 4.05 (bt, 4H), 3.61 (bm, 4H), 2.06 (bm, 8H), 1.58 (bd, 12H), 1.45 (bm, 4H), 0.95 (bd, 24H)

^{13}C NMR (CDCl$_3$/125MHz): δ 172.9, 151.5, 151.3, 125.0, 124.7, 105.9, 58.7, 42.1, 40.6, 31.4, 26.0, 22.8, 22.7, 12.8

HRMS (ESI) calculated for $C_{60}H_{85}N_4O_{16}$ $[M+H]^+$: 1117.5961; found: 1117.5967.

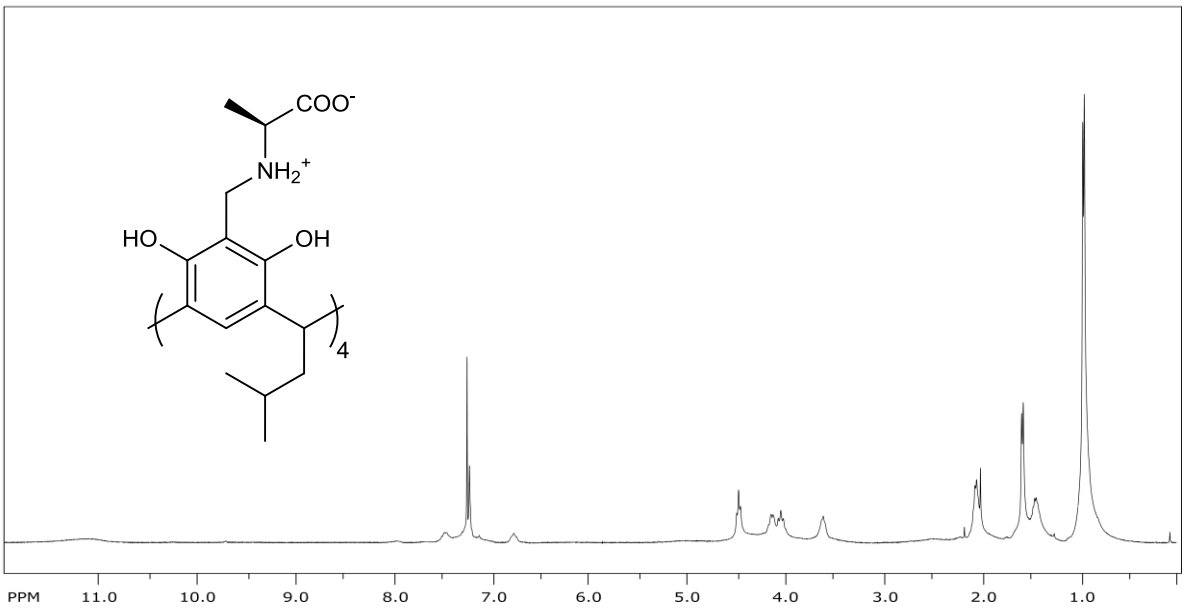

Figure 1. ^{1}H NMR spectrum of (L-**2b**)$_2$

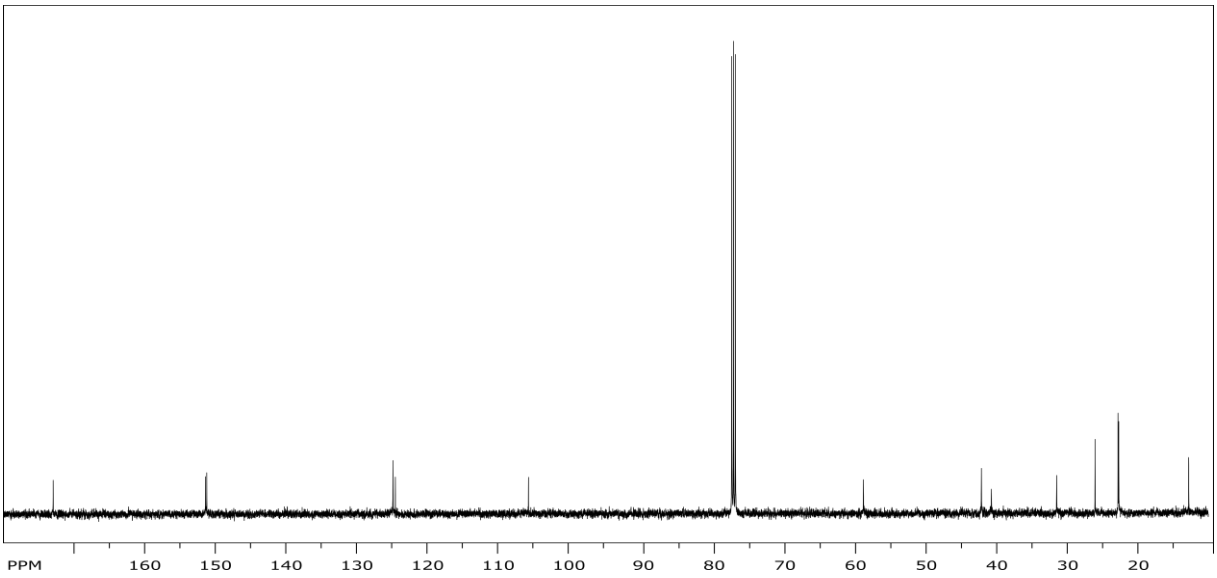

Figure 2. ^{13}C NMR spectrum of (L-**2b**)$_2$

*(L-**2c**)$_2$*

^{1}H NMR ($CDCl_3$, 600MHz): complicated spectrum with many overlapping signals

HRMS (ESI) calculated for $C_{72}H_{109}N_4O_{16}$ $[M+H]^+$: 285.7839; found: 1285.7832.

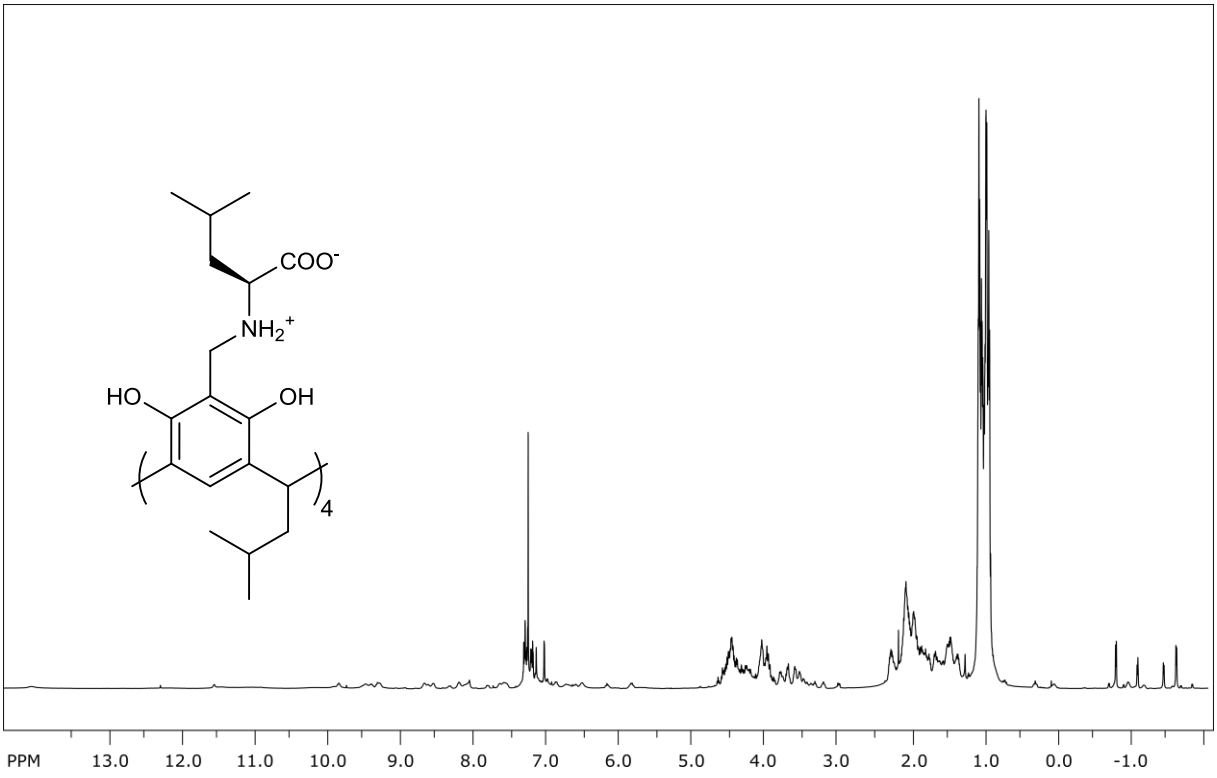

Figure 3. ^{1}H NMR spectrum of (L-**2c**)$_2$

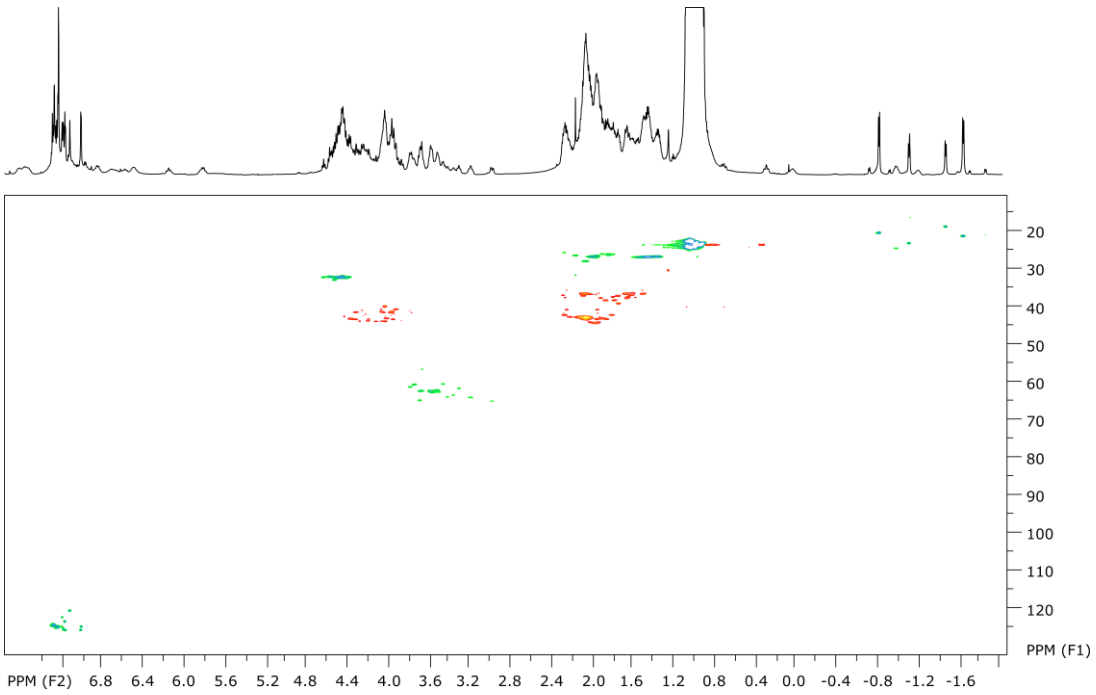

Figure 4. HSQC spectrum of (L-**2c**)$_2$ ($CDCl_3$, 298 K, 600 MHz)

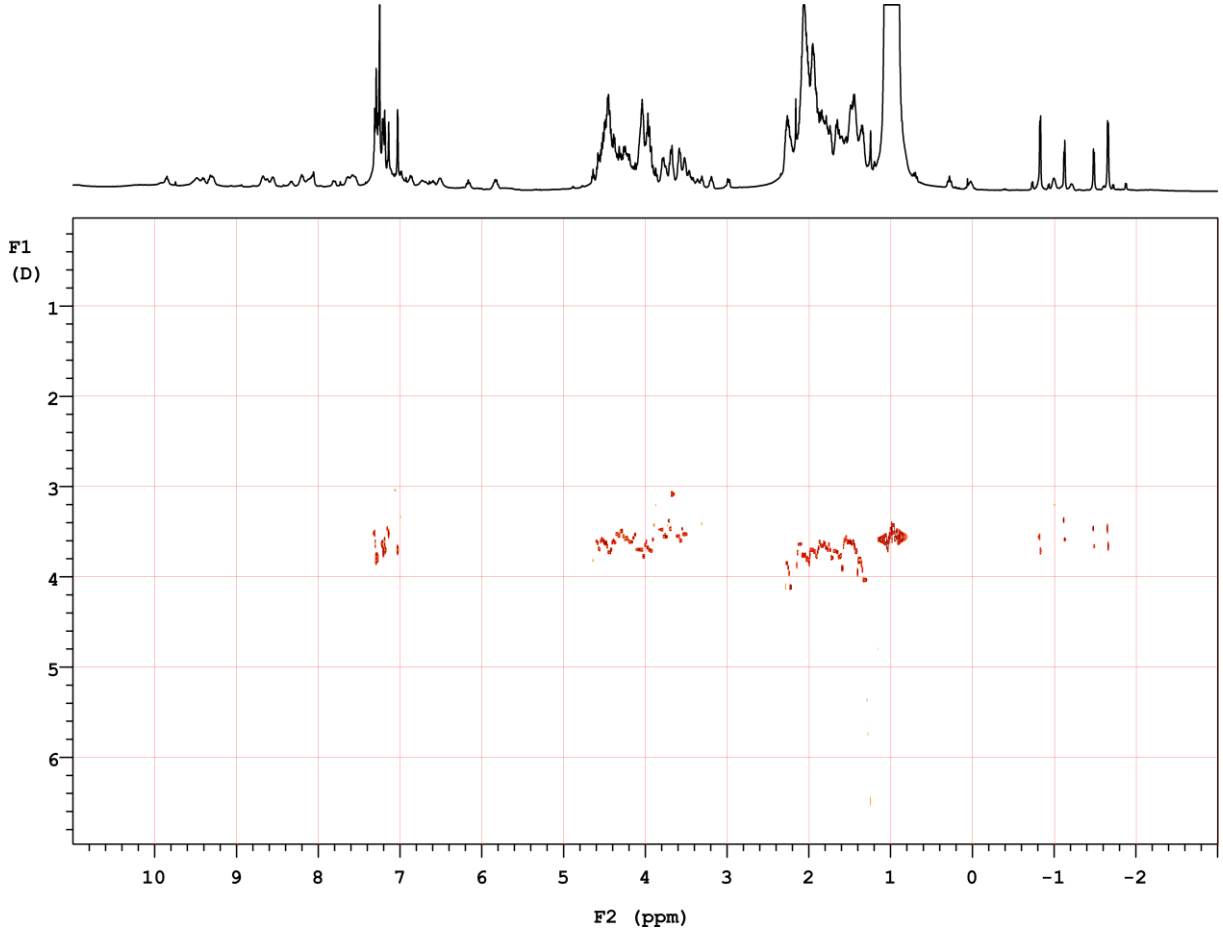

Figure 5. DOSY spectrum of (L-**2c**)$_2$ ($CDCl_3$, 298 K, 600 MHz)

(L-2d)(D-2d)

^{1}H NMR (CDCl$_3$/400MHz): δ 12.8 (bs, 4H), 9.97 (bm, 4H), 9.12 (bs, 4H), 7.29 (s, 4H), 6.30 (bm, 4H), 4.46 (bt, 4H), 4.09 (bm, 8H), 3.38 (bd, 4H), 2.42 (bm, 4H), 2.09 (bm, 4H), 2.00 (bm, 4H), 1.42 (bm, 4H), 1.31 (bd, 12H), 1.16 (bd, 12H), 0.94 (bd, 24H),

^{13}C NMR (CDCl$_3$/150MHz): δ 171.3, 152.1, 150.3, 125.4, 124.6, 123.5, 104.7, 65.4, 42.8, 38.7, 31.1, 26.0, 25.1, 22.9, 22.7, 20.6, 17.3,

HRMS (ESI) calculated for $C_{68}H_{101}N_4O_{16}$ $[M+H]^+$: 1229.7213; found: 1229.7240.

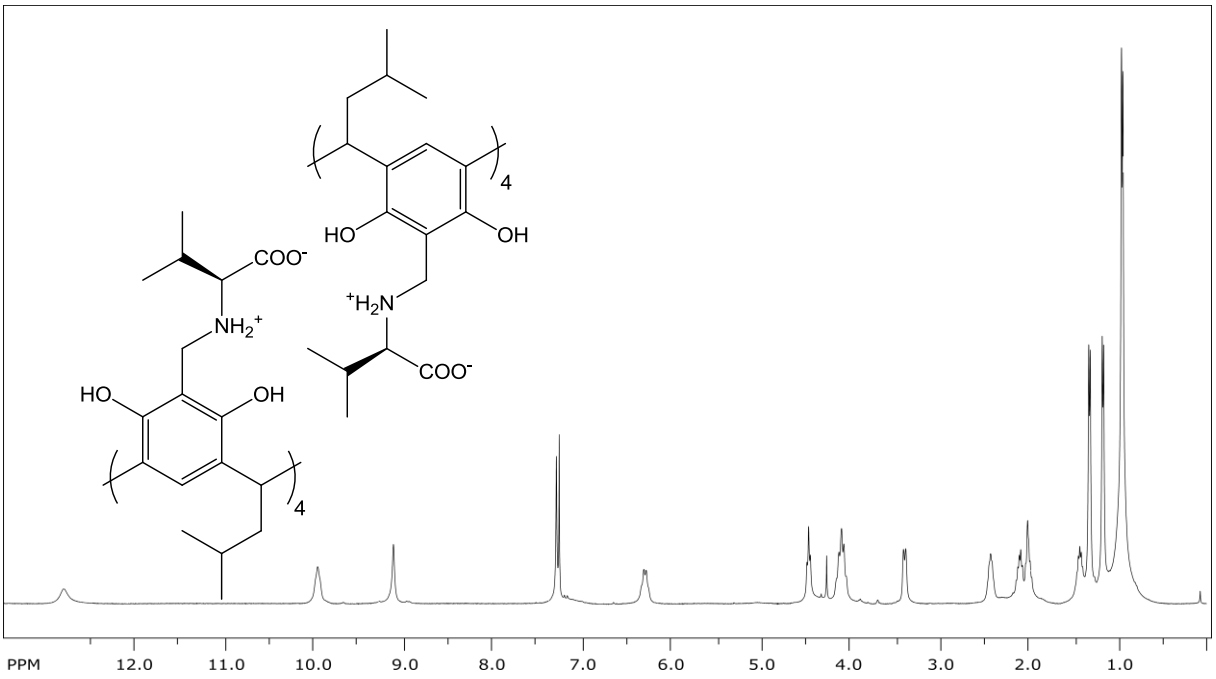

Figure 6. ^{1}H NMR spectrum of (L-**2d**)(D-**2d**)

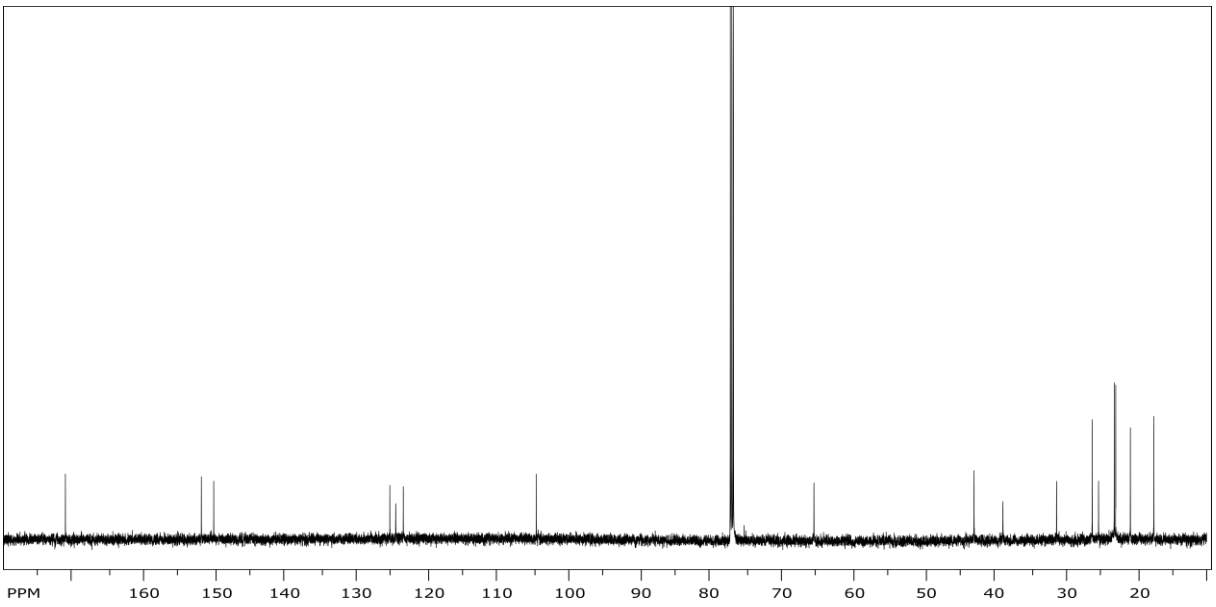

Figure 7. ^{13}C NMR spectrum of (L-**2d**)(D-**2d**)

*(L-**2e**)(D-**2d**)*

^{1}H NMR ($CDCl_3$/400MHz): δ 12.8 (bs, 4H), 10.97 (bm, 8H), 9.11 (bs, 8H), 7.28 (s, 8H), 6.30 (bm, 8H), 4.46 (bt, 8H), 4.08 (bm, 16H), 3.42 (bdd, 8H), 2.41 (bm, 4H), 2.08 (bm, 12H), 1.99 (bm, 8H), 1.71 (bm, 8H), 1.41 (bm, 8H), 1.30 (bd, 12H), 1.15 (bt, 24H), 1.01 (bt, 12H), 0.94 (bd, 48H)

^{13}C NMR ($CDCl_3$/100MHz): 171.4, 171.3, 152.0, 150.3, 125.4, 125.3, 124.5, 123.5, 104.6(3), 104.6(1), 77.2, 65.3, 64.2, 42.7, 38.6, 38.5, 32.0, 31.0, 27.6, 26.0, 26.0, 25.0, 22.9(1), 22.9(0), 22.6(8), 22.6(6), 20.6, 17.4, 14.7, 12.5

HRMS (ESI) calculated for $C_{68}H_{101}N_4O_{16}$ $[M_{2d}+H]^+$: 1229.7213; found: 1229.7194.
calculated for $C_{72}H_{109}N_4O_{16}$ $[M_{2e}+H]^+$: 1285.7839; found: 1285.7814.

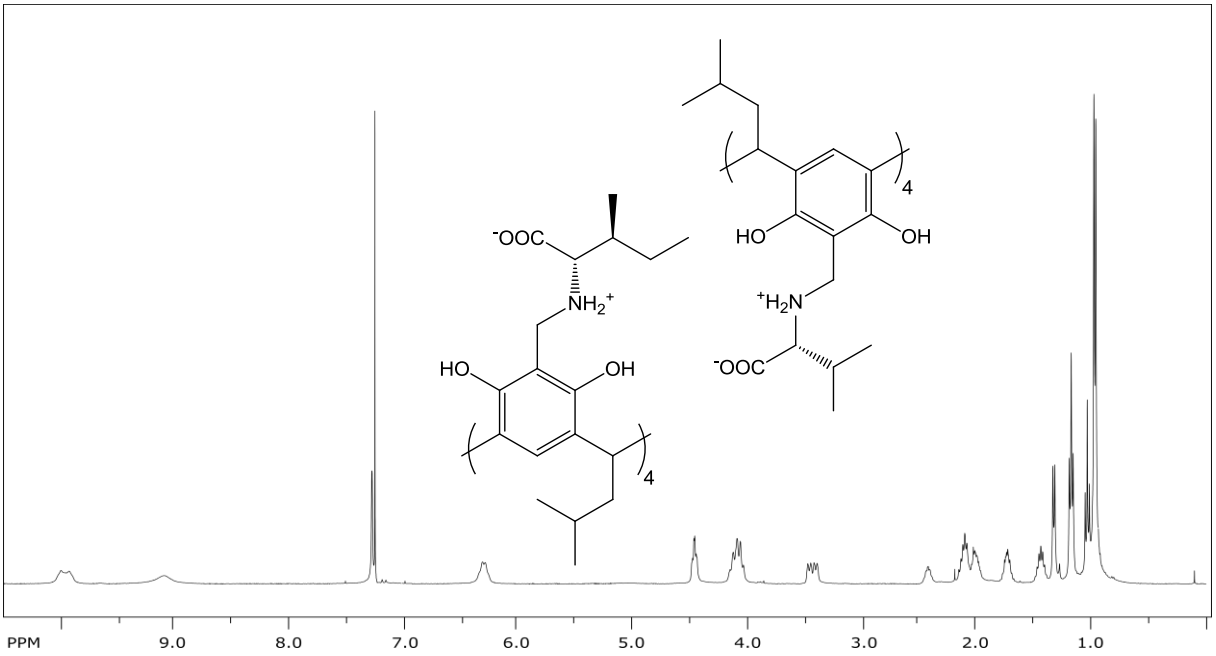

Figure 8. ^{1}H NMR spectrum of (L-**2e**)(D-**2d**)

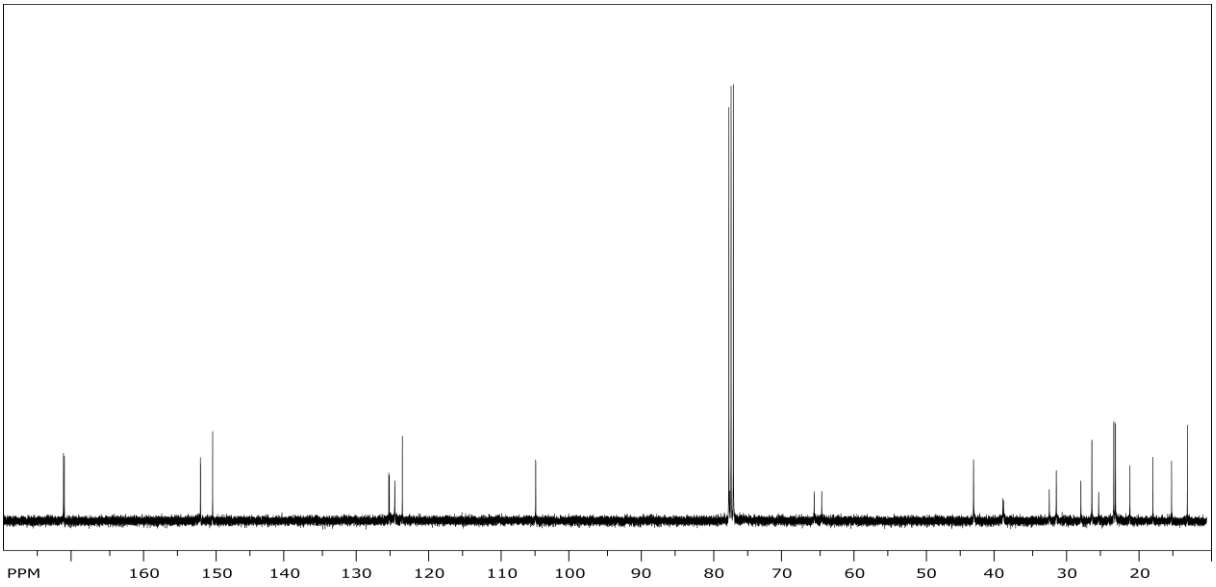

Figure 9. ^{13}C NMR spectrum of (L-**2e**)(D-**2d**)

*(L-**2a**)(D-**2d**)*

^{1}H NMR ($CDCl_3$/400MHz): δ 10.36 (bs, 4H), 10.00 (bs, 4H), 9.09 (bs, 4H), 7.40 – 7.13 (m, 28H), 6.22 (bs, 4H), 5.92 (bq, 4H), 4.39 (bm, 8H), 4.03 (bt, 8H), 3.88 (bt, 4H), 3.78 (bm, 4H), 3.62 (bm, 4H), 3.45 (bd, 4H), 3.26 (bdd, 4H), 3.05 (bd, 4H), 2.34 (bt, 4H), 2.12 – 1.79 (bm, 16H), 1.35 (bm, 8H), 1.22 (bd, 12H), 1.11 (bd, 12H), 1.02 – 0.70 (bm, 48H)

^{13}C NMR ($CDCl_3$/125MHz): δ 173.7, 170.8, 152.1, 151.6, 150.3, 149.9, 138.5, 129.0, 128.6, 127.0, 125.6, 125.4, 124.7, 124.6, 124.0, 123.6, 105.6, 104.9, 66.1, 62.4, 42.7, 42.6, 40.1, 39.2, 36.6, 31.2, 31.1, 26.0, 26.0, 25.2, 23.0, 22.8, 22.7, 22.5, 20.6, 17.0

HRMS (ESI) calculated for $C_{68}H_{101}N_4O_{16}$ $[M_{2d}+H]^+$: 1229.7213; found: 1229.7211.
calculated for $C_{84}H_{101}N_4O_{16}$ $[M_{2a}+H]^+$: 1421.7213; found: 1421.7194.

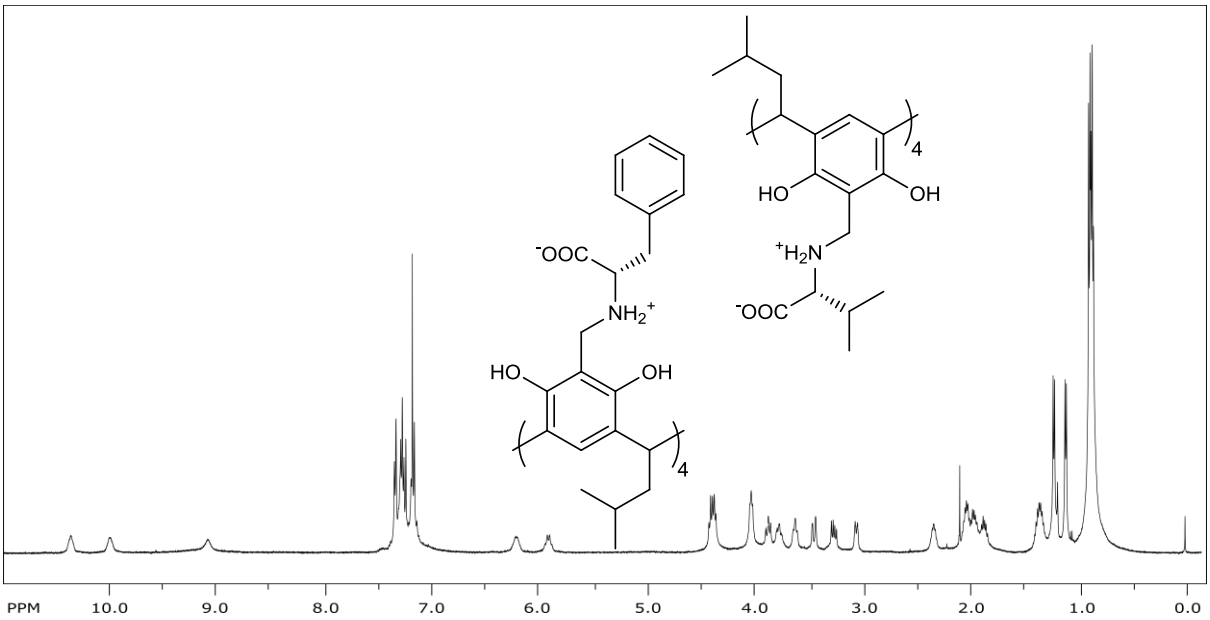

Figure 10. ^{1}H NMR spectrum of (L-**2a**)(D-**2d**)

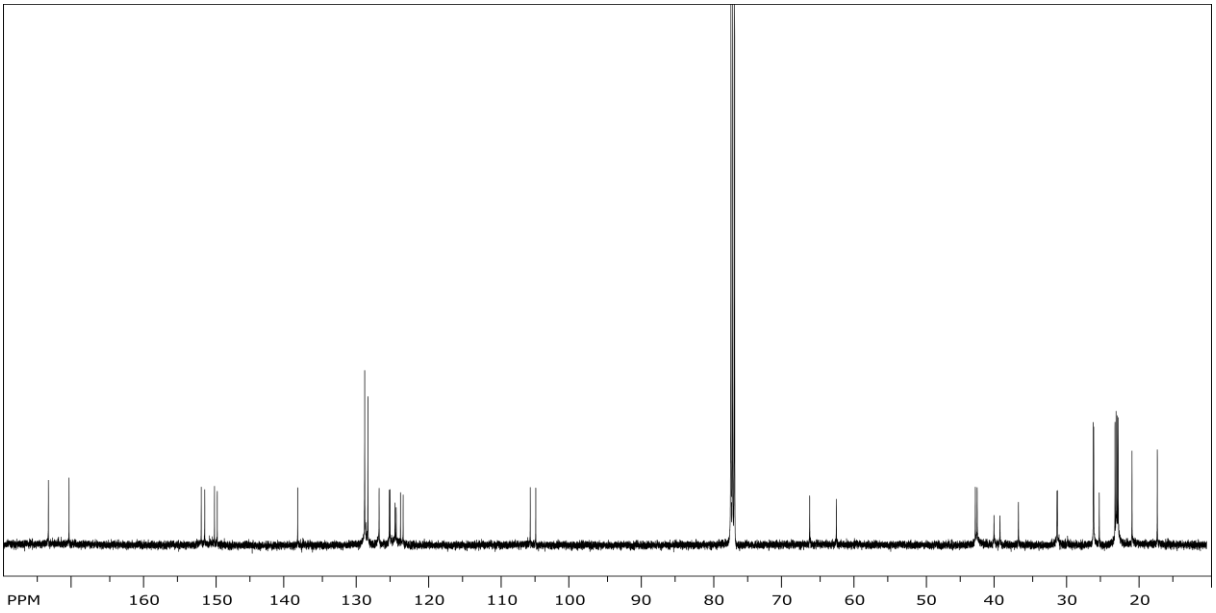

Figure 11. ^{13}C NMR spectrum of (L-**2a**)(D-**2d**)

Reaction kinetics - 2D NMR spectra

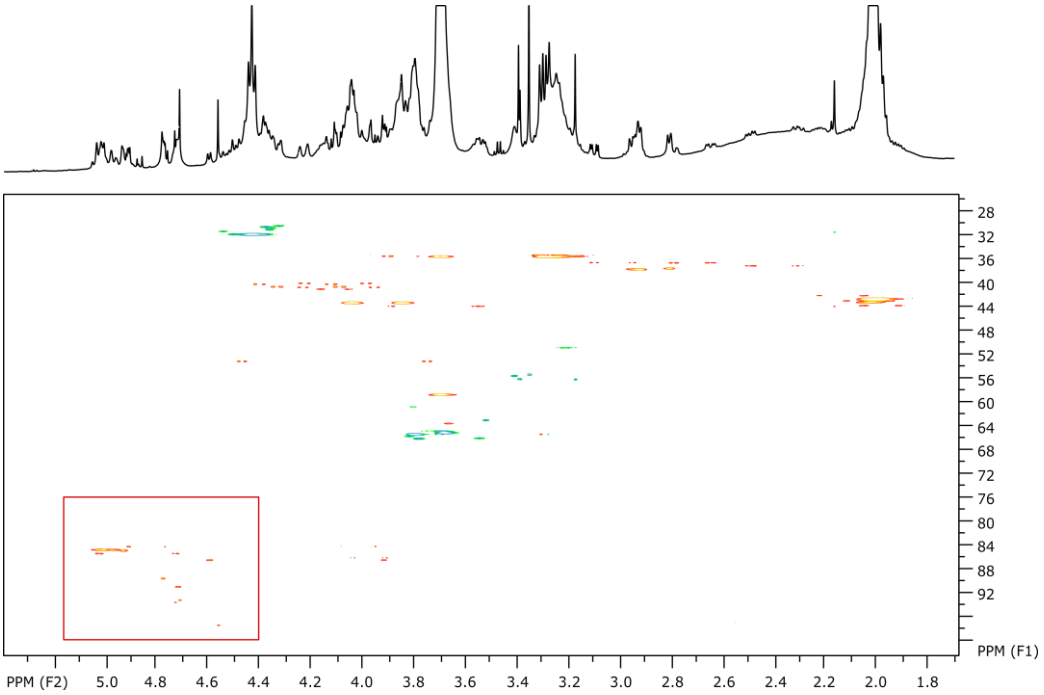

Figure 12. HSQC spectrum of a reaction mixture after 1 day ($CDCl_3$, 298 K, 600 MHz). The highlighted peaks are for the benzoxazine N,O-acetal bridge.

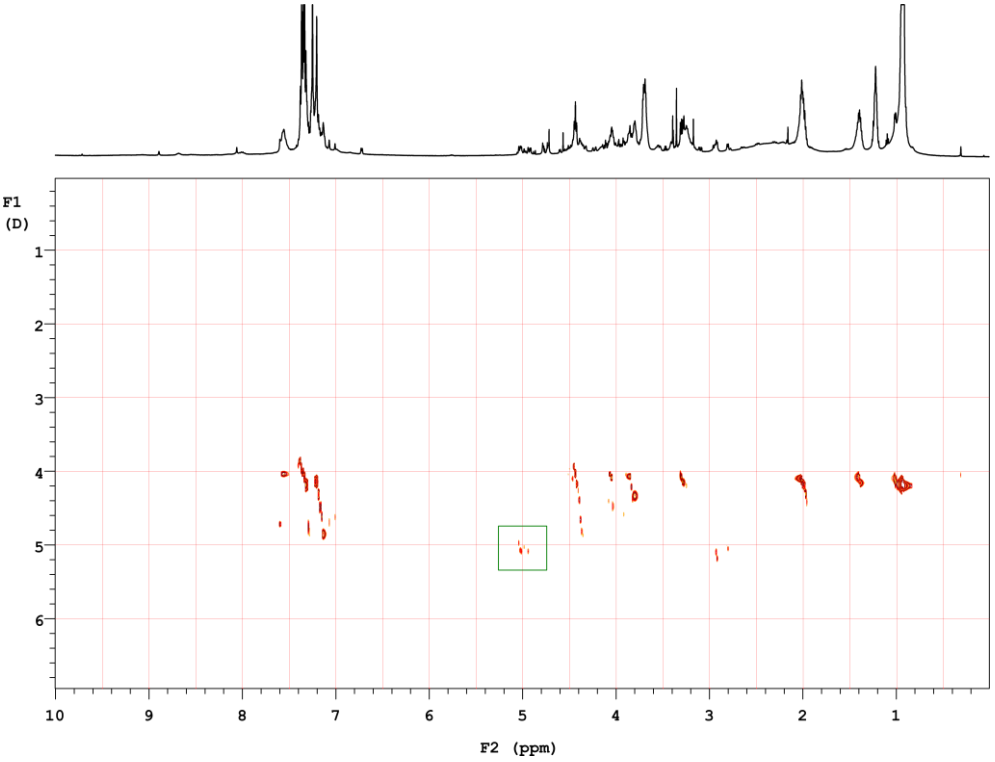

Figure 13. DOSY spectrum of a reaction mixture after 1 day ($CDCl_3$, 298 K, 600 MHz). The highlighted peaks are for the benzoxazine N,O-acetal bridge.