Supplementary Material

The influence of salt additives on the macrocyclic product distributions in double-amidation reactions

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Analytical and spectroscopic data of macrocyclic di- and tetramides

Diamide 9: 77% yield; mp. 224-225 °C; $^1$H NMR (400 MHz, CDCl$_3$), δ 7.38 (br s, 2H), 7.01-6.85 (m, 4 arom. H), 4.48 (s, 4H), 3.67 (m, 4H), 3.64 (m, 4H); $^{13}$C NMR (100 MHz, CDCl$_3$), δ 167.2, 146.1, 122.1, 112.5, 69.0, 66.9, 38.4.

Diamide 10: 75% yield; mp. 175-176 °C; $^1$H NMR (400 MHz, DMSO-d$_6$) δ 7.36 (s, 2H), 7.04-6.95 (m, 2H), 6.91-6.82 (m, 2H), 4.48 (s, 4H), 3.74-3.55 (m, 12H); $^{13}$C NMR (100 MHz, DMSO-d$_6$) δ 167.87, 146.75, 122.41, 113.24, 70.70, 69.70, 67.68, 38.69.

Diamide 11: 29% yield; 125-127 °C; $^1$H NMR (400 MHz, CDCl$_3$) δ 7.25 (bs, 2H), 7.03-6.95 (m, 2H), 6.94-6.83 (m, 2H), 4.57 (s, 4H), 3.75-3.33 (m, 16H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ 168.38, 147.64, 142.88, 114.71, 70.75, 70.68, 69.76, 69.12, 38.97.

Diamide 12: 40% yield; mp. 134-136 °C; $^1$H NMR (400 MHz, CDCl$_3$) δ 7.49 (s, 2H), 7.05-6.96 (m, 2H), 6.95-6.85 (m, 2H), 4.50 (s, 4H), 3.53-3.43 (m, 8H), 3.29-3.19 (m, 4H), 1.84-1.74 (m, 4H), 1.58-1.46 (m, 4H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ 168.24, 143.88, 123.26, 116.39, 71.12, 70.88, 69.95, 38.71, 38.21, 26.47.

Diamide 13: 55% yield, 117-118 °C; $^1$H NMR (400 MHz, CDCl$_3$) δ 7.61 (bs, 2H), 7.01-6.98 (m, 2H), 6.96-6.93 (m, 2H), 4.51 (s, 4H), 3.57-3.49 (m, 16H), 1.85-1.80 (m, 4H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ 168.28, 148.06, 123.08, 115.79, 70.28, 70.15, 69.55, 37.94, 28.42.

Diamide 14: 25% yield; mp. 230-231 °C; $^1$H-NMR (400 MHz, CDCl$_3$), δ 7.26 (br s, 2H), 7.17 (t, J=8.5 Hz, 1H), 6.67 (dd, J=8.5 Hz, J=2.5 Hz, 2 H), 6.65 (t, J=2.5 Hz, 1H), 4.65 (s, 4H), 3.39-3.59 (m, 8H); $^{13}$C-NMR (100 MHz, CDCl$_3$), δ 168.5, 158.8, 131.1, 109.0, 102.8, 69.5, 67.7, 38.9.

Diamide 15: 22% yield; mp. 144-147 °C; $^1$H NMR (400 MHz, CDCl$_3$) δ 7.24-7.12 (m, 1H), 6.68 (bs, 2H), 6.55-6.52 (m, 3H), 4.53 (s, 4H), 3.51-3.45 (m, 8H), 3.41 (s, 4H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ 168.50, 158.87, 130.50, 107.61, 102.94, 70.71, 69.69, 67.75, 38.87.

Diamide 16: 29% yield; mp. 125-127 °C; $^1$H NMR (400 MHz, CDCl$_3$) δ 7.26 (d, J=8.2 Hz, 1H), 7.01 (s, 2H), 6.63 (t, J=2.4 Hz, 1H), 6.59 (d, J=2.4 Hz, 1H), 6.57 (d, J=2.4 Hz, 1H), 4.53 (s, 4H), 3.65-3.60 (m, 4H), 3.57-3.48 (m, 12H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ 167.95, 158.77, 130.73, 107.43, 105.16, 70.81, 69.70, 69.53, 67.93, 38.52.

Diamide 17: 42% yield; mp. 103-104 °C; $^1$H NMR (400 MHz, CDCl$_3$) δ 7.49 (s, 2H), 7.05-6.96 (m, 2H), 6.95-6.85 (m, 2H), 4.50 (s, 4H), 3.53-3.43 (m, 8H), 3.29-3.19 (m, 4H), 1.84-1.74 (m, 4H), 1.58-1.46 (m, 4H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ 167.57, 158.55, 130.63, 106.06, 105.82, 71.44, 71.12, 67.29, 39.13, 28.04, 26.46.

Diamide 18: 40% yield; mp. 117-118 °C; $^1$H NMR (400 MHz, CDCl$_3$) δ 7.53 (bs, 2H), 7.27 (t, J=8.3 Hz, 1H), 6.76 (t, J=2.4 Hz, 1H), 6.56 (dd, J=8.4, 2.5 Hz, 2H), 4.47 (s, 4H), 3.74-3.57 (m, 12H), 3.55-3.42 (m, 4H), 1.91-1.75 (m, 4H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ 167.55, 158.60, 130.67, 106.26, 105.71, 71.99, 70.30, 70.21, 67.42, 39.09, 28.06.

Diamide 19: 1% yield; 177-179 °C; $^1$H NMR (400 MHz, DMSO-d$_6$) δ 7.91 (t, J=5.4 Hz, 2H), 6.81 (s, 4H), 4.35 (s, 4H), 3.47 (m, 4H), 3.32-3.27 (m, 4H); $^{13}$C NMR (100 MHz, DMSO) δ 167.68, 152.04, 115.57, 68.40, 67.54, 38.18.

Diamide 20: 20% yield; mp. 197-198 °C; $^1$H NMR (400 MHz, CDCl$_3$) δ 6.84 (s, 4H), 6.62 (bs, 2H), 4.54 (s, 4H), 3.53-3.32 (m, 8H), 3.20 (s, 4H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ 168.82, 152.02, 114.98, 69.96, 69.73, 67.51, 38.51.
Diamide 21: 18% yield; mp. 155-157 °C; $^1$H NMR (400 MHz, CDCl$_3$) δ 6.88 (s, 4H), 6.80 (s, 2H), 4.51 (s, 4H), 3.51-3.43 (m, 8H), 3.42-3.28 (m, 8H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ 168.74, 152.80, 116.13, 70.62, 70.35, 69.63, 68.70, 38.62.

Diamide 22: 35% yield; mp. 165-167 °C; $^1$H NMR (400 MHz, CDCl$_3$) δ 7.16 (bs, 2H), 6.86 (s, 4H), 4.45 (s, 4H), 3.51-3.29 (m, 8H), 3.18 (bs, 4H), 1.80-1.62 (m, 4H), 1.36-1.25 (m, 4H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ 168.36, 152.75, 116.11, 71.05, 70.41, 68.63, 38.19, 28.49, 26.07.

Diamide 23: 28% yield; mp. 136-137 °C; $^1$H NMR (400 MHz, DMSO-d$_6$) δ 7.80 (bt, $J$=5.5 Hz, 2H), 6.89 (s, 4H), 4.42 (s, 4H), 3.45-3.40 (m, 4H), 3.39-3.34 (m, 4H), 3.28 (t, $J$=6.3 Hz, 4H), 2.21-3.31 (m, 4H), 1.66-1.53 (m, 4H); $^{13}$C NMR (100 MHz, DMSO-d$_6$) δ 167.71, 152.13, 115.68, 69.53, 69.32, 68.82, 67.71, 36.16, 28.61.

Tetraamide 24: 2% yield; mp. 219-220 °C; $^1$H-NMR (400 MHz, CDCl$_3$), δ 6.97-6.96 (m, 4 arom. H), 6.82-6.81 (m, 4 arom. H), 4.42 (s, 8H), 3.59-3.52 (m, 16H); $^{13}$C-NMR (100 MHz, CDCl$_3$), δ 168.4, 147.6, 123.2, 115.4, 69.3, 69.2, 38.7.

Tetraamide 25: 5% yield; mp. 198-199 °C; $^1$H NMR (400 MHz, DMSO-d$_6$) δ $^1$H NMR (400 MHz, DMSO) δ 8.01 (t, $J$=5.4 Hz, 4H), 7.10-6.91 (m, 8H), 4.52 (s, 8H), 3.48-3.42 (m, 12H), 3.36-3.25 (m, 12H); $^{13}$C NMR (100 MHz, DMSO-d$_6$) δ 167.83, 147.68, 122.15, 115.13, 69.43, 68.72, 68.37, 38.19.

Tetraamide 27: 8% yield; mp. 185-187 °C; $^1$H NMR (400 MHz, DMSO-d$_6$) δ 7.27-7.16 (m, 6H), 6.57-6.53 (m, 6H), 4.44 (s, 8H), 3.47-3.36 (m, 24H), 1.79-1.78 (m, 8H), 1.59 (bs, 8H); $^{13}$C NMR (100 MHz, DMSO-d$_6$) δ 168.10, 147.79, 123.01, 115.47, 70.77, 69.30, 69.19, 37.52, 29.15, 26.30.

Tetraamide 28: 6% yield; mp. 122-124 °C; $^1$H NMR (500 MHz, CDCl$_3$) δ 7.40 (bt, $J$=5 Hz, 4H), 7.00-6.97 (m, 4H), 6.92-6.89 (m, 4H), 4.51 (s, 8H), 3.53-3.52 (m, 24H), 3.45 (dd, $J_1$=12.5 Hz, $J_2$=6.5 Hz, $J_3$=6.0Hz, 4H), 1.80 (dt, $J_1$=12.5 Hz, $J_2$=6.5 Hz, $J_3$=6.0 Hz, 4H); $^{13}$C NMR (100 MHz, DMSO-d$_6$) δ 168.10, 147.79, 123.01, 115.47, 70.77, 69.30, 69.19, 37.52, 29.15, 26.30.

Tetraamide 29: 4% yield; mp. 257-259 °C; $^1$H NMR (400 MHz, DMSO-d$_6$) δ 7.92 (t, $J$=5.5 Hz, 4H), 7.16 (t, $J$=8.1 Hz, 2H), 6.63-6.45 (m, 6H), 4.43 (s, 8H), 3.44 (t, $J$=5.4 Hz, 8H), 3.33- 3.23 (m, 8H); $^{13}$C NMR (100 MHz, DMSO) δ 167.58, 158.72, 129.91, 107.61, 101.93, 68.46, 66.99, 38.17.

Tetraamide 30: 6% yield; mp. 213-214 °C; $^1$H NMR (400 MHz, DMSO-d$_6$) δ 7.95 (t, $J$=5.5 Hz, 4H), 7.19 (t, $J$=8.2 Hz, 2H), 6.61-6.51 (m, 6H), 4.44 (s, 8H), 3.50-3.40 (m, 16H), 3.34- 3.22 (m, 8H); $^{13}$C NMR (100 MHz, DMSO-d$_6$) δ 167.53, 158.73, 129.95, 107.61, 101.96, 69.47, 68.74, 66.98, 38.25.

Tetraamide 32: 18% yield; mp. 150-153 °C; $^1$H NMR (400 MHz, CDCl$_3$) 7.21-7.16 (m, 6H), 6.57-6.53 (m, 6H), 4.44(s, 8H), 3.47-3.36 (m, 24H), 1.79-1.76 (m, 8H), 1.59 (bs, 8H); $^{13}$C NMR (100 MHz, DMSO-d$_6$) δ 167.72, 158.71, 130.51, 107.90, 102.99, 70.58, 69.75, 67.67, 37.85, 28.90, 26.40.

Tetraamide 33: 3% yield; mp. 157-158 °C; $^1$H NMR (400 MHz, CDCl$_3$) δ 7.21 (t, $J$=8.2 Hz, 2H), 7.16 (bt, $J$=5.3 Hz, 4H), 6.63-6.51 (m, 6H), 4.44 (s, 8H), 3.64-3.49 (m, 24H), 3.48-3.35 (m, 8H), 1.79 (p, $J$=6.4, 5.6 Hz, 8H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ 167.85, 158.74, 130.48, 107.86, 103.02, 70.36, 70.22, 69.82, 67.60, 37.43, 28.94.
Tetraamide 34: 10% yield; mp. 251-252 °C; $^{1}H$ NMR (400 MHz, DMSO-d$_6$) δ 7.92 (t, J = 5.5 Hz, 4H), 7.16 (t, J = 8.1 Hz, 2H), 6.63-6.45 (m, 6H), 4.43 (s, 8H), 3.44 (t, J = 5.4 Hz, 8H), 3.33-3.23 (m, 8H); $^{13}$C NMR (100 MHz, DMSO) δ 167.64, 152.04, 115.56, 68.39, 67.55, 38.17.  
Tetraamide 35: 11% yield; mp. 200-201 °C; $^{1}H$ NMR (400 MHz, DMSO-d$_6$) δ 7.91 (bs, 4H), 6.87 (s, 8H), 4.39 (s, 8H), 3.46-3.40 (m, 8H), 3.33-3.22 (m, 8H); $^{13}$C NMR (100 MHz, DMSO) δ 167.85, 152.20, 115.62, 69.50, 68.74, 67.60, 39.50, 38.23.  
Tetraamide 36: 2% yield; mp. 162-163 °C; $^{1}H$ NMR (400 MHz, DMSO-d$_6$) δ 7.91 (bs, 4H), 6.87 (s, 8H), 4.44 (s, 8H), 3.47-3.45 (m, 8H), 3.41-3.38 (m, 16H), 3.27-3.23 (m, 8H); $^{13}$C NMR (100 MHz, DMSO) δ 167.85, 152.20, 115.62, 69.50, 68.74, 67.60, 39.50, 26.34.  
Tetraamide 37: 6% yield; mp. 138-140 °C; $^{1}H$ NMR (400 MHz, CDCl$_3$) δ 7.52 (bs, 4H), 6.85 (s, 8H), 4.41 (s, 8H), 3.50-3.43 (m, 16H), 3.36-3.34 (m, 8H), 1.81-1.76 (m, 8H), 1.58-1.56 (m, 8H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ 168.10, 152.43, 115.89, 70.35, 70.21, 70.10, 68.15, 37.56, 26.82.  
Tetraamide 38: 4% yield; mp. 170-172 °C; $^{1}H$ NMR (400 MHz, CDCl$_3$) δ 7.52 (bs, 4H), 6.85 (s, 8H), 4.41 (s, 8H), 3.50-3.43 (m, 16H), 3.36-3.34 (m, 8H), 1.81-1.76 (m, 8H), 1.58-1.56 (m, 8H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ 168.10, 152.43, 115.89, 70.35, 70.21, 70.10, 68.15, 37.56, 28.82.  

### Calibration of HPLC UV-detector

We prepared three-component mixtures in methanol containing one diester, one diamide and one tetraamide in equal molar concentration of 0.80, 1.15, 1.30 mM. Each mixture was analyzed by HPLC using reversed-phase column Bionacom Velocity C18-2, 4.6 x 250 mm, gain size 5 μm, λ=195 nm, gradient: 25% → 50% acetonitrile in water t=30 min. The results of these experiments were used to determine linear dependence between UV-detector data and concentration (Table 1, Figure 1).

#### Table S1. Calibration data

| Mixed compounds | Concentration [mM] | averaged UV-detector data |
|-----------------|-------------------|---------------------------|
|                 |                   | diaminel | tetraamide | ester     |
| 29 + 30 + 7     | 0.80              | 1083699  | 1702793    | 1083533   |
| 35 + 35 + 8     | 1.30              | 2958070  | 4717045    | 3190803   |
| 15 + 16 + 6     | 1.15              | 2375623  | 3835689    | 2404382   |
Figure S1

Based on these data we have calculated correlation coefficients for concentration of 1.2 mM: diamide 1.000, tetraamide 1.593±0.007, diester 1.014±0.034 what have been used to determined reaction mixtures quantitatively.