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Palladium-catalyzed amination in the synthesis of macrocycles comprising cholane, polyamine and pyridine units

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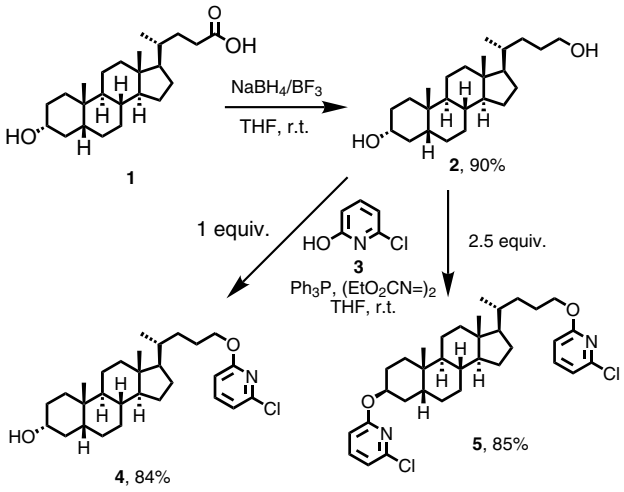
Abstract

3,24-Bis(6-chloropyridin-2-yloxy)cholane, obtained from 3,24-cholandiol via a Mitsunobu reaction, was successfully used for the synthesis of a variety of polyazamacrocycles using Pd-catalyzed amination reaction with linear polyamines. The competing formation of cyclodimers and other cyclic oligomers was found to be strongly dependent on the nature of the polyamines employed.

Macrocycles which contain 2–4 cholic acid fragments linked with various spacers are known as cholaphanes and are of great interest as molecular sensors. Steroidal fragments can be bridged with amide,[1–3] ester[4–8] groups, or with ethyleneglycol fragments.[9] Another type of steroid-based macrocycles resembles crown ethers and are formed from compounds with one steroid unit and one polyoxyalkyl chain attached.[10–13] Recently, we have elaborated another approach to steroid-based macrocycles which is based on the palladium-catalyzed amination of haloaryl derivatives of cholanediol with linear polyamines.[14,15] Now we have attempted the catalytic synthesis of steroid-based polyazamacrocycles using pyridine moieties as aromatic linkers. This choice is explained by the presence of an additional nitrogen atom in pyridine which can facilitate complexation towards cations and polar molecules and also by a possible increase in biological activity of the resulting compounds.

The synthesis of 3,24-cholanediol **2** in 90% yield was achieved by the reduction of the lithocholic acid **1** with borane in absolute THF. The Mitsunobu reaction[16] with 1 equiv of 6-chloropyridin-2-ol **3** provided monopyridinoxy derivative **4** in 84% yield (Scheme 1), in this case selective and complete substitution at C(24) occurred, which was not the case when using 3-bromophenol.[14] Treatment



Scheme 1. Synthesis of mono- and di(6-chloropyridin-2-yloxy)cholanes **4** and **5**.

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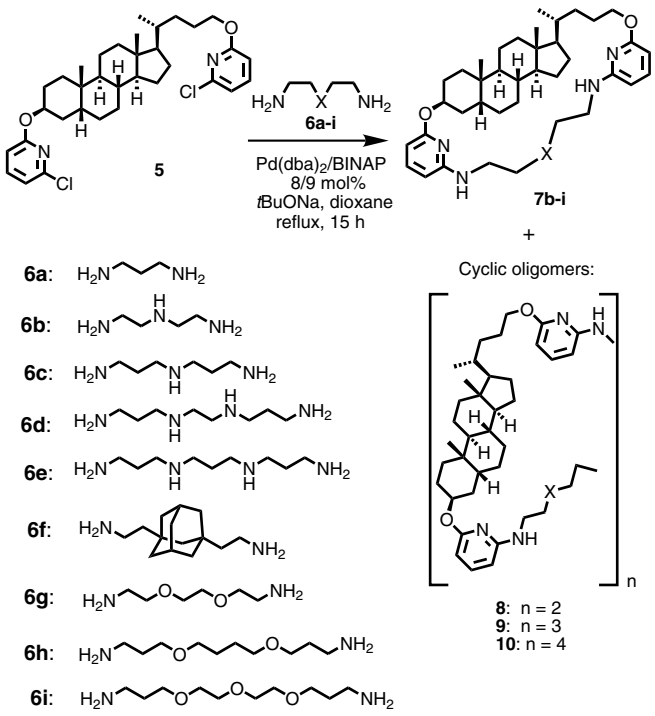

Scheme 2. Synthesis of macrocycles **7**.

of cholanediol **2** with 2.5 equiv of chloropyridinol under Mitsunobu conditions gave an 85% yield of 3,24-di(6-chloropyridin-2-yloxy)cholane **5** (Scheme 1).

Compound **5** was reacted in the palladium-catalyzed amination reactions[17,18] with various polyamines **6a–i** using 8 mol % $Pd(dba)_2$ and 9 mol % BINAP in boiling dioxane ($c = 0.02$ M), sodium *tert*-butoxide was employed as a base (Scheme 2). The reactions were complete in 15 h, and the composition of the reaction mixtures was identified by ^1H and ^{13}C NMR spectra prior to isolation of the products by column chromatography on silica gel. The yields of the target macrocycles **7** were found to be strongly dependent on the nature of the starting polyamines **6**, especially on the length of the aminoalkyl chains.

Application of the shortest 1,3-diaminopropane **6a** resulted in the formation of only cyclodimer **8a** in 38% yield (Table 1, entry 1). An additional amount (21%) of cyclodimer **8a** was obtained as a separate fraction in a 4:1:2 mole ratio with BINAP dioxide and dioxane. The same reaction with triamine **6b** gave 25% of cyclodimer **8b** and 46% of a mixture of cyclodimer **8b**, cyclotrimer **9b** and cyclotetramer **10b** (entry 2). The desired macrocycle **7b** was registered only as a tiny component of a mixture with cyclodimer **8b**, in a MALDI mass spectrum (m/z 615.7 [M^+]). The longer chain triamine **6c** provided the target macrocycle **7c** (10%) as a mixture with cyclodimer **8c** in ca. equimolar ratio, and a mixture of cyclodimer **8c**, cyclotrimer **9c** and cyclotetramer **10c** was obtained separately in 33% yield (entry 3). A better result was observed in the case of tetraamine **6d**, macrocycle **7d** was obtained in 26% yield though it contained cyclodimer **8d** as an admixture (entry 4). A slightly longer tetraamine **6e** provided the best yield of monomeric macrocycle **7e** with its cyclodimer **8e**, their yields being 29% and 66%, respectively (entry 5). 1,3-Bis(2-aminoethyl)adamantane **6f** reacted with di(chloropyridinyloxy)cholane **5** to afford macrocycle **7f** with a valuable adamantyl spacer in 15% yield, and cyclic oligomers were obtained as mixtures (22%, entry 6). Similar results were obtained with oxadiamines **6g–i**. While the shortest dioxadiamine **6g** afforded macrocycle **7g** in a low 6% yield (entry 7), the longer dioxadiamine **6h** gave **7h** in 22% yield (entry 8) and the reaction with trioxadiamine **6i** resulted in a 21% yield of macrocycle **7i** (entry 9). In these reactions cyclooligomers were isolated in 35–75% yields.

The results of the catalytic amination with 3,24-di(6-chloropyridin-2-yloxy)cholane **5** were found to be different from those described earlier for 3,24-di(3-bromophenoxy)cholane.[14] Yields of the target macrocycles **7** proved to be in general lower and also the formation of large amounts of cyclodimers and cyclic oligomers was observed.

This could be due to the lower reactivity of the chlorine in the amination reaction compared to bromine, which could lead to a lower rate of intramolecular amination after the first chlorine substitution with the nitrogen of the polyamine. This intermediate could react with a second molecule of compound **5** giving rise to oligomeric products though sufficiently dilute solutions ($c = 0.02$ M) were employed to suppress this undesirable effect. It should be noted that cyclodimers **8** can exist as two regioisomers (head-to-head and head-to-tail) which could not be distinguished using NMR spectra. For cyclic oligomers **9** and **10** of higher mass a greater number of possible regioisomers can be proposed. However, cyclic monomers **7** and

Table 1
Yields of macrocycles **7**

Entry	Amine	Yield of **7**	Yield of cyclic oligomers
1	**6a**	0	**8a**, 38%; in a 4:1:2 mole ratio with BINAP dioxide and dioxane, 21%
2	**6b**	Traces	**8b**, 25%; **8b**+**9b**+**10b**, 46%
3	**6c**	**7c**, 10%	**8c**, 11%; **8c**+**9c**+**10c**, 33%
4	**6d**	**7d**, 26%	
5	**6e**	**7e**, 29%	**8e**, 66%
6	**6f**	**7f**, 15%	Higher oligomers, 22%
7	**6g**	**7g**, 6%	**8g**, 7%; **9g**, 7%; higher oligomers, 61%
8	**6h**	**7h**, 22%	**8h**, 12%; higher oligomers, 23%
9	**6i**	**7i**, 21%	**8i**, 10%; higher oligomers, 33%

cyclodimers **8** can be distinguished from ^{1}H and ^{13}C NMR spectra of their pyridine moieties.[19]

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19. *Synthesis of 24-(6-chloropyridin-2-yloxy)cholane* **4**: A two-neck flask (250 ml) flushed with dry argon and equipped with a magnetic stirrer was charged with 3,24-cholanediol (3 mmol, 1.086 g, obtained from lithocholic acid[14]), absolute THF (75 ml), 2-chloro-6-hydroxypyridine **3** (3 mmol, 377 mg), triphenylphosphine (3 mmol, 786 mg) and diethyl azodicarboxylate (DEAD) (3 mmol, 534 mg, 1.38 ml of a 40% soln in toluene), and the reaction mixture was stirred at room temperature overnight. THF was partially evaporated in vacuo, diethyl ether was added to precipitate the majority of the triphenylphosphine oxide which was filtered off. The resulting clear solution was evaporated and chromatographed on silica gel using CH_2Cl_2 as eluent. Product **4** was obtained as a colorless oil, yield 1.186 g (84%). For the synthesis of 3,24-di(6-chloropyridin-2-yloxy)cholane **5**, 2.5 equiv of 2-chloro-6-hydroxypyridine **3**, triphenylphosphine and diethyl azodicarboxylate were employed. Yield (from 3.7 mmol, 1.344 g of 3,24-cholanediol **2**) 1.841 g (85%).
24-(6-Chloropyridin-2-yloxy)cholan-3-ol **4**: ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 0.60$ (s, 3H), 0.87 (s, 3H), 0.90 (d, $J = 6.5$ Hz, 3H), 0.95–1.96 (m, 28H), 2.14 (br s, 1H), 3.52–3.61 (m, 1H), 4.15–4.24 (m, 2H), 6.58 (d, $J = 8.0$ Hz, 1H), 6.82 (d, $J = 7.6$ Hz, 1H), 7.45 (t, $J = 7.8$ Hz, 1H); ^{13}C NMR (100.6 MHz, $CDCl_3$): $\delta = 12.1$, 18.6, 20.8, 23.4, 24.2, 25.5, 26.4, 27.2, 28.2, 30.6, 32.0, 34.6, 35.3, 35.5, 35.8, 36.5, 40.2, 40.4, 42.1, 42.7, 56.2, 56.5, 67.2, 71.9, 109.1, 116.0, 140.4, 148.3, 163.8; MALDI-TOF *m/z* 473.44 M^+.
3,24-Di(6-chloropyridin-2-yloxy)cholane **5**: ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 0.65$ (s, 3H), 0.94 (d, $J = 6.4$ Hz, 3H), 0.97 (s, 3H), 1.02–2.03 (m, 28H), 4.20–4.28 (m, 2H), 5.31 (br s, 1H), 6.60 (dd, $J = 8.2$, 0.6 Hz, 1H), 6.62 (dd, $J = 8.2$, 0.6, 1H), 6.82 (dd, $J = 7.4$, 0.6 Hz, 1H), 6.86 (dd, $J = 7.4$, 0.6 Hz, 1H), 7.46 (t, $J = 7.8$ Hz, 1H), 7.49 (t, $J = 7.8$ Hz, 1H); ^{13}C NMR (100.6 MHz, $CDCl_3$): $\delta = 12.1$, 18.6, 21.1, 23.8, 24.2, 24.8, 25.4, 26.2, 26.6, 28.2, 30.4, 30.6, 32.0, 34.9, 35.4, 35.7, 37.2, 39.9, 40.2, 42.7, 56.1, 56.6, 67.2, 71.9, 109.1, 109.7, 115.6, 115.9, 140.4 (2C), 148.3 (2C), 163.2, 163.7; MALDI-TOF *m/z* 584.48 M^+.
Typical procedure for the amination of steroid compounds **4** *and* **5**: A two-neck flask equipped with a magnetic stirrer and a condenser was charged with steroid compound **4** or **5** (0.5 mmol), absolute dioxane (25 ml), $Pd(dba)_2$ (24 mg, 8 mol %) and BINAP(28 mg, 9 mol %). The mixture was stirred for 2 min, and then appropriate polyamine **6** was added (0.5 mmol), and the reaction mixture was refluxed for 15 h. After cooling to ambient temperature and filtration dioxane was evaporated in vacuo and the residue was chromatographed on silica gel using a sequence of eluents: CH_2Cl_2, CH_2Cl_2–MeOH 500:1–3:1, CH_2Cl_2–MeOH–aqNH_3 100:20:1–10:4:1.
Selected spectroscopic data: *Cyclodimer* **8a**: 0.65 (s, 6H), 0.94 (d, $J = 6.4$ Hz, 6H), 0.96 (s, 6H), 0.99–2.03 (m, 60H), 3.35 (dt, $J = 7.3$, 6.1 Hz, 8H), 4.08–4.18 (m, 4H), 4.49 (br s, 4H), 5.15 (s, 2H), 5.88 (d, $J = 7.9$ Hz, 2H), 5.91 (d, $J = 8.1$ Hz, 2H), 5.98 (d, $J = 7.9$ Hz, 4H), 7.29 (t, $J = 7.6$ Hz, 2H), 7.30 (t, $J = 7.7$ Hz, 2H); 12.1 (2C), 18.7 (2C), 21.1 (2C), 23.8 (2C), 24.2 (2C), 25.0 (2C), 25.8 (2C), 26.3 (2C), 26.7 (2C), 28.3 (2C), 29.8 (2C), 30.7 (4C), 32.2 (2C), 34.9 (2C), 35.6 (2C), 35.7 (2C), 37.2 (2C), 39.8 (4C), 40.0 (2C), 40.3 (2C), 42.8 (2C), 56.3 (2C), 56.7 (2C), 66.3 (2C), 70.5 (2C), 97.3 (4C), 97.7 (2C), 98.2 (2C), 139.8 (2C), 139.9 (2C), 157.8 (4C), 163.0 (2C), 163.5 (2C); MALDI-TOF *m/z* 1173.23 M^+.
Macrocycle **7d**: ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 0.62$ (s, 3H), 0.92 (br s, 6H), 0.95–2.02 (m, 32H), 2.70–3.05 (m, 8H), 3.32 (br s, 4H), 4.06 (br s, 2H), 5.09 (br s, 1H), 5.30 (br s, 2H), 5.85–5.97 (m, 4H), 7.19–7.26 (m, 2H) (two NH protons of dialkylamino groups were not unambiguously assigned); ^{13}C NMR (100.6 MHz, $CDCl_3$): $\delta = 12.0$, 18.6, 21.0, 23.8, 24.1, 24.9, 25.6, 26.2, 26.6, 28.2, 30.2 (2C), 20.6 (2C), 32.1, 34.8, 35.6 (2C), 37.1, 39.9 (2C), 40.2, 40.3, 42.6, 46.6 (2C), 47.1, 47.6, 56.1, 56.5, 66.2, 70.4, 97.4, 97.6, 98.5, 98.6, 139.7, 139.9, 157.7, 157.8, 162.7, 163.3; MALDI-TOF *m/z* 686.63 M^+.
Macrocycle **7e**: ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 0.63$ (s, 3H), 0.92 (d, $J = 6.8$ Hz, 3H), 0.94 (s, 3H), 0.96–2.15 (m, 34H), 2.78–2.95 (m, 8H), 3.35–3.50 (m, 4H), 4.08 (br s, 2H), 4.14–4.28 (m, 2H), 5.30 (br s, 1H), 5.84 (d, $J = 7.6$ Hz, 1H), 5.93 (d, $J = 7.8$ Hz, 1H), 5.96 (d, $J = 7.6$ Hz, 2H), 7.23 (t, $J = 7.8$ Hz, 1H), 7.25 (d, $J = 7.6$ Hz, 1H) (two NH protons of dialkylamino groups were not unambiguously assigned); ^{13}C NMR (100.6 MHz, $CDCl_3$): $\delta = 12.0$, 18.8, 21.1, 23.0, 23.6, 24.1, 25.5, 26.3, 26.4, 27.7, 27.9, 28.2, 30.5, 31.0 (2C), 32.1, 34.2, 34.6, 35.3, 37.1, 39.0, 39.5, 40.3 (2C), 42.5, 46.6, 46.8, 46.9, 47.0, 53.9, 57.2, 66.3, 69.7, 97.2, 98.2,98.6, 99.0, 139.5, 139.7, 157.5, 157.6, 162.8, 163.1; MALDI-TOF *m/z* 701.44 $[M+H]^+$.
Cyclodimer **8e**: ^{1}H NMR (400 MHz, DMSO-d_6): $\delta = 0.58$ (s, 6H), 0.87 (br s, 12H), 0.90–2.02 (m, 68H), 2.75–3.00 (m, 16H), 3.24 (br s, 8H), 4.07 (br s, 4H), 5.13 (br s, 2H), 5.76 (br s, 4H), 5.96 (br s, 4H), 6.59 (br s, 4H), 7.19 (br s, 4H); (four NH protons of dialkylamino groups were not unambiguously assigned); ^{13}C NMR (100.6 MHz, DMSO-d_6): $\delta = 11.9$ (2C), 18.5 (2C), 23.0 (2C), 23.4 (2C), 23.7 (2C), 24.6 (2C), 25.3 (2C), 25.9 (2C), 26.1 (2C), 26.2 (2C), 27.8 (2C), 27.9 (2C), 28.6 (2C), 30.5 (2C), 30.6 (2C), 31.9 (2C), 34.5 (2C), 35.1 (2C), 35.2 (2C), 36.5 (2C), 38.0 (4C), 42.3 (2C), 44.5 (2C), 44.7 (2C), 44.8 (2C), 45.2 (2C), 55.7 (2C), 56.0 (2C), 65.2 (2C), 69.3 (2C), 95.4 (2C), 96.3 (2C), 99.0 (4C), 139.4 (4C), 157.7 (4C), 162.2 (2C), 162.8 (2C) (four carbon atoms in 39–40 ppm were hidden by CD_3 multiplet of the solvent); MALDI-TOF *m/z* 1402.15 $[M+H]^+$.
Macrocycle **7f**: ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 0.64$ (s, 3H), 0.92 (d, $J = 6.2$ Hz, 3H), 0.96 (s, 3H), 1.00–2.03 (m, 44H), 2.04 (s, 2H), 3.19 (br s, 4H), 4.09–4.16 (m, 2H), 4.23 (br s, 2H), 5.15 (br s, 1H), 5.85 (d, $J = 8.0$ Hz, 1H), 5.88 (d, $J = 7.9$ Hz, 1H), 5.97 (d, $J = 7.8$ Hz, 2H),

7.30 (t, $J = 7.9$ Hz, 1H), 7.31 (t, $J = 7.8$ Hz, 1H); ^{13}C NMR (100.6 MHz, $CDCl_3$): $\delta = 12.1$, 18.7, 21.1, 23.9, 24.3, 25.0, 25.8, 26.3, 26.7, 28.3, 29.0 (2C), 30.8 (2C), 32.2, 32.7 (2C), 34.9, 35.6, 35.7, 36.5, 37.2 (3C), 40.0, 40.3, 42.0 (4C), 42.8, 43.7 (2C), 47.7, 56.3, 56.7, 66.2, 70.4, 96.7, 97.2, 97.3, 98.2, 139.9 (2C), 157.8, 157.9, 162.9, 163.5; MALDI-TOF m/z 734.77 M^+.

Macrocycle **7g**: ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 0.64$ (s, 3H), 0.94 (d, $J = 7.0$ Hz, 3H), 0.95 (s, 3H), 0.99–2.05 (m, 28H), 3.40–3.48 (m, 2H), 3.58 (q, $J = 4.9$ Hz, 2H), 3.61–3.72 (m, 8H), 4.07–4.17 (m, 1H), 4.28–4.34 (m, 1H), 4.36 (br s, 1H), 4.67 (t, $J = 4.8$ Hz, 1H), 5.35 (br s, 1H), 5.87 (d, $J = 7.5$ Hz, 1H), 5.94 ($J = 8.1$ Hz, 1H), 5.96 (d, $J = 7.8$ Hz, 1H), 5.98 (d, $J = 7.9$ Hz, 1H), 7.24 (t, $J = 8.0$ Hz, 1H), 7.28 (t, $J = 7.9$ Hz, 1H); ^{13}C NMR (100.6 MHz, $CDCl_3$): $\delta = 12.1$, 18.6, 21.2, 22.6, 23.5, 24.0, 25.3, 26.0, 26.2, 28.3, 30.0, 30.3, 31.3, 34.5 (2C), 35.2, 37.2, 40.6, 40.7, 41.2, 41.4, 42.5, 53.4, 58.0, 66.3, 70.1, 70.2, 70.3, 70.5, 70.7, 98.2, 98.3, 98.6, 98.7, 139.5, 139.7, 157.1, 157.4, 163.0, 163.1; MALDI-TOF m/z 660.65 M^+.

Cyclodimer **8g**: ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 0.64$ (s, 6H), 0.92 (d, $J = 6.0$ Hz, 6H), 0.95 (s, 6H), 0.99–2.00 (m, 56H), 3.45 (br s, 8H), 3.64 (s, 8H), 3.67 (br s, 8H), 4.12 (br s, 4H), 4.79 (br s, 4H), 5.20 (br s, 2H), 5.86 (d, $J = 7.7$ Hz, 2H), 5.90 (d, $J = 7.8$ Hz, 2H), 5.98 (d, $J = 7.7$ Hz, 4H), 7.29 (t, $J = 7.7$ Hz, 4H); ^{13}C NMR (100.6 MHz, $CDCl_3$): $\delta = 12.0$ (2C), 18.6 (2C), 21.1 (2C), 23.8 (2C), 24.2 (2C), 24.9 (2C), 25.7 (2C), 26.3 (2C), 26.6 (2C), 28.3 (2C), 30.6 (2C), 30.7 (2C), 21.1 (2C), 34.8 (2C), 35.5 (2C), 35.6 (2C), 37.1 (2C), 39.9 (2C), 40.3 (2C), 41.7 (4C), 42.7 (2C), 56.1 (2C), 56.6 (2C), 66.2 (2C), 69.9 (4C), 70.2 (6C), 97.3 (4C), 98.0 (2C), 98.5 (2C), 139.7 (2C), 139.8 (2C), 157.6 (4C), 162.8 (2C), 163.4 (2C); MALDI-TOF m/z 1321.15 M^+.

Macrocycle **7h**: ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 0.64$ (s, 3H), 0.92 (d, $J = 6.8$ Hz, 3H), 0.95 (s, 3H), 0.99–2.05 (m, 36H), 3.25–3.48 (m, 8H), 3.55 (t, $J = 6.2$ Hz, 4H), 4.12–4.20 (m, 1H), 4.25–4.33 (m, 1H), 4.43 (br s, 1H), 5.00 (br s, 1H), 5.30 (br s, 1H), 5.80 (d, $J = 7.7$ Hz, 1H), 5.91 (d, $J = 7.8$ Hz, 1H), 5.95 (d, $J = 7.9$ Hz, 1H), 5.96 (d, $J = 7.7$ Hz, 1H), 7.28 (t, $J = 7.8$ Hz, 2H); ^{13}C NMR (100.6 MHz, $CDCl_3$): $\delta = 12.0$, 18.7, 21.1, 22.7, 23.8, 24.1, 25.2, 26.2, 26.4, 26.8, 26.9, 28.1, 29.3, 29.7, 30.3, 30.7, 30.9, 34.3, 34.7, 35.4, 37.2, 39.4, 40.3, 40.4, 41.6, 42.3, 53.8, 57.3, 66.4, 69.1, 69.6, 70.7, 71.0, 71.2, 96.4, 97.9, 98.2, 98.6, 139.6, 139.7, 157.6, 157.8, 162.8, 163.1; MALDI-TOF m/z 716.72 M^+.

Cyclodimer **8h**: 0.64 (s, 6H), 0.93 (d, $J = 5.9$ Hz, 6H), 0.96 (s, 6H), 1.00–2.02 (m, 72H), 3.32 (br s, 8H), 3.44 (br s, 8H), 3.52 (br s, 8H), 4.13 t, $J = 6.4$ Hz + 4.15–4.25 m (4H), 4.67 (br s, 4H), 5.16 br s + 5.21 br s (2H), 5.85 (d, $J = 7.4$ Hz, 2H), 5.89 (d, $J = 8.4$ Hz, 2H), 5.96 (d, $J = 7.8$ Hz, 4H), 7.28 (t, $J = 7.6$ Hz, 2H), 7.30 (d, $J = 7.7$ Hz, 2H); ^{13}C NMR (100.6 MHz, $CDCl_3$): $\delta = 12.0$ (2C), 18.6 (2C), 21.1 (2C), 23.8 (2C), 24.2 (2C), 25.0 (2C), 25.7 (2C), 26.2 (2C), 26.5 (4C), 26.6 (2C), 28.3 (2C), 29.4 (4C), 30.7 (4C), 32.1 (2C), 34.9 (2C), 35.5 (2C), 35.6 (2C), 37.1 (2C), 40.0 (2C), 40.1 (2C), 40.2 (2C), 40.3 (2C), 42.7 (2C), 56.1 + 56.2 (2C), 56.7 (2C), 66.1 (2C), 69.1 (2C), 69.2 (2C), 70.1 + 70.3 (2C), 70.8 (4C), 96.8 + 96.9 (2C), 97.1 + 97.2 (4C), 98.0 + 98.3 (2C), 139.7 + 139.8 (4C), 157.9 (4C), 162.8 (2C), 163.4 (2C); MALDI-TOF m/z 1433.33 M^+.

Macrocycle **7i**: ^{1}H NMR(400 MHz, $CDCl_3$): $\delta = 0.64$ (s, 3H), 0.91 (d, $J = 6.7$ Hz, 3H), 0.95 (s, 3H), 1.00–2.01 (m, 28H), 1.87 (quintet, $J = 6.1$ Hz, 2H), 1.91 (quintet, $J = 6.3$ Hz, 2H), 3.33 (br s, 2H), 3.38 (q, $J = 6.0$ Hz, 2H), 3.56–3.65 (m, 12H), 4.17–4.23 (m, 1H), 4.24–4.31 (m, 1H), 4.47 (br s, 1H), 4.75 (br s, 1H), 5.31 (br s, 1H), 5.81 (d, $J = 7.9$ Hz, 1H), 5.89 (d, $J = 7.7$ Hz, 1H), 5.94 (d, $J = 7.7$ Hz, 1H), 5.96 (d, $J = 7.8$ Hz, 1H), 7.26 (t, $J = 7.9$ Hz, 1H), 7.28 (t, $J = 7.9$ Hz, 1H); ^{13}C NMR (100.6 MHz, $CDCl_3$): $\delta = 12.0$, 18.7, 21.1, 23.0, 23.7, 24.1, 25.1, 26.1, 26.4, 28.0, 29.4, 29.5, 30.4, 30.9, 31.0, 34.4., 34.7, 35.4, 37.2, 39.3, 40.2, 40.3, 40.6, 42.5, 54.0, 57.2, 66.2, 69.4, 69.7, 70.1, 70.2, 70.5, 70.6, 70.7, 96.9, 97.8 (2C), 98.5, 139.6, 139.7, 157.5, 157.6, 162.8, 163.0; MALDI-TOF m/z 732.73 M^+.

Cyclodimer **8i**: ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 0.64$ (s, 6H), 0.92 (d, $J = 6.2$ Hz, 6H), 0.95 (s, 6H), 0.99–2.00 (m, 64H), 3.32 (q, $J = 6.9$ Hz, 8H), 3.52–3.67 (m, 24H), 4.12 (t, 5.6 Hz, 4H), 4.71 (br s, 4H), 5.19 (br s, 2H), 5.86 (d, $J = 7.9$ Hz, 2H), 5.89 (d, $J = 8.0$ Hz, 2H), 5.95 (d, $J = 7.8$ Hz, 4H), 7.27 (t, $J = 7.7$ Hz, 2H), 7.28 (t, $J = 8.0$ Hz, 2H); ^{13}C NMR (100.6 MHz, $CDCl_3$): $\delta = 12.1$ (2C), 18.6 (2C), 21.1 (2C), 23.8 (2C), 24.2 (2C), 25.0 (2C), 25.7 (2C), 26.3 (2C), 26.6 (2C), 28.3 (2C), 29.3 (4C), 30.7 (4C), 32.1 (2C), 34.9 (2C), 35.6 (2C), 35.7 (2C), 37.1 (2C), 39.7 (2C), 39.8 (2C), 40.0 (2C), 40.3 (2C), 42.7 (2C), 56.2 (2C), 56.7 (2C), 66.2 (2C), 69.4 (6C), 70.2 (4C), 70.6 (4C), 97.0 (4C), 97.1 (2C), 97.5 (2C), 139.8 (4C), 157.9 (4C), 162.8 (2C), 163.4 (2C); MALDI-TOF m/z 1465.33 M^+.