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Expedient Solution-Phase Synthesis and NMR Studies of Arylopeptoids

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The development of a highly convenient and efficient protocol for iterative solution-phase synthesis of shorter oligomers of *para*- and *meta*-arylopeptoids is described. Peptide coupling methods for accessing longer oligomers were studied: use of the new coupling reagent COMU was found to be the most efficient for creation of the tertiary benzamide bonds. The *cis*/*trans* isomerism of arylopeptoid backbones was studied by NMR and was found to be highly dependent on the nature of the side chains. Increasing bulkiness of the side chains favored the *cis* amide bond conformation; arylopeptoids possessing *tert*-butyl side chains contained exclusively *cis* amide bonds.

Introduction

There is ever growing interest in the development of foldamers, a term that covers non-natural oligomers with reduced complexity that are capable of mimicking the structures and functions of folded biopolymers in biomedical applications without drawbacks such as low half-lives and limited bioavailability.[1] Highly bio-inspired peptidomimetics (Figure 1, top) such as β-peptides[2] and peptoids[3] (*N*-substituted glycines and β-alanines) thus closely mimic the core structures of peptides and can adopt specific secondary or tertiary structures resembling those of naturally occurring biopolymers. Consequently, a range of interesting biological applications of these compounds have already been identified.[2,3] A more recently emerged area of interest is proteomimetics[4] that incorporate aromatics in their backbones, such as *N*-alkylated oligobenzanilides[5] and pyridine oligoamides[6] (Figure 1, bottom). Although the core structures are inherently only distantly related to the parent peptides, the aim is still to mimic the side chain presentation of biopolymers. To this end, limited studies on arylopeptoids,[7] a new class of peptoid-inspired oligomers with aromatic backbones, have recently been reported.[8] However, the reported solid-phase methodology is limited in scope and provides only mediocre yields and no conformational studies were undertaken.

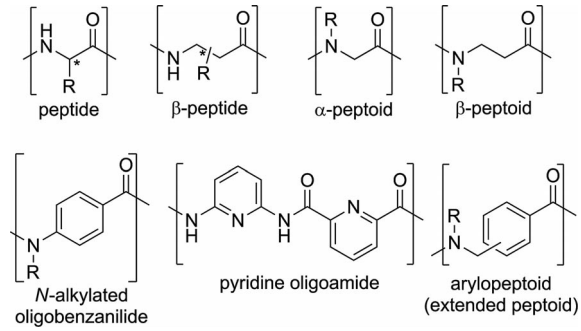

Figure 1. Peptides and peptidomimetics (top) and examples of proteomimetics and the structurally related arylopeptoids (bottom); * denotes a stereogenic centre.

We believe that these novel arylopeptoids might represent a new group of oligomers possessing folding propensities as a result of their relatively rigid aromatic backbones while still retaining the favorable characteristics of peptoids, such as large potential for diversity and straightforward synthesis amenable to automation. Here we present our results relating to the first solution-phase synthesis and conformational studies of a selected library of *para*- and *meta*-arylopeptoids. In an effort to elucidate the conformational preferences of these novel oligomers, we synthesized series bearing side chains of different bulk, including methyl, ethyl, isopropyl, or *tert*-butyl.

Results and Discussion

Thanks to the simplicity of their backbones, peptoids can be synthesized by a unique "submonomer" method in which the peptoid residues are created in a stepwise, iterative manner directly on the growing chain.[3] α-Peptoid residues are thus synthesized by an acylation/substitution cycle whereas β-peptoids are synthesized by an acylation/ad-

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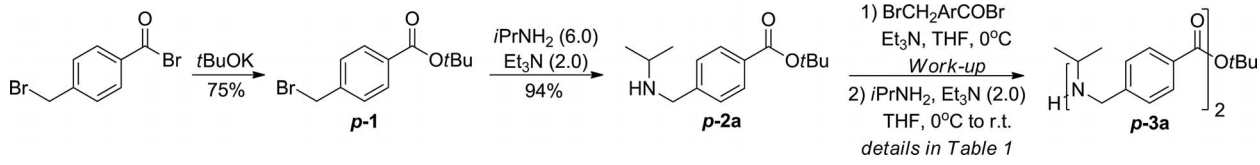


Scheme 1. "Submonomer" synthesis of arylopeptoids; see Table 1 for details.

Table 1. Optimization of the "submonomer" synthesis of arylopeptoids.

Entry	$BrCH_2ArCOBr$ [equiv.]	Et_3N [equiv.]	Workup	$iPrNH_2$ [equiv.]	Yield of ***p*-3a** [%][a]	Purity [%][b]
1	1.20	1.20	filtration	6.0	93	97
2	1.05	1.05	one-pot	2.0	76	>99
3	1.05	1.05	one-pot	4.0	85	>99
4	1.05	1.05	one-pot	6.0	87	>99
5	1.05	1.05	one-pot	8.0	92	>99
6	1.05	1.05	one-pot	10.0	94	>99
7	1.05	1.05	one-pot	20.0	96	>99

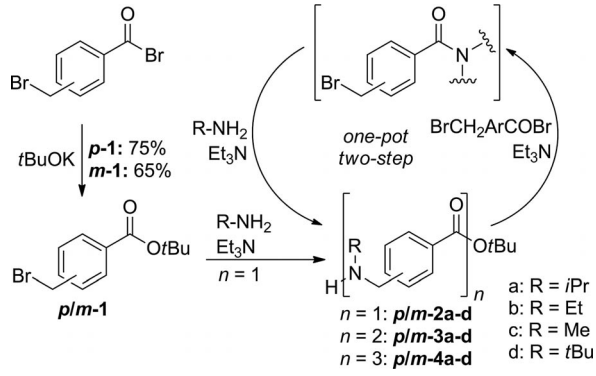
[a] Isolated yield after column chromatography. [b] Purity measured by HPLC.

dition cycle. In spite of the obvious structural differences, we hypothesized that we could adapt the convenient protocols we have previously developed for "submonomer" synthesis of α-peptoid residues to the synthesis of arylopeptoid residues.[9] As a model system for optimization of arylopeptoid chain elongation, we used the *para* family with the moderately bulky isopropyl side chain (see Scheme 1 and Table 1).

tert-Butyl 4-(bromomethyl)benzoate (***p*-1**), obtained from commercially available 4-(bromomethyl)benzoyl bromide, was thus treated with isopropylamine in THF in the presence of triethylamine to give the desired monomer ***p*-2a** in 94% yield. In comparison with α-peptoid residue synthesis,[9] we found it necessary to substitute filtration of the crude product to eliminate the formed ammonium salts with a basic aqueous wash before column chromatography.

We then turned to the ensuing chain elongation optimization. The monomer ***p*-2a** was treated with 4-(bromomethyl)benzoyl bromide (1.2 equiv.) in THF in the presence of triethylamine (1.2 equiv.), filtered, and then subjected to the same substitution reaction conditions as above. The desired dimer ***p*-3a** was obtained in an excellent 93% yield and 97% HPLC purity for the two steps (Table 1, Entry 1). We then found that with the use of only a slight excess of acylating reagent (1.05 equiv.) the whole residue synthesis could be performed as a highly convenient two-step one-pot procedure giving the desired product in 87% yield and >99% HPLC purity (Table 1, Entry 4). The overall yield of the residue synthesis depended strongly on the excess of isopropylamine used in the substitution step (Table 1, Entries 2–7) and the best compromise between amount of reagent amine needed and yield was 10 equiv. isopropylamine, which gave the dimer ***p*-3a** in 94% yield (Table 1, Entry 6).

The optimized protocol was then used for stepwise iterative synthesis of the monomers ***p*/*m*-2a**–**c**, the dimers ***p*/*m*-3a**–**c**, and the trimers ***p*/*m*-4a**–**c** in good to excellent yields and with excellent purities (see Scheme 2 and Table 2) by



Scheme 2. Iterative solution-phase synthesis of arylopeptoids; see Table 2 for yields.

Table 2. Yields for iterative solution-phase synthesis of arylopeptoids containing up to three residues.[a]

	n	*i*Pr	Yield [%][b]	Et	Yield [%][b]	Me	Yield [%][b]	*t*Bu	Yield [%][b]
para	1	***p*-2a**	96	***p*-2b**	93	***p*-2c**	87	***p*-2d**	85
	2	***p*-3a**	93	***p*-3b**	95	***p*-3c**	87	***p*-3d**	82
	3	***p*-4a**	92	***p*-4b**	86	***p*-4c**	79	***p*-4d**	82
meta	1	***m*-2a**	96	***m*-2b**	87	***m*-2c**	70	***m*-2d**	75
	2	***m*-3a**	90	***m*-3b**	83	***m*-3c**	65	***m*-3d**	81
	3	***m*-4a**	83	***m*-4b**	87	***m*-4c**	74	***m*-4d**	67

[a] For R = *i*Pr, Et, and Me the optimized conditions (Table 1, Entry 6) were used. For R = *t*Bu, 2.0 equiv. of acylating reagent was used and the acylated intermediates were purified by column chromatography. [b] Isolated yield after column chromatography; HPLC purity ≥ 97%.

starting from 4- and 3-(bromomethyl)benzoyl bromide. However, in the case of the series with the very bulky *tert*-butyl side chain, we found that use of a larger excess (2.0 equiv.) of the acylating reagents was needed in order to drive the reactions to completion. The acylated intermediates were therefore also purified by column chromatography in these series.

Although the iterative chain elongation may be continued, we instead envisioned the production of longer oligomers through coupling of shorter fragments by peptide-type coupling methods. Examples of more or less successful protocols for coupling of simple benzoic acids with secondary benzylic amines using a range of coupling reagents have been reported.[10] In order to find the optimal conditions for coupling of arylopeptoids we therefore screened a representative selection of coupling reagents and solvent compositions (Figure 2). The coupling of the arylopeptoid trimer ***p*-4a** with the acid ***p*-6a** to form the hexamer ***p*-7a** was used as a model system. The degrees of conversion of the coupling reactions were evaluated by quantitative HPLC determination of the free amine ***p*-4a** and hexamer ***p*-7a** (see the Supporting Information for details). The coupling reagents were initially tested in CH_2Cl_2 and the highest levels of conversion after 24 h were observed for COMU[11] (79%) and HATU (72%), followed by PyBOP (65%) and PyBroP (41%), and, by some distance, DPPA (7%) and DIC (1%). Accordingly, HPLC monitoring revealed that conversion of the free acids into the corresponding activated species was fastest with COMU (<2 min), HATU (<5 min), and PyBOP (<5 min).

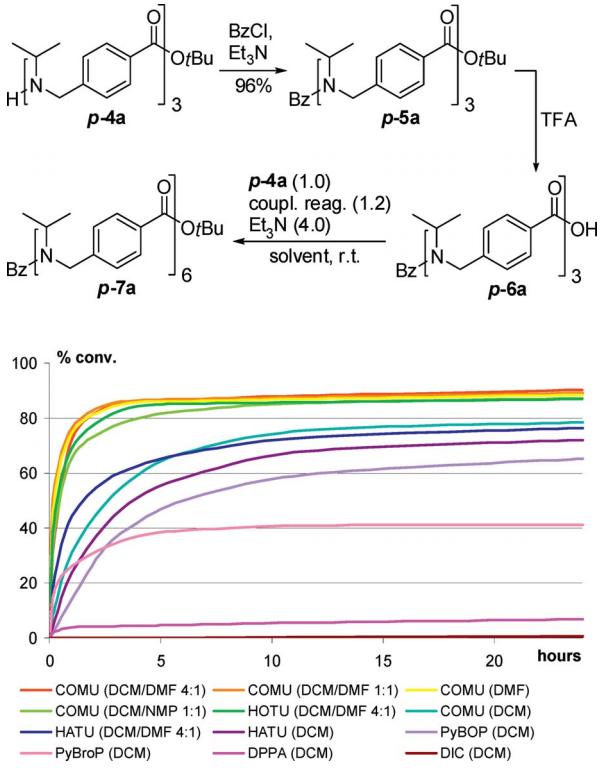
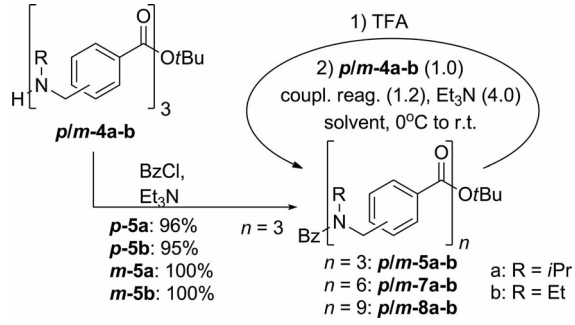


Figure 2. Screening of coupling reagents and conditions for peptide-type coupling of arylopeptoid fragments. Levels of conversion were determined by quantitative HPLC measurements (see the Supporting Information for details and larger versions of the chart).

As might be expected, the coupling reactions proceeded more rapidly and with higher levels of conversion in pure DMF or in CH_2Cl_2/DMF mixtures than in pure CH_2Cl_2. The most significant improvement in terms of overall level of conversion was observed for COMU (89–90%) whereas a less dramatic change was observed for HATU (76%). We furthermore found that DMF could be substituted with the less toxic NMP, and COMU with HOTU without any decrease in overall conversion. This study demonstrates the efficacy of the new uronium salt derived from Oxyma (COMU), which is safer and less expensive than benzotriazole-based uronium coupling reagents such as HATU.

Using these findings we then synthesized the hexamers ***p*/*m*-7a–b** and the nonamers ***p*/*m*-8a–b** (Scheme 3 and Table 3). For the *para* family we found, as expected, COMU in CH_2Cl_2/DMF (4:1) to be the best conditions and thanks to their low solubilities these oligomers were most easily purified by washing the obtained crude solids with EtOAc. The hexamers of the *para* family were obtained in pure form in very good yields in this way, but the inherent insolubility of these oligomers made the purification of the nonamers very difficult.



Scheme 3. Synthesis of arylopeptoid oligomers; see Table 3 for detailed conditions and yields.

Table 3. Detailed conditions and yields for synthesis of arylopeptoid oligomers.

	n	Conditions	*i*Pr	Yield [%]	Et	Yield [%]
para	6	COMU, CH_2Cl_2/DMF (4:1)	***p*-7a**	80[a]	***p*-7b**	74[a,c]
	9	COMU, CH_2Cl_2/DMF (4:1)	***p*-8a**	82[a]	***p*-8b**	55[a]
meta	6	HATU, DMF	***m*-7a**	77[b,d]	***m*-7b**	78[b]
	9	HATU, DMF	***m*-8a**	21[a]	***m*-8b**	32[b]

[a] Isolated yield; HPLC purity not determinable due to insolubility. [b] Isolated yield; HPLC purity ≥ 95%. [c] Use of HATU in DMF gave 72% yield. [d] Use of COMU or HOTU in CH_2Cl_2/DMF (4:1) gave lower yields and impure products.

For the *meta* family the use of COMU or HOTU proved problematic because separation of the oligomers from urea side products was impossible. We instead opted for coupling using HATU, which gave the desired pure oligomers after flash chromatography. Overall, the combination of submonomer- and peptide-type coupling methods allows facile access to longer oligomers of arylopeptoids than can be obtained from the current solid-phase methodology.[8]

It is well known that both *cis* and *trans* amide conformations may be significantly populated in aliphatic peptoids,[9b,12] and that the equilibrium may be controlled to some degree by appropriate choice of side chains.[13] Interestingly, we found the *cis*/*trans* conformations of arylopeptoid amides to be very sensitive towards the bulkiness of the side chains. Thus, in $CDCl_3$ at room temperature, only single sets of sharp signals were observed in the NMR spectra of *para*- and *meta*-arylopeptoids containing the highly bulky *tert*-butyl side chain. NOESY experiments with ***p*-3d** and ***m*-3d** showed these single sets of signals to correspond to the *cis* amide conformations (Figure 3; see the Supporting Information for details).

In contrast, the less bulky methyl, ethyl, and isopropyl series produced spectra with very broad signals in $CDCl_3$ at room temperature, indicating that these series existed in the intermediate exchange regime on the NMR timescale.

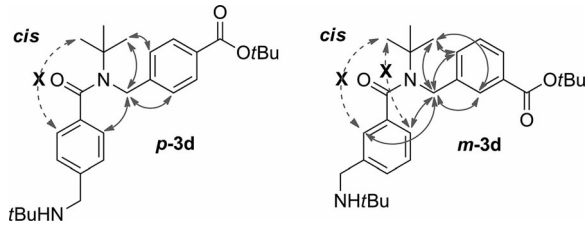


Figure 3. Most important NOESY correlations establishing the *cis* amide conformations of ***p*-3d** and ***m*-3d**.

Furthermore, partly overlapping sets of signals for carbons and/or protons in close proximity to the amide nitrogen(s) caused by the presence of *cis*/*trans* mixtures were observed. In general, the most pronounced difference in NMR chemical shift between the *cis* and *trans* isomers was observed for the backbone benzylic carbons and/or protons (i.e., CON-CH_2Ar). Throughout all three series, and independently of chain length and *para* or *meta* substitution patterns, the isomer showing a relative downfield chemical shift (approx. 4.8–4.6 ppm vs. 4.6–4.4 ppm) for the backbone benzylic protons remained the major isomer: approx. $56 \pm 2\%$ for the least bulky methyl series, $60 \pm 3\%$ for the ethyl series, and seemingly close to 100% for the moderately bulky isopropyl series. Unfortunately, *cis*/*trans* attribution through

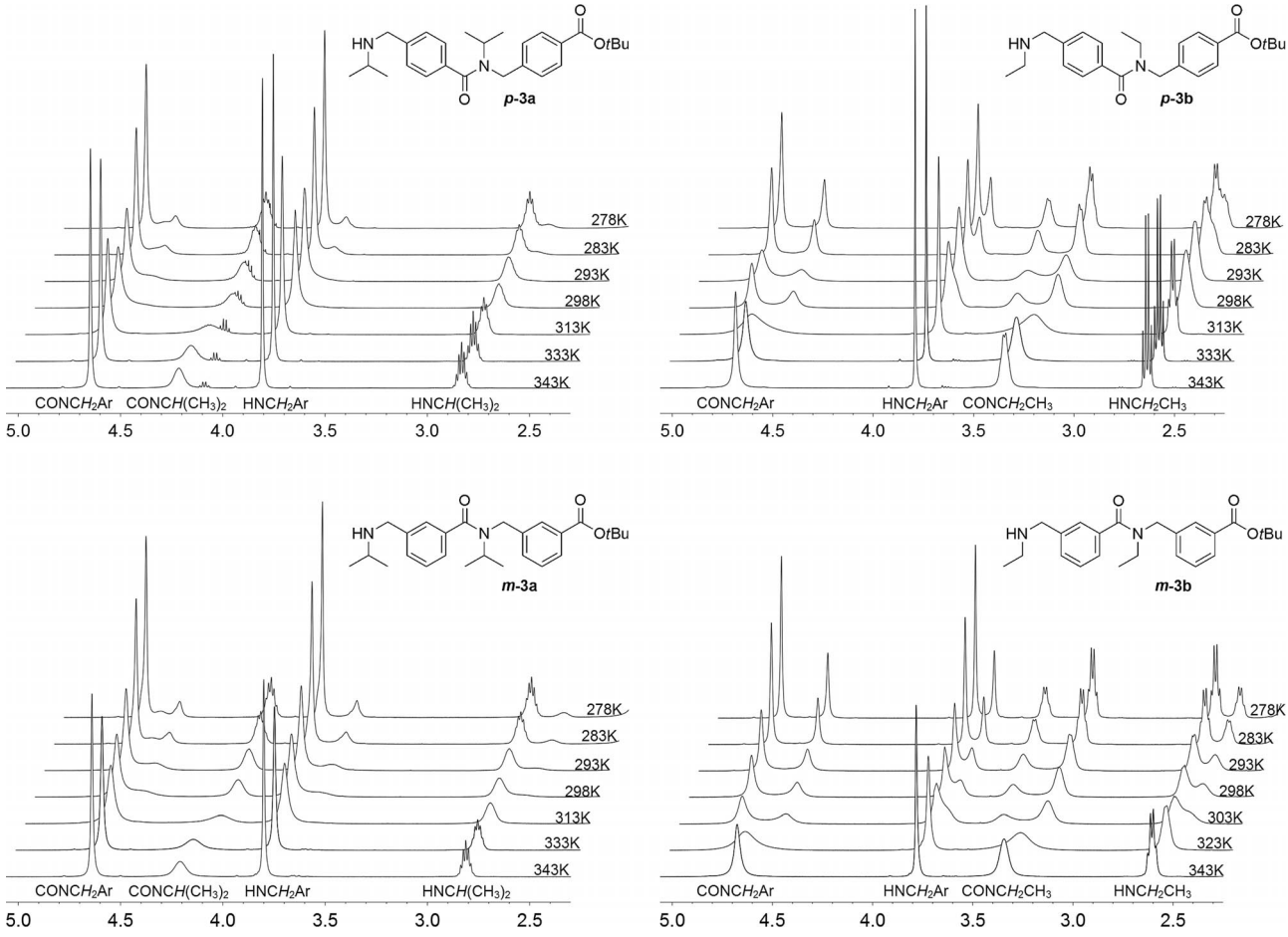


Figure 4. NMR temperature study on the dimers ***plm*-3a** and ***plm*-3b** in CD_3CN. Only a selected region of aliphatic protons is shown.

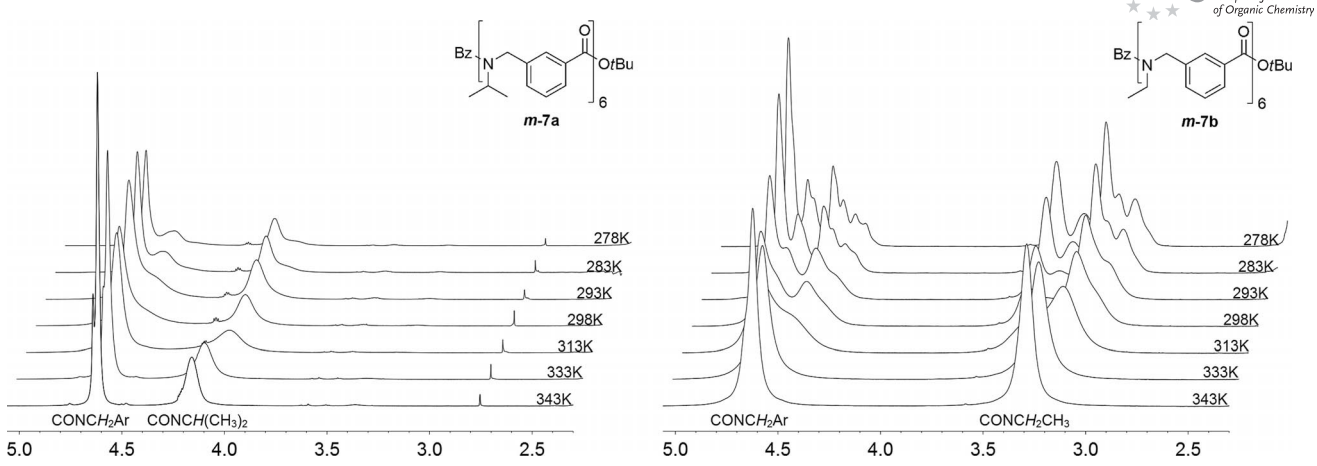


Figure 5. NMR temperature study on the hexamers ***m*-7a** and ***m*-7b** in CD_3CN. Only a selected region of aliphatic protons is shown.

NOESY experiments was not possible, due to overlapping signals in the aromatic region of the spectra. However, it can be assumed that the major isomers correspond to the *cis* isomers because it would be expected that the proportion of *cis* isomer should increase with increasing bulk of the side chains. Indeed, similar features have been observed in α-peptoids, in which an increase in the aliphatic side chain steric bulk likewise leads to a slightly favored *cis* amide configuration.[13] In the case of arylopeptoids this trend is thus much more pronounced and the *cis* amide configuration is always predominant over the *trans* one.

To investigate our observations further, we recorded the ^1H NMR spectra of the dimers ***p*/*m*-3a**, ***p*/*m*-3b**, and ***p*-3d** in CD_3CN over the 278–343 K temperature range.[14] As expected, no change was observed in the spectra of ***p*-3d**. In the spectra of ***p*-3b** (Figure 4, top right) and ***m*-3b** (Figure 4, bottom right), from the ethyl series, two distinct *cis*/*trans* signals in 64:36 and 65:35 ratios, respectively, were observed below room temperature. Above room temperature only a single, gradually sharpening set of signals was observed in each case. This indicates that these ethyl series compounds exist in a *cis*/*trans* ratio of approximately 65:35 below room temperature whereas the energy barrier of rotation about the amide bond is low enough to be overcome by heating above room temperature. As expected, the temperature studies likewise allowed for a more precise estimation of the *cis*/*trans* ratios in the isopropyl series. Thus, for ***p*-3a** (Figure 4, top left) and ***m*-3a** (Figure 4, bottom left), *cis*/*trans* ratios of 82:18 and 84:16, respectively, were observed below room temperature.

Although little or no differences between the *cis*/*trans* ratios of the *para* and *meta* families were observed in the above temperature study, better separation of the signals was observed in the *meta* families than in the *para* families. A similar study was therefore undertaken on the hexamers ***m*-7a** and ***m*-7b** (Figure 5). It is notable that whereas the hexamer ***m*-7a** (isopropyl series) showed a temperature profile reminiscent of that of the dimer ***m*-3a**, a very complex mixture of *cis*/*trans* rotamers was observed for the hexamer ***m*-7b** (ethyl series) below room temperature.

Conclusions

In summary, we have developed highly convenient and efficient protocols for the first solution-phase synthesis of *para*- and *meta*-arylopeptoids in which the residues are created in an iterative manner by one-pot two-step procedures. This methodology is scalable and therefore amenable to gram-scale synthesis. By development of efficient coupling protocols we have furthermore demonstrated a facile route to longer oligomers than previously possible. The amide conformations of arylopeptoids were found to be very sensitive towards the natures of the side chains attached to the amide nitrogens: increasing bulkiness of these favored the *cis* amide bond conformation, a phenomenon less marked in the parent peptoid family. Arylopeptoids with *tert*-butyl side chains thus contained exclusively *cis* amide bonds. Overall, these observations offer the promise of possible control of secondary structures for development as foldamers. We will continue to explore all aspects of arylopeptoids as potential foldamers, such as proteomimetics, and will report our findings in due course.

Experimental Section

General: CH_2Cl_2, DMF, Et_3N, Et_2O, NMP, and THF were dried with molecular sieves (4 Å). Technical grade 3-(bromomethyl)benzoyl bromide obtained from Matrix Scientific was distilled under reduced pressure before use. All other solvents and chemicals obtained from commercial sources (Acros Organics, Alfa Aesar, Fluka, and Sigma–Aldrich) were used as received. Melting points were determined with a Mettler Toledo MP70 melting point system (arylopeptoids **1**–**5**) or a Reichert microscope apparatus (arylopeptoids **7**–**8**) and are referenced to the melting points of benzophenone and benzoic acid. IR spectra were recorded with a Shimadzu FTIR-8400S spectrometer fitted with a Pike Technologies MIRacle™ ATR and $\tilde{\nu}$ values are expressed in cm^{-1}. NMR spectra were recorded with a Bruker Avance 300 MHz spectrometer (arylopeptoids **1**–**5**), a 400 MHz Bruker AC 400 spectrometer (arylopeptoids **7**–**8**), or a 500 MHz Bruker Avance 500 instrument (temperature studies). Chemical shifts are referenced to the residual solvent peak and *J* values are given in Hz. The following multiplicity abbrevi-

ations are used: (s) singlet, (d) doublet, (t) triplet, (q) quartet, (m) multiplet, and (br) broad. Where applicable, assignments were based on COSY, HMBC, HSQC and *J*-mod experiments. TLC was performed on Merck TLC aluminum sheets (silica gel 60, F_{254}). Progress of reactions was, when applicable, followed by HPLC, NMR, and/or TLC. Visualization of spots in TLC was achieved with UV light and/or ninhydrin in EtOH/AcOH. Flash chromatography was performed with Merck silica gel (60, 40–63 μm). Unless otherwise stated, flash chromatography was performed in the eluent system for which the R_f values are given. HRMS were recorded with a Micromass LCT apparatus fitted with an AP-ESI probe calibrated with Leu-enkephalin (arylopeptoids **2**–**5**) or a Micromass Q-Tof Micro (3000 V) apparatus with an internal lock mass (H_3PO_4) and an external lock mass (Leu-enkephalin) (arylopeptoids **7**–**8**). See the Supporting Information for details relating to HPLC analysis.

Method A. General Procedure for Synthesis of the First Arylopeptoid Residue: To a solution of ***p*-1** or ***m*-1** (1.0 equiv., 0.2 M) in THF at 0 °C under N_2 was added Et_3N (2.0 equiv.) followed by the chosen primary amine (10.0 equiv., either neat or as a 2 M solution in THF). After stirring overnight at room temp., the resulting mixture was concentrated under reduced pressure. The residue was taken up in EtOAc and washed with satd. aq. $NaHCO_3$ (1 ×) and brine (1 ×). The combined aqueous layers were extracted with EtOAc (1 ×) and the combined organic layers were dried with Na_2SO_4, filtered, and concentrated under reduced pressure. Flash chromatography of the residue yielded the desired product.

Method B. General Procedure for Synthesis of Arylopeptoid Residues (except those with *tert*-butyl side chains): To a solution of the secondary amine (1.0 equiv., 0.2 M) in THF at 0 °C under N_2 was added Et_3N (1.05 equiv.) followed by 4- or 3-(bromomethyl)benzoyl bromide (1.05 equiv.). After the mixture had been stirred for 1 h at 0 °C, Et_3N (2.0 equiv.) and then the chosen primary amine (10.0 equiv., either neat or as a 2 M solution in THF) were added. After stirring overnight at room temp., the resulting mixture was concentrated under reduced pressure. The residue was taken up in EtOAc (dimers) or CH_2Cl_2 (trimers) and washed with satd. aq. $NaHCO_3$ (1 ×) and brine (1 ×). The combined aqueous layers were extracted with EtOAc (dimers, 1 ×) or CH_2Cl_2 (trimers, 1 ×) and the combined organic layers were dried with Na_2SO_4, filtered, and concentrated under reduced pressure. Flash chromatography of the residue yielded the desired product.

Method C. General Procedure for Synthesis of Arylopeptoid Residues (*tert*-butyl side chains only): To a solution of the secondary amine (1.0 equiv., 0.2 M) in THF at 0 °C under N_2 was added Et_3N (2.0 equiv.) followed by 4- or 3-(bromomethyl)benzoyl bromide (2.0 equiv.). After stirring for 1 h at 0 °C, the resulting mixture was concentrated under reduced pressure. The residue was taken up in CH_2Cl_2 and washed with satd. aq. $NaHCO_3$/brine (1:1, 1 ×). The aqueous layer was extracted with CH_2Cl_2 (1 ×) and the combined organic layers were dried with Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was passed through a short silica gel column to yield the sufficiently pure acylated intermediate. To a solution of the acylated intermediate (1.0 equiv., 0.2 M) in THF at 0 °C under N_2 was added Et_3N (2.0 equiv.) followed by *tert*-butylamine (10.0 equiv.). After stirring overnight at room temp., the resulting mixture was concentrated under reduced pressure. The residue was taken up in CH_2Cl_2 and washed with satd. aq. $NaHCO_3$ (1 ×) and brine (1 ×). The combined aqueous layers were extracted with CH_2Cl_2 (1 ×) and the combined organic layers were dried with Na_2SO_4, filtered, and concentrated under reduced pressure. Flash chromatography of the residue yielded the desired product.

Method D. General Procedure for *N*-Terminal Benzoyl Protection of Arylopeptoids: To a solution of the secondary amine (1.0 equiv., 0.1 M) in CH_2Cl_2 at 0 °C under N_2 was added Et_3N (1.2 equiv.) followed by benzoyl chloride (1.1 equiv.). After stirring for 1 h at 0 °C, the resulting mixture was washed with satd. aq. $NaHCO_3$ (1 ×). The aqueous layer was extracted with CH_2Cl_2 (1 ×) and the combined organic layers were dried with Na_2SO_4, filtered, and concentrated under reduced pressure. Flash chromatography of the residue yielded the desired product.

Method E. General Procedure for *C*-Terminal Deprotection of Arylopeptoids: To a solution of the *C*-terminally protected arylopeptoid (0.080 mmol) in CH_2Cl_2 (0.8 mL) at 0 °C was added TFA (0.8 mL), and the resulting mixture was stirred for 3 h at 0 °C. The solvents were evaporated under reduced pressure and the residue was dried in vacuo to yield the crude acid intermediate as a pale yellowish foam.

Method F. General Procedure for Coupling of Arylopeptoid Oligomers with COMU: To a suspension of the *C*-terminally deprotected arylopeptoid (0.080 mmol) and *N*-terminally deprotected arylopeptoid (0.080 mmol) in CH_2Cl_2/DMF (4:1, 1.6 mL) at 0 °C under N_2 was added Et_3N (0.320 mmol, 4 equiv.) followed by COMU (0.096 mmol, 1.2 equiv.). The mixture was stirred for 72 h while being allowed to warm slowly to room temperature. CH_2Cl_2 (20 mL) was added to the mixture and the organic layer was washed with water (2 × 10 mL) and brine (10 mL). The organic layer was dried with Na_2SO_4, filtered, concentrated, and dried in vacuo. The pale yellow solid was washed with AcOEt (5 × 5 mL) to give the pure arylopeptoid oligomer.

Method G. General Procedure for Coupling of Arylopeptoid Oligomers with HATU: To a suspension of the *C*-terminally deprotected arylopeptoid (0.080 mmol) and *N*-terminally deprotected arylopeptoid (0.080 mmol) in DMF (1.6 mL) at 0 °C under N_2 was added Et_3N (0.320 mmol, 4 equiv.) followed by HATU (0.096 mmol, 1.2 equiv.). The mixture was stirred for 72 h while being allowed to warm slowly to room temperature. CH_2Cl_2 (20 mL) was added to the mixture and the organic layer was washed with water (4 × 10 mL) and brine (10 mL). The organic layer was dried with Na_2SO_4, filtered, concentrated and dried in vacuo. Flash chromatography of the residue yielded the desired product.

***tert*-Butyl 4-(Bromomethyl)benzoate (*p*-1):** A modified literature procedure was used.[15] A suspension of finely ground potassium *tert*-butoxide (2.24 g, 20.0 mmol) in Et_2O (200 mL) was added dropwise over 1.5 h at room temp. under N_2 to a solution of 4-(bromomethyl)benzoyl bromide (5.56 g, 20.0 mmol) in Et_2O (150 mL). The mixture was stirred for 2 h further at room temp. and was then filtered. The filtrate was washed with satd. aq. $NaHCO_3$ (50 mL), HCl (1 M, 50 mL), and brine (50 mL). The organic layer was dried with Na_2SO_4, filtered, and concentrated under reduced pressure. Flash chromatography of the residue yielded ***p*-1** (4.09 g, 75%) as a colorless solid. R_f (heptane/EtOAc 99:1) = 0.09; m.p. 54–56 °C (lit.[15] m.p. 58–59 °C). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.99–7.93 (m, 2 H), 7.46–7.40 (m, 2 H), 4.50 (s, 2 H), 1.59 (s, 9 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 165.1 (C_q), 142.0 (C_q), 131.9 (C_q), 129.9 (2 × CH), 128.8 (2 × CH), 81.2 (C_q), 32.4 (CH_2), 28.1 (3 × CH_3) ppm. NMR spectra were in full accordance with those reported in the literature.[15]

***tert*-Butyl 3-(Bromomethyl)benzoate (*m*-1):** Treatment of 3-(bromomethyl)benzoyl bromide (1.39 g, 5.00 mmol) by the same procedure as used in the synthesis of ***p*-1** yielded ***m*-1** (877 mg, 65%) as a colorless solid. R_f (heptane/EtOAc 99:1) = 0.05; m.p. 48–48.5 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.01–7.98 (m, 1 H), 7.96–7.90 (m, J = 7.7 Hz, 1 H), 7.58–7.53 (m, J = 7.7 Hz, 1 H),

7.40 (t, J = 7.7 Hz, 1 H), 4.52 (s, 2 H), 1.60 (s, 9 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 165.1 (C_q), 137.9 (C_q), 133.0 (CH), 132.6 (C_q), 129.8 (CH), 129.4 (CH), 128.8 (CH), 81.3 (C_q), 32.7 (CH_2), 28.2 (3 × CH_3) ppm. NMR spectra were in full accordance with those reported in the literature.[16]

***tert*-Butyl 4-[(Propan-2-ylamino)methyl]benzoate (*p*-2a):** Treatment of ***p*-1** (543 mg, 2.00 mmol) by Method A with isopropylamine yielded ***p*-2a** (480 mg, 96%) as a colorless oil. R_f (EtOAc/MeOH 95:5) = 0.19. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.96–7.90 (m, 2 H), 7.39–7.33 (m, 2 H), 3.82 (s, 2 H), 2.82 (dq, J = 6.2 Hz, 1 H), 1.58 (s, 9 H), 1.31–1.23 (br. s, 1 H), 1.08 (d, J = 6.2 Hz, 6 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 165.7 (C_q), 145.6 (C_q), 130.6 (C_q), 129.5 (2 × CH), 127.7 (2 × CH), 80.8 (C_q), 51.2 (CH_2), 48.0 (CH), 28.2 (3 × CH_3), 22.9 (2 × CH_3) ppm. HRMS (TOF MS ES$^+$): calcd. for $C_{15}H_{24}NO_2$ [M + H]$^+$ 250.1802; found 250.1803. HPLC purity: 99.9%.

Arylopeptoid Dimer *p*-3a: Treatment of ***p*-2a** (599 mg, 2.40 mmol) by Method B with isopropylamine yielded ***p*-3a** (946 mg, 93%) as a colorless solid. R_f (EtOAc/MeOH 80:20) = 0.13; m.p. 119.5–121.5 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.97–7.87 (m, 2 H), 7.46–7.20 (br. m, 6 H), 4.78–4.46 (br. s, 2 H, CONCH_2Ar), 4.26–4.02 [br. m, 1 H, CONCH(CH_3)$_2$], 3.78 (s, 2 H, HNCH_2Ar), 2.92–2.75 [m, 1 H, HNCH(CH_3)$_2$], 2.56–2.36 (br. s, 1 H), 1.56 (s, 9 H), 1.25–0.94 (br. m, 12 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 172.1 (C_q), 165.4 (C_q), 144.1 (C_q), 141.6 (C_q), 135.5 (C_q), 130.5 (C_q), 129.5 (2 × CH), 128.2 (2 × CH), 126.6 (2 × CH), 126.2 (2 × CH), 80.7 (C_q), 50.8 (CH_2, HNCH$_2$Ar), 50.6 [br, CH, CONCH(CH_3)$_2$], 48.0 [CH, HNCH(CH_3)$_2$], 43.3 (br, CH_2, CONCH$_2$Ar), 28.1 (3 × CH_3), 22.6 (2 × CH_3), 21.3 (br, 2 × CH_3) ppm. HRMS (TOF MS ES$^+$): calcd. for $C_{26}H_{37}N_2O_3$ [M + H]$^+$ 425.2799; found 425.2796. HPLC purity: 99.9%.

Arylopeptoid Trimer *p*-4a: Treatment of ***p*-3a** (1.27 g, 2.99 mmol) by Method B with isopropylamine yielded ***p*-4a** (1.65 g, 92%) as a colorless solid. R_f (EtOAc/MeOH 80:20) = 0.12; m.p. 153.5–155 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.97–7.91 (m, 2 H), 7.47–7.24 (br. m, 10 H), 4.78–4.46 (br. s, 4 H, 2 × CONCH_2Ar), 4.31–4.03 [br. m, 2 H, 2 × CONCH(CH_3)$_2$], 3.81 (s, 2 H, HNCH_2Ar), 2.87 [dq, J = 6.2 Hz, 1 H, HNCH(CH_3)$_2$], 1.59 (s, 9 H), 1.22–1.03 (br. m, 18 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 172.0, 171.9 (2 × C_q), 165.4 (C_q), 144.0 (C_q), 141.8, 140.6 (2 × C_q), 135.4, 135.3 (2 × C_q), 130.4 (C_q), 129.4 (2 × CH), 128.1, 126.8, 126.6, 126.3, 126.2 (10 × CH), 80.6 (C_q), 50.9 (CH_2, HNCH$_2$Ar), 50.6 [br, 2 × CH, 2 × CONCH(CH_3)$_2$], 48.1 [CH, HNCH(CH_3)$_2$], 43.1 (br, 2 × CH_2, 2 × CONCH$_2$Ar), 28.0 (3 × CH_3), 22.6 (2 × CH_3), 21.2 (br, 4 × CH_3) ppm. HRMS (TOF MS ES$^+$): calcd. for $C_{37}H_{50}N_3O_4$ [M + H]$^+$ 600.3796; found 600.3786. HPLC purity: 98.8%.

***tert*-Butyl 3-[(Propan-2-ylamino)methyl]benzoate (*m*-2a):** Treatment of ***m*-1** (548 mg, 2.02 mmol) by Method A with isopropylamine yielded ***m*-2a** (486 mg, 96%) as a pale yellowish oil. R_f (EtOAc/MeOH 95:5) = 0.16. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.93–7.90 (m, 1 H), 7.88–7.83 (m, J = 7.6 Hz, 1 H), 7.52–7.47 (m, J = 7.6 Hz, 1 H), 7.36 (t, J = 7.6 Hz, 1 H), 3.81 (s, 2 H), 2.85 (dq, J = 6.2 Hz, 1 H), 1.59 (s, 9 H), 1.44–1.34 (br. s, 1 H), 1.10 (d, J = 6.2 Hz, 6 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 165.8 (C_q), 140.9 (C_q), 132.2 (CH), 132.1 (C_q), 129.0 (CH), 128.2 (CH), 127.9 (CH), 80.9 (C_q), 51.2 (CH_2), 48.1 (CH), 28.2 (3 × CH_3), 22.9 (2 × CH_3) ppm. HRMS (TOF MS ES$^+$): calcd. for $C_{15}H_{24}NO_2$ [M + H]$^+$ 250.1802; found 250.1809. HPLC purity: 99.9%.

Arylopeptoid Dimer *m*-3a: Treatment of ***m*-2a** (425 mg, 1.70 mmol) by Method B with isopropylamine yielded ***m*-3a** (654 mg, 90%) as a pale yellowish oil. R_f (EtOAc/MeOH 80:20) = 0.15. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.98–7.86 (br. m, 1 H), 7.86–7.79 (m, J = 7.5 Hz, 1 H), 7.57–7.45 (br. m, 1 H), 7.45–7.15 (m, 5 H), 4.74–4.45 (br. s, 2 H, CONCH_2Ar), 4.21–4.03 [br. m, 1 H, CONCH(CH_3)$_2$], 3.85–3.65 (br. s, 2 H, HNCH_2Ar), 2.90–2.69 [m, 1 H, HNCH-(CH_3)$_2$], 2.02–1.80 (br. s, 1 H), 1.56 (s, 9 H), 1.30–0.95 (br. m, 12 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 172.1 (C_q), 165.4 (C_q), 141.0 (C_q), 139.3 (C_q), 137.1 (C_q), 132.0 (C_q), 131.0 (CH), 129.0 (CH), 128.4 (CH), 128.2 (CH), 125.8 (CH), 124.5 (CH), 127.8 (CH), 127.6 (CH), 80.8 (C_q), 50.9 (CH_2, HNCH$_2$Ar), 50.6 [br, CH, CONCH(CH_3)$_2$], 48.0 [CH, HNCH(CH_3)$_2$], 43.2 (br, CH_2, CON-CH$_2$Ar), 28.1 (3 × CH_3), 22.6 (2 × CH_3), 21.3 (br, 2 × CH_3) ppm. HRMS (TOF MS ES$^+$): calcd. for $C_{26}H_{37}N_2O_3$ [M + H]$^+$ 425.2799; found 425.2801. HPLC purity: 99.5%.

Arylopeptoid Trimer *m*-4a: Treatment of ***m*-3a** (510 mg, 1.20 mmol) by Method B with isopropylamine yielded ***m*-4a** (601 mg, 83%) as a colorless amorphous solid. R_f (EtOAc/MeOH 80:20) = 0.10. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.98–7.85 (br. m, 1 H), 7.82 (d, J = 7.6 Hz, 1 H), 7.58–7.12 (m, 10 H), 4.74–4.44 (br. s, 4 H, 2 × CONCH_2Ar), 4.22–4.00 [br. m, 2 H, 2 × CONCH(CH_3)$_2$], 3.82–3.68 (br. s, 2 H, HNCH_2Ar), 2.87–2.74 [m, 1 H, HNCH(CH_3)$_2$], 2.25–2.03 (br. s, 1 H), 1.56 (s, 9 H), 1.30–0.93 (br. m, 18 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 172.1 (C_q), 172.0 (C_q), 165.4 (C_q), 141.0, 139.6, 139.2, 137.1 (5C_q), 132.0 (C_q), 130.8 (CH), 129.0, 128.6, 128.4, 128.2, 125.8, 124.6, 124.5, 124.4 (9 × CH), 127.5 (CH), 80.8 (C_q), 50.9 (CH_2, HNCH$_2$Ar), 50.6 [br, 2 × CH, 2 × CONCH(CH_3)$_2$], 48.1 [CH, HNCH(CH_3)$_2$], 43.2 (br, 2 × CH_2, 2 × CONCH$_2$Ar), 28.0 (3 × CH_3), 22.6 (2 × CH_3), 21.3 (4 × CH_3) ppm. HRMS (TOF MS ES$^+$): calcd. for $C_{37}H_{50}N_3O_4$ [M + H]$^+$ 600.3796; found 600.3806. HPLC purity: 99.3%.

***tert*-Butyl 4-[(Ethylamino)methyl]benzoate (*p*-2b):** Treatment of ***p*-1** (543 mg, 2.00 mmol) by Method A with ethylamine (2 M) in THF yielded ***p*-2b** (438 mg, 93%) as a colorless gel. R_f (EtOAc/MeOH 90:10) = 0.16. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.96–7.90 (m, 2 H), 7.38–7.33 (m, 2 H), 3.83 (s, 2 H), 2.66 (q, J = 7.1 Hz, 2 H), 1.58 (s, 9 H), 1.45–1.40 (br. s, 1 H), 1.12 (t, J = 7.1 Hz, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 165.7 (C_q), 145.2 (C_q), 130.6 (C_q), 129.5 (2 × CH), 127.7 (2 × CH), 80.8 (C_q), 53.5 (CH_2), 43.6 (CH_2), 28.2 (3 × CH_3), 15.2 (CH_3) ppm. HRMS (TOF MS ES$^+$): calcd. for $C_{13}H_{20}NO_2$ [M + H]$^+$ 236.1645; found 236.1649. HPLC purity: 99.9%.

Arylopeptoid Dimer *p*-3b: Treatment of ***p*-2b** (377 mg, 1.60 mmol) by Method B with ethylamine (2 M) in THF and flash column chromatography in EtOAc/MeOH 90:10 to 80:20 yielded ***p*-3b** (604 mg, 95%) as a pale yellowish oil. R_f (EtOAc/MeOH 80:20) = 0.09. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.96–7.90 (m, 2 H), 7.41–7.15 (br. m, 6 H), 4.86–4.63 [br. s, 1.16 H, (c)-CONCH_2Ar], 4.63–4.39 [br. s, 0.84 H, (t)-CONCH_2Ar], 3.75 (s, 2 H, HNCH_2Ar), 3.56–3.32 [br. m, 0.84 H, (t)-CONCH_2CH$_3$], 3.32–3.05 [br. m, 1.16 H, (c)-CONCH_2CH$_3$], 2.62 (q, J = 6.9 Hz, 2 H, HNCH_2CH$_3$), 1.73–1.64 (br. s, 1 H), 1.54 (s, 9 H), 1.21–0.95 (br. m, 6 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 171.7 (C_q), 165.2 (C_q), 142.1 (br, C_q), 141.7 (C_q), 134.8 (C_q), 131.1 (C_q), 129.7 (2 × CH), 128.0 (2 × CH), 127.6, 126.4 (4 × CH), 80.8 (C_q), 53.3 (CH_2, HNCH$_2$Ar), 51.8 [br, 0.42 × CH_2, (t)-CONCH$_2$Ar], 46.9 [br, 0.58 × CH_2, (c)-CON-CH$_2$Ar], 43.5 (CH_2, HNCH$_2$CH$_3$), 43.0 [br, 0.58 × CH_2, (c)-CONCH$_2$CH$_3$], 39.8 [br, 0.42 × CH_2, (t)-CONCH$_2$CH$_3$], 28.0 (3 × CH_3), 15.0 (CH_3), 13.6 [br, 0.58 × CH_3, (c)-CONCH$_2$$CH_3$], 12.1 [br, 0.42 × CH_3, (t)-CONCH$_2$$CH_3$] ppm. HRMS (TOF MS ES$^+$): calcd. for $C_{24}H_{33}N_2O_3$ [M + H]$^+$ 397.2486; found 397.2481. HPLC purity: 99.9%.

Arylopeptoid Trimer *p*-4b: Treatment of ***p*-3b** (872 mg, 2.20 mmol) by Method B with ethylamine (2 M) in THF yielded ***p*-4b** (1.05 g, 86%) as a thick, colorless oil. R_f (EtOAc/MeOH 70:30) = 0.10. ^{1}H

NMR (300 MHz, $CDCl_3$): δ = 7.96–7.90 (m, 2 H), 7.42–7.08 (br. m, 10 H), 4.87–4.62 [br. s, 2.32 H, 2× (c)-CONCH_2Ar], 4.62–4.39 [br. s, 1.68 H, 2× (t)-CONCH_2Ar], 3.75 (s, 2 H, HNCH_2Ar), 3.56–3.32 [br. m, 1.68 H, 2× (t)-CONCH_2CH$_3$], 3.32–3.05 [br. m, 2.32 H, 2× (c)-CONCH_2CH$_3$], 2.62 (q, J = 7.0 Hz, 2 H, HNCH_2CH$_3$), 1.54 (s, 9 H), 1.42–1.37 (br. s, 1 H), 1.21–0.95 (br. m, 9 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 171.7 (C_q), 171.4 (C_q), 165.2 (C_q), 142.0, 139.0 (3×C_q), 135.4 (C_q), 134.8 (C_q), 131.1 (C_q), 129.7 (2×CH), 128.0, 127.5, 126.7, 126.4 (10×CH), 80.9 (C_q), 53.3 (CH_2, HNCH_2Ar), 51.8 [br, 0.84×CH_2, 2× (t)-CONCH_2Ar], 46.8 [br, 1.16×CH_2, 2× (c)-CONCH_2Ar], 43.5 (CH_2, HNCH_2CH$_3$), 43.0 [br, 1.16×CH_2, 2× (c)-CONCH_2CH$_3$], 39.8 [br, 0.84×CH_2, 2× (t)-CONCH_2CH$_3$], 28.0 (3×CH_3), 15.1 (CH_3), 13.6 [br, 1.16×CH_3, 2× (c)-CONCH$_2$CH_3], 12.1 [br, 0.84×CH_3, 2× (t)-CONCH$_2$CH_3] ppm. HRMS (TOF MS ES$^+$): calcd. for $C_{34}H_{44}N_3O_4$ [M + H]$^+$ 558.3326; found 558.3333. HPLC purity: 98.9%.

***tert*-Butyl 3-[(Ethylamino)methyl]benzoate (*m*-2b):** Treatment of ***m*-1** (814 mg, 3.00 mmol) by Method A with ethylamine (2 M) in THF yielded ***m*-2b** (649 mg, 87%) as a pale yellowish oil. R_f (EtOAc/MeOH 90:10) = 0.10. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.93–7.90 (m, 1 H), 7.89–7.84 (m, J = 7.6 Hz, 1 H), 7.52–7.47 (m, J = 7.6 Hz, 1 H), 7.36 (t, J = 7.6 Hz, 1 H), 3.83 (s, 2 H), 2.67 (q, J = 7.1 Hz, 2 H), 1.59 (s, 9 H), 1.51–1.45 (br. s, 1 H), 1.13 (t, J = 7.1 Hz, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 165.8 (C_q), 140.6 (C_q), 132.2 (CH), 132.1 (C_q), 129.0 (CH), 128.2 (CH), 128.0 (CH), 80.9 (C_q), 53.6 (CH_2), 43.6 (CH_2), 28.2 (3×CH_3), 15.2 (CH_3) ppm. HRMS (TOF MS ES$^+$): calcd. for $C_{13}H_{20}NO_2$ [M + H]$^+$ 236.1645; found 236.1642. HPLC purity: 99.9%.

Arylopeptoid Dimer *m*-3b: Treatment of ***m*-2b** (565 mg, 2.40 mmol) by Method B with ethylamine (2 M) in THF yielded ***m*-3b** (794 mg, 83%) as a pale yellowish oil. R_f (EtOAc/MeOH 80:20) = 0.10. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.94–7.70 (br. m, 2 H), 7.56–7.21 (br. m, 6 H), 4.88–4.62 [br. s, 1.16 H, (c)-CONCH_2Ar], 4.62–4.38 [br. s, 0.84 H, (t)-CONCH_2Ar], 3.76 (s, 2 H, HNCH_2Ar), 3.58–3.33 [br. m, 0.84 H, (t)-CONCH_2CH$_3$], 3.33–3.05 [br. m, 1.16 H, (c)-CONCH_2CH$_3$], 2.70–2.50 (m, 2 H, HNCH_2CH$_3$), 1.84–1.75 (br. s, 1 H), 1.55 (s, 9 H), 1.23–0.96 (br. m, 6 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 171.8 (C_q), 165.3 (C_q), 140.7 (C_q), 137.5 (C_q), 136.5 (C_q), 132.2 (C_q), 131.8 (CH), 130.5 (CH), 129.1 (CH), 128.5 (CH), 128.3 (CH), 127.8 (CH), 126.0 (CH), 124.7 (CH), 81.0 (C_q), 53.3 (CH_2, HNCH$_2$Ar), 51.8 [br, 0.42×CH_2, (t)-CONCH$_2$Ar], 46.7 [br, 0.58×CH_2, (c)-CONCH$_2$Ar], 43.4 (CH_2, HNCH$_2$CH$_3$), 43.0 [br, 0.58×CH_2, (c)-CONCH$_2$CH$_3$], 39.6 [br, 0.42×CH_2, (t)-CONCH$_2$CH$_3$], 28.0 (3×CH_3), 14.9 (CH_3), 13.6 [br, 0.58×CH_3, (c)-CONCH$_2$CH_3], 12.1 [br, 0.42×CH_3, (t)-CONCH$_2$CH_3] ppm. HRMS (TOF MS ES): calcd. for $C_{24}H_{33}N_2O_3$ [M + H]$^+$ 397.2486; found 397.2486. HPLC purity: 99.9%.

Arylopeptoid Trimer *m*-4b: Treatment of ***m*-3b** (635 mg, 1.60 mmol) by Method B with ethylamine (2 M) in THF yielded ***m*-4b** (781 mg, 87%) as a thick colorless oil. R_f (EtOAc/MeOH 70:30) = 0.11. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.96–7.69 (br. m, 2 H), 7.56–7.12 (br. m, 10 H), 4.88–4.60 [br. s, 2.40 H, 2× (c)-CONCH_2Ar], 4.60–4.32 [br. s, 1.60 H, 2× (t)-CONCH_2Ar], 3.76 (s, 2 H, HNCH_2Ar), 3.58–3.32 [br. m, 1.60 H, 2× (t)-CONCH_2CH$_3$], 3.33–3.02 [br. m, 2.40 H, 2× (c)-CONCH_2CH$_3$], 2.70–2.51 (m, 2 H, HNCH_2CH$_3$), 1.55 (s, 9 H), 1.39–1.28 (br. s, 1 H), 1.25–0.92 (br. m, 9 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 171.8 (C_q), 171.5 (C_q), 165.3 (C_q), 141.0 (C_q), 137.9 (C_q), 137.5 (C_q), 136.9 (C_q), 136.4 (C_q), 132.2 (C_q), 131.8, 129.0, 128.8, 128.6, 128.4, 128.3, 127.7, 126.9, 125.3, 124.6 (12×CH), 81.0 (C_q), 53.4 (CH_2, HNCH$_2$Ar), 51.7 [br, 0.80×CH_2, 2× (t)-CONCH$_2$Ar], 46.7 [br, 1.20×CH_2, 2× (c)-CONCH$_2$Ar], 43.3 (CH_2, HNCH$_2$CH$_3$), 43.0 [br, 1.20×CH_2, 2× (c)-CONCH$_2$CH$_3$], 39.6 [br, 0.80×CH_2, 2× (t)-CONCH$_2$CH$_3$], 28.0 (3×CH_3), 15.1 (CH_3), 13.6 [br, 1.20×CH_3, 2× (c)-CONCH$_2$CH_3], 12.1 [br, 0.80×CH_3, 2× (t)-CONCH$_2$CH_3] ppm. HRMS (TOF MS ES$^+$): calcd. for $C_{34}H_{44}N_3O_4$ [M + H]$^+$ 558.3326; found 558.3317. HPLC purity: 98.8%.

***tert*-Butyl 4-[(Methylamino)methyl]benzoate (*p*-2c):** Treatment of ***p*-1** (543 mg, 2.00 mmol) by Method A with methylamine (2 M) in THF yielded ***p*-2c** (387 mg, 87%) as a colorless gel. R_f (EtOAc/MeOH 80:20) = 0.12. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.96–7.92 (m, 2 H), 7.38–7.33 (m, 2 H), 3.79 (s, 2 H), 2.44 (s, 3 H), 1.66–1.63 (br. s, 1 H), 1.58 (s, 9 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 165.7 (C_q), 144.8 (C_q), 130.8 (C_q), 129.5 (2×CH), 127.8 (2×CH), 80.8 (C_q), 55.6 (CH_2), 35.9 (CH_3), 28.2 (3×CH_3) ppm. HRMS (TOF MS ES$^+$): calcd. for $C_{13}H_{20}NO_2$ [M + H]$^+$ 222.1489; found 222.1491. HPLC purity: 99.9%.

Arylopeptoid Dimer *p*-3c: Treatment of ***p*-2c** (354 mg, 1.60 mmol) by Method B with methylamine (2 M) in THF and flash column chromatography in EtOAc/MeOH 80:20 to 70:30 yielded ***p*-3c** (513 mg, 87%) as a pale yellowish solid. R_f (EtOAc/MeOH 70:30) = 0.05; m.p. 64–66 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.97–7.91 (m, 2 H), 7.41–7.24 (br. m, 4.90 H), 7.24–7.11 (br. m, 1.10 H), 4.84–4.65 [br. s, 1.10 H, (c)-CONCH_2Ar], 4.64–4.41 [br. s, 0.90 H, (t)-CONCH_2Ar], 3.71 (s, 2 H, HNCH_2Ar), 3.06–2.90 [br. s, 1.35 H, (t)-CONCH_3], 2.90–2.74 [br. s, 1.65 H, (c)-CONCH_3], 2.38 (s, 3 H, HNCH_3), 1.74–1.65 (br. s, 1 H), 1.54 (s, 9 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 172.1, 171.4 (C_q), 165.2 (C_q), 141.9 (C_q), 141.6 (0.55×C_q), 141.3 (0.45×C_q), 134.4 (C_q), 131.2 (C_q), 129.7 (2×CH), 128.0 (2×CH), 127.7, 126.9, 126.8, 126.2 (4×C_q), 80.9 (C_q), 55.4 (CH_2, HNCH$_2$Ar), 54.8 [br, 0.45×CH_2, (t)-CONCH$_2$Ar], 50.5 [br, 0.55×CH_2, (c)-CONCH$_2$Ar], 37.0 [br, 0.55×CH_3, (c)-CONCH_3], 35.8 (CH_3, HNCH_3), 33.2 [br, 0.45×CH_3, (t)-CONCH_3], 28.0 (3×CH_3) ppm. HRMS (TOF MS ES$^+$): calcd. for $C_{22}H_{29}N_2O_3$ [M + H]$^+$ 369.2173; found 369.2180. HPLC purity: 98.6%.

Arylopeptoid Trimer *p*-4c: Treatment of ***p*-3c** (442 mg, 1.20 mmol) by Method B with methylamine (2 M) in THF yielded ***p*-4c** (490 mg, 79%) as a colorless, amorphous solid. R_f (EtOAc/MeOH 70:30) = 0.05. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.97–7.92 (m, 2 H), 7.44–7.06 (br. m, 10 H), 4.83–4.62 [br. s, 2.20 H, 2× (c)-CONCH_2Ar], 4.62–4.39 [br. s, 1.80 H, 2× (t)-CONCH_2Ar], 3.71 (s, 2 H, HNCH_2Ar), 3.08–2.90 [br. m, 2.70 H, 2× (t)-CONCH_3], 2.90–2.74 [br. m, 3.30 H, 2× (c)-CONCH_3], 2.38 (s, 3 H, HNCH_3), 1.73–1.64 (br. s, 1 H), 1.55 (s, 9 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 172.0, 171.4, 171.1 (2×C_q), 165.2 (C_q), 141.9, 141.5, 141.0, 138.7, 138.4 (3×C_q), 135.0 (C_q), 134.4 (C_q), 131.2 (C_q), 129.7 (2×CH), 128.0, 127.7, 127.3, 127.0, 126.2 (10×CH), 80.9 (C_q), 55.4 (CH_2, HNCH_2Ar), 54.8 [br, 0.90×CH_2, 2× (t)-CONCH_2Ar], 50.4 [br, 1.10×CH_2, 2× (c)-CONCH_2Ar], 37.0 [br, 1.10×CH_3, 2× (c)-CONCH_3], 35.8 (CH_3, HNCH_3), 33.2 [br, 0.90×CH_3, 2× (t)-CONCH_3], 28.0 (3×CH_3) ppm. HRMS (TOF MS ES$^+$): calcd. for $C_{31}H_{38}N_3O_4$ [M + H]$^+$ 516.2857; found 516.2853. HPLC purity: 97.5%.

***tert*-Butyl 3-[(Methylamino)methyl]benzoate (*m*-2c):** Treatment of ***m*-1** (543 mg, 2.00 mmol) by Method A with methylamine (2 M) in THF yielded ***m*-2c** (312 mg, 70%) as a pale yellowish oil. R_f (EtOAc/MeOH 80:20) = 0.13. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.92–7.89 (m, 1 H), 7.89–7.84 (m, J = 7.6 Hz, 1 H), 7.52–7.46 (m, J = 7.6 Hz, 1 H), 7.36 (t, J = 7.6 Hz, 1 H), 3.78 (s, 2 H), 2.44 (s, 3 H), 2.05–2.00 (br. s, 1 H), 1.58 (s, 9 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 165.7 (C_q), 140.0 (C_q), 132.3 (CH), 132.1 (C_q), 129.1

(CH), 128.2 (CH), 128.1 (CH), 80.9 (C_q), 55.5 (CH_2), 35.8 (CH_3), 28.1 ($3\times CH_3$) ppm. HRMS (TOF MS ES$^+$): calcd. for $C_{13}H_{20}NO_2$ [M + H]$^+$ 222.1497; found 222.1491. HPLC purity: 99.9%.

Arylopeptoid Dimer *m*-3c: Treatment of ***m*-2c** (243 mg, 1.10 mmol) by Method B with methylamine (2 M) in THF yielded ***m*-3c** (264 mg, 65%) as a pale yellowish oil. R_f (EtOAc/MeOH 70:30) = 0.08. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.95–7.70 (br. m, 2 H), 7.55–7.24 (br. m, 6 H), 4.83–4.61 [br. s, 1.15 H, (c)-CONCH_2Ar], 4.61–4.40 [br. s, 0.85 H, (t)-CONCH_2Ar], 3.73 (s, 2 H, HNCH_2Ar), 3.06–2.91 [br. s, 1.27 H, (t)-CONCH_3], 2.91–2.76 [br. s, 1.73 H, (c)-CONCH_3], 2.44–2.32 (br. s, 3 H, HNCH_3), 2.30–2.23 (br. s, 1 H), 1.56 (s, 9 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 172.1, 171.5 (C_q), 165.3 (C_q), 140.3 (C_q), 137.1 (C_q), 136.1 (C_q), 132.3 (C_q), 131.9, 130.5 (CH), 129.3, 128.6, 128.5, 128.4, 127.7, 126.5, 125.4, 125.2 (7CH), 81.0 (C_q), 55.3 (CH_2, HNCH_2Ar), 54.8 [br, $0.42\times CH_2$, (t)-CONCH_2Ar], 50.4 [br, $0.58\times CH_2$, (c)-CONCH_2Ar], 37.0 [br, $0.58\times CH_3$, (c)-CONCH_3], 35.7 (CH_3, HNCH_3), 33.0 [br, $0.42\times CH_3$, (t)-CONCH_3], 28.0 ($3\times CH_3$) ppm. HRMS (TOF MS ES$^+$): calcd. for $C_{22}H_{29}N_2O_3$ [M + H]$^+$ 369.2173; found 369.2168. HPLC purity: 97.5%.

Arylopeptoid Trimer *m*-4c: Treatment of ***m*-3c** (206 mg, 0.56 mmol) by Method B with methylamine (2 M) in THF yielded ***m*-4c** (213 mg, 74%) as a pale yellowish oil. R_f (EtOAc/MeOH 70:30) = 0.05. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.96–7.70 (br. m, 2 H), 7.56–7.08 (br. m, 10 H), 4.82–4.61 [br. s, 2.28 H, 2× (c)-CONCH_2Ar], 4.61–4.38 [br. s, 1.72 H, 2× (t)-CONCH_2Ar], 3.73 (s, 2 H, HNCH_2Ar), 3.06–2.91 [br. s, 2.58 H, 2× (t)-CONCH_3], 2.91–2.74 [br. s, 3.42 H, 2× (c)-CONCH_3], 2.45–2.30 (br. s, 3 H, HNCH_3), 1.96–1.88 (br. s, 1 H), 1.56 (s, 9 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 171.5 (C_q), 171.2 (C_q), 165.3 (C_q), 140.5 (C_q), 137.4 (C_q), 137.0 (C_q), 136.5 (C_q), 136.0 (C_q), 132.3 (C_q), 131.9, 129.3, 128.8, 128.7, 128.6, 128.3, 127.7, 126.5, 126.0, 125.7, 125.4, 125.1 ($12\times CH$), 81.1 (C_q), 55.4 (CH_2, HNCH_2Ar), 54.7 [br, $0.86\times CH_2$, 2× (t)-CONCH_2Ar], 50.4 [br, $1.14\times CH_2$, 2× (c)-CONCH_2Ar], 37.0 [br, $1.14\times CH_3$, 2× (c)-CONCH_3], 35.8 (CH_3, HNCH_3), 33.1 [br, $0.86\times CH_3$, 2× (t)-CONCH_3], 28.0 ($3\times CH_3$) ppm. HRMS (TOF MS ES$^+$): calcd. for $C_{31}H_{38}N_3O_4$ [M + H]$^+$ 516.2857; found 516.2860. HPLC purity: 97.1%.

***tert*-Butyl 4-[(*tert*-Butylamino)methyl]benzoate (*p*-2d):** Treatment of ***p*-1** (543 mg, 2.00 mmol) by Method A with *tert*-butylamine yielded ***p*-2d** (446 mg, 85%) as a colorless solid. R_f (heptane/EtOAc 50:50) = 0.13; m.p. 24–25 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.95–7.90 (m, 2 H), 7.42–7.34 (m, 2 H), 3.78 (s, 2 H), 1.59 (s, 9 H), 1.17 (s, 9 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 165.7 (C_q), 146.4 (C_q), 130.4 (C_q), 129.4 ($2\times CH$), 127.8 ($2\times CH$), 80.7 (C_q), 50.7 (C_q), 46.9 (CH_2), 29.1 ($3\times CH_3$), 28.1 ($3\times CH_3$) ppm. HRMS (TOF MS ES$^+$): calcd. for $C_{16}H_{26}NO_2$ [M + H]$^+$ 264.1958; found 264.1961. HPLC purity: 99.9%.

Arylopeptoid Dimer *p*-3d: Treatment of ***p*-2d** (422 mg, 1.60 mmol) by Method C yielded ***p*-3d** (596 mg, 82%) as a colorless solid. Acylated intermediate: R_f (heptane/EtOAc 75:25) = 0.30. Data for ***p*-3d**: R_f (EtOAc/MeOH 95:5) = 0.12; m.p. 116.5–118 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.99–7.93 (m, 2 H, *o*-C_6H_4COO), 7.38–7.32 (m, 2 H, *o*-C_6H_4CON), 7.32–7.24 (m, 4 H, *m*-C_6H_4COO and *m*-C_6H_4CON), 4.64 (s, 2 H, CONCH_2Ar), 3.69 (s, 2 H, HNCH_2Ar), 1.61 (s, 9 H, O*t*Bu), 1.50 (s, 9 H, CON*t*Bu), 1.15 (s, 9 H, HN*t*Bu) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 173.7 (C_q, *C*ON), 165.3 (C_q, *C*OO), 144.8 (C_q, *p*-C_6H_4COO), 142.5 (C_q, *p*-C_6H_4CON), 137.4 (C_q, *ipso*-C_6H_4CON), 130.7 (C_q, *ipso*-C_6H_4COO), 129.5 ($2\times CH$, *o*-C_6H_4COO), 128.0 ($2\times CH$, *m*-C_6H_4CON), 126.0 ($2\times CH$, *o*-C_6H_4CON), 125.9 ($2\times CH$, *m*-C_6H_4COO), 80.9 (C_q, O*t*Bu), 58.0 (C_q, CON*t*Bu), 51.4 (CH_2, CONCH_2Ar), 50.6 (C_q, HN*t*Bu), 46.7 (CH_2, HNCH_2Ar), 29.0 ($3\times CH_3$, HN*t*Bu), 28.6 ($3\times CH_3$, CON*t*Bu), 28.1 ($3\times CH_3$, O*t*Bu) ppm. HRMS (TOF MS ES$^+$): calcd. for $C_{28}H_{41}N_2O_3$ [M + H]$^+$ 453.3112; found 453.3112. HPLC purity: 99.3%.

Arylopeptoid Trimer *p*-4d: Treatment of ***p*-3d** (362 mg, 0.80 mmol) by Method C yielded ***p*-4d** (422 mg, 82%) as a colorless solid. Acylated intermediate: R_f (heptane/EtOAc 60:40) = 0.31. Data for ***p*-4d**: R_f (EtOAc/MeOH 80:20) = 0.22; m.p. 88.5–90.5 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.94–7.89 (m, 2 H), 7.32–7.18 (m, 8 H), 7.10–7.05 (m, 2 H), 4.58 (s, 2 H, CONCH_2Ar), 4.49 (s, 2 H, CONCH_2Ar), 3.63 (s, 2 H, HNCH_2Ar), 1.56 (s, 9 H), 1.46 (s, 9 H), 1.40 (s, 9 H), 1.13 (s, 9 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 173.6 (C_q), 173.3 (C_q), 165.2 (C_q), 144.7 (C_q), 141.1, 137.6, 137.5 ($4\times C_q$), 130.8 (C_q), 129.6, 128.3, 126.3, 126.1, 126.0, 125.9 ($12\times CH$), 80.9 (C_q), 58.1 (C_q), 57.9 (C_q), 51.4, 51.2 ($2\times CH_2$ and C_q, 2× CON-*C*H_2Ar and HN*t*Bu), 46.6 (CH_2, HNCH_2Ar), 28.7, 28.6 ($9\times CH_3$), 28.1 ($3\times CH_3$) ppm. HRMS (TOF MS ES$^+$): calcd. for $C_{40}H_{56}N_3O_4$ [M + H]$^+$ 642.4265; found 642.4260. HPLC purity: 99.7%.

***tert*-Butyl 3-[(*tert*-Butylamino)methyl]benzoate (*m*-2d):** Treatment of ***m*-1** (543 mg, 2.00 mmol) by Method A with *tert*-butylamine yielded ***m*-2d** (393 mg, 75%) as a colorless oil. R_f (heptane/EtOAc 50:50) = 0.13. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.95–7.92 (m, 1 H), 7.88–7.82 (m, 1 H), 7.55–7.49 (m, 1 H), 7.35 (t, J = 7.6 Hz, 1 H), 3.76 (s, 2 H), 1.59 (s, 9 H), 1.18 (s, 9 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 165.9 (C_q), 141.7 (C_q), 132.4 (CH), 132.1 (C_q), 129.1 (CH), 128.2 (CH), 127.8 (CH), 80.9 (C_q), 50.7 (C_q), 47.0 (CH_2), 29.1 ($3\times CH_3$), 28.2 ($3\times CH_3$) ppm. HRMS (TOF MS ES$^+$): calcd. for $C_{16}H_{26}NO_2$ [M + H]$^+$ 264.1958; found 264.1955. HPLC purity: 99.6%.

Arylopeptoid Dimer *m*-3d: Treatment of ***m*-2d** (290 mg, 1.10 mmol) by Method C yielded ***m*-3d** (406 mg, 81%) as a colorless oil. Acylated intermediate: R_f (heptane/EtOAc 75:25) = 0.32. Data for ***m*-3d**: R_f (EtOAc/MeOH 90:10) = 0.22. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.87–7.82 (m, 1 H, *o*-C_6H_4COO), 7.84–7.80 (s, 1 H, *o*′-C_6H_4COO), 7.45–7.36 (m, 2 H, *m*-C_6H_4COO and *p*-C_6H_4COO), 7.34–7.30 (s, 1 H, *o*′-C_6H_4CON), 7.30–7.24 (m, 1 H, *p*-C_6H_4CON), 7.23–7.16 (m, 2 H, *o*-C_6H_4CON and *m*-C_6H_4CON), 4.61 (s, 2 H, CONCH_2Ar), 3.62 (s, 2 H, HNCH_2Ar), 1.59 (s, 9 H, O*t*Bu), 1.51 (s, 9 H, CON*t*Bu), 1.10 (s, 9 H, HN*t*Bu) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 173.8 (C_q, *C*ON), 165.3 (C_q, *C*OO), 141.3 (C_q, *m*′-C_6H_4CON), 140.4 (C_q, *m*′-C_6H_4COO), 139.1 (C_q, *ipso*-C_6H_4CON), 132.2 (C_q, *ipso*-C_6H_4COO), 130.0 (CH, *p*-C_6H_4COO), 129.0 (CH, *p*-C_6H_4CON), 128.3 (CH, *m*-C_6H_4CON), 128.3 (CH, *m*-C_6H_4COO), 127.9 (CH, *o*-C_6H_4COO), 127.1 (CH, *o*′-C_6H_4COO), 125.6 (CH, *o*′-C_6H_4CON), 124.2 (CH, *o*-C_6H_4CON), 81.1 (C_q, O*t*Bu), 58.0 (C_q, CON*t*Bu), 51.2 (CH_2, CONCH_2Ar), 50.8 (C_q, HN*t*Bu), 46.8 (CH_2, HNCH_2Ar), 28.9 ($3\times CH_3$, HN*t*Bu), 28.6 ($3\times CH_3$, CON*t*Bu), 28.1 ($3\times CH_3$, O*t*Bu) ppm. HRMS (TOF MS ES$^+$): calcd. for $C_{28}H_{41}N_2O_3$ [M + H]$^+$ 453.3112; found 453.3112. HPLC purity: 99.3%.

Arylopeptoid Trimer *m*-4d: Treatment of ***m*-3d** (294 mg, 0.65 mmol) by Method C yielded ***m*-4d** (280 mg, 67%) as a colorless solid. Acylated intermediate: R_f (heptane/EtOAc 60:40) = 0.39. Data for ***m*-4d**: R_f (EtOAc/MeOH 80:20) = 0.20; m.p. 73–76 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.85–7.79 (m, 1 H), 7.79–7.76 (s, 1 H), 7.36–7.31 (m, 2 H), 7.31–7.17 (m, 5 H), 7.15–7.06 (m, 3 H), 4.56 (s, 2 H, CONCH_2Ar), 4.46 (s, 2 H, CONCH_2Ar), 3.60 (s, 2 H, HNCH_2Ar), 1.56 (s, 9 H), 1.47 (s, 9 H), 1.38 (s, 9 H), 1.11 (s, 9 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 173.7 (C_q), 173.3 (C_q), 165.2 (C_q), 140.4, 140.0, 139.3, 139.0 ($5C_q$), 132.3 (C_q), 129.0 (CH), 129.2 (CH), 128.4 (CH), 128.3 (CH), 128.0 (CH), 126.8 (CH), 126.0

(CH), 124.5 (CH), 124.4 (CH), 124.0 (CH), 128.5 (CH), 127.0 (CH), 81.1 (C_q), 58.1 (C_q), 57.9 (C_q), 51.5 (C_q), 51.2 (CH_2, CON-*C*H_2Ar), 51.1 (CH_2, CON*C*H_2Ar), 46.6 (CH_2, HN*C*H_2Ar), 28.6 (3 × CH_3), 28.6 (3 × CH_3), 28.6 (3 × CH_3), 28.1 (3 × CH_3) ppm. HRMS (TOF MS ES$^+$): calcd. for $C_{40}H_{56}N_3O_4$ [M + H]$^+$ 642.4265; found 642.4261. HPLC purity: 99.9%.

Arylopeptoid Trimer *p*-5a: Treatment of ***p*-4a** (600 mg, 1.00 mmol) by Method D yielded ***p*-5a** (674 mg, 96%) as a colorless solid. R_f (EtOAc) = 0.59; m.p. 193.5–195 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.96–7.87 (m, 2 H), 7.47–7.21 (br. m, 15 H), 4.76–4.49 (br. s, 6 H, 3 × CONC*H*$_2$Ar), 4.30–4.00 [br. m, 3 H, 3 × CONC*H*$(CH_3)_2$], 1.55 (s, 9 H), 1.27–0.95 (br. m, 18 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 172.1, 172.0 (3 × C_q), 165.4 (C_q), 144.0 (C_q), 140.6, 136.9, 135.3 (5 × C_q), 130.5 (C_q), 129.4 (2 × CH), 129.2, 128.4, 126.8, 126.6, 126.3, 126.0 (15 × CH), 80.7 (C_q), 50.6 [br, 3 × CH, 3 × CONC*H*$(CH_3)_2$], 43.2 (br, 3 × CH_2, 3 × CONC*H*$_2$Ar), 28.0 (3 × CH_3), 21.2 (6 × CH_3) ppm. HRMS (TOF MS ES$^+$): calcd. for $C_{44}H_{54}N_3O_5$ [M + H]$^+$ 704.4058; found 704.4055. HPLC purity: 99.2%.

Arylopeptoid Hexamer *p*-7a: Deprotection of ***p*-5a** (56 mg, 0.080 mmol) by Method E and subsequent coupling with ***p*-4a** (48 mg, 0.080 mmol) by Method F yielded ***p*-7a** (79 mg, 80%) as a colorless solid. R_f (CH_2Cl_2/MeOH 95:5) = 0.21; m.p. 226 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.91 (d, J = 8 Hz, 2 H), 7.49–7.21 (br. m, 27 H), 4.65 (br. s, 12 H, 6 × CONC*H*$_2$Ar), 4.40–4.02 [br. m, 6 H, 6 × CONC*H*$(CH_3)_2$], 1.56 (s, 9 H), 1.29–0.95 (br. m, 36 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 172.2 (6 × C_q), 165.7 (C_q), 142.9 (C_q), 140.8, 137.0, 135.4 (11 × C_q), 130.6 (C_q), 129.4 (2 × CH), 129.6, 128.6, 126.9, 126.5, 126.2 (27 × CH), 80.9 (C_q), 50.8 [br, 6 × CH, 6 × CONC*H*$(CH_3)_2$], 43.4 (br, 6 × CH_2, 6 × CONC*H*$_2$Ar), 28.2 (3 × CH_3), 21.4 (br, 12 × CH_3) ppm. HRMS (TOF MS ES$^+$): calcd. for $C_{77}H_{94}N_6O_8$ [M + 2H]$^{2+}$ *m*/*z* 615.3567; found 615.3547. HPLC purity indeterminable due to insolubility.

Arylopeptoid Nonamer *p*-8a: Deprotection of ***p*-7a** (37 mg, 0.030 mmol) by Method E and subsequent coupling with ***p*-4a** (18 mg, 0.030 mmol) by Method F yielded ***p*-8a** (43 mg, 82%) as a colorless solid. R_f (CH_2Cl_2/MeOH 95:5) = 0.31; m.p. 270 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.93 (br. s, 2 H), 7.51–7.28 (br. m, 39 H), 4.85–4.48 (m, 18 H, 9 × CONC*H*$_2$Ar), 4.30–4.02 [m, 9 H, 9 × CONC*H*$(CH_3)_2$], 1.57 (s, 9 H), 1.32–0.91 (m, 54 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 172.3 (9 × C_q), 165.7 (C_q), 144.3 (C_q), 140.8, 137.0, 135.3 (14 × C_q), 130.9 (C_q), 130.2, 129.7, 129.5, 128.7, 127.1, 126.6, 126.3 (39 × CH), 80.9 (C_q), 50.9 [br, 9 × CH, 9 × CONC*H*$(CH_3)_2$], 43.4 (br, 9 × CH_2, 9 × CONC*H*$_2$Ar), 28.3 (3 × CH_3), 21.5 (br, 18 × CH_3) ppm. HRMS (TOF MS ES$^+$): calcd. for $C_{110}H_{131}N_9O_{11}Na_2$ [M + 2Na]$^{2+}$ *m*/*z* 899.9882; found 899.9861. HPLC purity indeterminable due to insolubility.

Arylopeptoid Trimer *m*-5a: Treatment of ***m*-4a** (300 mg, 0.50 mmol) by Method D yielded ***m*-5a** (353 mg, 100%) as a colorless solid. R_f (EtOAc) = 0.63; m.p. 68–71 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.00–7.87 (br. m, 1 H), 7.84 (d, J = 7.6 Hz, 1 H), 7.56–7.08 (m, 15 H), 4.76–4.45 (br. s, 6 H, 3 × CONC*H*$_2$Ar), 4.30–4.95 [br. m, 3 H, 3 × CONC*H*$(CH_3)_2$], 1.57 (s, 9 H), 1.35–0.90 (br. m, 18 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 172.1, 172.0 (3 × C_q), 165.4 (C_q), 139.7, 139.3, 137.1, 136.9 (6 × C_q), 132.0 (C_q), 130.8 (CH), 129.2, 128.6, 128.4, 128.2, 126.0, 124.5 (14 × CH), 127.7 (CH), 127.6 (CH), 80.8 (C_q), 50.6 [br, 3 × CH, 3 × CONC*H*$(CH_3)_2$], 43.2 (br, 3 × CH_2, 3 × CONC*H*$_2$Ar), 28.1 (3 × CH_3), 21.2 (br, 6 × CH_3) ppm. HRMS (TOF MS ES$^+$): calcd. for $C_{44}H_{54}N_3O_5$ [M + H]$^+$ 704.4058; found 704.4064. HPLC purity: 98.5%.

Arylopeptoid Hexamer *m*-7a: Deprotection of ***m*-5a** (56 mg, 0.080 mmol) by Method E and subsequent coupling with ***m*-4a** (48 mg, 0.080 mmol) by Method G yielded ***m*-7a** (75 mg, 77%) as a colorless foam. R_f (AcOEt/MeOH 95:5) = 0.31. ^{1}H NMR (400 MHz, CD_3OD): δ = 8.11–8.00 (m, 1 H), 7.94–7.81 (m, 1 H), 7.66–7.12 (m, 27 H), 4.85–4.48 (br. s, 12 H, 6 × CONC*H*$_2$Ar), 4.28–4.00 [br. m, 6 H, 6 × CONC*H*$(CH_3)_2$], 1.61 (s, 9 H), 1.42–0.95 (br. m, 36 H) ppm. ^{13}C NMR (100 MHz, CD_3OD): δ = 174.3 (6C_q), 167.1 (C_q), 141.5, 140.9, 138.2 (12 × C_q), 133.3 (C_q), 132.3 (CH), 130.8, 130.1, 129.9, 129.6, 129.3, 127.1, 125.7 (26 × CH), 128.6 (CH), 128.5 (CH), 82.3 (C_q), 52.6 [br, 6 × CH, 6 × CONC*H*-$(CH_3)_2$], 44.4 (br, 6 × CH_2, 6 × CONC*H*$_2$Ar), 28.5 (3 × CH_3), 21.5 (br, 12 × CH_3) ppm. HRMS (TOF MS ES$^+$): calcd. for $C_{77}H_{92}N_6O_8Na_2$ [M + 2Na]$^{2+}$ *m*/*z* 637.3386; found 637.3380. HPLC purity: 95.5%.

Arylopeptoid Nonamer *m*-8a: Deprotection of ***m*-7a** (49 mg, 0.040 mmol) by Method E and subsequent coupling with ***m*-4a** (24 mg, 0.040 mmol) by Method G yielded ***m*-8a** (15 mg, 21%) as a colorless oil. R_f (AcOEt/MeOH 95:5) = 0.14. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.00–7.93 (m, 1 H), 7.89–7.80 (m, 1 H), 7.59–7.10 (m, 39 H), 4.81–4.43 (br. s, 18 H, 9 × CONC*H*$_2$Ar), 4.28–4.00 [br. m, 9 H, 9 × CONC*H*$(CH_3)_2$], 1.59 (s, 9 H), 1.34–0.90 (br. m, 54 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 172.4 (9C_q), 164.5 (C_q), 140.0, 139.9, 137.2 (18 × C_q), 132.2 (C_q), 131.1 (CH), 129.5, 128.9, 128.8, 128.5, 126.3, 124.7 (38 × CH), 128.1 (CH), 128.0 (CH), 81.1 (C_q), 50.9 [br, 9 × CH, 9 × CONC*H*$(CH_3)_2$], 43.5 (br, 9 × CH_2, 9 × CONC*H*$_2$Ar), 28.3 (3 × CH_3), 21.6 (br, 18 × CH_3) ppm. HRMS (TOF MS ES$^+$): calcd. for $C_{110}H_{131}N_9O_{11}Na_2$ [M + 2Na]$^{2+}$ *m*/*z* 899.9882; found 899.9974. HPLC purity indeterminable due to insolubility.

Arylopeptoid Trimer *p*-5b: Treatment of ***p*-4b** (391 mg, 0.70 mmol) by Method D yielded ***p*-5b** (442 mg, 95%) as a colorless solid. R_f (EtOAc) = 0.40; m.p. 60–61.5 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.98–7.92 (m, 2 H), 7.47–7.02 (br. m, 15 H), 4.89–4.63 [br. s, 3.48 H, 3 × (c)-CONC*H*$_2$Ar], 4.63–4.33 [br. s, 2.52 H, 3 × (t)-CON-C*H*$_2$Ar], 3.62–3.32 [br. m, 2.52 H, 3 × (t)-CONC*H*$_2$$CH_3$], 3.32–3.05 [br. m, 3.48 H, 3 × (c)-CONC*H*$_2$$CH_3$], 1.56 (s, 9 H), 1.27–0.92 (br. m, 9 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 171.8, 171.4 (3 × C_q), 165.2 (C_q), 142.0, 141.5, 138.9, 138.9, 136.3, 135.4, (6 × C_q), 131.1 (C_q), 129.7 (2 × CH), 129.3, 128.3, 127.8, 127.8, 127.6, 126.8, 126.2 (15 × CH), 80.9 (C_q), 51.7 [br, 1.26 × CH_2, 3 × (t)-CONC*H*$_2$Ar], 46.7 [br, 1.74 × CH_2, 3 × (c)-CONC*H*$_2$Ar], 43.0 [br, 1.74 × CH_2, 3 × (c)-CONC*H*$_2$$CH_3$], 39.8 [br, 1.26 × CH_2, 3 × (t)-CONC*H*$_2$$CH_3$], 28.0 (3 × CH_3), 13.6 [br, 1.74 × CH_3, 3 × (c)-CONCH$_2$C*H*$_3$], 12.1 [br, 1.26 × CH_3, 3 × (t)-CONCH$_2$C*H*$_3$] ppm. HRMS (TOF MS ES$^+$): calcd. for $C_{41}H_{48}N_3O_5$ [M + H]$^+$ 662.3588; found 662.3593. HPLC purity: 99.5%.

Arylopeptoid Hexamer *p*-7b: Deprotection of ***p*-5b** (53 mg, 0.080 mmol) by Method E and subsequent coupling with ***p*-4b** (48 mg, 0.080 mmol) by Method F yielded ***p*-7b** (68 mg, 74%) as a colorless solid. R_f (CH_2Cl_2/MeOH 95:5) = 0.34; m.p. 134 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.97 (d, J = 7.6 Hz, 2 H), 7.50–7.08 (br. m, 29 H), 4.98–4.68 [br. s, 7.20 H, 6 × (c)-CONC*H*$_2$Ar], 4.67–4.44 [br. s, 4.80 H, 6 × (t)-CONC*H*$_2$Ar], 3.65–3.40 [br. s, 4.80 H, 6 × (t)-CONC*H*$_2$$CH_3$], 3.39–3.12 [br. s, 7.20 H, 6 × (c)-CONC*H*$_2$$CH_3$], 1.58 (s, 9 H), 1.26–0.95 (m, 18 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 171.8 (6 × C_q), 165.5 (C_q), 142.2, 139.2, 136.5, 135.7 (12 × C_q), 131.4 (C_q), 129.6 (2 × CH), 130.0, 128.6, 128.1, 127.1, 126.5 (27 × CH), 81.2 (C_q), 52.1 [br, 2.40 × CH_2, 6 × (t)-CONC*H*$_2$Ar], 47.0 [br, 3.60 × CH_2, 6 × (c)-CONC*H*$_2$Ar], 43.3 [br, 3.60 × CH_2, 6 × (c)-CONC*H*$_2$$CH_3$], 40.0 [br, 2.40 × CH_2, 6 × (t)-CONC*H*$_2$$CH_3$], 28.3 (3 × CH_3), 13.8 [br, 3.60 × CH_3, 6 × (c)-CONCH$_2$C*H*$_3$], 12.3 [br, 2.40 × CH_3, 6 × (t)-CONCH$_2$C*H*$_3$] ppm. HRMS (TOF MS ES$^+$): calcd. for $C_{71}H_{82}N_6O_8$ [M + 2H]$^{2+}$ *m*/*z*

573.3097; found 573.3080. HPLC purity indeterminable due to insolubility.

Arylopeptoid Nonamer *p*-8b: Deprotection of ***p*-7b** (46 mg, 0.040 mmol) by Method E and subsequent coupling with ***p*-4b** (23 mg, 0.040 mmol) by Method F yielded ***p*-8b** (36 mg, 55%) as an off-white solid. R_f (CH_2Cl_2/MeOH 95:5) = 0.29; m.p. 154 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.01–7.75 (m, 2 H), 7.52–7.18 (br. m, 39 H), 4.88–4.45 (br. m, 18 H, 9× CONCH_2Ar), 3.60–3.12 (br. m, 18 H, 9-CONCH_2CH$_3$), 1.59 (s, 9 H), 1.29–1.01 (br. m, 27 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$/CD_3OD 1:1): δ = 172.2, 172.0, 171.8 (9×C_q), 164.5 (C_q), 141.6, 139.3, 138.8, 138.1, 137.6, 135.4, 134.9, 134.6 (18×C_q), 131.0 (C_q), 129.3, 128.1, 127.5, 126.4, 125.6 (41×CH), 81.0 (C_q), 51.5, 46.6 (9×CH_2, br, 9× CON*C*H$_2$Ar), 43.2, 39.8 (9×CH_2, br, 9× CONCH_2CH$_3$), 27.2 (3×CH_3), 12.9, 11.2 (9×CH_3, br, 9× CONCH$_2$*C*H$_3$). HRMS (TOF MS ES$^+$): calcd. for $C_{101}H_{113}N_9O_{11}Na_2$ [M + 2Na]$^{2+}$ *m*/*z* 836.9177; found 836.9174. HPLC purity indeterminable due to insolubility.

Arylopeptoid Trimer *m*-5b: Treatment of ***m*-4b** (391 mg, 0.70 mmol) by Method D yielded ***m*-5b** (466 mg, 100%) as a colorless solid. R_f (EtOAc) = 0.48; m.p. 45–48 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.96–7.72 (br. m, 2 H), 7.56–7.08 (br. m, 15 H), 4.85–4.61 [br. s, 3.66 H, 3× (c)-CONCH_2Ar], 4.61–4.31 [br. s, 2.34 H, 3× (t)-CONCH_2Ar], 3.61–3.32 [br. m, 2.34 H, 3× (t)-CONCH_2CH$_3$], 3.32–3.01 [br. m, 3.66 H, 3× (c)-CONCH_2CH$_3$], 1.56 (s, 9 H), 1.27–0.91 (br. m, 9 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 171.7, 171.5 (3×C_q), 165.3 (C_q), 137.8, 137.4, 136.8, 136.3 (6×C_q), 132.2 (C_q), 131.8 (CH), 129.3, 128.8, 128.8, 128.6, 128.3, 127.6, 126.2, 125.4, 125.3 (16×CH), 81.0 (C_q), 51.7 [br, 1.17CH_2, 3× (t)-CON*C*H$_2$Ar], 46.8 [br, 1.83×CH_2, 3× (c)-CON*C*H$_2$Ar], 43.0 [br, 1.83×CH_2, 3× (c)-CON*C*H$_2$CH$_3$], 39.7 [br, 1.17×CH_2, 3× (t)-CON*C*H$_2$CH$_3$], 28.0 (3×CH_3), 13.6 [br, 1.83×CH_3, 3× (c)-CONCH$_2$*C*H$_3$], 12.1 [br, 1.17×CH_3, 3× (t)-CONCH$_2$*C*H$_3$] ppm. HRMS (TOF MS ES$^+$): calcd. for $C_{41}H_{48}N_3O_5$ [M + H]$^+$ 662.3588; found 662.3591. HPLC purity: 99.9%.

Arylopeptoid Hexamer *m*-7b: Deprotection of ***m*-5b** (53 mg, 0.080 mmol) by Method E and subsequent coupling with ***m*-4b** (45 mg, 0.080 mmol) by Method G yielded ***m*-7b** (72 mg, 78%) as a colorless foam. R_f (AcOEt/MeOH 95:5) = 0.36. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.91–7.78 (br. m, 2 H), 7.59–7.15 (br. m, 27 H), 4.88–4.65 [br. m, 7.44 H, 6× (c)-CONCH_2Ar], 4.64–4.49 [br. m, 4.56 H, 6× (t)-CONCH_2Ar], 3.62–3.34 [br. m, 4.56 H, 6× (t)-CONCH_2CH$_3$], 3.33–3.05 [br. m, 7.44 H, 6× (c)-CONCH_2CH$_3$], 1.59 (s, 9 H), 1.30–0.99 (br. m, 18 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 171.7 (6C_q), 165.5 (C_q), 138.0, 137.6, 137.0, 136.5 (12C_q), 132.4 (C_q), 132.0 (CH), 129.5, 129.0, 128.8, 128.5, 127.8, 126.4, 125.5 (28×CH), 81.2 (C_q), 51.9 [br, 2.28×CH_2, 6× (t)-CON*C*H$_2$Ar], 47.0 [br, 3.72×CH_2, 6× (c)-CON*C*H$_2$Ar], 43.2 [br, 3.72×CH_2, 6× (c)-CON*C*H$_2$CH$_3$], 39.9 [br, 2.28×CH_2, 6× (t)-CON*C*H$_2$CH$_3$], 28.2 (3×CH_3), 13.8 [br, 3.72×CH_3, 6× (c)-CONCH$_2$*C*H$_3$], 12.3 [br, 2.28×CH_3, 6× (t)-CONCH$_2$*C*H$_3$] ppm. HRMS (TOF MS ES$^+$): calcd. for $C_{71}H_{80}N_6O_8Na_2$ [M + 2Na]$^{2+}$ *m*/*z* 595.2917; found 595.2903. HPLC purity: 98.4%.

Arylopeptoid Nonamer *m*-8b: Deprotection of ***m*-7b** (46 mg, 0.040 mmol) by Method E and subsequent coupling with ***m*-4b** (22 mg, 0.040 mmol) by Method G yielded ***m*-8b** (21 mg, 32%) as a colorless foam. R_f (AcOEt/MeOH 90:10) = 0.26. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.92–7.76 (br. m, 2 H), 7.60–7.12 (br. m, 39 H), 4.88–4.63 [br. m, 11.34 H, 9× (c)-CONCH_2Ar], 4.62–4.40 [br. m, 6.66 H, 9× (t)-CONCH_2Ar], 3.65–3.31 [br. m, 6.66 H, 9× (t)-CONCH_2CH$_3$], 3.30–3.08 [br. m, 11.34 H, 9× (c)-CONCH_2CH$_3$], 1.59 (s, 9 H), 1.28–0.95 (br. m, 27 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 172.0, 171.9 (9C_q), 165.7 (C_q), 138.1, 137.6, 137.0 (18×C_q), 132.5 (C_q), 132.1 (CH), 129.6, 129.1, 128.9, 128.7, 127.8, 126.5, 126.2, 125.6, 125.2 (40×CH), 81.4 (C_q), 52.0 [br, 3.33×CH_2, 9× (t)-CON*C*H$_2$Ar], 47.0 [br, 5.67CH_2, 9× (c)-CON*C*H$_2$Ar], 43.2 [br, 5.67×CH_2, 9× (c)-CON*C*H$_2$CH$_3$], 39.9 [br, 3.33CH_2, 9× (t)-CON*C*H$_2$CH$_3$], 28.3 (3×CH_3), 13.9 [br, 5.67×CH_3, 9× (c)-CONCH$_2$*C*H$_3$], 12.4 [br, 3.33×CH_3, 9× (t)-CONCH$_2$*C*H$_3$] ppm. HRMS (TOF MS ES$^+$): calcd. for $C_{101}H_{113}N_9O_{11}Na_2$ [M + 2Na]$^{2+}$ *m*/*z* 836.9177; found 836.9194. HPLC purity: 98.4%.

Supporting Information (see footnote on the first page of this article): General experimental methods for HPLC analysis; NMR spectra and HPLC profiles; details for coupling optimization; NOESY and temperature NMR spectroscopy.

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