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Axially Chiral Facial Amphiphiles with a Dihydronaphthopentaphene Structure as Molecular Tweezers for SWNTs

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In memory of Charles Mioskowski who initiated this work

Abstract: Syntheses of chiral 6,15-dihydronaphtho[2,3-*c*]pentaphene derivatives of opposite configurations are reported. Starting from anthracene, the strategy involves two key steps: a Diels–Alder reaction on a prochiral dianthraquinone, and an enantiomeric resolution using (−)-menthol. The final molecules exhibit very strong optical activity, as shown by their circular dichroism spectra, and are examples of chiral facial amphiphiles. Their adsorption at the surface of single-walled carbon nanotubes (SWNTs) has also been studied, and has been found to occur preferentially on 0.8–1.0 nm diameter nanotubes among the population of a high-pressure CO conversion (HiPco) SWNT sample (0.8–1.2 nm). The synthesised facial amphiphiles act as nano-tweezers for the diameter-selective solubilisation of SWNTs in water. The expected optical activities of the SWNT samples solubilised by each of the chiral amphiphiles have been studied by circular dichroism spectroscopy, but the results are not yet conclusive.

Keywords: amphiphiles · anthracenes · carbon nanotubes · chirality · pi interactions

Introduction

Typical amphiphiles, such as lipids, have a head-to-tail structure, usually consisting of a polar head-group and a long hydrocarbon chain; *facial amphiphiles*, on the contrary, present a hydrophobic face and a hydrophilic face.[1] Bile salts and certain helical peptides are natural examples of such compounds.[2] Numerous original facial amphiphiles have been synthesised and examined with regard to their two- and three-dimensional assembly behaviour, their abilities to solubilise specific types of molecules, and their lack of susceptibility to aggregation.[3]

Pursuing our effort to design geometrically constrained polyaromatic molecules for the supramolecular recognition and sorting of single-walled carbon nanotubes (SWNTs),[4] we conceived the facial amphiphiles (6*R*,15*R*)-**1** and (6*S*,15*S*)-**1** (Figure 1). The structural control of SWNTs (diameter and helicity) during their production is difficult. Nevertheless, obtaining refined SWNT samples possessing well-defined properties is a critical hurdle that has to be overcome with regard to their fundamental study and for many technological applications. For instance, discrimination according to diameter is highly valuable for nanoelectronic applications, since diameter plays a key role in determining the electronic properties of carbon nanotube field-effect transistors (on-current varying by several orders of magnitude depending on the SWNT band gap).[5] Therefore, the development of methods for sorting SWNTs according to their electronic properties and/or structural parameters has attracted a lot of attention, the ultimate goal being the production of samples of SWNTs with a single structure.[6] In pursuit of this goal, "host–guest strategies" are the most sophisticated and promising; they have been adopted by several groups, including our own. These strategies involve the use of small amphiphilic anchor molecules with constrained shapes that are able to specifically solubilise a sub-population of SWNTs in an as-produced SWNTs mixture. These

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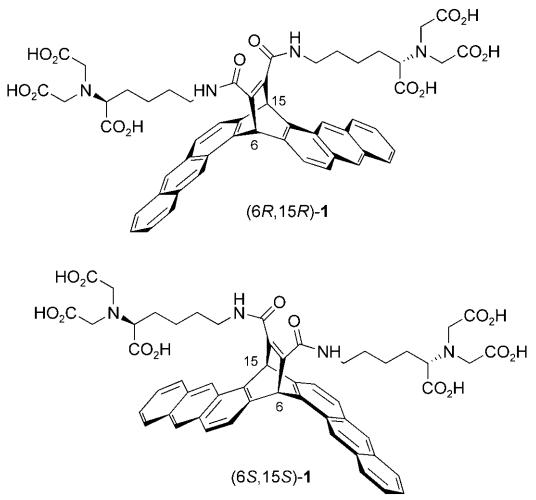


Figure 1. Chiral facial amphiphiles.

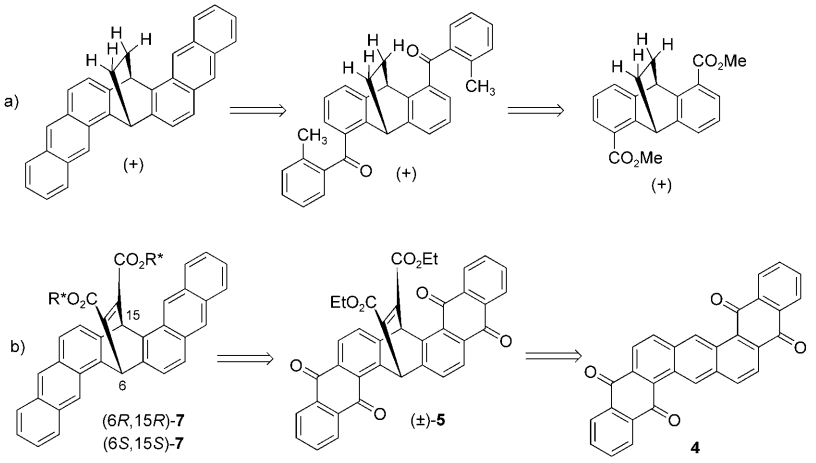
approaches often allow the attainment of high specificities in the diameter or the helicity (e.g., zigzag or armchair) and thus the conductivity of the selected SWNTs by virtue of the precise molecular design of the anchor molecules.[7] The most advanced development of such a "host–guest strategy" was recently proposed by N. Komatsu, who reported the selective solubilisation of optical isomers of SWNTs (left- or right-handed helicity along the nanotube axis) by using chiral zinc(II) diporphyrins.[8] To the best of our knowledge, this is unique work concerning the separation of isomers of SWNTs, and is noteworthy in that the corresponding anchor molecules do not discriminate a particular helicity angle. In our previous report, we presented two polyaromatic amphiphilic molecules for the selection of either armchair or zigzag SWNTs by virtue of optimised π–π stacking interactions with the nanotube graphene-type atomic structure.[4] In the work presented herein, the same strategy is followed, but inspired by the pioneering work of N. Komatsu, we envisaged the sorting of SWNTs according to more advanced structural parameters; we wished to design polyaromatic molecules that would allow for the first time the diameter-selective chiral discrimination of SWNTs. Remarkably, in parallel, N. Komatsu has recently reported the enrichment of larger diameter SWNTs using chiral monoporphyrins.[8d] The aim of this communication is to describe the synthesis of the two chiral facial amphiphiles (6*R*,15*R*)-**1** and (6*S*,15*S*)-**1** and to present the results of SWNT-sorting experiments in terms of diameter discrimination and optical enrichment.

Compounds **1** (Figure 1) are two 6,15-dihydronaphtho[2,3-*c*]pentaphene derivatives.[9] They are not exact enantiomers because the asymmetric centres of the nitrilotriacetic side chains are of the same configuration in the two structures; however, the two asymmetric carbons of the 6,15-dihydronaphtho[2,3-*c*]pentaphene fragment (C6 and C15, Figure 1) are of opposite stereochemistry. To the best of our knowledge, only one example of a chiral 6,15-dihydronaphtho[2,3-*c*]pentaphene has hitherto been described in the literature. In 1976, Harada et al. reported the synthesis of (6*R*,15*R*)-(+)-6,15-dihydro-6,15-ethanonaphtho-[2,3-*c*]pentaphene (Scheme 1a) from chiral (9*R*,10*R*)-(+)-1,5-dimethoxycarbonyl-9,10-dihydro-9,10-ethanoanthracene by a sequence of Grignard addition, oxidation, Friedel–Crafts acylation, and aromatisation.[10] Notably, the opposite enantiomer of the final product was not synthesised. Furthermore, this hydrocarbon molecule does not bear chemical functions that would enable the grafting of the polar headgroups required in our application; thus, we had to follow a completely different synthetic strategy. To access our target molecules, and especially the two isomers of the dihydronaphthopentaphene, we envisaged using the dianthraquinone **4** as a key intermediate (Scheme 1b).

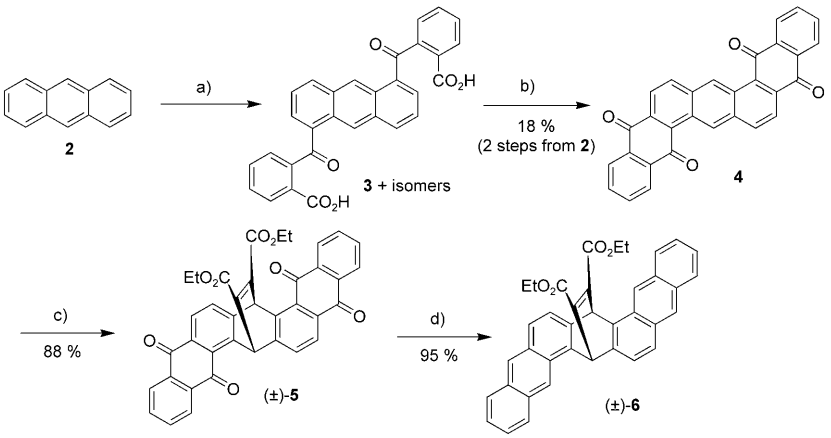
A report by Clar in 1948[11] suggests that the central anthracene ring in **4** should be the most favourable reactive site in a Diels–Alder reaction. With diethyl acetylenedicarboxylate as the dienophile, (±)-**5** would be obtained as a racemic mixture. Reduction and aromatisation of this diquinone, followed by transesterification with a chiral alcohol, should allow us to separate the two diastereoisomers of **7**. Each of them could subsequently be converted to the target molecules **1**.

Results and Discussion

Synthesis: Compound **4** was synthesised following the strategy reported by Clar,[11] in two steps from anthracene **2** (Scheme 2). The diacid **3** was obtained among a mixture of other regioisomers and could not be purified. Heating of the



Scheme 1. Retrosynthetic strategy followed by a) Harada et al. and b) that used herein.



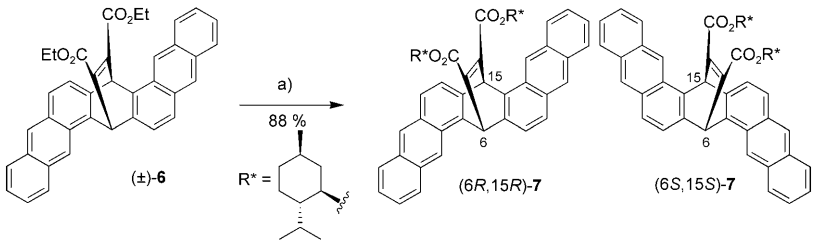
Scheme 2. Synthesis of racemic 6,15-dihydronaphthopentaphene (±)-**6**. a) Phthalic anhydride, $AlCl_3$, $(CHCl_2)_2$, 2 h at 95 °C; b) benzoyl chloride, $ZnCl_2$, nitrobenzene, 30 min at 205 °C; c) diethyl acetylenedicarboxylate, nitrobenzene, 45 h at 210 °C; d) 1) $NaBH_4$, MeOH/diglyme, −20 °C to RT; 2) $SnCl_2$, aqueous 10 % HCl.

mixture at 205 °C for 30 min in the presence of zinc(II) chloride and benzoyl chloride allowed the formation of **4**, which could be cleanly isolated as a purple solid after repeated washing with nitrobenzene and diethyl ether. A ^{1}H NMR spectrum of this highly insoluble compound could only be recorded in deuterated nitrobenzene by heating the sample to 190 °C. Notably, the overall yield of this synthesis of **4** was higher than that reported by Clar (18 % instead of 9 %).

Diels–Alder reactions of acetylenes and **4** were found to be regiospecific because of the high reactivity of the central ring of the anthracene fragment, as previously reported.[12] By heating **4** in nitrobenzene in the presence of 10 equiv of diethyl acetylenedicarboxylate for 45 h in a sealed tube, racemic compound (±)-**5** could be obtained in a very good yield (Scheme 2) and was thoroughly characterised after recrystallisation. Furthermore, the structure of (±)-**5**, and especially the dihedral angle (approximately 120°) formed by the two anthraquinone units, was confirmed by X-ray crystallographic analysis of monocrystals grown by diffusion of petroleum ether into a solution in chloroform. Notably, the Diels–Alder reaction of **4** with di-(−)-menthyl acetylenedicarboxylate was unsuccessful. Reduction of the two quinone moieties of (±)-**5** followed by the sensitive aromatisation of the anthracene units to afford (±)-**6** was performed in a one-pot sequence.

In order to separate the two enantiomers of the 6,15-dihydronaphtho[2,3-*c*]pentaphene **6**, twofold transesterification of the ethyl esters with (−)-menthol was studied. Heating (±)-**6** with (−)-menthol in the presence of a catalyst such as $TiCl_4$, $Ti(OiPr)_4$, or *p*-toluenesulfonic acid (PTSA) did not afford the expected menthyl esters. In order to achieve this transformation, we extended the indium triiodide-catalysed transesterification reaction reported by Ranu et al.,[13] using molten (−)-menthol as the solvent. Indeed, at 80 °C in molten (−)-menthol, indium triiodide, prepared in situ by stirring indium metal and iodine, efficiently afforded the di-(−)-menthyl esters **7** from (±)-**6** in 88 % yield (Scheme 3).

The resulting equimolar mixture of the two diastereoisomers could be very efficiently separated by column chromatography on silica gel, affording the two enantiomerically

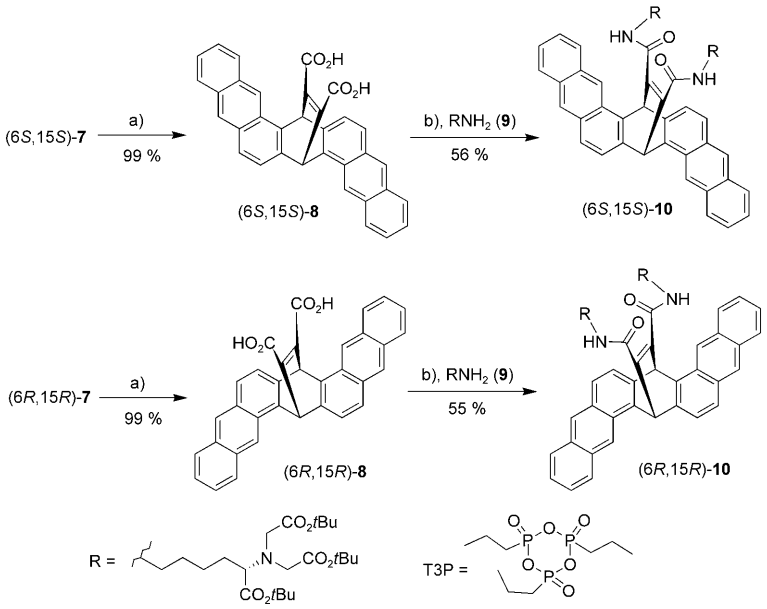


Scheme 3. Synthesis and separation of diastereoisomers **7**. a) (−)-menthol, In, I_2, 48 h at 80 °C.

pure compounds (6*R*,15*R*)-**7** and (6*S*,15*S*)-**7** (*de* > 99 % by HPLC; see the Supporting Information).

Each of the two diastereoisomers of **7** was quantitatively saponified to afford the two enantiomers of diacid **8** (Scheme 4). Attempted bis-coupling of the *tert*-butyl-nitrilotriacetate (**9**)[14] with compounds **8** was unsuccessful using the benzotriazole-1-yloxytris(dimethylamino)phosphonium hexafluorophosphate (BOP) reagent or the 1-hydroxybenzotriazole (HOBt)/*N*′-(3-dimethylaminopropyl)-*N*-ethylcarbodiimide (EDC) coupling system in DMF, 1,4-dioxane, or 1,4-dioxane/benzene (1:1) as solvents. In the presence of 6 equiv of *n*-propylphosphonic anhydride (T3P, Scheme 4)[15] no reaction was observed in 1,4-dioxane; however, the presence of benzene as a co-solvent allowed the reaction to proceed such that the two desired products (6*R*,15*R*)-**10** and (6*S*,15*S*)-**10** were obtained in moderate yields. Benzene might prevent compounds **8** from aggregating by keeping them in solution by virtue of intermolecular π–π stacking interactions. The specific rotations of the compounds **10** could be measured in chloroform: for (6*R*,15*R*)-**10**: $[\alpha]_D = +182°$ ($c = 1.9 \times 10^{-3}$, $CHCl_3$) and for (6*S*,15*S*)-**10**: $[\alpha]_D = -190°$ ($c = 0.6 \times 10^{-3}$, $CHCl_3$).

Since we observed a certain degree of retro Diels–Alder reactions of 6,15-dihydronaphthopentaphenes **10** or similar substrates when using sodium hydroxide, lithium hydroxide, or potassium hydroxide, acidic conditions were preferred for the deprotection of the 6-carboxylic acids of (6*R*,15*R*)-**10**

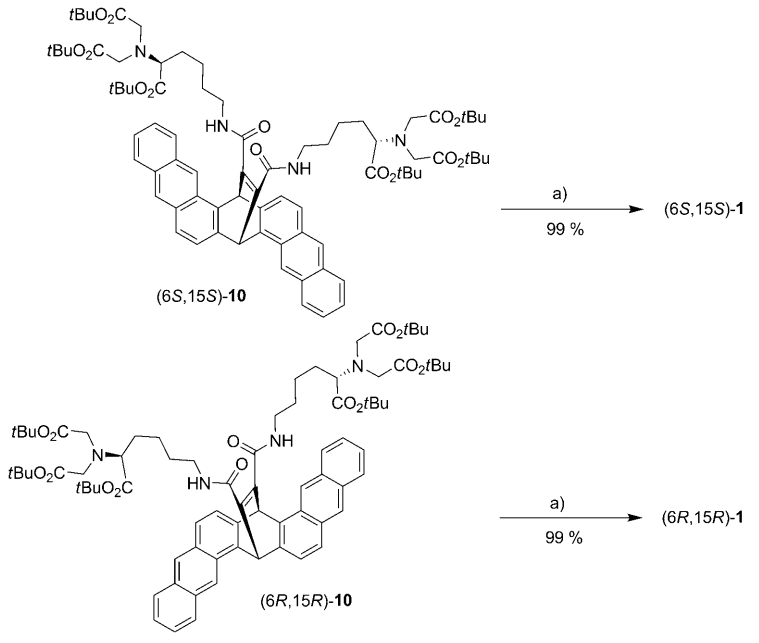


Scheme 4. Synthesis of the two 6,15-dihydronaphthopentaphene diastereoisomers **10**. a) LiOH, EtOH, 6 h at reflux; b) **9**, T3P, EDIPA, 1,4-dioxane/benzene 1:1, 4 d at RT.

and (6*S*,15*S*)-**10**. Cleavage of the 6-*tert*-butyl esters was achieved by treating each of the two compounds **10** in trifluoroacetic acid for 30 h (HPLC monitoring; Scheme 5). The structures of the obtained compounds, (6*R*,15*R*)-**1** and (6*S*,15*S*)-**1**, were confirmed by ^{1}H and ^{13}C NMR as well as by mass spectrometry in negative-ion mode on a MALDI-TOF instrument.

Circular dichroism (CD) spectra of compounds **1** allowed assignment of the absolute configurations of the 6,15-dihydronaphthopentaphene moieties. Both CD spectra, recorded in Tris buffer (pH 8), feature very strong typical split Cotton effects for such compounds in the 220–300 nm region (Figure 2). By comparison with the CD spectrum of (6*R*,15*R*)-(+)-6,15-dihydro-6,15-ethanonaphtho[2,3-*c*]pentaphene,[10a] the (6*R*,15*R*)-**1** configuration was assigned to the sample displaying a CD spectrum with a positive first and a negative second Cotton effect ($\Delta\varepsilon_{272}=+255\,000$, $\Delta\varepsilon_{250}=-269\,000$, $A(\Delta\varepsilon_{272}-\Delta\varepsilon_{250})=+524\,000$). The CD spectrum showing a negative first and a positive second Cotton effect ($\Delta\varepsilon_{272}=-254\,000$, $\Delta\varepsilon_{250}=+277\,000$, $A(\Delta\varepsilon_{272}-\Delta\varepsilon_{250})=-531\,000$) was assigned to the (6*S*,15*S*)-**1** configuration. Interestingly, despite the fact that the two compounds are not strictly enantiomers (the asymmetric centres of the nitrilotriacetic side chains are of the same configuration), the CD spectra are virtually identical but of opposite sign, showing that the optical activity is largely dictated by the enantiomerically pure 6,15-dihydronaphthopentaphene fragments (similarly, the UV/Vis absorption spectra are almost identical; Figure 2). Notably, to the best of our knowledge, this is the first report of a CD spectrum of a (6*S*,15*S*)-dihydronaphthopentaphene.

The absolute configurations of the synthesised intermediates were determined on the basis of the configuration of the final compounds **1**.



Scheme 5. Synthesis of the two 6,15-dihydronaphthopentaphene diastereoisomers **1**. a) TFA, 30 h at RT.

Selective solubilisation of SWNTs: The properties of the compounds **1** for the discrimination of SWNTs in terms of diameter and chirality were studied according to a previously reported strategy.[4] The previously optimised protocol was applied, starting from high-pressure CO conversion (HiPco) SWNTs dispersed in an aqueous solution of sodium dodecyl sulfate (SDS; 1 wt%). Briefly, (6*R*,15*R*)-**1** or (6*S*,15*S*)-**1** was added to a suspension of SWNTs, SDS was removed by extended dialysis, and finally the samples were centrifuged

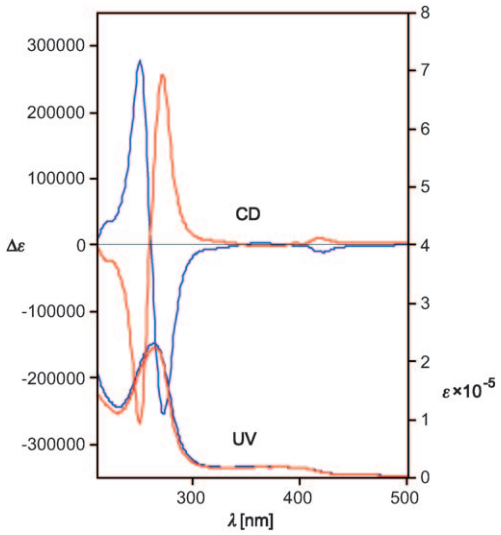


Figure 2. CD (left axis) and UV (right axis) spectra of (6*R*,15*R*)-**1** (red trace) and (6*S*,15*S*)-**1** (blue trace) in Tris buffer (pH 8).

to separate the solubilised fraction of SWNTs remaining in the supernatant from the aggregated SWNTs in the pellet. Control experiments in the absence of facial amphiphiles **1** showed that no SWNTs remained in the supernatant at this stage. The aqueous supernatants obtained, containing the SWNTs selected by (6*R*,15*R*)-**1** or (6*S*,15*S*)-**1**, were dialysed against D_2O in order to reach an H_2O content below 0.2% and to allow their analysis by photoluminescence (PL). This experiment permits analysis of the semiconducting (*n*,*m*) SWNT population and thus allows comparison of the two obtained samples with the population of the starting HiPco nanotubes in terms of diameter selection (photoluminescence phenomena would be expected to be identical for two enantiomeric SWNTs). The PL protocol involves measuring the luminescence of the sample using excitation wavelengths in the range 500–900 nm (in 3 nm increments). The result is a three-dimensional map showing absorption peaks that can be precisely assigned to a specific nanotube structure (*n*,*m*).[16] The PL experimental conditions used herein cover the whole distribution of the (*n*,*m*) semiconducting nanotubes in the HiPco material (note that metallic tubes are not detected by this technique).[17]

The PL results show that the fractions of SWNTs solubilised by compounds (6*R*,15*R*)-**1** and (6*S*,15*S*)-**1** are virtually identical since the maps recorded for these two samples are very similar (Figure 3b, c). Under the hypothesis that the solubilisation of SWNTs is driven by the two enantiomerically pure 6,15-dihydronaphthopentaphene fragments of **1**, this demonstrates the specificity of our sorting procedure.[4] Comparing the population of SWNTs sorted by one of the two compounds **1** with the starting HiPco mixture (Figure 3a/b or a/c), a clear selection in terms of diameter is observed, since only nanotubes in the range 0.8–1.0 nm are detected. These results can be related to the work of Tromp et al., in which it was reported that pentacene–maleimide Diels–Alder adducts serve as diameter-selective molecular anchors for the separation of SWNTs in the 1–2 nm diameter range,[7c] though we demonstrate here the finer selection of smaller SWNTs in an HiPco mixture. In our case, the observed selection in size could also be due to the three-dimensional shape of compounds **1**, which makes them suitable for effective interaction with the tubular shape of SWNTs of optimum diameter (see the Supporting Information for a schematic representation, Scheme S1). Notably, a discrimination of SWNTs in favour of large helicity angle is also observed with compounds **1**, as tubes (7,6) show the largest increases of abundance in comparison with the starting mixture.

As shown in Figure 4, the selections achieved with compounds **1** are very different from those obtained in previous studies using a pentacene- or a quaterrylene-based amphiphile.[4] This confirms that the geometry of the polyaromatic anchor molecule, most probably interacting by π–π stacking with the nanotube wall, is a crucial factor for the tuning of the SWNTs discrimination. Also, in comparison with previous amphiphiles used, running the sorting experiments with **1** was facilitated by virtue of their lower self-aggregating behaviour, a feature that is inherent to *facial* amphiphiles.

After having studied the diameter-based discrimination of SWNTs achieved by compounds **1** by PL, the optical activity of the purified nanotube samples was studied with the aim of characterising the optical enrichment. We adopted the experimental set-up reported by Peng et al. in his pioneering work on the preparation of optically active SWNT samples using two enantiomers of chiral diporphyrins.[8] Thus, the optical activities of SWNT samples extracted by using (6*R*,15*R*)-**1** and (6*S*,15*S*)-**1** were studied by CD after removal of compounds **1** from the samples (by repeated aqueous and acidic methanolic washes).[4] Unfortunately, all our attempts to record an unequivocal signal by CD (in the range 300–1100 nm) attributable to carbon nanotubes under the conditions described by Peng et al. have been unsuccessful due to the low SWNT contents in the final samples.[18] Therefore, our experiments are not yet conclusive in terms of optical enrichment in the SWNT samples purified by compound **1**.

In the light of reports by N. Komatsu, we had not anticipated that the amount of purified SWNT necessary for CD studies would have been higher than the amount of material that our experimental strategy can deliver (after extensive washings of compound **1**). Instead of pursuing an optimisation of the experimental procedure, this observation and the very promising selection results shown above led us to rethink our strategy toward our foremost objective, which is to deliver a large-scale preparative procedure based on our amphiphilic anchor molecules for the fine selection of SWNTs. To this end, we are currently working on a supported version of our amphiphiles and on the adaptation of our experimental procedures to a pH-dependent continuous-extraction set-up.

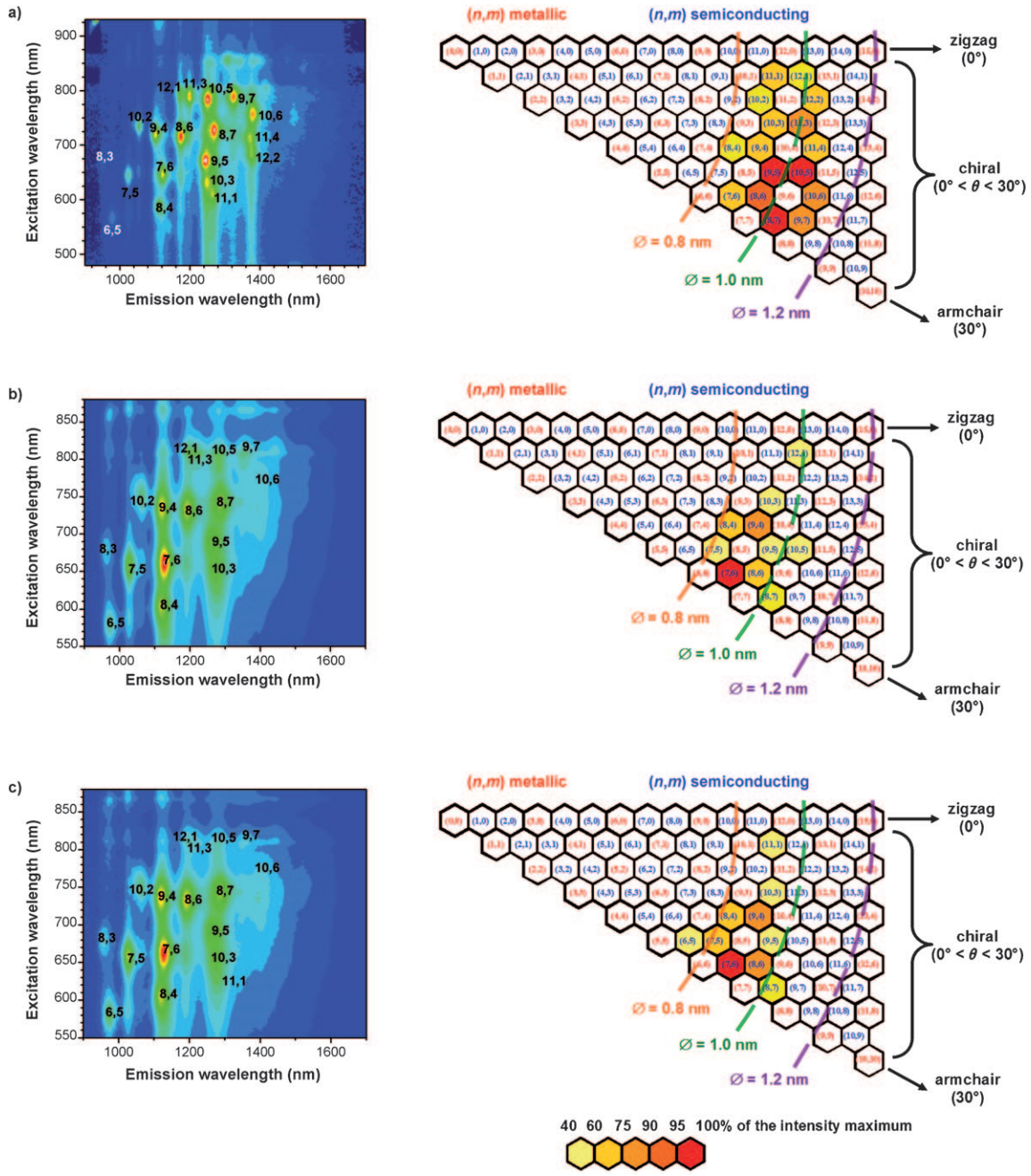


Figure 3. Photoluminescence spectra of HiPco SWNT samples before and after the selection protocol. a) PL intensity versus excitation and emission wavelengths for a HiPco SWNT sample suspended in SDS and deuterium oxide (the colours from blue to red indicate the strength of the emission). b), c) Spectra of the extracted fractions of the previous HiPco SWNT sample using the reported selection protocol[4] and starting with facial amphiphile (6*R*,15*R*)-**1** (b) or (6*S*,15*S*)-**1** (c) at a concentration of 2×10^{-4} mol L^{-1}. PL emission intensities are reported in Hamada plots to illustrate the selections obtained.

Conclusion

A pair of chiral facial amphiphiles with a dihydronaphthopentaphene structure has been synthesised for the first time. Compounds (6*R*,15*R*)-**1** and (6*S*,15*S*)-**1** exhibit very high optical activities and could be of utility in studies of optical devices or for the selective solubilisation of chiral guest molecules. In this report, we have focused on their use as sorting agents for SWNTs and have demonstrated that compounds **1** permit very fine size selections. Theoretical calculations are ongoing for the further interpretation of this experimental result. CD experiments on the final samples, which were not conclusive in terms of SWNT optical enrichment, have encouraged us to pursue our effort towards the development of preparative methods based on our collection of amphiphilic anchor molecules for the sorting of various types of

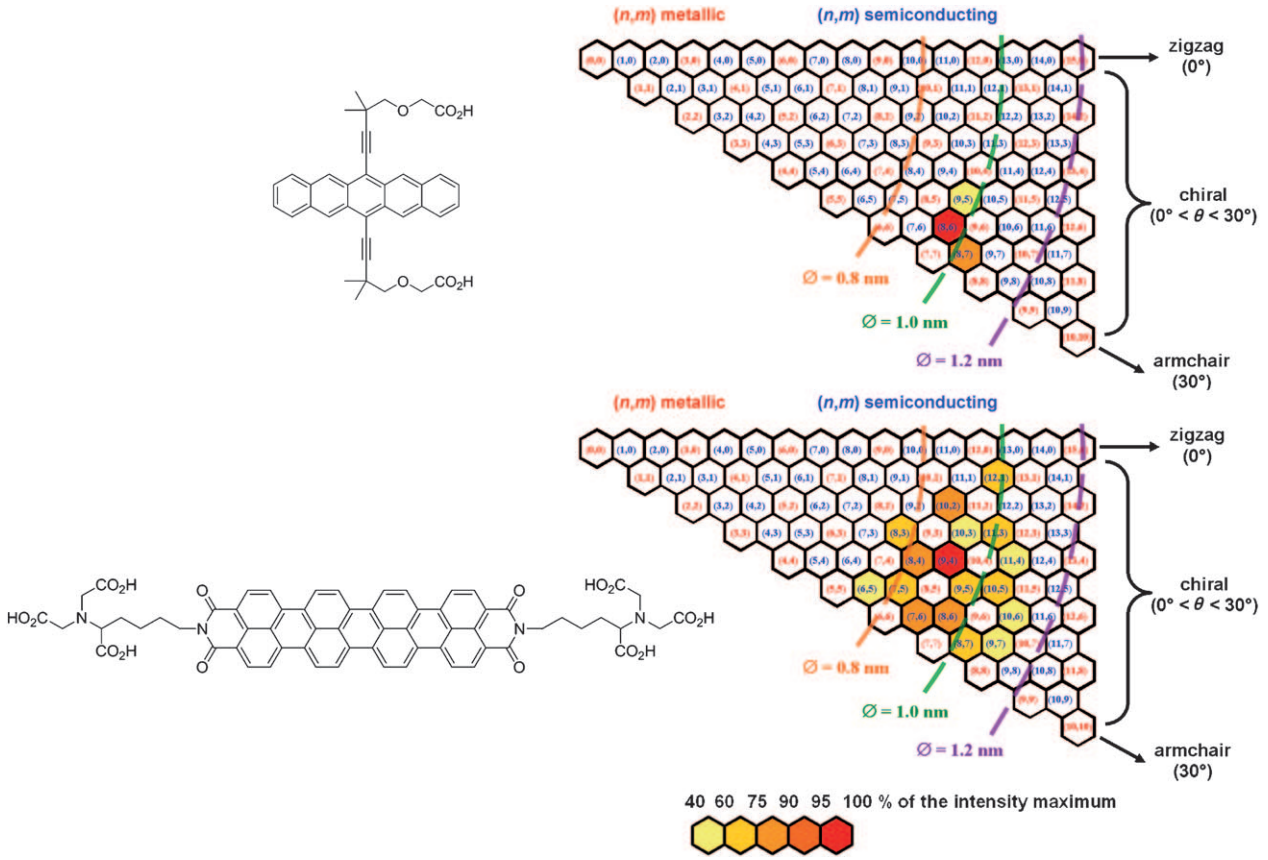


Figure 4. Selection of SWNTs from HiPco samples by using a pentacene-based (top) or quaterrylene-based (bottom) amphiphile. PL emission intensities are reported in Hamada plots to illustrate the selections obtained. For spectra, refer to ref. [4].

SWNTs, with the ultimate goal being the delivery of bulk quantities of a single-structure SWNT.

Experimental Section

General: All experiments were carried out under an argon atmosphere. TLC was performed on Merck silica gel 60F_{254} and spots were revealed by exposure to UV at 254 nm and vanillin. Silica gel (Merck 60, 40–63 μm) was used for flash column chromatography. For the separation of compounds (6*R*,15*R*)-**7** and (6*S*,15*S*)-**7**, a finer silica gel (Merck 60, 14–40 μm) was preferred. NMR spectra were recorded at 300 or 200 MHz for ^{1}H and at 75 or 50 MHz for ^{13}C. Infra-red spectra were recorded on a Perkin–Elmer spectrometer (1600 FT-IR) from samples in KBr discs. Melting points were measured on a Bibby Sterilin device (Stuart Scientific SMP3). Elemental analyses were performed by the Service Central d'Analyses du CNRS at Vernaison. High-resolution mass spectra were recorded using a MicroTOF instrument (Bruker). UV/Vis absorption spectra were recorded on a UVIkon XL instrument (BioTek). CD spectra were recorded on a Jasco spectrometer (J-810).

Naphtho[2,3-*c*]pentaphene-5,18:9,14-diquinone (4): A mixture of anthracene (5.4 g, 30.3 mmol) and phthalic anhydride (10.3 g, 69.5 mmol, 2.3 equiv) was heated to 150 °C under vigorous stirring. 1,1,2,2-Tetrachloroethene (120 mL) was then slowly added, the resulting mixture was cooled to 95 °C, and freshly prepared finely divided aluminium chloride (18 g, 135 mmol, 1.5 equiv) was added portionwise. The reaction mixture was stirred for 2 h at 95 °C, then cooled, diluted with chloroform (300 mL), and hydrolysed with 10 % HCl (300 mL) for 12 h under vigorous stirring. The aqueous phase was extracted with chloroform; the obtained emulsions were collected at each extraction step, pooled, and centrifuged. The solids recovered from the centrifugation and the organic phases were combined and dried under reduced pressure. The obtained residue was washed with acetic acid and diethyl ether to afford crude 1,5-bis(2-carboxybenzoyl)anthracene as a light-brown solid (5.22 g). This residue (5.22 g, 11 mmol based on the sole presence of 1,5-bis(2-carboxybenzoyl)anthracene) was mixed with benzoyl chloride (17.6 mL, 154 mmol, 14 equiv), zinc(II) chloride (3.07 g, 22.5 mmol, 2.05 equiv), and nitrobenzene (60 mL). The resulting mixture was gradually heated to 205 °C and kept at this temperature for 30 min. After cooling to 60–80 °C, the reaction mixture was filtered. The brown residue was washed with nitrobenzene and diethyl ether to afford **4** as a violet solid (2.41 g, 5.5 mmol, 18 % from anthracene). M.p. > 350 °C; ^{1}H NMR (300 MHz, [D_5]nitrobenzene, 190 °C, TMS): δ = 10.6 (s, 2H; H6,15), 8.60–8.68 (m, 2H; H7,16), 8.52–8.60 (m, 2H; H8,17), 8.44–8.52 (m, 2H; H4,13), 8.34–8.41 (m, 2H; H1,10), 7.82–7.99 ppm (m, 4H; H2,3,11,12); IR: $\tilde{\nu}$ = 1668 (C=O), 1591, 1332, 1300, 1271, 709 cm^{-1}.

Diquinone (±)-5: A mixture of compound **4** (220 mg, 0.50 mmol), diethyl acetylenedicarboxylate (0.80 mL, 4.7 mmol, 9.4 equiv), and nitrobenzene (1.5 mL) was heated at 210 °C in a sealed tube for 45 h. The crude product was purified by flash chromatography on silica, eluting first with ethyl acetate/dichloromethane/cyclohexane 1:80:19 and then with ethyl acetate/dichloromethane (gradient to 4:96). The obtained solid was recrystallised twice from ethyl acetate/cyclohexane 3:2 to yield (±)-**5** as a brown solid (260 mg, 0.43 mmol, 88 %). R_f = 0.25 (AcOEt/CH_2Cl_2/cyclohexane, 1:80:19); ^{1}H NMR (300 MHz, $CDCl_3$, 20 °C, TMS): δ = 8.34 (d, ^3J(H,H) = 8.2 Hz, 2H; H4,13), 8.26 (d, ^3J(H,H) = 8.0 Hz, 2H; H1,10), 8.18 (d, ^3J(H,H) = 7.8 Hz, 2H; H7,16), 7.95 (d, ^3J(H,H) = 7.8 Hz, 2H; H8,17), 7.85–7.79 (m, 2H; H3,12), 7.82–7.75 (m, 2H; H2,11), 7.79 (s, 2H; H6,15), 4.29 (q, ^3J(H,H) = 7.1 Hz, 4H; 2×CH_2), 1.31 ppm (t, ^3J(H,H) = 7.1 Hz, 6H; 2×CH_3); ^{13}C NMR (75 MHz, $CDCl_3$, 20 °C, TMS): δ = 185.2, 182.8, 165.2 (2×CO_2Et), 151.9 (2×*C*CO_2Et), 146.6, 145.9, 134.5 (C4a,13a), 134.5

(C4,13), 133.3 (C5a,14a), 132.1 (C8a,17a), 130.2 (C1,10), 128.8 (C9a,18a), 127.8 (C2,3,11,12), 127.3 (C8,17), 127.1 (C7,16), 62.2 (2×CH_2), 48.6 (C6,15), 14.4 ppm (2×CH_3); elemental analysis calcd (%) for $C_{38}H_{24}O_8$: C 74.99, H 3.97; found: C 74.2, H 4.1; MS (CI): *m/z*: 609 [M^++H], 608 [M^+].

Diethyl ester (±)-6: Sodium borohydride (62 mg, 1.6 mmol, 12 equiv) was added portionwise to a suspension of (±)-**5** (100 mg, 0.16 mmol) in dry methanol (3.5 mL) at −20 °C over 15 min. After a further 15 min of stirring, diglyme (3 mL) was added. After the addition of further sodium borohydride, the reaction was monitored by TLC until complete consumption of the starting material. Once homogeneous, the reaction mixture was warmed to −5 °C, diluted with cold dry methanol (3.5 mL), and slowly poured into a cold (5 °C) saturated solution of tin(II) chloride in 10% HCl (100 mL) under stirring. The aqueous phase was extracted with chloroform. The combined organic layers were dried over sodium sulfate, filtered, and concentrated and the residue was purified by flash chromatography on silica eluting with dichloromethane/cyclohexane 70:30 to afford (±)-**6** as a yellow solid (85 mg, 0.15 mmol, 94%). R_f=0.20 (CH_2Cl_2/cyclohexane, 70:30); ^{1}H NMR (300 MHz, $CDCl_3$, 20 °C, TMS): δ=8.90 (s, 2H; H5,14), 8.42 (s, 2H; H9,18), 8.13 (d, ^3J(H,H)=8.7 Hz, 2H; H4,13), 7.94 (d, ^3J(H,H)=8.1 Hz, 2H; H1,10), 7.79 (d, ^3J(H,H)=8.6 Hz, 2H; H7,16), 7.76 (d, ^3J(H,H)=8.6 Hz, 2H; H8,17), 7.53–7.45 (m, 2H; H3,12), 7.49–7.41 (m, 2H; H2,11), 6.72 (s, 2H; H6,15), 4.28 (q, ^3J(H,H)=7.1 Hz, 4H; 2×CH_2), 1.28 ppm (t, ^3J(H,H)=7.1 Hz, 6H; 2×CH_3); ^{13}C NMR (75 MHz, $CDCl_3$, 20 °C, TMS): δ=166.0 (2×CO_2Et), 149.2 (2×*C*CO_2Et), 143.41, 143.36, 132.1 (C4a,13a), 131.3 (C5a,14a), 130.3 (C6a,17a), 128.5 (C4,13), 128.3 (C1,10), 127.8 (C9a,18a), 127.5 (C9,18), 125.8 (C2,3,11,12), 125.5 (C8,17), 122.8 (C7,16), 120.3 (C5,14), 61.7 (2×CH_2), 50.5 (C6,15), 14.2 ppm (2×CH_3); MS (CI): *m/z*: 548 [M^+].

Di(−)-menthyl esters (6*R*,15*R*)-7 and **(6*S*,15*S*)-7**: Powdered indium (163 mg, 1.4 mmol, 3.7 equiv) and doubly sublimed iodine (540 mg, 2.1 mmol, 5.6 equiv) were added to molten (−)-menthol (3.5 g, 22 mmol, 60 equiv) at 45 °C. The reaction mixture was stirred at 45 °C for 30 min and then (±)-**6** (210 mg, 0.38 mmol) was added. The resulting mixture was stirred at 80 °C for 40 h. Most of the excess of (−)-menthol was removed by sublimation. The remaining material was dissolved in diethyl ether, and the solution was washed with a saturated solution of sodium thiosulfate and brine, dried over sodium sulfate, filtered, and concentrated. The residue was purified by flash chromatography on silica eluting with ethyl acetate/dichloromethane (gradient from 1:99 to 4:96) to afford (6*R*,15*R*)-**7** and (6*S*,15*S*)-**7** (255 mg, 0.33 mmol, 88%). The two diastereoisomers were separated by column chromatography on fine silica eluting with ethyl acetate/cyclohexane 90:10 (*de* >99%, Chiralcel OD-H column, 0.46×25 cm, 0.5 mL min^{-1}, ethanol/hexane (0.8:99.2), $t_{R(6R,15R)\text{-}7}$=14.1 min and $t_{R(6S,15S)\text{-}7}$=15.4 min; see the Supporting Information for chromatograms). Data for (6*R*,15*R*)-**7**: R_f=0.29 (AcOEt/cyclohexane, 10:90); ^{1}H NMR (200 MHz, $CDCl_3$, 20 °C, TMS): δ=8.83 (s, 2H; H5,14), 8.35 (s, 2H; H9,18), 8.05 (d, ^3J(H,H)=8.2 Hz, 2H; H4,13), 7.87 (d, ^3J(H,H)=8.0 Hz, 2H; H1,10), 7.72 (m, 4H; H7,8,16,17), 7.48–7.38 (m, 2H; H3,12), 7.42–7.32 (m, 2H; H2,11), 6.67 (s, 2H; H6,15), 4.87 (td, ^3J(H,H)=10.8 Hz, ^3J(H,H)=4.2 Hz, 2H; 2×OCH), 2.10–0.75 ppm (m, 36H); ^{13}C NMR (50 MHz, $CDCl_3$, 20 °C, TMS): δ=165.3 (2×CO_2), 149.0 (2×*C*CO_2), 143.44, 143.38, 132.1 (C4a,13a), 131.3 (C5a,14a), 130.3 (C8a,17a), 128.4 (C4,13), 128.3 (C1,10), 127.9 (C9a,18a), 127.4 (C9,18), 125.8, 125.7, 125.4 (C8,17), 122.8 (C7,16), 120.2 (C5,14), 76.0 (2×OCH), 50.7 (C6,15), 47.1 (2×OCHCH_2*C*H), 41.0 (2×OCHCHCH_2*C*H_2), 34.4 (2×OCHCH*C*H_2), 31.6 (2×$(CH_3)_2$*C*H), 26.2 (2×OCH*C*H), 23.3 (2×OCH*C*H_2), 22.2 (2×CHCH*C*H_3), 21.1 (2×CHCH*C*H_3), 16.4 ppm (2×CH_2CH*C*H_3). Data for (6*S*,15*S*)-**7**: R_f=0.29 (AcOEt/cyclohexane, 10:90); ^{1}H NMR (200 MHz, $CDCl_3$, 20 °C, TMS): δ=8.83 (s, 2H; 2×H5,14), 8.33 (s, 2H; H9,18), 8.07 (d, ^3J(H,H)=8.2 Hz, 2H; H4,13), 7.86 (d, ^3J(H,H)=8.0 Hz, 2H; H1,10), 7.76 (d, ^3J(H,H)=8.4 Hz, 2H; H7,16), 7.68 (d, ^3J(H,H)=8.4 Hz, 2H; H8,17), 7.48–7.38 (m, 2H; 2×H3,12), 7.43–7.33 (m, 2H; H2,11), 6.67 (s, 2H; H6,15), 4.85 (td, ^3J(H,H)=10.8 Hz, ^3J(H,H)=4.1 Hz, 2H; 2×OCH), 2.21–0.70 ppm (m, 36H); ^{13}C NMR (50 MHz, $CDCl_3$, 20 °C, TMS): δ=165.5 (2×CO_2), 148.6 (2×*C*CO_2), 143.5 (C5b,6a,14b,15a), 132.0 (C4a,13a), 131.2 (C5a,14a), 130.3 (C8a,17a), 128.4 (C4,13), 128.3 (C1,10), 127.8 (C9a,18a), 127.4 (C9,18), 125.8, 125.7, 125.4 (C8,17), 122.9 (C7,16), 120.1 (C5,14), 76.0 (2×O*C*H), 50.6 (C6,15), 46.9 (2×OCHCH_2CH), 41.0 (2×OCHCHCH_2CH_2), 34.3 (2×OCHCH*C*H_2), 31.6 (2×$(CH_3)_2$*C*H), 26.0 (2×OCH*C*H), 23.2 (2×OCH*C*H_2), 22.2 (2×CHCH*C*H_3), 20.9 (2×CHCH*C*H_3), 16.2 ppm (2×CH_2CH*C*H_3).

Diacid (6*R*,15*R*)-8: Lithium hydroxide (50 mg, 2.3 mmol, 23 equiv) was added to a solution of (6*R*,15*R*)-**7** (76 mg, 0.10 mmol, 1.0 equiv) in ethanol (20 mL) and the mixture was refluxed for 6 h. Water (60 mL) and 1 N HCl were then added to the cooled reaction mixture, and the aqueous phase was extracted with ethyl acetate. The combined organic phases were dried over sodium sulfate, filtered, and concentrated to dryness. The crude residue was purified by flash chromatography on silica eluting with methanol/ethyl acetate (gradient from 0:100 to 40:60). The purified product was dried under reduced pressure and redissolved in chloroform (10 mL). The solution obtained was filtered to remove the silica and concentrated once more to afford (6*R*,15*R*)-**8** (49 mg, 0.10 mmol, 99%). R_f=0.20 (MeOH/AcOEt, 5:95); ^{1}H NMR (300 MHz, CD_3OD, 20 °C, TMS): δ=9.04 (s, 2H; H5,14), 8.38 (s, 2H; 2×H9,17), 8.12 (d, ^3J(H,H)=8.3 Hz, 2H; H4,13), 7.90 (d, ^3J(H,H)=8.3 Hz, 2H; H1,10), 7.81 (d, ^3J(H,H)=8.3 Hz, 2H; H7,16), 7.72 (d, ^3J(H,H)=8.3 Hz, 2H; H8,17), 7.47–7.40 (m, 2H; H3,12), 7.42–7.35 (m, 2H; H2,11), 7.29 ppm (s, 2H; H6,15); ^{13}C NMR (75 MHz, CD_3OD, 20 °C, TMS): δ=169.5 (2×CO_2H), 154.2 (2×*C*CO_2H), 145.2, 145.0, 133.4 (C4a,13a), 132.5 (C5a,14a), 131.6 (C8a,17a), 129.4 (C4,13), 129.2 (C9a,18a), 129.1 (C1,10), 128.2 (C9,18), 126.6, 126.4, 126.2 (C8,17), 123.8 (C7,16), 121.4 (C5,14), 53.0 ppm (C6,15); HRMS: calcd for $C_{34}H_{20}O_4$: 491.1278 [M^++H]; found (ESI-TOF): *m/z*: 491.1286.

Diacid (6*S*,15*S*)-8: Following the same procedure as that used for the synthesis of (6*R*,15*R*)-**8**, but using (6*S*,15*S*)-**7** (77 mg, 0.10 mmol, 1.0 equiv) instead of (6*R*,15*R*)-**7**, gave (6*S*,15*S*)-**8** (49 mg, 0.10 mmol, 99%). HRMS (ESI-TOF): *m/z*: 491.1314 [M^++H].

Compound (6*R*,15*R*)-10: The formate salt of *tert*-butyl (*S*)-6-amino-2-{bis[(*tert*-butoxycarbonyl)methyl]amino}hexanoate[14] (115 mg, 0.22 mmol, 6.4 equiv) was dissolved in a saturated aqueous solution of potassium carbonate (20 mL), which was then extracted with ethyl acetate. The combined organic phases were dried over magnesium sulfate, filtered, and concentrated to dryness to give the free base, which was redissolved in benzene (5.5 mL) and 1,4-dioxane (5.5 mL) and added to a solution of (6*R*,15*R*)-**8** (17 mg, 0.034 mmol, 1.0 equiv) in a mixture of benzene (1.5 mL) and 1,4-dioxane (1.5 mL). A 50% solution of *n*-propylphosphonic anhydride (T3P) in ethyl acetate (61 μL, 0.66 mmol, 3.0 equiv) was added, followed by *N*-ethyl-*N*,*N*-diisopropylamine (42 μL, 1.54 mmol, 7.0 equiv). More T3P (61 μL, 0.66 mmol, 3.0 equiv) was added after 2 h of stirring at room temperature. Once all of the starting material and intermediates (TLC on silica, methanol/ethyl acetate, 10:90, R_f=0.5) had been consumed, the reaction mixture was washed with brine (2×10 mL). The combined aqueous phases were extracted with ethyl acetate (10 mL). The combined organic phases were dried over sodium sulfate, filtered, and concentrated to dryness. The crude residue was purified by flash chromatography on silica eluting with ethyl acetate/dichloromethane 10:90 to afford (6*R*,15*R*)-**10** (9 mg, 0.007 mmol, 20%) as a yellow solid. R_f=0.20 (AcOEt/CH_2Cl_2, 5:95); ^{1}H NMR (300 MHz, $CDCl_3$, 20 °C, TMS): δ=8.95 (s, 2H; H5,14), 8.41 (s, 2H; H9,18), 8.13 (d, ^3J(H,H)=8.1 Hz, 2H; H4,13), 7.94 (d, ^3J(H,H)=8.1 Hz, 2H; H1,10), 7.85 (d, ^3J(H,H)=8.4 Hz, 2H; H7,16), 7.93 (d, ^3J(H,H)=8.4 Hz, 2H; H8,17), 7.52–7.45 (m, 2H; H3,12), 7.47–7.40 (m, 2H; H2,11), 7.13 (br t, ^3J(H,H)=7 Hz, 2H; 2×NH), 6.86 (s, 2H; H6,15), 3.49 (d, ^3J(H,H)=17.3 Hz, 4H; 2×N(C$H_A$$H_B$)$_2$), 3.41 (d, ^3J(H,H)=17.3 Hz, 4H; 2×N(C$H_A$$H_B$)$_2$), 3.45–3.20 (m, 6H; 2×NHCH_2, 2×NCH), 1.41 (s, 18H; 2×C(CH_3)$_3$), 1.40 (s, 36H; 4×C(CH_3)$_3$), 1.70–1.25 ppm (m, 12H; 2×NHCH$_2$CH_2CH_2CH_2); ^{13}C NMR (50 MHz, $CDCl_3$, 20 °C, TMS): δ=172.4 (2×CO_2*t*Bu), 170.8 (4×CO_2*t*Bu), 166.6 (2×CON), 149.4 (2×*C*CON), 143.7, 143.4, 132.2 (C4a,13a), 131.3 (C5a,14a), 130.3 (C8a,17a), 128.5 (C4,13), 128.3 (C9a,18a), 127.8 (C1,10), 127.5 (C9,18), 125.9, 125.7, 125.5 (C8,17), 123.0 (C7,16), 120.1 (C5,14), 81.2 (2×*C*(CH$_3$)$_3$), 80.8 (4×*C*(CH$_3$)$_3$), 65.3 (2×NCH), 53.8 (2×N(CH$_2$)$_2$), 51.6 (C6,15), 40.0 (2×NHCH$_2$), 30.4 (2×NHCH$_2$CH_2), 29.2 (2×NCH*C*H$_2$), 28.3 (6×CH$_3$), 28.2 (12×CH$_3$), 23.5 ppm (2×NHCH$_2$CH$_2$CH_2CH$_2$); UV/Vis (1,4-dioxane/chloroform, 92:8): λ_{max} (ε)=484 (10000), 404 (200000), 384 (220000), 366 (200000), 346 (160000), 272 nm (3700000 mol^{-1}m^{3}cm^{-1}); HRMS: calcd for

$C_{78}H_{100}N_4O_{14}$: 1317.7309 [M^++H]; found (ESI-TOF): m/z: 1317.7236. The CD spectrum is displayed in the Supporting Information.

Compound (6*S*,15*S*)-10: Following the same procedure as that used for the synthesis of (6*R*,15*R*)-**10**, but using (6*S*,15*S*)-**8** (22 mg, 0.044 mmol, 1.0 equiv) instead of (6*R*,15*R*)-**8**, gave (6*S*,15*S*)-**10** (12 mg, 0.009 mmol, 20%) as a yellow solid. R_f = 0.20 (AcOEt/CH_2Cl_2, 5:95); ^{1}H NMR (300 MHz, $CDCl_3$, 20°C, TMS): δ = 8.96 (s, 2H; H5,14), 8.41 (s, 2H; H9,18), 8.14 (d, ^3J(H,H) = 8.1 Hz, 2H; H4,13), 7.93 (d, ^3J(H,H) = 8.1 Hz, 2H; H1,10), 7.84 (d, ^3J(H,H) = 8.4 Hz, 2H; H7,16), 7.75 (d, ^3J(H,H) = 8.4 Hz, 2H; H8,17), 7.52–7.45 (m, 2H; H3,12), 7.47–7.40 (m, 2H; H2,11), 7.18 (br m, 2H; 2×NH), 6.86 (s, 2H; H6,15), 3.50 (d, ^3J(H,H) = 17.6 Hz, 4H; 2×N(C$H_A$$H_B$)$_2$), 3.43 (d, ^3J(H,H) = 17.6 Hz, 4H; 2×N(CH$_A$$H_B$)$_2$), 3.45–3.20 (m, 6H; 2×NHCH_2, 2×NCH), 1.42 (s, 18H; 2×C(CH$_3$)$_3$), 1.39 (s, 36H; 4×C(CH$_3$)$_3$), 1.65–1.20 ppm (m, 12H; 2×NHCH$_2$CH_2CH_2CH_2); ^{13}C NMR (50 MHz, $CDCl_3$, 20°C, TMS): δ = 172.4 (2×CO_2*t*Bu), 170.8 (4×CO_2*t*Bu), 166.6 (2×CON), 149.4 (2×*C*CON), 143.7, 143.4, 132.2 (C4a,13a), 131.3 (C5a,14a), 130.4 (C8a,17a), 128.6 (C4,13), 128.3 (C9a,18a), 127.8 (C1,10), 127.5 (C9,18), 125.9, 125.7, 125.4 (C8,17), 123.0 (C7,16), 120.2 (C5,14), 81.2 (2×*C*(CH$_3$)$_3$), 80.8 (4×*C*(CH$_3$)$_3$), 65.4 (2×NCH), 53.9 (2×N(CH$_2$)$_2$), 51.6 (C6,15), 40.0 (2×NHCH$_2$), 30.4 (2×NHCH$_2$CH_2), 29.2 (2×NCHCH_2), 28.34 (6×CH$_3$), 28.25 (12×CH$_3$), 23.6 ppm (2×NHCH$_2$CH$_2$CH_2); UV/Vis (1,4-dioxane/chloroform, 92:8): λ_{max} (ε) = 484 (10000), 404 (220000), 384 (240000), 366 (220000), 346 (180000), 272 nm (4100000 mol^{-1}m^{3}cm^{-1}); HRMS: calcd for $C_{78}H_{100}N_4O_{14}$: 1339.7128 [M^++Na]; found (ESI-TOF): m/z: 1339.7078. The CD spectrum is displayed in the Supporting Information.

Compound (6*R*,15*R*)-1: A large excess of trifluoroacetic acid (1 mL) was added to a solution of (6*R*,15*R*)-**10** (16 mg, 0.012 mmol, 1.0 equiv) in chloroform (0.05 mL). The reaction mixture was stirred for 30 h at room temperature, and then diethyl ether (2 mL) was added and the resulting mixture was concentrated under reduced pressure. Twice more, diethyl ether (2 mL) was added and the solution obtained was concentrated to dryness to yield a yellow solid (12 mg, 0.012 mmol, 99%). $t_{R(6R,15R)\text{-}10}$ = 16.4 min (Dionex Acclaim 120-C18, 0.46×25 cm, 1.0 mL min^{-1}, acetonitrile/50 mM $AcONH_4$, pH 6.8, gradient from 0:100 to 100:0 in 30 min); ^{1}H NMR (300 MHz, CD_3OD, 20°C, TMS): δ = 9.04 (s, 2H; H5,14), 8.39 (s, 2H; H9,18), 8.14 (d, ^3J(H,H) = 8.1 Hz, 2H; H4,13), 7.91 (d, ^3J(H,H) = 8.7 Hz, 2H; H1,10), 7.87 (d, ^3J(H,H) = 8.1 Hz, 2H; H7,16), 7.74 (d, ^3J(H,H) = 8.1 Hz, 2H; H8,17), 7.50–7.35 (m, 6H; H2,3,11,12, 2×NH), 6.80 (s, 2H; H6,15), 3.85–3.50 (m, 14H; 2×NHCH_2, 2×NCH, 2×N(CH$_2$)$_2$), 1.90–1.10 ppm (m, 12H; 2×NHCH$_2$CH_2CH_2CH_2); ^{13}C NMR (75 MHz, CD_3OD, 20°C, TMS): δ = 172.8 (2×CO_2H), 174.5 (4×CO_2H), 168.7 (2×CON), 150.5 (2×*C*CON), 145.2, 145.1, 133.5 (C4a,13a), 132.6 (C5a,14a), 131.6 (C8a,17a), 129.4 (C4,13), 129.2 (C9a,18a), 129.0 (C1,10), 128.3 (C9,18), 126.8, 126.6, 126.4 (C8,17), 123.8 (C7,16), 121.3 (C5,14), 67.0 (2×NCH), 55.2 (2×N(CH$_2$)$_2$), 52.0 (C6,15), 40.4 (2×NHCH$_2$), 30.5 (2×NHCH$_2$CH_2), 29.8 (2×NCHCH_2), 24.7 ppm (2×NHCH$_2$CH$_2$CH_2); MS (MALDI-TOF negative-ion mode, α-cyano-4-hydroxycinnamic acid (HCCA), MeCN/H_2O, 99:1): m/z: 979 [M^+−H]. The CD spectrum is displayed in Figure 2.

Compound (6*S*,15*S*)-1: Following the same procedure as that used for the synthesis of (6*R*,15*R*)-**1**, but using (6*S*,15*S*)-**10** (20 mg, 0.015 mmol, 1.0 equiv) instead of (6*R*,15*R*)-**10**, gave (6*S*,15*S*)-**1** (15 mg, 0.015 mmol, 99%) as a yellow solid. $t_{R(6S,15S)\text{-}10}$ = 16.7 min (Dionex Acclaim 120-C18, 0.46×25 cm, 1.0 mL min^{-1}, acetonitrile/50 mM $AcONH_4$, pH 6.8, gradient from 0:100 to 100:0 in 30 min); ^{1}H NMR (300 MHz, CD_3OD, 20°C, TMS): δ = 9.04 (br s, 2H; H5,14), 8.38 (br s, 2H; H9,18), 8.20–8.10 (m, 2H; H4,13), 7.97–7.81 (m, 4H; H1,7,10,16), 7.77–7.69 (m, 2H; H8,17), 7.50–7.35 (m, 6H; H2,3,11,12, 2×NH), 6.79 (s, 2H; H6,15), 3.85–3.50 (m, 14H; 2×NHCH_2, 2×NCH, 2×N(CH$_2$)$_2$), 1.90–1.10 ppm (m, 12H; 2×NHCH$_2$CH_2CH_2CH_2); ^{13}C NMR (50 MHz, CD_3OD, 20°C, TMS): δ = 175.8 (2×CO_2H), 175.1 (4×CO_2H), 168.7 (2×CON), 150.5 (2×*C*CON), 145.2 (C5b,6a,14b,15a), 133.5 (C4a,13a), 132.6 (C5a,14a), 131.6 (C8a,17a), 129.5 (C4,13), 129.2 (C9a,18a), 129.0 (C1,10), 128.2 (C9,18), 126.8, 126.5, 126.4 (C8,17), 123.9 (C7,16), 121.3 (C5,14), 66.9 (2×NCH), 55.3 (2×N-(CH$_2$)$_2$), 52.0 (C6,15), 40.5 (2×NHCH$_2$), 30.5 (2×NHCH$_2$CH$_2$), 29.9 (2×NCHCH_2), 24.8 ppm (2×NHCH$_2$CH$_2$CH_2); MS (MALDI-TOF negative-ion mode, HCCA, MeCN/H_2O, 99:1): m/z: 979 [M^+−H]. The CD and absorbance spectra are displayed in Figure 2.

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[1] Y. Cheng, D. M. Ho, G. R. Gottlieb, D. Kahne, *J. Am. Chem. Soc.* **1992**, *114*, 7319–7320.
[2] a) E. T. Kaiser, F. J. Kezdy, *Science* **1984**, *223*, 249–255; b) S. Takahashi, *Biochemistry* **1990**, *29*, 6257–6264.
[3] a) F. M. Menger, J. L. Sorrells, *J. Am. Chem. Soc.* **2006**, *128*, 4960–4961; b) U. Taotafa, D. B. McMullin, S. C. Lee, L. D. Hansen, P. B. Sauvage, *Org. Lett.* **2000**, *2*, 4117–4120; c) J. Lu, S.-Z. Kang, S. L. Xu, Q.-D. Zeng, C. Wang, L.-J. Wan, C.-L. Bai, *Chem. Commun.* **2003**, 1498–1499; d) Z. Zhong, J. Yan, Y. Zhao, *Langmuir* **2005**, *21*, 6235–6239; e) S.-L. Xu, S.-Z. Kang, J. Lu, Y.-H. Liu, C. Wang, L.-J. Wan, C.-L. Bai, *Surfactant Sci. Ser.* **2003**, *527*, L171–L176.
[4] R. Marquis, C. Greco, I. Sadokierska, S. Lebedkin, M. M. Kappes, T. Michel, L. Alvarez, J.-L. Sauvajol, S. Meunier, C. Mioskowski, *Nano Lett.* **2008**, *8*, 1830–1835.
[5] Z. Chen, J. Appenzeller, J. Knoch, Y.-M. Lin, P. Avouris, *Nano Lett.* **2005**, *5*, 1497–1502.
[6] a) D. Yuan, J. Liu, *Small* **2007**, *3*, 366–367; b) R. Krupke, F. Hennrich, H. V. Loehneysen, M. M. Kappes, *Science* **2003**, *301*, 344–347; c) M. S. Arnold, A. A. Green, J. F. Hulvat, S. I. Stupp, M. C. Hersam, *Nat. Nanotechnol.* **2006**, *1*, 60–65; d) M. S. Strano, M. Zheng, A. Jagota, G. B. Onoa, D. A. Heller, P. W. Barone, M. L. Usrey, *Nano Lett.* **2004**, *4*, 543–550; e) A. Nish, J.-Y. Hwang, J. Doig, R. J. Nicholas, *Nat. Nanotechnol.* **2007**, *2*, 640.
[7] a) N. Nish, J.-Y. Hwang, J. Doig, R. J. Nicholas, *Nat. Nanotechnol.* **2007**, *2*, 640–646; b) F. Chen, B. Wang, Y. Chen, L.-J. Li, *Nano Lett.* **2007**, *7*, 3013–3017; c) R. M. Tromp, A. Afzali, M. Freitag, D. B. Mitzi, Z. Chen, *Nano Lett.* **2008**, *8*, 469–472.
[8] a) N. Komatsu, *J. Inclusion Phenom. Macrocyclic Chem.* **2008**, *61*, 195–216; b) X. Peng, N. Komatsu, S. Bhattacharya, T. Shimawaki, J. Aonuma, T. Kimura, A. Osuka, *Nat. Nanotechnol.* **2007**, *2*, 361–365; c) X. Peng, N. Komatsu, T. Kimura, A. Osuka, *J. Am. Chem. Soc.* **2007**, *129*, 15947–15953; d) X. Peng, F. Wang, T. Kimura, N. Komatsu, A. Osuka, *J. Phys. Chem. C* **2009**, *113*, 9108–9113.
[9] D. Biermann, W. Schmidt, *J. Am. Chem. Soc.* **1980**, *102*, 3173–3181.
[10] a) N. Harada, Y. Takuma, H. Uda, *J. Am. Chem. Soc.* **1976**, *98*, 5408–5409; b) N. Harada, Y. Takuma, H. Uda, *Bull. Chem. Soc. Jpn.* **1977**, *50*, 2033–2038.
[11] E. Clar, *Chem. Ber.* **1948**, *81*, 169–175.
[12] a) A. Sygula, R. Sygula, A. Ellern, P. W. Rabideau, *Org. Lett.* **2003**, *5*, 2595–2597; b) R. Schwenninger, Y. Ramondenc, K. Wurst, J. Schlögl, B. Kräutler, *Chem. Eur. J.* **2000**, *6*, 1214–1223; c) J. C. Adrian, Jr., T. M. Ovitt, *Tetrahedron: Asymmetry* **1996**, *7*, 2407–2410; d) M. A. Petti, T. J. Shepodd, R. E. Barrans, D. A. Dougherty, *J. Am. Chem. Soc.* **1988**, *110*, 6825–6840.
[13] B. C. Ranu, P. Dutta, A. Sarkar, *J. Org. Chem.* **1998**, *63*, 6027–6028.
[14] a) M. N. Tahir, P. Theato, W. E. G. Mueller, H. C. Schroeder, A. Janshoff, J. Zhang, J. Huth, W. Tremel, *Chem. Commun.* **2004**, 2848–2849; b) Z. Huang, J. I. Park, D. S. Watson, P. Hwang, F. C. Szoka, Jr., *Bioconjugate Chem.* **2006**, *17*, 1592–1600.
[15] a) H. Wissmann, H. J. Kleiner, *Angew. Chem.* **1980**, *92*, 129–130; *Angew. Chem. Int. Ed.* **1980**, *19*, 133–134; b) J. Klose, C. Mollenkopf, D. Wehle, C.-W. Zhang, L. A. Carpino, P. Henklein, *Chem. Commun.* **1999**, 1847–1848; c) M. Schwarz, *Synlett* **2000**, 1369.
[16] S. M. Bachilo, M. S. Strano, C. Kittrell, R. H. Hauge, R. E. Smalley, R. B. Weisman, *Science* **2002**, *298*, 2361–2366.
[17] S. Lebedkin, K. Arnold, F. Hennrich, R. Krupke, B. Renker, M. M. Kappes, *New J. Phys.* **2003**, *5*, 140.

[18] To date, and as underlined by N. Komatsu (ref. [8]), CD measurements do not allow the discrimination of optical activity due to SWNTs and induced optical activity of racemic SWNTs (as observed, for example, by adsorbing DNA on a racemic mixture of SWNTs; G. Dukovic, M. Balaz, P. Doak, N. D. Berova, M. Zheng, R. S. Mclean, L. E. Brus, *J. Am. Chem. Soc.* **2006**, *128*, 9004–9005). For this reason, and because of the very high optical activity of compounds **1**, extensive washings were required for its complete removal from the SWNT samples in order to unequivocally measure the optical enrichment due to the chiral SWNTs. In this process, we incurred a dramatic loss in material, which prevented us from recording CD signals strong enough to be conclusive.

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