Campestarenes: new building blocks with 5-fold symmetry†

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Campestarene is a planar, shape-persistent macrocycle with 5-fold symmetry. A range of derivatives bearing peripheral functional groups suitable for generating supramolecular interactions has been designed and synthesised for potential applications in creating 2D quasicrystal molecular assemblies. The new campestarene derivatives bear ester, carboxylic acid, methoxy, bromo, 4-pyridyl, 4-cyanophenyl and 4-phenyl carboxylic acid groups, including further derivatives of the latter two bearing alkyl chains on the phenyl groups to improve solubility. The campestarene derivatives were prepared by reductive condensation of phenol precursors bearing nitro and formyl groups using Na2S2O4. The target functional groups were installed either by pre-cyclisation derivatisation or by synthesis of methoxy-substituted campestarene and subsequent derivatisation. The cyclisation reaction is tolerant of the functional groups introduced. The ten new campestarene derivatives were characterised by NMR spectroscopy and MALDI-TOF MS, although the poor solubility of some examples precluded their detailed characterisation.

Introduction

Architects and builders designing and constructing houses need supply yards full of building materials of the right size, shape and material properties to create buildings with the desired dimensions, features and functions. The same is true for nano-architects and builders whose supplies of suitable molecular building blocks need to develop to keep pace with the increasing sophistication of their supramolecular nanoarchitectures. Just as the shape of an individual brick has a relationship with the symmetry and properties of the wall it is used to build, individual molecular building blocks also determine the symmetry and properties of supramolecular nanoarchitectures. For this reason, shape-persistent molecular building blocks have proved extremely useful for the design and construction of ordered 2D and 3D materials on the nanoscale. Amongst these, macrocycles with full or partial conjugation have proved especially useful. The macrocycles themselves often contain aryl units as integral components linked by amide, ethynyl or imine bridges which have well-defined spatial configurations and organise the overall shape of the macrocycles.1–6 Porphyrins, with their well-defined 4-fold symmetry and planar geometry, are quintessential examples.7,8 Shape-persistent building blocks with 2-, 3-, 4- and 6-fold symmetry are common, with many synthetically accessible examples available, and have been extensively studied for 2D and 3D assemblies which typically replicate the symmetry of their components.1,7,8 However, extending this principle to the use of building blocks with 5-fold symmetry to generate assemblies which demonstrate 5-fold symmetry in extended arrays has proved much more challenging, primarily because the expression of 5-fold symmetry in 2D and 3D assemblies is inherently more complex. The building blocks cannot pack regularly, as evidenced by the particular properties of Penrose tiling patterns in 2D and quasicrystal packing in 3D.

This challenge has received growing interest in recent times, prompted in part by the observation that 3D quasicrystalline metal alloys show unusual properties in a range of applications.9–13 However, the rational design and assembly of 2D quasicrystal packing using molecular pentagons as building blocks remains an elusive goal. It requires an understanding of the unique symmetry properties of 2D crystal tiling patterns based on a pentagonal tile, which are ordered but translationally aperiodic.14–18 Amongst the conceivable experimental approaches, the most obvious is the deposition of planar molecular pentagons on a surface. Attempts to do this have shown that the hexagonal symmetry of the underlying surface rather than the pentagonal shape of the molecule determines the packing arrangement.19 In a serendipitous discovery, regions of 2D quasicrystalline, Penrose tile ordering of ferrocene carboxylic acid molecules on a surface were observed in which the ordering was directed by supramolecular interactions between the ferrocene carboxylic acid groups.20,21 This points to the need for inclusion of functional groups suitable
for generating supramolecular interactions on the periphery of the building blocks. This approach has been shown to play a significant role in the packing orientation in 2D self-assembly.22

A further barrier to the exploration of quasicrystalline packing in 2D is the paucity of synthetically available, shape-persistent macrocyclic building blocks with 5-fold symmetry.23–25 Examples from the recent literature are the family of macrocyclic pentamers from Zeng’s group,31,33,34 cyanostar reported by Flood et al.,32 and MacLachlan’s campestarene.30,35 Although these molecules are planar and rigorously 5-fold symmetric, all of them bear alkyl groups as the peripheral substituents and so are not ideal as building blocks for 2D supramolecular assemblies.19,30,32,34 Suitably functionalised macrocyclic pentamers could be useful for this purpose, and also for dendrimer design and as building blocks for metal- or covalent-organic frameworks (MOFs or COFs).36 The goal of this study was to elaborate the synthesis of the campestarene framework to allow the inclusion of a range of different functional groups on the periphery which could serve as a supply of 5-fold symmetric building blocks for supramolecular assemblies.

Campestarenes are cyclic pentamers comprised of imine-linked phenol groups. Several tautomers can be envisaged, with enol-imine and keto-enamine forms as well as a zwitterionic structure. Overall, the regular, planar shape is reinforced by the 3-centered hydrogen bonds between the imines and hydroxy groups (Fig. 1).30 Campestarenes are prepared by sequential formylation and nitration of the corresponding phenols, followed by cyclisation via a Schiff base amine-aldehyde condensation which gives a homogeneous product in high yield. The high selectivity for the pentameric structure from the one-pot cyclisation is accounted for based on ab initio DFT calculations, which for both tautomers of the pentamer were in accord with the experimentally observed planar structure, whereas the hexamer was calculated to adopt a twisted confirmation.30 The planar structure favours intermolecular π–π stacking leading to aggregation in solution and in the gas phase.37,38 Substitution with bulky organosilyl groups improved their solubility in both polar and non-polar solvents allowing full characterisation, including a molecular structure determination.35 Experimental studies on the tautomerisation behaviour of campestarenes concluded that the location of the interior protons was on nitrogen (keto-enamine form) in polar solvents and on oxygen (enol-imine form) in non-polar solvents, in agreement with DFT calculations. Campestarene derivatives reported to date bear tert-butyl,30 1,1-dimethyl-propyl,30 1,1,3,3-tetramethyl-buty1,30 triphenylsilyl35 and trisopropylsilyl groups35 on the periphery 1a–1e (Table 1).

The current study extends the synthetic routes to campestarene derivatives containing ester, carboxylic acid, methoxy, bromo, 4-pyridyl, 4-cyanophenyl and 4-phenyl carboxylic acid groups, 1f–1o, chosen for their potential utility as supramolecular recognition groups for the construction of molecular assemblies.

### Results and discussion

The first approach to functionalising campestarenes is pre-cyclisation derivatisation where the target functional group is installed in the para-position of the monomeric phenol before the cyclisation. Scheme 1 shows three synthetic routes to the mono-substituted hydroquinones (5g-Et, 5f tBu and 5f) required to prepare the precursors 2f–2h to the ester- and carboxylic acid-substituted campestarenes 1f–1h. Route 1 is a single substitution on hydroquinone using bromoacetate t-butyl ester to yield 5g-tBu. Surprisingly, if the bromoacetate ethyl ester was used then a mixture of the di-substituted product and unreacted hydroquinone resulted even when the reaction time, temperature, stoichiometry and solvent were varied. In routes 2 and 3 one hydroquinone hydroxyl group is protected by benzyl and sulfate groups, respectively, resulting in 5g-Et, 5f tBu and 5f after deprotection. The next steps, formylation to give 6g-Et, 6g-tBu and 6f, followed by nitration, yielded the target ester-substituted campestarene precursors, 2g-Et, 2g-tBu and 2f, of which only 2f was taken on directly to the cyclisation step.

Cyclisation of 2f using sodium dithionite in refluxing ethanol/water gave the ester-substituted campestarene 1f. De-esterification of 1f to afford the penta-carboxylic acid...
campestarene 1h using 1 or 2 M NaOH at 50 °C was unsuccessful. In the presence of strong base and heat the 3-centered hydrogen bonds in the macrocycle core were disrupted. Under milder conditions, <1 M NaOH with or without heating, the ester could not be converted into the carboxylic acid. However, the ester precursors 2g-Et and 2g-tBu could be de-esterified to form the carboxylic acid precursors 2g and 2h which were then successfully cyclised to produce the carboxylic acid campestarenes 1g and 1h.

Compound 1f was purified by flash column chromatography on alumina using dichloromethane/methanol as eluent to give a pure purple solid product after solvent removal. Both silica and alumina column chromatography decomposed 1g and 1h. Presumably, the five polar carboxylic acid groups on the macrocycles were excessively adsorbed onto silica and alumina. However, washing 1g and 1h with 0.1 M HCl followed by 0.1 M NaOH removed most of the organic by-products and chromatography on Sephadex G-10 gave solid purple products, 1g and 1h.

Compared to t-butyl campestarene (1a) which is observed to aggregate and exists as a dimer in the gas phase and in solution, the 1H NMR spectra for 1f–1h in DMSO-d6 show no evidence for aggregation (Fig. 2). The signals near 17 and 9 ppm can be assigned to the core hydrogens and the imine protons (N=CH), respectively. The two aromatic protons can be observed near 7.2 and 7.7 ppm. Both 1g and 1h are soluble in methanol, although 1h is the more soluble of the two. The ester campestarene 1f is soluble in both methanol and dichloromethane indicating that the presence of the ester groups confers better solubility in organic solvents than the carboxylic acids. Compounds 1f–1h show limited solubility in methanol and dichloromethane. DMSO dissolved 1f–1h best among organic solvents. Due to the poor solubility of 1f, 1g and 1h, 13C NMR, HSQC and HMBC spectra could not be obtained even after more than 100 000 scans. The assignments of the 1H NMR spectra for 1f–1h are based on comparison with t-butyl campestarene (1a).

An alternative approach to functionalisation of campestarene was conceived via the synthesis of methoxy campestarene, 1i, with a plan to subsequently substitute the methoxy groups. 4-Methoxyphenol was formylated to form 7i and nitrated to prepare the precursor 2i which was cyclised to give 1i (Scheme 2). This purple solid was insoluble in most organic solvents except DMSO and DMF. The crude product 1i was purified by Soxhlet extraction with multiple solvents to remove
imperatives. Although aggregation of 1i with its very flat geometry was expected, no evidence of aggregation was observed by \( ^1H \) NMR spectroscopy in DMSO-\( d_6 \) (Fig. S44†) or MALDI-TOF MS. It is noted that ESI mass spectra could not be recorded for campestarenes. The attempted de-methylation of 1j to form hydroxy campestarene did not proceed to completion, even after addition of excess BBr3. As shown in Fig. S46(b) and (c), the signals assigned to the methoxy protons at 3.9 ppm could still be observed although with diminished intensities. The same difficulty in achieving complete de-methylation has also been reported for another 5-fold symmetric macrocycle.39

The brominated reagent 7j was used because halogens are useful synthons for coupling reactions. Commercially available reagent 7j was nitrate using fuming HNO3 to yield 7j. As shown in Fig. S46(b) and (c),† the signals assigned to the methoxy protons at 3.9 ppm could still be observed although with diminished intensities. The same difficulty in achieving complete de-methylation has also been reported for another 5-fold symmetric macrocycle.39

The third approach to preparing peripherally substituted campestarenes was to begin with boronic acid reagents and employ Suzuki cross-coupling to install the substituents on the precursors 2k–2m (Scheme 2). The boronic acid reagents bearing 4-pyridyl, 4-cyanophenyl and 4-carboxyphenyl groups were coupled to 2j, catalysed by tetrakis(triphenylphosphine) palladium(0), to give 2k–2m. Cyclisation of 2k–2m to synthesise the corresponding campestarenes was successfully achieved to yield the distinctive purple solid products 1k–1m, indicating that the condensation reaction is also tolerant to cyano and pyridyl groups. MALDI-TOF MS confirmed the presence of 1k–1m.

Unfortunately the solubilities of 1k–1m were too poor to complete their purification and characterisation beyond MALDI-TOF MS measurements. Even after multiple purification attempts with washing using the Soxhlet technique for 1k and 1l and acid–base washing followed by Sephadex G-10 column chromatography for 1m, the \( ^1H \) NMR spectra of 1k–1m in DMSO-\( d_6 \) showed broad signals at 7–8 ppm. Based on a report that the solubility of campestarenes could be improved by appending \( n \)-alkyl groups,30 \( n \)-butyl and \( n \)-heptyl groups were attached to the boronic acid reagents, 1o and 1o, which were coupled to the intermediate 2j to synthesise the precursors 2n and 2o (which are alkyl-substituted derivatives of 2m). Cyclisations of 2n and 2o to synthesise campestarenes 1n and 1o were carried out under the same conditions (Scheme 3) and their presence confirmed by MALDI-TOF MS. The solubility of the resulting purple solid products was improved: the \( n \)-butyl campestarene, 1n, is soluble in methanol and the \( n \)-heptyl campestarene, 1o, can even be dissolved in dichloromethane. However, even with improved solubility, broadening of the signals in their \( ^1H \) NMR spectra in DMSO-\( d_6 \) (Fig. S44 and S45†) is still observed even after various attempts at further purification via silica or alumina flash column chromatography, washing using the Soxhlet technique and acid–base washing followed by Sephadex G-10 column chromatography. In addition to the broadening, the NMR spectra show additional structure in the region of the imine N=CH and aryl CH peaks, as reported for 1a–1c and interpreted as evidence for aggregation.30 Aggregation probably also causes
the poor solubility of 1k-1m and for all of 1k-1o most likely arises from the presence of 10 aromatic rings in each campestarene derivative.

Conclusions
Campestarenes substituted with methoxy, alkyl ester and alkyl carboxylic acid can be prepared via sequential formylation and nitration of appropriately substituted precursor monomers followed by cyclisation. The cyclisation method is tolerant of several functional groups on the monomers. The products could be purified by Soxhlet extraction or acid–base washing followed by Sephadex G-10 column chromatography, allowing characterisation by 1H NMR spectroscopy and MALDI-TOF MS. Difficulties with postcyclisation substitution on some of the campestarenes may be attributed to the lower reactivity of campestarenes in comparison with the monomer molecules, for example in the de-methylation reaction. Disruption of the 3-centered hydrogen bonds in the macrocycle core by deprotonation in strongly basic media means that such conditions need to be avoided. The 4-bromophenyl-substituted campestarenes are potentially a useful synthon but difficulties with postcyclisation substitution on some of the sparingly soluble products. Presumably, the additional five aryl groups result in some aggregation with evidence of five equivalents of MgCl2 and 2.2 equivalents of paraformaldehyde. Spectra recorded in CDCl3, D2O, CD3OD, and DMSO-d6 were referenced to TSP-d4 for D2O, or the respective residual solvent peaks. Alkylation40, boronation40, formylation30,41 nitration30, Suzuki coupling42 and cyclisation30 were performed according to literature. Analytical grades of precursors 3, 7j, 8, hydroquinone, phenol, reagents and solvents were purchased and used without further purification.2f,43 2j,44 2m,42 4,45 4g-Et,46 4f,46 5g-Et,45,46 5g-fBu,47 5f,45,46 and 7l48 were synthesised using either reported or modified procedures. Their characterisation data matched literature values. Compounds 6g-Et and 6g-fBu were prepared using Method A, 2g-Et, 2g-fBu and 2f using Method B, 1f–1o using Method C and 2k, 2l, 2n and 20 using Method D.

Method A (6g-Et and 6g-fBu)30
Two equivalents of Et3N were added dropwise to a mixture of 1 equivalents of the corresponding phenol (5g-Et or 5g-fBu), 2 equivalents of MgCl2 and 2.2 equivalents of paraformaldehyde in dry THF. The reaction mixture was refluxed for 24 h, cooled to r.t. and dilute HCl was added until the remaining solid was completely dissolved. The organic phase was removed by rotary evaporation and then the aqueous phase was extracted with CH2Cl2. The combined extracts were dried over MgSO4, filtered and the solvent removed under vacuum. The crude products were purified by silica gel flash column chromatography.

Method B (2g-Et, 2g-fBu and 2f)30
1.1 Equivalents of fuming HNO3 were added dropwise to the corresponding hydroxybenzaldehyde (6g-Et, 6g-fBu or 6f) in glacial acetic acid. After stirring at r.t. for 2 h, water was added to the reaction mixture and a white precipitate formed. The crude product was collected by filtration and recrystallized from hot EtOH by addition of cold water.

Method C (1f–1o)30
Six equivalents of sodium dithionite (Na2S2O4) were added to the corresponding 2-hydroxy-3-nitrobenzaldehyde (2f–2o) in EtOH and water. The reaction mixture was refluxed for 2 h, cooled to r.t. and the solvent removed under vacuum.
Method D (2k, 2l and 2o)\textsuperscript{41}

One equivalent of 2j, 1.2 equivalents of the corresponding boronic acid, 6 equivalents of sodium carbonate and 0.05 equivalents of tetrakis(triphenylphosphine)palladium(0) were dissolved/suspended in DMF/water (1:1). The reaction mixture was heated at 105 °C under N\textsubscript{2} for 6 h. After cooling to r.t., 1 M NaOH was added to the reaction mixture which was then washed with CH\textsubscript{2}Cl\textsubscript{2}. The aqueous phase was acidified with 6 M HCl to give an orange/yellow precipitate which was washed with water and diethyl ether and then dried under vacuum.

Ethyl 2-(3-formyl-4-hydroxyphenoxy) acetate, 6g-Et

Method A. 5g-Et (1.80 g, 9.17 mmol), THF (80 mL) and 5% HCl (150 mL). Purified by flash silica column chromatography (eluent: 10% EtOAc in CH\textsubscript{2}Cl\textsubscript{2}) to give a yellow oil product. The first band was the product. Yield: 0.380 g, 18.5%; HRMS (ESI) \([M + Na]^+ = \text{calcd 261.0739}\).

The crude product was extracted with diethyl ether, refluxed for 24 h, cooled to r.t. and poured into 5% HCl (150 mL). The crude product was extracted with diethyl ether, refluxed for 24 h, cooled to r.t. and poured into 5% HCl (150 mL). Purified by flash silica column chromatography (eluent: 10% EtOAc in CH\textsubscript{2}Cl\textsubscript{2}) to give a yellow oil product. The 1H NMR (500 MHz, CDCl\textsubscript{3}; \(\delta = 10.91\) (s, 1 H), 10.42 (s, 1 H), 7.90 (d, 1 H, \(J = 3.1\) Hz), 7.72 (d, 1 H, \(J = 3.2\) Hz), 4.67 (s, 2 H), 4.31 (q, 2 H, \(J = 7.1\) Hz), 1.33 (t, 3 H, \(J = 7.1\) Hz); \(^{13}\)C NMR (75 MHz, CDCl\textsubscript{3}; \(\delta = 187.97, 167.92, 151.85, 150.39, 134.75\) (found in HMBC), 126.38, 123.56, 116.97, 66.22, 61.97, 14.28.

tert-Butyl 2-(3-formyl-4-hydroxy-5-nitrophenoxy) acetate, 2g-tBu

Method B. 6g-tBu (0.073 g, 0.089 mmol), acetic acid (1 mL) and water (20 mL). Purified by flash silica column chromatography (eluent: 33% EtOAc in CH\textsubscript{2}Cl\textsubscript{2}) to give a yellow/orange oil. The 2nd band was the product. Yield: 0.027 g, 63.5%; HRMS (ESI) \([M + Na]^+ = \text{calcld 320.0746}\), found 320.0736 m/z; \(^{1}\)H NMR (400 MHz, CDCl\textsubscript{3}; \(\delta = 10.90\) (s, 1 H), 10.43 (s, 1 H), 7.88 (d, 1 H, \(J = 3.2\) Hz), 7.71 (d, 1 H, \(J = 3.2\) Hz), 4.57 (s, 2 H), 1.50 (s, 9 H).

Ethyl 2-(3-formyl-4-hydroxy-5-nitrophenoxy) propanoate, 2f

Method B. 6f (0.467 g, 1.96 mmol), acetic acid (2 mL) and water (100 mL). An orange oil product. Yield: 0.251 g, 45.2%; HRMS (ESI) \([M + Na]^+ = \text{calcd 320.0746}\), found 320.0736 m/z; \(^{1}\)H NMR (500 MHz, CDCl\textsubscript{3}; \(\delta = 188.04, 171.02, 151.75, 150.17, 135.31\) (found in HMBC), 126.32, 124.22, 117.44, 73.93, 61.93, 29.84, 18.44.

2-(3-Formyl-4-hydroxy-5-nitrophenoxy) acetophenone, 2g

1 M NaOH (40 mL) was added to a solution of 2g-Et (0.184 g, 0.683 mmol) in MeOH (50 mL). The yellow/orange solution turned to dark red in colour immediately after the addition of 1 M NaOH. The reaction mixture was stirred at r.t. overnight. MeOH was removed under reduced pressure. 1 M HCl (25 mL) was added to the remaining solution to form a yellow solution (pH 1) which was extracted with CH\textsubscript{2}Cl\textsubscript{2}, dried over Na\textsubscript{2}SO\textsubscript{4} and the solvent removed under vacuum to give yellow oily solid. Yield: 0.164 g, 99.6%.

2g-tBu (0.027 g, 0.091 mmol) was dissolved in CH\textsubscript{2}Cl\textsubscript{2} (5 mL) and TFA (0.02 mL, 0.272 mmol) was added at r.t. The reaction mixture was then stirred at r.t. overnight. The solvent was removed under vacuum and the remaining acid was co-evaporated with dioxane twice to give a yellow oil. Yield: 0.201 g, 95.8%; HRMS (ESI) \([M + H]^+ = \text{calcd 240.0233}\), found 240.0168 m/z; \(^{1}\)H NMR (500 MHz, CDCl\textsubscript{3}; \(\delta = 11.85\) (s, 1 H), 10.95 (s, 1 H), 10.45 (s, 1 H), 7.94 (d, 1 H, \(J = 3.4\) Hz), 7.77 (d, 1 H, \(J = 3.4\) Hz), 4.76 (s, 2 H); \(^{13}\)C NMR (125 MHz, CDCl\textsubscript{3}; \(\delta = 187.96, 172.38, 151.94, 150.19, 126.43, 124.29, 123.48, 117.70, 65.67.\)
2-(3-Formyl-4-hydroxy-5-nitrophenox) propanoic acid, 2h

1 M NaOH (80 mL) was added to a solution of 2f (0.356 g, 1.26 mmol) in MeOH (100 mL). The yellow/orange solution turned dark red in colour immediately after the addition of 1 M NaOH. The reaction mixture was stirred at r.t. overnight. MeOH was removed under reduced pressure. 1 M HCl (50 mL) was added to the remaining solution to form a yellow solution (pH 1) which was extracted with CH2Cl2 dried over Na2SO4 and the solvent removed under vacuum to give yellow oily solid. Yield: 0.320 g, 99.6%; HRMS (ESI) [M + Na]+ = calcd 267.0484, m/z; 1H NMR (500 MHz, DMSO-d6): δ = 11.59 (s, 1 H), 7.93 (s, 1 H, J = 7.8 Hz), 7.04 (m, 2 H), 2.98 (t, 2 H, J = 7.8 Hz), 1.64–1.59 (m, 2 H), 1.36–1.24 (m, 6 H), 0.90 (t, 3 H, J = 7.0 Hz); 13C NMR (100 MHz, DMSO-d6): δ = 170.07, 162.72, 161.53, 152.42, 134.13, 124.29, 116.97, 35.90, 31.84, 31.64, 30.76, 29.17, 22.76, 14.16.

2-Hydroxy-3-nitro-5-(pyrid-4-yl)benzaldehyde, 2k

Method D. 4-Pyridinylboronic acid (0.148 g, 1.2 mmol), DMF (20 mL)/water (20 mL), 6 M HCl (20 mL), CH2Cl2 (3 × 10 mL), 1 M NaOH (60 mL) and diethyl ether (3 × 5 mL). Yield: 0.108 g, 40.3%; HRMS (ESI) [M + Na]+ = calcd 267.0484, m/z; 1H NMR (500 MHz, DMSO-d6): δ = 10.25 (s, 1 H), 8.47 (d, 2 H, J = 4.8 Hz), 8.30 (d, 1 H, J = 4.8 Hz), 7.95 (d, 1 H, J = 2.6 Hz), 7.55 (d, 1 H, J = 2.6 Hz); 13C NMR (125 MHz, DMSO-d6): δ = 190.56, 168.71, 149.97, 146.00, 143.11, 130.98, 130.05, 130.00, 118.96, 112.98.

3′-Formyl-4-hydroxy-5′-nitro-[1,1′-biphenyl]-4-carbonitrile, 2l

Method D. 4-Cyanophenylboronic acid (0.176 g, 1.20 mmol), 4-Borono-2-heptylbenzoic acid, 4-(2,5-diethyl-2-methyl-1,3,4-oxidiazol-5-yl)benzene-1-carboxylic acid, 10a

2.5 M n-butyllithium in n-hexane (21.5 mL, 53.9 mmol) was added dropwise to a solution of 9n (3.96 g, 15.4 mmol) in dry THF (300 mL) at −78 °C and the mixture was stirred at −78 °C for 10 min. Trisopropyl borate (12.5 mL, 53.9 mmol) was then added dropwise at −78 °C and the mixture was then stirred at −78 °C for 3 h. After warmed up to 0 °C, the reaction mixture was quenched with 2 M HCl (60.0 mL) and extracted with EtOAc (2 × 300 mL). The combined organic layers were washed with brine, dried over Na2SO4 and the solvent removed under vacuum to give a white solid. The crude product was purified by flash silica chromatography (eluent: CHCl3 to 30% of MeOH in CHCl3) to give a yellow solid. Yield: 1.82 g, 26.7%; 1H NMR (400 MHz, CDCl3): δ = 11.59 (s, 1 H), 7.93 (t, 1 H, J = 7.8 Hz), 7.04 (m, 2 H), 2.98 (t, 2 H, J = 7.8 Hz), 1.64–1.59 (m, 2 H), 1.36–1.24 (m, 6 H), 0.90 (t, 3 H, J = 7.0 Hz); 13C NMR (100 MHz, CDCl3): δ = 170.07, 162.72, 161.53, 152.42, 134.13, 124.29, 116.97, 35.90, 31.84, 31.64, 30.76, 29.17, 22.76, 14.16.

4-Bromo-2-butylbenzoic acid, 10n

2.5 M n-butyllithium in n-hexane (21.5 mL, 53.9 mmol) was added dropwise to a solution of 9n (3.96 g, 15.4 mmol) in dry THF (300 mL) at −78 °C and the mixture was stirred at −78 °C for 10 min. Trisopropyl borate (12.5 mL, 53.9 mmol) was then added dropwise at −78 °C and the mixture was then stirred at −78 °C for 3 h. After warmed up to 0 °C, the reaction mixture was quenched with 2 M HCl (60.0 mL) and extracted with EtOAc (2 × 300 mL). The combined organic layers were stirred with 2.5 M NaOH (160 mL) for 10 min. The collected aqueous layer was acidified to pH 3 with 6 M HCl, extracted with EtOAc, dried over Na2SO4 and concentrated to give a white precipitate which was collected by filtration, washed with CH2Cl2 and dried under vacuum. Yield: 1.33 g, 39.0%; HRMS (ESI) [M – H]− = calcd 221.0993 m/z, found 221.0988 m/z; 1H NMR (500 MHz, MeOD): δ = 7.87–7.46 (m, 3 H), 2.97 (t, 2 H, J = 8.0 Hz), 1.60–1.54 (m, 2 H), 1.41–1.35 (m, 4 H), 0.95 (t, 3 H, J = 7.3 Hz); 13C NMR (125 MHz, MeOD): δ = 171.81, 144.02, 137.43, 133.07, 131.98, 130.39, 125.46, 35.39, 35.07, 23.81, 14.28; 11B NMR (160 MHz, MeOD): δ = 18.54 (s, 1 B).
Method C. 2g (0.020 g, 0.083 mmol) in EtOH (2 mL) and water (0.3 mL). Purification: after addition of water (10 mL), the mixture was acidified with 0.1 M HCl to give purple precipitate which was re-dissolved in 0.1 M NaOH (1 mL) and purified by Sephadex G-10 column chromatography. The collected purple solution was acidified with 0.1 M HCl to give purple precipitate which was collected by centrifuge, washed with minimum amount of water and dried under vacuum to give purple solid products. Yield: 2.00 mg, 12.5%; MALDI-TOF-MS [M + H]+ = calcd 1052.2556 m/z, found 1058.4048 m/z, [M + K] = calcd 1074.2295 m/z, found 1074.4120 m/z; 1H NMR (400 MHz, DMSO-d6): δ = 16.49 (s, 5 H, OH), 9.30 (s, 5 H, HC=NH), 7.66 (s, 5 H, Ar–H), 7.06 (s, 5 H, Ar–H), 4.90 (d, 5 H, J = 7.0 Hz, CH), 1.57 (d, 15 H, J = 7.0 Hz, CH3). UV-vis (λmax/nm (ε/M–1 cm–1), DMSO): 551 (5303), 450 (4807), 319 (6429).

Pentapropionoxy-campestarene, 1h

Method C. 2h (0.320 g, 1.26 mmol) in EtOH (35 mL) and water (4 mL). Purification: after addition of water (20 mL), the mixture was acidified with 0.1 M HCl to give purple precipitate which was re-dissolved in 0.1 M NaOH (1 mL) and purified by Sephadex G-10 column chromatography. The collected purple solution was acidified with 0.1 M HCl to give purple precipitate which was collected by centrifuge, washed with minimum amount of water and dried under vacuum to give purple solid products. Yield: 28.0 mg, 10.8%; MALDI-TOF-MS [M + H]+ = calcd 1036.2658 m/z, found 1036.4210 m/z, [M + Na] = calcd 1058.2556 m/z, found 1058.4048 m/z, [M + K] = calcd 1074.2295 m/z, found 1074.4120 m/z; 1H NMR (400 MHz, DMSO-d6): δ = 16.49 (s, 5 H, OH), 9.30 (s, 5 H, HC=NH), 7.66 (s, 5 H, Ar–H), 7.06 (s, 5 H, Ar–H), 4.90 (d, 5 H, J = 7.0 Hz, CH), 1.57 (d, 15 H, J = 7.0 Hz, CH3). UV-vis (λmax/nm (ε/M–1 cm–1), DMSO): 551 (5303), 450 (4807), 319 (6429).

Pentamethoxy-campestarene, 1i

Method C. 2i (0.182 g, 0.923 mmol) in EtOH (20 mL) and water (3 mL). The purple crude product was purified twice by Soxhlet technique using CH2Cl2 and MeOH as solvents for 24 h each and multiple washing with water using an ultrasonic bath. Yield: 0.082 g, 59.4%; MALDI-TOF-MS [M + H]+ = calcd 746.2384 m/z, found 746.3896 m/z, [M + Na]+ = calcd 768.2282 m/z, found 768.3630 m/z, [M + K]+ = calcd 784.2021 m/z, found 784.3323 m/z; 1H NMR (400 MHz, DMSO-d6): δ = 16.34 (s, 5 H, OH), 9.26 (s, 5 H, HC=NH), 7.53 (s, 5 H, Ar–H), 7.51 (s, 5 H, Ar–H), 3.84 (s, 15 H, CH3). UV-vis (λmax/nm (ε/M–1 cm–1), DMSO): 442 (966), 303 (1148).

Pentabromo-campestarene, 1j

Method C. 2j (1 g, 4.06 mmol) in EtOH (20 mL) and water (3 mL). The purple crude product was purified twice by Soxhlet technique using CH2Cl2 and MeOH as solvents for 24 h each and multiple washing with water using an ultrasonic bath. Yield: 0.764 g, 94.9%; MALDI-TOF-MS [M + H]+ = calcd 989.7340 m/z, found 989.7634 m/z, [M + Na]+ = calcd 1011.7238
Penta(pyridyl)-campestarene, 1k
Method C. 2k (0.134 g, 0.549 mmol) in EtOH (20 mL) and water (3 mL). The purple crude product was purified twice by Soxhlet technique using CH₂Cl₂ and MeOH as solvents for 24 h each and multiple washing with water using an ultra-sonic bath. Yield: 0.062 g, 57.4%; MALDI-TOF-MS [M + Na]⁺ = calcd 1218.5125 m/z, found 1218.5125 m/z, [M + K]⁺ = calcd 1724.8027 m/z, found 1724.7983 m/z, [M + Na]⁺ = calcd 1686.8390 m/z, found 1686.8390 m/z, [M + Na]⁺ = calcd 1686.8390 m/z, [M + K]⁺ = calcd 1724.8027 m/z, found 1724.7983 m/z, [M + Na]⁺ = calcd 1686.8390 m/z, found 1686.8390 m/z.

Penta(cyanoaryl)-campestarene, 1l
Method C. 2l (0.108 g, 0.402 mmol) in EtOH (20 mL) and water (3 mL). The purple crude product was purified twice by Soxhlet technique using CH₂Cl₂ and MeOH as solvents for 24 h each and multiple washing with water using an ultra-sonic bath. Yield: 0.049 g, 55.1%; MALDI-TOF-MS [M + H]⁺ = calcd 1218.5125 m/z, found 1218.5125 m/z, [M + Na]⁺ = calcd 1686.8390 m/z, found 1686.8390 m/z, [M + K]⁺ = calcd 1724.8027 m/z, found 1724.7983 m/z, [M + Na]⁺ = calcd 1686.8390 m/z, found 1686.8390 m/z.

Penta(arylcarboxylic acid)-campestarene, 1m
Method C. 2m (0.176 g, 0.612 mmol) in EtOH (20 mL) and water (3 mL). The purple crude product was purified twice by Soxhlet technique using CH₂Cl₂ and MeOH as solvents for 24 h each and multiple washing with water using an ultra-sonic bath. Yield: 0.113 g, 57.4%; MALDI-TOF-MS [M + Na]⁺ = calcd 1218.5125 m/z, found 1218.5125 m/z, [M + K]⁺ = calcd 1724.8027 m/z, found 1724.7983 m/z, [M + Na]⁺ = calcd 1686.8390 m/z, found 1686.8390 m/z, [M + K]⁺ = calcd 1724.8027 m/z, found 1724.7983 m/z.

Penta(α-butylarylcarboxylic acid)-campestarene, 1n
Method C. 2n (0.167 g, 0.486 mmol) in EtOH (17 mL) and water (2 mL). Purification: after addition of water (10 mL), the mixture was acidified with 0.1 M HCl to give purple precipitate which was collected by centrifuge, washed with minimum amount of water and dried under vacuum to give purple solid products. Yield: 0.091 g, 62.3%; MALDI-TOF-MS [M + Na]⁺ = calcd 1043.3911 m/z, found 1043.3911 m/z, [M + K]⁺ = calcd 1518.5559 m/z, found 1518.5559 m/z, [M + Na]⁺ = calcd 1666.8390 m/z, found 1666.8390 m/z, [M + Na]⁺ = calcd 1666.8390 m/z.

Penta(α-heptylarylcarboxylic acid)-campestarene, 1o
Method C. 2o (0.113 g, 0.293 mmol) in EtOH (17 mL) and water (2 mL). Purification: after addition of water (10 mL), the mixture was acidified with 0.1 M HCl to give purple precipitate which was collected by centrifuge, washed with minimum amount of water and dried under vacuum to give purple solid products. Yield: 0.062 g, 57.4%; MALDI-TOF-MS [M + Na]⁺ = calcd 1218.5125 m/z, found 1218.5125 m/z, [M + K]⁺ = calcd 1724.8027 m/z, found 1724.7983 m/z, [M + Na]⁺ = calcd 1686.8390 m/z, found 1686.8390 m/z, [M + K]⁺ = calcd 1724.8027 m/z, found 1724.7983 m/z, [M + Na]⁺ = calcd 1686.8390 m/z, found 1686.8390 m/z.

Notes and references