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# Syntheses of four new pyridinium phenolates with caged phenolate functionalities as chromophores for quadratic optics

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ABSTRACT

Semi-empirical calculations as well as our preliminary studies indicate an increase of the nonlinear response of pyridinium phenolates with the raise of their interplanar angle. Unfortunately, the tendency of previously synthesized zwitterionic compounds to form aggregates prevents their use in electro-optical devices. In order to understand the process of aggregation and to circumvent it, the syntheses of new pyridinium phenolates bearing alkyl chains of various length, caging the phenolate functionality, have been achieved and are described herein.

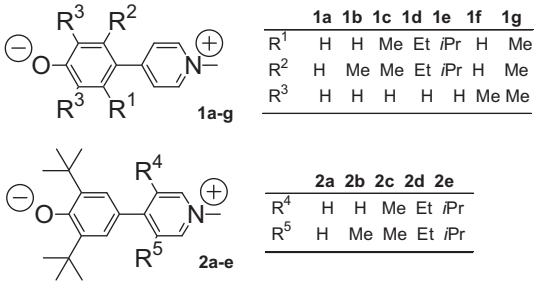


## 1. Introduction

Pyridinium phenolates have shown to be model push–pull molecules with large nonlinear optical properties. These are twisted intramolecular charge-transfer molecules, that is, in other word, tictoïds. They are characterized by a large permanent dipole moment in the electronic ground state. Semi-empirical calculations[1–4] as well as previous work,[5] indicated that increasing the interplanar angle between the two aromatic rings could enhance their NLO properties.

Since a few years our objective is the preparation of pyridinium phenolates with various interplanar angles and bearing (or not) protecting groups at *ortho* position of the phenolate functionality (Scheme 1). The medium-term purpose of our work is the selection of the most promising compound with respect to its high hyperpolarisability and solubility in order to dope polymers for the development of promising electro-optical materials.

Until now, two series of pyridinium phenolates, sterically hindered at the *ortho* position of the intercyclic bond, have been synthesized. Unfortunately, the low solubilities of compounds **1a**–**e** made their NLO characterization difficult.[8] Much more reliable results were obtained with compounds **2a**–**e** in which two *tert*-butyl groups are anchored at the *ortho* positions of the phenolate ring.[5] Actually, *tert*-butyl groups are known to notably reduce the formation of aggregates. In addition, the enhancement of the molecular mass led to a better solubility of the corresponding tictoïds in organic solvents. Unfortunately, the solubilities obtained are not yet sufficient and aggregation is still a persistent phenomenon, which precludes a potential use in integrated optical devises. In order to circumvent these two main drawbacks and to understand the process of aggregation better, aliphatic chains of various lengths were linked, via ether functions, at both *ortho* positions of the phenolate ring. A restricted torsion angle was obtained by introduction of two methyl groups at the *meta* position of the pyridine ring, leading to a twist angle of about 45° as for **2c**.[5] The




| | 1a | 1b | 1c | 1d | 1e | 1f | 1g |
|---|---|---|---|---|---|---|---|
| $R^1$ | H | H | Me | Et | *i*Pr | H | Me |
| $R^2$ | H | Me | Me | Et | *i*Pr | H | Me |
| $R^3$ | H | H | H | H | H | Me | Me |

| | 2a | 2b | 2c | 2d | 2e |
|---|---|---|---|---|---|
| $R^4$ | H | H | Me | Et | *i*Pr |
| $R^5$ | H | Me | Me | Et | *i*Pr |

**Scheme 1.** Zwitterionic compounds previously synthesized.[6,7]

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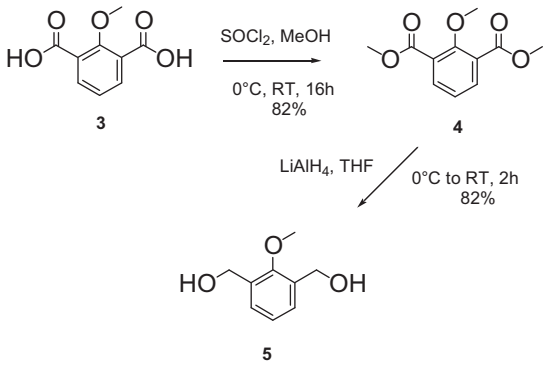
synthesis of four new betaine chromophores having these last mentioned characteristics is described herein.

## 2. Results and discussion

### 2.1. Syntheses of bromocyclophanes 10a–d

In a first approach, **5** was readily synthesized in two steps from the known 2-methoxy*iso*-phthalic acid **3**.[9] Compound **3** was first converted into its dimethylester **4** by reaction with $SOCl_2$ in anhydrous MeOH (Scheme 2).[10] Then, reduction with $LiAlH_4$ afforded **5** in 67% total yield from diacid **3**.



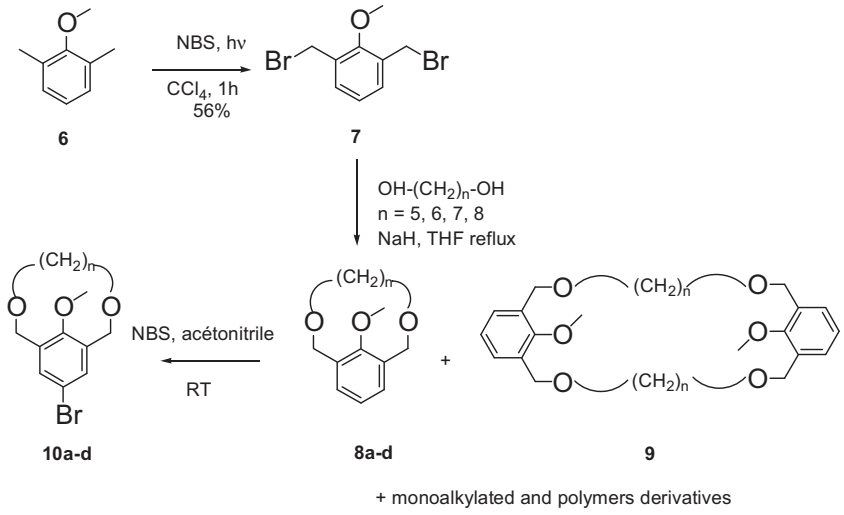

**Scheme 2.** Preparation of **5**.

The preparation of the boronic ester **12** from the known 4-bromo-3,5-dimethylpyridine **11**[7] was easily performed, in 61% yield, via a classical bromide/lithium exchange followed by treatment with tributylborate and then pinacol.

### 2.2. Synthesis of boronic ester 12

### 2.3. Suzuki–Miyaura coupling reaction–deprotection–quaternisation

The following three steps, namely the cross-coupling reaction followed by deprotection and quaternisation, were performed under the same conditions as previously described for the syntheses of **1a–e** and **2a–e**.[6,7] The Suzuki–Miyaura coupling reaction of **11a–d** with boronic ester **12** afforded the 4-pyridinylanisoles **13a–d** in good to excellent yields (from 75 to 82%), using our usual conditions [$Pd(PPh_3)_4$ as catalyst and $Cs_2CO_3$ as base in anhydrous THF] (Table 1, Scheme 4). Then, the phenol functions were deprotected, in DMF, at 100 °C, using sodium ethanethiolate, pre-




**Scheme 3.** Preparation of **8a–d** and **10a–d** (n = 5, 6, 7, 8).

A condensation between 1,5-dibromopentane and the bis(hydroxymethyl) compound **5** was then attempted under high-dilution condition. Unfortunately, using *t*-BuOK as base, as well as in THF and in DMF, the reaction led to a complete decay of **5**. On the contrary, in 1,4-dioxane, or in the presence of NaH in THF, no reaction occurred and **5** was recovered quantitatively.

We therefore decided to invert the reactive functionalities of the two partners as described in the literature for the syntheses of 2-methoxy-1,3-xylyl crown compounds.[11–14] The known 2,6-dimethylanisole **6** was therefore brominated using NBS under irradiation, via a radical substitution, to obtain bis(bromomethyl) anisole **7** in 56% yield.

Condensation of 2,6-bis(bromomethyl)anisole with alkanes-1,*n*-diols (*n*=5–8) of various lengths, conducted in the presence of sodium hydride in anhydrous THF at reflux and under high-dilution conditions, afforded the desired cyclophanes **8a–d**. Despite a meticulous optimisation of the reaction conditions, the cyclophanes were obtained mixed with by-products (i.e., 25% of various monosubstituted anisoles and about 20% of dimer **9**) (Scheme 3). Cyclophanes **8a–d** were subsequently purified by flash chromatography and recovered in yields ranged between 15 and 43% (Table 1). Finally, they were readily brominated into 4-bromoanisoles **10a–d**, using NBS.

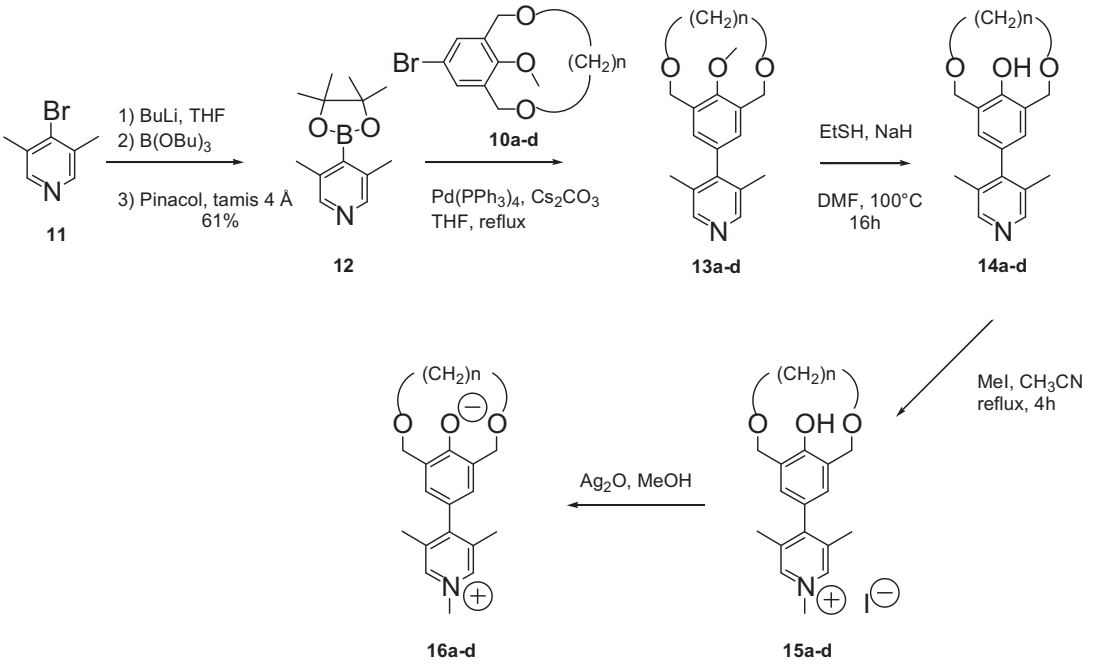
**Table 1**
Yields leading from **7** to **16a–d**

| | *n* | Cyclisation | | | Bromination | | Suzuki–Miyaura coupling yield/% | |
|---|---|---|---|---|---|---|---|---|
| | | Time/h | Yield/% | | Time/h | Yield/% | | |
| **8a** | 5 | 96 | 15 | **10a** | 8 | 85 | **13a** | 85 |
| **8b** | 6 | 96 | 25 | **10b** | 8 | 95 | **13b** | 75 |
| **8c** | 7 | 48 | 38 | **10c** | 1 | 88 | **13c** | 80 |
| **8d** | 8 | 48 | 43 | **10d** | 1 | 90 | **13d** | 85 |

| Deprotection yield/% | | Quaternisation yield/% | | Deprotonation yield/% | |
|---|---|---|---|---|---|
| **14a** | 66 | **15a** | 70 | **16a** | 60 |
| **14b** | 65 | **15b** | 80 | **16b** | 65 |

pared in situ by deprotonation of ethanethiol. The four corresponding free phenols **14a**–**d** were recovered in yields ranging from 65 to 83%. The quaternisation of pyridines **14a**–**d** with iodomethane was also performed very easily to give the corresponding 4-pyridinio phenol iodide salts **15a**–**d**.

three representative solvents of different polarity (Fig. 1). In order to avoid the protonation of phenolate oxygen, all measurements were conducted in the presence of an excess of tetramethylguanidine as base. As for 4-[*N*-methyl-4-pyridinio]phenolate, POMP, the absorption bands are moderately large and structureless.[15] The $\tilde{\nu}_{max}$




**Scheme 4.** Preparation of **16a**–**d** ($n$=5, 6, 7, 8).

## 2.4. Deprotonation

Deprotonation of **15a**–**d** has to afford the tictoïds **16a**–**d** free from traces of salts. Previously, we used a small excess of $Bu_4N^+HO^-$.[6,7] The zwitterions **1a**–**e** and **2a**–**e** were weakly soluble and were therefore easily purified by making use of their differences in solubility with tetra-*n*-butylammonium iodide in solvent mixtures such as $CH_2Cl_2/Et_2O$ or $CH_2Cl_2$/cyclohexane. One advantage of this method was the possibility to detect traces of $Bu_4N^+I^-$ by NMR spectroscopy using duroquinone in $CD_3OD$ as an internal reference. Analogous attempts with our new tictoïds have proved to be negative because of their far better solubilities in organic solvents as compared to that of the zwitterions of the first two series, i.e., compounds **1a**–**g** and **2a**–**e**. This property admittedly confronted us with a synthetic problem but, in other respects, bodes well for a future incorporation in organic NLO devices.

Therefore, we have elaborated an alternative procedure using $Ag_2O$ as an efficient reagent, knowing that $Ag_2O$ and AgI are insoluble in organic solvents and precipitate in them. After treatment with $Ag_2O$ for a few minutes, all new tictoïds were recovered, after a meticulous centrifugation, free from any inorganic salts. In order to definitively validate this new deprotonation method, we compared the EFISHG responses of two batches of compound **2b**. One batch was obtained, as previously, using $Bu_4N^+HO^-$, and the second one, using our new method, namely $Ag_2O$. In both cases similar results were obtained. The small differences lay in the range of measurement errors.

## 2.5. UV/visible absorption spectra of 16d

Logically, the chain length should not significantly influence the UV/visible absorption spectra. So, we only recorded those of **16d** in values undergo a severe blue shift (negative solvatochromism) from THF to MeOH ($\Delta\tilde{\nu}_{max} = 5000\ cm^{-1}$), which indicates that the dipole moment of **16d** decreases largely upon excitation. This result is in agreement with the charge-transfer nature of the electron transition from the phenolate to the pyridinium ring, experimentally observed using femtosecond spectroscopy in the case of the related compounds **2a**–**c** and **2d**.[16]

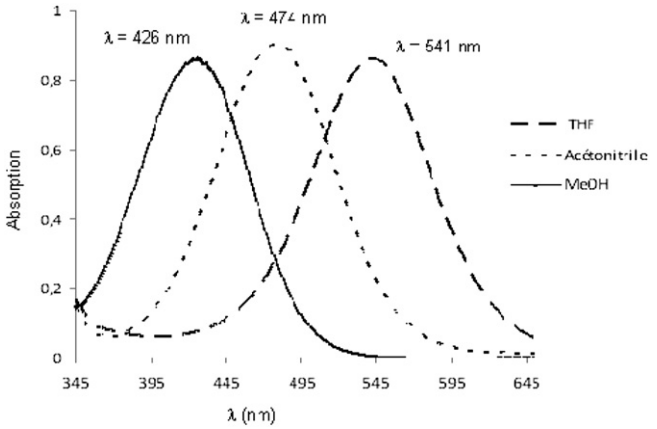



**Fig. 1.** UV/visible absorption spectra of **16d** measured in three solvents of different polarity

## 2.6. Preliminary EFISHG results

Compounds **16a**–**d** and **2c** possess equivalent interplanar angles. Moreover, the phenolate function of each derivative is congested at the *ortho* positions by the presence of alkyl groups: a saturated chain with 7–10 methylene groups or *tert*-butyl groups

at each *ortho* position. As a consequence, the NLO response for **16a**–**d** was expected to be of the same magnitude as that previously obtained for **2c**.[5] Preliminary EFISHG experiments have been performed with tictoïds **16b**–**d** under the conditions described in the literature[5] in order to determine the magnitude of $\mu$, the permanent dipole moment. While the measurements with **2a** led to a value of $\mu$ equal to $-950\times10^{-48}$ esu, for **16b**, **16c**, and **16d** we obtained values of $-750$, $-930$, and $-1400\times10^{-48}$ esu, respectively, as was to be expected.

## 3. Conclusion

In summary, four new tictoïds of the pyridinium phenolate type have been readily synthesized. Their solubilities are notably improved. However, the *ortho* alkyl chains at the phenolate ring seem not to be bulky enough to protect the phenolate function against protonation both in acidic and in neutral media as it was reported in literature for related pyridinium phenolates betaine dyes.[5,8,17] To hinder protonation, the chain substitution at the *ortho* position of the phenolate ring at is now considered. Nevertheless, no significant aggregation has been highlighted, allowing preliminary EFISGH measurements.

## 4. Experimental section

### 4.1. General points

Reagents were purchased from commercial suppliers and used without further purification. THF, diethyl ether, and toluene were freshly distilled from sodium/benzophenone, MeOH from Mg/$I_2$. A freshly opened DMF bottle was used and DMF was dried over 3 Å molecular sieves. All melting points were taken on a Kofler bench. IR spectra ($cm^{-1}$) were recorded on either a Bruker Vertex 70 or an Equinox 55 spectrometer. $^1$H NMR (400 MHz) and $^{13}$C NMR (100.6 MHz) spectra were measured with a Bruker Avance (Serie 400) at 295 K. Microanalyses were performed by the analytical service of the *Service de Microanalyse du CNRS* in Vernaison and high resolution MS were measured with an Agilent Technologies 6510 (Q-TOF) Spectrometer using a dual ESI source. Irradiations were performed using a Hanau mercury vapour lamp HPK 125.

UV/visible spectra were carried out with an Agilent 8453 spectrometer. Acetonitrile, MeOH, and $CH_3CN$ employed were of spectroscopic grade. The absorption of all solvents was subtracted from the sample spectra. In order to maintain exclusively the zwitterionic form, an excess of tetramethylguanidine was added to each sample.

Previously reported procedures were used to prepare 1,3-dimethylanisole **6**, 2-methoxy*iso*-phthalic acid **3**,[9] and 4-bromo-3,5-dimethylpyridine **11**.[7]

$Pd(PPh_3)_4$ was prepared according to Ref. 18 and used directly or within three months at longest while stored under $N_2$ at $-30$ °C.

### 4.2. General procedures

*4.2.1. Procedure A: synthesis of cyclophanes **8a**–**d**.* Under an atmosphere of Ar, to NaH (13 equiv), suspended in anhydrous THF (500 mL per mmol of **7**) at reflux was added dropwise a solution of **7** (1 equiv) and alkane-1,*n*-diol (1.1 equiv) in THF (120 mL per mmol of **7**). The reaction mixture was stirred under reflux until completion of the reaction, which was monitored by NMR spectroscopy. An aqueous solution of $NH_4Cl$ (10%) was then added at 0 °C until neutralization. THF was evaporated under reduced pressure. The crude residue was dissolved in $Et_2O$. This organic layer was then extracted twice with water, dried with $MgSO_4$, and evaporated under reduced pressure. Purification by chromatography on silicagel (cyclohexane/AcOEt) afforded the pure cyclophanes **8a**–**d** and dimer **9**.

*4.2.2. Procedure B: bromination of cyclophanes.* Under an atmosphere of Ar, to a solution of cyclophanes **8a**–**d** (1 equiv) in MeCN (8 mL per mmol of **8a**–**d**) was added NBS (1.4 equiv). The reaction mixture was stirred at room temperature overnight. The solvent was then evaporated under reduced pressure. Cyclohexane was added to the crude residue. Insoluble solids were filtered off and rinsed with another portion of cyclohexane. The filtrate was evaporated under reduced pressure. Purification by chromatography on silicagel (cyclohexane/AcOEt) afforded the pure bromo cyclophanes **10a**–**d**.

*4.2.3. Procedure C: Suzuki–Miyaura coupling reaction.* Under an atmosphere of Ar, $Cs_2CO_3$ (1.2 equiv), the boronic ester **12** (1.2 equiv), and $Pd(PPh_3)_4$ (0.08 equiv) were successively added to a solution of **10a**–**d** (1 equiv) in anhydrous THF (10 mL per mmol of **10a**–**d**). The reaction mixture was stirred overnight. The suspension was then filtered through *Celite* with $CH_2Cl_2$. The reaction mixture was concentrated under reduced pressure and the residue was purified by chromatography on silicagel (cyclohexane/AcOEt) to afford pure **13a**–**d**.

*4.2.4. Procedure D: deprotection of phenols.* Under an atmosphere of Ar, EtSH (7 equiv) was added dropwise to NaH (8 equiv) suspended in DMF (14 mL per mmol of **13a**–**d**). On completion of $H_2$ emission, **13a**–**d** (1 equiv) was introduced in the reaction mixture. After an overnight stirring at 100 °C, $H_2O$ (2.5 mL per mmol of **13a**–**d**), aqueous HCl (1 M, 8 mL per mmol of **13a**–**d**), and a phosphate buffer (0.5 M, pH=2) were successively added. The aqueous layer was extracted three times with $Et_2O$. The combined organic layers were extracted twice with $H_2O$ and dried with $MgSO_4$. The solution was concentrated under reduced pressure and the residue was purified by chromatography on silicagel (cyclohexane/AcOEt) to afford pure **14a**–**d**.

*4.2.5. Procedure E: alkylation reaction.* Under an atmosphere of Ar, to a suspension of the biaryl compounds **14a**–**d** (1 equiv) in acetone (16 mL per mmol of **14a**–**d**), iodomethane (4 equiv) was added dropwise. The reaction mixture was refluxed for 4 h. The solvent was then removed under reduced pressure. The residue was washed first with $Et_2O$ then with AcOEt. The crude iodides **15a**–**d** were not further purified and only characterized by NMR spectroscopy.

*4.2.6. Procedure F: deprotonation.* $Ag_2O$ (2 equiv) was added to a solution of **15a**–**d** in MeOH (11 mL per mmol of **15a**–**d**). After 10 min of reaction an excess of both $Ag_2O$ and AgI precipitated. The suspension was then centrifugated. The supernatant organic phase was centrifugated once more and was then evaporated under reduced pressure to afford the pure tictoïds **16a**–**d**.

### 4.3. Synthesis of derivatives

*4.3.1. 2-Methoxy-1,3-benzenedicarboxylic acid dimethyl ester **4**.* Under an atmosphere of Ar, $SOCl_2$ (0.4 mL, 5.5 mmol) was added dropwise at 0 °C to 2-methoxy*iso*-phthalic acid **3** (500 mg, 2.5 mmol) in anhydrous methanol (4 mL). The reaction mixture was then allowed to reach room temperature. After stirring overnight, the reaction mixture was evaporated under reduced pressure. The crude residue was then dissolved in AcOEt. This organic layer was successively washed with a saturated aqueous solution of $NaHCO_3$ and water. After drying with $MgSO_4$, the solvent was evaporated under reduced pressure to afford **4** (468 mg, 82%),

which was used in the next step without further purification. Mp and $^1$H NMR were in agreement with the literature values.[9,19]

*4.3.2. 2,6-Bis(hydroxymethyl)anisole **5**.* Under an atmosphere of Ar, at 0 °C, a solution of **4** (116 mg, 0.52 mmol) in anhydrous THF (2.5 mL per mmol of **4**, 1.3 mL) was added dropwise to a suspension of $LiAlH_4$ (49 mg, 1.26 mmol) in anhydrous THF (2.5 mL per mmol of **4**, 1.3 mL). The reaction mixture was stirred overnight at room temperature. AcOEt was then carefully added at 0 °C in order to neutralize $LiAlH_4$ in excess. $Na_2SO_4$, $10\times H_2O$ (152 mg) and an aqueous solution of NaOH (0.25 M, 0.2 mL) were then added. The solution was filtered through *Celite* with AcOEt. The aqueous solution was separated and extracted twice with AcOEt. The combined organic layers were dried with $MgSO_4$, and evaporated under reduced pressure to afford **5** (71 mg, 82%), which was used in the next step without further purification. Mp and $^1$H NMR were in agreement with literature values.[20]

*4.3.3. 2,6-Bis(bromomethyl)anisole **7**.* Under an atmosphere of Ar, 1,6-dimethylanisole **6** (488 mg, 3.59 mmol) was added dropwise to a suspension of NBS (1.278 mg, 7.18 mmol) in $CCl_4$ (25 mL). After stirring for 60 min under irradiation (125 nm), the reaction mixture was filtered and evaporated under reduced pressure. The crude residue was dissolved in $CH_2Cl_2$ and extracted twice with an aqueous solution of $NH_4Cl$ (10%). The organic layer was then dried with $MgSO_4$ and evaporated under reduced pressure to afford **7** (590 mg, 56%), which was used in the next step without further purification (**7** is a lachrymator). Mp was in agreement with the literature values.[11]

*4.3.4. 3,9-Dioxa-1[2,6]-(1$^1$-methoxy)benzenacyclodecaphane **8a**.* After purification by chromatography on silicagel (cyclohexane/AcOEt, 7:3), compound **8a** (60.5 mg, 15%) was obtained as colourless crystals from bis(bromomethyl)anisole **7** (500 mg, 1.7 mmol) by using procedure A (96 h at reflux). Mp 82 °C. $^1$H NMR (400 MHz, $CDCl_3$): $\delta$=0.38–0.51 (m, 2H), 0.89–1.10 (m, 1H), 1.09–1.22 (m, 2H), 1.78–1.93 (m, 1H), 3.15 (ddd, $^3J_{H,H}$=4.0 Hz, $^3J_{H,H}$=8.0 Hz, $^2J_{H,H}$=12.0 Hz, 2H), 3.51 (ddd, $^3J_{H,H}$=4.0 Hz, $^3J_{H,H}$=8.0 Hz, $^2J_{H,H}$=12.0 Hz, 2H), 3.93 (s, 3H), 4.08 (d, $^2J_{H,H}$=12.4 Hz, 2H), 5.18 (d, $^2J_{H,H}$=12.4 Hz, 2H), 7.00 (t, $^2J_{H,H}$=7.4 Hz, 1H), 7.20 (d, $^2J_{H,H}$=7.4 Hz, 2H) ppm. $^{13}$C NMR (100.6 MHz, $CDCl_3$): $\delta$=19.6, 28.2 (2C), 61.1, 66.6 (2C), 70.6 (2C), 122.2, 132.1(2C), 132.4 (2C), 160.7 ppm. IR (KBr): $\tilde{\nu}$ = 651, 728, 780, 834, 854, 885, 951, 991, 1017, 1046, 1079, 1129, 1183, 1219, 1263, 1287, 1360, 1427, 1472, 1592, 2857, 2920 cm$^{-1}$. HRMS (ESI-Q-Tof): calcd for $C_{14}H_{21}O_3Na$ $[M+H]^{\bullet+}$ 237.1485; found 237.1485.

*4.3.5. 3,10-Dioxa-1[2,6]-(1$^1$-methoxy)benzenacycloundecaphane **8b**.* After purification by chromatography on silicagel (cyclohexane/AcOEt, 8:2), compound **8b** (12.8 mg, 18%) was obtained as colourless oil from bis(bromomethyl)anisole **7** (84.5 mg, 2.8 mmol) by using procedure A (96 h at reflux). $^1$H NMR (400 MHz, $CDCl_3$): $\delta$=0.62–0.74 (m, 2H), 1.00–1.12 (m, 2H), 1.15–1.26 (m, 2H), 1.2–1.39 (m, 2H), 3.43 (ddd, $^3J_{H,H}$=4.0 Hz, $^3J_{H,H}$=7.2 Hz, $^2J_{H,H}$=10.5 Hz, 2H), 3.61 (ddd, $^3J_{H,H}$=4.0 Hz, $^3J_{H,H}$=7.2 Hz, $^3J_{H,H}$=10.5 Hz, 2H), 3.62 (s, 3H), 4.22 (d, $^2J_{H,H}$=12.4 Hz, 2H), 4.95 (d, $^2J_{H,H}$=12.4 Hz, 2H), 7.09 (t, $^2J_{H,H}$=7.6 Hz, 1H), 7.27 (d, $^2J_{H,H}$=7.6 Hz, 2H) ppm. $^{13}$C NMR (100.6 MHz, $CDCl_3$): $\delta$=23.3 (2C), 29.7 (2C), 62.3, 67.7 (2C), 69.1 (2C), 123.8, 132.5 (4C), 158.6 ppm. IR (KBr): $\tilde{\nu}$ = 651, 771, 828, 917, 1014, 1064, 1090, 1124, 1175, 1219, 1274, 1369, 1429, 1470, 1593, 2857, 2929 cm$^{-1}$. HRMS (ESI-Q-Tof): calcd for $C_{15}H_{22}NaO_3$ $[M+Na]^{\bullet+}$ 273.1461; found 273.1463.

*4.3.6. 3,11-Dioxa-1[2,6]-(1$^1$-methoxy)benzenacyclododecaphane **8c**.* After purification by chromatography on silicagel (cyclohexane/AcOEt, 9:1), compound **8c** (341 mg, 38%) was obtained as colourless oil from bis(bromomethyl)anisole **7** (1 g, 3.4 mmol) by using procedure A with 48 h at reflux. $^1$H NMR (400 MHz, $CDCl_3$): $\delta$=0.53–0.72 (m, 2H), 1.00–1.15 (m, 2H), 1.15–1.26 (m, 2H), 1.26–1.40 (m, 2H), 1.60–1.75 (m, 2H), 3.13–3.18 (m, 2H), 3.31–3.32 (m, 2H), 3.39(s, 3H), 4.14 (d, $^2J_{H,H}$=12.2 Hz, 2H), 5.04 (t, $^2J_{H,H}$=12.2 Hz, 2H), 7.02 (d, $^2J_{H,H}$=7.3 Hz, 1H), 7.22 (d, $^2J_{H,H}$=7.3 Hz, 2H) ppm. $^{13}$C NMR (100.6 MHz, $CDCl_3$): $\delta$=24.9, 25.1 (2C), 28.7 (2C), 61.8, 65.4 (2C), 69.3 (2C), 122.8, 131.4 (2C), 133.2 (2C), 159.6 ppm. IR (KBr): $\tilde{\nu}$ = 666, 716, 770, 833, 879, 942, 1013, 1047, 1094, 1131, 1171, 1232, 1280, 1364, 1428, 1472, 1593, 1728, 2855, 2935 cm$^{-1}$. HRMS (ESI-Q-Tof): calcd for $C_{32}H_{52}NO_6$ $[2M+NH_4]^{\bullet+}$ 546.7743; found 546.3780.

*4.3.7. 3,12-Dioxa-1[2,6]-(1$^1$-methoxy)benzenacyclotridecaphane **8d** and 1$^1$,14$^1$-dimethoxy-1,14(2,6)-dibenzena-3,12,16,25-tetraoxacyclohexacosane **9**.* After purification by chromatography on silicagel (cyclohexane/AcOEt, 9:1), compounds **8d** (610 mg, 43%) and **9** (284 mg, 20%) were obtained as from bis(bromomethyl)anisole **7** (1.5 g, 5.1 mmol) by using procedure A with 48 h at reflux.

Compound **8d**: colourless oil. $^1$H NMR (400 MHz, $CDCl_3$): $\delta$=0.81–0.94 (m, 2H), 0.94–1.02 (m, 2H), 1.02–1.10 (m, 2H), 1.10–1.18 (m, 2H), 1.18–1.29 (m, 2H), 1.44–1.63 (m, 2H), 3.35–3.45 (m, 4H), 3.83 (s, 3H), 4.25 (d, $^2J_{H,H}$=12.2 Hz, 2H), 4.88 (d, $^2J_{H,H}$=12.2 Hz, 2H), 7.09 (t, $^2J_{H,H}$=7.6 Hz, 1H), 7.31 (d, $^2J_{H,H}$=7.6 Hz, 2H) ppm. $^{13}$C NMR (100.6 MHz, $CDCl_3$): $\delta$=24.3 (2C), 26.6 (2C), 28.4 (2C), 62.8, 67.6 (2C), 67.72 (2C), 123.5, 131.6 (2C), 132.1 (2C), 158.4 ppm. IR (KBr): $\tilde{\nu}$ = 664, 770, 1012, 1092, 1171, 1221, 1268, 1361, 1430, 1471, 1594, 2856, 2930 cm$^{-1}$. HRMS (ESI-Q-Tof): calcd for $C_{17}H_{27}O_3$ $[M+H]^{\bullet+}$ 279.1955; found 279.1943.

Compound **9**: colourless crystals. Mp 84 °C. $^1$H NMR (400 MHz, $CDCl_3$): $\delta$=1.20–1.40 (m, 16H), 1.59 (quint, $^3J_{H,H}$=6.3 Hz, 8H), 3.48 (t, $^3J_{H,H}$=6.3 Hz, 8H), 3.81 (s, 6H), 4.53 (s, 8H), 7.08 (t, $^2J_{H,H}$=7.6 Hz, 2H), 7.33 (d, $^2J_{H,H}$=7.6 Hz, 4H) ppm. $^{13}$C NMR (100.6 MHz, $CDCl_3$): $\delta$=25.8 (4C), 28.9 (4C), 29.6 (4C), 62.6 (2C), 67.6 (4C), 70.3 (4C), 124.1 (2C), 129.6 (4C), 131.6 (4C), 156.7 (2C) ppm. IR (KBr): $\tilde{\nu}$ = 494, 531, 589, 604, 717, 773, 787, 817, 865, 902, 979, 1013, 1050, 1070, 1098, 1113, 1173, 1212, 1228, 1267, 1280, 1295, 1351, 1393, 1430, 1468, 1594, 1727, 2855, 2926 cm$^{-1}$. HRMS (ESI-Q-Tof): calcd for $C_{34}H_{56}NO_6$ $[M+NH_4]^{\bullet+}$ 574.4108; found 574.4112.

*4.3.8. 1$^4$-Bromo-3,9-dioxa-1(2,6)-(1$^1$-methoxy)benzenacyclodecaphane **10a**.* After purification by chromatography on silicagel (cyclohexane/AcOEt, 7:3), compound **10a** (155 mg, 85%) was obtained as colourless crystals from cyclophane **8a** (136 mg, 0.58 mmol) by using procedure B with 8 h of stirring. Mp 119.5 °C. $^1$H NMR (400 MHz, $CDCl_3$): $\delta$=0.45–0.60 (m, 2H), 0.90–1.02 (m, 1H), 1.11–1.26 (m, 2H), 1.75–1.90 (m, 1H), 3.11–3.20 (m, 2H), 3.48–3.56 (m, 2H), 3.91 (s, 3H), 4.00 (d, $^2J_{H,H}$=12.6 Hz, 2H), 5.11 (d, $^2J_{H,H}$=12.6 Hz, 2H), 7.31 (s, 2H) ppm. $^{13}$C NMR (100.6 MHz, $CDCl_3$): $\delta$=19.5, 28.2 (2C), 61.0, 67.0 (2C), 70.2 (2C), 114.3, 134.2 (2C), 134.5 (2C), 159.8 ppm. IR (KBr): $\tilde{\nu}$ = 612, 656, 690, 777, 845, 868, 999, 1048, 1079, 1129, 1182, 1228, 1264, 1359, 1425, 1470, 1692, 2856, 2922 cm$^{-1}$. HRMS (ESI-Q-Tof): calcd for $C_{14}H_{19}BrNaO_3$ $[M+Na]^{\bullet+}$ 337.0409; found 237.0413.

*4.3.9. 1$^4$-Bromo-3,10-dioxa-1(2,6)-(1$^1$-methoxy)benzenacycloundecaphane **10b**.* After purification by chromatography on silicagel (cyclohexane/AcOEt, 8:2), compound **10a** (678 mg, 95%) was obtained as colourless oil from cyclophane **8b** (542 mg, 2.17 mmol) by using procedure B with 8 h of stirring. $^1$H NMR (400 MHz, $CDCl_3$): 0.65–0.82 (m, 2H), 1.08–1.19 (m, 2H), 1.19–1.29 (m, 2H), 1.32–1.43 (m, 2H), 3.42 (ddd, $^3J_{H,H}$=4.0 Hz, $^3J_{H,H}$=7.6 Hz, $^2J_{H,H}$=11.2 Hz, 2H), 3.60 (ddd, $^3J_{H,H}$=4.0 Hz, $^3J_{H,H}$=7.6 Hz, $^2J_{H,H}$=11.2 Hz, 2H), 3.82 (s, 3H), 4.17 (d, $^2J_{H,H}$=12.4 Hz, 2H), 4.89 (d, $^2J_{H,H}$=12.4 Hz, 2H), 7.40 (s, 2H) ppm. $^{13}$C NMR (100.6 MHz, $CDCl_3$): $\delta$=23.4 (2C), 29.6 (2C), 62.2, 67.9 (2C), 68.6 (2C), 116.0, 134.7 (2C), 134.8 (2C), 157.7 ppm. IR (KBr):

$\tilde{\nu}$ = 573, 614, 654, 692, 878, 1013, 1091, 1172, 1217, 1469, 2858, 2929 $cm^{-1}$. HRMS (ESI-Q-Tof): calcd for $C_{15}H_{21}BrNaO_3$ $[M+Na]^{\bullet+}$ 351.0566; found 251.0554.

*4.3.10. 1⁴-Bromo-3,11-dioxa-1(2,6)-(1¹-methoxy)benzenacyclododecaphane* ***10c***. After purification by chromatography on silicagel (cyclohexane/AcOEt, 9:1), compound **10c** (286 mg, 88%) was obtained as colourless crystals from cyclophane **8b** (238 mg, 0.9 mmol) by using procedure B with 1 h of stirring. Mp 118.5–120.5 °C. $^1$H NMR (400 MHz, $CDCl_3$): 0.55–079 (m, 2H), 1.04–1.16 (m, 2H), 1.16–1.27 (m, 2H), 1.27–1.41 (m, 2H), 1.62–1.76 (m, 2H), 3.13–3.21 (m, 2H), 3.28–3.35 (m, 2H), 3.88 (s, 3H), 4.08 (d, $^2J_{H,H}$=12.4 Hz, 2H), 4.99 (d, $^2J_{H,H}$=12.4 Hz, 2H), 7.34 (s, 2H) ppm. $^{13}$C NMR (100.6 MHz, $CDCl_3$): $\delta$=24.5, 24.7 (2C), 28.2 (2C), 61.2, 65.3 (2C), 68.6 (2C), 114.6, 133.1 (2C), 135.0 (2C), 158.3 ppm. IR (KBr): $\tilde{\nu}$ = 626, 685, 716, 852, 916, 943, 1015, 1051, 1094, 1134, 1223, 1284, 1362, 1426, 1453, 1470, 2852, 2932 $cm^{-1}$. HRMS (ESI-Q-Tof): calcd for $C_{16}H_{24}BrO_3$ $[M+H]^{\bullet+}$ 343.0909; found 343.0894.

*4.3.11. 1⁴-Bromo-3,12-dioxa-1(2,6)-(1¹-methoxy)benzenacyclotridecaphane* ***10d***. After purification by chromatography on silicagel (cyclohexane/AcOEt, 9:1), compound **10d** (647 mg, 90%) was obtained as colourless crystals from cyclophane **8d** (560 mg, 2 mmol) by using procedure B with 1 h of stirring. Mp 62 °C. $^1$H NMR (400 MHz, $CDCl_3$): $\delta$=0.80–0.95 (m, 2H), 0.95–1.07 (m, 2H), 1.07–1.23 (m, 4H), 1.25–1.35 (m, 2H), 1.45–1.60 (m, 2H), 3.35–3.48 (m, 4H), 3.82 (s, 3H), 4.20 (d, $^2J_{H,H}$=12.0 Hz, 2H), 4.82 (d, $^2J_{H,H}$=12.0 Hz, 2H), 7.44 (s, 2H) ppm. $^{13}$C NMR (100.6 MHz, $CDCl_3$): $\delta$=24.4 (2C), 26.8 (2C), 28.4 (2C), 62.8, 67.3 (2C), 68.2 (2C), 116.1, 134.0 (2C), 134.6 (2C), 157.5 ppm. IR (KBr): $\tilde{\nu}$ = 793, 854, 882, 1008, 1047, 1088, 1171, 1220, 1426, 1470, 2861, 2923, 2954 $cm^{-1}$. HRMS (ESI-Q-Tof): calcd for $C_{17}H_{25}BrNaO_3$ $[M+Na]^{\bullet+}$379.0893; found 379.0877.

*4.3.12. 3,5-Dimethyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2yl)-pyridine* ***12***. Under an atmosphere of Ar, at −78 °C, a solution of *n*-BuLi (2.5 M in cyclohexane, 0.53 mL, 1.29 mmol) was added dropwise to a stirred solution of 4-bromopyridine **11** (200 mg, 1.07 mmol) in anhydrous $Et_2O$ (8 mL). Fifteen minutes later, $B(OBu)_3$ (0.35 mL, 1.29 mmol) was added dropwise. The reaction mixture was then warmed up to room temperature. Acetic acid (65 μL, 1 mmol) was added. The suspension was filtered and the solid was removed with anhydrous $Et_2O$. The combined solvents were evaporated under reduced pressure and 1-butanol was taken off via azeotropic distillation with toluene. The crude residue was then dissolved in anhydrous toluene (5 mL), $MgSO_4$ (1 g) and pinacol (153 mg, 1.29 mmol) were successively added. This reaction mixture was stirred at reflux for 2 h. The obtained suspension was filtered and the solvent was evaporated under reduced pressure. The crude material was purified by chromatography on silicagel (cyclohexane/AcOEt, 3:7) to afford pure **12** as a colourless solid (153 mg, 61%), which can be sublimated (100 °C, 1 mmHg). Mp 133 °C. $^1$H NMR (400 MHz, $CDCl_3$): $\delta$=1.39 (s, 12H), 2.35 (s, 6H), 8.20 (s, 2H) ppm. $^{13}$C NMR ($CDCl_3$): $\delta$=19.0 (2C), 25.0 (4C), 84.4 (2C), 136.0 (3C), 147.3 (2C) ppm. IR (KBr): $\tilde{\nu}$ = 680, 856, 1085, 1145, 1168, 1273, 1314, 1338, 1371, 1380, 1391, 1411, 1456, 2975 $cm^{-1}$. Anal. Calcd for $C_{13}H_{20}BNO_2$ (233.12) C, 66.98; H, 8.65; B, 4.64; N, 6.01. Found: C, 66.84; H, 8.68; B, 4.66; N, 5.88.

*4.3.13. 4-[(3,5-Dimethyl)pyridin-4-yl]-2,6-[(2,8-dioxa)nonan-1,9-diyle]-1-methoxybenzene* ***13a***. After purification by chromatography on silicagel (cyclohexane/AcOEt, 7:3), compound **13a** (126 mg, 85%) was obtained as colourless crystals from bromocyclophane **10a** (137 mg, 0.43 mmol) by using procedure C. Mp 128 °C. $^1$H NMR (400 MHz, $CDCl_3$): $\delta$=0.50–0.65 (m, 2H), 0.95–1.09 (m, 1H), 1.15–1.29 (m, 2H), 1.82–2.20 (m, 1H), 2.00 (s, 3H), 2.16 (s, 3H), 3.16–3.25 (m, 2H), 3.52–3.62 (m, 2H), 4.03 (s, 3H), 4.07 (d, $^2J_{H,H}$=12.5 Hz, 2H), 5.24 (d, $^2J_{H,H}$=12.5 Hz, 2H), 6.97 (s, 2H), 8.34 (s, 1H), 8.38 (s, 1H) ppm. $^{13}$C NMR (100.6 MHz, $CDCl_3$): $\delta$=17.3, 17.5, 19.5, 28.3 (2C), 61.1, 66.7 (2C), 70.7 (2C), 130.7, 131.0, 131.7, 131.9 (2C), 132.4 (2C), 145.8, 148.2, 148.5, 160.2 ppm. IR (KBr): $\tilde{\nu}$ = 539, 661, 697, 722, 852, 885, 1003, 1019, 1047, 1078, 1100, 1121, 1129, 1161, 1194, 1229, 1259, 1282, 1358, 1375, 1439, 1467, 1584, 2853, 2922, 2956 $cm^{-1}$. HRMS (ESI-Q-Tof): calcd for $C_{21}H_{28}NO_3$ $[M+H]^{\bullet+}$ 342.2064; found 242.2064.

*4.3.14. 4-[(3,5-Dimethyl)pyridin-4-yl]-2,6-[(2,9-dioxa)decan-1,10-diyle]-1-methoxybenzene* ***13b***. After purification by chromatography on silicagel (cyclohexane/AcOEt, 5:5), compound **13b** (497 mg, 75%) was obtained as colourless crystals from bromocyclophane **10b** (608 mg, 1.84 mmol) by using procedure C. Mp 119 °C. $^1$H NMR (400 MHz, $CDCl_3$): $\delta$=0.69–0.80 (m, 2H), 1.05–1.17 (m, 2H), 1.17–1.40 (m, 4H), 2.00 (s, 3H), 2.10 (s, 3H), 3.42–3.51 (m, 2H), 3.61–3.69 (m, 2H), 3.90 (s, 3H), 4.21 (d, $^2J_{H,H}$=12.4 Hz, 2H), 4.99 (d, $^2J_{H,H}$=12.4 Hz, 2H), 7.04 (s, 2H), 8.33 (s, 1H), 8.35 (s, 1H) ppm. $^{13}$C NMR (100.6 MHz, $CDCl_3$): $\delta$=17.3, 17.6, 23.4 (2C), 29.7 (2C), 62.4, 67.9 (2C), 69.1 (2C), 130.8, 130.9, 132.2 (2C), 133.1 (2C), 133.6, 148.3, 148.4, 148.5, 158.0 ppm. IR (KBr): $\tilde{\nu}$ = 538, 651, 673, 693, 723, 877, 904, 920, 1015, 1040, 1065, 1094, 1125, 1160, 1196, 1233, 1272, 1358, 1468, 1587, 2733, 2759, 2858, 2921, 2956, 2995 $cm^{-1}$. HRMS (ESI-Q-Tof): calcd for $C_{22}H_{30}NO_3$ $[M+H]^{\bullet+}$ 356.2220; found 356.2212.

*4.3.15. 4-[(3,5-Dimethyl)pyridin-4-yl]-2,6-[(2,10-dioxa)undecan-1,11-diyle]-1-methoxybenzene* ***13c***. After purification by chromatography on silicagel (cyclohexane/AcOEt, 5.5:4.5), compound **10c** (126 mg, 80%) was obtained as colourless crystals from bromocyclophane **8c** (146 mg, 0.42 mmol) by using procedure C. Mp 151–153 °C. $^1$H NMR (400 MHz, $CDCl_3$): $\delta$=0.61–0.74 (m, 2H), 1.04–1.15 (m, 2H), 1.17–1.40 (m, 6H), 1.60–1.75 (m, 2H), 2.01 (s, 3H), 2.07 (s, 3H), 3.18–3.30 (m, 2H), 3.32–3.42 (m, 2H), 3.96 (m, 3H), 4.14 (d, $^2J_{H,H}$=12.3 Hz, 2H), 5.07 (d, $^2J_{H,H}$=12.3 Hz, 2H), 7.00 (s, 2H), 8.33 (s, 1H), 8.34 (s, 1H) ppm. $^{13}$C NMR (100.6 MHz, $CDCl_3$): $\delta$=17.3, 17.4, 24.5, 24.6 (2C), 28.3 (2C), 61.9, 65.2 (2C), 68.6 (2C), 130.8, 130.9, 131.5 (2C), 132.2, 132.4 (2C), 148.3, 148.4 (2C), 158.4 ppm. IR (KBr): $\tilde{\nu}$ = 526, 670, 718, 877, 899, 940, 1015, 1048, 1093, 1131, 1161, 1195, 1248, 1278, 1360, 1376, 1430, 1477, 1584, 2697, 2728, 2757, 2853, 2896, 2935, 3018 $cm^{-1}$. HRMS (ESI-Q-Tof): calcd for $C_{23}H_{32}NO_3$ $[M+H]^{\bullet+}$ 370.2382; found 370.2374.

*4.3.16. 4-[(3,5-Dimethyl)pyridin-4-yl]-2,6-[(2,11-dioxa)dodecan-1,12-diyle]-1-methoxybenzene* ***13d***. After purification by chromatography on silicagel (cyclohexane/AcOEt, 5.5:4.5), compound **13d** (596 mg, 85%) was obtained as colourless crystals from bromocyclophane **10d** (654 mg, 1.83 mmol) by using procedure C. Mp 88 °C. $^1$H NMR (400 MHz, $CDCl_3$): $\delta$=0.86–0.98 (m, 2H), 0.98–1.15 (m, 4H), 1.15–1.31 (m, 4H), 1.44–1.58 (m, 2H), 2.01 (s, 3H), 2.08 (s, 3H), 3.43–3.48 (m, 4H), 3.92 (s, 3H), 4.24 (d, $^2J_{H,H}$=12.4 Hz, 2H), 4.95 (d, $^2J_{H,H}$=12.4 Hz, 2H), 7.08 (s, 2H), 8.33 (ls, 2H) ppm. $^{13}$C NMR (100.6 MHz, $CDCl_3$): $\delta$=17.3, 17.5, 24.3 (2C), 26.7 (2C), 28.6 (2C), 63.2, 67.7 (2C), 67.9 (2C), 130.8, 130.9, 131.8 (2C), 132.3 (2C), 133.2, 148.3, 148.4, 148.5, 157.8 ppm. IR (KBr): $\tilde{\nu}$ = 518, 675, 857, 875, 1008, 1045, 1086, 1162, 1198, 1235, 1268, 1314, 1378, 1472, 1584, 2860, 2931 $cm^{-1}$. HRMS (ESI-Q-Tof): calcd for $C_{24}H_{34}NO_3$ $[M+H]^{\bullet+}$ 384.2533; found 384.2530.

*4.3.17. 4-[(3,5-Dimethyl)pyridin-4-yl]-2,6-[(2,8-dioxa)nonan-1,9-diyle]phenol* ***14a***. After purification by chromatography on silicagel (cyclohexane/AcOEt, 8:2), compound **14a** (66 mg, 66%) was obtained as colourless crystals from biaryl **13a** (116 mg, 0.34 mmol) by using procedure D. Mp 118.5 °C. $^1$H NMR (400 MHz, $CDCl_3$): $\delta$=0.75–0.90 (m, 2H), 1.10–1.25 (m, 1H), 1.25–1.39 (m, 2H), 1.91–2.06 (m, 2H), 2.01 (s, 3H), 2.14 (s, 3H), 3.24–3.34 (m, 2H),

3.63–3.71 (m, 2H), 4.14 (d, $^2J_{H,H}$=13.0 Hz, 2H), 5.32 (d, $^2J_{H,H}$=13.0 Hz, 2H), 6.88 (s, 2H), 8.37 (br s, 2H) ppm. $^{13}$C NMR (100.6 MHz, $CDCl_3$): $\delta$=17.3, 17.5, 20.4, 27.9 (2C), 68.0 (2C), 71.0 (2C), 128.0 (2C), 129.0, 130.0 (2C), 131.9, 131.95, 147.7, 147.8, 149.1, 155.6 ppm. IR (KBr): $\tilde{\nu}$ = 542, 668, 695, 721, 991, 1029, 1044, 1077, 1097, 1120, 1129, 1160, 1195, 1222, 1236, 1281, 1319, 1338, 1438, 1455, 1474, 1496, 1590, 2852, 2907, 2948, 3034 cm$^{-1}$. HRMS (ESI-Q-Tof): calcd for $C_{20}H_{26}O_3N$ $[M+H]^{\bullet+}$ 328.1907; found 328.1904.

*4.3.18. 4-[(3,5-Dimethyl)pyridin-4-yl]-2,6-[(2,9-dioxa)decan-1,10-diyle]phenol* ***14b****.* After purification by chromatography on silicagel (cyclohexane/AcOEt, 5:5), compound **14b** (268 mg, 65%) was obtained as colourless crystals from biaryl **13b** (429 mg, 1.2 mmol) by using procedure D. Mp 163 °C. $^1$H NMR (400 MHz, $CDCl_3$): $\delta$=0.93–1.05 (m, 2H), 1.29–1.43 (m, 4H), 1.46–1.57 (m, 2H), 1.99 (s, 3H), 2.08 (s, 3H), 3.40–3.49 (m, 2H), 3.72–3.80 (m, 2H), 4.19 (d, $^2J_{H,H}$=12.8 Hz, 2H), 5.16 (d, $^2J_{H,H}$=12.8 Hz, 2H), 6.86 (s, 2H), 7.90 (s, 1H), 8.31 (s, 1H), 8.33 (s, 1H) ppm. $^{13}$C NMR (100.6 MHz, $CDCl_3$): $\delta$=17.3, 17.4, 24.3 (2C), 29.3 (2C), 69.0 (2C), 70.0 (2C), 126.6 (2C), 129.2, 129.9 (2C), 131.0, 131.1, 148.3 (2C), 148.6, 154.2 ppm. IR (KBr): $\tilde{\nu}$ = 514, 535, 658, 673, 787, 863, 881, 900, 969, 1012, 1031, 1053, 1082, 1123, 1161, 1193, 1221, 1282, 1312, 1339, 1468, 1496, 1585, 2867, 2882, 2925, 3016, 3288 cm$^{-1}$. HRMS (ESI-Q-Tof): calcd for $C_{21}H_{28}NO_3$ $[M+H]^{\bullet+}$ 342.2063; found 342.2056.

*4.3.19. 4-[(3,5-Dimethyl)pyridin-4-yl]-2,6-[(2,10-dioxa)undecane-1,11-diyle]phenol* ***14c****.* After purification by chromatography on silicagel (cyclohexane/AcOEt, 5.5:4.5), compound **14c** (89 mg, 79%) was obtained as colourless crystals from biaryl **13c** (117 mg, 0.32 mmol) by using procedure D. Mp 187–189 °C. $^1$H NMR (400 MHz, $CDCl_3$): $\delta$=0.70–1.00 (m, 2H), 1.36–1.50 (m, 4H), 1.50–1.70 (m, 4H), 2.04 (s, 6H), 3.32 (t, $^3J_{H,H}$=5.5, 4H), 4.80 (br m, 4H), 6.86 (s, 2H), 7.52 (s, 1H), 8.34 (ls, 2H) ppm. $^{13}$C NMR (100.6 MHz, $CDCl_3$): $\delta$=17.3 (2C), 23.2, 24.8 (2C), 27.9 (2C), 65.0 (2C), 70.1 (2C), 124.9 (2C), 128.7, 130.5 (2C), 131.1 (2C), 148.4 (2C), 148.5, 154.9 ppm. IR (KBr): $\tilde{\nu}$ = 679, 704, 877, 896, 909, 939, 960, 986, 1045, 1091, 1129, 1160, 1195, 1223, 1278, 1317, 1346, 1378, 1456, 1474, 1496, 1592, 1615, 2850, 2927, 2941, 3129 cm$^{-1}$. HRMS (ESI-Q-Tof): calcd for $C_{22}H_{30}NO_3$ $[M+H]^{\bullet+}$356.2226; found 356.2237.

*4.3.20. 4-[(3,5-Dimethyl)pyridin-4-yl]-2,6-[(2,11-dioxa)dodecane-1,12-diyle]phenol* ***14d****.* After purification by chromatography on silicagel (cyclohexane/AcOEt, 5.5:4.5), compound **14d** (300 mg, 83%) was obtained as colourless crystals from biaryl **13d** (374 mg, 0.98 mmol) by using procedure D. Mp 135 °C. $^1$H NMR (400 MHz, $CDCl_3$): $\delta$=1.10–1.20 (m, 4H), 1.23–1.35 (m, 4H), 1.51 (q, $^3J_{H,H}$=6.0 Hz, 4H), 2.03 (s, 6H), 3.52 (t, $^3J_{H,H}$=6.0 Hz, 4H), 4.65 (s, 4H), 6.87 (s, 2H), 7.78 (br s, 1H), 8.32 (s, 2H) ppm. $^{13}$C NMR (100.6 MHz, $CDCl_3$): $\delta$=17.3 (2C), 24.6 (2C), 26.9 (2C), 28.7 (2C), 69.0 (2C), 69.9 (2C), 125.0 (2C), 128.9, 130.0 (2C), 131.1 (2C), 148.4 (2C), 148.6, 154.6 ppm. IR (KBr): $\tilde{\nu}$ = 481, 669, 714, 886, 1016, 1047, 1079, 1157, 1215, 1274, 1340, 1476, 1592, 1614, 2851, 2934 cm$^{-1}$. HRMS (ESI-Q-Tof): calcd for $C_{23}H_{32}N\,O_3$ $[M+H]^{\bullet+}$ 370.2376; found 370.2375.

*4.3.21. 4-{4-[3,9-Dioxa-1(2,6)-(1$^1$-hydroxy)benzenacyclodecaphanyl]-1,3,5-trimethylpyridinium iodide* ***15a****.* Compound **15a** (80 mg, 70%) was obtained as colourless crystals from pyridinylphenol **14a** (80 mg, 0.24 mmol) by using procedure E. Mp 240 °C. $^1$H NMR (400 MHz, $CD_3OD$): $\delta$=0.66–079 (m, 2H), 0.98–1.10 (m, 1H), 1.16–1.28 (m, 2H), 2.01–2.16 (m, 1H), 2.20 (s, 3H), 2.39 (s, 3H), 3.24–3.35 (m, 2H), 3.55–3.63 (m, 2H), 4.14 (d, $^2J_{H,H}$=12.6 Hz, 2H), 4.36 (s, 3H), 5.29 (d, $^2J_{H,H}$=12.6 Hz, 2H), 7.10 (s, 2H), 8.59 (s, 1H), 8.73 (s, 1H) ppm. $^{13}$C NMR (100.6 MHz, $CD_3OD$): $\delta$=18.0, 18.4, 21.0 (2C), 29.4 (2C), 48.1, 67.9 (2C), 71.0 (2C), 125.6, 129.1 (2C), 131.6 (2C), 138.8, 139.1, 144.0, 144.1, 158.9, 159.5 ppm. IR (KBr): $\tilde{\nu}$ = 548, 660, 676, 731, 775, 845, 918, 935, 984, 1061, 1128, 1178, 1226, 1292, 1319, 1384, 1434, 1479, 1603, 1634, 2853, 2899, 2951, 3202 cm$^{-1}$. HRMS (ESI-Q-Tof): calcd for $C_{21}H_{28}NO_3$ $[M]^{\bullet+}$ 342.2063; found 342.2064.

*4.3.22. 4-{4-[3,10-Dioxa-1(2,6)-(1$^1$-hydroxy)benzenacycloundecaphanyl]-1,3,5-trimethylpyridinium iodide* ***15b****.* Compound **15b** (174 mg, 80%) was obtained as colourless crystals from pyridinylphenol **14b** (154 mg, 0.45 mmol) by using procedure E. Mp 270 °C. $^1$H NMR (400 MHz, $CD_3OD$): $\delta$=0.80–1.01 (m, 2H), 1.20–1.41 (m, 4H), 1.41–1.56 (m, 2H), 2.22 (s, 3H), 2.34 (s, 3H), 3.40–3.54 (m, 2H), 3.68–3.83 (m, 2H), 4.26 (d, $^2J_{H,H}$=12.8 Hz, 2H), 4.36 (s, 3H), 5.15 (d, $^2J_{H,H}$=12.8 Hz, 2H), 7.10 (s, 2H), 8.68 (s, 1H), 8.69 (s, 1H) ppm. $^{13}$C NMR (100.6 MHz, $CD_3OD$): $\delta$=18.0, 18.3, 25.2 (2C), 30.7 (2C), 48.2, 69.6 (2C), 70.0 (2C), 126.5, 128.7 (2C), 131.3 (2C), 138.9, 139.0, 144.0 (2C), 157.0, 159.6 ppm. IR (KBr): $\tilde{\nu}$ = 658, 786, 862, 899, 928, 966, 979, 1012, 1050, 1122, 1178, 1224, 1285, 1307, 1357, 1379, 1432, 1482, 1595, 1613, 1638, 1834, 2880, 2899, 2918, 2987, 3257 cm$^{-1}$. HRMS (ESI-Q-Tof): calcd for $C_{22}H_{30}NO_3$ $[M]^{\bullet+}$ 356.2220; found 356.2214.

*4.3.23. 4-{4-[3,11-Dioxa-1(2,6)-(1$^1$-hydroxy)benzenacyclododecaphanyl]-1,3,5-trimethylpyridinium iodide* ***15c****.* Compound **15c** (81 mg, 96%) was obtained as colourless crystals from pyridinylphenol **14c** (60 mg, 0.17 mmol) by using procedure E. Mp 264 °C. $^1$H NMR (400 MHz, $CD_3OD$): $\delta$=0.60–1.00 (br m, 2H), 1.25–1.85 (m, 8H), 2.27 (s, 6H), 4.00–5.5 (br m, 8H), 4.36 (s, 4H), 7.12 (s, 2H), 8.71 (s, 2H) ppm. $^{13}$C NMR (100.6 MHz, $CD_3OD$): $\delta$=18.1 (2C), 24.6, 26.0 (2C), 29.2 (2C), 48.2, 65.6 (2C), 70.1 (2C), 125.6, 126.9 (2C), 132.0 (2C), 138.9 (2C), 144.1 (2C), 157.9, 159.5 ppm. IR (KBr): $\tilde{\nu}$ = 589, 617, 671, 687, 760, 889, 921, 932, 1038, 1087, 1099, 1130, 1176, 1208, 1243, 1289, 1317, 1362, 1384, 1434, 1475, 1602, 1634, 1838, 2856, 2913, 2844, 2981, 3414 cm$^{-1}$. HRMS (ESI-Q-Tof): calcd for $C_{23}H_{32}NO_3$ $[M]^{\bullet+}$ 370.2377; found 370.2372.

*4.3.24. 4-{4-[3,12-Dioxa-1(2,6)-(1$^1$-hydroxy)benzenacyclotridecaphanyl]-1,3,5-trimethylpyridinium iodide* ***15d****.* Compound **15d** (235 mg, 75%) was obtained as colourless crystals from pyridinylphenol **14d** (226 mg, 0.61 mmol) by using procedure E. Mp 254 °C. $^1$H NMR (400 MHz, $CD_3OD$): $\delta$=1.15–1.20 (m, 4H), 1.22–1.35 (m, 4H), 1.47 (quint, $^3J_{H,H}$=6 Hz, 4H), 2.27 (s, 6H), 3.55 (t, $^3J_{H,H}$=6 Hz, 4H), 4.37 (s, 3H), 4.85 (s, 4H), 7.13 (s, 2H), 8.71 (s, 2H) ppm. $^{13}$C NMR (100.6 MHz, $CD_3OD$): $\delta$=18.2 (2C), 25.7 (2C), 28.2 (2C), 30.0 (2C), 48.2, 69.7 (2C), 69.9 (2C), 126.2, 127.4 (2C), 131.4 (2C), 138.9 (2C), 144.1 (2C), 157.5, 159.6 ppm. IR (KBr): $\tilde{\nu}$ = 664, 863, 913, 1015, 1038, 1074, 1179, 1218, 1289, 1363, 1479, 1613, 1643, 2853, 2834, 2996, 3285 cm$^{-1}$. HRMS (ESI-Q-Tof): calcd for $C_{24}H_{34}NO_3$ $[M+H]^{\bullet+}$ 384.2533; found 384.2527.

*4.3.25. 4-[(1,3,5-Trimethyl)-4-pyridinio]-2,6-[2,8-dioxanonan-1,9-diyle]phenolate* ***16a****.* Compound **16b** (13 mg, 60%) was obtained as red crystals from iodide **15b** (30 mg, 0.06 mmol) by using procedure F. Mp (dec) 84 °C. $^1$H NMR (400 MHz, $CD_3OD$): $\delta$=0.73–0.87 (m, 2H), 0.87–1.00 (m, 1H), 1.20–1.35 (m, 2H), 1.83–1.98 (m, 1H), 2.36 (s, 6H), 3.26–3.38 (m, 2H), 3.47–3.58 (m, 2H), 3.94 (d, $^2J_{H,H}$=11.7 Hz, 2H), 4.28 (s, 3H), 5.35 (d, $^2J_{H,H}$=11.7 Hz, 2H), 6.92 (s, 2H), 8.55 (s, 2H) ppm. $^{13}$C NMR (100.6 MHz, $CD_3OD$): $\delta$=18.6 (2C), 22.2, 29.5 (2C), 47.5, 67.1 (2C), 71.3 (2C), 117.5, 129.0 (2C), 132.8 (2C), 138.3 (2C), 143.5 (2C), 161.1, 169.8 ppm. IR (KBr): $\tilde{\nu}$ = 651, 665, 752, 1066, 1128, 1097, 1306, 1355, 1594, 1416, 1642, 2845, 2921, 2954, 3042, 3415 cm$^{-1}$. HRMS (ESI-Q-Tof): calcd for $C_{21}H_{28}NO_3$ $[M+H]^{\bullet+}$ 342.2064; found 342.2061.

*4.3.26. 4-[(1,3,5-Trimethyl)-4-pyridinio]-2,6-[2,9-dioxadecan-1,10-diyle]phenolate* ***16b****.* Compound **16b** (19 mg, 65%) was obtained as red crystals from iodide **15b** (40 mg, 0.08 mmol) by using procedure F. Mp (dec) 94 °C. $^1$H NMR (400 MHz, $CD_3OD$): $\delta$=0.84–0.97 (m, 2H), 1.15–1.26 (m, 2H), 1.26–1.45(m, 4H), 2.36 (br s, 6H), 3.49–3.3.57 (m, 2H), 3.72–3.8 (m, 2H), 4.03 (d, $^2J_{H,H}$=11.6 Hz, 2H),

4.29 (s, 3H), 5.26 (d, $^{2}J_{H,H}$=11.6 Hz, 2H), 6.94 (s, 2H), 8.55 (s, 2H) ppm. $^{13}$C NMR (100.6 MHz, $CD_3OD$): $\delta$=18.7 (2C), 24.7 (2C), 30.9 (2C), 47.5, 68.9 (2C), 70.5 (2C), 117.7, 129.7 (2C), 132.8 (2C), 138.4 (2C), 143.5 (2C), 161.4, 169.3 ppm. IR (KBr): $\tilde{\nu}$ = 649, 752, 902, 966, 1053, 1083, 1122, 1178, 1220, 1305, 1334, 1417, 1466, 1595, 1645, 2341, 2361, 2851, 2927, 3333 cm$^{-1}$. HRMS (ESI-Q-Tof): calcd for $C_{22}H_{30}NO_3$ $[M+H]^{\bullet+}$ 356.2220; found 356.2211.

*4.3.27. 4-[(1,3,5-Trimethyl)-4-pyridinio]-2,6-[2,10-dioxaundecan-1,11-diyle]phenolate* ***16c****.* Compound **16c** (35 mg, 65%) was obtained as orange crystals from iodide **15c** (60 mg, 0.12 mmol) by using procedure F. Mp (dec) 99 °C. $^{1}$H NMR (400 MHz, $CD_3OD$): $\delta$=0.80–0.97 (m, 2H), 0.97–1.18 (m, 2H), 1.18–1.44 (m, 4H), 1.44–1.70 (m, 2H), 2.35 (br s, 6H), 3.40–3.6 (m, 4H), 3.88–4.14 (m, 2H), 4.28 (s, 3H), 5.11–5.37 (m, 2H), 6.93 (s, 2H), 8.54 (s, 2H) ppm. $^{13}$C NMR (100.6 MHz, $CD_3OD$): $\delta$=18.6 (2C), 25.8 (2C), 26.6, 30.0 (2C), 47.5, 66.9 (2C), 69.7 (2C), 117.2, 128.8 (2C), 133.1 (2C), 138.4 (2C), 143.5 (2C), 161.5, 169.1 ppm. IR (KBr): $\tilde{\nu}$ = 658, 750, 910, 1032, 1092, 1130, 1177, 1217, 1302, 1338, 1417, 1468, 1593, 1644, 2850, 2924, 3337 cm$^{-1}$. HRMS (ESI-Q-Tof): calcd for $C_{23}H_{32}NO_3$ $[M+H]^{\bullet+}$370.2377; found 370.2370.

*4.3.28. 4-[(1,3,5-Trimethyl)-4-pyridinio]-2,6-[2,11-dioxadodecan-1,12-diyle]phenolate* ***16d****.* Compound **16d** (116 mg, 86%) was obtained as red crystals from iodide **15d** (180 mg, 0.35 mmol) by using procedure F. Mp (dec) 157 °C. $^{1}$H NMR (400 MHz, $CD_3OD$): $\delta$=0.99–1.08 (m, 4H), 1.17–1.28 (m, 4H), 1.41 (q, $^{3}J_{H,H}$=6.5 Hz, 4H), 2.34 (s, 6H), 3.52 (t, $^{3}J_{H,H}$=6.5 Hz, 4H), 4.28 (s, 3H), 4.62 (br s, 4H), 6.97 (s, 2H), 8.55 (s, 2H) ppm. $^{13}$C NMR (100.6 MHz, $CD_3OD$): $\delta$=18.6 (2C), 25.4 (2C), 27.8 (2C), 29.8 (2C), 47.5, 68.3 (2C), 69.2 (2C), 117.9, 128.8 (2C), 132.6 (2C), 138.4 (2C), 143.5 (2C), 161.5, 168.7 ppm. IR (KBr): $\tilde{\nu}$ = 656, 753, 861, 891, 1013, 1042, 1087, 1178, 1221, 1342, 1387, 1416, 1466, 1598, 1643, 2851, 2923, 3392 cm$^{-1}$. HRMS (ESI-Q-Tof): calcd for $C_{24}H_{34}NO_3$ $[M+H]^{\bullet+}$384.2533; found 384.2524.

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