A Shape-Persistent Macrocycle With Two Opposing 2,2′:6′,2"-Terpyridine Units

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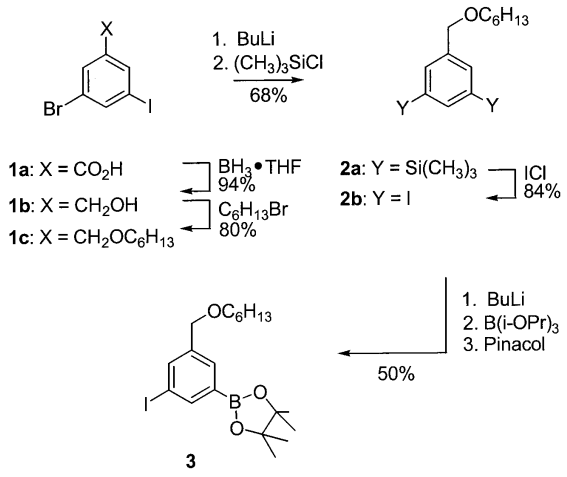
The synthesis reported here of the shape-persistent macrocycle **9** with two opposing terpyridine units, and with pendant flexible chains for solubility reasons, was achieved by Suzuki cross-coupling of two "half-cycles", the bisboronic acid ester **7** and its diiodo counterpart **8**. Cycle **9** was obtained on a 100 mg scale in a yield of 20%. It was characterized by FAB mass spectrometry and ^{1}H and ^{13}C NMR spectroscopy. Cycle **9** is the first shape-persistent cycle containing terpyridine units that is larger than cyclosexipyridine. An improved synthesis of the important building block dibromoterpyridine **12** is also presented.

Introduction

As part of a long-term project aimed at soluble, shape-persistent macrocycles for metal complexation and aggregation into cylindrically shaped stacks, we have recently reported the synthesis of a series of building blocks,[1−3] as well as the first examples in which these building blocks were actually put together to form hexagonal cyclic molecules with two opposing bipyridine (bpy) units.[2b] These bpy′s can rotate more or less freely, and should allow for *endo* and *exo* metal complexation. Parallel to this work we have been investigating related cycles with terpyridine (tpy) units located at a hexagon′s corners.[1,4] Here the chelating moiety can only lead to *endo* complexation. The present contribution describes the synthesis of a macrocycle that has two opposing tpy units, and is decorated with four flexible chains for solubility reasons. A considerably improved synthesis of 5,5"-dibromo-2,2′:6′,2"-tpy, an important building block within this general theme, is also reported, which makes it conveniently available on the 2 g scale.

Results and Discussion

A variety of tpy-containing cycles are known;[5,6] however, except for the small cyclosexipyridine and its derivatives,[5] they all contain flexible units and are therefore not considered as shape-persistent (rigid). From liquid crystalline compounds, one knows that shape-persistence favors aggregation of molecules into ordered arrays. It reduces the conformational space available and stacking, in entropy terms, is no longer so costly.[7] With regard to the synthesis of macrocycles, shape persistence adds an additional aspect, that of the efficiency with which the cycles can be obtained from their precursor(s). Generally, the more rigid the precursor(s) is(are), the higher the cycle′s yield is,[8] providing, of course, that the geometry is such that it enhances the efficiency of ring-closure.



Scheme 1

The synthesis of cycle **9** is shown in Schemes 1 to 3. It is constructed from the two symmetrical half-cycles **7** and **8**,[1] whose tpy units were obtained using different strategies. Whereas unit **7** was built from the central pyridine **6** and the terminal phenylpyridine **5**, the half-cycle **8** was obtained using an already preformed tpy building block from our construction set.[1] Changing the coupling functionalities from halo to boronic acid, in the dihalo "half-cycles" of type **8** was not feasible.[9] For the synthesis of the terminal phenylpyridine **5**, the suitably functionalized benzene derivative **3** was obtained according to the sequence in Scheme 1. Some comments to the schemes are given below.

Scheme 1: The conversion from **1c** to **2a** converts an unsymmetrical into a symmetrical compound, which at first glance may be considered unattractive. Compound **1c** however, is the most easily accessible *meta*-dihalobenzene derivative with a flexible chain, and was therefore taken as starting material.

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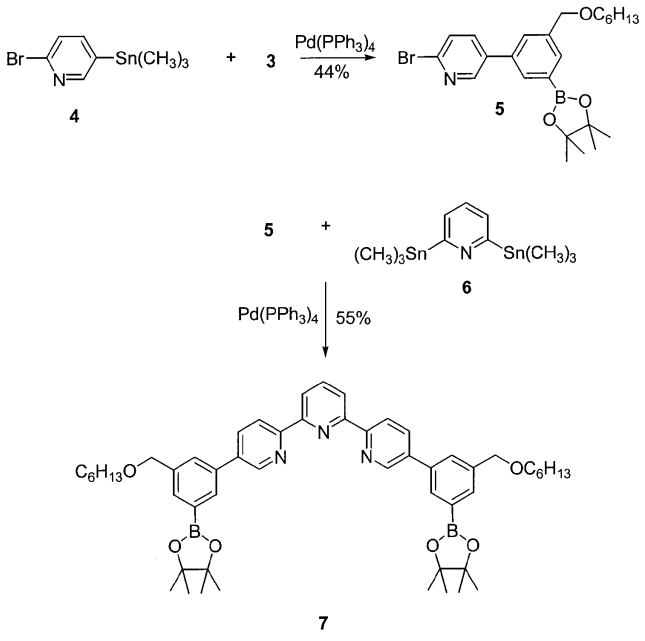
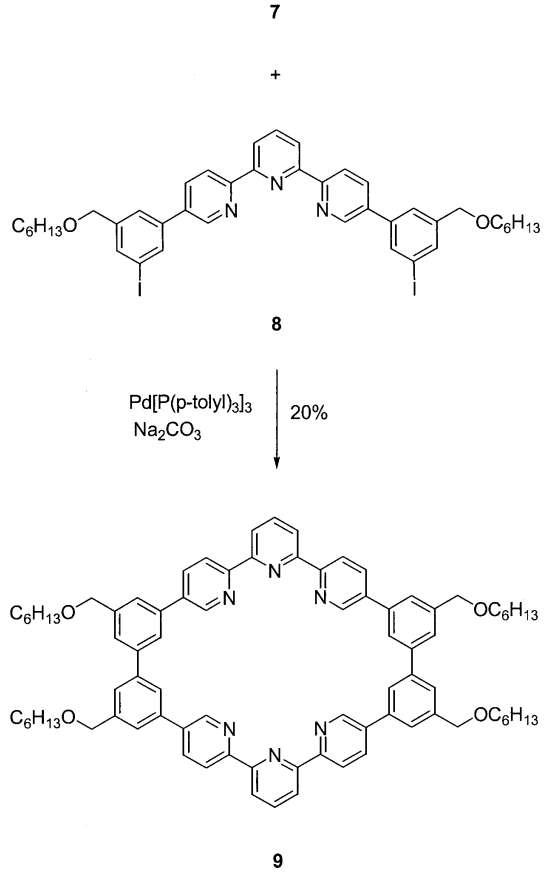


Scheme 2



Scheme 3

Scheme 2: Compounds **3** and **4** have four potential sites for cross-coupling. The Stille-type coupling reaction shown utilizes the known high selectivity of iodo over bromo carbons,[10] and trimethylstannyl (TMSn) over boronic acid ester groups.[11] There was, however, some side reaction caused by homocoupling of **4** to give 6,6′-dibromo-3,3′-bipyridine which reduced the yield to 44%.[12,13]

The cross-coupling of **5** and **6** occurred with a conversion of at least 80% (NMR spectroscopy of the reaction mixture). The chromatographic purification was difficult, and led to pure product in a yield of 55%. Compounds **5** and **7** are both stable on silica gel. Deboronification was not observed as is sometimes the case in structurally related compounds.[14]

The cyclization in Scheme 3 uses Suzuki conditions and the results depend on the reaction conditions.[15] Figure 1 shows typical GPC elution curves taken directly from the cyclization experiments. The top curve was obtained when the reported standard conditions for cyclizations to oligophenylene rings were applied.[16] The signal at 1904 (molar mass relative to polystyrene standard) reflects cycle **9**. If the conditions were varied, as described in the Experimental Section, essentially leading to an increased concentration of catalyst precursor, the amount of cyclic product **9** could be greatly improved (Figure 1b). Purification of **9** was done by preparative GPC to a degree illustrated by the trace in Figure 1c. Despite this nice looking elution curve, compound

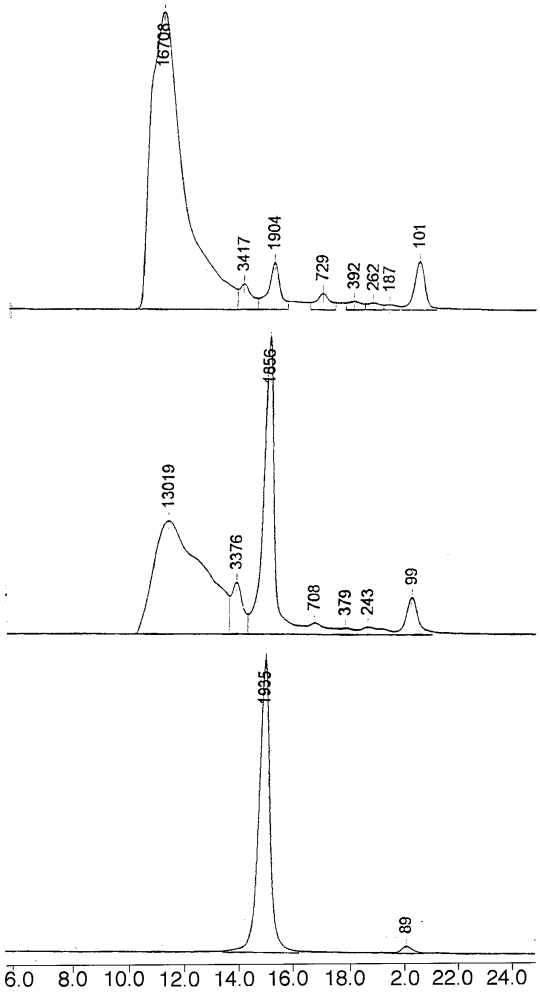
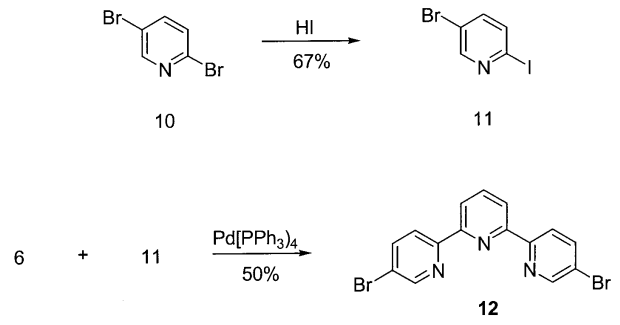


Figure 1. Gel permeation chromatography elugrams of a crude product of the reaction between the "half-cycles" **7** and **8** (a) under standard cyclization conditions (ref. 16) and (b) under optimized conditions (reported here), and of the purified cycle **9** (c)

9 was not completely pure. The FAB mass spectrum, in addition to the peak for the molecular ion at $m/z = 1224$ [M + H$^+$], with the expected isotope distribution, showed a low intensity signal at $m/z = 1240$ whose nature is not yet clear.[17] Also, the data from combustion analysis were not completely satisfactory. The carbon value was 1% off. There is however, no reasonable doubt that the cycle really exists, because the ^{1}H and ^{13}C NMR spectra show all required signals at the expected shifts. Furthermore, the shifts of the ^{1}H NMR spectrum of **9** depend on concentration — with increasing dilution the aromatic signals are shifted downfield by up to 0.7 ppm, and the benzylic protons by up to 0.2 ppm. This effect has not yet been correlated with a structural model, but supports the assignment of **9** as a cycle, because neither half cycle **7** nor **8** shows this dependence. Also, the polymeric side product[18] does not show this effect. The same observation was made by Moore et al.[7] in the case of phenylacetylene macrocycles, where the cycles also show a pronounced shift/concentration dependence whereas the open chain analogues do not.

Scheme 4 shows the improved sequence in forming the dibromo tpy building block **12**.[1] It utilizes iodobromopyridine **4**, which was easily obtained by reacting compound **10** with hydroiodic acid on the 14 g scale. Stille cross-coupling of **11** with **6** gave **12** in a yield of 50%.



Scheme 4

Experimental Section

General: Compound **1c** was previously reported without an experimental procedure,[2a] which is now given here. Compounds **4**,[2a] **6**,[19] and **8**[1] were prepared according to the literature.

1-Bromo-3-hydroxymethyl-5-iodobenzene (1b): To a solution of 3-bromo-5-iodobenzenecarboxylic acid **(1a)** (25 g, 76 mmol) in THF (150 mL) at 0 °C was added BH_3 (1 M, 100 mL) in THF, dropwise. The reaction mixture was stirred at room temp. for 12 h, before a 1:1 mixture of THF and H_2O was added carefully. The resulting mixture was made alkaline with potassium carbonate, and subsequently extracted with CH_2Cl_2 (2 × 200 mL). The combined organic layers were dried over $MgSO_4$ and filtered, and the solvent was removed. This gave **1b** (22.7 g, 94%) as a white solid. A further purification was not necessary. − M.p. 120 °C. − ^{1}H NMR ($CDCl_3$, 270 MHz): δ = 1.90 (br s, 1 H, ArCH$_2$O*H*), 4.60 (s, 2 H, ArC*H*$_2$OH), 7.46 (s, 1 H), 7.62 (s, 1 H), 7.74 (s, 1 H). − ^{13}C NMR ($CDCl_3$, 68 MHz): δ = 63.54 (ArCH$_2$OH), 94.48 (*C*−I), 123.04, 129.07, 134.25, 138.61, 144.68. − MS (EI, 80 eV); *m/z* (%): 314 (93.83), 312 (100.00) [M$^+$], 233 (24.43) [M$^+$ − Br]. − C_7H_6BrIO (360.19): calcd. C 26.86, H 1.93; found C 26.72, H 1.80.

1-Bromo-3-hexoxymethyl-5-iodobenzene (1c): A solution of **1b** (33 g, 105 mmol), hexyl bromide (34.8 g, 211 mmol), KO*t*Bu (23.6 g, 210 mmol) and 18-crown-6 (0.28 g, 1 mmol) in THF (400 mL) was heated under reflux and stirred vigorously for 24 h. Then the reaction mixture was allowed to cool to room temp. and treated with H_2O (150 mL). The aqueous layer was separated and washed with CH_2Cl_2 (2 × 100 mL). The combined organic extracts were dried over $MgSO_4$. Removal of the solvent and chromatographic separation on silica gel with CH_2Cl_2 as eluent afforded **1c** (33.8 g, 80%) as a light yellow oil. − ^{1}H NMR ($CDCl_3$, 270 MHz): δ = 0.87 (t, *J* = 6.5 Hz, 3 H, C*H*$_3$), 1.19−1.39 (m, 6 H, C*H*$_2$), 1.59 (q, *J* = 6.6 Hz, 2 H, β-C*H*$_2$), 3.42 (t, *J* = 6.6 Hz, 2 H, α-C*H*$_2$), 4.37 (s, 2 H, Ar−C*H*$_2$), 7.41 (s, 1 H), 7.57 (s, 1 H), 7.72 (s, 1 H). − ^{13}C NMR ($CDCl_3$, 68 MHz): δ = 14.01, 22.51, 25.71, 29.50, 31.53, 70.83, 70.90, 94.34 (*C*−I), 122.81, 129.47, 134.65, 138.30, 142.81. − MS (EI, 80 eV); *m/z* (%): 396 (6.25) [M$^+$], 296 (100.00) [M$^+$ − OC_6H_{13} + H], 217 (17.78) [M$^+$ − OC_6H_{13} − Br + H]. − $C_{13}H_{18}BrIO$ (397.09): calcd. C 39.32, H 4.56; found C 39.33, H 4.47.

1-Hexoxymethyl-3,5-bis(trimethylsilyl)benzene (2a): Compound **1c** (5 g, 12.6 mmol) was dissolved in a mixture of Et_2O (50 mL) and THF (50 mL). At −78 °C *n*BuLi (1.6 M, 31 mL) was added dropwise. The suspension was stirred at this temperature for 1 h before it was warmed to room temp., so that the precipitate dissolved. Before trimethylsilyl chloride (8.5 g, 78.8 mmol) was added, the reaction mixture was cooled again to −78 °C. After warming to room temp. overnight, H_2O (100 mL) was added, the layers were separated, and the aqueous layer was washed with Et_2O (2 × 100 mL). The combined organic layers were dried over $MgSO_4$ and filtered, and the solvent was removed. Chromatography on silica gel with hexane/EtOAc (30:1) as eluent gave **2a** (2.91 g, 68%) as a colorless oil. − ^{1}H NMR ($CDCl_3$, 270 MHz): δ = 0.30 [s, 18 H, Si(C*H*$_3$)$_3$], 0.91 (t, *J* = 6.5 Hz, 3 H, C*H*$_3$), 1.31−1.46 (m, 6 H, C*H*$_2$), 1.65 (q, *J* = 6.6 Hz, 2 H, β-C*H*$_2$), 3.51 (t, *J* = 6.6 Hz, 2 H, α-C*H*$_2$), 4.54 (s, 2 H, Ar−C*H*$_2$ 7.51 (s, 2 H), 7.61 (s, 1 H). − ^{13}C NMR ($CDCl_3$, 68 MHz): δ = − 1.08 [Si(*C*H$_3$)$_3$], 14.03, 22.62, 25.94, 29.75, 31.71, 70.53, 73.20, 133.26, 136.75, 137.36, 139.45. − MS (EI, 80 eV); *m/z* (%): 336 (7.10) [M$^+$], 321 (100) [M$^+$ − CH$_3$], 251 (25.50) [M$^+$ − C_6H_{13}], 236 (42.81) [M$^+$ − C_6H_{13} − CH$_3$], 221 (16.41) [M$^+$ − C_6H_{13} − 2 CH$_3$], 148 (67.69) [M$^+$ − C_6H_{13} −2 CH$_3$ − Si(CH$_3$)$_3$]. − HRMS: *m/z* calcd. for $C_{19}H_{36}OSi_2$ 336.23047; found 336.23446.

1-Hexoxymethyl-3,5-diiodobenzene (2b): A solution of ICl (10.3 g, 63.4 mmol) in CH_2Cl_2 (100 mL) was added at −70 °C to a solution of **2a** (7.15 g, 21.2 mmol) in CH_2Cl_2 (100 mL). Then, the solution was allowed to warm to −40 °C before $Na_2S_2O_5$ (1 M, 100 mL) was added. After warming to room temp. the layers were separated and the aqueous layer was extracted with CH_2Cl_2 (2 × 100 mL). The combined organic extracts were dried over $MgSO_4$, and the solvent was evaporated in vacuum. Chromatographic separation on silica gel with hexane/EtOAc (30:1) as eluent afforded **2b** (7.93 g, 84%) as a colorless oil. − ^{1}H NMR ($CDCl_3$, 270 MHz): δ = 0.87 (t, *J* = 6.6 Hz, 3 H, C*H*$_3$), 1.19−1.38 (m, 6 H, C*H*$_2$), 1.58 (q, *J* = 6.5 Hz, 2 H, β-C*H*$_2$), 3.41 (t, *J* = 6.5 Hz, 2 H, α-C*H*$_2$), 4.39 (s, 2 H, Ar−C*H*$_2$), 7.59 (s, 1 H), 7.90 (s, 2 H). − ^{13}C NMR ($CDCl_3$, 68 MHz): δ = 14.04, 22.52, 25.71, 29.50, 29.55, 31.52, 70.80, 94.79 (*C*−I), 135.33, 142.85, 143.77. − MS (EI, 80 eV); *m/z* (%): 444 (10.29) [M$^+$], 343 (67.86) [M$^+$ − OC_6H_{13}], 217 (100.00) [M$^+$ − OC_6H_{13} − I + H], 89 (88.10) [M$^+$ − OC_6H_{13} −2I]. − HRMS: *m/z* calcd. for $C_{13}H_{18}I_2O$ 443.94471; found 443.94931.

2-(3-Hexoxymethyl-5-iodophenyl)-4,4,5,5-tetramethyl-[1,3,2]dioxaborolan (3): BuLi (1.6 M, 14 mL) in hexane was added dropwise to a solution of compound **2b** (7.93 g, 17.8 mmol) in Et_2O (100 mL),

while the temperature was kept at −78 °C. After stirring at −78 °C for 1 h, a solution of triisopropyl borate (10 g, 53 mmol) in Et_2O (30 mL) was added dropwise. Then the mixture was allowed to warm to room temp. overnight. The reaction mixture was treated with H_2O (100 mL). The layers were separated, and the aqueous layer was washed with Et_2O (2 × 100 mL). The combined organic extracts were dried over $MgSO_4$ and concentrated under reduced pressure. Some impurities were separated by chromatography on silica gel with CH_2Cl_2 as eluent. The crude boronic acid was eluted with EtOAc and was then dissolved with 2,3-dimethylbutane-2,3-diol (1.72 g, 14.6 mmol) in 1,4-dioxane (50 mL). The solvent was evaporated under reduced pressure at 60 °C, and the residue was purified by chromatography on silica gel with CH_2Cl_2 as eluent to give **3** (4.01 g, 50%) as a colorless oil. − ^{1}H NMR ($CDCl_3$, 270 MHz): δ = 0.85 (t, J = 6.5 Hz, 3 H, $O(CH_2)_5-CH_3$), 1.19−1.37 (m, 6 H, CH_2), 1.29 (s, 12 H, pinacole−CH_3), 1.57 (q, J = 6.6 Hz, 2 H, β-CH_2), 3.41 (t, J = 6.6 Hz, 2 H, α-CH_2), 4.39 (s, 2 H, Ar−CH_2), 7.65 (s, 1 H), 7.78 (s, 1 H), 8.01 (s, 1 H). − ^{13}C NMR ($CDCl_3$, 68 MHz): δ = 14.01, 22.54, 24.77, 25.76, 29.57, 31.58, 70.69, 71.80, 84.00 [$C(CH_3)_2$], 94.50 (C−I), 132.85, 139.11, 140.34, 142.41. − MS (EI, 80 eV); *m/z* (%): 444 (3.50) [M^+], 359 (1.63) [$M^+ - C_6H_{13}$], 343 (19.44) [$M^+ - OC_6H_{13}$], 217 (100) [$M^+ - OC_6H_{13} - I$]. − $C_{19}H_{30}BIO_3$ (444.16): calcd. C 51.37, H 6.80; found C 51.31, H 6.58.

2-Bromo-5-[3-hexoxymethyl-5-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-phenyl]pyridine (5): Compound **3** (4.13 g, 9.3 mmol) and 2-bromo-5-trimethylstannylpyridine (**4**) (2.98 g, 9.3 mmol) were dissolved in toluene (50 mL). The solution was degassed twice. Then $(Ph_3P)_4Pd$ (0.214 g, 0.185 mmol) was added, and the solution was degassed again. After the mixture was heated under reflux for 24 h, a saturated solution of KF (20 mL) was added, and the inorganic precipitate removed by filtration. The organic phase was separated and the aqueous was extracted with CH_2Cl_2 (2 × 30 mL). The organic phases were combined, dried over $MgSO_4$ and evaporated. Some nonpolar impurities were separated by chromatography on silica gel with CH_2Cl_2 as eluent and some other polar impurities by chromatography on silica gel with hexane/EtOAc (5:1) as eluent. This gave **5** (1.95 g, 44%) as a white solid, m.p. 73 °C. − ^{1}H NMR ($CDCl_3$, 270 MHz): δ = 0.85 [t, J = 6.6 Hz, 3 H, $O(CH_2)_5CH_3$], 1.18−1.41 (m, 6 H, CH_2), 1.33 (s, 12 H, pinacol−CH_3), 1.60 (q, J = 6.5 Hz, 2 H, β-CH_2), 3.47 (t, J = 6.5 Hz, 2 H, α-CH_2), 4.54 (s, 2 H, Ar−CH_2), 7.51 (d, $J_{H\text{-}3,H\text{-}4}$ = 8.3 Hz, 1 H, H_{pyr}-3), 7.63 (s, 1 H), 7.76 (dd, $J_{H\text{-}4,H\text{-}6}$ = 2.5 Hz, $J_{H\text{-}4,H\text{-}3}$ = 8.3 Hz, 1 H, H_{pyr}-4), 7.78 (s, 1 H), 7.86 (s, 1 H), 8.58 (d, $J_{H\text{-}6,H\text{-}4}$ = 2.5 Hz, 1 H, H_{pyr}-6). − ^{13}C NMR ($CDCl_3$, 68 MHz): δ = 14.01, 22.57, 24.83, 25.83, 29.65, 31.62, 70.85, 72.45, 84.06 [$C(CH_3)_2$], 127.84, 128.94, 132.43, 134.08, 135.89, 136.05, 137.09, 139.14, 140.79, 148.52; MS (EI, 80 eV): *m/z* (%): 476 (4.86), 475 (18.41), 474 (9.92), 473 (18.39), 472 (5.18) [M^+], 376 (21.52), 375 (91.31), 374 (67.36), 373 (100.00), 372 (47.47) [$M^+ - OC_6H_{13}$]. − HRMS: *m/z* calcd. for $C_{24}H_{33}BBrNO_3$ 473.17368; found 473.17822.

5,5′′-Bis[3-hexoxymethyl-5-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-phenyl]-2,2′:6′,2′′-terpyridine (7): Terpyridine **7** was obtained from 2,6-bis(trimethylstannyl)pyridine **(6)** (0.736 g, 1.81 mmol), **5** (1.9 g, 4.0 mmol) and $(Ph_3P)_4Pd$ (84 mg, 0.072 mmol) in toluene (20 mL), using the procedure described for **5**, by heating under reflux over 65 h. The crude product was purified by chromatography on silica gel with hexane/EtOAc (5:1) as eluent to afford **7** (0.869 g, 55%) as a white solid, m.p. 123 °C. − ^{1}H NMR ($CDCl_3$, 270 MHz): δ = 0.87 (t, J = 6.5 Hz, 6 H, $O(CH_2)_5CH_3$), 1.25−1.47 (m, 12 H, CH_2), 1.36 (s, 24 H, pinacol−CH_3), 1.63 (q, J = 6.6 Hz, 4 H, β-CH_2), 3.51 (t, J = 6.6 Hz, 4 H, α-CH_2), 4.58 (s, 4 H, Ar−CH_2), 7.77 (s, 2 H), 7.80 (s, 2 H), 7.97 (t, $J_{H\text{-}4',H\text{-}3'}$ = 7.8 Hz, 1 H, H-4′), 8.02 (s, 2 H), 8.11 (dd, $J_{H\text{-}4,H\text{-}6}$ = 2.4 Hz, $J_{H\text{-}4,H\text{-}3}$ = 8.2 Hz, 2 H, H-4,4′′), 8.49 (d, $J_{H\text{-}3',H\text{-}4'}$ = 7.8 Hz, 2 H, H-3′,5′) 8.68 (d, $J_{H\text{-}3,H\text{-}4}$ = 8.2 Hz, 2 H, H-3,3′′), 8.96 (d, $J_{H\text{-}6,H\text{-}4}$ = 2.4 Hz, 2 H, H-6,6′′). − ^{13}C NMR ($CDCl_3$, 68 MHz): δ = 13.99, 22.54, 24.81, 25.82, 29.66, 31.62, 70.74, 72.56, 83.93 [$C(CH_3)_2$], 120.86, 129.06, 132.59, 133.76, 135.21, 136.34, 137.24, 137.76, 138.94, 147.64, 154.90, 155.12. − MS (EI, 80 eV): *m/z* (%): 867 (16.62), 866 (54.76), 865 (100.00), 864 (43.55) [M^+], 782 (4.52), 781 (16.21), 780 (32.90), 779 (13.61) [$M^+ - C_6H_{13}$], 767 (5.69), 766 (19.33), 765 (37.22), 764 (22.73) [$M^+ - C_6H_{13} - CH_3$]. − $C_{53}H_{69}B_2N_3O_6$ (865.76): calcd. C 73.52, H 8.03, N 4.85; found C 73.52, H 7.85, N 4.78.

Cycle 9: A degassed solution of **7** (0.455 g, 0.525 mmol), **8** (0.455 g, 0.525 mmol) and $Pd[P(p\text{-tolyl})_3]_3$ (8 mg, 1.5 mol-%) in 1,2-dimethoxyethane (18 mL) was added with a syringe pump within 65 h to a degassed boiling mixture of $Pd[P(p\text{-tolyl})_3]_3$ (8 mg, 1.5 mol-%) in an aqueous solution of Na_2CO_3 (1 M, 37 mL) and 1,2-dimethoxyethane (37 mL). After heating the reaction mixture under reflux for 3 d, the solution was cooled to room temp. and the phases separated. The organic solvent was evaporated and the residue was dissolved in $CHCl_3$. The aqueous layer was washed with $CHCl_3$ (3 × 20 mL). The combined organic phases were dried over $MgSO_4$, and the solvent was removed in vacuum. Purification by preparative GPC gave **9** (132 mg, 20.5%) as a white solid. ^{1}H NMR (270 MHz, $CDCl_3$): δ = 0.91 (t, J = 6.6 Hz, 12 H, CH_3), 1.22 (s, unknown) 1.22−1.46 (m, 24 H, CH_2), 1.71 (q, J = 6.6 Hz, 8 H, β-CH_2), 3.58 (t, J = 6.6 Hz, 8 H, α-CH_2), 4.57 (s, 8 H, Ar−CH_2), 7.41 (s, 4 H), 7.50 (s, 4 H), 7.56 (s, 4 H), 7.71 (t, $J_{H\text{-}4',H\text{-}3'}$ = 7.8 Hz, 2 H, H-4′), 7.92 (d, $J_{H\text{-}4,H\text{-}3}$ = 6.8 Hz, 4 H, H-4,4′′), 8.13 (d, $J_{H\text{-}3',H\text{-}4'}$ = 7.8 Hz, 4 H, H-3′,5′), 8.62 (d, $J_{H\text{-}3,H\text{-}4}$ = 6.8 Hz, 4 H, H-3,3′′), 8.70 (s, 4 H, H-6,6′′). − ^{13}C NMR (68 MHz, $CDCl_3$): δ = 14.10 (CH_3), 22.67, 25.97 (γ-CH_2), 29.66 (unknown), 29.80 (β-CH_2), 31.75, 71.00 (α-CH_2), 72.71 (Ar−CH_2), 120.26, 121.08, 124.25, 125.02, 134.70, 135.04 (C-4,4′′), 137.34, 137.57 (C-4′), 140.11, 140.28, 146.61 (C-6,6′′), 154.07 (C-2′,6′), 154.78 (C-2,2′′). − MS (FAB^+, Xenon, CH_2Cl_2/*m*-nitrobenzyl alcohol); *m/z* (%): 1226 (39.77), 1225 (83.80), 1224 (100.00), 1223 (75.56), 1222 (29.82) [$M^+ + H$].

5-Bromo-2-iodopyridine (11): 2,5-Dibromopyridine **10** (14.4 g, 60.8 mmol) in 67% HI (48 mL) was heated at 100 °C for 12 h, and then at 170 °C for 4 h. After cooling to room temp. the mixture was poured into 40% NaOH (50 mL) and ice, and extracted with Et_2O (2 × 100 mL). The extracts were dried over $MgSO_4$ and filtered, and the solvent removed. Further purification was not necessary. When there was still some starting material in the product, the whole procedure was repeated. This gave **11** (13.6 g, 78%) as a slightly yellow solid, m.p. 113 °C. − ^{1}H NMR (270 MHz, $CDCl_3$): δ = 7.42 (dd, $J_{H\text{-}4,H\text{-}6}$ = 2.9 Hz, $J_{H\text{-}4,H\text{-}3}$ = 8.3 Hz, 1 H, H-4), 7.58 (d, $J_{H\text{-}3,H\text{-}4}$ = 8.3 Hz, 1 H, H-3), 8.42 (d, $J_{H\text{-}6,H\text{-}4}$ = 2.9 Hz, 1 H, H-6). − ^{13}C NMR (68 MHz, $CDCl_3$): δ = 115.15, 121.01, 135.96, 140.19, 151.71. − MS (80 eV, EI); *m/z* (%): 285 (76.04), 283 (78.07) [M^+], 158 (99.13), 156 (100.00) [$M^+ - I$]. − C_5H_3BrIN (283.89): calcd. C 21.15, H 1.06, N 4.93; found C 21.01, H 0.95, N 4.61.

5,5′′-Dibromo-2,2′:6′,2′′-terpyridine (12): 5-Bromo-2-iodopyridine **(11)** (6.1 g, 21.5 mmol) and 2,6-bis(trimethylstannyl)pyridine **(6)** (3.5 g, 8.6 mmol) were dissolved in toluene (50 mL). The solution was degassed twice. Then, $(Ph_3P)_4Pd$ (0.4 g, 0.346 mmol) was added, and the mixture was degassed again. After the mixture was heated under reflux for 60 h, a saturated solution of KF (30 mL) was added, and the inorganic precipitate removed by filtration. The organic phase was separated and the aqueous was extracted with

CH_2Cl_2 (2 × 30 mL). The organic phases were combined and evaporated. Chromatography of the residue on silica gel with CH_2Cl_2 as eluent gave **12** (1.68 g, 50%) as a white solid, m.p. 205 °C. – ^{1}H NMR ($CDCl_3$, 270 MHz,): δ = 7.93 (t, $J_{H\text{-}4'H\text{-}3'}$ = 7.8 Hz, 1 H, H-4′), 7.95 (dd, $J_{H\text{-}4,H\text{-}6}$ = 2.2 Hz, $J_{H\text{-}4,H\text{-}3}$ = 8.4 Hz, 2 H, H-4,4′′), 8.41 (d, $J_{H\text{-}3',H\text{-}4'}$ = 7.8 Hz, 2 H, H-3′,5′), 8.47 (d, $J_{H\text{-}3,H\text{-}4}$ = 8.4 Hz, 2 H, H-3,3′′), 8.72 (d, $J_{H\text{-}6,\ H\text{-}4}$ = 2.2 Hz, 2 H, H-6,6′′). – ^{13}C NMR ($CDCl_3$, 68 MHz): δ = 121.17, 121.23, 122.33, 138.10, 139.43,150.18, 154.47. – MS (EI, 80 eV); *m/z* (%): 393 (51.13), 391 (100.00), 389 (53.41) [M^+], 312 (10.72), 310 (10.84), [M^+ – Br]. – $C_{15}H_9Br_2N_3$ (391.06): calcd. C 46.07, H 2.31, N 10.74; found C 45.85, H 2.40, N 10.74.

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[1] U. Lehmann, O. Henze, A. D. Schlüter, *Chem. Eur. J.* **1999**, *5*, 854–859.
[2] [2a] O. Henze, U. Lehmann, A. D. Schlüter, *Synthesis* **1999**, 683–687. – [2b] O. Henze, D. Lentz, A. D. Schlüter, *Chem. Eur. J.* **2000**, *6*, 2362–2367.
[3] For related work with homoaromatic building blocks, for example, see: V. Hensel, A. D. Schlüter, *Chem. Eur. J.* **1999**, *5*, 421–429; V. Hensel, A. D. Schlüter, *Eur. J. Org. Chem*. **1999**, 451–458.
[4] U. Lehmann, O. Henze, A. D. Schlüter, *Am. Chem. Soc. Polym. Mater. Sci. Engin.* **1999**, *80*, 165, 233.
[5] G. R. Newkome, H.-W. Lee, *J. Am. Chem. Soc*. **1983**, *105*, 5956–5957; J. L. Toner, *Tetrahedron Lett*. **1983**, *24*, 2707–2710; T. W. Bell, A. Firestone, *J. Am. Chem. Soc*. **1986**, *108*, 8109–8111; T. W. Bell, A. Firestone, R. Ludwig, *J. Chem. Soc., Chem. Commun*. **1989**, 1902–1904; T. W. Bell, P. J. Cragg, M. G. B. Drew, A. Firestone, D. –I. A. Kwok, *Angew. Chem*. **1992**, *104*, 319–321; *Angew. Chem. Int. Ed. Engl*. **1992**, *31*, 345–347; T. W. Bell, P. J. Cragg, M. G. B. Drew, A. Firestone, A. D.-I. Kwok, J. Liu, R. T. Ludwig, A. T. Papoulis, *Pure Appl. Chem*. **1993**, *65*, 361–366.
[6] E. C. Constable, *Prog. Inorg. Chem*. **1994**, *42*, 67–138. For some other cycles with interior donor groups, see: S. Höger, A.-D. Meckenstock, H. Pellen, *J. Org. Chem*. **1997**, *62*, 4556–4557; Y. Tobe, N. Utsumi, A. Nagano, K. Naemura, *Angew. Chem*. **1998**, *110*, 1347–1349*, Angew. Chem. Int. Ed. Engl*. **1998**, *37*, 1285–1287; U. Velten, M. Rehahn, *Macromol. Chem. Phys.* **1998**, *199*, 127–135. For additional related work, mostly on noncyclic oligo(het)arylenes, see: G. S. Hanan, C. R. Arana, J.-M. Lehn, D. Fenske, *Angew. Chem. Int. Ed.* **1995**, *34*, 1122–1125; M. Fujita, H. Oka, K. Ogura, *Tetrahedron Lett.* **1995**, *36*, 5247–5250; J. A. Zoltewicz, M. P. Cruskie Jr., *Tetrahedron* **1995**, *51*, 11401–11410; D. J. Cardenas, J.-P. Sauvage, *Synlett* **1996**, 916–918; V. Grosshenny, F. M. Romero, R. Ziessel, *J. Org. Chem*. **1997**, *62*, 1491–1500; T. R. Kelly, Y.-J. Lee, R. J. Mears, *J. Org. Chem*. **1997**, *62*, 2774–2781.
[7] J. Zhang, J. S. Moore, *J. Am. Chem. Soc.* **1994**, *116*, 2655–2656; D. Venkataraman, S. Lee, J. Zhang, J. S. Moore, *Nature* **1994**, *371*, 591–593; A. S. Shatty, J. Zhang, J. S. Moore, *J. Am. Chem. Soc.* **1996**, *118*, 1019–1027.
[8] G. Illuminati, L. Mandolini, *Acc. Chem. Res.* **1981**, *14*, 95–102.
[9] Lithiation followed by reaction with boric acid triisopropyl ester did not proceed sufficiently well, specifically considering the amount of work involved in the synthesis of **8**.
[10] G. W. Gray, M. Hird, D. Lacey, K. J. Toyne, *J. Chem. Soc., Perkin. Trans.2* **1989**, 2041–2053.
[11] Y. Yamamoto, T. Seko, H, Nemoto, *J. Org. Chem.* **1989**, *54*, 4734–4736.
[12] V. Farina, B. Krishnan, D. R. Marshall, G. P. Roth, *J. Org. Chem*. **1993**, *58*, 5434–5444.
[13] The homocoupling product of **4** was not isolated but proven by mass spectrometry and NMR spectroscopy.
[14] G. Manickam, A. D. Schlüter, *Synthesis* **2000**, 442–446.
[15] N. Miyaura, A. Suzuki, *Chem. Rev.* **1995**, *95*, 2457–2483.
[16] C. Lützow, PhD Thesis, Free University Berlin, 1997.
[17] This signal may be due to a water molecule complexed to one of the tpy units through hydrogen bonds. For an X-ray structure of a cycle containing tpy crytallized as a dihydrate, see: G. R. Newkome, H. W. Lee, F. R. Fronczek, *Isr. J. Chem.* **1986**, *27*, 87–95.
[18] This material has a GPC molar mass referenced to polystyrene of M_{peak} = 16,000
[19] Y. Yamamoto, A. Yanagi, *Chem. Pharm. Bull*. **1982**, *30*, 1731.

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