Supporting Information for:

Calix[6]arene Derivatives Selectively Functionalised at Alternate Sites on the Smaller Rim with 2-Phenylpyridine and 2-Fluorenylpyridine Substituents to Provide Deep Cavities

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General. All synthetic reagents were used as supplied. Solvents were dried and distilled using standard procedures.

4-(Pyridin-2-yl)benzaldehyde (1). A mixture of 4-formylbenzeneboronic acid (1.50 g, 10.0 mmol), 2-bromopyridine (1.90 g, 12.0 mmol), THF (50 mL), toluene (50 mL) and Na_2CO_3 (1 M, 10 mL) was stirred under argon for 30 min, then tetrakis(triphenylphosphino)palladium (138 mg, 0.12 mmol) was added in one portion. The yellow solution was stirred for 48 h at 80 °C. Water (100 mL) was added. The yellow organic phase was separated and the aqueous phase was extracted with dichloromethane (3×30 mL). The combined organic extracts were dried (anhyd. MgSO_4). The solvent was removed and the red residue was purified by column chromatography (SiO_2 , dichloromethane:acetone, 100:2 v/v) to give **1** (0.81 g, 44% yield) as a yellow solid, mp 54-56 °C, with spectroscopic data consistent with that reported previously.¹

[4-(Pyridin-2-yl)phenyl]methanol (2). To a solution of compound **1** (480 mg, 2.62 mmol) in ethanol (30 mL) was added sodium borohydride (256 mg, 6.0 mmol) in one portion. The solution was stirred for 30 min at room temperature. The solvent was removed under reduced pressure. The residue was dissolved in dichloromethane (30 mL) and water (100 mL). To this two-layered mixture, sodium carbonate (1.06 g, 10 mmol) was added in one portion. The mixture was stirred at room temperature for 30 min. The organic layer was separated and the aqueous layer was extracted with dichloromethane (5×30 mL). The combined organic phases were dried (anhyd. MgSO_4) and the solvent was removed under reduced pressure to yield **2** (476 mg, 99%) as a viscous yellow oil which was sufficiently pure for use in the next reaction. Spectroscopic data were consistent with the literature.²

2-[4-(Bromomethyl)phenyl]pyridine (3)³ To a solution of compound **2** (476 mg, 2.60 mmol) in dichloromethane (30 mL) at 0 °C was added phosphorus tribromide (1.5 mL) dropwise. The suspension was stirred overnight at room temperature then cooled to 0 °C and treated with saturated aqueous carbonate solution while maintaining the temperature at < 5 °C. After the solution became basic, the organic phase was separated. The aqueous phase was extracted with dichloromethane (3×30 mL). The combined organic phases were dried (anhyd. MgSO_4) and the solvent removed to give compound **3** as a white powder (530 mg, 83% yield), mp 45 °C (dec.). ¹H NMR (400 MHz, CDCl_3): 8.68 (ddd, 1H, $J = 5.6$ Hz, 1.2 Hz, 0.8 Hz), 7.98 (d, 2H, $J = 8.4$ Hz), 7.78-7.71 (m, 2H), 7.50 (d, 2H, $J = 8.4$ Hz), 7.23 (ddd, 1H,

$J = 7.8$ Hz, 2.4 Hz, 1.6 Hz), 4.55 (s, $2H$). ^{13}C NMR (100 MHz, $CDCl_3$): 156.7 , 149.7 , 139.5 , 138.5 , 136.8 , 129.5 , 127.3 , 122.3 , 120.5 , 33.1 .

6-Phenylpyridine-3-carbaldehyde (6). A mixture of benzenboronic acid (1.22 g, 10.0 mmol), 6-bromopyridine-3-carbaldehyde (1.86 g, 10.0 mmol), THF (50 mL), toluene (50 mL) and Na_2CO_3 (1 M, 10 mL) was stirred under argon for 30 min, and then tetrakis(triphenylphosphino)palladium (138 mg, 0.12 mmol) was added in one portion. The yellow solution was stirred for 48 h at 80 °C. Workup as described for **1** gave a red residue which was purified by column chromatography (SiO_2 , dichloromethane to dichloromethane/acetone: $100:1$ v/v) to give compound **6** (1.74 g, 94% yield) as a yellow solid, mp 60 °C (lit.⁴ $58-59$ °C). Spectroscopic data were consistent with the literature.⁵

(6-Phenylpyridin-3-yl)methanol (7). To a solution of compound **6** (1.72 g, 9.39 mmol) in ethanol (50 mL), sodium borohydride (567 mg, 15.0 mmol) was added in one portion. The solution was stirred for 30 min at room temperature. Workup as described for **2** gave **7** (1.70 g, 99%) as a viscous white oil which was sufficiently pure for the next reaction. Spectroscopic data were consistent with the literature.⁵

5-(Bromomethyl)-2-phenylpyridine (8). A solution of compound **7** (1.70 g, 9.18 mmol) in dichloromethane (50 mL) was cooled to 0 °C under argon. Phosphorus tribromide (2 mL) was added dropwise, the suspension was stirred for 5 h at room temperature then cooled to 0 °C. Workup as described for **3** gave compound **8** as a white powder (2.03 g, 89% yield) mp $75-76$ °C. 1H NMR (400 MHz, $CDCl_3$): 8.68 (dd, $1H$, $J = 2.0$ Hz, 0.8 Hz), $7.97-7.95$ (m, $2H$), 7.77 (dd, $1H$, $J = 8.4$ Hz, 2.0 Hz), 7.70 (dd, $1H$, $J = 8.4$ Hz, 0.8 Hz), $7.48-7.39$ (m, $3H$), 4.50 (s, $2H$). ^{13}C NMR (100 MHz, $CDCl_3$): 157.4 , 149.7 , 138.7 , 137.4 , 132.0 , 129.3 , 128.8 , 127.0 , 120.4 , 29.8 . Anal. Calcd. for $C_{12}H_{10}BrN$: C, 58.09 ; H, 4.06 ; N, 5.65 . Found C, 57.99 ; H, 4.15 ; N, 5.56 .

6-(9,9-Dihexylfluoren-2-yl)pyridine-3-carbaldehyde (11). A mixture of borolane **10**⁶ (4.20 g, 10.5 mmol), 6-bromopyridine-3-carbaldehyde (1.86 g, 10 mmol), THF (50 mL), toluene (50 mL) and Na_2CO_3 (1 M, 10 mL) was stirred under argon flow for 30 min, and then tetrakis(triphenylphosphino)palladium (138 mg, 0.12 mmol) was added in one portion. The yellow solution was stirred for 48 h at 80 °C. Workup as described for **1** with column chromatography (SiO_2 , dichloromethane) gave **11** as light yellow oil (3.85 g, 88% yield). 1H

NMR (400 MHz, CDCl₃): 10.17 (s, 1H), 9.17 (dd, 1H, *J* = 2.4 Hz, 0.8 Hz), 8.26 (dd, 1H, *J* = 8.0 Hz, 2.4 Hz), 8.13 (dd, 1H, *J* = 1.6 Hz, 0.8 Hz), 8.11 (dd, 1H, *J* = 8.0 Hz, 1.6 Hz), 8.00 (dd, 1H, *J* = 8.0 Hz, 0.8 Hz), 7.84 (dd, 1H, *J* = 8.0 Hz, 0.8 Hz), 7.79-7.76 (m, 1H), 7.42-7.36 (m, 3H), 2.08-2.05 (m, 4H), 1.12-1.04 (m, 12H), 0.76 (t, 6H, *J* = 7.2 Hz), 0.68-0.62 (m, 4H). ¹³C NMR (100 MHz, CDCl₃): 190.4, 162.6, 152.5, 151.6, 151.5, 143.7, 140.2, 136.6, 136.3, 129.7, 127.8, 126.9, 126.7, 123.0, 121.9, 120.5, 120.3, 120.1, 55.4, 40.4, 31.5, 29.7, 23.8, 22.5, 13.9. MS (ES⁺): *m/z* 440.5 (M+1). Anal. Calcd. for C₃₁H₃₇NO: C, 84.69; H, 8.48; N, 3.19. Found C, 84.48; H, 8.52; N, 3.01.

[6-(9,9-Dihexylfluoren-2-yl)pyridine-3-yl]methanol (12). To a solution of **11** (1.95 g, 4.44 mmol), dichloromethane (20 mL) and ethanol (50 mL), sodium borohydride (256 mg, 6.0 mmol) was added in one portion. The solution was stirred for 30 min at room temperature. Workup as described for **2** gave product **12** (1.95 g, 100% yield) as a viscous white oil which sufficiently pure enough for the next reaction. ¹H NMR (400 MHz, CDCl₃): 8.64 (dd, 1H, *J* = 1.6 Hz, 0.8 Hz), 7.96 (d, 1H, *J* = 1.6 Hz), 7.94 (dd, 1H, *J* = 7.6 Hz, 1.6 Hz), 7.77 (d, 2H, *J* = 0.8 Hz), 7.76 (dd, 1H, *J* = 7.6 Hz, 0.8 Hz), 7.73-7.70 (m, 1H), 7.36-7.27 (m, 3H), 4.73 (d, 2H, *J* = 5.6 Hz), 2.35 (s, 1H), 2.04-1.47 (m, 4H), 1.11-0.94 (m, 12H), 0.71 (t, 6H, *J* = 6.8 Hz), 0.68-0.58 (m, 4H). ¹³C NMR (100 MHz, CDCl₃): 157.4, 151.4, 151.3, 148.5, 142.2, 140.6, 137.8, 135.7, 134.3, 127.3, 126.8, 125.9, 122.9, 121.2, 120.5, 120.0, 119.9, 62.7, 55.3, 40.4, 31.5, 29.7, 23.8, 22.6, 14.0. MS (ES⁺): *m/z* 442.5 (M+1). Anal. Calcd. for C₃₁H₃₉NO: C, 84.31; H, 8.90; N, 3.17. Found C, 84.45; H, 9.02; N, 3.09.

5-(Bromomethyl)-2-(9,9-di-*n*-hexylfluorenyl)pyridine (13). To a solution of **12** (1.85 g, 4.188 mmol) in dichloromethane (50 mL) at 0 °C phosphorus tribromide (2 mL) was added dropwise. The reaction was stirred overnight at room temperature. The solution was cooled again to 0 °C and workup as described for **3** gave **13** as a pale yellow oil (2.08 g, 98% yield) of sufficient purity for the next reaction. ¹H NMR (400 MHz, CDCl₃): 8.72 (dd, 1H, *J* = 2.0 Hz, 0.8 Hz), 8.00 (d, 1H, *J* = 1.6 Hz), 7.97 (dd, 1H, *J* = 7.6 Hz, 2.0 Hz), 7.79 (d, 2H, *J* = 1.6 Hz), 7.77 (dd, 1H, *J* = 7.6 Hz, 0.8 Hz), 7.74-7.72 (m, 1H), 7.37-7.29 (m, 3H), 4.53 (s, 2H), 2.08-1.96 (m, 2H), 2.08-1.96 (m, 4H), 1.12-0.95 (m, 12H), 0.74 (t, 6H, *J* = 6.8 Hz), 0.68-0.58 (m, 4H). ¹³C NMR (100 MHz, CDCl₃): 157.7, 151.5, 151.4, 149.6, 142.6, 140.5, 137.5, 137.3, 131.7, 127.5, 126.8, 125.9, 123.0, 121.3, 120.5, 120.1, 120.0, 55.3, 40.4, 31.5, 29.9, 29.7, 23.8, 22.6, 14.0. Anal. Calcd. for C₃₁H₃₈BrN: C, 73.80; H, 7.59; N, 2.78. Found C, 74.02; H, 7.49; N, 2.73.

Table S1. ^1H NMR data for compound **4** in CDCl_3 at variable temperatures.

T ($^{\circ}\text{C}$)	C_{3v} conformer	C_s conformer*	Percentage of C_s conformer [#]
60	8.67(d, 3H, $J = 2.4$ Hz), 8.01(d, 6H, $J = 6.4$ Hz), 7.71(m, 6H), 7.63(d, 6H, $J = 6.4$ Hz), 7.26(s, 6H), 7.18(m, 3H), 6.72(s, 6H), 5.04(s, 6H), 4.62(d, 6H, $J = 12.0$ Hz), 3.40(d, 6H, $J = 12.0$ Hz), 2.36(s, 9H), 1.37(s, 27H), 0.84(s, 27H).	7.96(d, 4H, $J = 6.4$ Hz), 7.53(d, 4H, $J = 6.4$ Hz), 7.26(s, 6H), 7.08(s, 2H), 6.97(s, 2H), 6.82(s, 2H), 6.77(s, 2H), 4.97(d, 2H, $J = 9.2$ Hz), 4.89(s, 2H), 4.74(d, 2H, $J = 9.2$ Hz), 4.48(d, 2H, $J = 12.4$ Hz), 4.35(d, 2H, $J = 12.4$ Hz), 4.18(d, 2H, $J = 11.6$ Hz), 3.70(d, 2H, $J = 11.6$ Hz), 3.47(d, 2H, $J = 12.4$ Hz), 3.34(d, 2H, $J = 12.4$ Hz), 2.43(s, 6H), 2.12(s, 3H), 1.32(s, 9H), 1.18(s, 18H), 1.06(s, 9H), 1.01(s, 18H).	24.8%
30	8.65(s, 3H), 7.99(d, 6H, $J = 6.0$ Hz), 7.73(bs, 6H), 7.63(d, 6H, $J = 6.0$ Hz), 7.26(s, 6H), 7.19(m, 3H), 6.69(s, 6H), 5.02(s, 6H), 4.62(d, 6H, $J = 12.0$ Hz), 3.39(d, 6H, $J = 12.0$ Hz), 2.30(s, 9H), 1.36(s, 27H), 0.82(s, 27H).	7.95(d, 4H, $J = 6.4$ Hz), 7.71(bs, 6H), 7.55(d, 2H, $J = 6.4$ Hz), 7.51(d, 4H, $J = 6.4$ Hz), 7.16(s, 2H), 7.11(s, 2H), 7.02(s, 2H), 6.79(s, 2H), 6.73(s, 2H), 4.96(d, 2H, $J = 13.2$ Hz), 4.89(s, 2H), 4.65(d, 2H, $J = 13.2$ Hz), 4.43(d, 2H, $J = 12.4$ Hz), 4.37(d, 2H, $J = 12.8$ Hz), 4.16(d, 2H, $J = 12.4$ Hz), 3.76(d, 2H, $J = 12.8$ Hz), 3.50(d, 2H, $J = 12.4$ Hz), 3.33(d, 2H, $J = 12.4$ Hz), 2.32(s, 6H), 2.09(s, 3H), 1.32(s, 9H), 1.17(s, 18H), 1.02(s, 9H), 1.01(s, 18H).	21.4%
0	8.69(d, 3H, $J = 4.8$ Hz), 7.99(d, 6H, $J = 6.4$ Hz), 7.75(bs, 6H), 7.64(d, 6H, $J = 6.4$ Hz), 7.28(s, 6H), 7.25(m, 3H, overlapped with CHCl_3), 6.68(s, 6H), 5.02(s, 6H), 4.63(d, 6H, $J =$	7.94(d, 4H, $J = 6.4$ Hz), 7.58(d, 2H, $J = 6.4$ Hz), 7.51(d, 4H, $J = 6.4$ Hz), 7.17(s, 2H), 7.15(s, 2H), 7.09(s, 2H), 6.76(s, 2H), 6.71(s, 2H), 4.97(d, 2H, $J = 8.8$ Hz), 4.90(s, 2H), 4.56(d, 2H, $J = 8.8$ Hz), 4.42(d, 2H, $J = 12.4$ Hz), 4.37(d, 2H, $J = 12.0$ Hz), 4.14(d, 2H, $J = 10.6$ Hz), 3.84(d, 2H, $J = 11.2$ Hz), 3.53(d, 2H, $J = 12.8$ Hz), 3.34(d, 2H, $J =$	21.8%

	11.2 Hz), 3.40 (d, 6H, $J = 11.2$ Hz), 2.23(s, 9H), 1.37(s, 27H), 0.81(s, 27H).	= 11.2 Hz, partially overlapped with the C _{3v} conformer), 2.21(s, 6H), 1.99(s, 3H), 1.32(s, 9H), 1.17(s, 18H), 1.03(s, 18H), 0.99(s, 9H).	
-30	8.66(s, 3H), 7.96(m, 6H), 7.75(m, 6H), 7.63(m, 6H), 7.25(bs, 9H), 6.63(s, 6H), 5.00(s, 6H), 4.63(bs, 6H), 3.37 (bs, 6H), 2.14(s, 9H), 1.36(s, 27H), 0.78(s, 27H).	7.92(d, 4H, $J = 6.0$ Hz), 7.49(bs, 6H), 7.17(s, 2H), 7.15(s, 2H), 6.70(s, 2H), 6.68(s, 2H), 5.37(s, 2H), 4.92(d, 2H, $J = 12.0$ Hz), 4.45(m, 4H), 4.32(m, 2H), 4.10(m, 2H), 3.89(m, 2H), 3.56(m, 2H), 2.08(s, 3H), 1.93(s, 6H), 1.31, 1.29(each s, 9H), 1.16, 1.14(each s, 18H), 1.03, 1.02(each s, 18H), 0.93, 0.91(each s, 9H).	22.4%
-60	8.67(d, 3H, $J = 3.6$ Hz), 7.93(d, 6H, $J = 6.0$ Hz), 7.79(t, 3H, $J = 4.4$ Hz), 7.74(d, 3H, $J = 6.4$ Hz), 7.61(d, 6H, $J = 6.0$ Hz), 7.26(s, 9H, Ar-H), 6.58(s, 6H), 4.98(s, 6H), 4.62(d, 6H, $J = 12.8$ Hz), 3.37 (d, 6H, $J = 12.8$ Hz), 2.09(s, 9H), 1.35(s, 27H), 0.74(s, 27H).	7.88(d, 4H, $J = 6.4$ Hz), 7.46(d, 4H, $J = 6.4$ Hz), 7.16(s, 4H), 7.16(s, 2H), 6.63(s, 4H), 4.91(d, 2H, $J = 9.6$ Hz), 4.87(s, 2H), 4.48(d, 2H, $J = 13.2$ Hz), 4.31(d, 2H, $J = 9.6$ Hz), 4.26(d, 2H, $J = 12.8$ Hz), 4.08(d, 2H, $J = 11.2$ Hz), 3.92(d, 2H, $J = 12.0$ Hz), 3.59(d, 2H, $J = 12.8$ Hz), 1.96(s, 6H), 1.79(s, 3H), 1.28(s, 9H), 1.14(s, 18H), 1.02(s, 9H), 0.86(s, 18H).	23.1%

*Due to overlap or low abundance of the 1,2,3-alternate conformers (C_s), not all the resonances could be assigned. # ± 0.2 %

Figure S1. Variable temperature ^1H NMR spectra for compound **4** in CDCl_3 .

Crystallographic studies. X-ray diffraction experiments (see Table S2) for **4** and **9** were carried out on a Bruker 3-circle diffractometer with a SMART 6K CCD area detector, using graphite-monochromated Mo- K_{α} radiation ($\bar{\lambda}$ =0.71073 Å) and a Cryostream open-flow N₂ cryostat (Oxford Cryosystems). Full sphere of reciprocal space was covered by 4 sets of 0.3° ω scans, each set with different ϕ and/or 2 θ angles. The structures were solved by direct methods in automatic mode, using OLEX2 program,⁷ and refined by full-matrix least squares against F^2 of all data, using SHELXTL software.⁸ The solvent content in **4** was tentatively estimated as 5.5 molecule of DCM and 4 molecules of ethanol per asymmetric unit, according to the void volumes and the total electron density therein using PLATON software (VOID and SQUEEZE routines),⁹ although not all of this has been actually located and refined. All hydrogen atoms (including hydroxyls) were treated as ‘riding’ in presumed positions. Crystal data and experimental details are listed in Table S2. CCDC number 612882.

The X-ray diffraction study of **9** was inconclusive. The triclinic unit cell contains four molecules of **9** and an uncertain amount of solvent of crystallisation (DCM and/or ethanol). The data indicate a mode of packing different from **4**: one phenylpyridyl group is plugged into the macrocyclic cavity of the opposing molecule. Unfortunately, the remaining phenylpyridyls, as well as the solvent molecules, are highly disordered, whereas the calixarene *t*-butyl groups display practically free rotation.

Table S2. Crystal data

Compound	4	9
Formula	$\text{C}_{105}\text{H}_{117}\text{N}_3\text{O}_6 \cdot 2.75 \text{CH}_2\text{Cl}_2 \cdot 2 \text{EtOH}$	$\text{C}_{105}\text{H}_{117}\text{N}_3\text{O}_6 \cdot x \text{CH}_2\text{Cl}_2 \cdot y \text{EtOH}$
Formula weight	1842.7	
T, K	120	120
Symmetry	triclinic	triclinic
Space group	$P\bar{1}$ (# 2)	
a , Å	21.979(2)	18.107(5)
b , Å	22.020(2)	22.556(6)
c , Å	26.603(3)	27.130(7)
α , °	107.85(1)	102.82(1)
β , °	94.80(1)	99.70(1)
γ , °	119.60(1)	106.11(1)
V , Å ³	10 217.2(17)	10 062(2)
Z	4	4
D_c , g cm ⁻³	1.198	
$\mu(\text{Mo-}K\alpha)$, mm ⁻¹	0.21	
Refls collected	118524	108028
Unique refls	46985, 22231*	35438, 13004*
R_{int}	0.112	0.144
No. of variables	2337	
$R(F)$	0.103*	
$wR(F^2)$	0.331	

* Reflections with $F^2 > 2\sigma(F^2)$

References for the Supporting Information

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