Supporting Information


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Experimental Section:

General experimental methods: \(^1\)H NMR spectra were determined on a Bruker 400 (400 MHz) spectrometer as solutions in CDCl\(_3\). Chemical shifts are expressed in parts per million (δ) and are referenced to tetramethyl silane (TMS) as internal standard and the signals were reported as s (singlet), d (doublet), t (triplet), m (multiplet) and coupling constants \(J\) were given in Hz. \(^13\)C NMR spectra were recorded at 100 MHz in CDCl\(_3\) solution. ESI-HRMS data were collected at Brucker MicrOTOF-Q II Instrument. MALDI-TOF data were obtained on Bruker Ultraflex III MALDI-TOF instrument using 4-nitroaniline or matrixes. Melting points were determined using the Boetius Block apparatus. All organic solvents were purified and dried in accordance with standard procedures before use. Additional control of the purity of compounds and monitoring of the reaction were carried out by thin-layer chromatography using Silica G, 200 μm plates, UV 254. Commercially available substrates were freshly distilled before the reaction. Solvents, reagents and chemicals were purchased from Aldrich, Fluka, Merck, SRL, Spectrochem and Process Chemicals and used as received without additional purification. The spectral data of all the synthesized products (2a-2d) are consistent with our previously reported method.\(^1\)

General procedure for the synthesis of 1,4-dialkoxybenzenes:

1,4-Dialkoxybenzenes were synthesized by the reported method.\(^2\) The adequate amounts of hydroquinone, TBAB and KOH were mixed at room temperature. The appropriate alkyl halide was then added and the reaction mixture was heated to 60-80 °C in an oil bath for the required time. The crude mixture was extracted with diethyl ether (50 mL). Filtration and evaporation of the solvent afforded the pure 1,4-dialkoxybenzene.

For 1,4-diethoxybenzene: 3 Equiv. of ethyl iodide, 9 mol% of TBAB and 2.5 equiv. of KOH were used with respect to hydroquinone. The reaction mixture was heated at 60 °C for 24 h.

For 1,4-dipropoxybenzene: 3 Equiv. of \(n\)-propyl bromide, 9 mol% of TBAB and 2.5 equiv. of KOH were used with respect to hydroquinone. The reaction mixture was heated at 70 °C for 5 h.

For 1,4-dibutoxybenzene: 2.5 Equiv. of \(n\)-butyl bromide, 9 mol% of TBAB and 2.5 equiv. of KOH were used with respect to hydroquinone. The reaction mixture was heated at 80 °C for 4 h.

For 1,4-diheptyloxy benzene: 2.5 Equiv. of heptyl iodide, 9 mol% of TBAB and 2.5 equiv. of KOH were used with respect to hydroquinone. The reaction mixture was heated at 80 °C for 4 h.
For 1,4-di-tert-butyloxy carbonyl methoxy benzene: 2.5 Equiv. of tert-butyl bromoacetate, 9 mol% of TBAB and 2.5 equiv. of KOH were used with respect to hydroquinone. The reaction mixture was heated at 80 ºC for 4 h.

General procedure for the synthesis of per-alkylated pillar[6]arenes (2a-2f) in presence of H$_2$SO$_4$:

To a solution of the appropriate 1,4-dialkoxy benzene (2 mmol) in 2 mL of acetonitrile, paraformaldehyde (124 mg, 4 mmol) was added. The reaction mixture was stirred for 5 minutes. Then conc. H$_2$SO$_4$ (32 µL, 30 mol%) was added to that reaction mixture and stirred at room temperature for 5 minutes. After that 5 mL of ethanol was poured into the reaction mixture. The resulting precipitate was filtered off, washed two-three times with ethanol, dried and purified by column chromatography [silica gel, hexane/ethyl acetate 30:1 (v/v)] to result in analytically pure per-alkylated pillar[6]arenes 2.

1,4-Bis(ethoxy)pillar[6]arene (2a): To a solution of 1,4-diethoxy benzene (0.33 g, 2 mmol) in 2 mL of acetonitrile, paraformaldehyde (124 mg, 4 mmol) was added. The reaction mixture was stirred for 5 minutes. Then conc. H$_2$SO$_4$ (32 µL, 30 mol%) was added to that reaction mixture and stirred at room temperature for 5 minutes. After that 5 mL of ethanol was poured into the reaction mixture. The resulting precipitate was filtered off, washed two-three times with ethanol, dried and purified by column chromatography [silica gel, hexane/ethyl acetate 30:1 (v/v)] to result in analytically pure 1,4-bis(ethoxy)pillar[6]arene (2a) as a white solid. Yield 71%, mp. 171-173 ºC (Lit. 170-172 ºC); $^1$H NMR (CDCl$_3$, 400 MHz): δ 6.67 (s, 12H, phenyl protons), 3.90-3.85 (m, 36H, methylene protons and methylene bridges), 1.31 (t, $J = 6.7$ Hz, 36H, methyl protons); $^{13}$C NMR (CDCl$_3$, 100 MHz): δ 150.7, 128.1, 115.0 (C of phenyl), 64.4 (C of oxymethylene groups), 29.7 (C of methylene bridge), 15.1 (C of methyl groups). Calcd. For C$_{66}$H$_{84}$O$_{12}$: m/z = 1068.60; Found: m/z = 1086.63 [M+NH$_4$]$^+$. Anal. Calcd for C$_{66}$H$_{84}$O$_{12}$: C, 74.13; H, 7.92%. Found: C, 73.97; H, 8.05%. HPLC Retention time = 22.7 min.

1,4-Bis(propoxy)pillar[6]arene (2b): To a solution of 1,4-dipropoxy benzene (0.39 g, 2 mmol) in 2 mL of acetonitrile, paraformaldehyde (124 mg, 4 mmol) was added. The reaction mixture was stirred for 5 minutes. Then conc. H$_2$SO$_4$ (32 µL, 30 mol%) was added to that reaction mixture and stirred at room temperature for 5 minutes. After that 5 mL of ethanol was poured into the reaction mixture. The resulting precipitate was filtered off, washed two-three times with ethanol, dried and purified by column chromatography [silica gel, hexane/ethyl acetate 30:1 (v/v)] to result in analytically pure 1,4-bis(propoxy)pillar[6]arene (2b) as a white solid. Yield 70%, mp. 118-120 ºC (Lit. 121-123 ºC); $^1$H NMR (CDCl$_3$, 400 MHz): δ 6.67 (s, 12H, phenyl protons), 3.88-3.83 (m, 36H, methylene protons and methylene bridges), 1.28 (t, $J = 6.8$ Hz, 36H, methyl protons); $^{13}$C NMR (CDCl$_3$, 100 MHz): δ 150.7, 128.1, 115.0 (C of phenyl), 64.4 (C of oxymethylene groups), 29.7 (C of methylene bridge), 15.1 (C of methyl groups). Calcd. For C$_{66}$H$_{84}$O$_{12}$: m/z = 1196.70; Found: m/z = 1210.61 [M+NH$_4$]$^+$. Anal. Calcd for C$_{66}$H$_{84}$O$_{12}$: C, 74.13; H, 7.92%. Found: C, 73.97; H, 8.05%. HPLC Retention time = 23.1 min.
protons), 3.90 (s, 12H, methylene bridges), 3.77 (t, \( J = 6.48 \) Hz, 24H, -OC\(\text{H}_2\text{CH}_2\text{CH}_3\)), 1.75-1.70 (m, 24H, -OCH\(\text{H}_2\text{CH}_2\)), 0.97 (t, \( J = 7.4 \) Hz, 36H, methyl protons); \(^{13}\)C NMR (CDCl\(_3\), 100 MHz): \( \delta \) 150.6, 128.0, 114.7 (C of phenyl), 70.3 (C of oxymethylene groups), 30.8 (C of methylene bridge), 22.8 (C of methylene groups), 10.5 (C of methyl groups). ESI-HRMS: Calcd. for C\(_{78}\)H\(_{108}\)O\(_{12}\) m/z = 1236.78, found 1254.82 [M+NH\(_4\)]\(^+\). Anal. Calcd for C\(_{78}\)H\(_{108}\)O\(_{12}\): C, 75.69; H, 8.80%; Found: C, 75.77; H, 8.68%.

**1,4-Bis(butoxy)pillar[6]arene (2c):** To a solution of 1,4-dibutoxy benzene (0.44 g, 2 mmol) in 2 mL of acetonitrile, paraformaldehyde (124 mg, 4 mmol) was added. The reaction mixture was stirred for 5 minutes. Then conc. H\(_2\)SO\(_4\) (32 \( \mu \)L, 30 mol%) was added to that reaction mixture and stirred at room temperature for 5 minutes. After that 5 mL of ethanol was poured into the reaction mixture. The resulting precipitate was filtered off, washed two-three times with ethanol, dried and purified by column chromatography [silica gel, hexane/ethyl acetate 30:1 (v/v)] to result in analytically pure 1,4-bis(butoxy)pillar[6]arene (2c) as a white solid. Yield 66%, mp. 92-93 °C (Lit.\(^1\) 90-92 °C); \(^1\)H NMR (CDCl\(_3\), 400 MHz): \( \delta \) 6.67 (s, 12H, phenyl protons), 3.87 (s, 12H, methylene bridges), 3.81 (t, \( J = 8.96 \) Hz, 24H, -OC\(\text{H}_2\text{CH}_2\)), 1.73-1.67 (m, 24H, -OCH\(\text{H}_2\text{CH}_2\)), 1.46-1.40 (m, 24H, -OCH\(\text{H}_2\text{CH}_2\)), 0.91 (t, \( J = 7.36 \) Hz, 36H, methyl protons); \(^{13}\)C NMR (CDCl\(_3\), 100 MHz): \( \delta \) 150.8, 128.2, 114.9 (C of phenyl), 68.7 (C of oxymethylene groups), 31.9 (C of methylene groups), 31.0 (C of methylene bridge), 19.5 (C of methylene groups), 14.0 (C of methyl groups). ESI-HRMS: Calcd. for C\(_{90}\)H\(_{132}\)O\(_{12}\) m/z = 1404.97, found 1423.01 [M+NH\(_4\)]\(^+\). Anal. Calcd for C\(_{90}\)H\(_{132}\)O\(_{12}\): C, 76.88; H, 9.46%; Found: C, 77.07; H, 9.22%.

**1,4-Bis(heptyloxy)pillar[6]arene (2d):** To a solution of 1,4-diheptyloxy benzene (0.61 g, 2 mmol) in 2 mL of acetonitrile, paraformaldehyde (124 mg, 4 mmol) was added. The reaction mixture was stirred for 5 minutes. Then conc. H\(_2\)SO\(_4\) (32 \( \mu \)L, 30 mol%) was added to that reaction mixture and stirred at room temperature for 5 minutes. After that 5 mL of ethanol was poured into the reaction mixture. The resulting precipitate was filtered off, washed two-three times with ethanol, dried and purified by column chromatography [silica gel, hexane/ethyl acetate 30:1 (v/v)] to result in analytically pure 1,4-bis(heptyloxy)pillar[6]arene (2d) as a white solid. Yield 61%, mp. 104-106 °C (Lit.\(^1\) 105-107 °C); \(^1\)H NMR (CDCl\(_3\), 400 MHz): \( \delta \) 6.67 (s, 12H, phenyl protons), 3.87 (s, 12H, methylene bridges), 3.81 (t, \( J = 8.96 \) Hz, 24H, -OCH\(\text{H}_2\text{CH}_2\)), 1.73-1.67 (m, 24H, -OCH\(\text{H}_2\text{CH}_2\)), 1.46-1.40 (m, 24H, -OCH\(\text{H}_2\text{CH}_2\)), 0.91 (t, \( J = 7.36 \) Hz, 36H, methyl protons); \(^{13}\)C NMR (CDCl\(_3\), 100 MHz): \( \delta \) 150.7, 128.2, 114.9 (C of phenyl), 68.7 (C of oxymethylene groups), 31.9 (C of methylene groups), 31.0 (C of methylene bridge), 19.5 (C of methylene groups), 14.0 (C of methyl groups). ESI-HRMS: Calcd. for C\(_{90}\)H\(_{132}\)O\(_{12}\) m/z = 1404.97, found 1423.01 [M+NH\(_4\)]\(^+\). Anal. Calcd for C\(_{90}\)H\(_{132}\)O\(_{12}\): C, 76.88; H, 9.46%; Found: C, 77.07; H, 9.22%.
Caled. For C_{126}H_{204}O_{12}: C, 79.19; H, 10.76%; Found: C, 79.13; H, 10.70%. MALDI-TOF Caled. For C_{126}H_{204}O_{12}: m/z = 1910.54; Found: m/z = 1911.9 [M+H]^+.

**tert-Butyloxy carbonylmethoxy-substituted Pillar[6]arene (2f):** To a solution of 1,4-di-tert-butyloxy carbonylmethoxy benzene (0.68 g, 2 mmol) in 2 mL of acetonitrile, paraformaldehyde (124 mg, 4 mmol) was added. The reaction mixture was stirred for 5 minutes. Then conc. H_2SO_4 (32 µL, 30 mol%) was added to that reaction mixture and stirred at room temperature for 5 minutes. After that 5 mL of methanol was poured into the reaction mixture. The resulting precipitate was filtered off, washed two-three times with methanol, dried and purified by column chromatography [silica gel, hexane/ethyl acetate 30:1 (v/v)] to result in analytically pure pillar[6]arene (2f) as a white solid. Yield 42%, mp. 160-162 ºC; ^1H NMR (CDCl_3, 400 MHz): δ 6.84 (s, 12H, phenyl protons), 4.88 (s, 24H, -OCH_2CO-), 3.89 (s, 12H, methylene bridges), 1.28 (s, 108H, methyl protons); ^13C NMR (CDCl_3, 100 MHz): δ 170.0 (C of carbonyl groups), 153.6, 129.1, 114.6 (C of phenyl), 81.2 (C of oxymethylene groups), 69.5 (tertiary carbons), 29.6 (C of methylene bridges), 28.1(C of methyl groups). Anal. Caled. For C_{114}H_{156}O_{36}: C, 65.13; H, 7.48%; Found: C, 65.02 H, 7.32%.

### Table 1. Optimization of the reaction conditions in presence of BF_3·OEt_2[a]

<table>
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<tr>
<th>Entry</th>
<th>Amount of PF used (equiv.)</th>
<th>Amount of BF_3·OEt_2</th>
<th>Time (min)[b]</th>
<th>Yields (%)[c]</th>
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<tbody>
<tr>
<td>1</td>
<td>2</td>
<td>1 equiv.</td>
<td>5</td>
<td>42</td>
</tr>
<tr>
<td>2</td>
<td>3</td>
<td>1 equiv.</td>
<td>10</td>
<td>60</td>
</tr>
<tr>
<td>3[a]</td>
<td>3</td>
<td>1 equiv.</td>
<td>15</td>
<td>67</td>
</tr>
<tr>
<td>4</td>
<td>3</td>
<td>0.5 equiv.</td>
<td>15</td>
<td>46</td>
</tr>
<tr>
<td>5</td>
<td>3</td>
<td>1 equiv.</td>
<td>20</td>
<td>68</td>
</tr>
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</table>

[a] All reactions were carried out on 2 mmol scale in 2 mL of acetonitrile. [b] Time was counted after addition of the catalyst. [c] Yields after washing with ethyl alcohol. PF = Paraformaldehyde.
Typical procedure for the synthesis of pillar[6]arene 2a in presence of BF$_3$·OEt$_2$:

Paraformaldehyde (186 mg, 6 mmol) was added to a solution of 1,4-diethoxybenzene (332 mg, 2 mmol) in acetonitrile (2 mL) and stirred for 5 min at room temperature for dissolving the reactants in solvent. Then BF$_3$·OEt$_2$ (0.25 mL, 2 mmol) was added to the solution, and the mixture was stirred at room temperature for 15 min. After that 5 mL of ethanol was poured into the reaction mixture. The resulting precipitate was filtered off, washed two-three times with ethanol, dried and purified by column chromatography [silica gel, hexane/ethyl acetate 30:1 (v/v)] to result in analytically pure per-alkylated pillar[6]arene 2a.

Typical procedure for the synthesis of 2,5-diethoxybenzyl alcohol (4a):

In a typical procedure a mixture of 1,4-diethoxy benzene (1.66 g, 10 mmol), paraformaldehyde (3 g, 100 mmol), H$_2$SO$_4$ (20 mg), and DDQ (4.54 g, 20 mmol) was stirred in 10 mL acetonitrile for 5 h at 80 °C. The reaction mixture was cooled to room temperature. The obtained precipitate was filtered off and washed with ethyl acetate. The crude product from the filtrate was purified by column chromatography (eluent: hexane/ethyl acetate) to get the corresponding 2,5-diethoxybenzaldehyde. The product was dissolved in 10 mL of MeOH. 1.5 equiv. of NaBH$_4$ was added by portion to that solution and stirred for 5 h. After evaporation of the solvent 20 mL of ethyl acetate and 5 mL of water were added. Then the combined organic layer was dried over anhydrous Na$_2$SO$_4$. Evaporation of solvent furnished the pure product 4a.

Same procedure was followed in case of 4b.
General procedure for the synthesis of 2a from 4a:

To a solution of 4a (392 mg, 2 mmol) in acetonitrile (2 mL) conc. H$_2$SO$_4$ (32 µL, 30 mol%) was added and stirred for 5 min at room temperature. After that 5 mL of ethanol was poured into the reaction mixture. The resulting precipitate was filtered off, washed two-three times with ethanol, dried and purified by column chromatography [silica gel, hexane/ethyl acetate 30:1 (v/v)] to result in analytically pure per-alkylated pillar[6]arene 2a.

Same procedure was followed for the synthesis of 2b from 4b, where 4b was taken as starting material instead of 4a.

![Scheme 1. Synthesis of 2a & 2b from 4a & 4b respectively.](image)

### Table 2. Solvent controlled synthesis of Pillar[n]arenes:[a]

<table>
<thead>
<tr>
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</thead>
<tbody>
<tr>
<td>1</td>
<td>H$_2$SO$_4$ (30 mol%)</td>
<td>1,2-DCE</td>
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<td>Traces</td>
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<td>H$_2$SO$_4$ (30 mol%)</td>
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<tr>
<td>3</td>
<td>H$_2$SO$_4$ (30 mol%)</td>
<td>1,2-DCE &amp; Acetonitrile (1:1)</td>
<td>0</td>
<td>68</td>
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<td>4[b]</td>
<td>BF$_3$.OEt$_2$ (1 equiv.)</td>
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<td>BF$_3$.OEt$_2$ (1 equiv.)</td>
<td>Acetonitrile</td>
<td>Traces</td>
<td>67</td>
</tr>
<tr>
<td>6</td>
<td>BF$_3$.OEt$_2$ (1 equiv.)</td>
<td>1,2-DCE &amp; Acetonitrile (1:1)</td>
<td>Traces</td>
<td>63</td>
</tr>
</tbody>
</table>

[a] All reactions were carried out on 2 mmol scale.  [b] Typical Ogoshi’s procedure. (Ref. 3)
**Scheme 2. Gram scale synthesis**

**Typical procedure for the synthesis of 2a on gram scale:**

**Using H$_2$SO$_4$.** To a solution of the appropriate 1,4-diethoxy benzene 1a (1.66 g, 10 mmol) in 10 mL of acetonitrile, paraformaldehyde (0.62 g, 20 mmol) was added. The reaction mixture was stirred for 10 minutes. Then conc. H$_2$SO$_4$ (160 µL, 30 mol%) was added to that reaction mixture and stirred at room temperature for 5 minutes. After that 20 mL of ethanol was poured into the reaction mixture. The resulting precipitate was filtered off, washed two-three times with ethanol, dried and purified by column chromatography [silica gel, hexane/ethyl acetate 30:1 (v/v)] to result in analytically pure per-alkylated pillar[6]arene 2a.

**Using BF$_3$·OEt$_2$.** To a solution of the appropriate 1,4-diethoxy benzene 1a (1.66 g, 10 mmol) in 10 mL of acetonitrile, paraformaldehyde (0.93 g, 30 mmol) was added. The reaction mixture was stirred for 10 minutes. Then BF$_3$·OEt$_2$ (1.25 mL, 10 mmol) was added to that reaction mixture and stirred at room temperature for 5 minutes. After that 20 mL of ethanol was poured into the reaction mixture. The resulting precipitate was filtered off, washed two-three times with ethanol, dried and purified by column chromatography [silica gel, hexane/ethyl acetate 30:1 (v/v)] to result in analytically pure per-alkylated pillar[6]arenes 2a.
1,4-Bis(ethoxy)pillar[6]arene (2a):
1,4-Bis(propoxy)pillar[6]arene (2b):
1,4-Bis(butoxy)pillar[6]arene (2c):
1,4-Bis(heptyloxy)pillar[6]arene (2d):
Fig. 1 Comparison of $^1$H NMR spectra (run in CDCl$_3$) of crude product (2a) in different solvent media.

References:

