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Supplementary Information

for

Insights into the Synthesis of Pillar[5]arene and its Conversion into Pillar[6]arene

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1. Materials and Method

Solvents used in the study were reagent grade and purchased from commercial national sources. Hydroquinone, iodoethane, iodoethane-d$_5$, paraformaldehyde, FeCl$_3$, tetramethylammonium chloride (TMAC), ammonium cerium (IV) nitrate (CAN), trifluoracetic acid (TFA) were reagent grade and purchased from Sigma-Aldrich. Deionized water was used in all experiments. ^{1}H and ^{13}C NMR spectra were collected on a Bruker-400 MHz NMR spectrometer. High-resolution ESI mass spectra were measured on an Agilent 6210 ESI-TOF device (Agilent Technologies) and on an Waters Xevo G2-XS Q-Tof device (Waters). HPLC grade solvents were used with a flow rate of 2-4 µL/min.

2. Synthesis and characterization of compounds

*Synthesis of 1,4-diethoxybenzene (**DEB**)*

Ethyl iodide (3.3 mL, 44.1 mmol) and NaOH (1.76 g, 44.1 mmol) were added to a solution of hydroquinone (**HQ)** (1.6 g, 14.7 mmol) in DMSO (50 mL) under air atmosphere at 25 °C. The mixture was stirred for 2 h and then poured into ice and water (100 mL). The solid precipitate was filtered and washed with water. Yield: 2.3 g (14 mmol, 95%) of **DEB** as white crystals. ^{1}H NMR spectrum of **DEB** is shown in Figure S1. ^{1}H NMR (400 MHz, CDCl$_3$, 298 K), δ 6.82 (s, 4H), 3.98 (q, J = 7.0 Hz, 4H), 1.40 (d, J = 7.0 Hz, 6H).

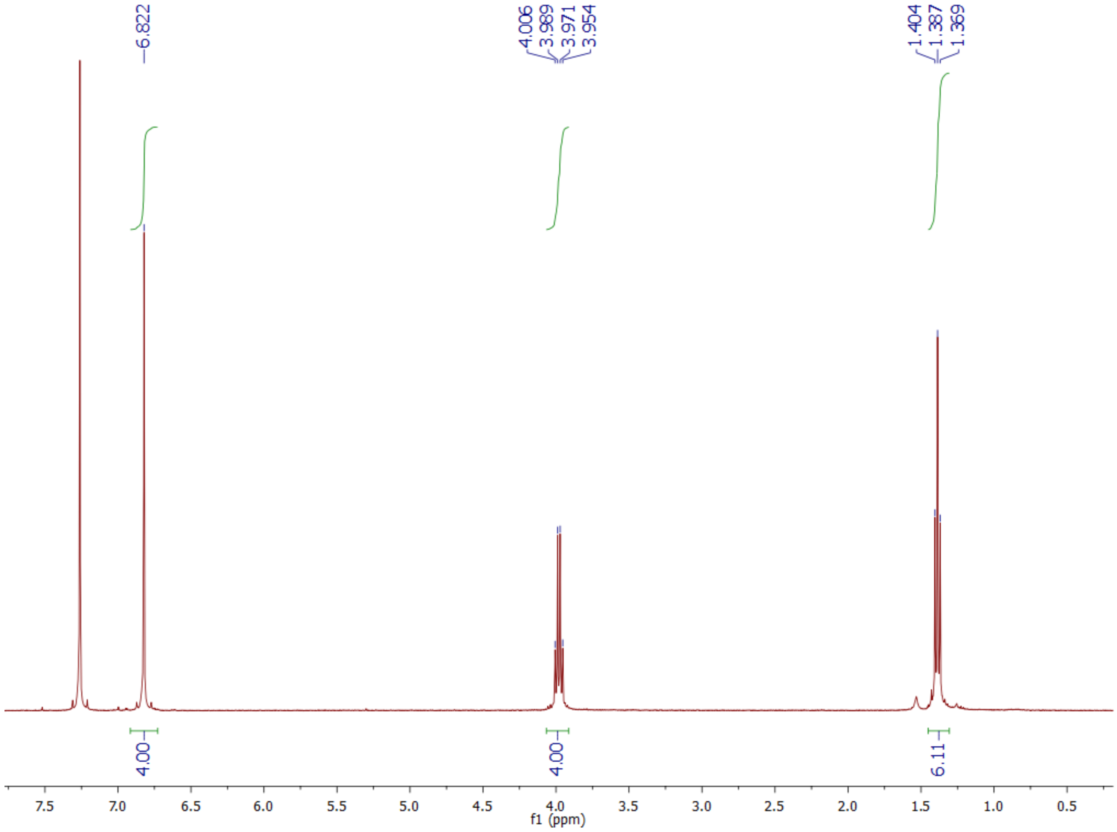

***Figure S1** ^{1}H NMR (400 MHz, CDCl$_3$, 298 K) spectrum of **DEB**.*

Synthesis of ***PEt[5]***

Trifluoracetic acid (7.5 mL, 9.8 mmol) and paraformaldehyde (420 mg, 14 mmol) were added to a solution of **DEB** (2.3 g, 14 mmol) in DCE (150 mL) at 55 °C under reflux. The mixture was stirred for 2 h and then was poured into MeOH (100 mL). The solid precipitate was filtered and washed with MeOH. The solid residue was crystallized from boiling EtOH, then filtered and washed with cold EtOH. Yield: 1.12 g (1.26 mmol, 53%) of **PEt[5]** as yellowish powder. NMR spectra of **PEt[5]** are shown in Figures S2-3. ^{1}H NMR (400 MHz, $CDCl_3$, 298 K), δ 6.72 (s, 10H), 3.83 (q, J = 7.0 Hz, 20H), 3.77 (s, 10H), 1.26 (t, J = 7.0 Hz, 30H). ^{13}C NMR (100 MHz, $CDCl_3$, 298 K) δ 149.72, 128.45, 114.74, 63.62, 29.66, 15.14.

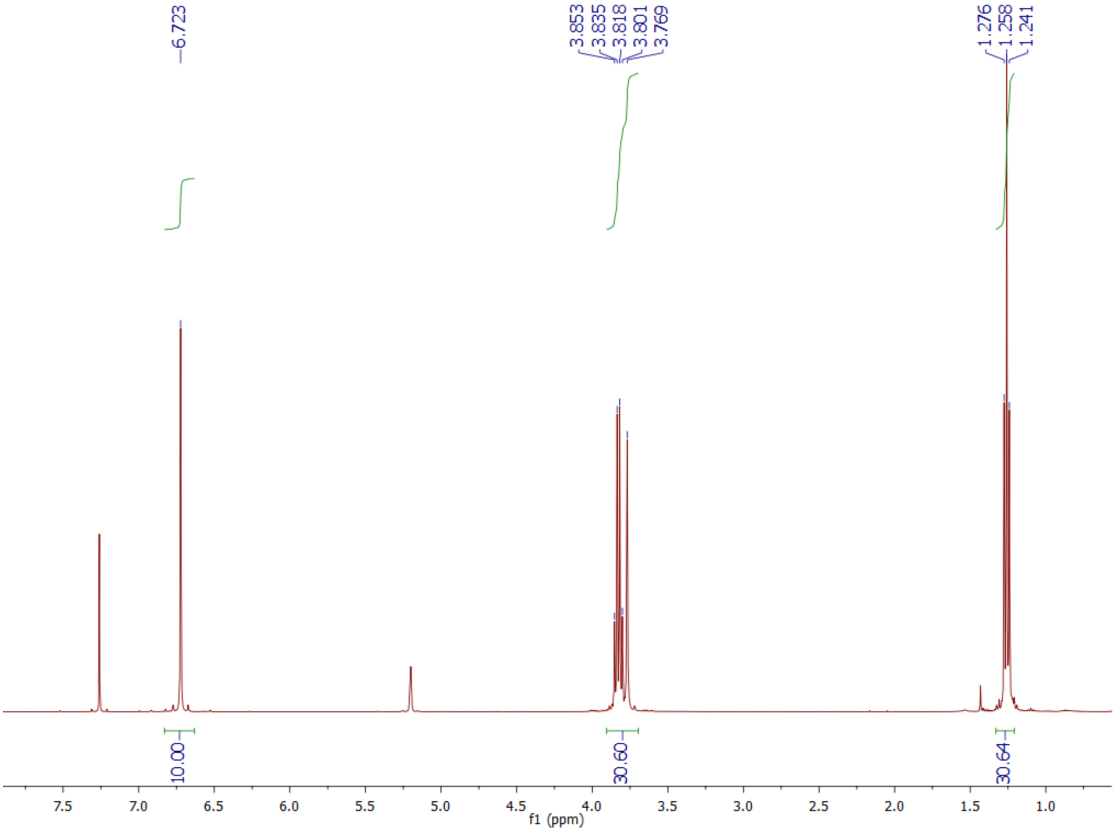

Figure S2 *^{1}H NMR (400 MHz, $CDCl_3$, 298 K) spectrum of* ***PEt[5]****.*

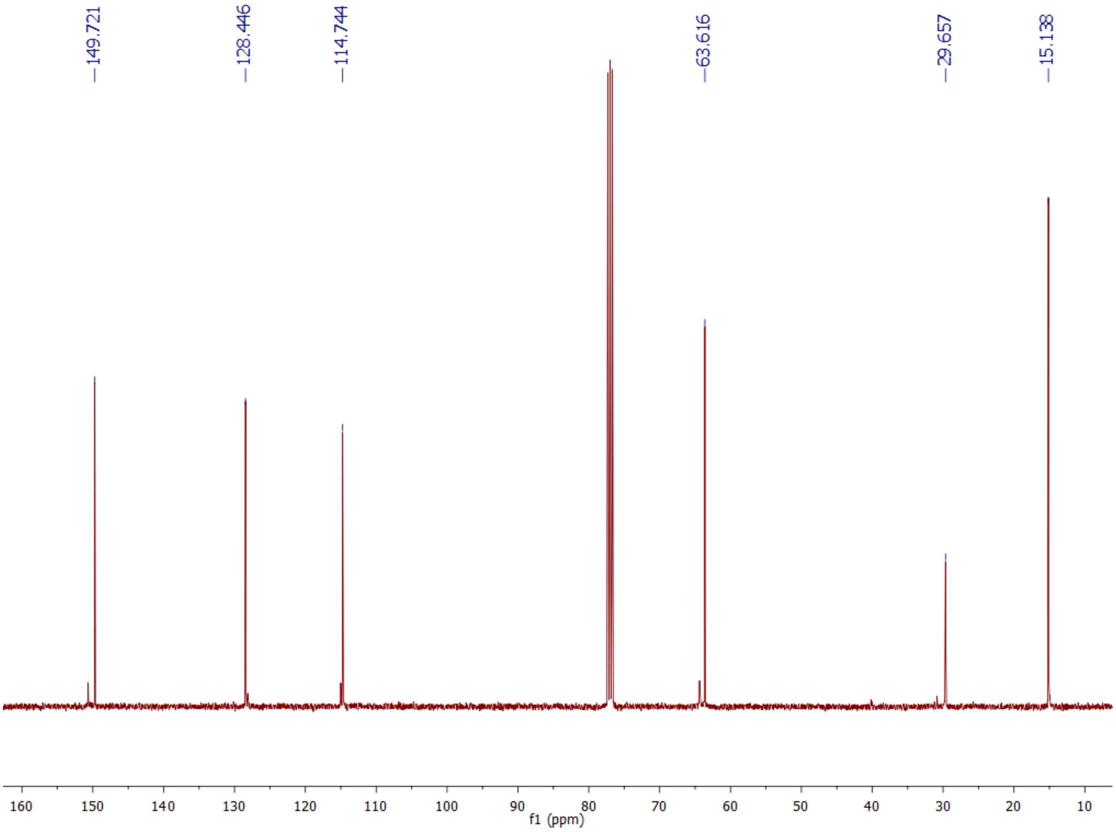

Figure S3 ^{13}C NMR *(100 MHz, CDCl$_3$, 298 K) spectrum of* ***PEt[5]****.*

*Synthesis of 1,4-dimethoxybenzene (****DMB****)*

Methyl iodide (2.7 mL, 44.1 mmol) and NaOH (1.76 g, 44.1 mmol) were added to a solution of hydroquinone (**HQ)** (1.62 g, 14.7 mmol) in DMSO (50 mL) under air atmosphere at 25 °C. The mixture was stirred for 2 h and then poured into ice and water (100 mL). The solid precipitate was filtered and washed with water. Yield: 1.89 g (13.7 mmol, 97%) of **DMB** as white crystals. ^{1}H NMR spectrum of **DMB** is shown in Figure S4. ^{1}H NMR (400 MHz, CDCl$_3$, 298 K), δ 6.84 (s, 4H), 3.77 (s, 6H).

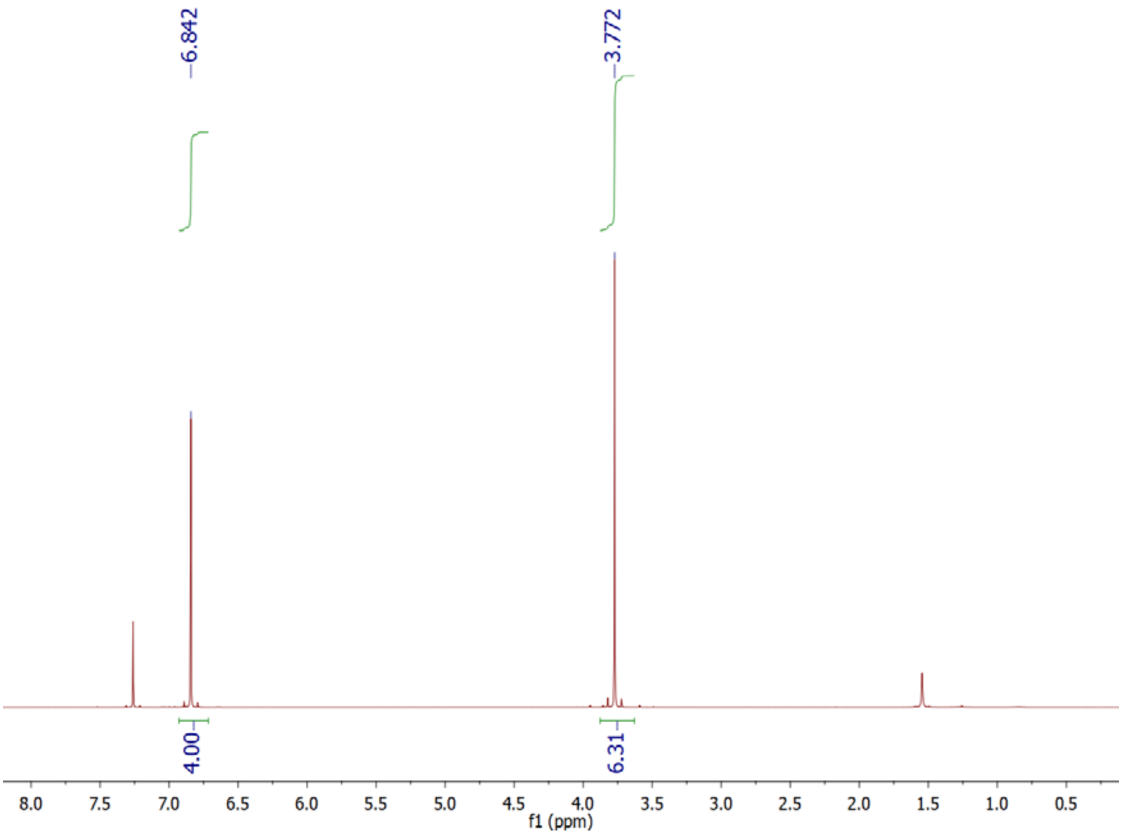

Figure S4 *^{1}H NMR (400 MHz, $CDCl_3$, 298 K) spectrum of* ***DMB****.*

Synthesis of ***PMe[5]***

Trifluoracetic acid (7.5 mL, 9.8 mmol) and paraformaldehyde (420 mg, 14 mmol) were added to a solution of **DMB** (1.89 g, 13.7 mmol) in DCE (150 mL) at 55 °C under reflux. The mixture was stirred for 2 h and then was poured into MeOH (100 mL). The solid precipitate was filtered and washed with MeOH. The solid residue was crystallized from boiling EtOH, then filtered and washed with cold EtOH. Yield: 1.35 g (1.8 mmol, 69%) of **PMe[5]** as yellowish powder. NMR spectra of **PMe[5]** are shown in Figures S5-6. ^{1}H NMR (400 MHz, $CDCl_3$, 298 K), δ 6.90 (s, 10H), 3.76 (s, 10H), 3.75 (s, 20H). ^{13}C NMR (100 MHz, $CDCl_3$, 298 K) δ 150.66, 128.21, 113.90, 55.70, 29.51.

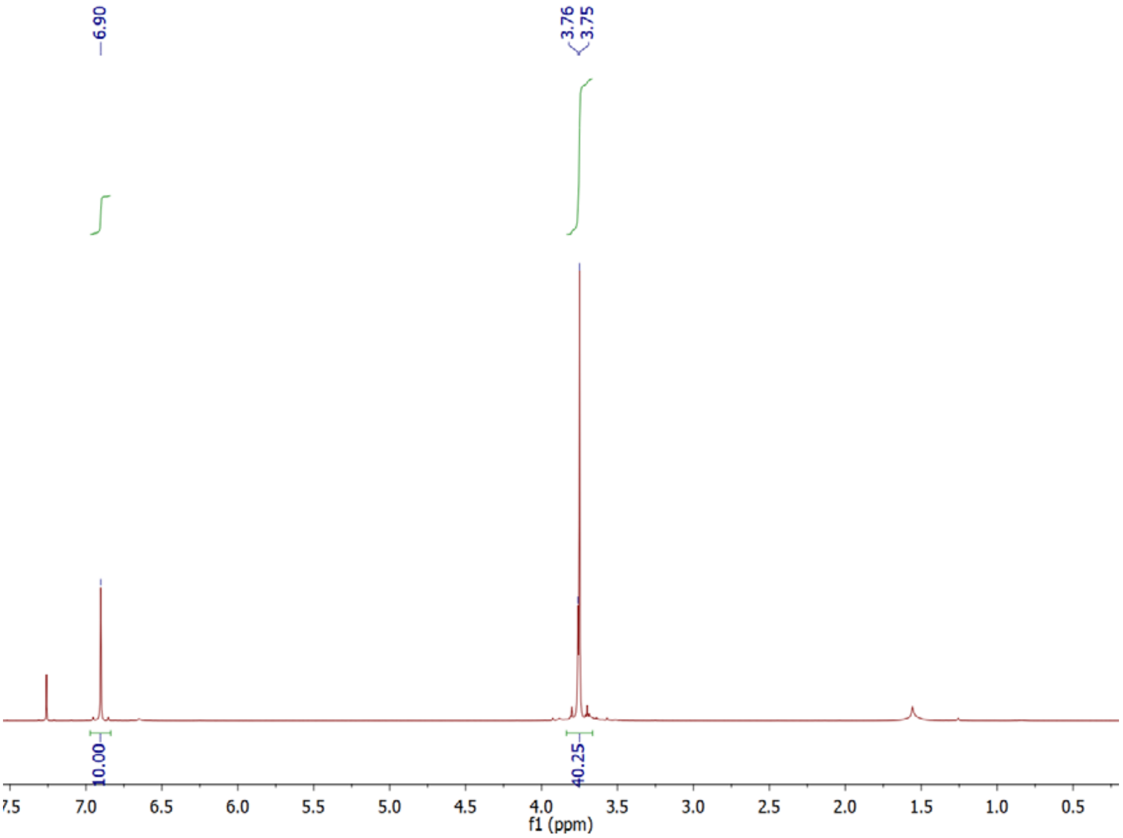

Figure S5 *^{1}H NMR (400 MHz, $CDCl_3$, 298 K) spectrum of* ***PMe[5]****.*

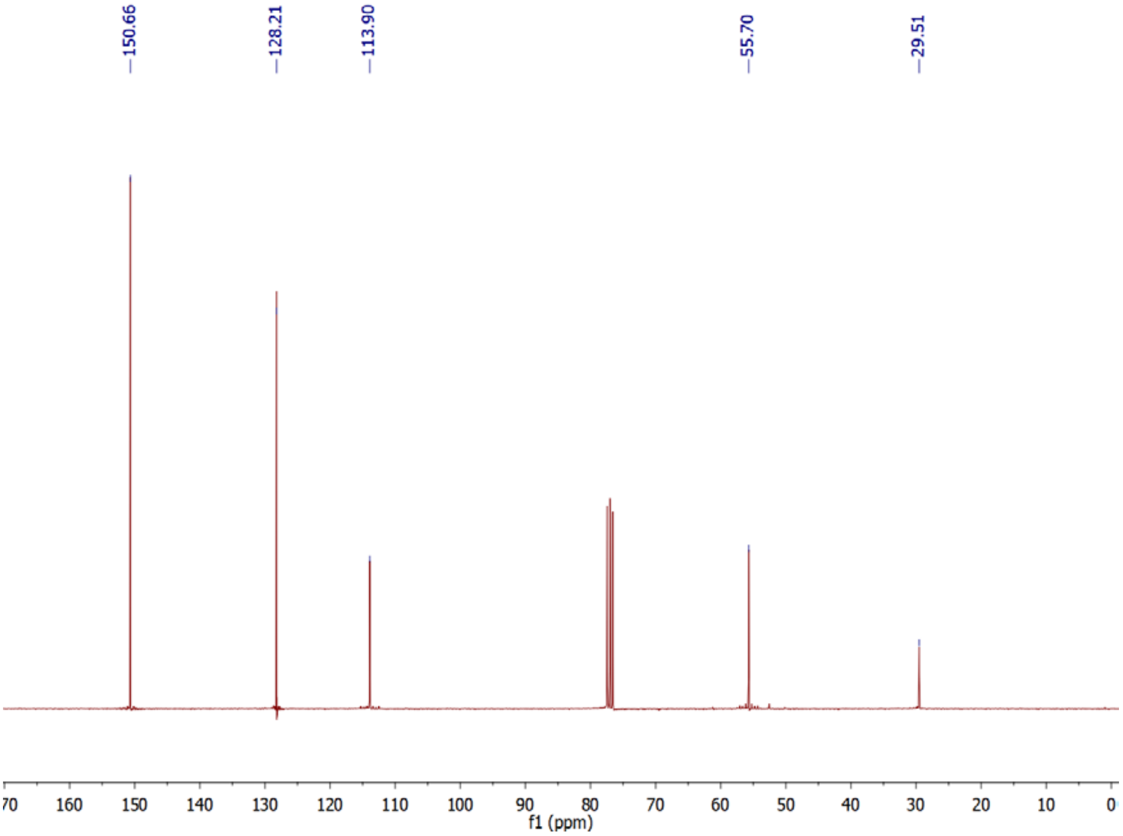

Figure S6 *^{13}C NMR (100 MHz, $CDCl_3$, 298 K) spectrum of* ***PMe[5]****.*

3. Oligomers mixture characterization

NMR and EI-MS spectra of **OEt[n]** are shown in Figures S7 and S8 respectively. ^{1}H NMR (400 MHz, CDCl$_3$, 298 K) δ 6.75-6.61 (m), 4.06-3.67 (m), 1.43-1.10 (m). MS (EI) *m/z* 534.3 [**OEt[6]**-OH]$^{2+}$, 891.1 [**OEt[5]**-OH]$^+$, 1069.1 [**OEt[6]**-OH]$^+$, 1247.8 [**OEt[6]**-OH]$^+$, *m/z* calcd for [**OEt[6]**-OH]$^+$ C$_{66}$H$_{84}$O$_{12}$: 1069.1; found 109.1 (100%).

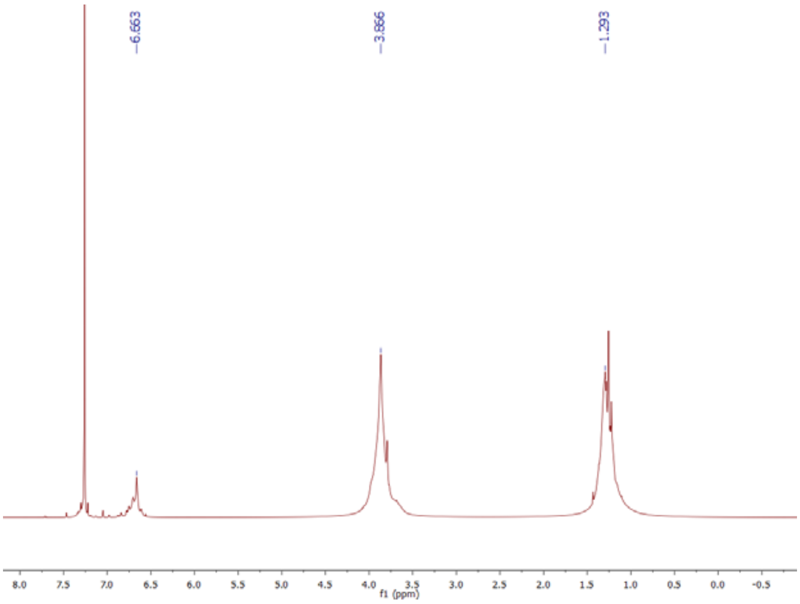

Figure S7 *^{1}H NMR (400 MHz, CDCl$_3$, 298 K) spectrum of **OEt[n]s** mixture (n = 5,6,7).*

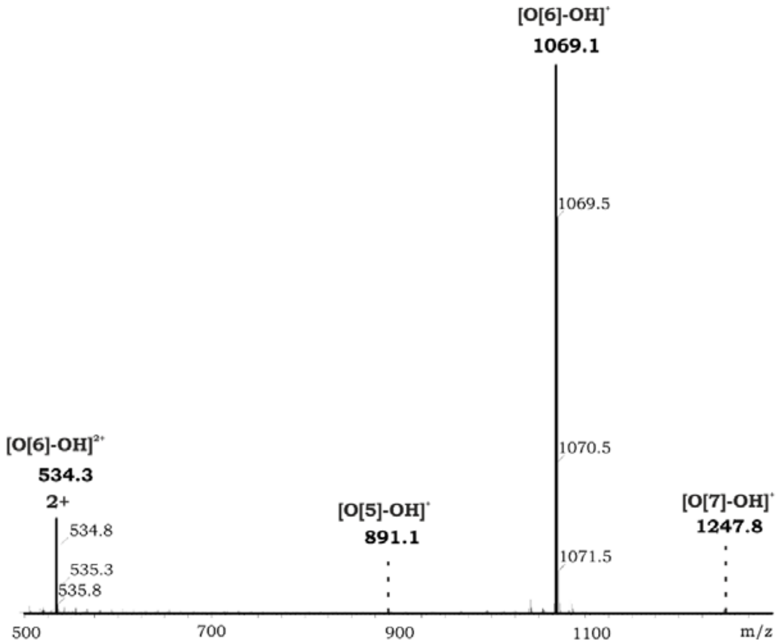

Figure S7 *EI-MS spectrum of **OEt[n]s** mixture (n = 5,6,7).*

4. General procedure for PEt[5] conversion experiments

All the conversion experiments have been performed omitting alternatively paraformaldehyde, $FeCl_3$ and TMAC as shown in Table S1.

Paraformaldehyde (40 mg, 1.32 mmol), $FeCl_3$ (118 mg, 0.71 mmol) and **TMAC** (56 mg, 0.51 mmol) were heated at 110 °C and gently stirred until a dark brown viscous liquid formed. Then a solution of **PEt[5]** (22 mg, 0.024 mmol) in DCM (20 mL) was added and the mixture was stirred at 25 °C for 2 minutes. Then water (20 mL) was added and the reaction mixture was stirred at 25 °C for 1 week. The reaction was monitored by FTICR-ESI-MS.

Table S1 *Synthesis of* ***PEt[6]*** *from* ***PEt[6]*** *in DCM at 25 °C, in the absence (a) presence (p) of paraformaldehyde,* $FeCl_3$ *and* ***TMAC***

#	Paraformaldehyde	$FeCl_3$	TMAC	Isolated Yield (%)
1	p	p	p	8
2	a	p	p	8
3	a	p	a	<1
4	a	a	p	<1

5. Oligomers conversion into PEt[6]

$FeCl_3$ (58 mg, 0.358 mmol) and **TMAC** (28 mg, 0.255 mmol) were heated at 110 °C and gently stirred until a dark brown viscous liquid formed. Then a solution of **OEt[6]** (10 mg, 0.009 mmol) in DCM (25 mL) was added and the mixture was stirred at 25 °C for 2 minutes. Then water (50 mL) was added and the reaction mixture was stirred at 25 °C for 1 week. The reaction was monitored by FTICR-ESI-MS (Figure S17). The organic layer was then washed with water and brine, dried over $MgSO_4$, filtered and dried over vacuum. The crude product was purified by preparative TLC with PET:Et_2O = 8:2 as eluent to give **PEt[6]** between 25% and 55% yield. ESI-MS spectrum of **PEt[6]** is shown in Figure S8. MS (ESI) *m/z* 186.6385 [**PEt[6]**+NH_4]$^+$, 1091.5928 [**PEt[6]**+Na]$^+$, 1107.5693 [**PEt[6]**+K]$^+$, 1169.7212 [**PEt[6]**+TEA]$^+$. *m/z* calcd for [**PEt[6]**+Na]$^+$ $C_{66}H_{84}NaO_{12}$: 1091.5855; found 1091.5928 (100%).

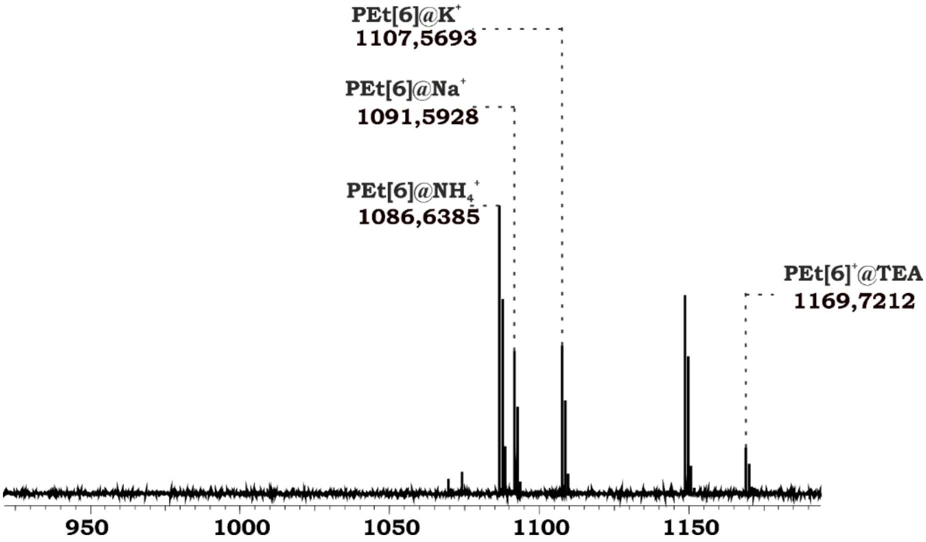

Figure S8 *ESI-MS spectrum of **OEt[6]** conversion into **PEt[6]** after 1 week, with* $FeCl_3$ *as catalysts and **TMAC** as template, in* DCM/H_2O *at 25 °C.*

6. Synthesis of co-pillar[6]arenes

*Synthesis of **PMe[5]Et[1]***

$FeCl_3$ (58 mg, 0.358 mmol) and **TMAC** (28 mg, 0.255 mmol) were heated at 110 °C and gently stirred until a dark brown viscous liquid formed. Then a solution of **PMe[5]** (8 mg, 0.011 mmol) and **DEB** (3 mg 0.018 mmol) in DCM (25 mL) was added and the mixture was stirred at 25 °C for 2 minutes. Then water (50 mL) was added and the reaction mixture was stirred at 25 °C for 1 week. The organic layer was then washed with water and brine, dried over $MgSO_4$, filtered and dried over vacuum. The crude product was purified by preparative TLC with PET:Et_2O = 8:2 as eluent. Four different fractions were collected and identified by FTICR-ESI-MS as **PMe[5]** (76%), **PMe[5]Et[1]** (8%) **PEt[5]** (3%) and **PEt[6]** (9%). Here we reported the mass characterization only for **PMe[5]Et[1]** which ESI-MS spectrum is shown in Figure S9**.** MS (ESI) *m/z* 929.448 [**PMe[5]Et[1]**+H]$^+$, 946.475 [**PMe[5]Et[1]**+NH_4]$^+$, 951.430 [**PMe[5]Et[1]**+Na]$^+$, 967.403 [**PMe[5]Et[1]**+K]$^+$, 1030.568 [**PMe[5]Et[1]**+TEAH]$^+$. *m/z* calcd for [**PMe[5]Et[1]**+Na]$^+$ $C_{56}H_{64}NaO_{12}$: 951.429; found 951.430 (100%).

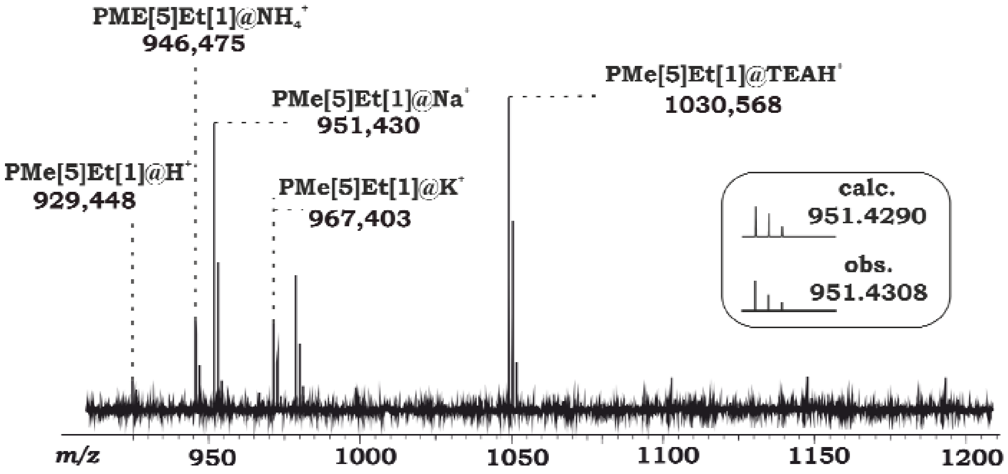

Figure S9 *ESI-MS spectrum of* ***PMe[5]Et[1]****.*

Synthesis of ***PMe[1]Et[5]***

$FeCl_3$ (58 mg, 0.358 mmol) and **TMAC** (28 mg, 0.255 mmol) were heated at 110 °C and gently stirred until a dark brown viscous liquid formed. Then a solution of **PEt[5]** (10 mg, 0.010 mmol) and **DMB** (3 mg 0.014 mmol) in DCM (25 mL) was added and the mixture was stirred at 25 °C for 2 minutes. Then water (50 mL) was added and the reaction mixture was stirred at 25 °C for 1 week. The organic layer was then washed with water and brine, dried over $MgSO_4$, filtered and dried over vacuum. The crude product was purified by preparative TLC with PET:Et_2O = 8:2 as eluent. Four different fractions were collected and identified by FTICR-ESI-MS as **PMe[5]** (12%), **PMe[1]Et[5]** (8%) **PEt[5]** (70%) and **PEt[6]** (7%). Here we reported the mass characterization only for **PMe[1]Et[5]** which ESI-MS spectrum is shown in Figure S10. MS (ESI) *m/z* 1041.569 [**PMe[1]Et[5]**+H]$^+$, 1058.595 [**PMe[1]Et[5]**+NH_4]$^+$, 1063.551 [**PMe[1]Et[5]**+Na]$^+$, 1079.525 [**PMe[1]Et[5]**+K]$^+$, 1142.689 [**PMe[1]Et[5]**+TEAH]$^+$. *m/z* calcd for [**PMe[1]Et[5]**+Na]$^+$ $C_{64}H_{80}NaO_{12}$: 1063.554; found 1063.551 (100%).

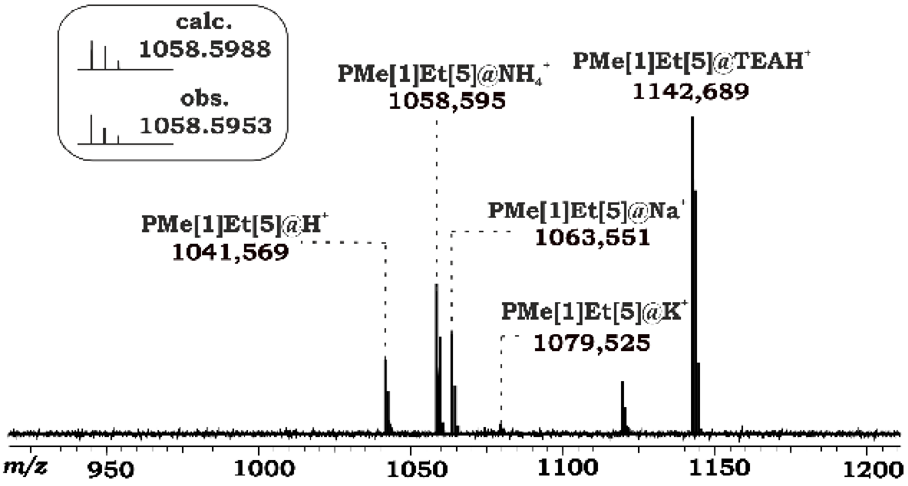

***Figure S10** ESI-MS spectrum of **PMe[1]Et[5]**.*

7. Scrambling experiment between two differently substituted P[5]s.

$FeCl_3$ (58 mg, 0.358 mmol) and **TMAC** (28 mg, 0.255 mmol) were heated at 110 °C and gently stirred until a dark brown viscous liquid formed. Then a solution of **PMe[5]** (8 mg, 0.011 mmol) and **PEt[5]** (10 mg, 0.010 mmol) in DCM (25 mL) was added and the mixture was stirred at 25 °C for 2 minutes. Then water (50 mL) was added and the reaction mixture was stirred at 25 °C for 1 week. The organic layer was then washed with water and brine, dried over $MgSO_4$, filtered and dried over vacuum. The crude product was analyzed by FTICR-ESI-MS.

8. PEt[5] conversion into PEt[6]

*Proposed mechanism for the conversion of **PEt[5]** into **PEt[6]***

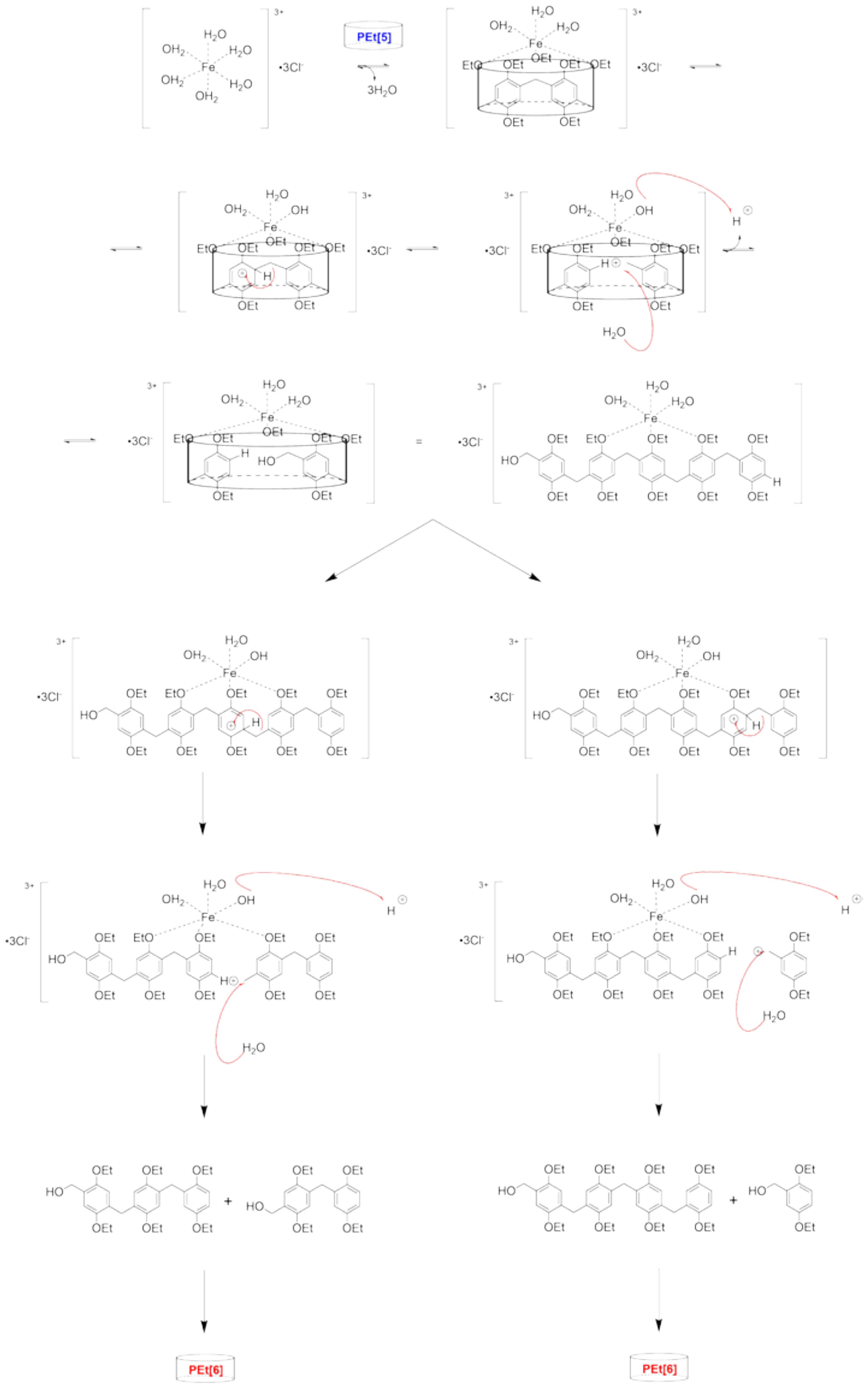

Figure S11 *Proposed mechanisms for the conversion of **PEt[5]** into **PEt[6]** considering two different series of cleavages (3+2 on the left and 4+1 on the right).*

9. PMe[5] and PEt[5] scrambling experiment

Table S2 *Peak assignment of the ESI-MS spectra showed in Figure 4 for the series of co-pillar[5]arenes (entries 1-12) and co-pillar[6]arenes (entries 13-22).*

#	*m/z*	**Abundance (%)**[a]	**Adduct**	**Assignment**
		Pillar[5]arenes Products		
1	751.348	23.2	$[M+H^+]$	**PMe[5]**
2	768.375	6.1	$[M+NH_4^+]$	**PMe[5]**
3	779.379	43.7	$[M+H^+]$	**PMe[4]Et[1]**
4	796.406	13.8	$[M+NH_4^+]$	**PMe[4]Et[1]**
5	807.411	94.3	$[M+H^+]$	**PMe[3]Et[2]**
6	824.437	35.7	$[M+NH_4^+]$	**PMe[3]Et[2]**
7	835.442	100.0[a]	$[M+H^+]$	**PMe[2]Et[3]**
8	852.468	47.2	$[M+NH_4^+]$	**PMe[2]Et[3]**
9	863.472	52.0	$[M+H^+]$	**PMe[1]Et[4]**
10	880.500	31.9	$[M+NH_4^+]$	**PMe[1]Et[4]**
11	891.504	22.0	$[M+H^+]$	**PEt[5]**
12	908.531	13.3	$[M+NH_4^+]$	**PEt[5]**
		Pillar[6]arenes Products		
13	929.447	1.3	$[M+H^+]$	**PMe[5]Et[1]**
14	957.477	2.8	$[M+H^+]$	**PMe[4]Et[2]**
15	974.504	0.9	$[M+NH_4^+]$	**PMe[4]Et[2]**
16	985.509	4.4	$[M+H^+]$	**PMe[3]Et[3]**
17	1002.535	1.3	$[M+NH_4^+]$	**PMe[3]Et[3]**
18	1013.540	4.0	$[M+H^+]$	**PMe[2]Et[4]**
19	1030.566	1.3	$[M+NH_4^+]$	**PMe[2]Et[4]**
20	1041.571	2.0	$[M+H^+]$	**PMe[1]Et[5]**
21	1058.630	0.8	$[M+NH_4^+]$	**PMe[1]Et[5]**
22	1069.605	0.9	$[M+H^+]$	**PEt[6]**

a) the relative percentage is calculated assigning 100 to the most abundant peak **PEt[3]Me[2]**.

Table S3 *Calculation of the normalized abundance of the different series of* ***P[5]*** *bearing n number of methoxy units (n=0-5) from the spectra showed in Figure 4.*

	% relative to the most abundant peak PMe[2]Et[3]	**Relative abundance**	**Normalized abundance**
PMe[5]	23,20		
PMe[5]	6,10	29,30	6,06
PMe[4]Et[1]	43,70		
PMe[4]Et[1]	13,80	57,50	11,90
PMe[3]Et[2]	94,30		
PMe[3]Et[2]	35,70	130,00	26,90
PMe[2]Et[3]	100,00		
PMe[2]Et[3]	47,20	147,20	30,46
PMe[1]Et[4]	52,00		
PMe[1]Et[4]	31,90	83,90	17,36
PEt[5]	22,00		
PEt[5]	13,30	35,30	7,31
		483,20	

Table S4 *Calculation of the normalized abundance of the different series of* ***P[6]*** *bearing m number of methoxy units (m=0-6) from the spectra showed in Figure 4.*

	% relative to the most abundant peak PMe[2]Et[3]	**Relative abundance**	**Normalized abundance**
PMe[5]Et[1]	1,30	1,30	6,60
PMe[4]Et[2]	2,80		
PMe[4]Et[2]	0,90	3,70	18,78
PMe[3]Et[3]	4,40		
PMe[3]Et[3]	1,30	5,70	28,93
PMe[2]Et[4]	4,00		
PMe[2]Et[4]	1,30	5,30	26,90
PMe[1]Et[5]	2,00		
PMe[1]Et[5]	0,80	2,80	14,21
PEt[6]	0,90	0,90	4,57
		19,70	