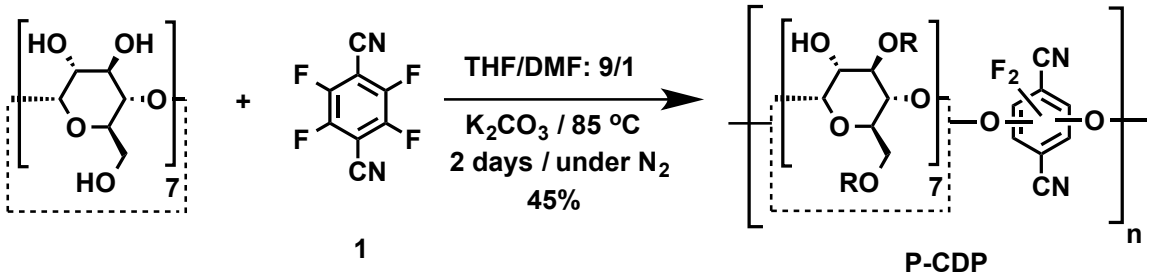
doi:10.1038/nature16185

Improved Synthesis of P-CDP



A flame dried 20 mL scintillation vial equipped with a magnetic stir bar was charged with β-CD (0.205 g, 0.181 mmol), **1** (0.100 g, 0.515 mmol), and K_2CO_3 (0.320 g, 2.32 mmol). The vial was flushed with N_2 gas for 5 min, then an anhydrous THF/DMF mixture (9:1 *v*/*v*, 8 mL) was added and the vial was sparged with N_2 for additional 2-3 min. The N_2 inlet was removed and the mixture was placed on a hot stirring plate (85 °C) and stirred at 500 rpm for 2 d. The orange suspension was cooled and then filtered, and the residual K_2CO_3 was removed by washing the solid on the filter paper with 1N HCl until CO_2 evolution stopped. The recovered light yellow solid was isolated and activated by soaking in H_2O (2 x 10 mL) for 15 min, THF (2 x 10 mL) for 30 min and CH_2Cl_2 (1 x 15 mL) for 15 min. Finally, the solid was dried under high vacuum at 77 K in a liquid nitrogen bath for 10 min and then at rt for 2-3 days. **P-CDP** (0.125 g, 45% yield) was obtained as a pale yellow powder and subsequently characterized. Anal. Calcd. for $(C_{42}H_{65}O_{35})_1 \bullet (C_8F_{1.4}N_2)_5 \bullet (CH_2Cl_2)_5 \bullet (H_2O)_{13}$: C, 43.43; H, 4.55; F, 4.96; N, 5.22. Found: C, 43.74; H, 4.67; F, 4.83; N, 5.05. S_{BET} (N_2 adsorption, 77K) = 118 $m^2\ g^{-1}$. FT-IR spectra and BPA uptake performance are given below to compare materials derived from this improved procedure with those prepared in neat THF.

Figure S1: FTIR spectra of **P-CDP** prepared using the original (top, red) and higher yielding (bottom, blue) procedures.

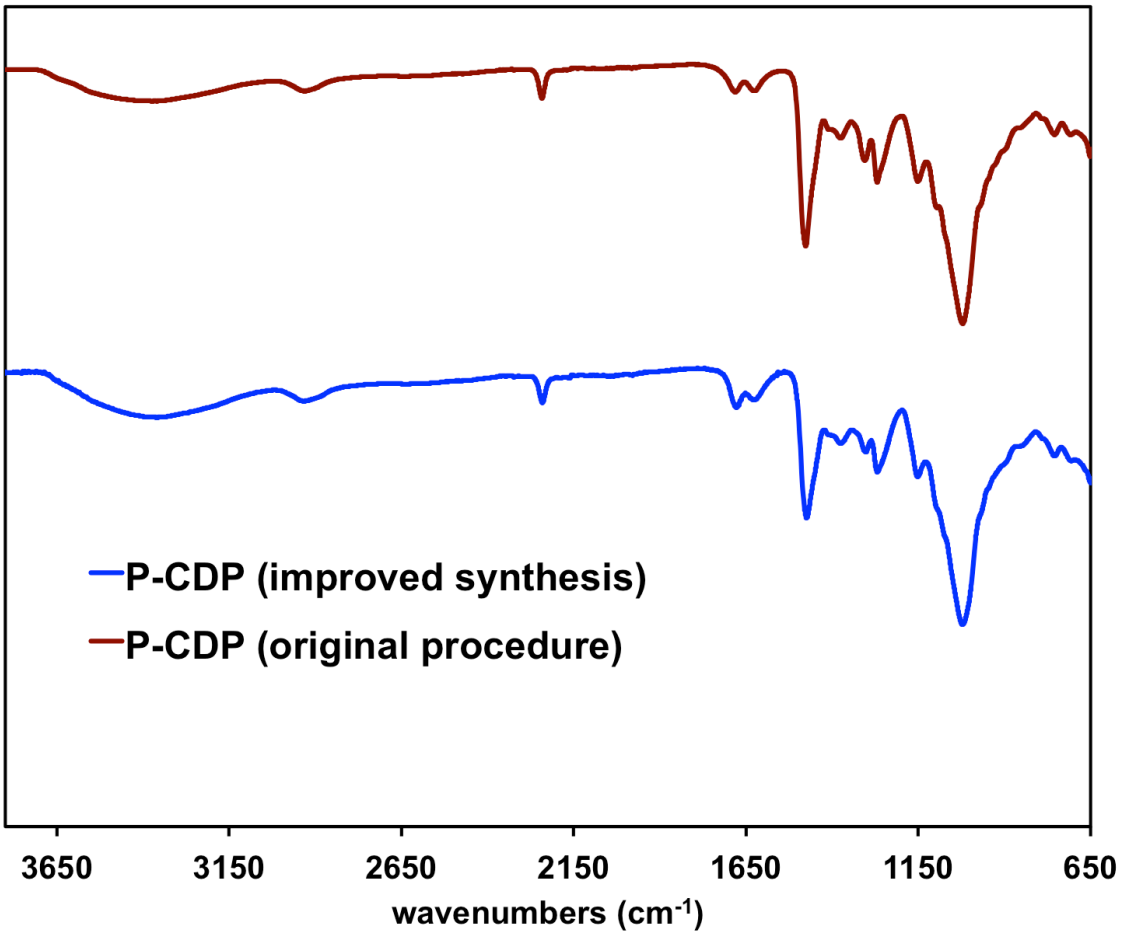
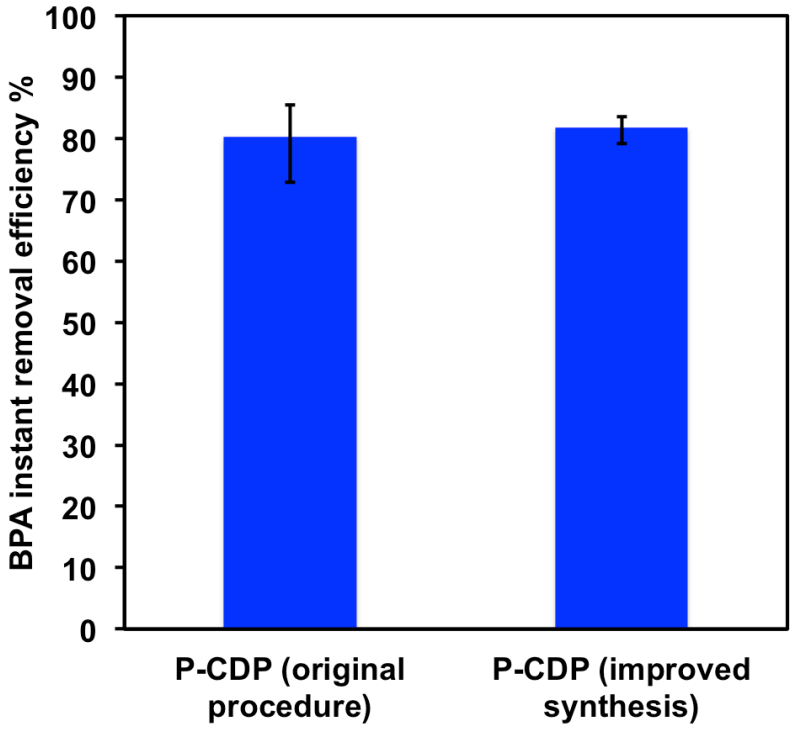
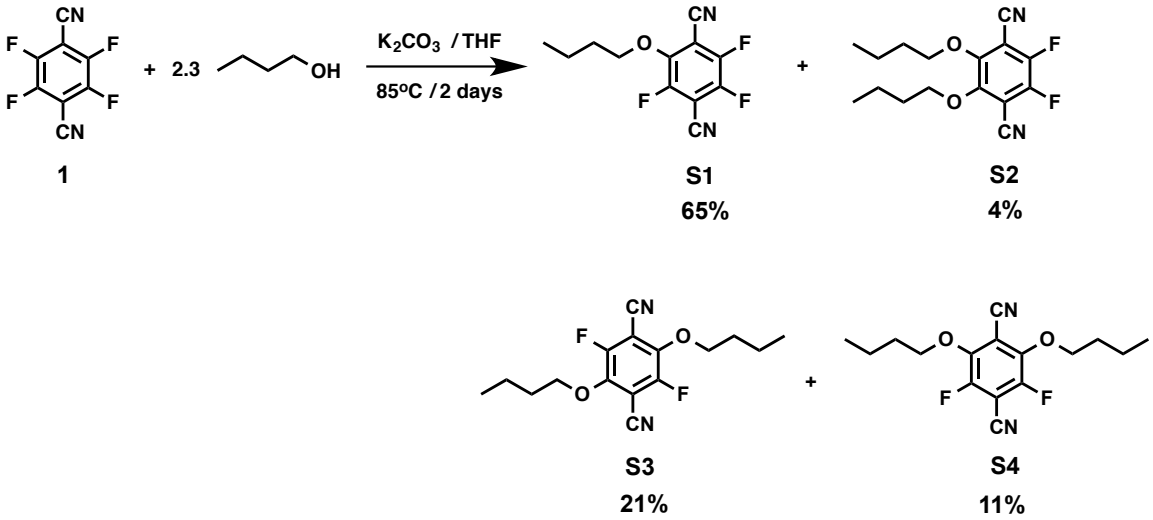


Figure S2: Instantaneous BPA uptake by **P-CDP** (1 mg/mL) prepared using the original (left) and higher yielding (right) synthetic procedures ($[BPA]_0$ = 0.1 mM, 9 mL/min flow rate). The data are an average of three measurements and the error bars represent the minimum and maximum uptake.

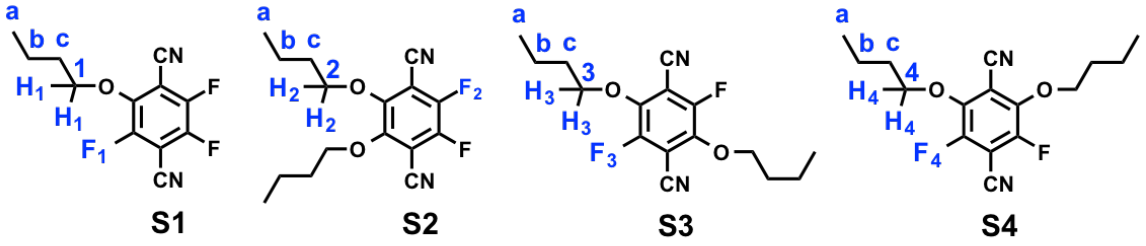


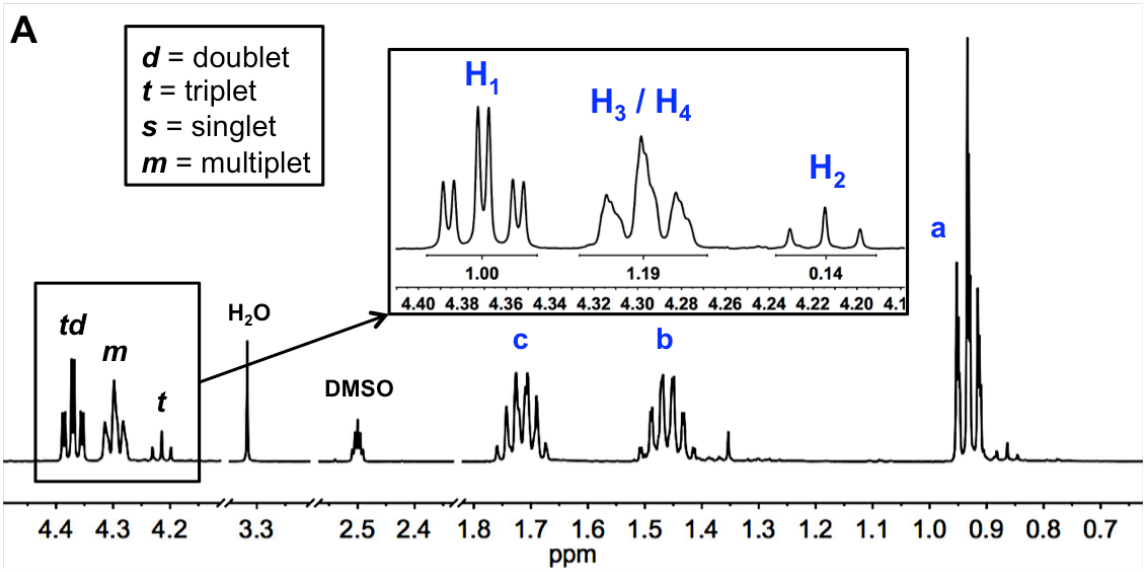
Model reaction S1

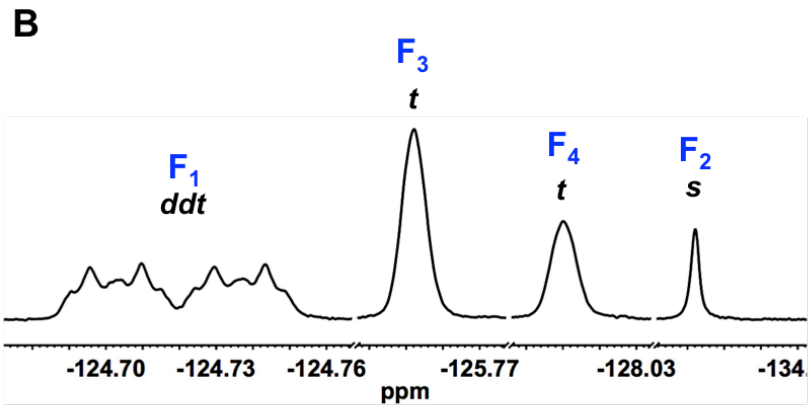


1 (1.00 g, 5.00 mmol), *n*-BuOH (1.10 mL, 12.0 mmol) and K_2CO_3 (2.76 g, 20.0 mmol) were added to a flame-dried 20 mL scintillation vial equipped with a magnetic stir bar. THF (16 mL) was then added and the vial was stirred at 85 °C for 2 d. The suspension was cooled to rt and filtered, from which a yellow solid was collected. THF was then removed under vacuum, and the remaining solid was suspended in hexanes, and the suspension was then filtered under vacuum. The filtrate was concentrated and thick yellow oil was isolated as a mixture of the above products, which were characterized by ^{1}H, ^{19}F and ^{13}C NMR spectroscopy and Direct Analysis in Real Time (DART) mass spectrometry (Fig. S3 and S4).

Figure S3: Partial NMR spectra (DMSO-d_6, 400 MHz, rt) of the crude product of model reaction S1. (A) ^{1}H NMR, (B) ^{19}F NMR, (C) ^{13}C NMR.







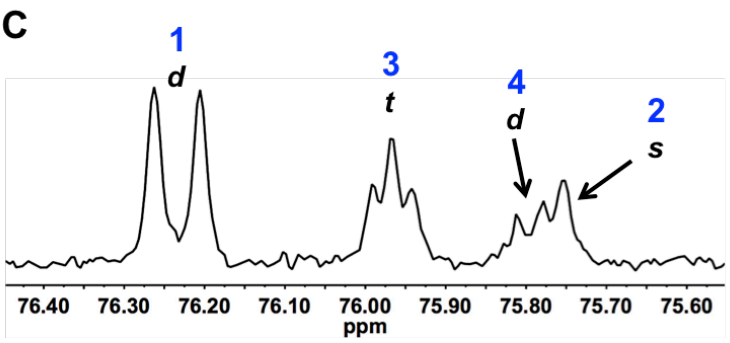
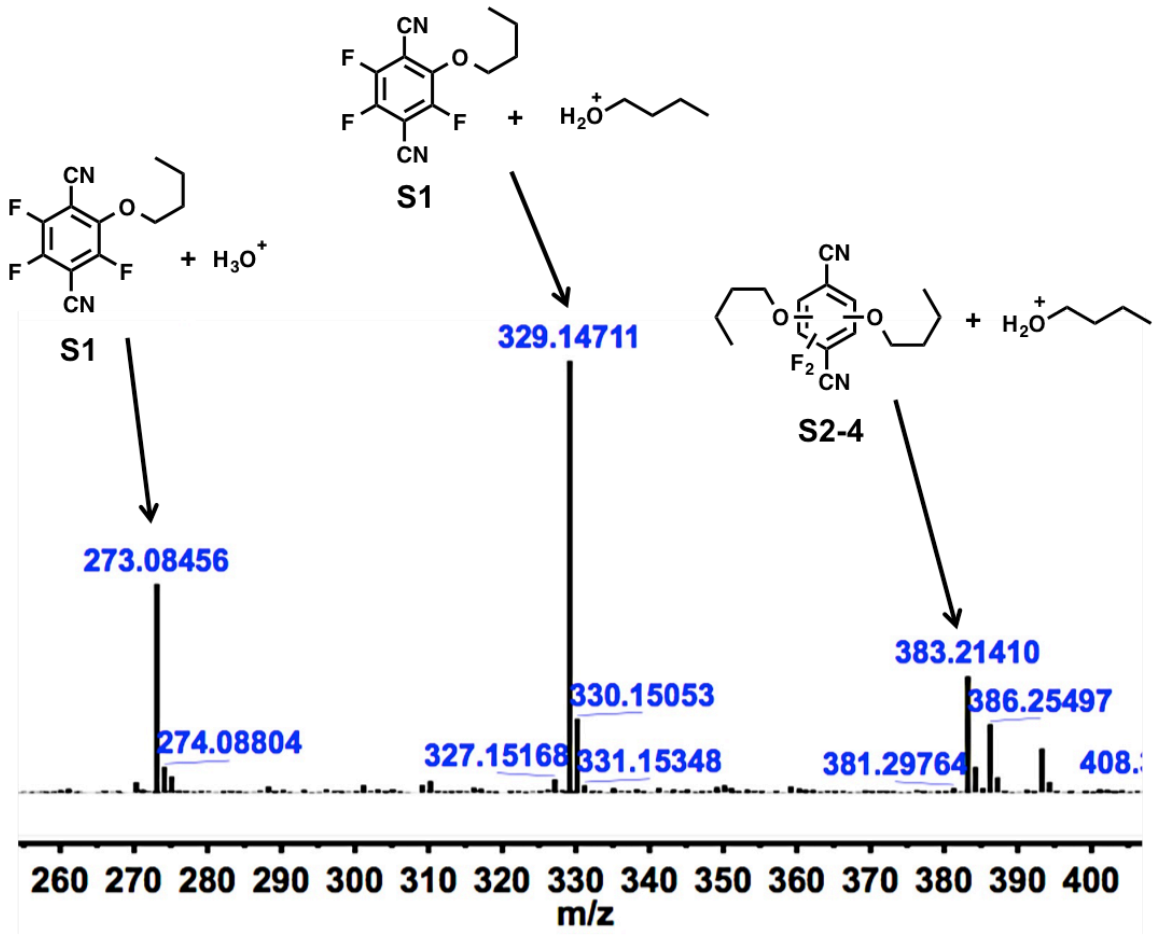
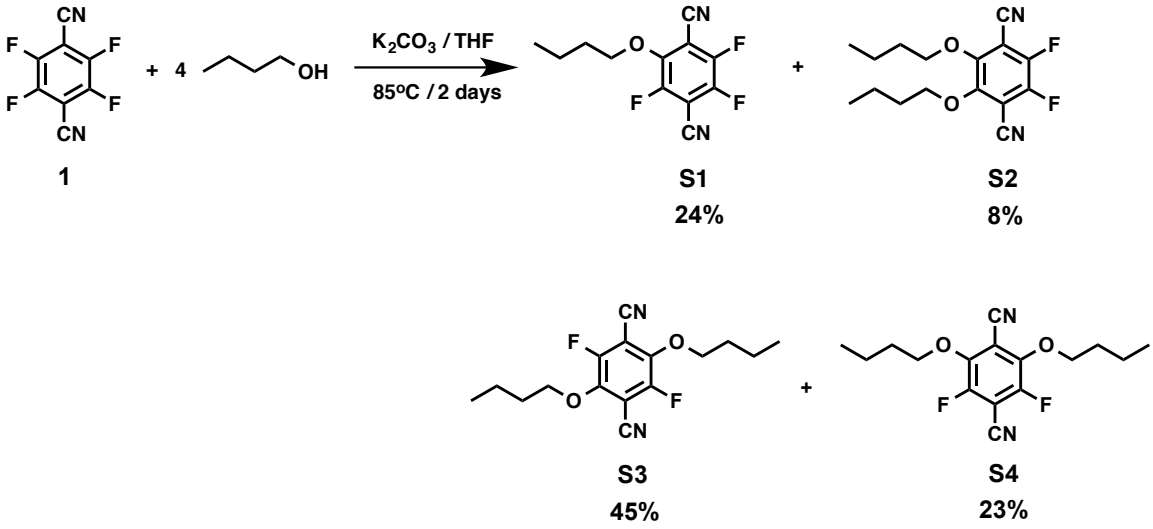


Figure S4: ESI spectrum of the crude product of model reaction S1 in positive ion mode.

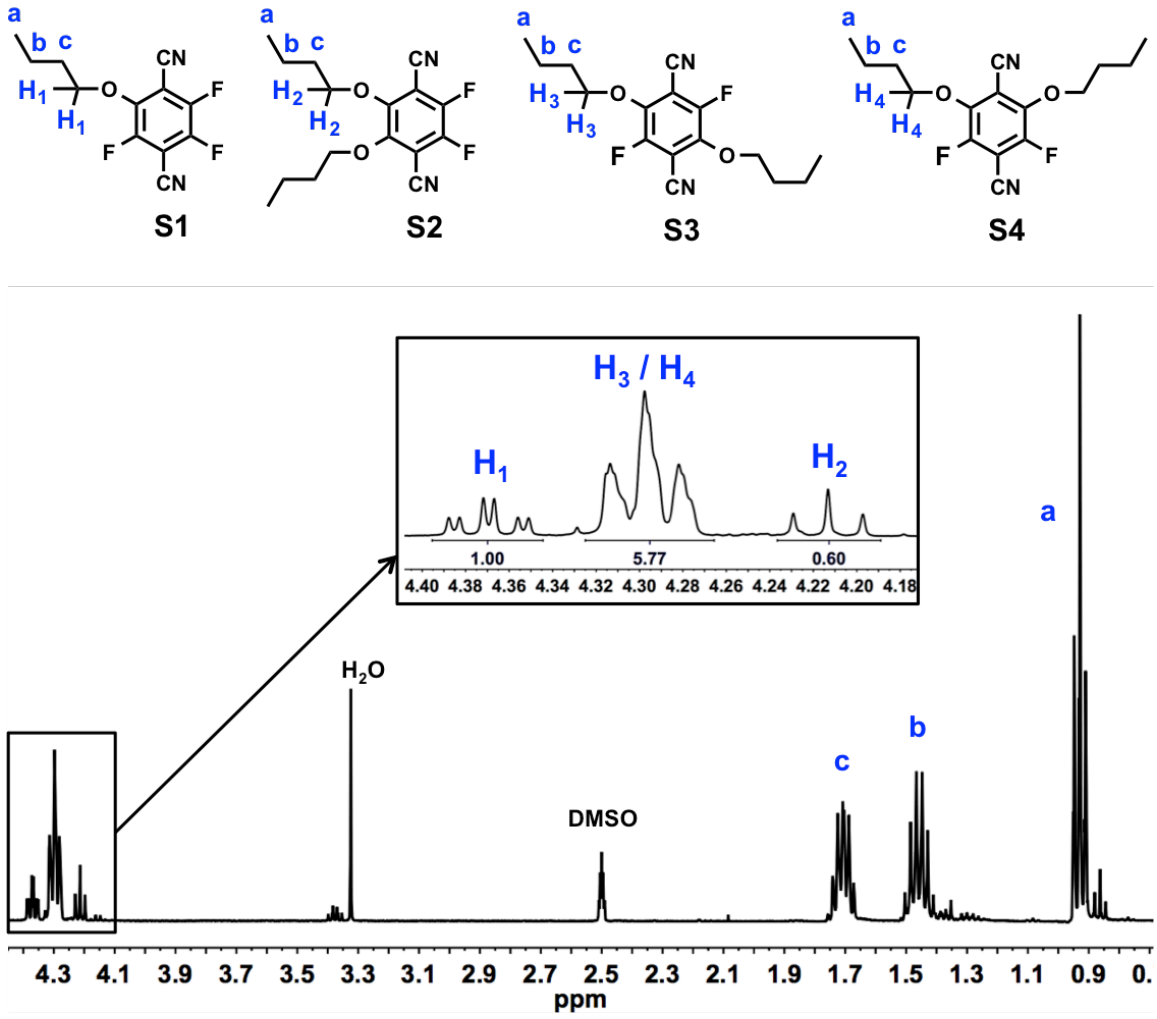


Model reaction S2.

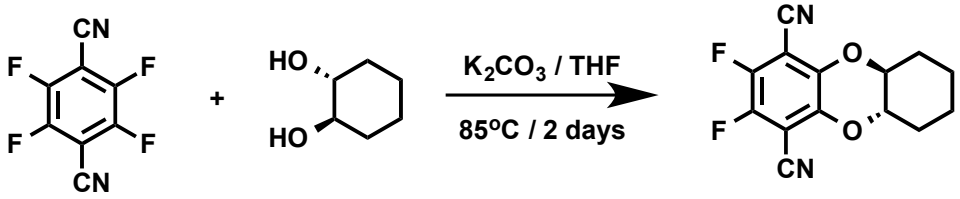


1 (1.00 g, 5.00 mmol), *n*-BuOH (1.80 mL, 19.7 mmol) and K_2CO_3 (3.50 g, 25.3 mmol), THF (16 mL) were combined in a flame-dried 20 mL scintillation vial equipped with a magnetic stir bar. The mixture was stirred at 85 °C for 2d. The suspension was filtered, and the filtrate was collected and concentrated under vacuum. The crude mixture, which was collected from the filtrate, was then suspended in hexanes, and the suspension was then filtered under vacuum. The filtrate was concentrated and the resulting viscous yellow oil was isolated and subsequently characterized by ^{1}H NMR spectroscopy (Fig. S5).

Figure S5: Partial ^{1}H NMR spectrum (DMSO-d_6, 400 MHz, rt) of the crude product of model reaction S2.



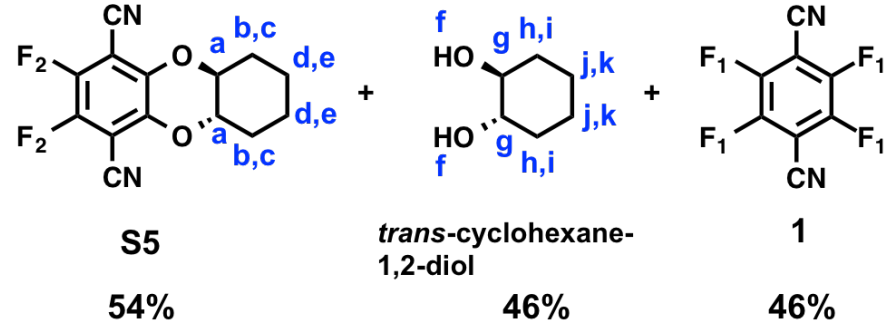
Model reaction S3.



1 **S5**

1 (200 mg, 1.00 mmol), trans-cyclohexane-1,2-diol (116 mg, 1.00 mmol) and K_2CO_3 (280 mg, 2.03 mmol) were added to a dry 20 mL scintillation vial. THF (16 mL) was then added and the mixture was stirred at 85 °C for 2 d. The mixture was filtered and then concentrated under vacuum. The crude yellow solid was characterized by ^{1}H NMR (Fig. S6), which revealed that the mono substituted product S5 was formed exclusively.

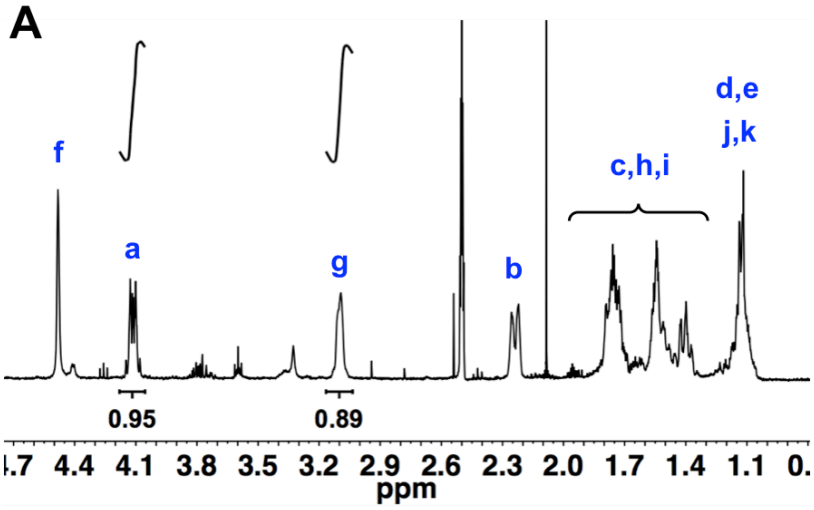
Figure S6: Partial ^{1}H NMR spectra (DMSO-d_6, 400 MHz, rt) of the crude products of model reaction S3. (A) ^{1}H NMR, and (B) ^{19}F NMR.

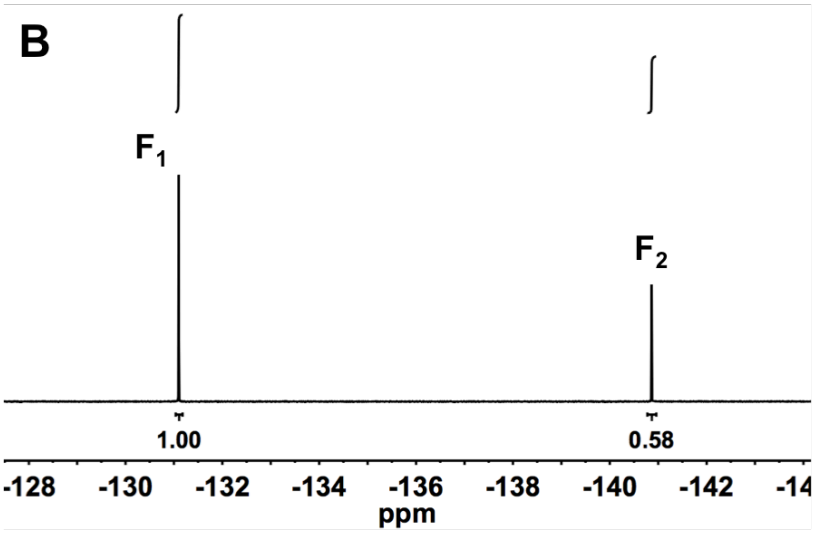


S5 54%

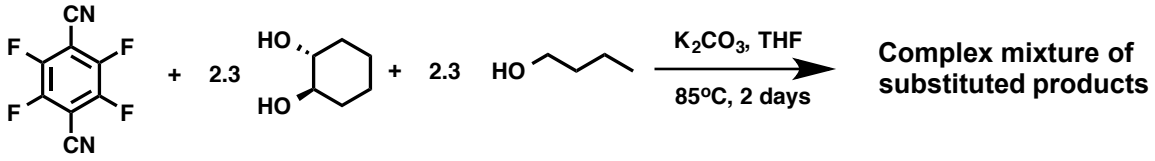
trans-cyclohexane-1,2-diol 46%

1 46%





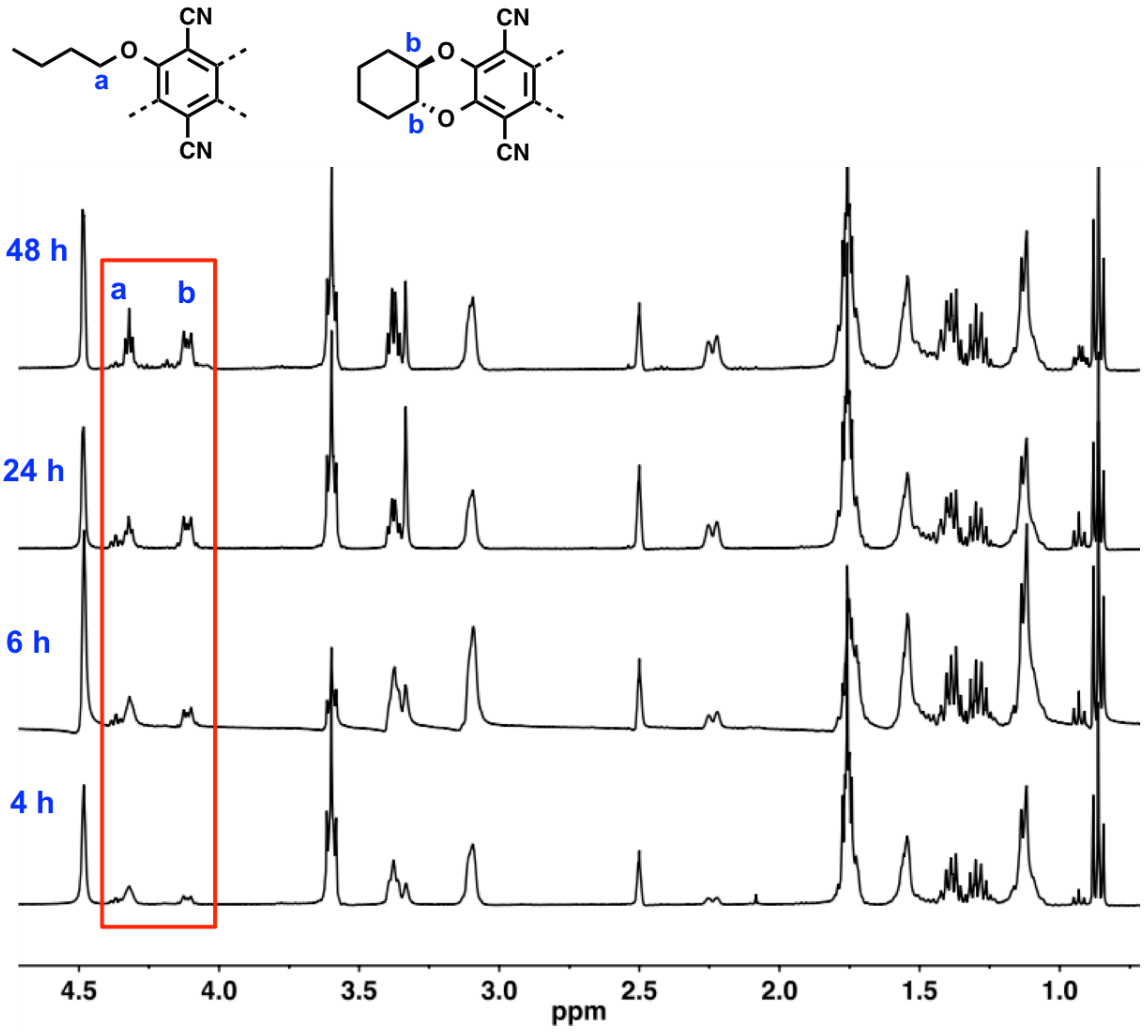
Competition substitution model reaction S4.



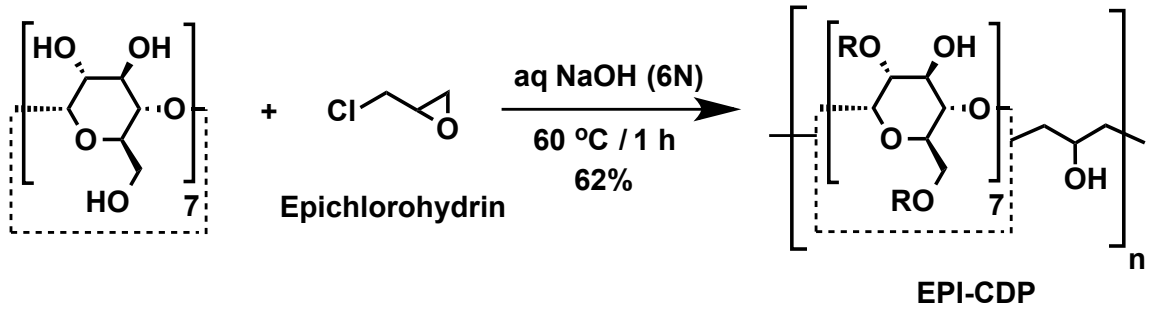
1

1 (200 mg, 1.00 mmol), trans-cyclohexane-1,2-diol (270 mg, 2.32 mmol), *n*-BuOH (0.213 mL, 2.33 mmol) and K_2CO_3 (610 mg, 4.41 mmol) were added to a dry 20 mL scintillation vial. THF (16 mL) was then added and the mixture was stirred at 85 °C for 2 d. Aliquots of the reaction were taken at certain intervals (4h, 6h, 24h, and 2d), which were filtered and concentrated under vacuum. The crude yellow solid was dissolved in DMSO-d_6 and characterized by ^{1}H NMR spectroscopy (Fig. S7).

Figure S7: ^{1}H NMR spectra (DMSO-d_6, 400 MHz, rt) of aliquots of the competition substitution model reaction S4 collected at various reaction times.

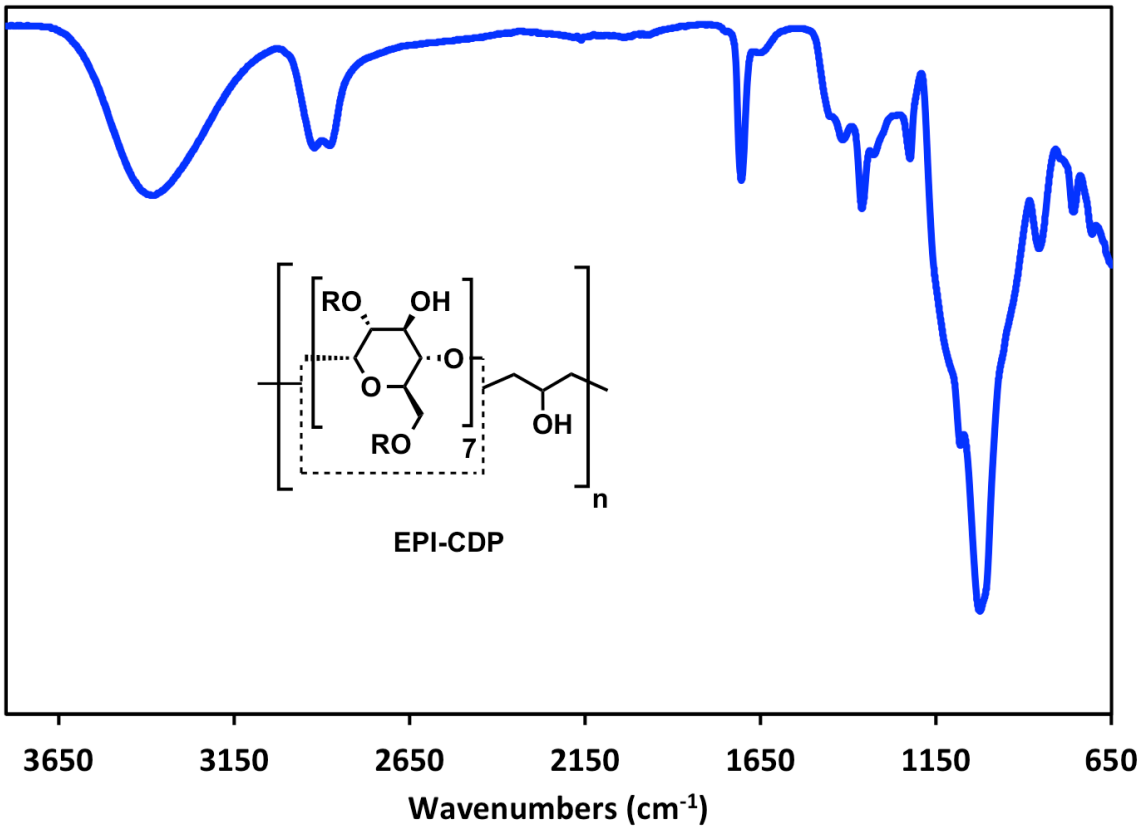


Epichlorohydrin β-cyclodextrin polymer (EPI-CDP) synthesis.



β-CD (0.300 g, 2.64 mmol) was dissolved in aqueous NaOH (6.25 N, 5.00 mL) at 60 °C. Epichlorohydrin (2.50 mL, 32.4 mmol,) was added to this solution dropwise while stirring vigorously at 60 °C. The mixture turned into a yellow gel within 1 h, after which 10 mL of deionized H_2O was added, and the mixture was filtered on a Büchner funnel. The solid was washed by soaking in deionized H_2O (2 x 150 mL) for 15 min, THF (3 x 15 mL) for 30 min and CH_2Cl_2 (1 x 15 mL) for 15 min. The solid was finally dried under high vacuum for 2 d at rt to give **EPI-CDP** (3.11 g, 62 % yield) as a white powder. ^{13}C-MAS SS-NMR (400 MHz): δ 100.1, 72.0 ppm. IR (solid, ATR) 3387, 2923, 2900, 1702, 1360, 1030 cm^{-1}. Anal. Calcd. For $(C_{42}H_{60}O_{35})_1 \bullet (C_3H_6O)_{10} \bullet (H_2O)_{4.5}$: C, 48.40; H, 7.28. Found: C, 48.23; H, 7.09.

Figure S8: FT-IR spectrum of as-synthesized **EPI-CDP**.



Functional Cost Analysis of P-CDP

Commercial activated carbons:

	Cost ($/kg)
Standard commercial ACs	2[a]
Advanced commercial ACs	9[a]
Norit RO 0.8 AC	47[b]
Granular AC (DARCO 12-20 mesh)	22[b]

[a] Prices obtained from wholesale suppliers (metric ton scale).
[b] Prices obtained from bulk suppliers (multiple kg scale).

Functional cost analysis of P-CDP:

Wholesale cost of reagents:

Reagent	Cost ($/kg)[a]
β-Cyclodextrin	1
Tetrafluoroterephthalonitrile	5
K_2CO_3	0.5

[a] Prices obtained from wholesale suppliers (metric ton scale).

Manufacturing cost analysis projections

Yield	Raw materials ($/kg)	Pilot-scale[b] ($/kg)	Dedicated manufacturing[c] ($/kg)
45% (Current yield)	8.5	25.5	12.1
100% (Limiting estimates)[a]	3.7	11.2	5.3

[a] Calculated based on raw materials required to produce 1 kg of P-CDP having 5.5:1 cross-linker:β-CD ratio in quantitative yield.
[b] The raw materials costs were scaled by 300% as a rough estimate of the cost associated with a pilot scale manufacturing cost.
[c] The raw materials costs were scaled by 142% as a rough estimate of the cost associated with an optimized process performed in a dedicated manufacturing plant.

Table S1: Molecular descriptor values for micropollutants used in the study.

Pollutant	$logK_{ow}$ [a]	logD [b]	MW (g/mol)	pKa	C_s (g/L) [c]	Min z L (Å) [d]	Max z L (Å) [e]
BPA	3.6	3.6	228.3	9.7	0.12	12.4	8.6
BPS	1.6	1.7	250.3	7.6 [f]	0.38 [f]	12.8	7.0
metolachlor	3.2	3.2	283.8	1.4 [f]	0.53	12.1	9.0
ethinyl estradiol	4.1	3.9	296.4	10.4	0.002	13.9	8.0
propranolol	2.6	1.1	259.3	9.5	0.050 (ref)	15.4	8.3
2-naphthol (2-NO)	2.7	2.9	144.2	9.5	0.76	9.6	4.0
1-naphthyl amine (1-NA)	2.2	2.3	143.2	3.9	1.7	9.5	4.1
2,4-dichlorophenol (DCP)	2.8	3.0	163.0	7.9	4.5	8.8	4.2

[a] Log octanol-water partition coefficient. Predicted using KOWWIN v1.67 software implemented in ChemSpider Database.
[b] Log distribution coefficient at pH = 7.4. Predicted using ACD/Labs Percepta software implemented in ChemSpider Database.
[c] Solubility in water. Experimental values.
[d] Minimal molecular z length. Defined as the length of the conformer perpendicular to its minimal projection area. Generated using ChemAxon software implemented in ChemSpider Database.
[e] Maximum molecular z length. Defined as the length of the conformer perpendicular to its maximal projection area. Generated using ChemAxon software implemented in ChemSpider Database.
[f] Calculated using Advanced Chemistry Development (ACD/Labs) Software V11.02, as implemented in the SciFinder CAS Database.

Table S2: Analytical data required for low concentration analyte quantification.

Compound	Molecular Formula	Exact Mass	Ionization Mode	Retention Time, (min)	Quantification Limit, (µg/L)
BPA	$C_{15}H_{16}O_2$	228.1145	negative	14.1	20
BPS	$C_{12}H_{10}O_4S$	250.0294	positive	10.83	0.05
metolachlor	$C_{15}H_{22}ClNO_2$	283.1334	positive	16.47	0.1
propranolol	$C_{16}H_{21}NO_2$	259.1567	positive	11.75	10
Ethynyl estradiol	$C_{20}H_{24}O_2$	296.1771	positive	15.22	1
1-NA	$C_{10}H_9N$	143.0729	positive	10.35	0.1
2-NO	$C_{10}H_8O$	144.0569	positive	13.16	0.5
2,4-DCP	$C_6H_4Cl_2O$	161.9634	negative	14.6	0.05