Electronic Supplementary Information

A CTV Analogue: Arene-persubstituted Cyclotrixylohydroquinoylene and Its Derivatives

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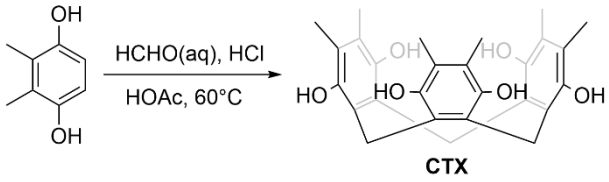
1. General information

All reactions were performed in air atmosphere unless otherwise stated. The commercially available reagents and solvents were either employed as purchased or dried according to procedures described in the literatures. Column chromatography was performed with silica gel (200 – 300 and 300 – 400 mesh) produced by Qingdao Marine Chemical Factory, Qingdao (China). All yields were given as isolated yields unless otherwise stated. NMR spectra were recorded on a Bruker DPX 400 MHz spectrometer with internal standard tetramethylsilane (TMS) and solvent signals as internal references at room temperature, and the chemical shifts (δ) were expressed in ppm and *J* values were given in Hz. High-resolution electrospray ionization mass spectra (HR-ESI-MS) were recorded on an Agilent 6540Q-TOF LCMS equipped with an electrospray ionization (ESI) probe operating in the positive-ion mode with direct infusion unless otherwise stated.

2. Synthetic procedures and characterization data



CTX

A general procedure for the synthesis of CTX

2,3-dimethylbenzene-1,4-diol (0.1 g, 0.72 mmol) was dissolved in AcOH (3 mL) and hydrochloric acid (37% aq, 0.6 mL) and aqueous formaldehyde solution (40%, 1.5 mL, 21.4 mmol) was added. The reaction mixture was stirred at 60℃ in oil bath for 1h. Upon completion, the cooled reaction mixture was poured into water (100 mL) and the obtained precipitate was filtered. The obtained product was brown solid and dried overnight in vacuo to give **CTX** (0.094 g, 0.21 mmol, 87%), which was used directly in the following reaction without purification. If needed, the product can be further purified by dissolved in small amount of DMSO and added dropwise to 100mL petroleum ether. The resulting precipitate was filtered to furnish the title compound as green solid. ^{1}H NMR (400 MHz, DMSO-d_6, 298 K) δ (ppm) = 9.76 (s, 6H), 4.65 (d, J = 14.8 Hz, 3H), 3.97 (d, J = 14.8 Hz, 3H), 2.06 (s, 18H). ^{13}C NMR (100 MHz, DMSO-d_6, 298 K) δ (ppm) = 145.5, 125.1, 123.4, 25.3, 13.2. HR-ESI-MS: m/z [M + H] $^{+}$ calcd for $[C_{27}H_{31}O_6]^{+}$ 451.2116, found 451.2132.

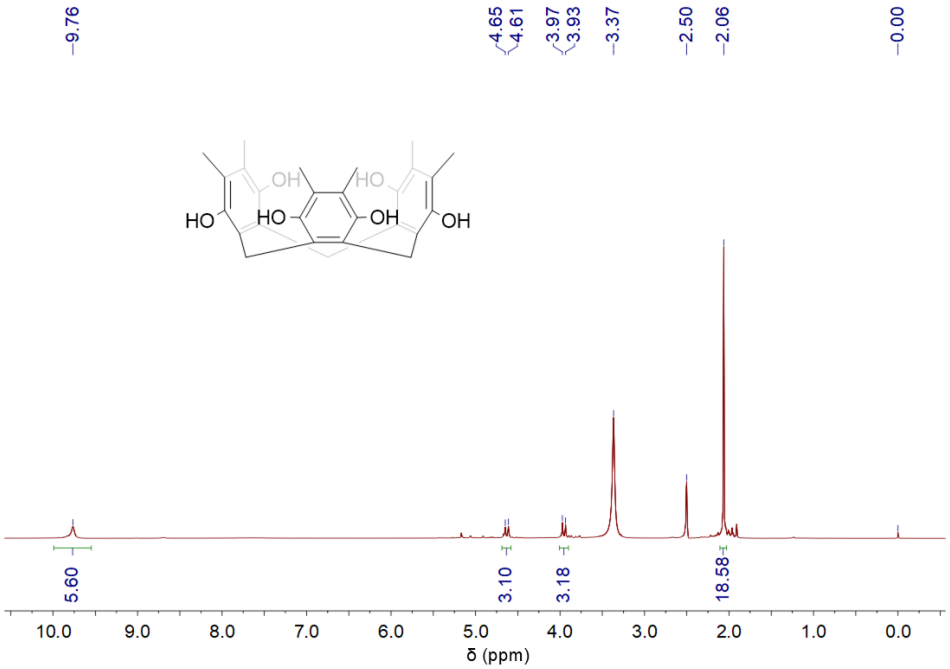


Fig. S1 ^{1}H NMR spectrum (400 MHz, DMSO-d_6, 298 K) of **CTX**.

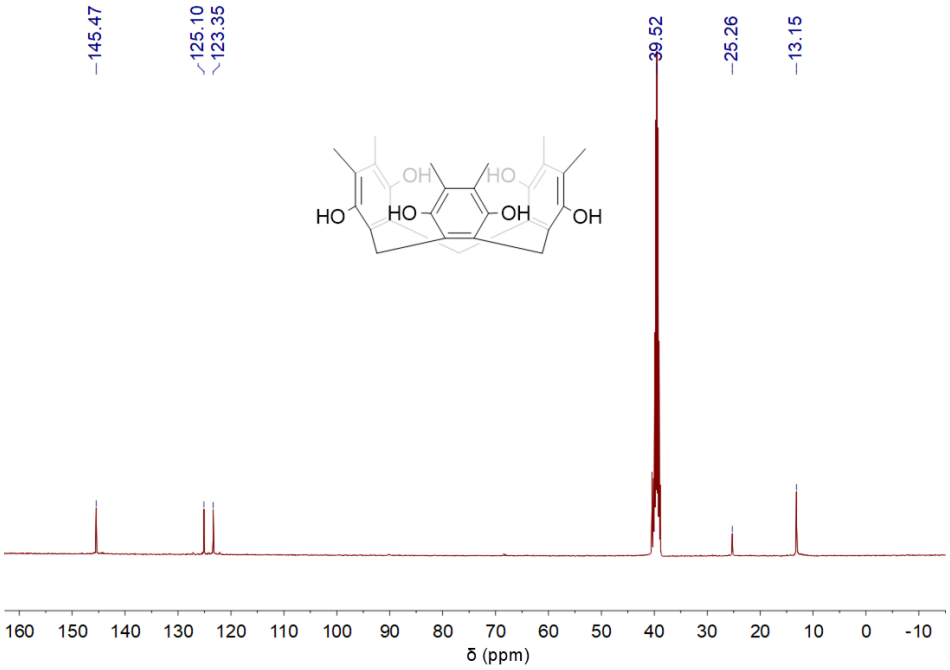


Fig. S2 ^{13}C NMR spectrum (100 MHz, DMSO-d_6, 298 K) of **CTX**.

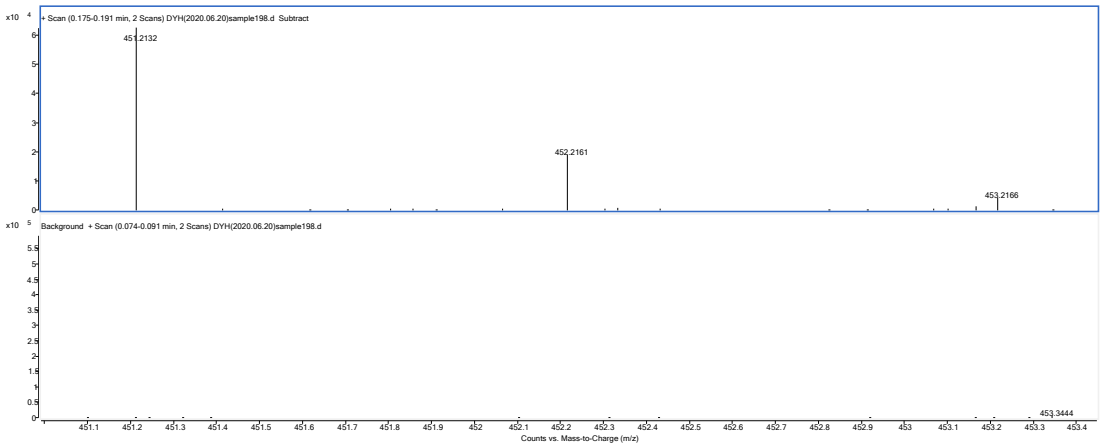
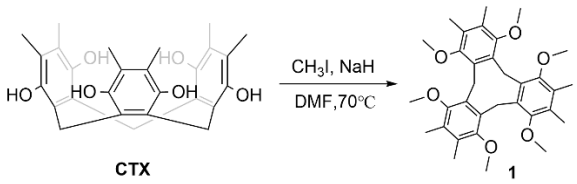


Fig. S3 HR-ESI-MS spectra of **CTX**.



Synthesis of compound 1

CTX (0.7 g, 1.56 mmol) was added to a suspension of NaH (60%, 1.85 g, 46.63 mmol) in DMF (30 mL) in an ice bath. CH_3I (1.4 mL, 23.3 mmol) was then added and the reaction mixture was stirred at 70°C in oil bath for 20h. When the reaction was completed, small amount of water was added to quench the reaction. Then the reaction mixture was filtered. The filtrate was poured into water and extracted with CH_2Cl_2, washed with water and brine, dried over Na_2SO_4, filtered, and concentrated to afford compound **1** as a yellow solid (0.73 g, 1.37 mmol, 88%). ^{1}H NMR (400 MHz, $CDCl_3$, 298 K) δ (ppm) = 4.13 (s, 6H), 3.45 (s, 6H), 2.16 (s, 18H). ^{13}C NMR (100 MHz, $CDCl_3$, 298 K) δ (ppm) = 153.2, 131.0, 128.5, 60.5, 24.7, 13.1. HR-ESI-MS: m/z $[M + Na]^+$ calcd for $[C_{33}H_{42}O_6Na]^+$ 557.2874, found 557.2899.

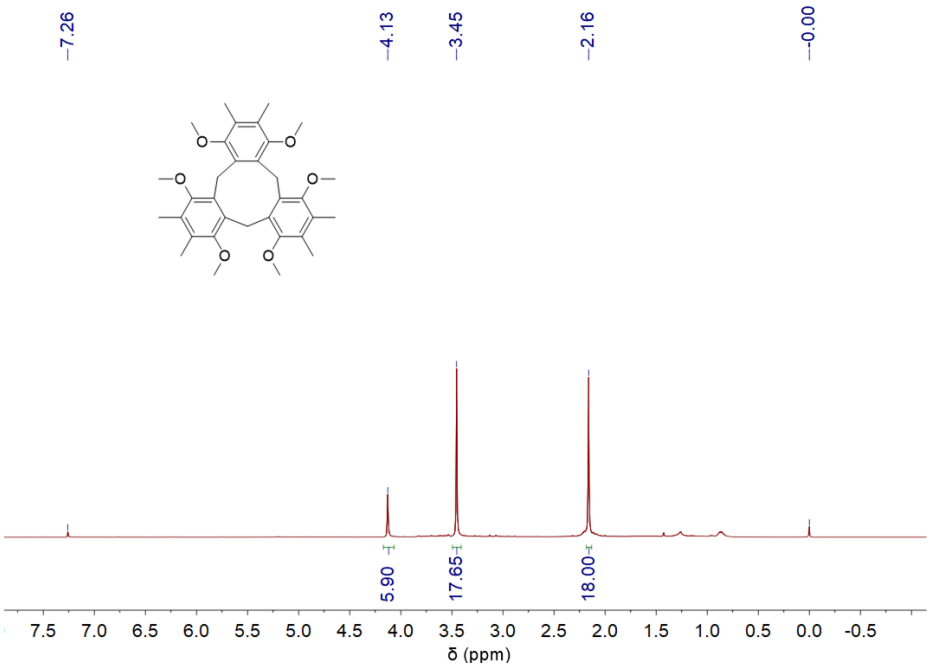


Fig. S4 ^{1}H NMR spectrum (400 MHz, $CDCl_3$, 298 K) of compound **1**.

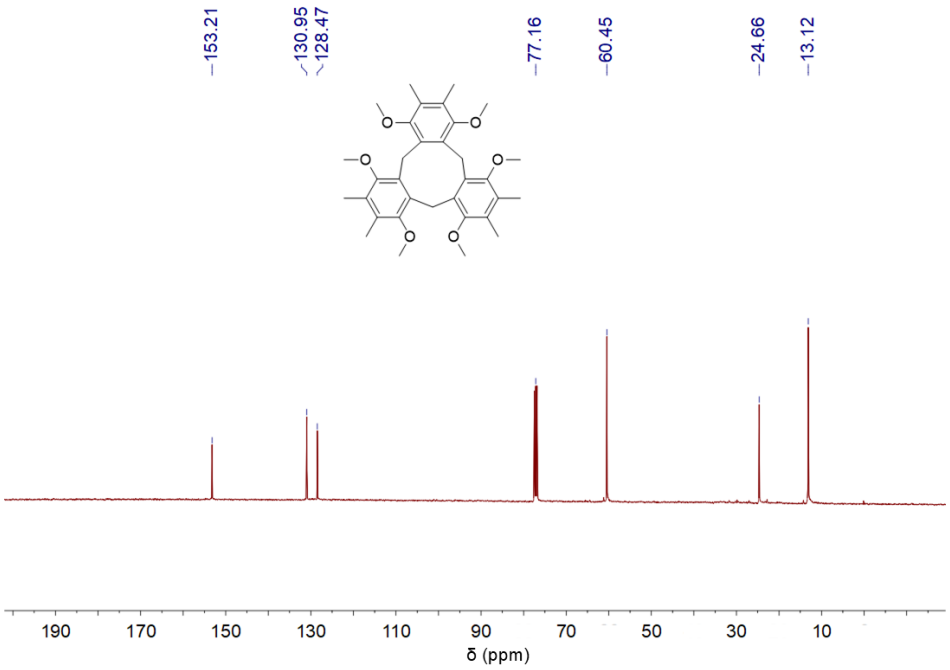


Fig. S5 ^{13}C NMR spectrum (100 MHz, $CDCl_3$, 298 K) of compound **1**.

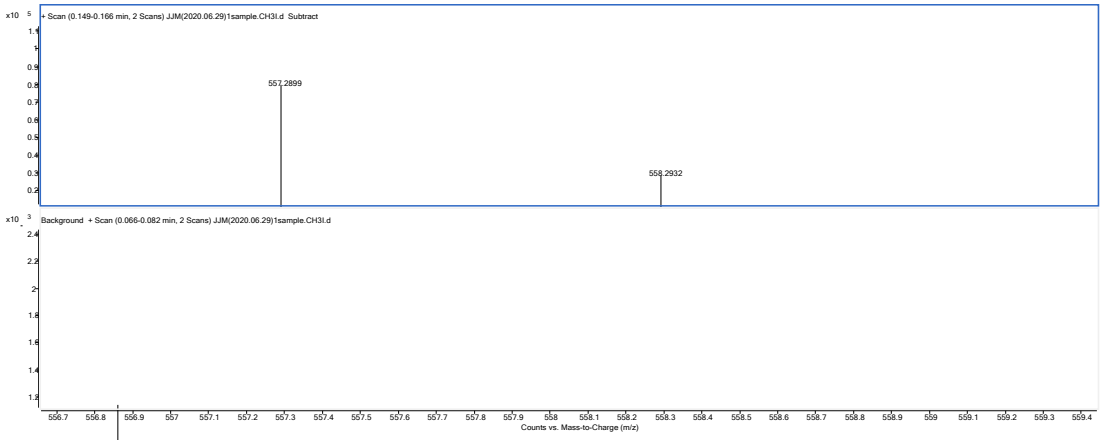
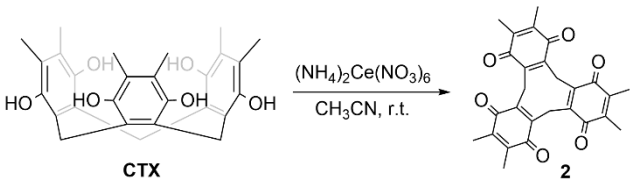


Fig. S6 HR-ESI-MS spectra of compound **1**.



Synthesis of compound 2

CTX (0.1 g, 0.22 mmol) was dissolved in CH_3CN (20 mL) in a 50 mL round-bottom flask and ceric ammonium nitrate (0.9 g, 1.69 mmol) was added. The reaction mixture was stirred at room temperature for 1 h. After the solvent was evaporated, the solid was washed with water by sonication to produce compound **2** as a yellow solid (0.088 g, 0.2 mmol, 89%). ^{1}H NMR (400 MHz, $CDCl_3$, 298 K) δ (ppm) = 3.88 (s, 6H), 2.03 (s, 18H). ^{13}C NMR (100 MHz, $CDCl_3$, 298 K) δ (ppm) = 185.9, 141.2, 141.0, 23.4, 12.8. HR-ESI-MS: m/z $[M+Na]^+$ calcd for $[C_{27}H_{24}O_6Na]^+$ 467.1466, found 467.1479.

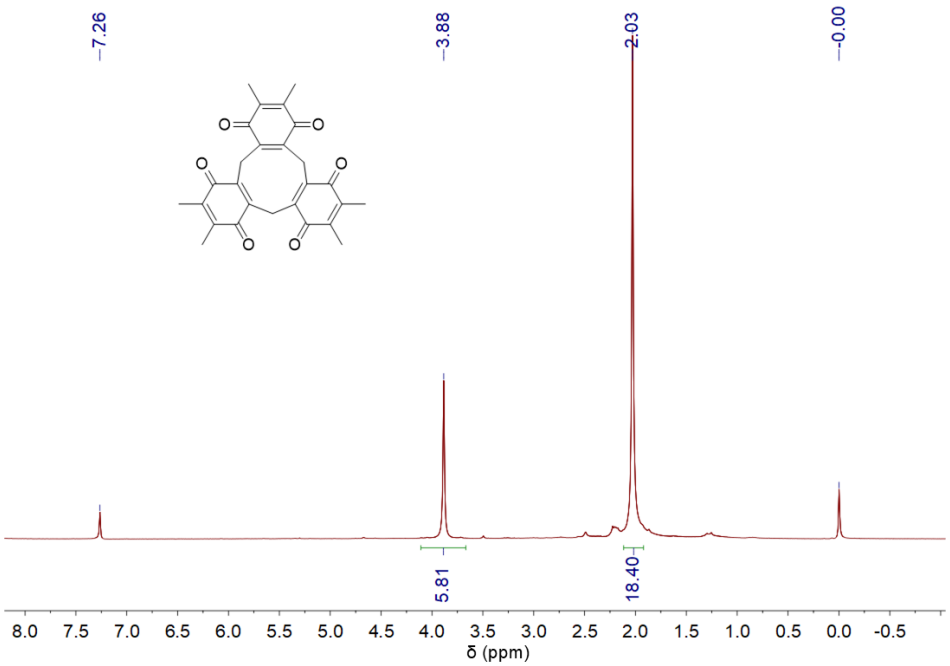


Fig. S7 ^{1}H NMR spectrum (400 MHz, $CDCl_3$, 298 K) of compound **2**.

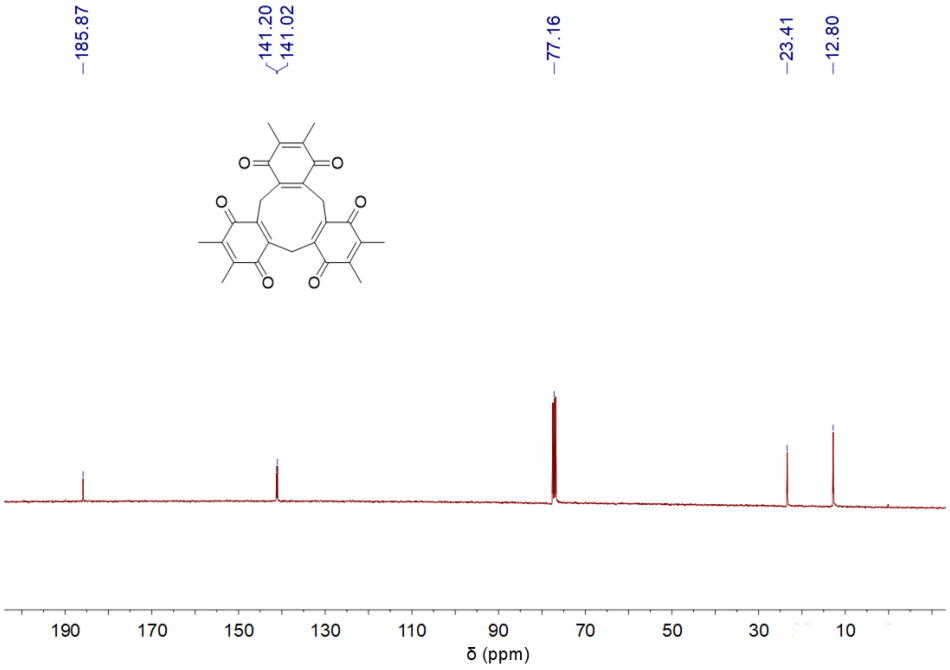


Fig. S8 ^{13}C NMR spectrum (100 MHz, $CDCl_3$, 298 K) of compound **2**.

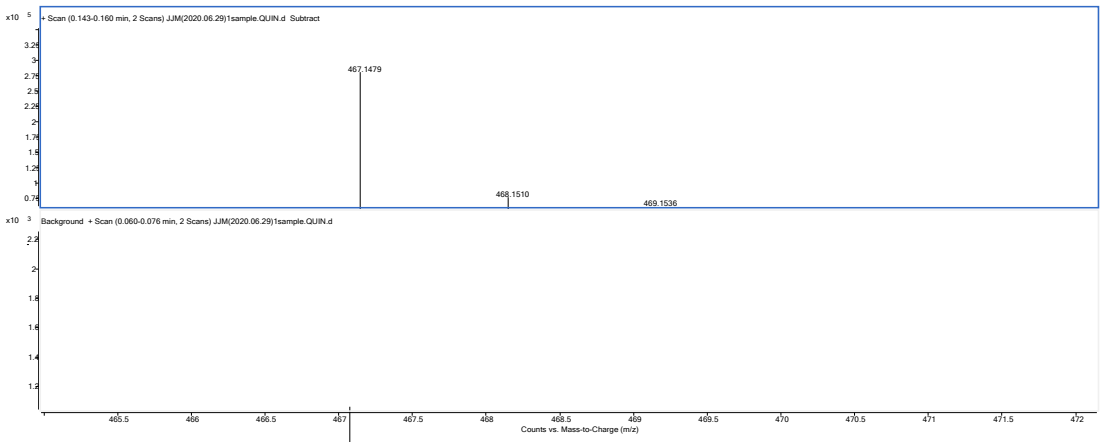
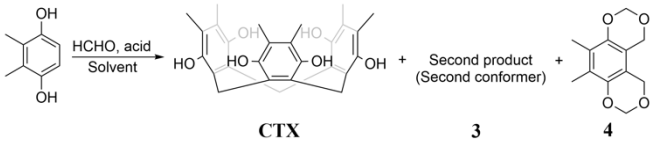


Fig. S9 HR-ESI-MS spectra of compound **2**.

Optimization of Reaction Conditions of Synthesis of CTX



CTX **3** **4**

Table S1 Optimization of Reaction Conditions of Synthesis of **CTX** [a, b]

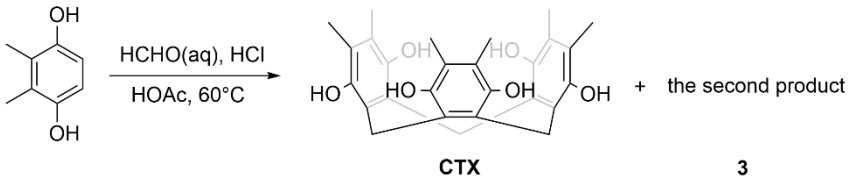
Entry	Formald-ehyde (eq)	Solvent	Acid	Temp. (°C)	Yield (%)		
					CTX	**3**	**4**
1	1	HOAc	HCl	60	68	25	0
2[c]	1	HOAc	HCl	60	45	37	0
3	5	HOAc	HCl	60	77	0	0
4	30	HOAc	HCl	60	83	0	0
5	30[d]	HOAc	HCl	60	0	0	51
6	30[e]	HOAc	HCl	60	0	0	58
7	30	CH_3OH	HCl	60	43	34	0
8	30	C_2H_5OH	HCl	60	78	0	0
9	30	DMSO	HCl	60	36	11	0
10	30	DMF	HCl	60	28	17	0
11	30	THF	HCl	60	41	6	0
12	30	HOAc	H_2SO_4	60	62	0	0
13	30	HOAc	HBr	60	78	0	0
14	30	HOAc	TFA	60	59	0	0
15	30	HOAc	TS	60	64	0	0
16	30	HOAc	—	60	0	0	0
17	30	HOAc	HCl	40	69	13	0
18	30	HOAc	HCl	110	0	0	0

a: Unless otherwise specified, all reactions were carried out with substrate (0.72 mmol), acid (7.2 mmol), and aqueous formaldehyde solution in solvent (3.0 mL) at indicated temperature for 1h. b: Yields were determined by ^{1}H NMR analysis of the crude reaction mixtures using 1,1,2,2-tetrachloroethane as the internal standard. c: It is based on a typical procedure for the synthesis of the mixture of **CTX** and the second product **3** described in page S10. d: Trioxane was employed. e: Paraformaldehyde was employed.

We started the optimization for the synthesis of **CTX**, and the corresponding results are shown in Table S1. Firstly, by using 1.0 eq formaldehyde instead of previous 30 eq, the synthetic reaction was carried out with *o*-xylohydroquinone (0.14 M) in HOAc (entry 1) and *o*-xylohydroquinone (0.75 M) in HOAc (entry 2), respectively, at 60 °C catalyzed by HCl, and then the obtained products were investigated by ^{1}H NMR spectroscopy. Based on the ^{1}H NMR spectra of both reaction products, it seemed that a mixture of **CTX** and second product were similarly obtained in each reaction, where more of second product in entry 2 was obtained than in entry 1. ^{1}H NMR spectrum of the mixture from entry 2 was shown in Figure 1C and S10, and it indicated that besides one set of signals corresponding to the expected crown-shaped **CTX**, there was the other set of signals from the second product, which showed one single peak at 2.07 ppm and one single peak at 3.97 ppm. Moreover, based on the integration of protons of these peaks, the second product might be another type of cyclic trimer, which could correspond to three possible compounds: second conformer of **CTX**, partially hydroquinone-oxidized product, or fully hydroquinone-oxidized product, owing to the possible oxidation of hydroquinone units, or it might be other cyclic oligomer, such as cyclic tetramer. Since the resulting mixture from entry 2 could not be separated, due to the poor solubility, it was then directly investigated by ^{13}C NMR spectroscopy. The ^{13}C NMR spectrum also showed clearly and exactly two sets of signals, one of which was corresponding to expected crown-shaped **CTX**, the other of which was very similar as **CTX**'s signals with only slight difference (Figure S11). More importantly, no carbonyl functional groups of quinone units were observed in ^{13}C NMR spectrum, which obviously eliminated the possibility of partially and fully hydroquinone-oxidized product. In order to further confirm its exact structure, the resulting mixture (entry 2) was directly and fully oxidized by **CAN**, which disclosed that only one pure quinone derivative **2** was obtained. Therefore, the possibility of other cyclic oligomers was also eliminated. Consequently, all of above results strongly indicated that the second product in the mixture from entry 2 is still a trimeric macrocycle and is much possibly the second conformer of **CTX**, which is saddle or twisted conformation.

Next, we tried the reactions with trioxane and paraformaldehyde, in which, surprisingly, the

third type of product was obtained as the major product instead of **CTX** (entries 5−6). The third product was then identified as compound **4**. Such product could be often observed in the reaction between phenol derivative and formaldehyde.[S1] With the use of aqueous formaldehyde solution, different solvents in the reaction (entries 7−11) were screened, and it was found that HOAc gave best yields with high purity. Other kinds of acids including sulfuric acid, hydrobromic acid, trifluoroacetic acid, and p-toluenesulfonic acid were also examined (entries 12−15), in which **CTX** was obtained with moderate yields in most cases. When the reaction was carried out in the absence of any strong acid as catalyst, no reaction occurred (entry 16). Additionally, a screen of reaction temperature was also investigated (entries 17−18). Eventually, to synthesize pure **CTX** with the single crown conformation, the optimized reaction conditions are: *o*-xylohydroquinone reacts with aqueous formaldehyde solution (30 eq) in HOAc, catalyzed by HCl (10 eq) at 60 °C for 1h (entry 4).



A typical procedure for the synthesis of the mixture of CTX and the second product 3

To a suspension of 2,3-dimethylbenzene-1,4-diol (0.69 g, 5 mmol) in a mixture of AcOH (5 mL) and hydrochloric acid (37% aq, 1.3 mL) at 60°C in oil bath, aqueous formaldehyde solution (40%, 0.34 mL, 5 mmol) was added dropwise. Large amounts of solids were precipitated from the solvent within 1 min until the stirring bar can't rotate any more. Then the reaction continued for another 15min. Upon completion, the cooled reaction mixture was poured into water (100 mL) and the obtained precipitate was filtered, dried overnight in vacuo to give the titled mixture (0.66 g, 1.47 mmol, 88%). ^{1}H NMR (400 MHz, DMSO-d_6, 298 K) for **CTX**: δ (ppm) = 9.78 (s, 6H), 4.65 (d, J = 14.8 Hz, 3H), 3.97 (d, J = 14.8 Hz, 3H), 2.07 (s, 18H); for compound **3**: δ (ppm) = 3.97 (s, 5H), 2.05(s, 15H). ^{13}C NMR (100 MHz, DMSO-d_6, 298 K) for **CTX**: δ (ppm) = 145.5, 125.1, 123.4, 25.3, 13.2; for compound **3**: δ (ppm) = 145.3, 124.1, 122.2, 24.1, 13.0.

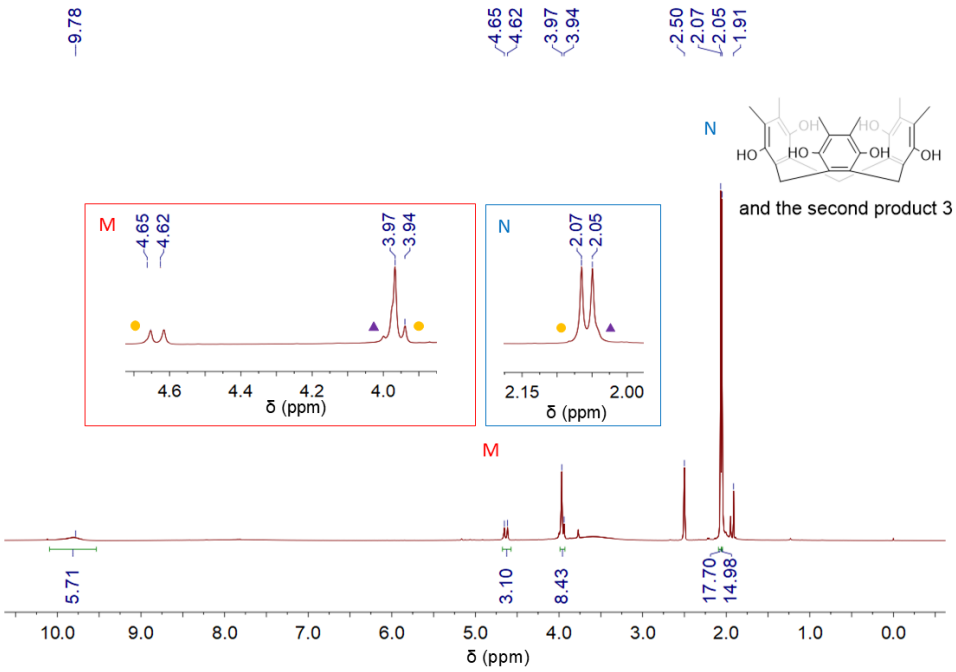


Fig. S10 ^{1}H NMR spectrum (400 MHz, DMSO-d_6, 298 K) of the mixture of **CTX** and second product **3**.

The yellow circle and purple triangle represent **CTX** and compound **3**, respectively.

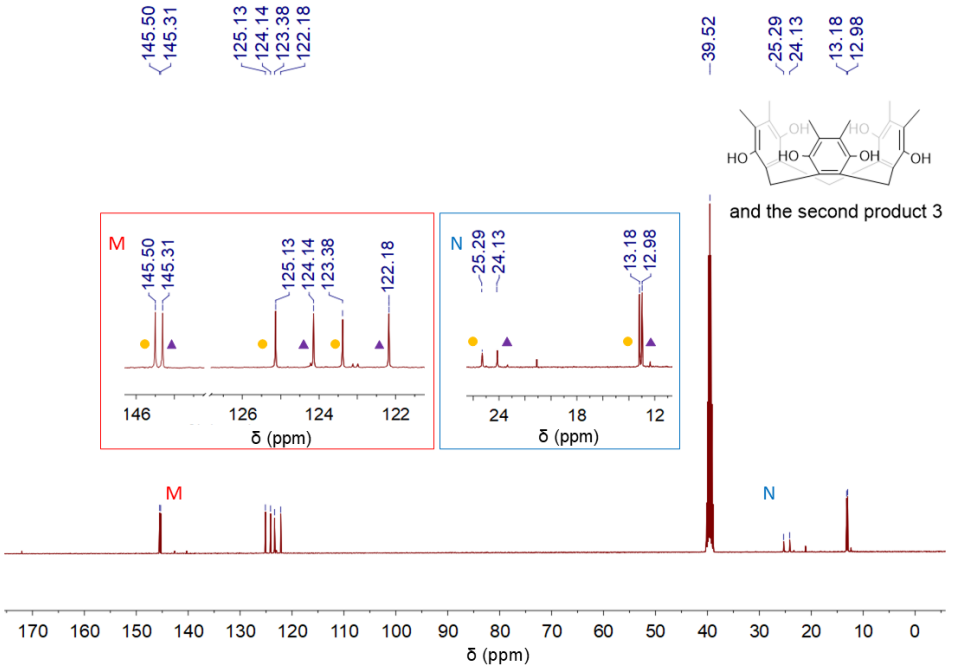


Fig. S11 ^{13}C NMR spectrum (100 MHz, DMSO-d_6, 298 K) of the mixture of **CTX** and second product **3**.

The yellow circle and purple triangle represent **CTX** and compound **3**, respectively.

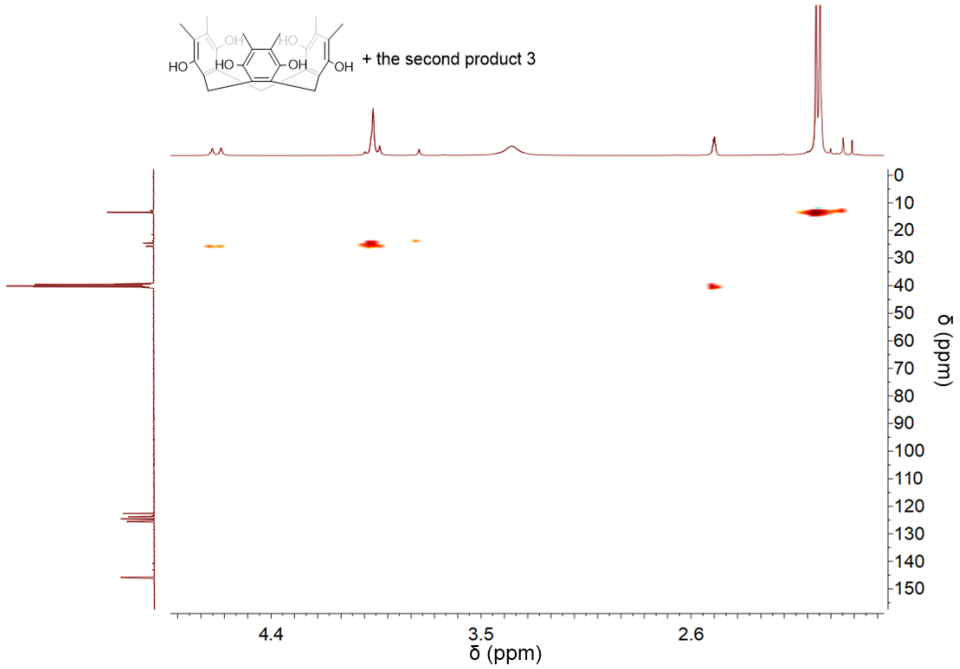


Fig. S12 HSQC spectrum (400 MHz, DMSO-d_6, 298 K) of the mixture of **CTX** and second product **3**.

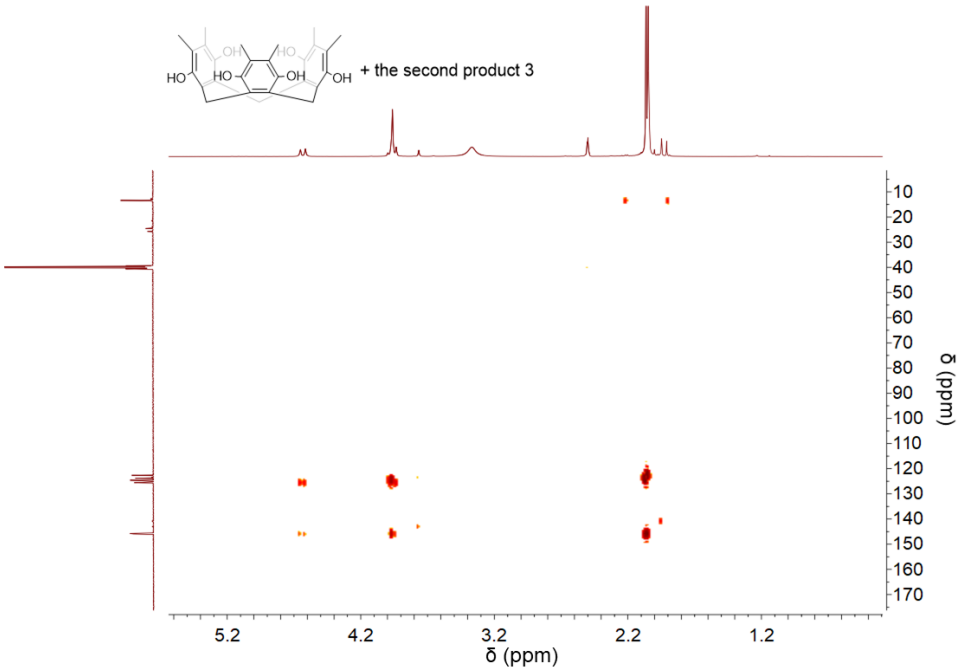


Fig. S13 HMBC spectrum (400 MHz, DMSO-d_6, 298 K) of the mixture of **CTX** and second product **3**.

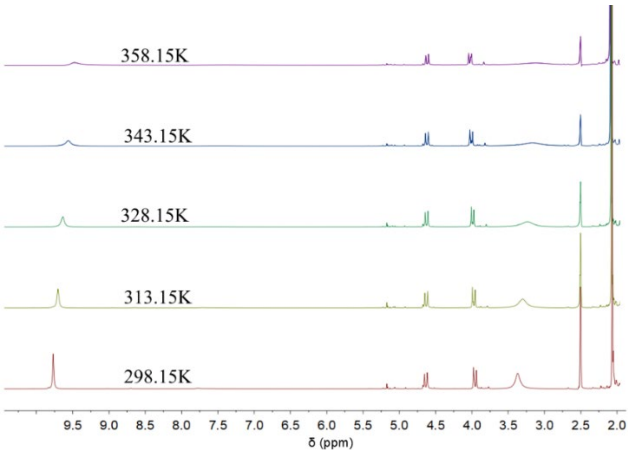


Fig. S14 Variable temperature ^{1}H NMR spectrum (400 MHz, DMSO-d_6, 298 K) of pure **CTX** from 298.15K to 358.15K.

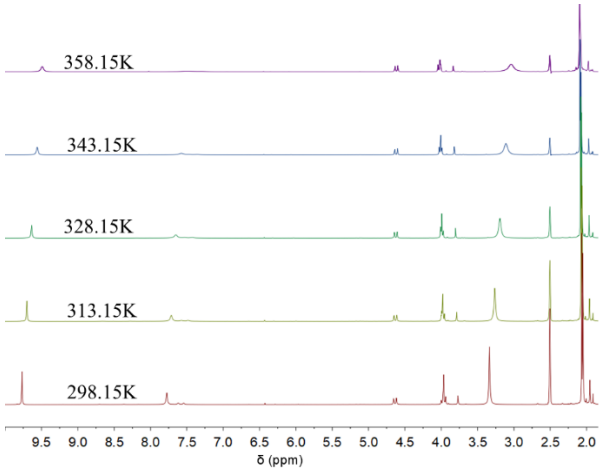


Fig. S15 Variable temperature ^{1}H NMR spectrum (400 MHz, DMSO-d_6, 298 K) of mixture of **CTX** (crown and twisted/saddle conformers) from 298.15K to 358.15K.

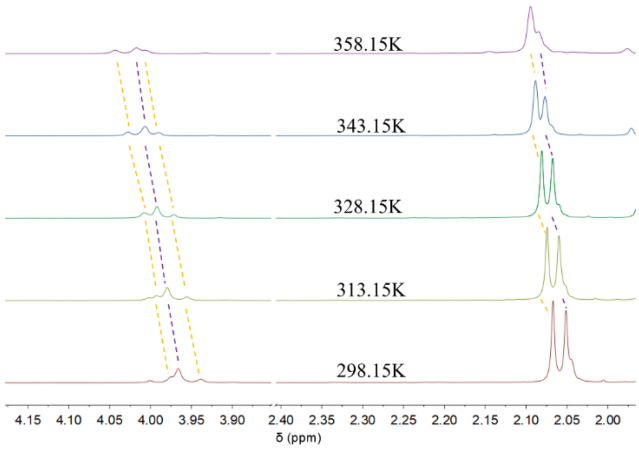
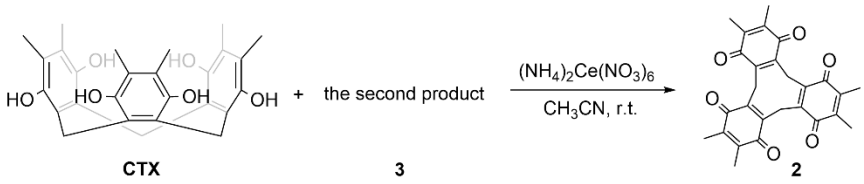
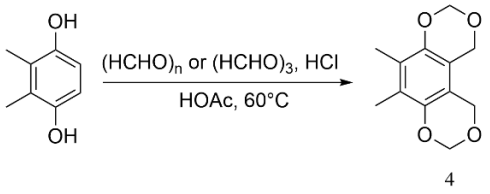


Fig. S16 Part of variable temperature ^{1}H NMR spectrum (400 MHz, DMSO-d_6, 298 K) of mixture of **CTX** (crown and twisted/saddle conformers) from 298.15K to 358.15K. Yellow and purple dash line points to crown and twisted/saddle conformers respectively.



Synthesis of compound 2 from the mixture of CTX and 3

All procedures were the same as the procedure for the synthesis of compound **2** above expect for the reactant is the mixture of **CTX** and **3** instead of the pure **CTX**. However, the NMR data of the product we obtained was exact the same as that of compound **2** above. Combined with the NMR data of the mixture of **CTX** and **3**, we inferred that compound **3** is another conformer of crown-shaped **CTX**.



Synthesis of compound 4

All procedures were the same as the general procedure for the synthesis of **CTX** expect for trioxane or paraformaldehyde employed instead of aqueous formaldehyde solution. In these two cases, we obtained compound **4** instead of **CTX**. ^{1}H NMR (400 MHz, DMSO-d_6, 298 K) δ (ppm) = 5.17 (s, 4H), 4.66 (s, 4H), 2.03(s, 6H). ^{13}C NMR (100 MHz, DMSO-d_6, 298 K) δ (ppm) = 144.2, 122.9, 114.7, 90.4, 62.7,11.0.

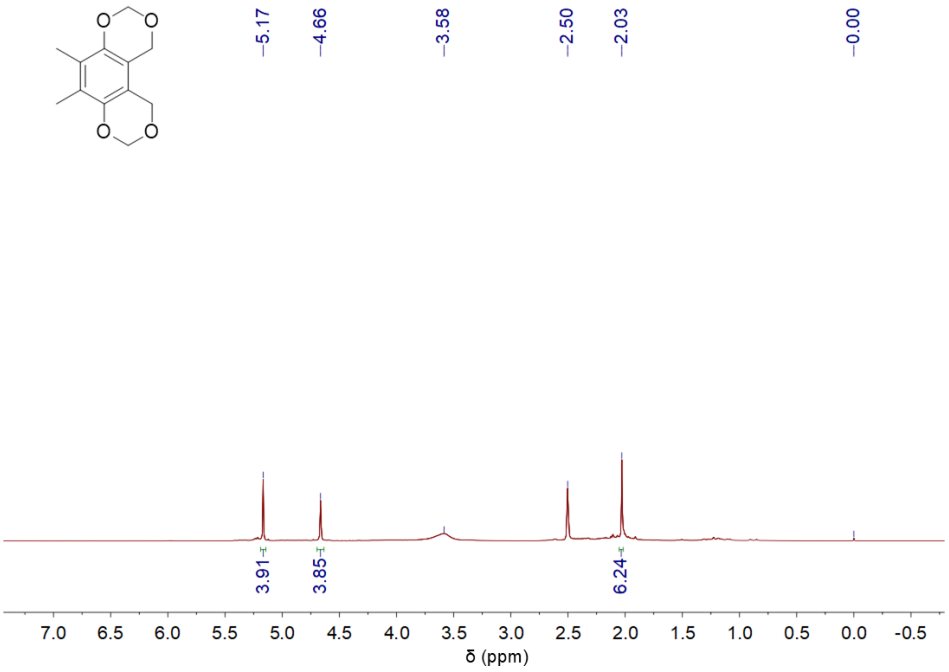


Fig. S17 ^{1}H NMR spectrum (400 MHz, DMSO-d_6, 298 K) of compound **4**.

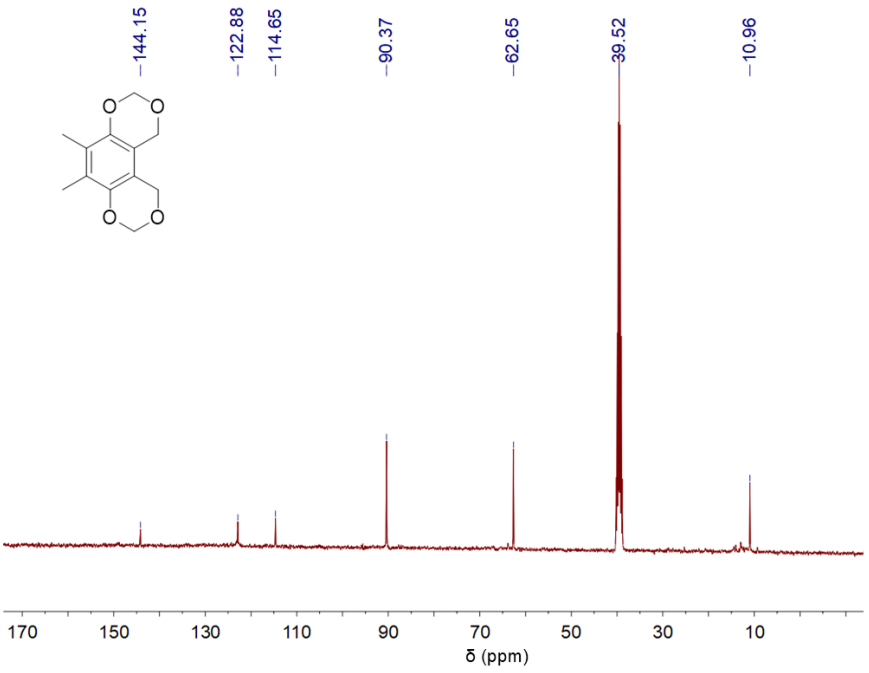
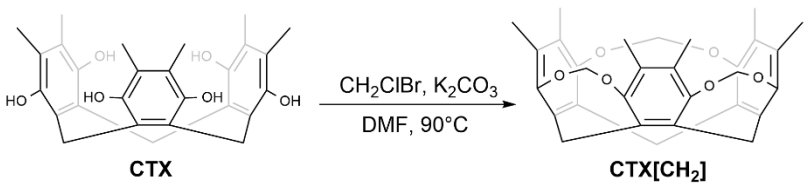


Fig. S18 ^{13}C NMR spectrum (100 MHz, DMSO-d_6, 298 K) of compound **4**.



Synthesis of CTX[CH_2]

CTX (0.6 g, 1.33 mmol) and bromochloromethane (1.32 ml, 19.80 mmol) was heated at 90°C in oil bath in the presence of K_2CO_3 (2.2 g, 15.94 mmol) in anhydrous DMF (10 mL) for 40h in a Schlenk tube. After the reaction mixture was cooled to room temperature, the solid was filtered and the filtrate was concentrated under vacuum. The obtained crude product was then purified by dissolved in 20 ml CH_2Cl_2 and then added to 120 mL petroleum ether. The precipitate was filtered off and the filtrate was concentrated under vacuum to give **CTX[CH_2]** as a light yellow solid (0.52 g, 1.07 mmol, 80%). ^{1}H NMR (400 MHz, $CDCl_3$, 298 K) δ (ppm) =6.03 (d, J = 6.8 Hz, 3H), 4.60 (d, J = 13.6 Hz, 3H), 4.48 (d, J = 13.6 Hz, 3H), 4.43 (d, J = 6.8 Hz, 3H), 2.07 (s, 18H). ^{13}C NMR (100 MHz, $CDCl_3$, 298 K) δ (ppm) = 152.8, 133.2, 129.0, 99.6, 27.4, 13.4. HR-ESI-MS: m/z [M +Na]$^+$ calcd for [$C_{30}H_{30}O_6$ Na]$^+$ 509.1935, found 509.1964.

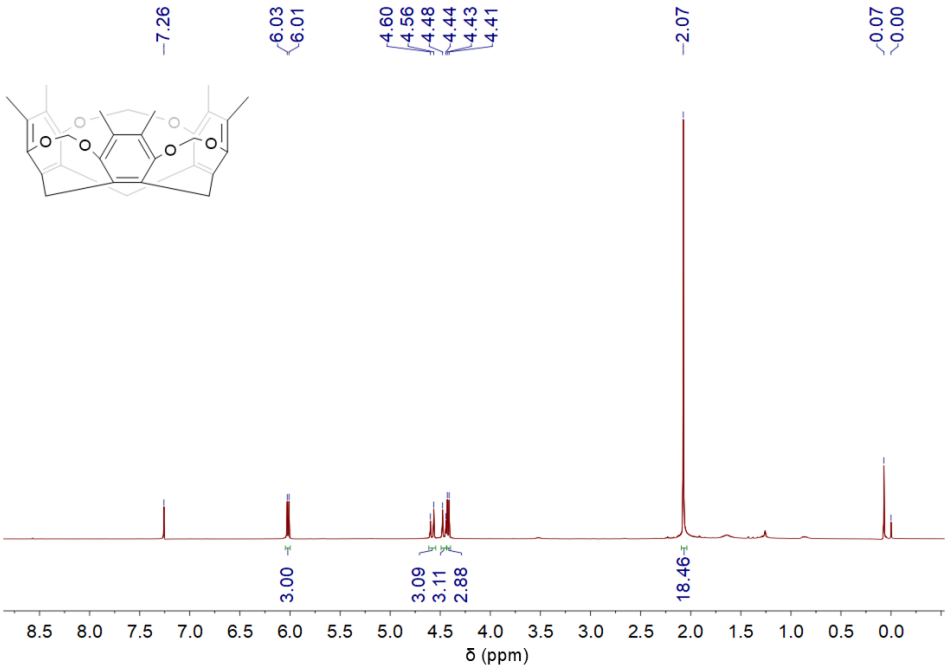


Fig. S19 ^{1}H NMR spectrum (400 MHz, $CDCl_3$, 298 K) of **CTX[CH_2]**.

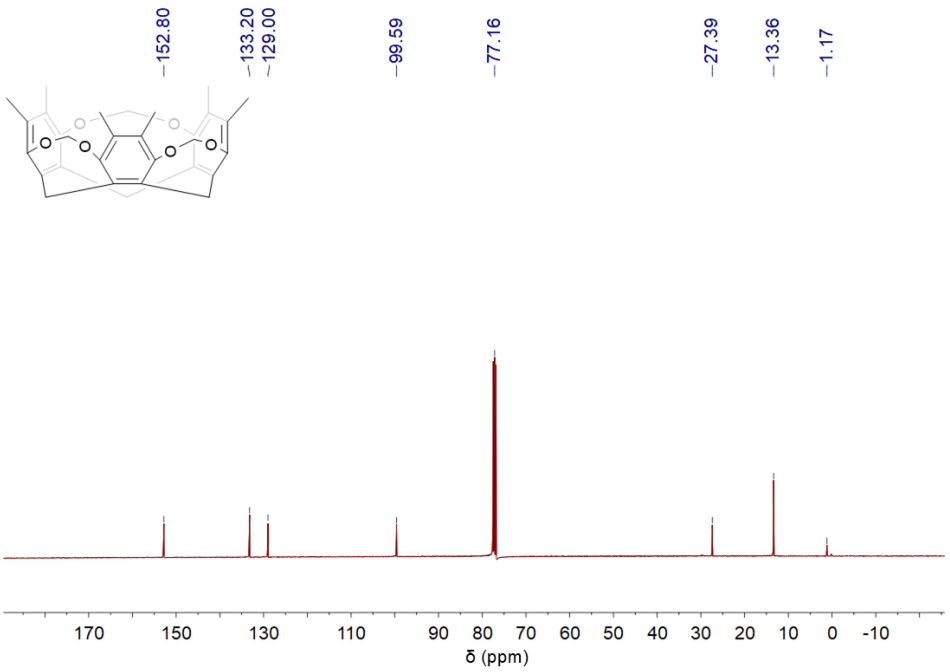


Fig. S20 ^{13}C NMR spectrum (100 MHz, $CDCl_3$, 298 K) of **CTX[CH$_2$]**.

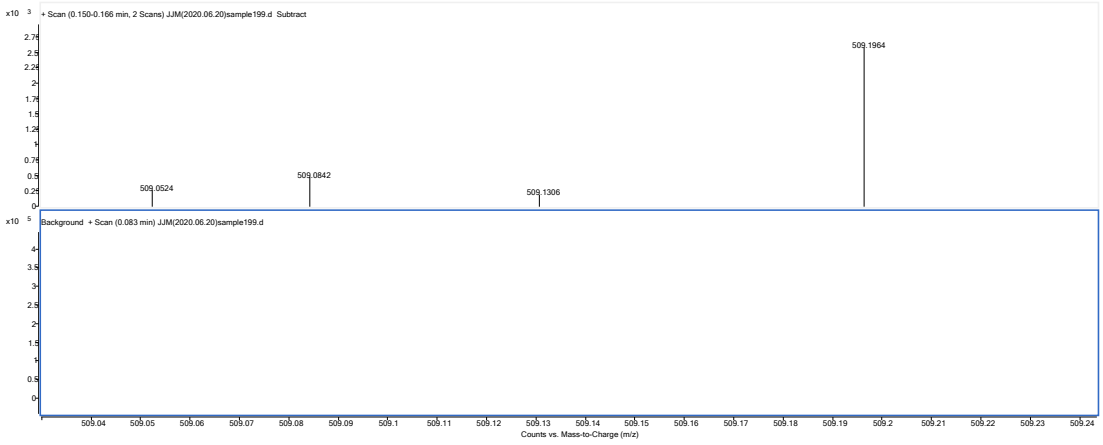
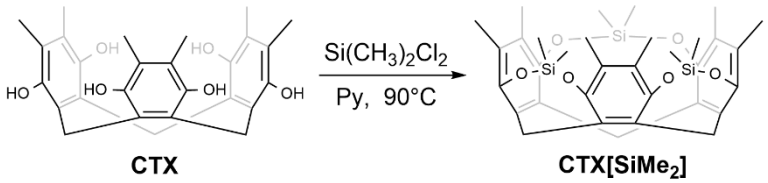


Fig. S21 HR-ESI-MS spectra of **CTX[CH$_2$]**.



Synthesis of compound CTX[SiMe$_2$]

CTX (0.2 g, 0.44 mmol) was dissolved in anhydrous pyridine and dichlorodimethylsilane (0.5 mL, 4 mmol) was added in an ice bath under argon atmosphere. Then the reaction mixture was heated at 90°C in oil bath for 5h. After the reaction mixture was cooled to room temperature and

removed the solvent under reduced pressure, anhydrous methanol was added, then the solid was filtered and washed two times by anhydrous methanol to give **CTX[SiMe$_2$]** as a pale yellow solid (0.17 g, 0.27 mmol, 61%). ^{1}H NMR (400 MHz, $CDCl_3$, 298 K) δ (ppm) =4.49 (d, J = 14.4 Hz, 3H), 4.42(d, J = 14.4 Hz, 3H), 2.09(s, 18H). 0.57(s, 9H), -0.08(s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$, 298 K) δ (ppm) = 146.2, 129.3, 126.7, 26.9, 13.8, -2.4, -4.1. HR-ESI-MS: m/z [M +H] $^+$ calcd for $[C_{33}H_{43}O_6Si_3]^+$ 619.2362, found 619.2391.

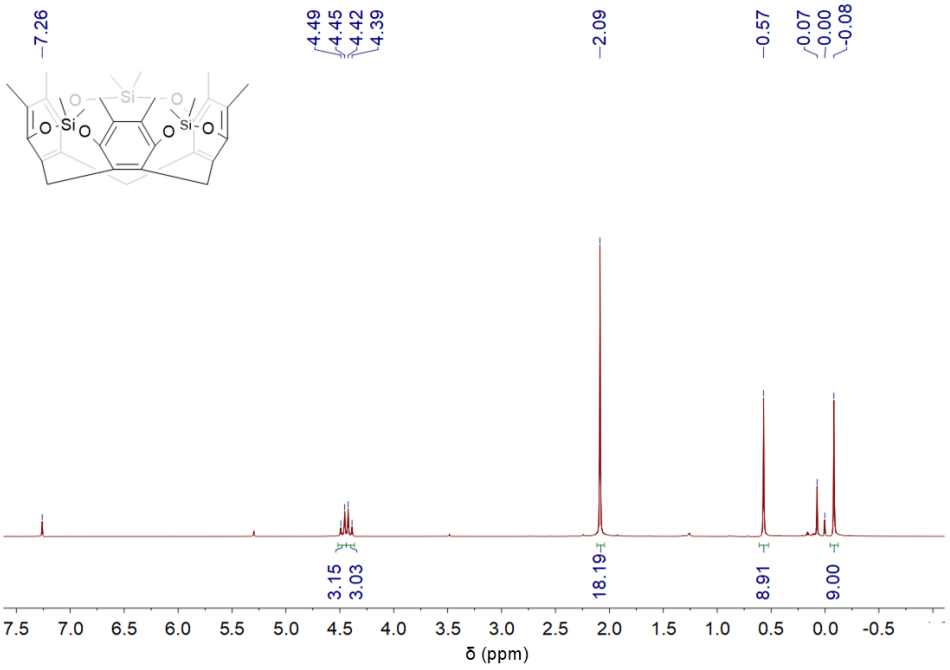


Fig. S22 ^{1}H NMR spectrum (400 MHz, $CDCl_3$, 298 K) of **CTX[SiMe$_2$]**.

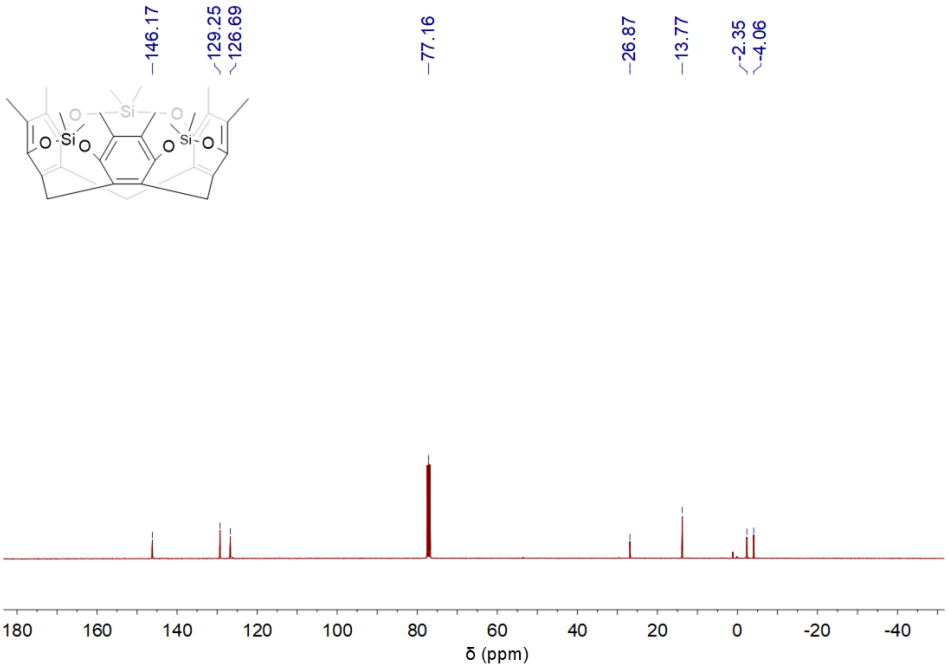


Fig. S23 ^{13}C NMR spectrum (100 MHz, $CDCl_3$, 298 K) of **CTX[SiMe$_2$]**.

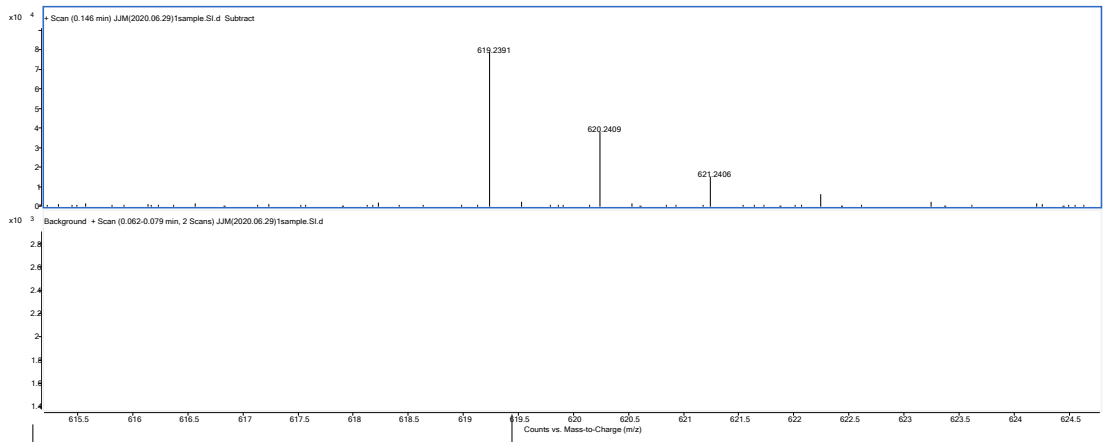
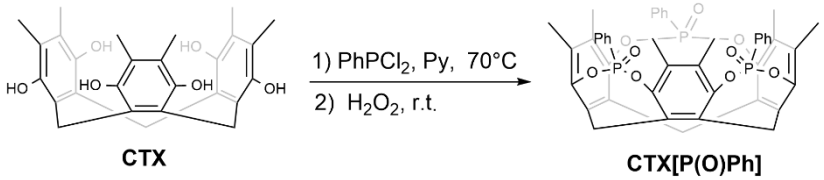


Fig. S24 HR-ESI-MS spectra of **CTX[SiMe$_2$]**.



Synthesis of CTX[P(O)Ph]

To a solution of **CTX** (0.3 g, 0.66 mmol) in dry pyridine (15 mL), dichlorophenylphosphine (0.45 ml, 3.3 mmol) were added under argon atmosphere. The solution was stirred at 70°C in oil bath for 3h. Afterwards, the mixture was cooled to room temperature and H_2O_2 (30% aq, 9 mL) was added. The mixture was stirred for additional 1h at room temperature, quenched in water and filtered. The crude product was purified by silica gel chromatography using CH_2Cl_2/CH_3OH (40:1, v/v) as the eluent to afford **CTX[P(O)Ph]** as a white solid (0.35 g, 0.39 mmol, 64%).^{1}H NMR (400 MHz, $CDCl_3$, 298 K) δ (ppm) =8.20-8.17 (m, 6H), 7.72-7.68(m, 3H), 7.63-7.59 (m, 6H), 4.72(d, J = 14.4 Hz, 3H), 4.63(d, J = 14 Hz, 3H), 2.21 (s, 18H). ^{13}C NMR (100 MHz, $CDCl_3$, 298 K) δ (ppm) = 144.9 (d, $J_{p,c}$ = 9 Hz), 133.4, 131.8 (d, $J_{p,c}$ = 10 Hz), 130.6 (d, $J_{p,c}$ = 3 Hz), 129.3, 129.0 (d, $J_{p,c}$ = 16 Hz), 128.0 (d, $J_{p,c}$ = 200 Hz) 26.9, 14.3. ^{31}P NMR (162 MHz, $CDCl_3$, 298 K): δ(ppm) 9.33 (s). HR-ESI-MS: m/z $[M + Na]^+$ calcd for $[C_{45}H_{39}O_9P_3Na]^+$ 839.1700, found 839.1726.

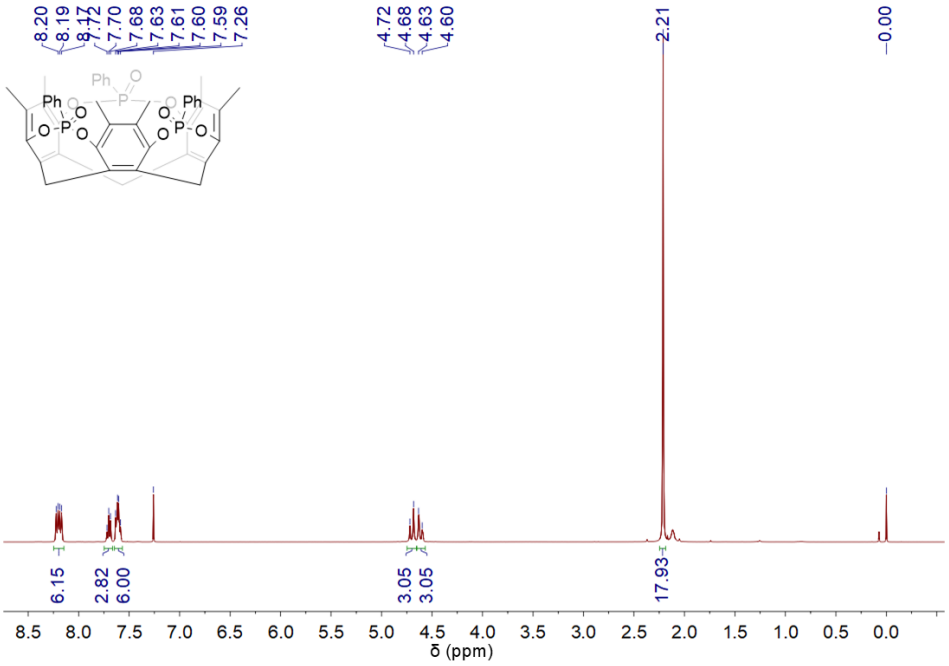


Fig. S25 ^{1}H NMR spectrum (400 MHz, $CDCl_3$, 298 K) of **CTX[P(O)Ph]**.

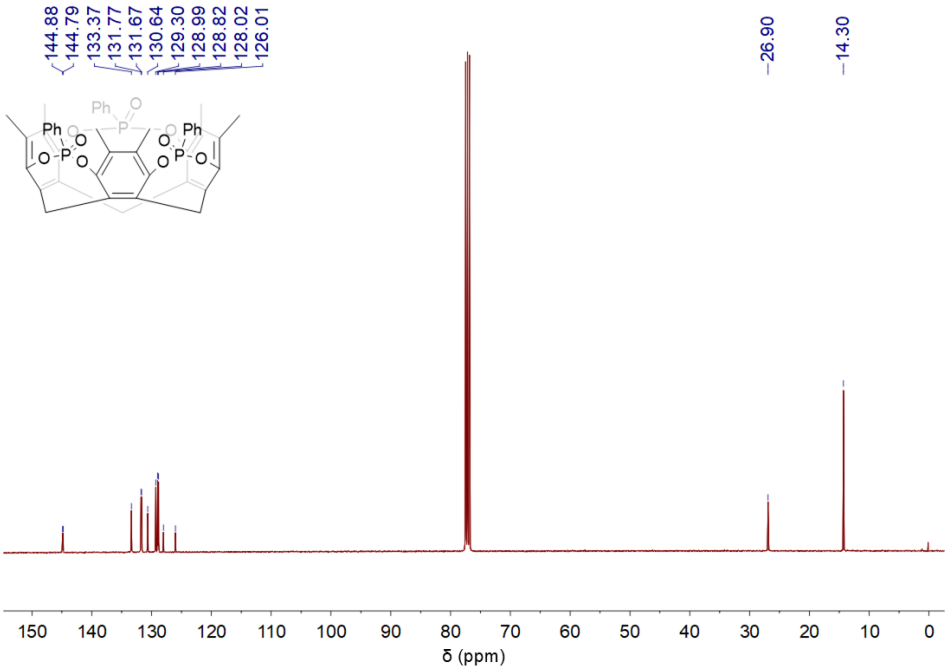


Fig. S26 ^{13}C NMR spectrum (100 MHz, $CDCl_3$, 298 K) of **CTX[P(O)Ph]**.

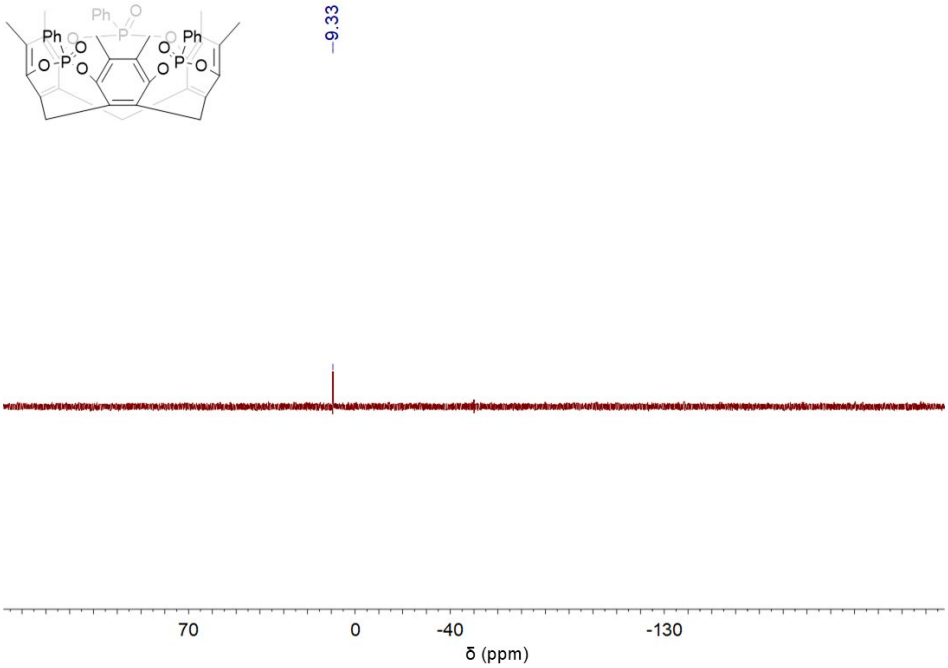


Fig. S27 ^{31}P NMR spectrum (162 MHz, $CDCl_3$, 298 K) of **CTX[P(O)Ph]**.

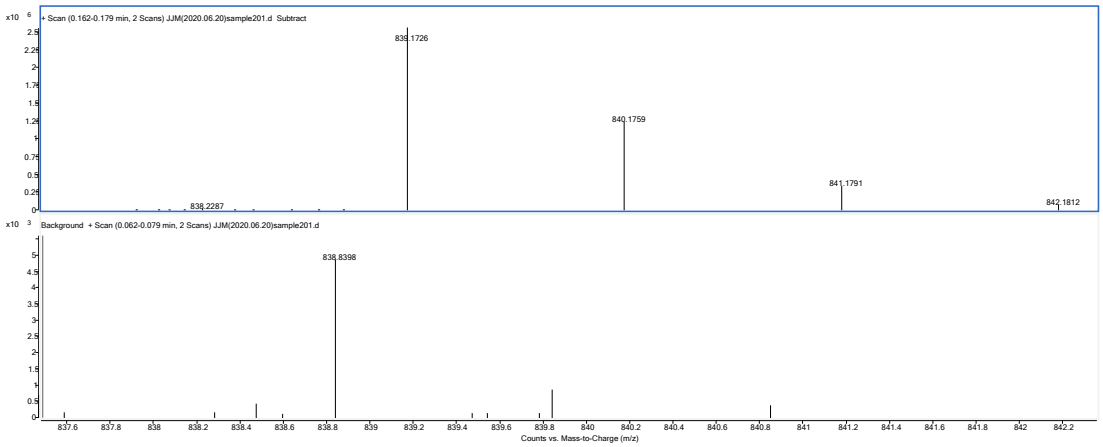
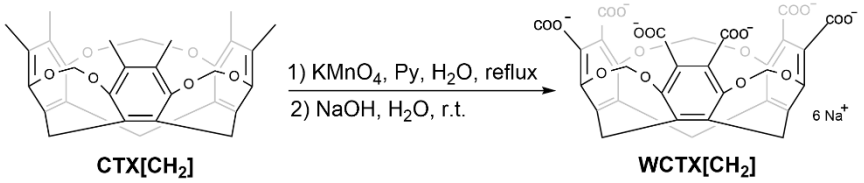


Fig. S28 HR-ESI-MS spectra of **CTX[P(O)Ph]**.



Synthesis of WCTX[CH_2]

To a refluxing solution of **CTX[CH_2]** (0.49 g, 1.0 mmol) in a mixture of pyridine (16 mL) and H_2O (12 mL), was added $KMnO_4$ (8.5 g, 54.0 mmol) portionwise, then the reaction mixture was refluxed at 100℃ in oil bath for 4h. After cooling to room temperature, the precipitated MnO_2 was

filtered off and washed with 1% aq. solution of KOH. The filtrate was concentrated and then acidified to pH 1 with aq. 3 M HCl. The precipitated solid was collected by filtration and dried under vacuum at 60 °C for 1h. To the suspension of the white solid in H_2O, NaOH was weighed and added in a 1:6 ratio quantitively to give a homogeneous solution. The resulting solution was evaporated under reduced pressure to furnish **WCTX[CH$_2$]** as a white solid (0.30g, 0.37mmol, 37%). ^{1}H NMR (400 MHz, D_2O, 298 K) δ (ppm) =5.87 (d, *J* = 7.6 Hz, 3H), 4.74 (d, *J* = 13.6 Hz, 3H), 4.67 (d, *J* = 7.6 Hz, 3H), 4.50(d, *J* = 14.0 Hz, 3H). ^{13}C NMR (100 MHz, D_2O, 298 K) δ (ppm) = 173.5, 149.5, 134.9, 131.4, 100.9, 26.6. HR-ESI-MS (in negative-ion mode): m/z [M - 2Na + K] $^-$ calcd for $[C_{30}H_{12}O_{18}Na_4K]^+$ 790.9256, found 790.9209.

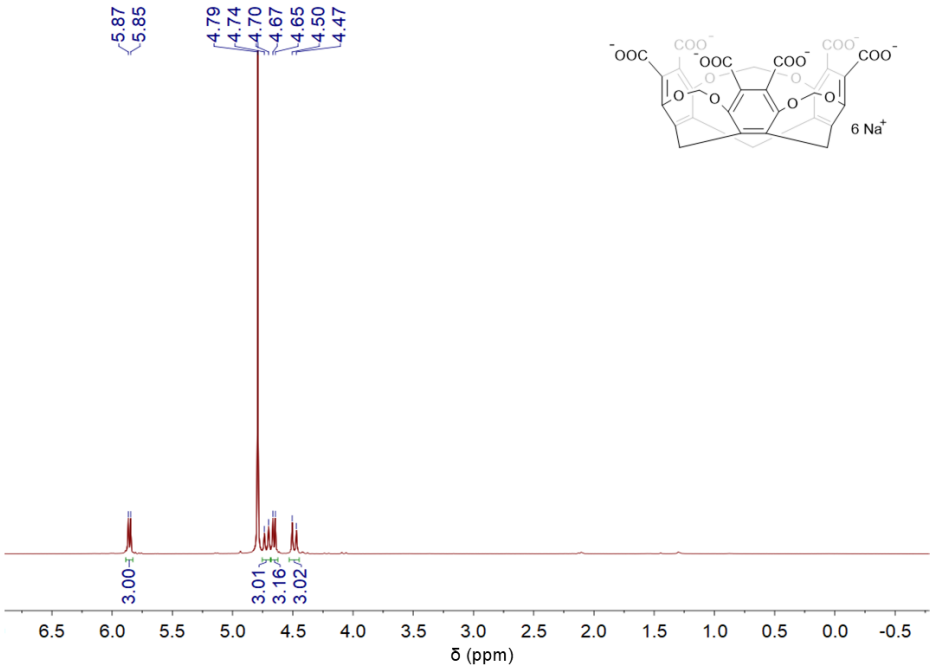


Fig. S29 ^{1}H NMR spectrum (400 MHz, D_2O, 298 K) of **WCTX[CH$_2$]**.

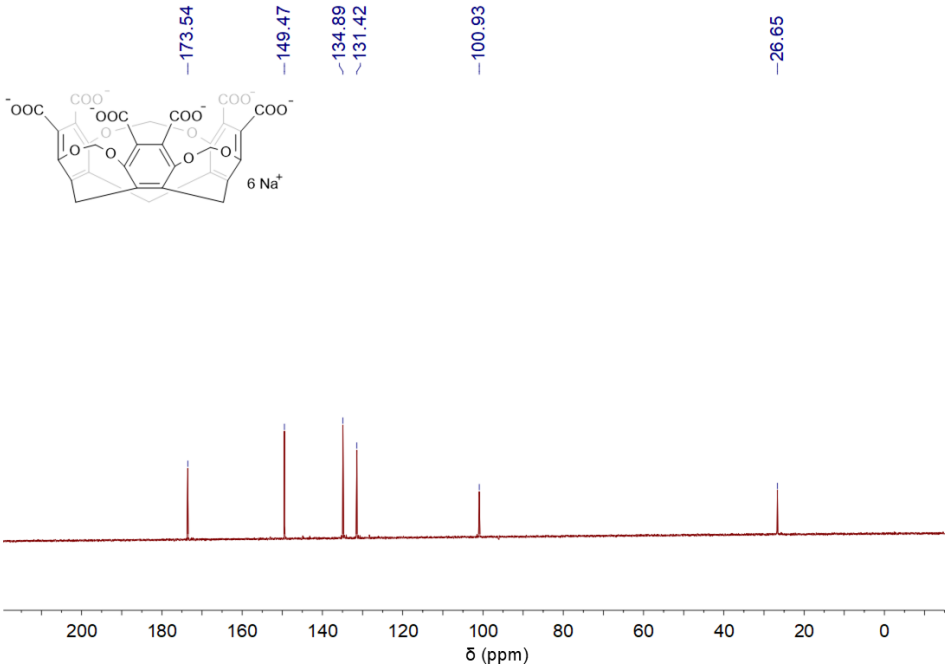


Fig. S30 ^{13}C NMR spectrum (100 MHz, D_2O, 298 K) of **WCTX[CH$_2$]**.

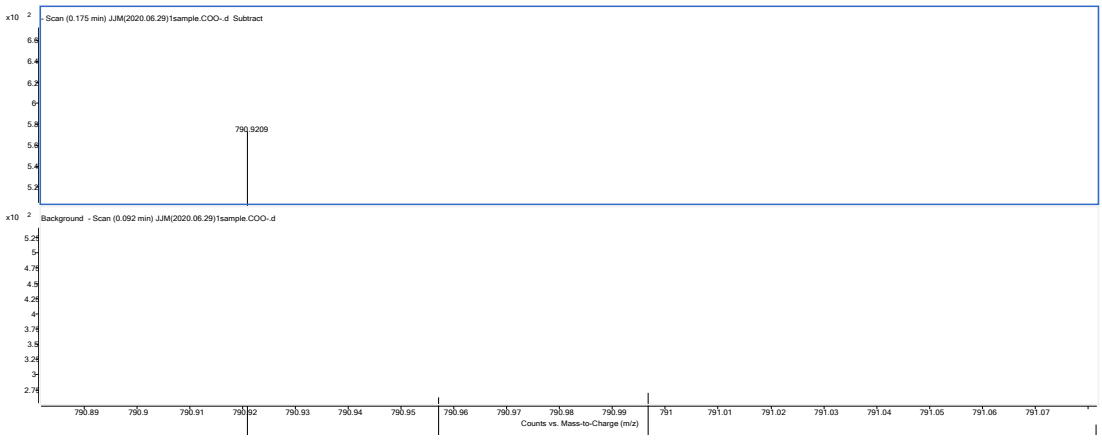


Fig. S31 HR-ESI-MS spectra of **WCTX[CH$_2$]**.

3. Host-guest interactions between H and G

Job plot of complex WCTX[CH$_2$]⊃G in water

(A) **(B)**

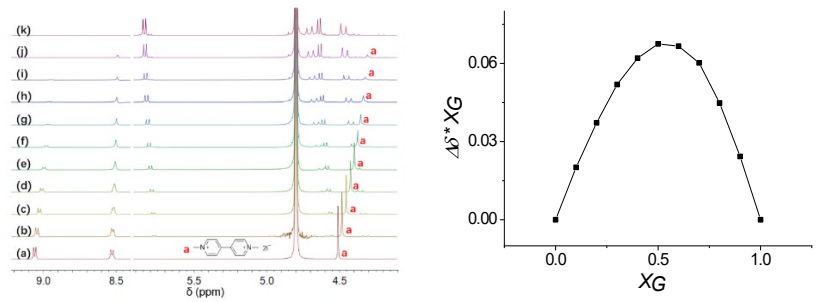


Fig. S32 (A) ^{1}H NMR spectrum (400 MHz, D_2O, 298 K) of complex **WCTX[CH$_2$]⊃G** with different concentrations of **WCTX[CH$_2$]** (mM): (a) 0.0, (b) 0.5, (c) 1.0, (d) 1.5, (e) 2.0, (f) 2.5, (g) 3.0, (h) 3.5, (i) 4.0, (j) 4.5, (k) 5.0 while [**WCTX[CH$_2$]**] + [**G**] = 5 mM. (B) Job plot of complex **WCTX[CH$_2$]⊃G** showing a 1:1 stoichiometry between **WCTX[CH$_2$]** and **G** by plotting the Δδ against the mole fraction of **G**.

Determination of the association constant (K_a) for WCTX[CH$_2$]⊃G complex in water

To determine the association constant between **WCTX[CH$_2$]** and **G**, ^{1}H NMR titrations were carried out in aqueous solution, which had a constant concentration of **G** (2.0 mM) and varying concentrations of **WCTX[CH$_2$]**. By a non-linear curve-fitting method, the association constant between **G** and **WCTX[CH$_2$]** was calculated. The non-linear curve-fitting was based on the following equation: $\Delta\delta = (\Delta\delta_\infty/[G]_0)(0.5[H]_0+0.5([G]_0+1/K_a)-(0.5([H]_0^2+(2[H]_0(1/K_a-[G]_0))+(1/K_a+[G]_0)^2)^{0.5}))$. Where Δδ is the chemical shift change of H_b on **G** at $[H]_0$, $\Delta\delta_\infty$ is the chemical shift change of H_b when the guest is completely complexed, $[G]_0$ is the fixed initial concentration of the guest (**G**), and $[H]_0$ is the varying concentrations of **WCTX[CH$_2$]**.

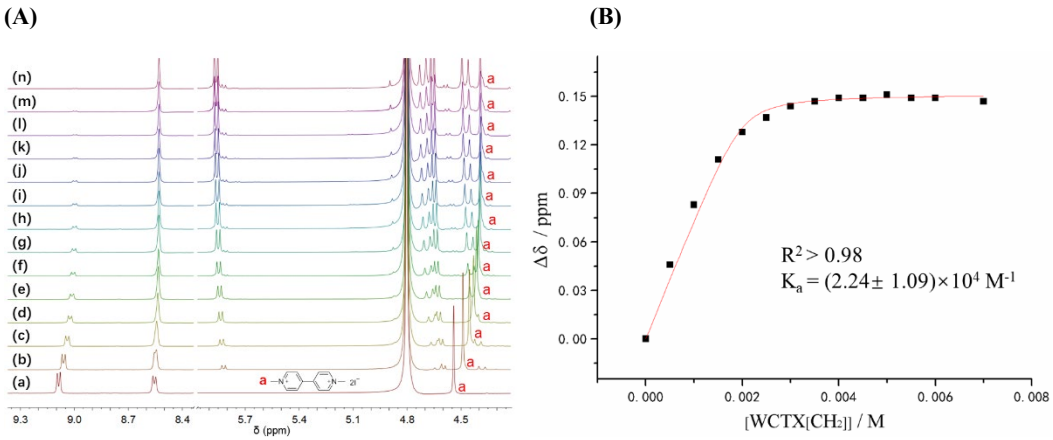


Fig. S33 (A) ^{1}H NMR spectra (400 MHz, D_2O, 298 K) of **G** at a constant concentration of 2.0 mM with different concentrations of **WCTX[CH$_2$]** (mM): (a) 0.0, (b) 0.5, (c) 1.0, (d) 1.5, (e) 2.0, (f) 2.5, (g) 3.0, (h) 3.5, (i) 4.0, (j) 4.5, (k) 5.0, (l) 5.5, (m) 6.0, (n) 7.0. (B) The chemical shift changes of H_a on **G** upon addition of **WCTX[CH$_2$]**. The red solid line was obtained from the non-linear curve-fitting using. The association constant (K_a) of **WCTX[CH$_2$]** and **G** was estimated to be about (2.24 ± 1.09) ×10^4 M^{-1}.

4. X-ray Crystallography Experimental, Data and Analysis

The crystal structures were determined by single-crystal X-ray analysis. Data collections were performed using a Bruker Apex Smart CCD diffractometer. The structures were solved with direct methods using the SHELXTL program[S2] and refined anisotropically with SHELXTL using full-matrix least-squares procedures. Crystallographic data and structural refinements parameters for all these crystals are given in Table S2 – S5.

Single crystals of compound **1** were obtained as colorless needles by slow evaporation of a mixed solvent of ethyl acetate and petroleum ether.

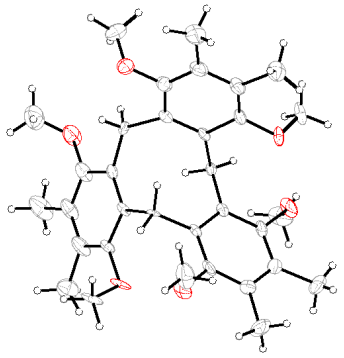


Fig. S34 X-ray structure of compound **1**. Thermal ellipsoids shown at 50% probability level.

Table S2 Crystal data and structure refinement for compound **1**

CCDC number	2020707
Empirical formula	$C_{66}H_{84}O_{12}$
Formula weight	1069.33
Temperature	296(2) K
Wavelength	0.71073 Å
Crystal system	monoclinic
Space group	$P2_1$
a	12.3747(19) Å
b	13.090(2) Å
c	17.605(3) Å
α	90°
β	90.106(7) °
γ	90°
Volume	2851.8(8) $Å^3$
Z	2
Density (calculated)	1.245 g/cm^3
Absorption coefficient	0.084 mm^{-1}
F (000)	1152.0
Crystal size	0.080 × 0.080 × 0.060 mm^3
Theta range for data collection	2.265 to 25.027°
Index ranges	-14<=h<=14 -15<=k<=15 -19<=l<=20
Reflections collected	20815
Independent reflections	9897 [R(int) = 0.0747]
Completeness to theta = 25.027°	99.8%
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	9897 / 1159 / 1045
Goodness-of-fit on F^2	1.013
Final R indices [I>2sigma(I)]	R1 = 0.1091, wR2 = 0.2672
R indices (all data)	R1 = 0.1599, wR2 = 0.3060
Largest diff. peak and hole	0.37 and -0.47 $e.Å^{-3}$

Single crystals of **CTX[CH$_2$]** were obtained as colorless needles by slow evaporation of a mixed solvent of methylene chloride and toluene.

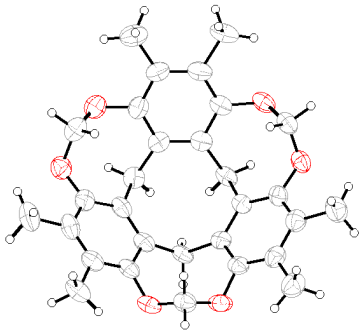


Fig. S35 X-ray structure of **CTX[CH$_2$]**. Thermal ellipsoids shown at 50% probability level.

Table S3 Crystal data and structure refinement for **CTX[CH$_2$]**

CCDC number	2020708
Empirical formula	$C_{60}H_{60}O_{12}$
Formula weight	973.08
Temperature	193(2) K
Wavelength	0.71073 Å
Crystal system	monoclinic
Space group	$P2_1/c$
a	22.521(4) Å
b	9.939(2) Å
c	22.841(5) Å
α	90°
β	112.881(5) °
γ	90°
Volume	4710.3(17) Å^3
Z	4
Density (calculated)	1.372 g/cm^3
Absorption coefficient	0.095 mm^{-1}
F (000)	2064.0
Crystal size	0.120 × 0.110 × 0.080 mm^3
Theta range for data collection	1.936 to 25.005°
Index ranges	-26<=h<=26, -11<=k<=10, -24<=l<=27
Reflections collected	29117
Independent reflections	8271 [R(int) = 0.0885]
Completeness to theta = 25.005°	99.7%
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	8271 / 0 / 662
Goodness-of-fit on F^2	1.081
Final R indices [I>2sigma(I)]	R1 = 0.1243, wR2 = 0.2457
R indices (all data)	R1 = 0.1899, wR2 = 0.2828
Largest diff. peak and hole	0.81 and -0.36 e.Å^{-3}

Single crystals of **CTX[P(O)Ph]** ⊃ acetone were obtained as colorless plates by slow evaporation of a mixed solvent of ethyl acetate and acetone.

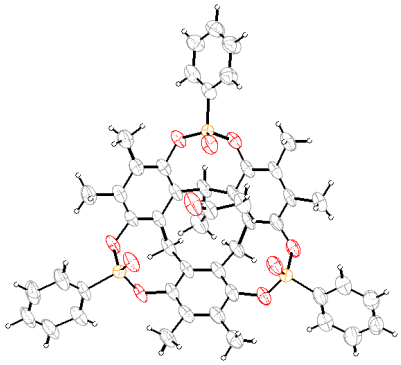


Fig. S36 X-ray structure of **CTX[P(O)Ph]** ⊃ acetone. Thermal ellipsoids shown at 50% probability level.

Table S4 Crystal data and structure refinement for **CTX[P(O)Ph]** ⊃ acetone

CCDC number	2020709
Empirical formula	$C_{48}H_{45}O_{10}P_3$
Formula weight	874.75
Temperature	193(2) K
Wavelength	1.34139 Å
Crystal system	monoclinic
Space group	$P2_1/n$
a	20.3643(16) Å
b	9.0027(7) Å
c	27.795(2) Å
α	90°
β	94.053(4) °
γ	90°
Volume	5083.0(7) $Å^3$
Z	4
Density (calculated)	1.143 g/cm^3
Absorption coefficient	0.974 mm^{-1}
F (000)	1832.0
Crystal size	0.120 × 0.110 × 0.090 mm^3
Theta range for data collection	2.265 to 54.503°
Index ranges	-24<=h<=24 -10<=k<=10 -33<=l<=33
Reflections collected	57367
Independent reflections	9301 [R(int) = 0.0982]
Completeness to theta = 54.503°	98.0%
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	9301 / 0 / 557
Goodness-of-fit on F^2	1.003
Final R indices [I>2sigma(I)]	R1 = 0.0674, wR2 = 0.1779
R indices (all data)	R1 = 0.0842, wR2 = 0.1905
Largest diff. peak and hole	0.45 and -0.51 $e.Å^{-3}$

Single crystals of **CTX[P(O)Ph]** ⊃ DMSO were obtained as colorless needles by slow evaporation of DMSO.

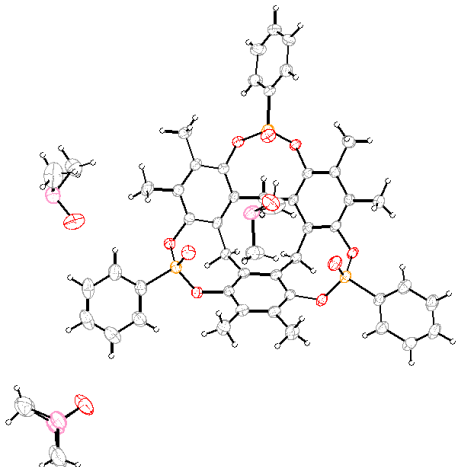


Fig. S37 X-ray structure of **CTX[P(O)Ph]** ⊃ DMSO. Thermal ellipsoids shown at 50% probability level.

Table S5 Crystal data and structure refinement for **CTX[P(O)Ph]** ⊃ DMSO

CCDC number	2024792
Empirical formula	$C_{51}H_{57}O_{12}P_3S_3$
Formula weight	1051.05
Temperature	190(2) K
Wavelength	1.34139 Å
Crystal system	monoclinic
Space group	$P2_1/n$
a	20.0545(6) Å
b	9.8273(3) Å
c	25.6769(8) Å
α	90°
β	90.7140(10) °
γ	90°
Volume	5060.1(3) $Å^3$
Z	4
Density (calculated)	1.380 g/cm^3
Absorption coefficient	1.805 mm^{-1}
F (000)	2208.0
Crystal size	0.200 × 0.180 × 0.180 mm^3
Theta range for data collection	2.418 to 54.02°
Index ranges	-23<=h<=24 -11<=k<=8 -29<=l<=30
Reflections collected	38159
Independent reflections	9241 [R(int) = 0.0491]
Completeness to theta = 54.02°	99.6%
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	9241 / 0 / 644
Goodness-of-fit on F^2	1.026

Final R indices [I>2sigma(I)]	R1 = 0.0535, wR2 = 0.1437
R indices (all data)	R1 = 0.0606, wR2 = 0.1489
Largest diff. peak and hole	0.63 and -0.42 e.Å^{-3}

5. References

S1. Kaslow, C. E.; Raymond, S., *J. Am. Chem. Soc.* **1948,** *70*, 3912-3914.
S2. Sheldrick, G. M., *Acta Crystallogr., Sect. C: Struct. Chem.* **2015**, 71, 3-8.