Electronic Supplementary Material (ESI) for New Journal of Chemistry.

Template-directed synthesis of cucurbituril analogues using propanediurea as building block

Yenan Shen, Lei Zou and Qiaochun Wang*

Key Laboratory for Advanced Materials and Institute of Fine Chemicals, School of Chemistry & Molecular Engineering, East China University of Science & Technology, Shanghai 200237, P.R. China.

* Corresponding author: qcwang@ecust.edu.cn

Supporting information

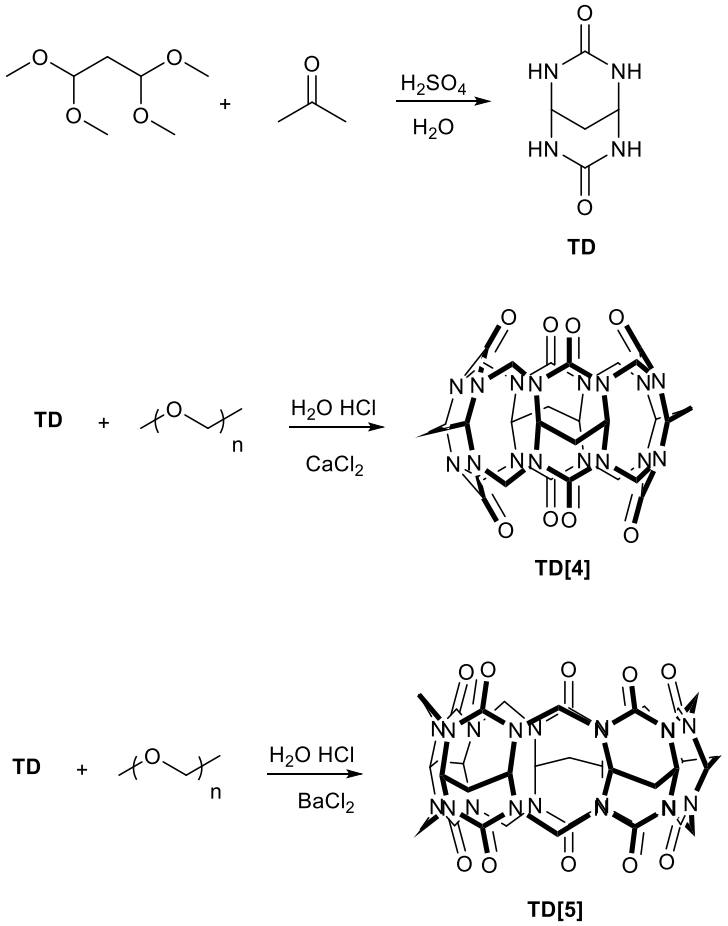
Table of contents:

1. General methods

^{1}H NMR and ^{13}C NMR spectra were measured on a Brüker AV-400 spectrometer. The molecular mass spectra were recorded on a Waters LCT Premier XE mass spectrometer. Thermal stability was measured by thermogravimetric analysis with model SDT Q600 V8.3 Build 101.

Materials: Paraformaldehyde, H_2SO_4, 1,1,3,3-tetramethoxypropane, urea, concentrated HCl, calcium chloride, barium chloride and solvents were used as supplied without further purification.

2. Experimental section



Scheme 1. The synthetic route of **TD[n]**s

1) Synthesis of propanediurea (**TD**)

1,1,3,3-tetramethoxypropane (100 ml, 0.61mol) was slowly dropped into the mixture of urea (84 g, 1.40mmol) and 1.8M H_2SO_4 (110 ml). The resulting solution was stirred and heated to 80℃ for 6h, then cooled to room temperature and the solid was collected by filtration. The product was washed with acetone/water (1:3) twice and dried to give **TD** (56 g, 59%) as the white powder.

^{1}H NMR (400 MHz, DMSO-d_6 , 298K): δ7.08(d, J=4Hz, 4H), 4.50(s, 2H), 1.96(s, 2H).

2) Synthesis of **TD[4]·2CaCl₂**

Paraformaldehyde (5.00g, 166.6mmol), **TD** (10g, 64.1mmol), $CaCl_2$ (1g, 9.0mmol) and 9M HCl (20ml) were mixed and the solution was heated to 100°C for 3.5h. The resulting mixture was cooled to room temperature. The precipitate was collected by filtration and transferred into 45ml water, after 12h of vigorous stirring, the insoluble part was removed. The filtrate was then concentrated and precipitate was collected and dried to give **TD[4]·2CaCl₂** (4.0g, 34%) as white powder.

^{1}H NMR (400 MHz, D_2O, 298 K): δ 6.35(d, J = 15.3 Hz, 8 H), 5.23(s, 8 H), 4.20(d, J = 15.2 Hz, 8H), 2.31(s, 8 H). ^{13}C NMR (100 MHz, D_2O): δ 152.27, 69.63, 61.36, 28.46. HRMS *m/z* 743.2486 $[M+Na]^+$. (calcd 743.2487)

3) Synthesis of **TD[5]·2BaCl₂**

The reaction was carried out as in the synthesis of **TD[4]·2CaCl₂** except $BaCl_2$ (1.5g, 7.2mmol) was used instead of $CaCl_2$. The precipitate was collected by filtration, and then washed with 8ml*2 water/acetone (1:3) and dried. **TD[5]·2BaCl₂** (4.3g, 37%) was obtained as white powder.

^{1}H NMR (400 MHz, D_2O, 298 K): δ 6.45(d, *J* = 15.0 Hz, 10 H), 5.27(s, 10 H), 4.17(d, *J* = 15.0 Hz, 10H), 2.31(s, 10 H). ^{13}C NMR (100 MHz, D_2O): δ 154.86, 69.42, 61.22, 25.13. HRMS *m/z* 923.3155 $[M+Na]^+$. (calcd 923.3434).

3. Removal of metal ions

1) Removal of Ca^{2+}

TD[4]·2CaCl₂ (4.00 g, 4.25 mmol) and EDTA(2.48 g, 8.50 mmol) were added into the aqueous solution of tetrabutylammonium hydroxide (15%wt, 29.5g) and the resulting mixture was stirred and heated to 50℃ for 5h. The solution was then cooled to room temperature and the precipitate was collected by filtration. The solid was washed with 5ml*2 H_2O and dried to give **TD[4]** (2.02 g, 66.5%) as white powder.

2) Removal of Ba^{2+}

TD[5]·2BaCl₂ (2 g, 1.52 mmol) was added into 0.9M sulfuric acid (20 ml) and the mixture was stirred at the room temperature for 3h. The $BaSO_4$ precipitate of was removed by filtration and the filtrate was poured into

100ml acetone. The solid was collected and washed with small amount of water/acetone 1: 3 and dried to give **TD[5]** (756 mg, 55%) as white powder.

4. Preparation of the single crystal of TD[n]s

The single crystals of **TD[4]·2CaCl$_2$** and **TD[5]·2BaCl$_2$** were prepared from their aqueous solutions (5.3mM and 7.6mM respectively) by slow diffusion of acetone vapor at room temperature. Colorless crystals were obtained after several weeks.

5. Supplementary Figures

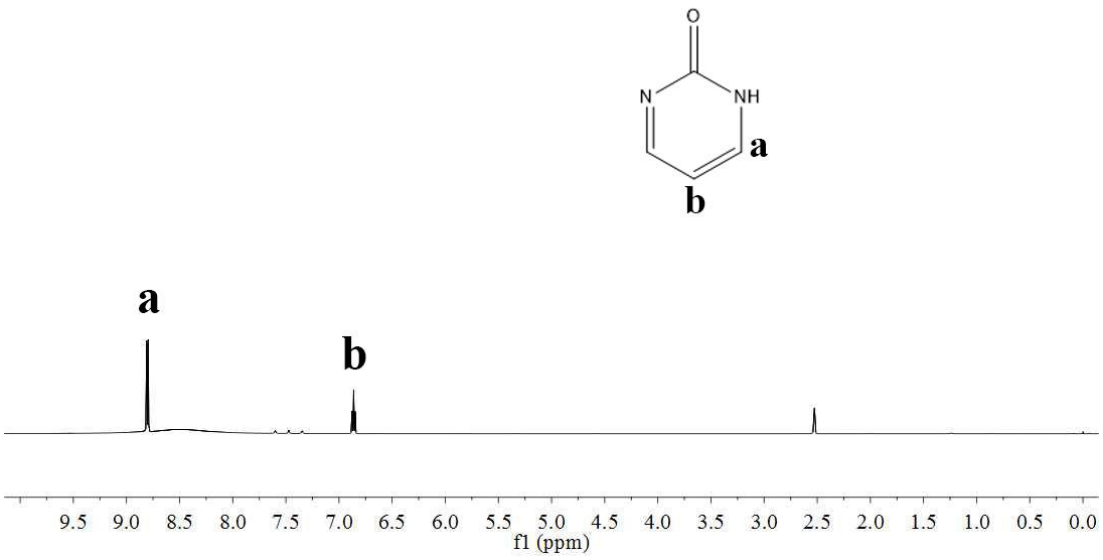


Fig S1. The ^{1}H NMR spectra (400 MHz, DMSO-d_6, 298 K) of **TD** and urea in HCI after heating for 4h at 100ºC, indicating the formation of high purity of pyrimidinone.

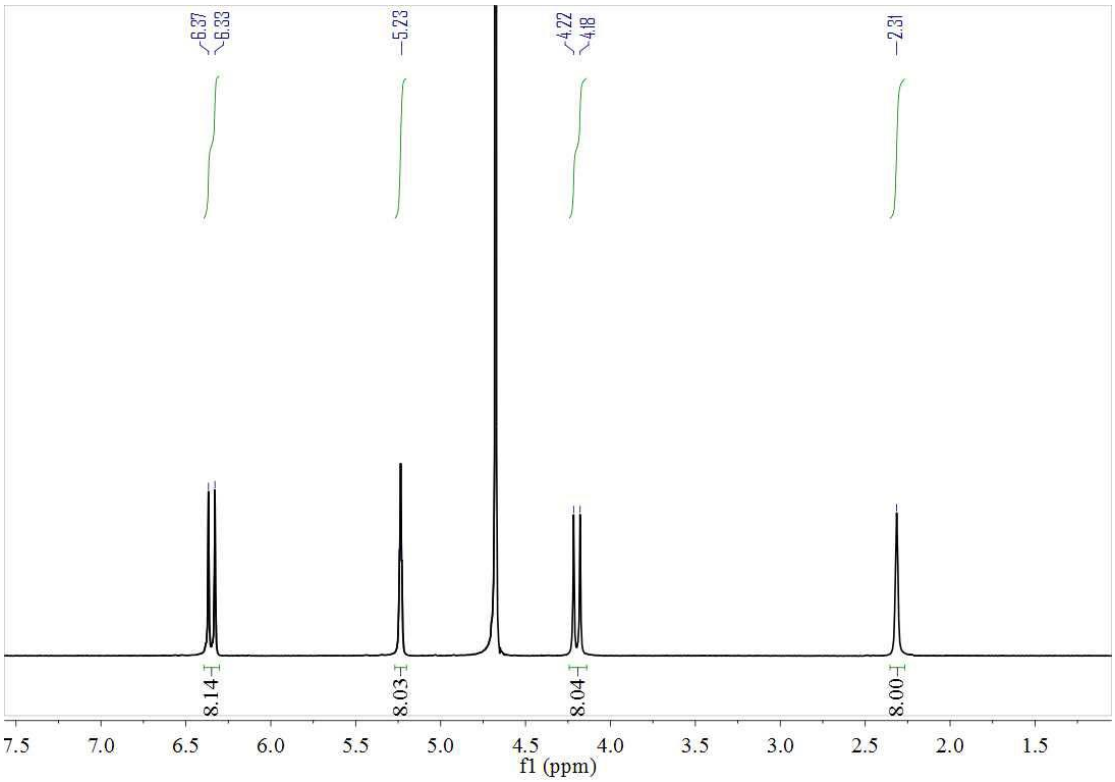


Fig S2. The ^{1}H NMR spectra (400 MHz, D_2O, 298 K) of **TD[4]·2CaCl$_2$**

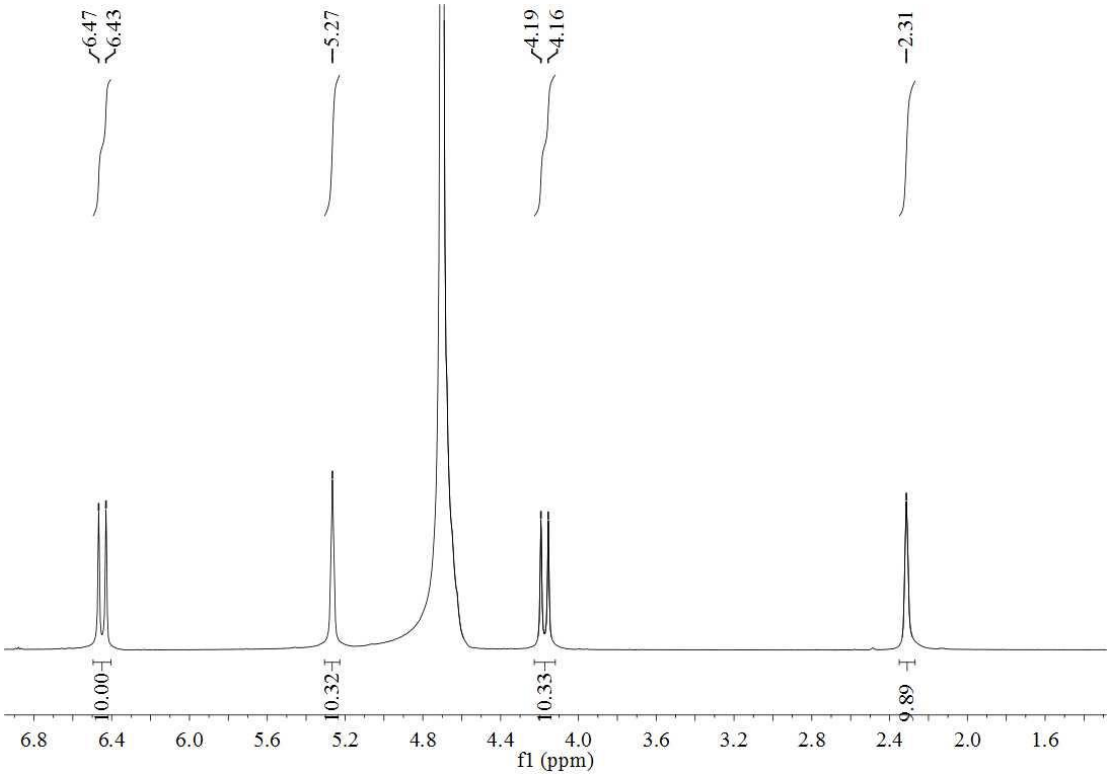


Fig S3. ^{1}H NMR spectra (400 MHz, D_2O, 298 K) of **TD[5]·2BaCl$_2$**

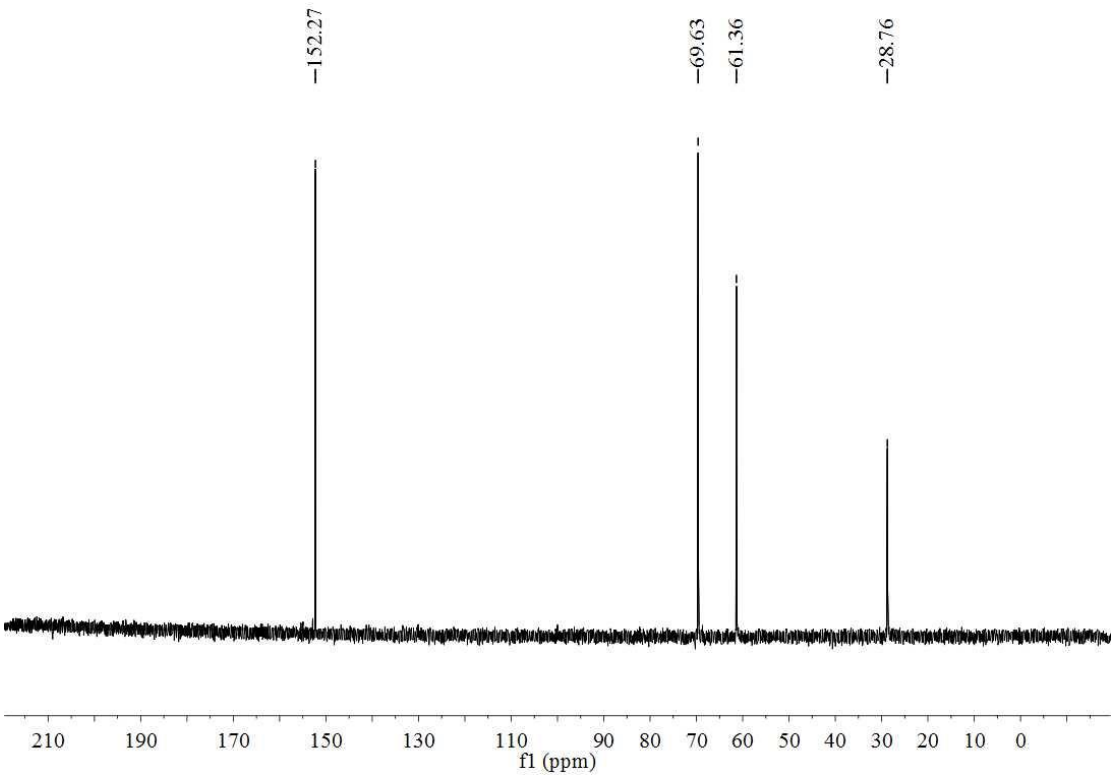


Fig S4. ^{13}C NMR spectra (100 MHz, D_2O, 298 K) of **TD[4]·2CaCl₂**

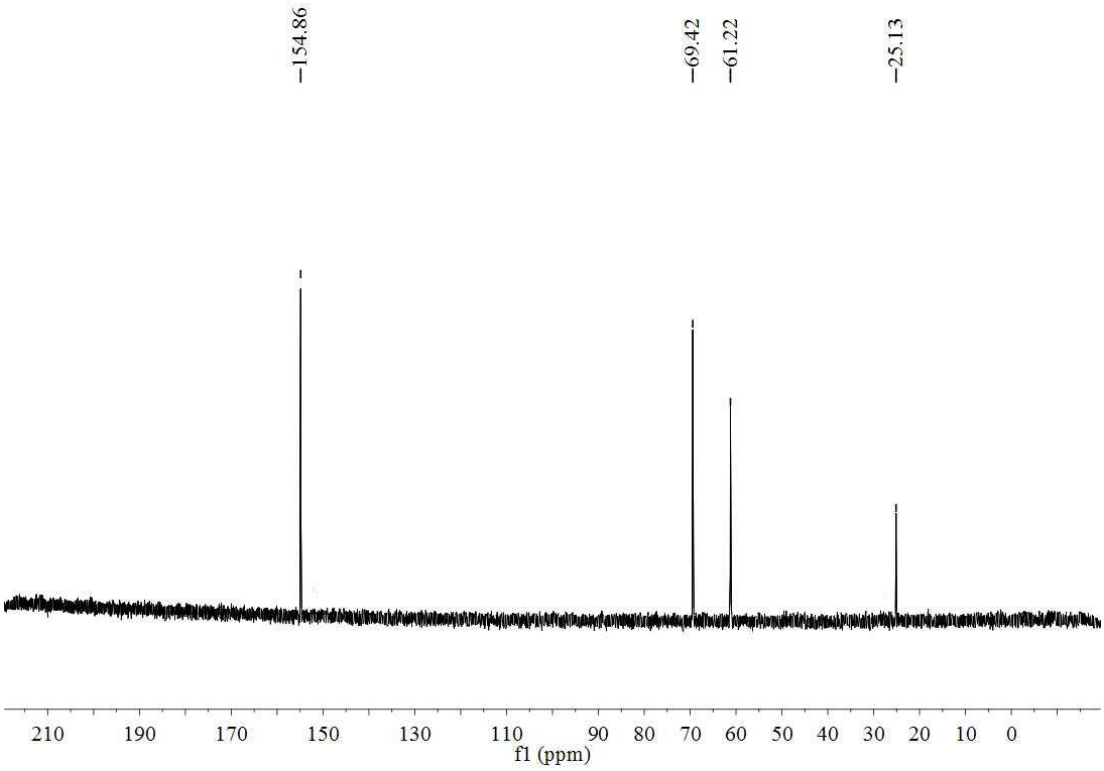


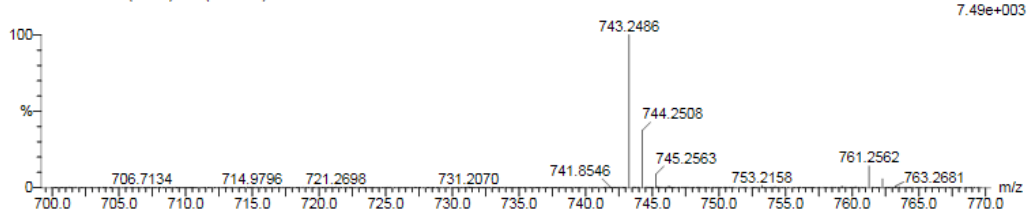
Fig S5. ^{13}C NMR spectra (100 MHz, D_2O, 298 K) of **TD[5]·2BaCl₂**

Elemental Composition Report **Page 1**

Single Mass Analysis
Tolerance = 50.0 PPM / DBE: min = -1.5, max = 100.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions
1166 formula(e) evaluated with 103 results within limits (up to 1 best isotopic matches for each mass)
Elements Used:
C: 0-49 H: 0-57 N: 0-16 O: 0-8 Na: 0-1

WANG-QC ECUST institute of Fine Chem 02-Mar-2017 14:10:30
WQ-SYN-201 233 (2.929) Cm (233:236) 1: TOF MS ES+ 7.49e+003



Minimum:				-1.5			
Maximum:		30.0	50.0	100.0			
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	i-FIT (Norm)	Formula
743.2486	743.2487	-0.1	-0.1	20.5	141.5	0.0	C28 H32 N16 O8 Na

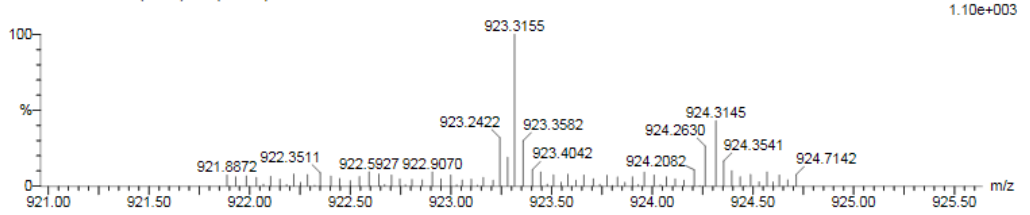
Fig S6. The HRMS spectra of **TD[4]**.

Elemental Composition Report **Page 1**

Single Mass Analysis
Tolerance = 50.0 PPM / DBE: min = -1.5, max = 100.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions
431 formula(e) evaluated with 9 results within limits (up to 1 best isotopic matches for each mass)
Elements Used:
C: 0-39 H: 0-45 N: 0-20 O: 0-10 Na: 0-1

WANG-QC ECUST institute of Fine Chem 23-Dec-2016 10:58:28
WQ-SYN-604-1 109 (3.440) Cm (21:185) 1: TOF MS ES+ 1.10e+003



Minimum:				-1.5			
Maximum:		30.0	50.0	100.0			
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	i-FIT (Norm)	Formula
923.3155	923.3134	2.1	2.3	25.5	308.0	0.0	C35 H40 N20 O10 Na

Fig S7. The HRMS spectra of **TD[5]**.

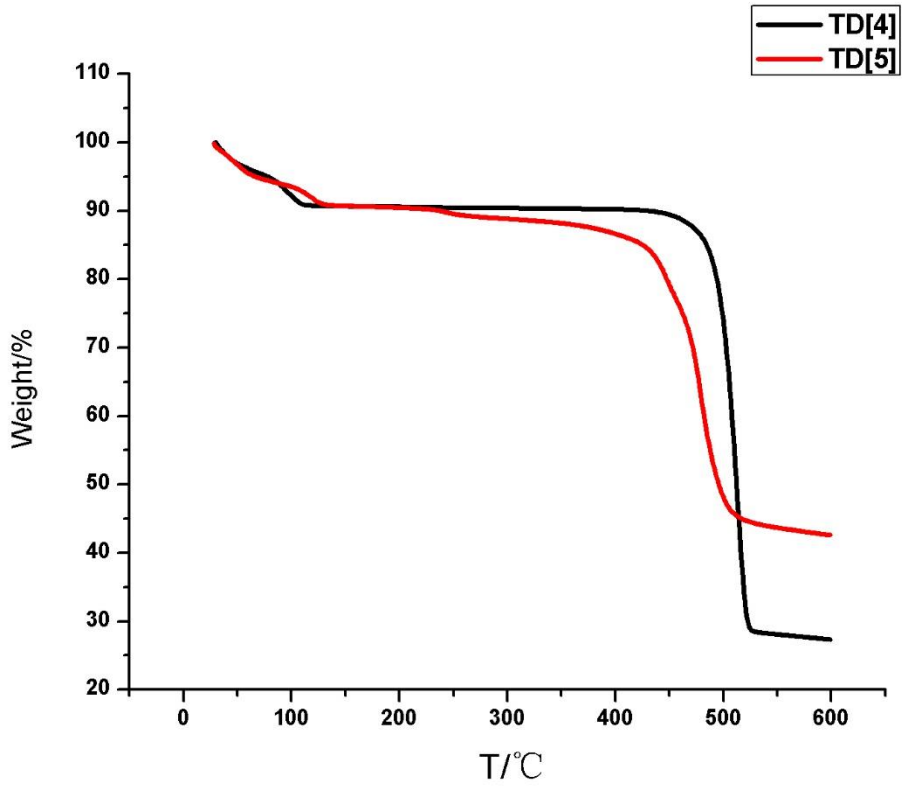


Fig S8. Thermogravimetric analysis of **TD[4]** and **TD[5]**

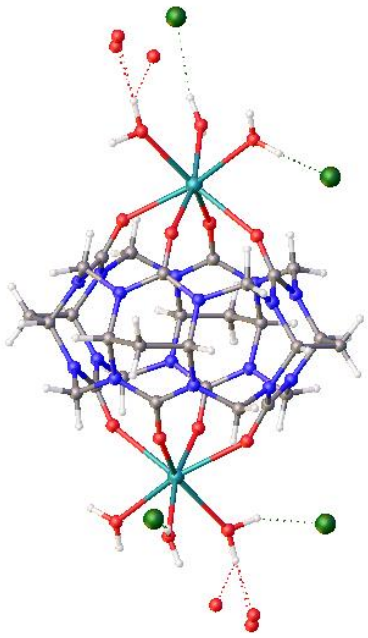


Fig S9. The single crystal structure of **TD[4]·2CaCl₂**

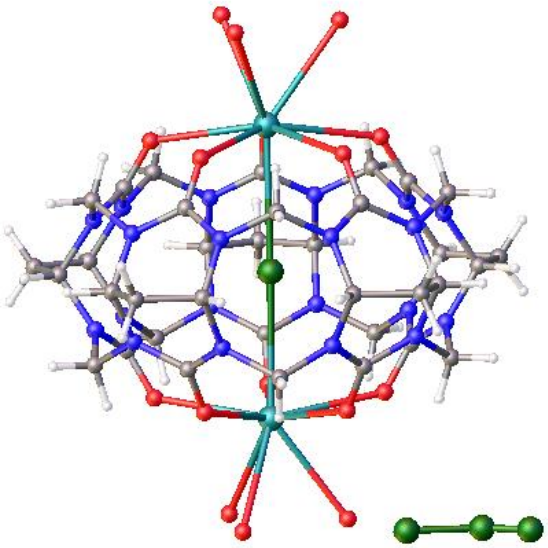
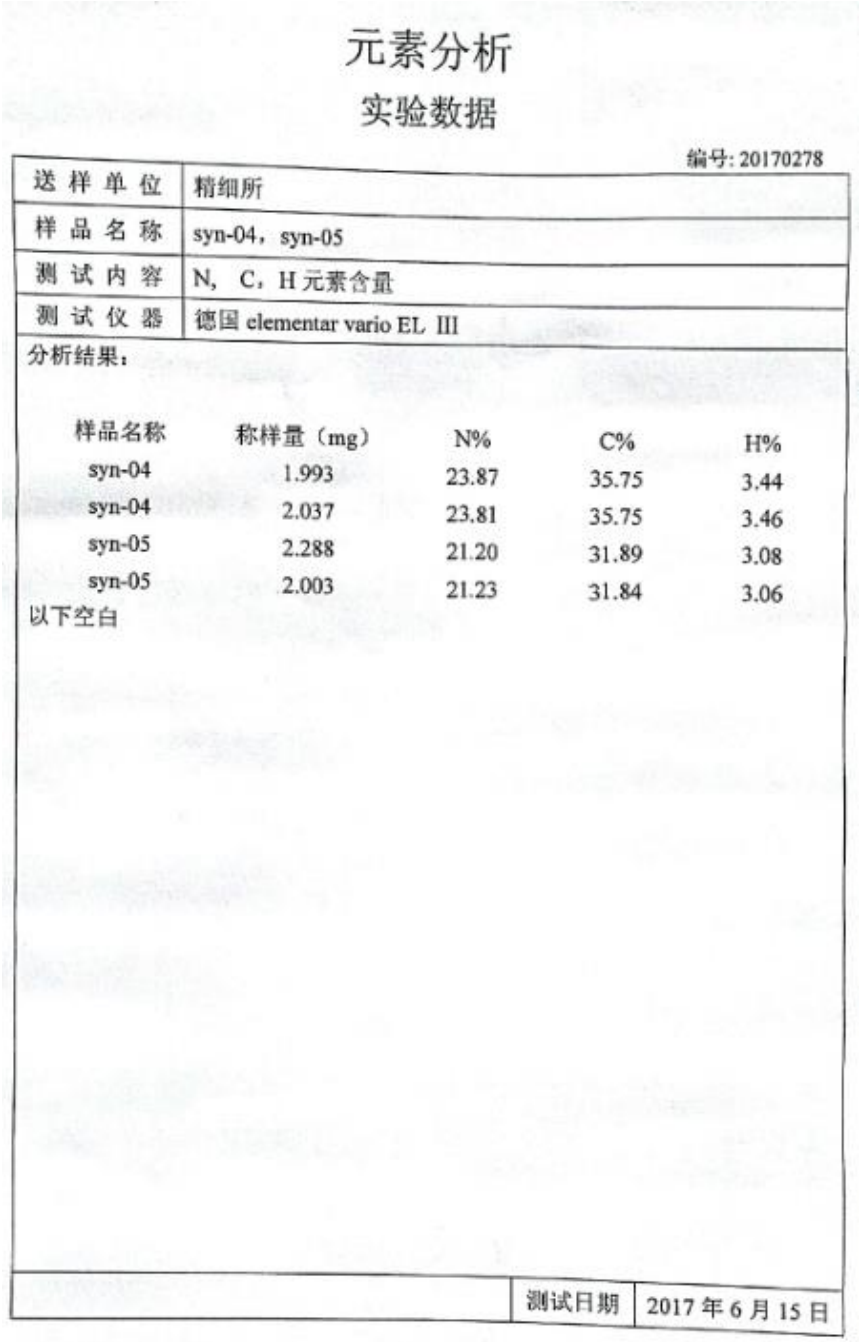


Fig S10. The single crystal structures **TD[5]·2BaCl$_2$**



元素分析

实验数据

编号: 20170278

送样单位	精细所
样品名称	syn-04，syn-05
测试内容	N，C，H元素含量
测试仪器	德国 elementar vario EL III

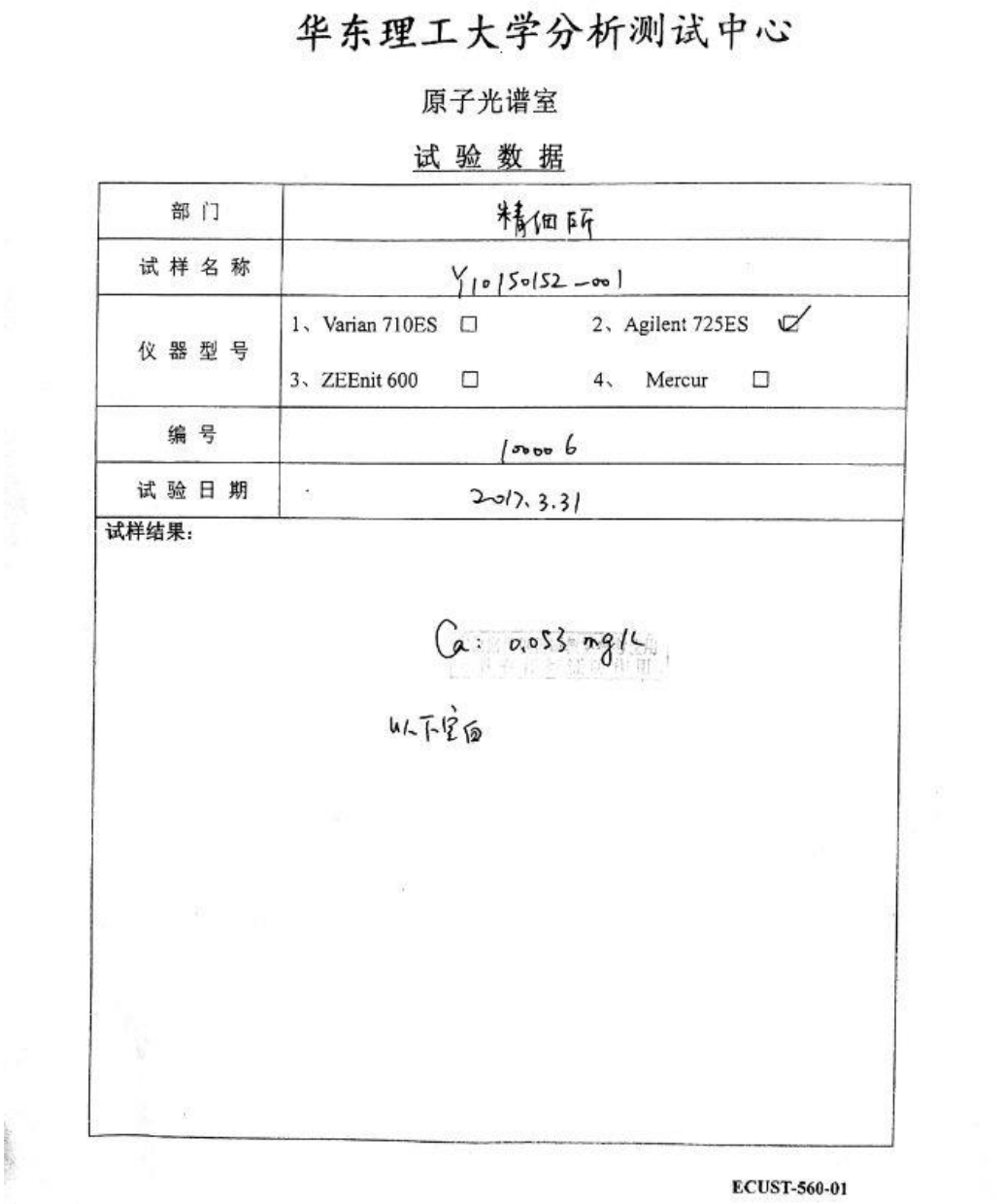
分析结果：

样品名称	称样量（mg）	N%	C%	H%
syn-04	1.993	23.87	35.75	3.44
syn-04	2.037	23.81	35.75	3.46
syn-05	2.288	21.20	31.89	3.08
syn-05	2.003	21.23	31.84	3.06

以下空白

测试日期 2017 年 6 月 15 日

Fig S11. The Elemental Analysis of **TD[4]·2CaCl₂** (syn-04) and **TD[5]·2BaCl₂** (syn-05). The found average percentages of C, N and H of **TD[4]·2CaCl₂** ($C_{28}H_{32}N_{16}O_8Ca_2Cl_4$) crystal were 35.75, 23.84 and 3.45, respectively (calculated values C: 35.74; N: 23.83; H: 3.43), and those of **TD[5]·2BaCl₂** ($C_{35}H_{40}N_{20}O_{10}Ba_2Cl_4$) crystal were 31.86, 21.22 and 3.07, respectively (calculated values C: 31.87; N: 21.25; H: 3.06).



华东理工大学分析测试中心

原子光谱室

试 验 数 据

部 门	精细所
试 样 名 称	Y10150152-001
仪 器 型 号	1、Varian 710ES ☐ 2、Agilent 725ES ☑ 3、ZEEnit 600 ☐ 4、 Mercur ☐
编 号	10006
试 验 日 期	2017.3.31

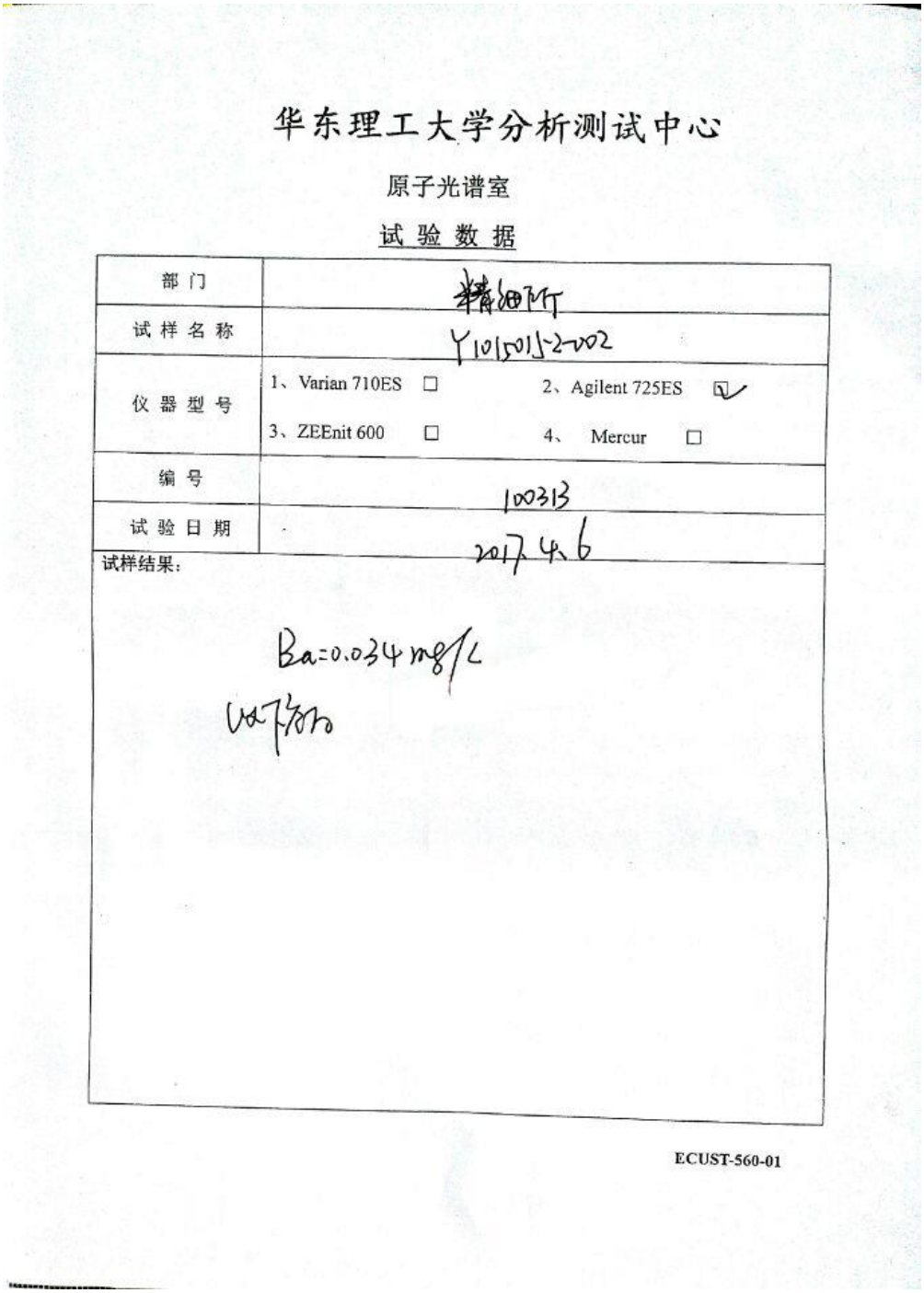
试样结果：

Ca: 0.053 mg/L

以下空白

ECUST-560-01

Fig S12. The result of the atomic absorption spectrum test for the calcium content of **TD[4]** solution (100 mg/L, 1.4×10^{-4}M). The concentration of Ca^{2+} was 0.053 mg/L (1.3×10^{-6}M), indicating that >99% of the calcium ions in **TD[4]·2CaCl₂** had been removed.



华东理工大学分析测试中心

原子光谱室

试 验 数 据

部 门	精细所
试 样 名 称	Y10150J-2-002
仪 器 型 号	1、Varian 710ES ☐ 2、Agilent 725ES ☑ 3、ZEEnit 600 ☐ 4、Mercur ☐
编 号	100313
试 验 日 期	2017.4.6

试样结果：

Ba=0.034 mg/L

ECUST-560-01

Figure S13. The result of the atomic absorption spectrum test for the barium content of **TD[5]** solution (100mg/L, 1.1×10^{-4}M). The concentration of Ba^{2+} was 0.034 mg/L (2.5×10^{-7}M), indicating that >99% of the barium ions in **TD[5]·2BaCl₂** had been removed.

元素分析

实验数据

编号: 20170138

送 样 单 位	化学院
样 品 名 称	Y10150152-001，Y10150152-002
测 试 内 容	N，C，H 元素含量
测 试 仪 器	德国 elementar vario EL III

分析结果：

样品名称	称样量（mg）	N%	C%	H%
Y10150152-001	1.574	31.14	46.65	4.42
Y10150152-001	1.540	31.18	46.67	4.48
Y10150152-002	1.840	31.11	46.65	4.40
Y10150152-002	1.954	31.10	46.65	4.43

以下空白

	测试日期	2017 年 4 月 6 日

Figure S14. The Elemental Analysis of **TD[4]** (Y10150152-001) and **TD[5]** (Y10150152-002).

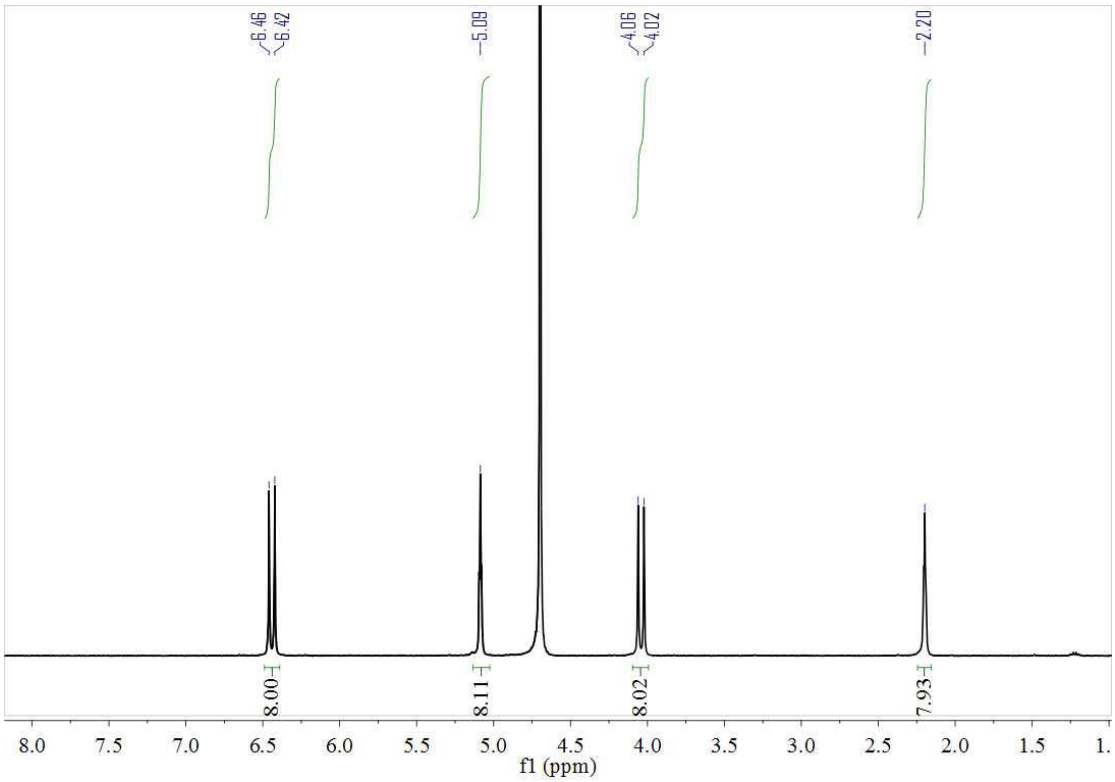


Fig S15. ^{1}H NMR spectra (400 MHz, D_2O, 298 K) of **TD[4].**

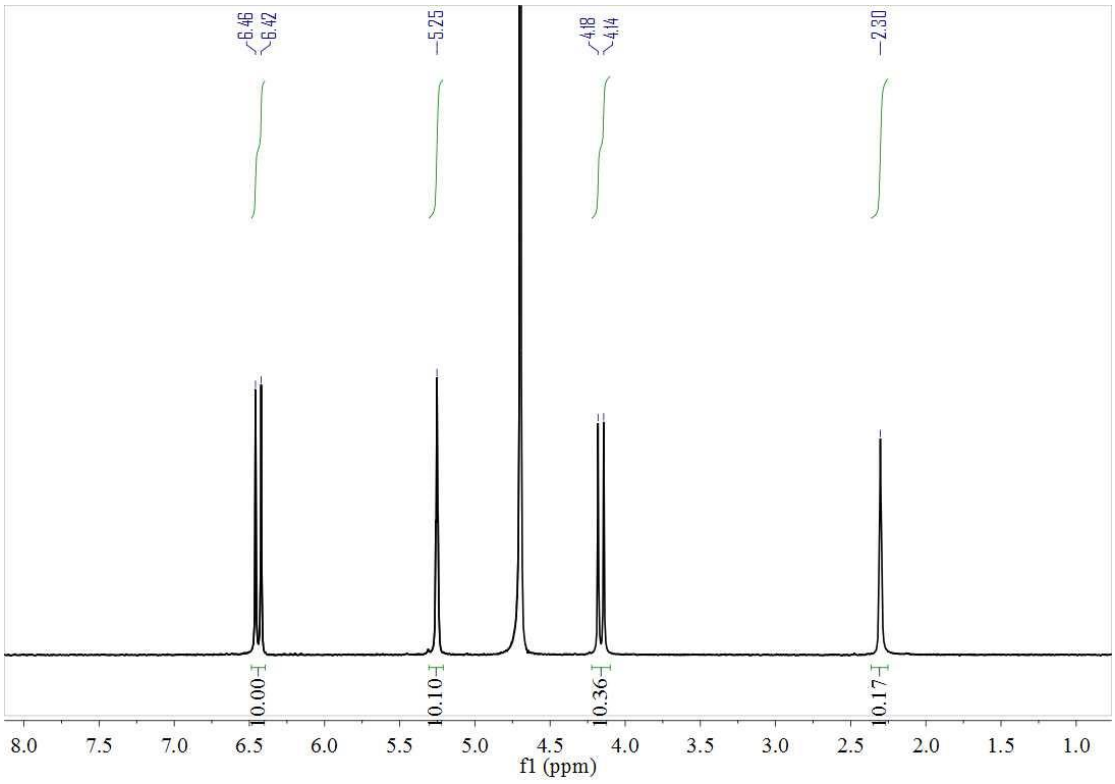


Fig S16. ^{1}H NMR spectra (400 MHz, D_2O, 298 K) of **TD[5].**

6. Details of the X-ray Crystal Structure

Table S1: crystal data and structure refinement for **TD[4]·2CaCl₂**

	TD[4]·2CaCl₂
Chemical formula	C28 H44 Ca2 Cl4 N16 O17
Formula weight	1098.75
Temperature	223(2) K
Wavelength	0.71073Å
Crystal system	Monoclinic
Space group	C2/m
Unit cell dimensions	a=14.953(2) Å α= 90 ° b=13.6358(18) Å β=95.389(2) ° c=11.0501(15) Å γ=90 °
Volume	2243.1(5) $Å^3$
Z	2
Density (calculated)	1.627 Mg/cm^3
Absorption coefficient	0.580 mm^{-1}
F(000)	1136
Crystal size	0.480×0.430×0.033 mm^3
Theta range for data collection	1.851 to 27.656°
Index ranges	-15<=h<=19, -17<=k<=17, -14<=l<=14
Reflections collected	8256
Independent reflections	2707 [R(int) = 0.0208]
Completeness to theta = 25.242 °	99.4%
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.746 and 0.672
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	2707 / 30 / 198
Goodness-of-fit on F^2	1.099
Final R indices [I>2sigma(I)]	R1 = 0.0554, wR2 = 0.1923
R indices (all data)	R1 = 0.0607, wR2 = 0.2019
Extinction coefficient	n/a
Largest diff. peak and hole	1.216 and -0.479 $e.Å^{-3}$

Table S2: crystal data and structure refinement for **TD[5]·2BaCl₂**

	TD[5]·2BaCl₂
Chemical formula	C35 H40 Ba2 Cl4 N20 O24
Formula weight	1541.33
Temperature	223(2) K
Wavelength	0.71073Å
Crystal system	Orthorhombic
Space group	Puma
Unit cell dimensions	a=19.356(3) Å α= 90 ° b=11.1923(16) Å β=90° c=26.552(4) Å γ=90 °
Volume	5752.2(15) $Å^3$
Z	4
Density (calculated)	1.780 Mg/cm^3
Absorption coefficient	1.642 mm^{-1}
F(000)	3048
Crystal size	0.780×0.400×0.200 mm^3
Theta range for data collection	1.534 to 27.585°
Index ranges	-22<=h<=25, -14<=k<=14, -34<=l<=30
Reflections collected	37628
Independent reflections	6994 [R(int) = 0.0360]
Completeness to theta = 25.242 °	99.7%
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.720 and 0.459
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	6994 / 60 / 446
Goodness-of-fit on F^2	1.199
Final R indices [I>2sigma(I)]	R1 = 0.0563, wR2 = 0.1527
R indices (all data)	R1 = 0.0647, wR2 = 0.1577
Extinction coefficient	n/a
Largest diff. peak and hole	2.255 and -0.636 $e.Å^{-3}$