Examination of the Dynamic Covalent Chemistry of [2+3]-Imine Cages

Tobias H.G. Schick, Frank Rominger and Michael Mastalerz*

Organisch-Chemisches Institut Ruprecht-Karls-Universität Heidelberg, Im Neuenheimer Feld 270, 69120 Heidelberg (Germany).

E-mail: michael.mastalerz@oci.uni-heidelberg.de

Table of Contents

1. NMR Spectra

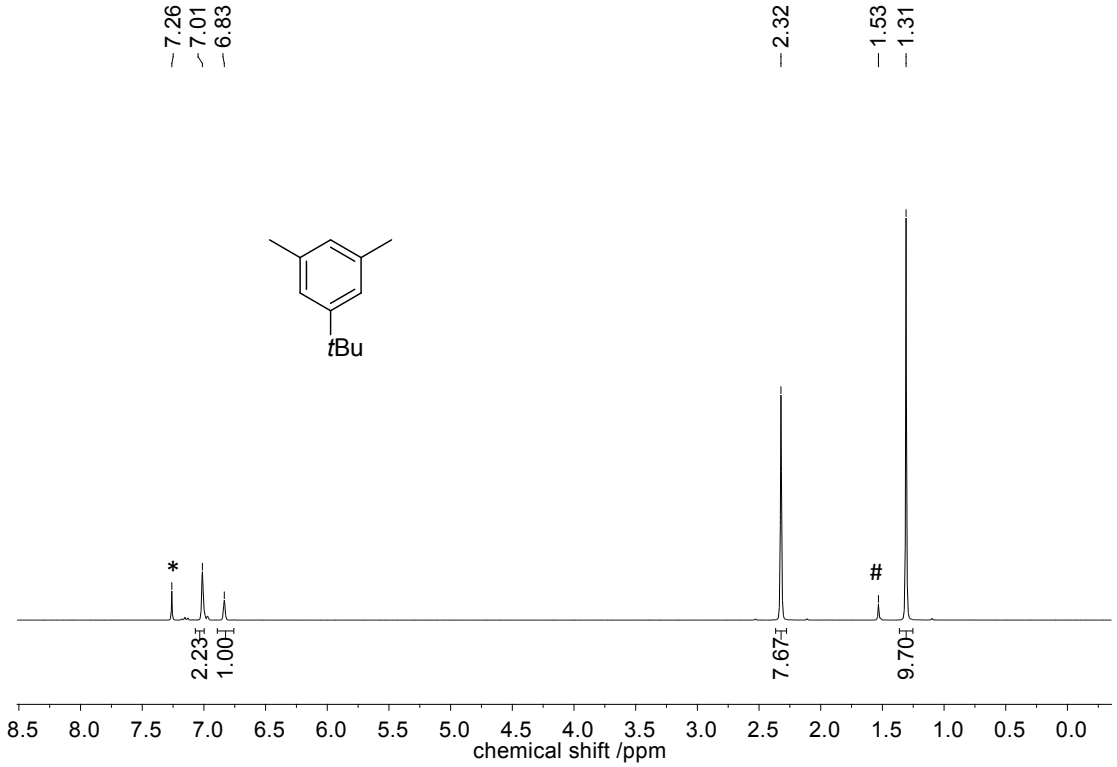


Figure S1. ^{1}H NMR spectrum ($CDCl_3$, 300 MHz) of 1-(*tert*-butyl)-3,5-dimethylbenzene.*$CHCl_3$, $^{\#}H_2O$.

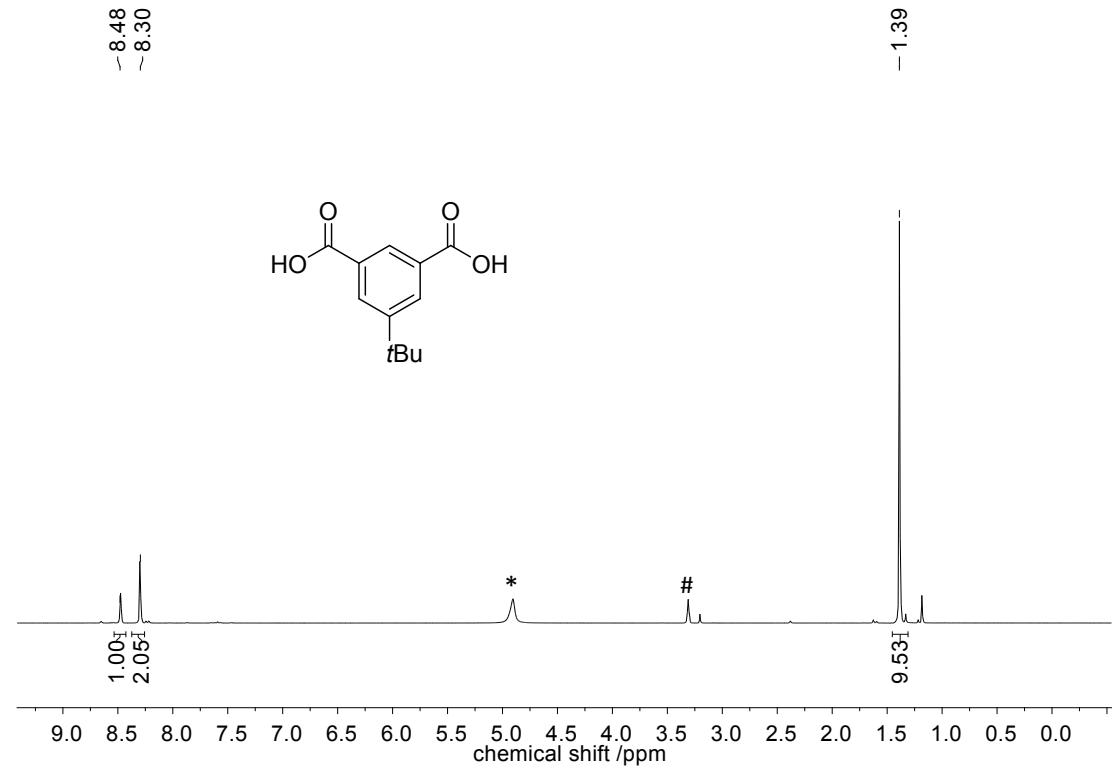


Figure S2. ^{1}H NMR spectrum of 5-(*tert*-butyl)isophthalic acid-d9 (MeOD, 300 MHz). *H_2O, $^{\#}$MeOH.

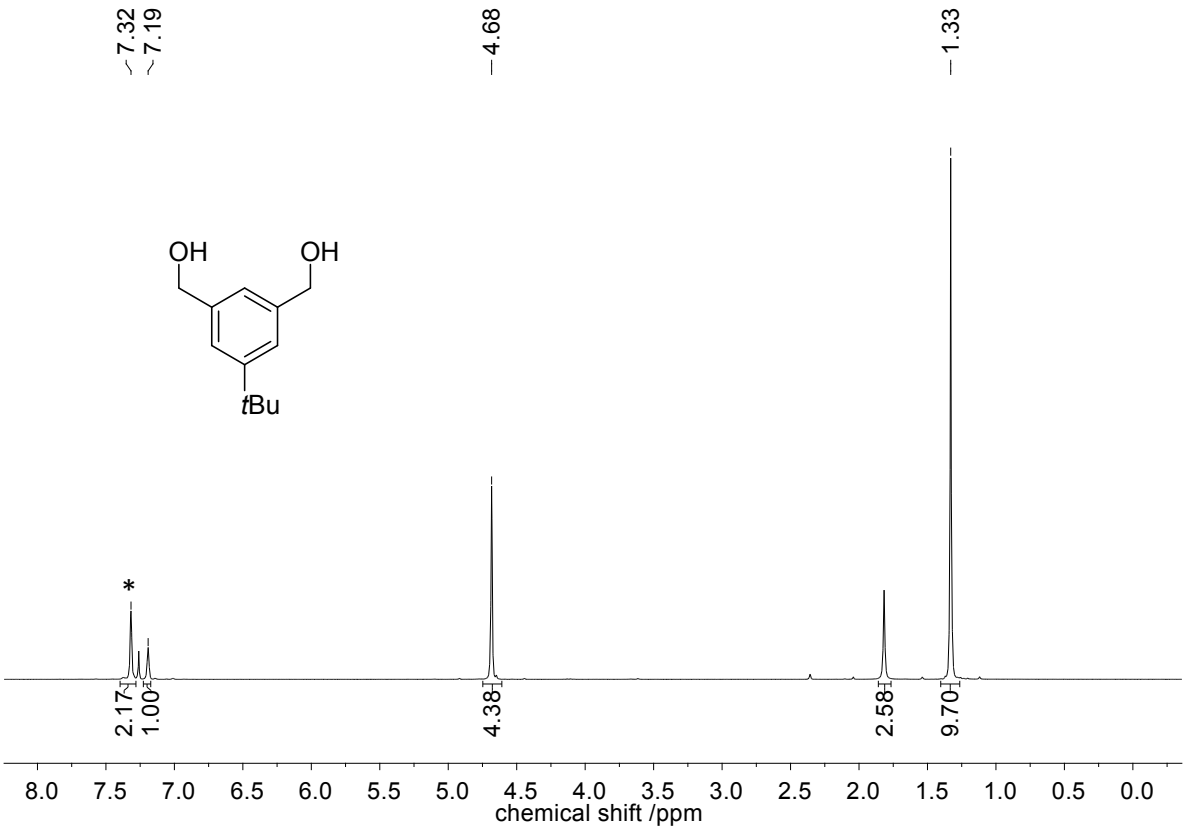


Figure S3. ^{1}H NMR spectrum ($CDCl_3$, 400 MHz) of (5-(*tert*-butyl)-1,3-dihydroxymethylenebenzene-d9. *$CHCl_3$.

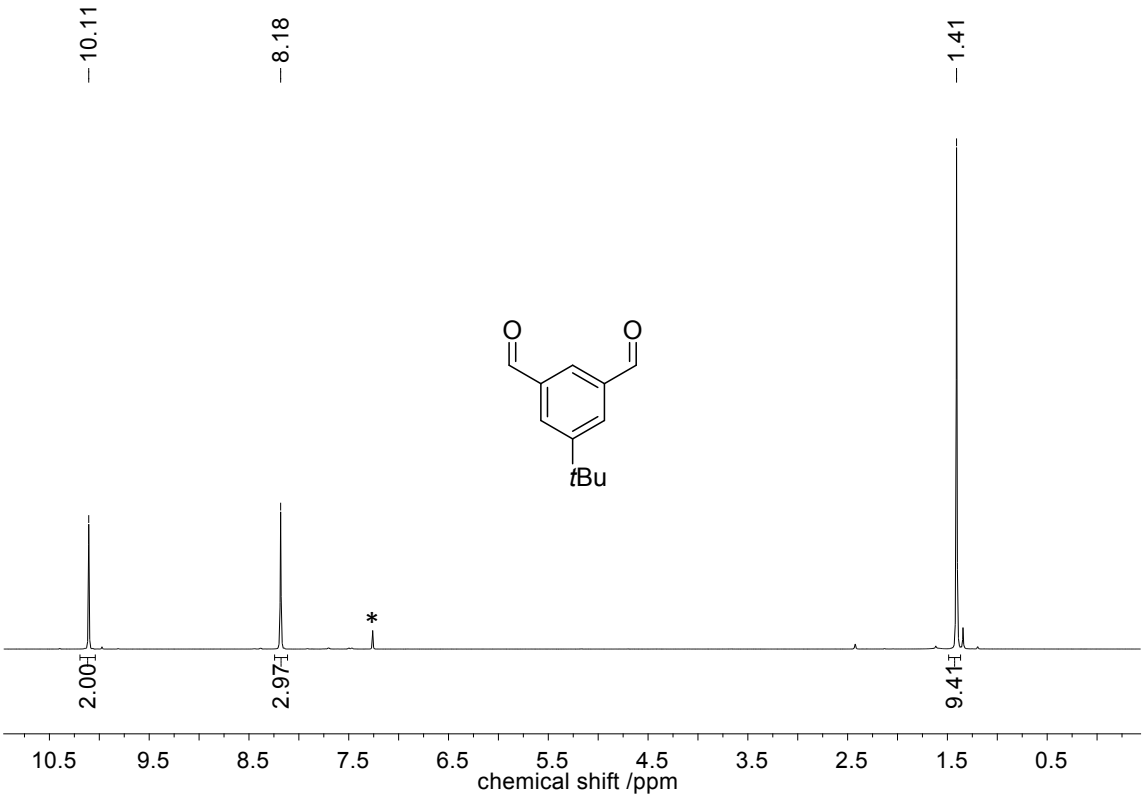


Figure S4. ^{1}H NMR spectrum ($CDCl_3$, 400 MHz) of compound **1-d9**. *$CHCl_3$.

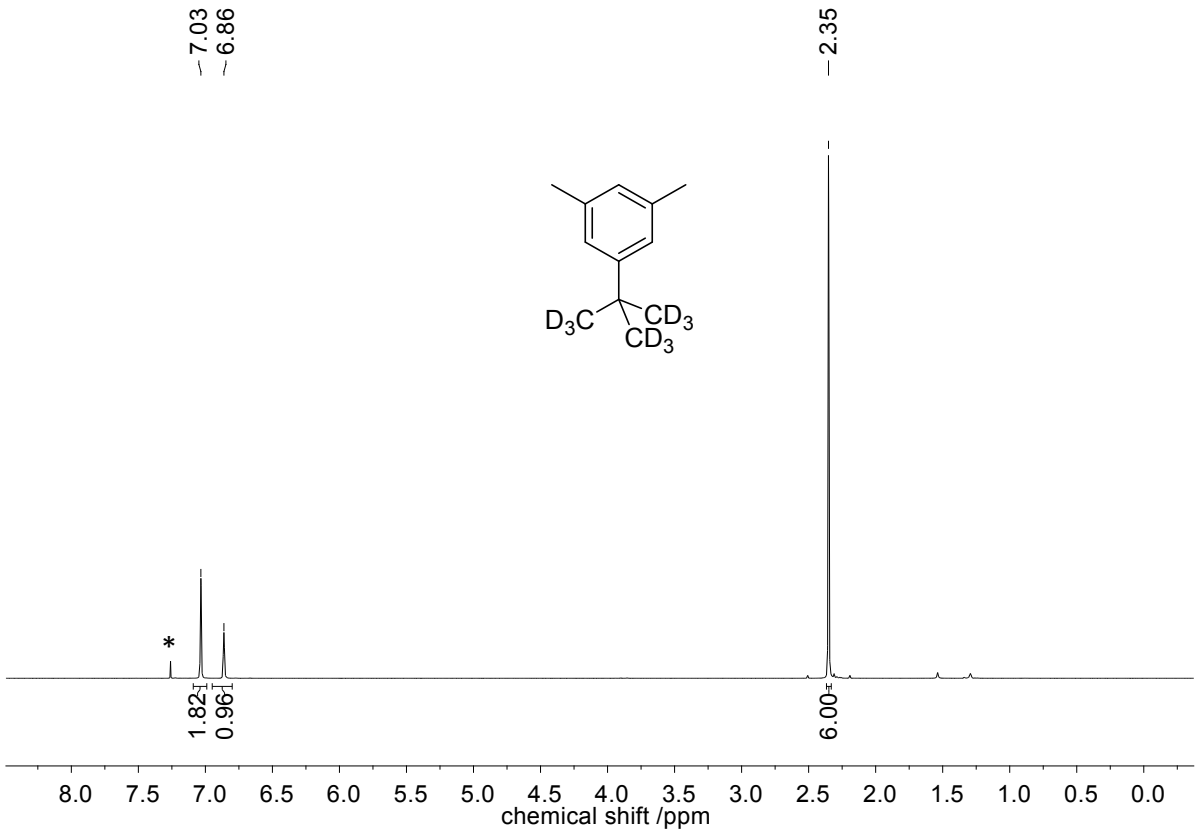


Figure S5. ^{1}H NMR spectrum ($CDCl_3$, 400 MHz) of 1-(*tert*-butyl)-3,5-dimethylbenzene-d9. *$CHCl_3$.

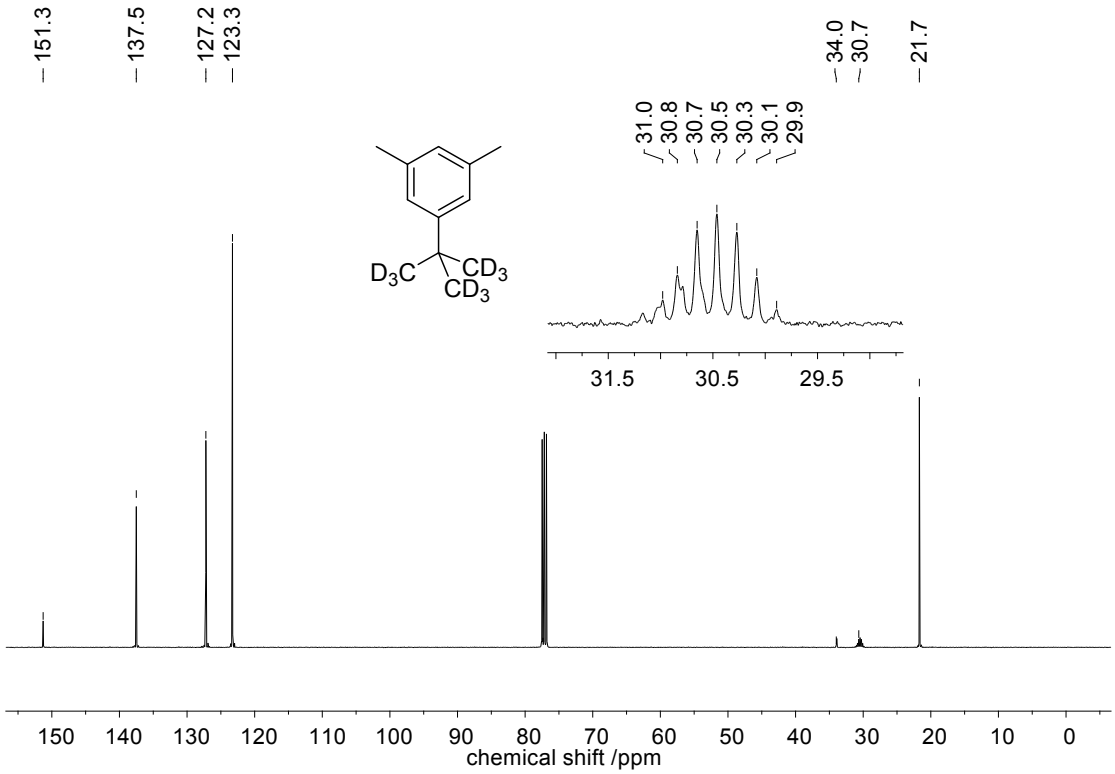


Figure S6. ^{13}C NMR spectrum ($CDCl_3$, 100 MHz) of compound 1-(*tert*-butyl)-3,5-dimethylbenzene-d9.

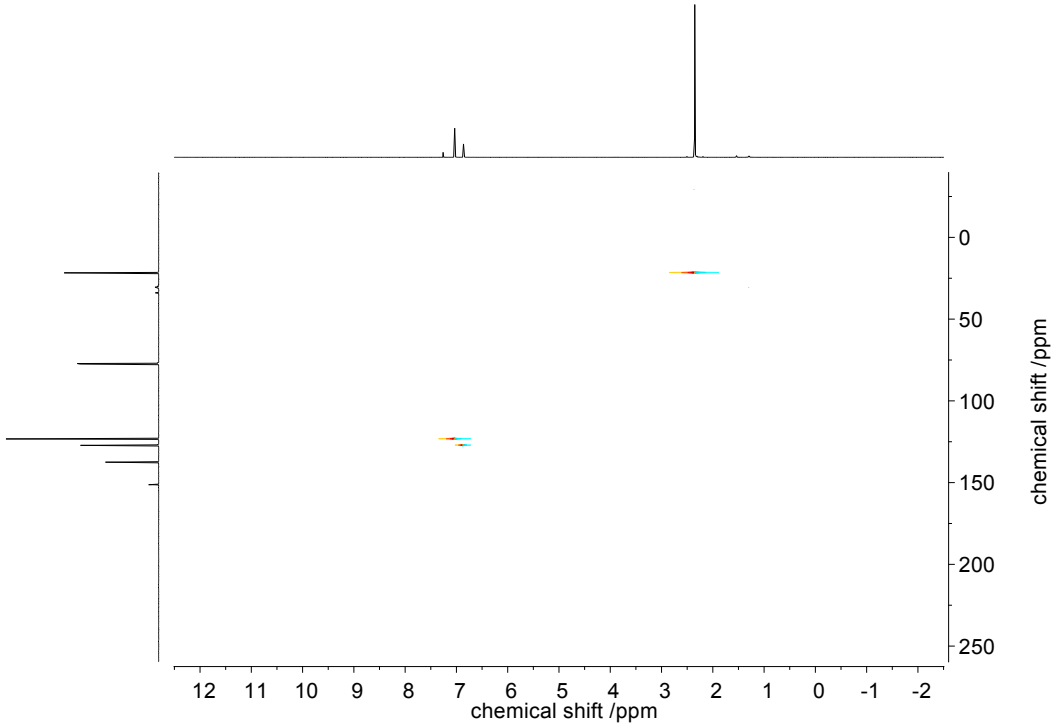


Figure S7. HSQC NMR spectrum $CDCl_3$, (400/100 MHz) of 1-(*tert*-butyl)-3,5-dimethylbenzene-d9.

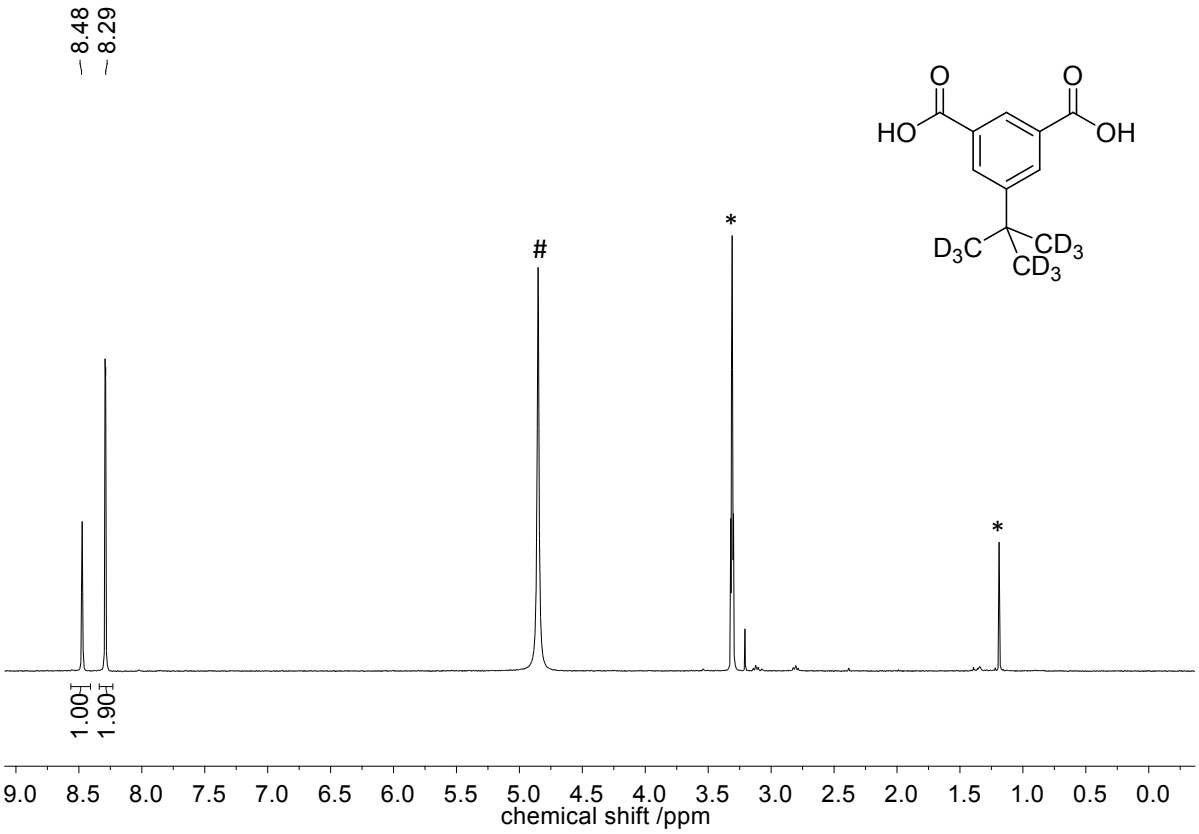


Figure S8. ^{1}H NMR spectrum of 5-(*tert*-butyl)isophthalic acid-d9 (MeOD, 300 MHz). *MeOH, $^{\#}H_2O$.

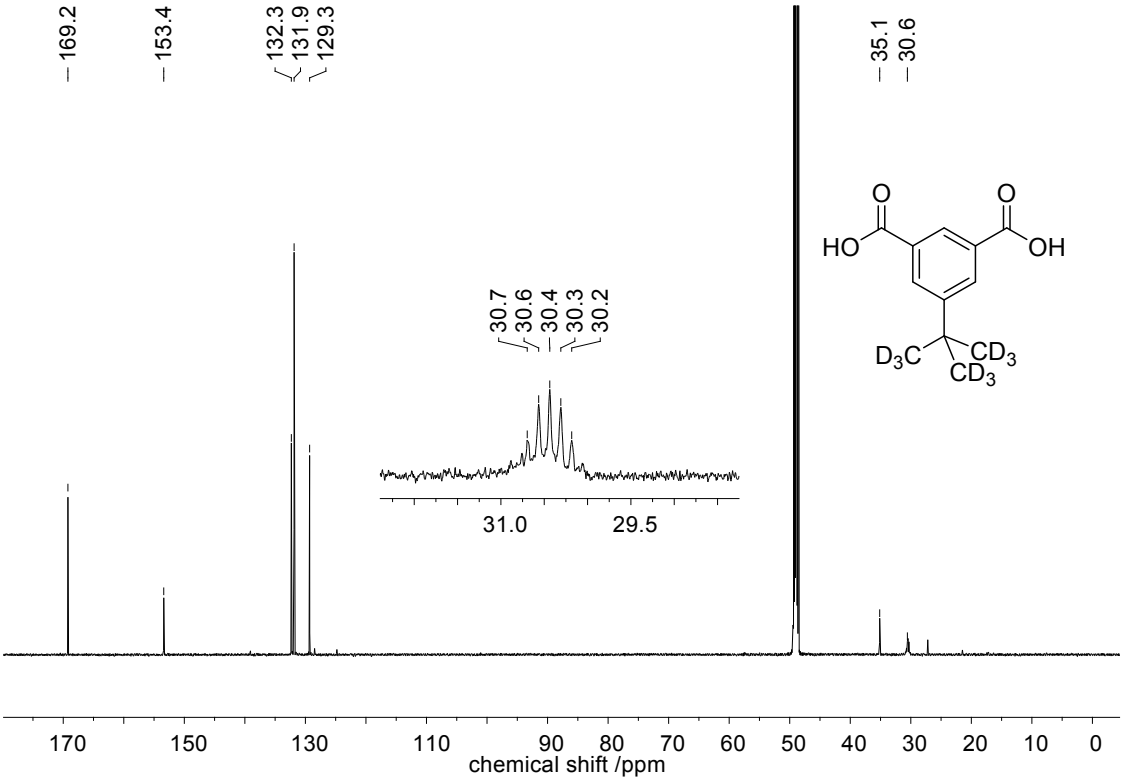


Figure S9. ^{13}C NMR spectrum (MeOD, 150 MHz) of 5-(*tert*-butyl)isophthalic acid-d9.

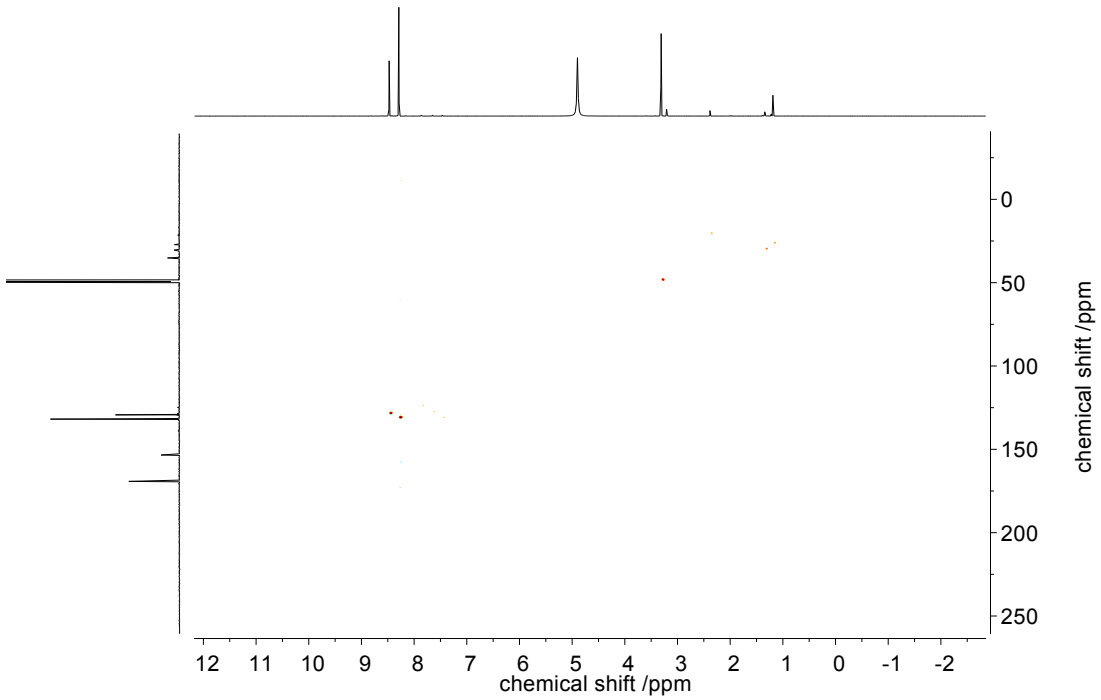


Figure S10. HSQC NMR spectrum (MeOD, 600 MHz) of 5-(*tert*-butyl)isophthalic acid-d9.

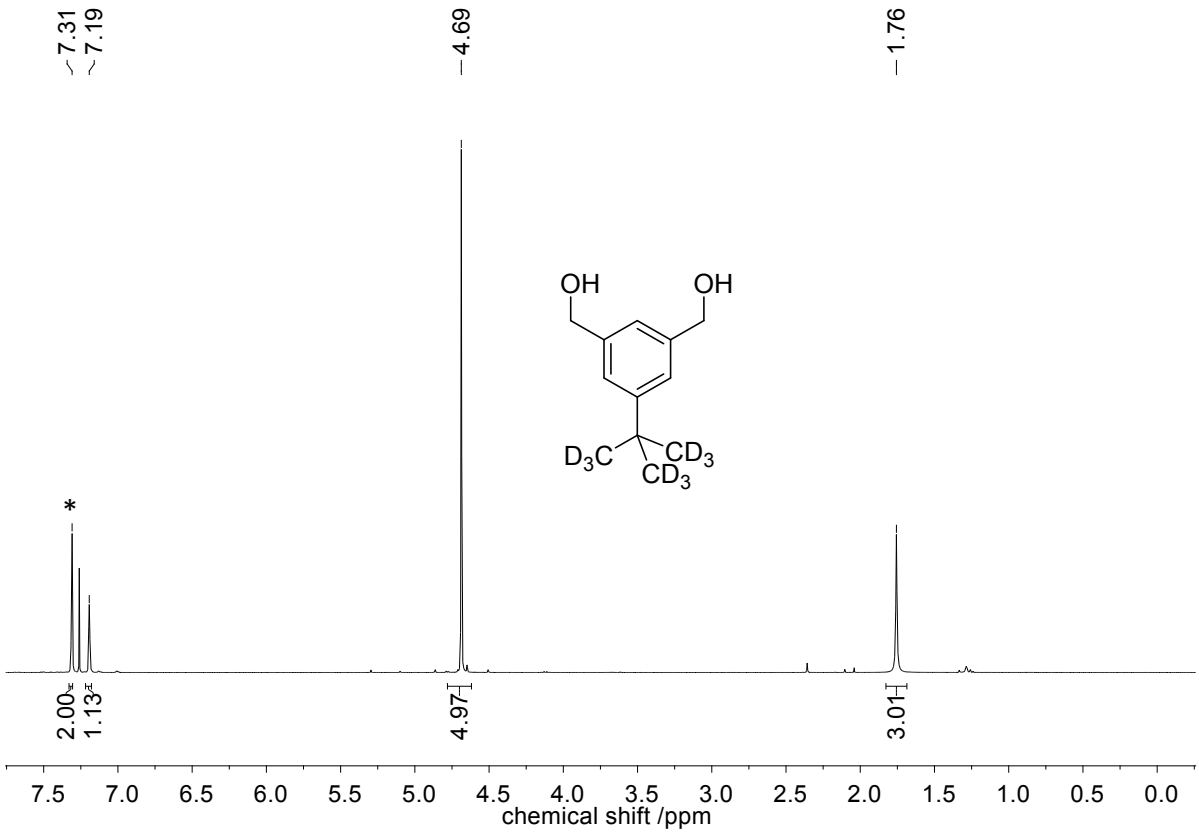


Figure S11. ^{1}H NMR spectrum ($CDCl_3$, 400 MHz) of (5-(*tert*-butyl)-1,3-dihydroxymethylenebenzene-d9. *$CHCl_3$.

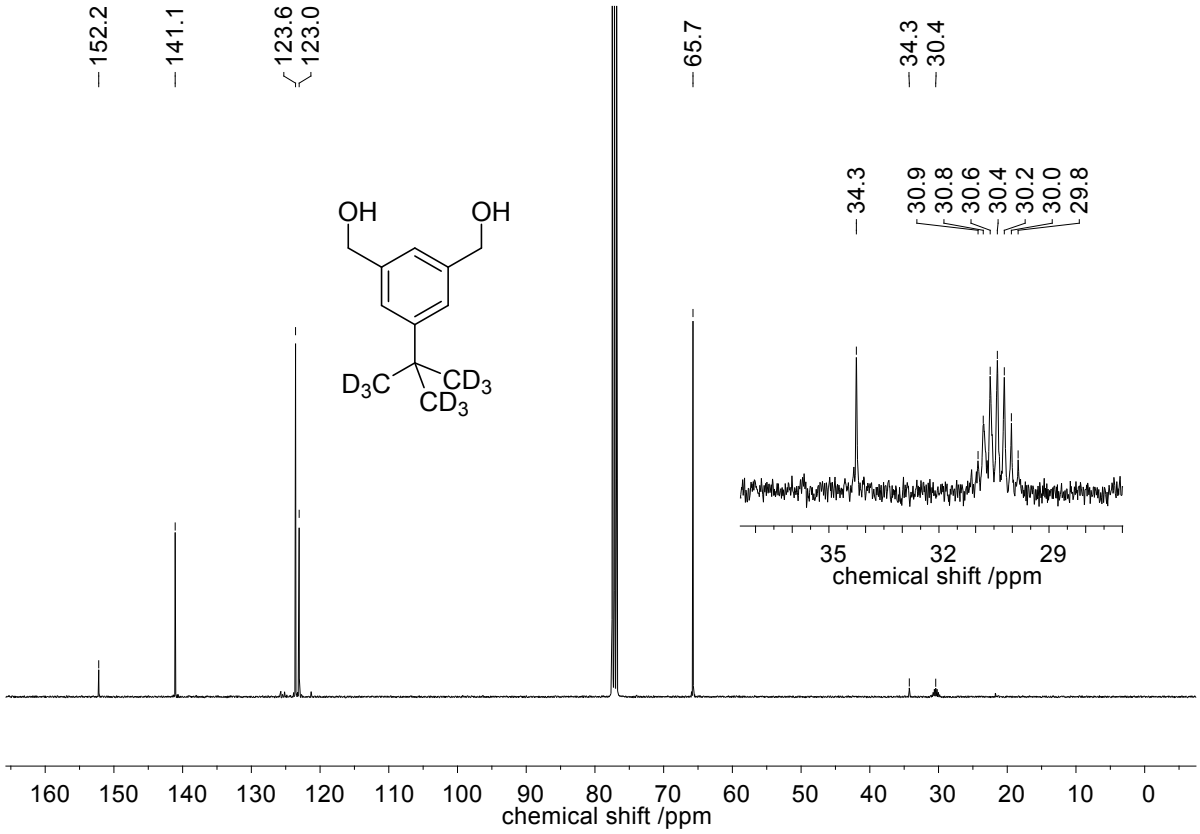


Figure S12. ^{13}C NMR spectrum ($CDCl_3$, 100 MHz) of (5-(*tert*-butyl)-1,3-dihydroxymethylenebenzene-d9.

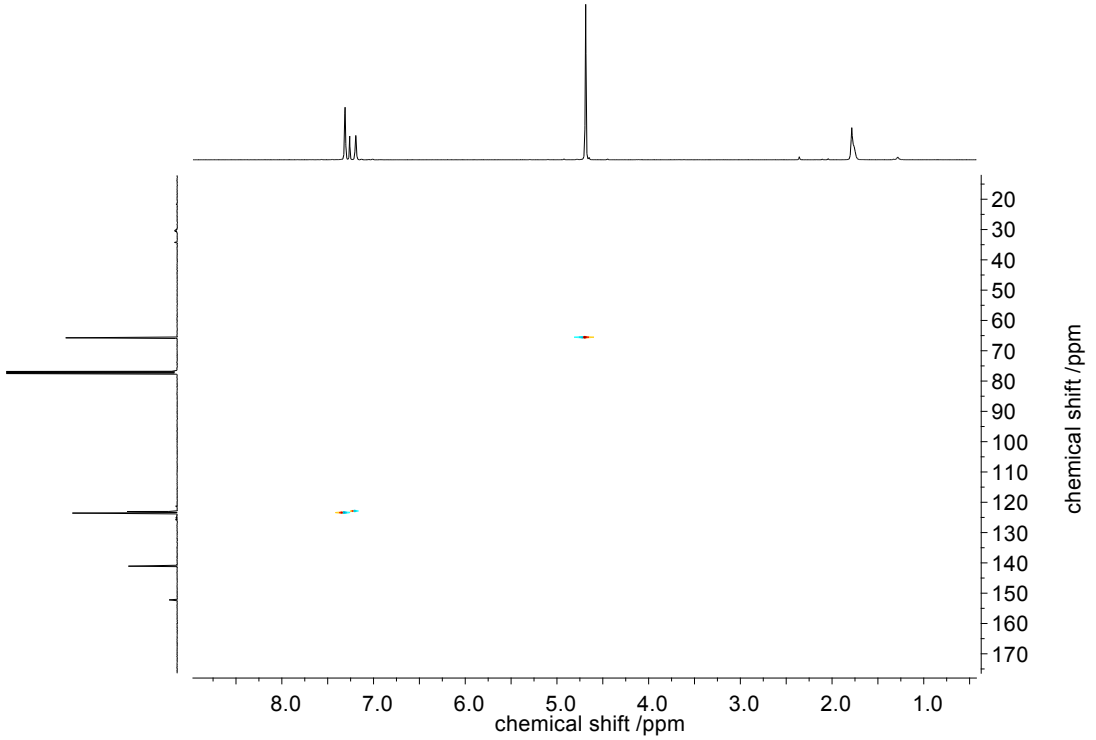


Figure S13. HSQC NMR spectrum ($CDCl_3$, 400 MHz) of (5-(*tert*-butyl)-1,3-dihydroxymethylenebenzene-d9.

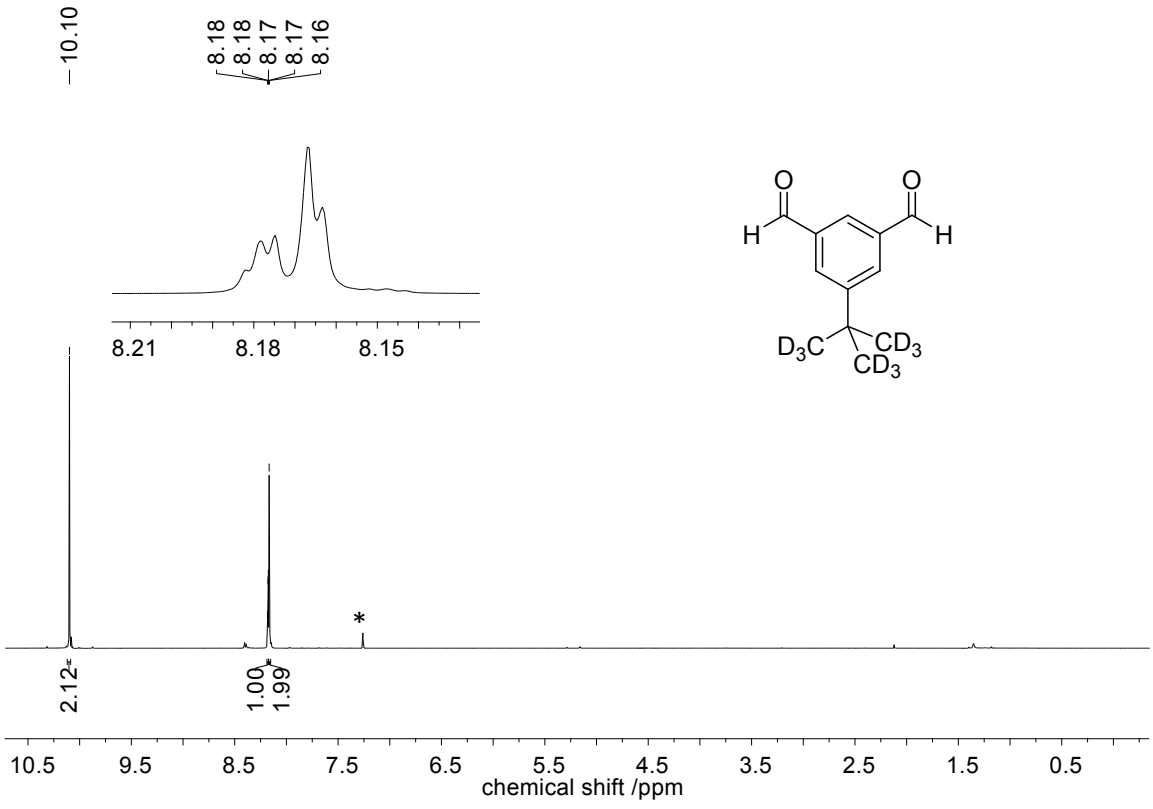


Figure S14. ^{1}H NMR spectrum ($CDCl_3$, 400 MHz) of **1-d9**. *$CHCl_3$.

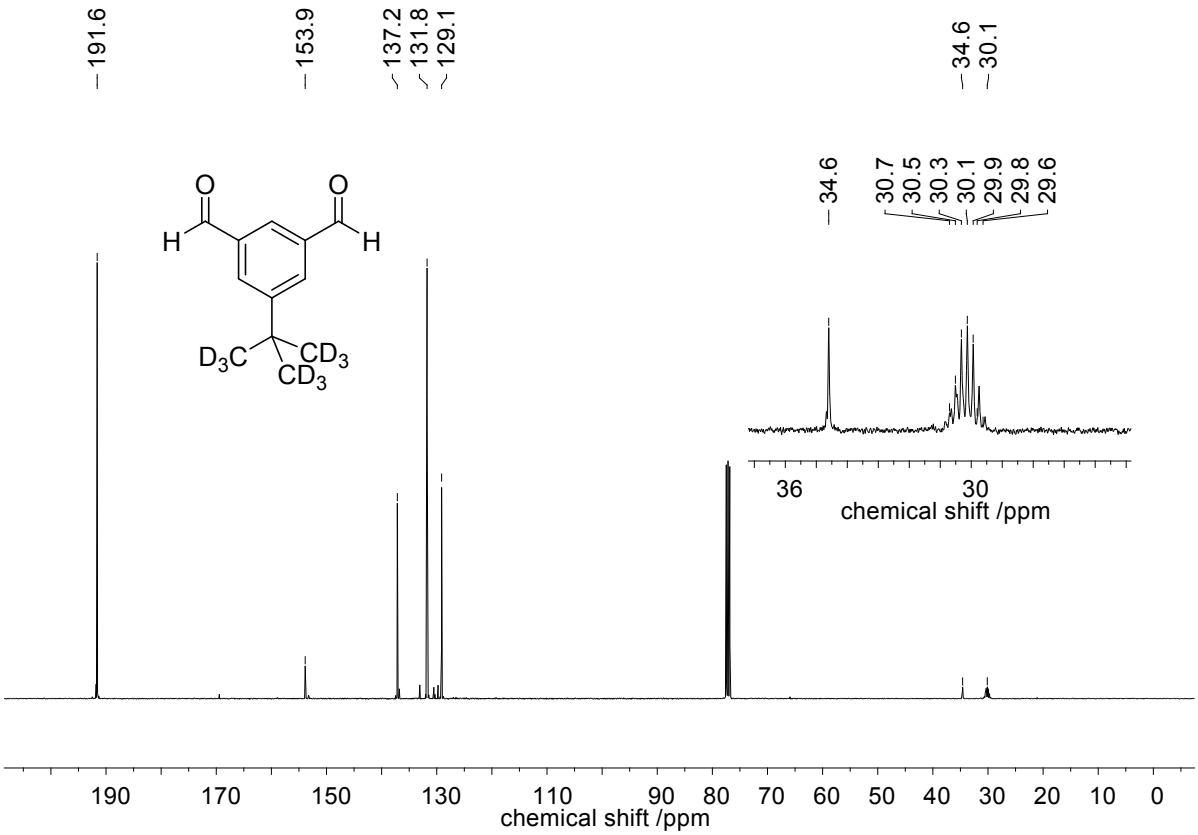


Figure S15. ^{13}C NMR spectrum ($CDCl_3$, 100 MHz) of **1d-9.**

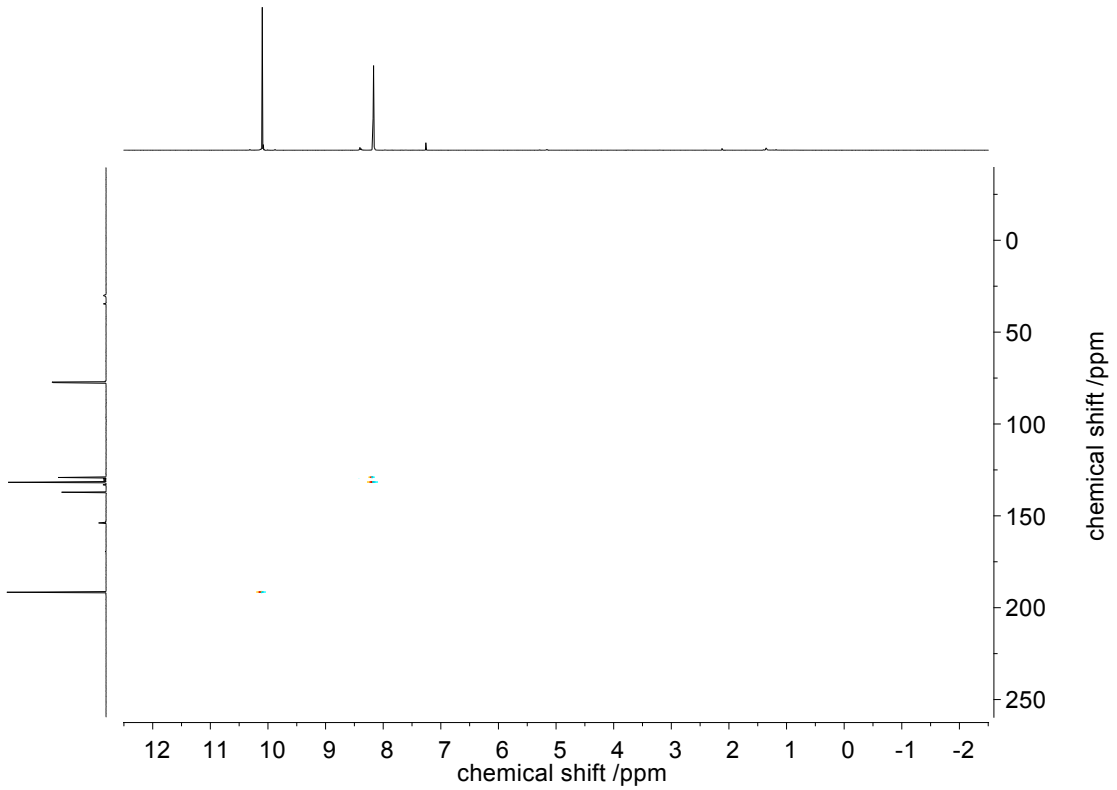


Figure S16. HSQC NMR spectrum ($CDCl_3$, 400 MHz) of **1d-9**.

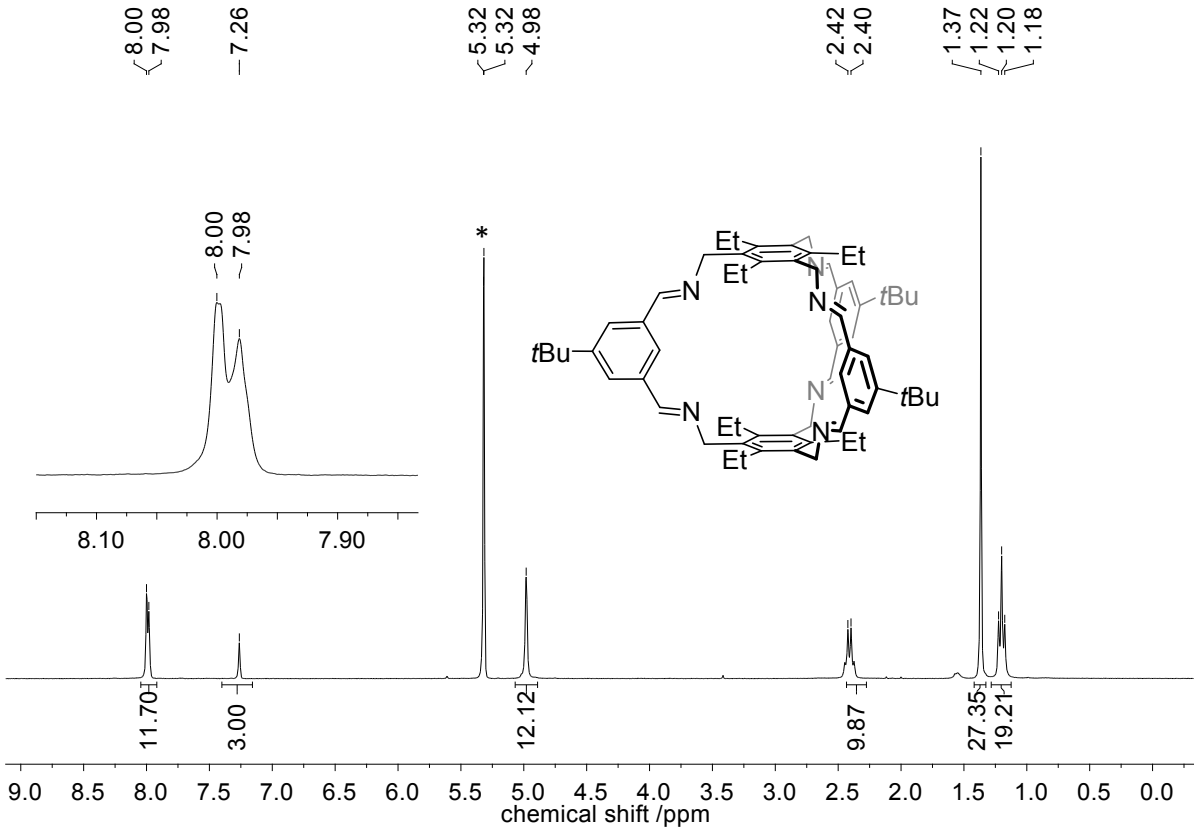


Figure S17. ^{1}H NMR spectrum of cage **4** (CD_2Cl_2, 600 MHz). *CH_2Cl_2.

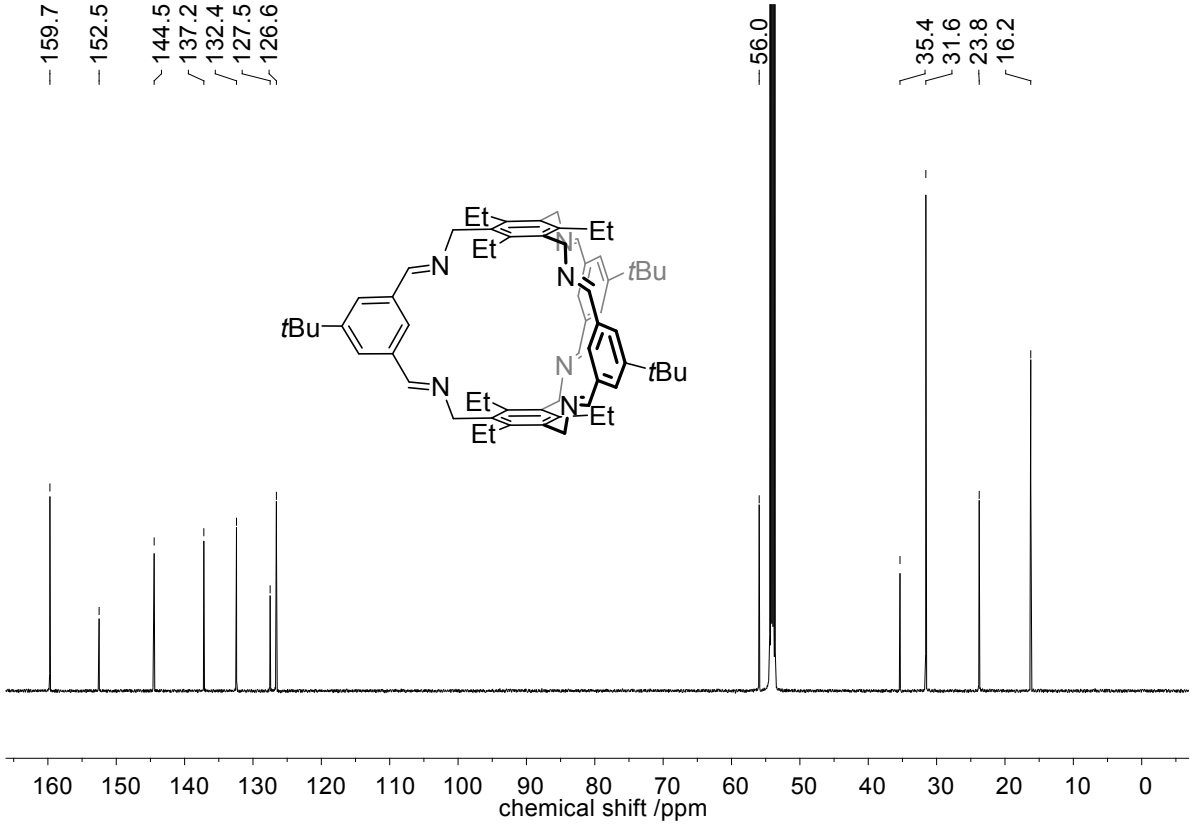


Figure S18. ^{13}C NMR spectrum (CD_2Cl_2, 150 MHz) of cage **4**.

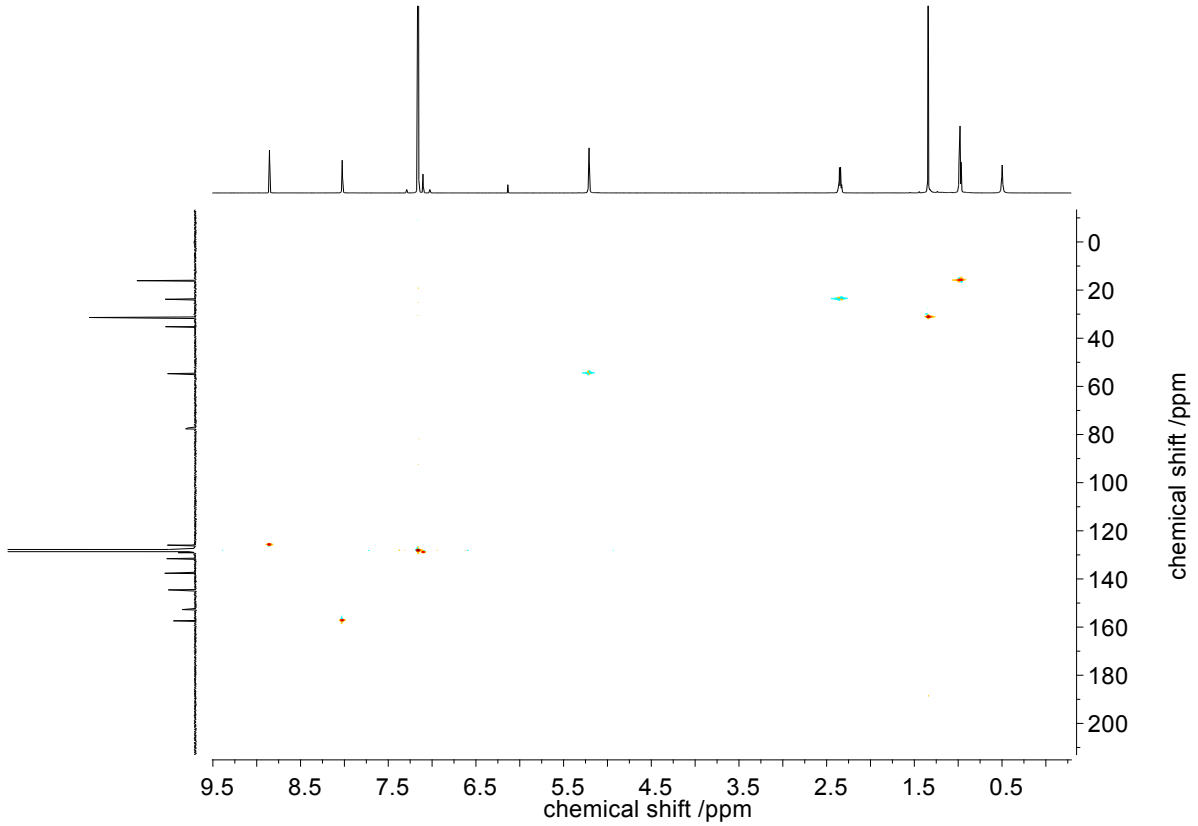


Figure S19. HSQC NMR spectrum of cage **4** (C_6D_6, 600/150 MHz).

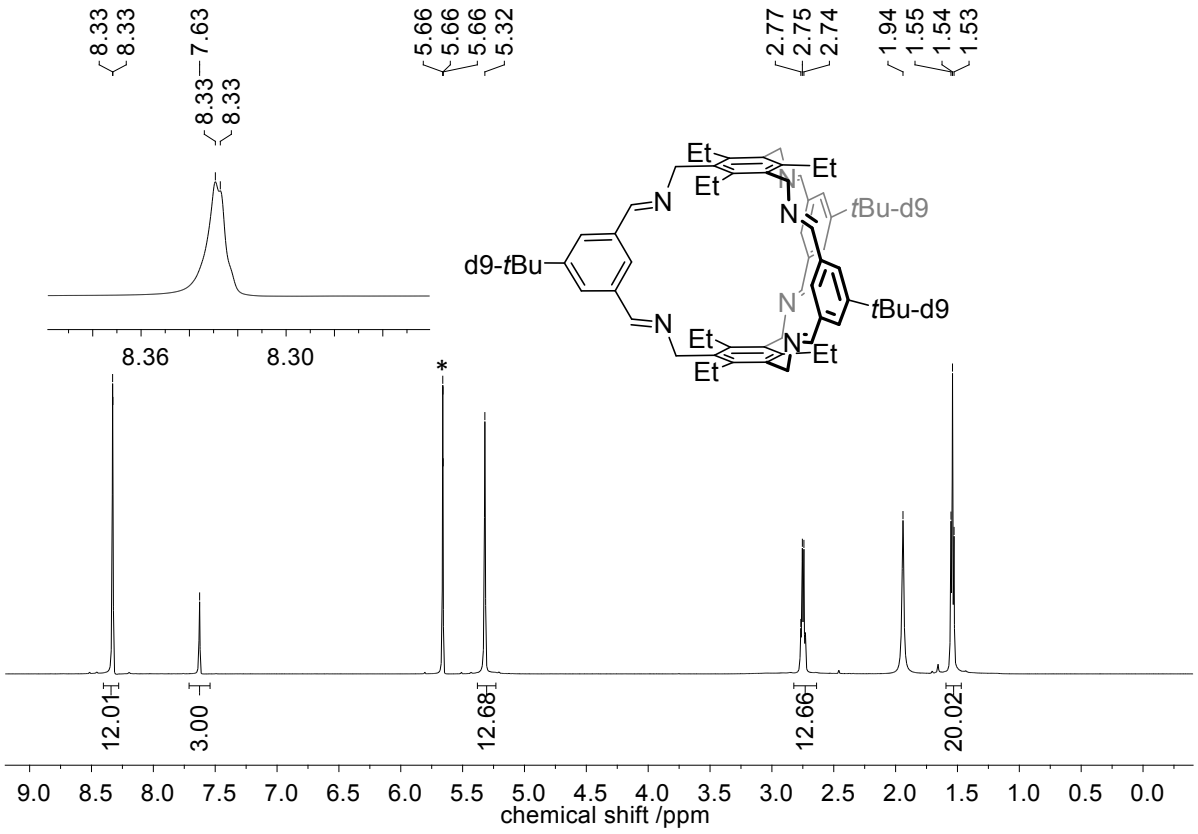


Figure S20. ^{1}H NMR spectrum (CD_2Cl_2, 600 MHz) of cage **4-d9**. *CH_2Cl_2.

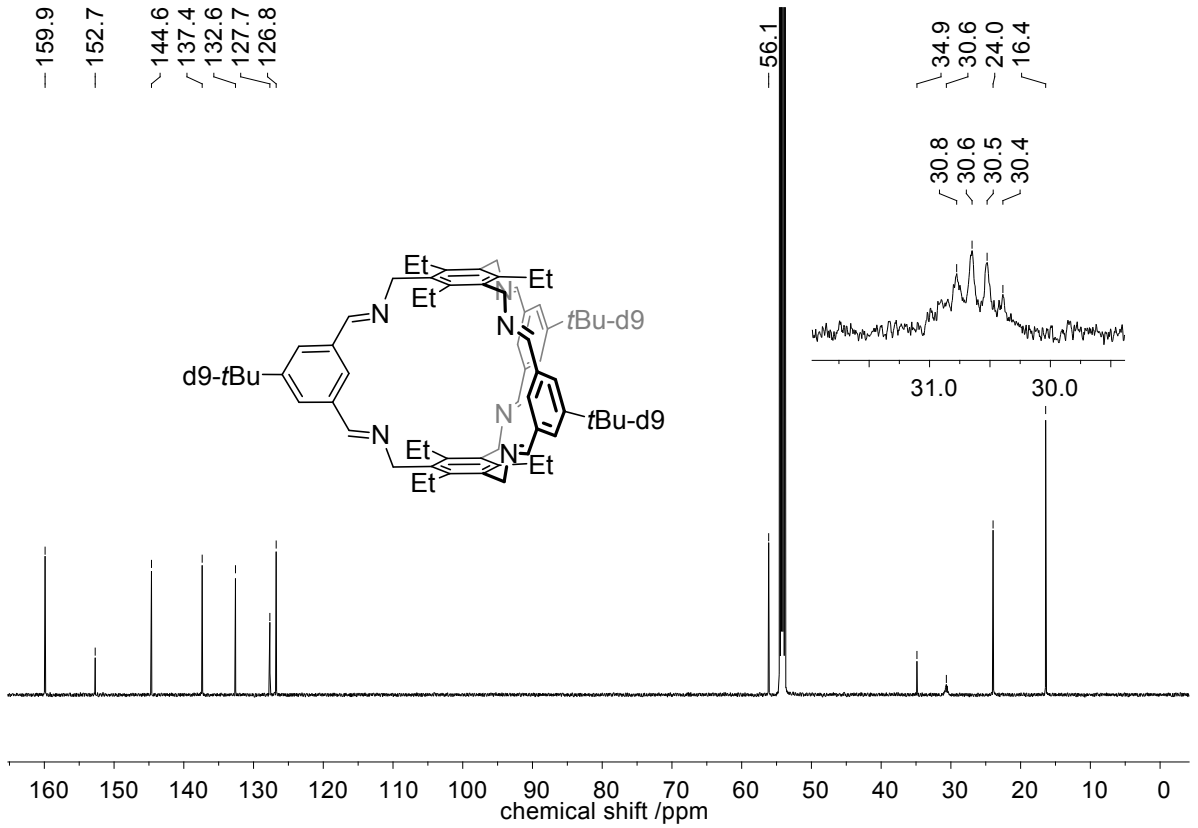


Figure S21. ^{13}C NMR spectrum (CD_2Cl_2, 150 MHz) of cage **4-d9**.

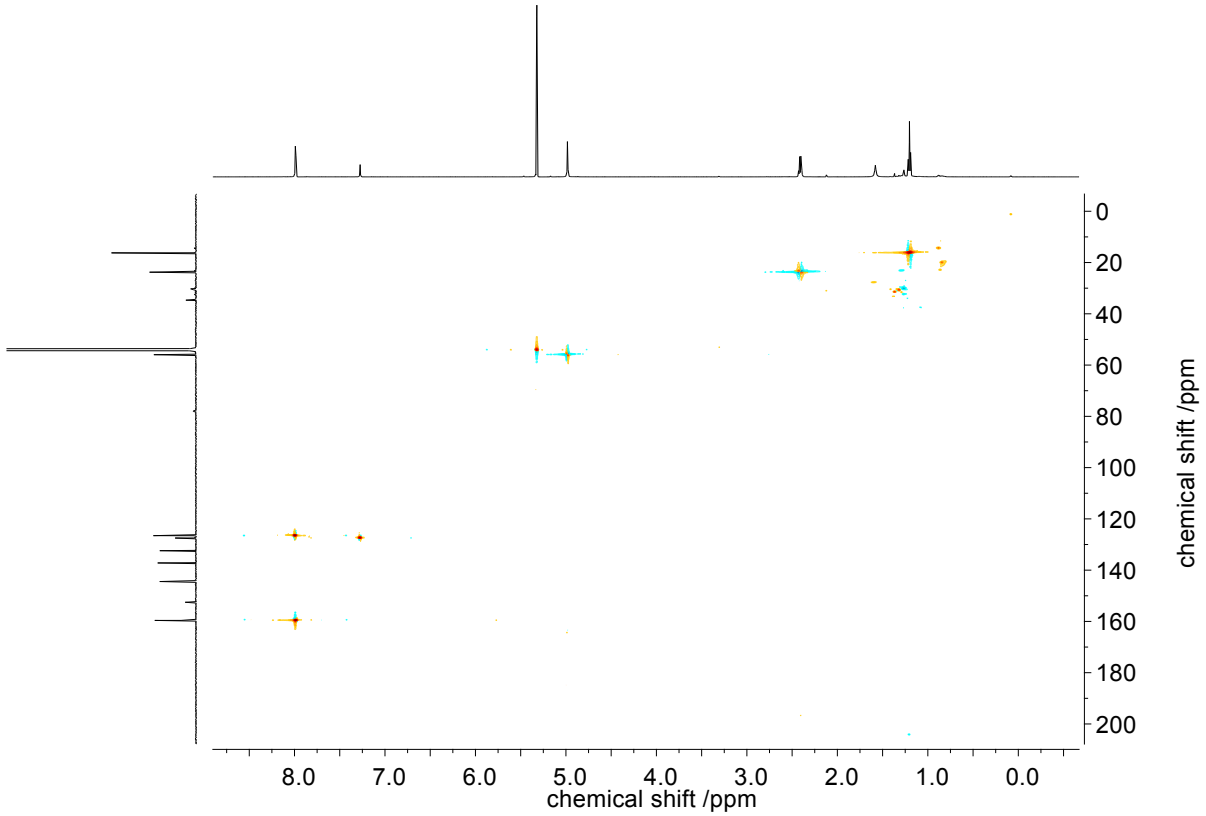


Figure S22. HSQC NMR spectrum (CD_2Cl_2, 600 MHz) of compound **4-d9**.

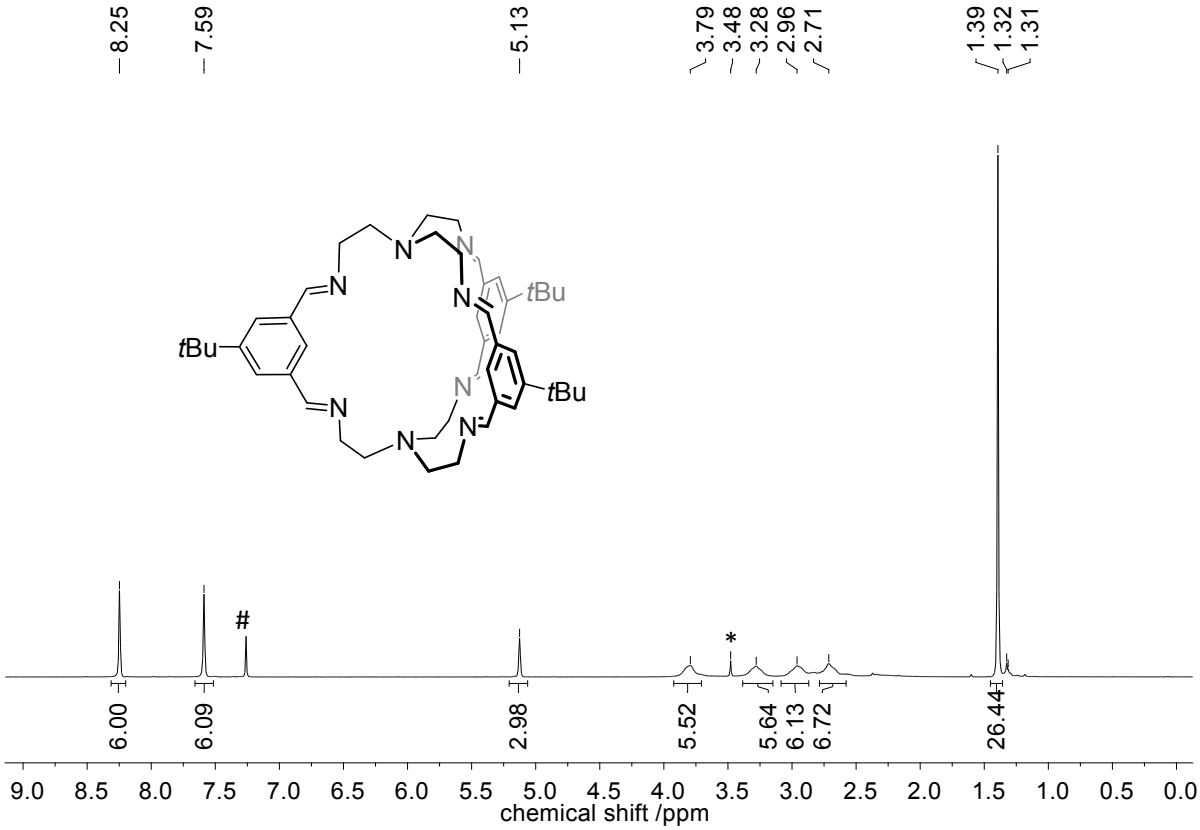


Figure S23. ^{1}H NMR spectrum ($CDCl_3$, 300 MHz) of cage **5**. $^{\#}CHCl_3$*MeOH.

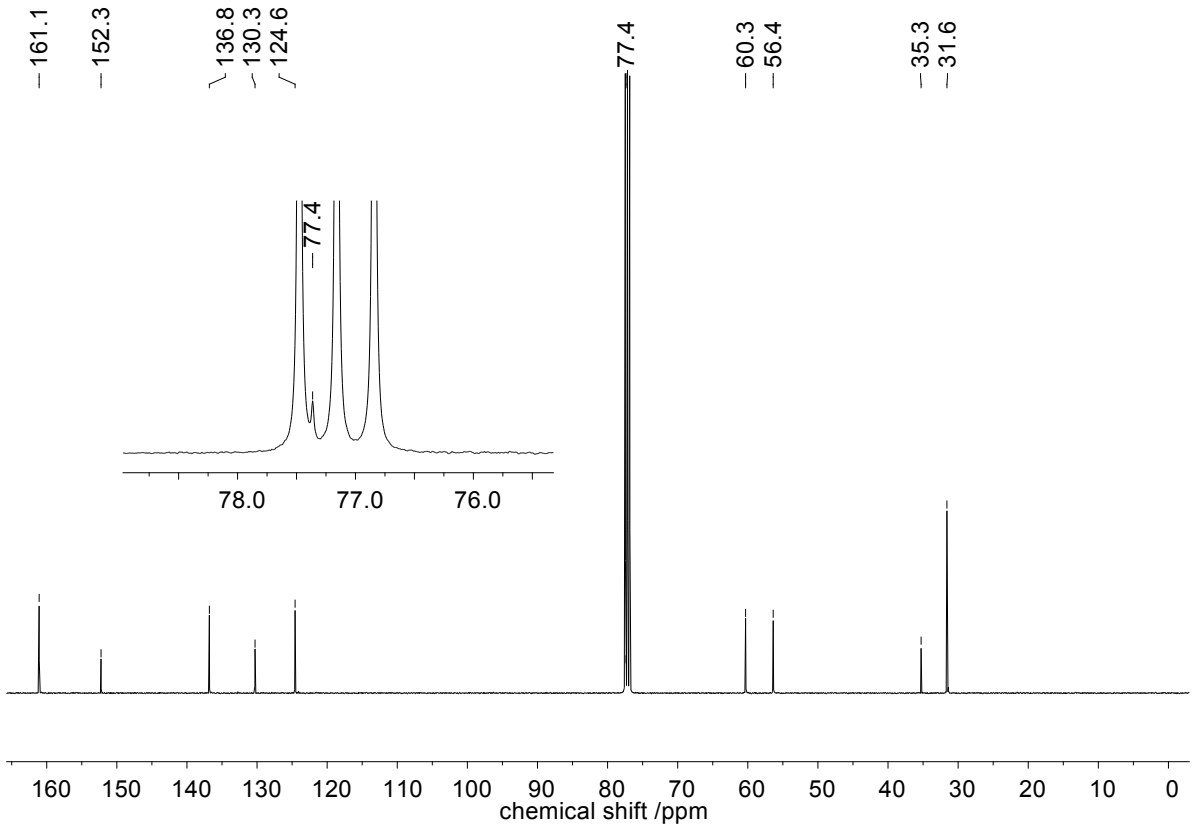


Figure S24. ^{13}C NMR spectrum ($CDCl_3$, 100 MHz) of cage **5**.

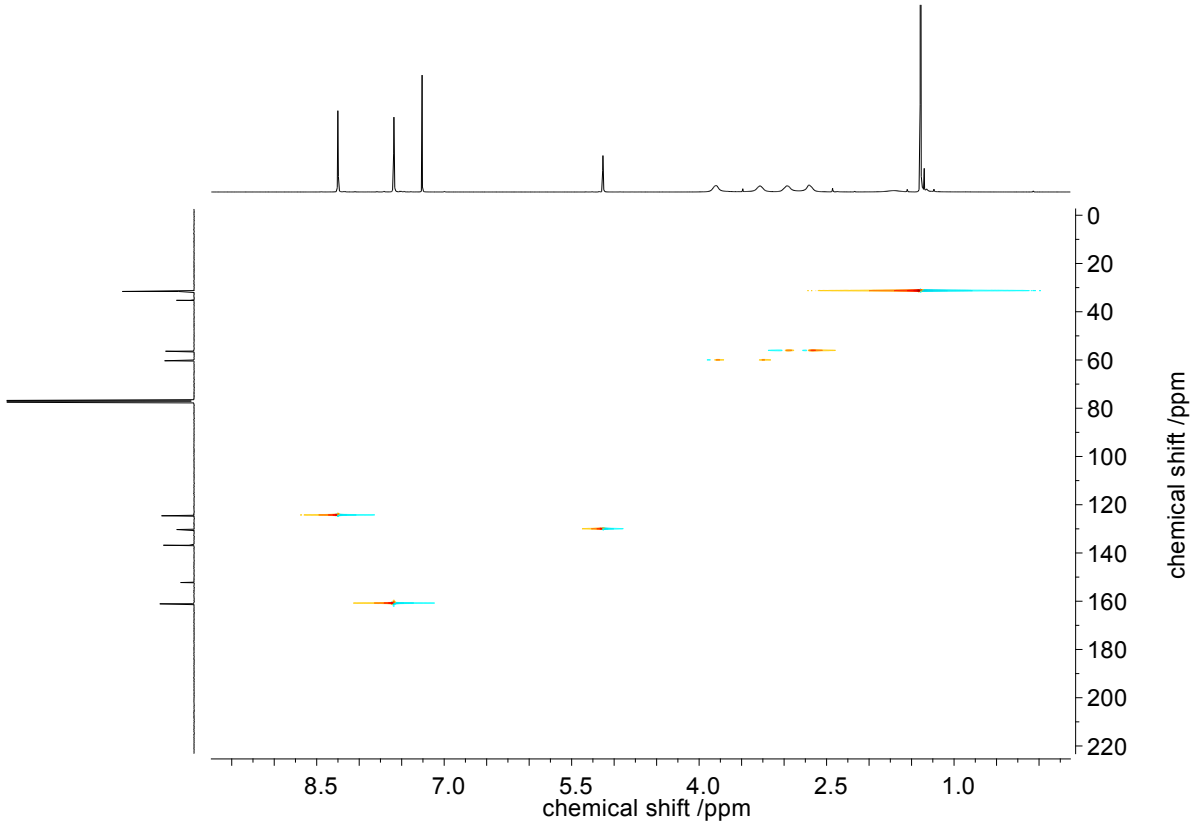


Figure S25. HSQC NMR spectrum ($CDCl_3$, 300 MHz) of compound **5**.

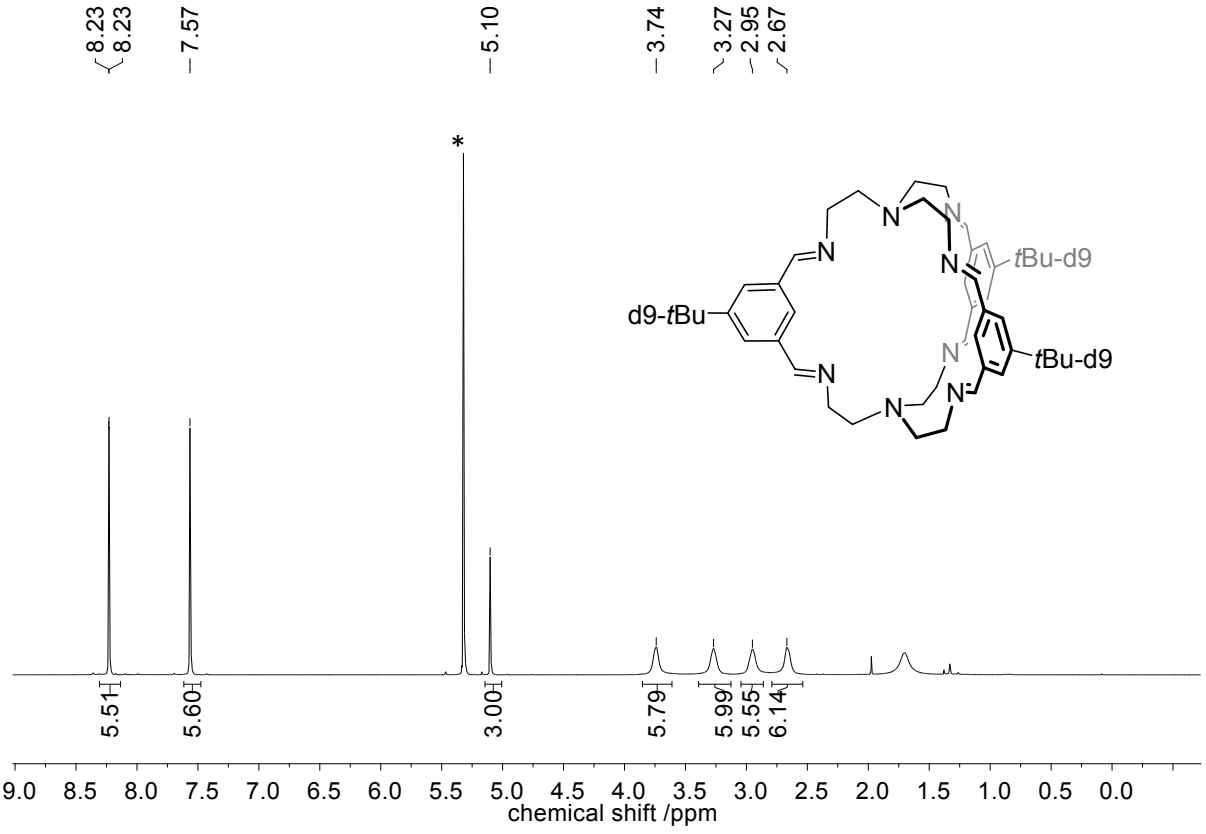


Figure S26. ^1H NMR spectrum (CD_2Cl_2, 600 MHz) of cage **5-d9**. *CH_2Cl_2

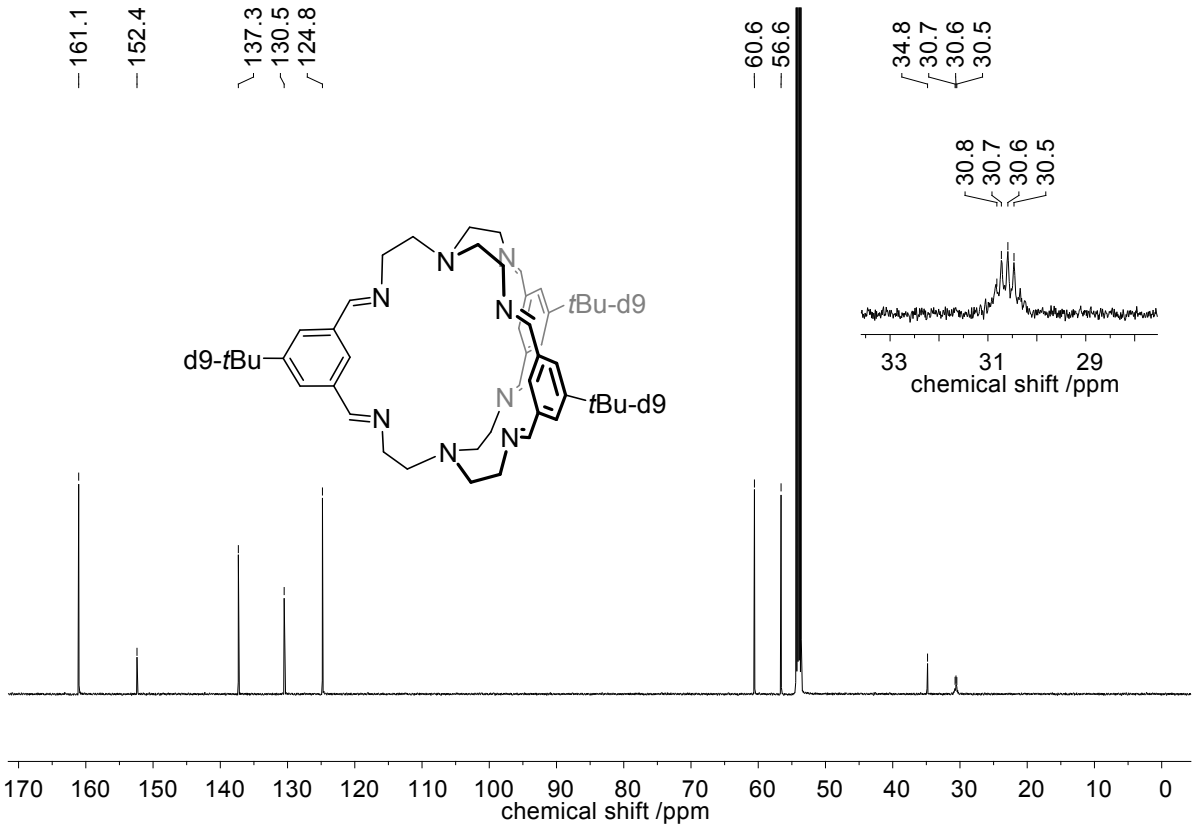


Figure S27. ^{13}C NMR spectrum (CD_2Cl_2, 150 MHz) of compound **5-d9**.

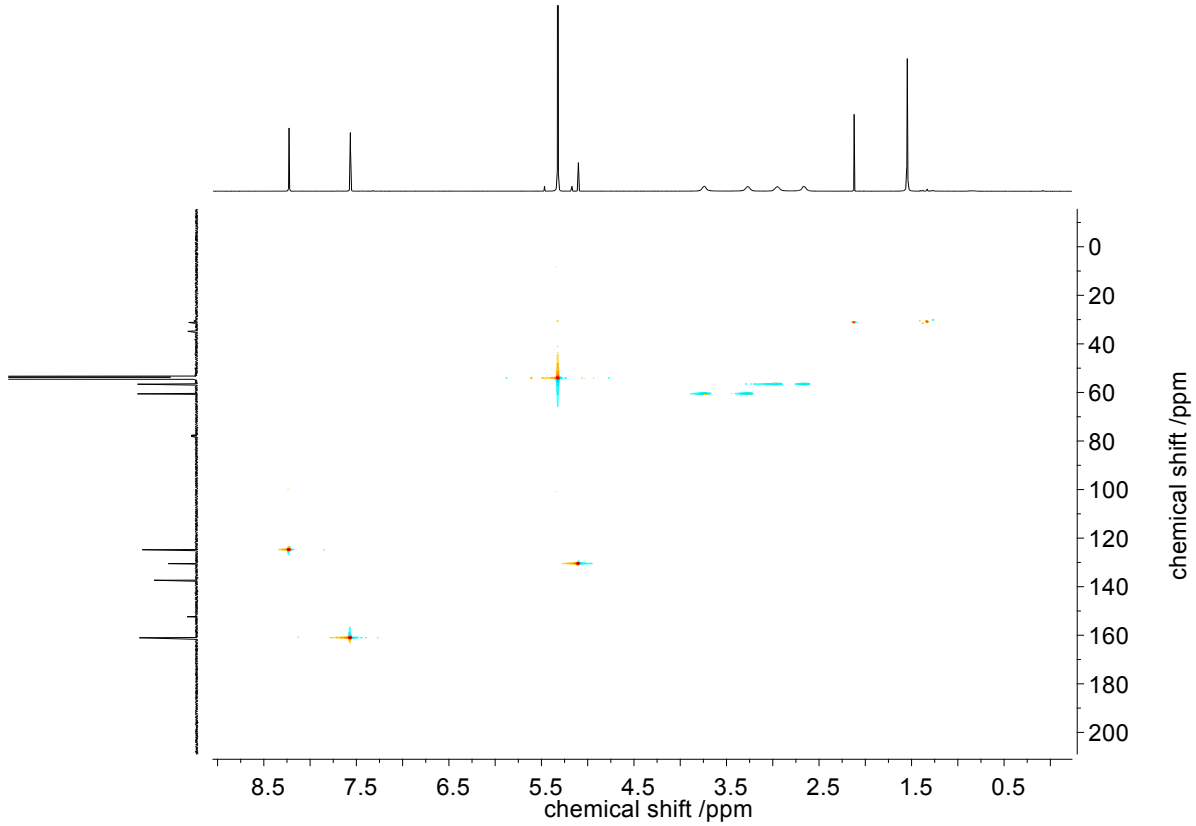


Figure S28. HSQC NMR spectrum (CD_2Cl_2, 600 MHz) of compound **5-d9**.

2. DOSY Experiments

DOSY NMR experiments were calibrated using known self-diffusion values for the solvents used (D_{solv}).[26] The solvodynamic radii were estimated using the semi-empirical modification of the Stokes-Einstein equation proposed by Chen and Chen.[27] This equation was solved for r_s using values of r_{solv} and η from the literature.[28]

$$D = \frac{k_B T}{\left(\frac{6}{1 + 0.695\left(\frac{r_{solv}}{r_s}\right)^{2.234}}\right)\pi\eta r_s}$$

D is the measured diffusion coefficient ($m^2 \cdot s^{-1}$)

k_B is Boltzmann constant (1.3806485 $\cdot 10$ $m^2 \cdot kg \cdot s^{-2} \cdot K^{-1}$)

T is the temperature (K)

r_{solv} is the hydrodynamic radius of the solvent (m)

r_s is the hydrodynamic radius of the analyte (m)

η is the viscosity of the solvent at temperature T ($kg \cdot m^{-1} \cdot s^{-1}$)

Table S1: Estimation of the hydrodynamic radius of cage compounds (r_h) in the corresponding solvents using parameters from literature and diffusion coefficients measured by DOSY NMR.

Compound	T [K]	Solvent	$D_{solv} \cdot 10^{-9}$ [$m^2 \cdot s^{-1}$]	r_{solv} [nm]	$\eta \cdot 10^{-3}$ [$kg \cdot m^{-1} \cdot s^{-1}$]	$D \cdot 10^{-10}$ [$m^2 \cdot s^{-1}$]	r_h [nm]
4	298	C_6D_6	2.18	0.270	0.603	4.89	0.73
5	298	$CDCl_3$	2.45	0.260	0.542	6.31	0.63

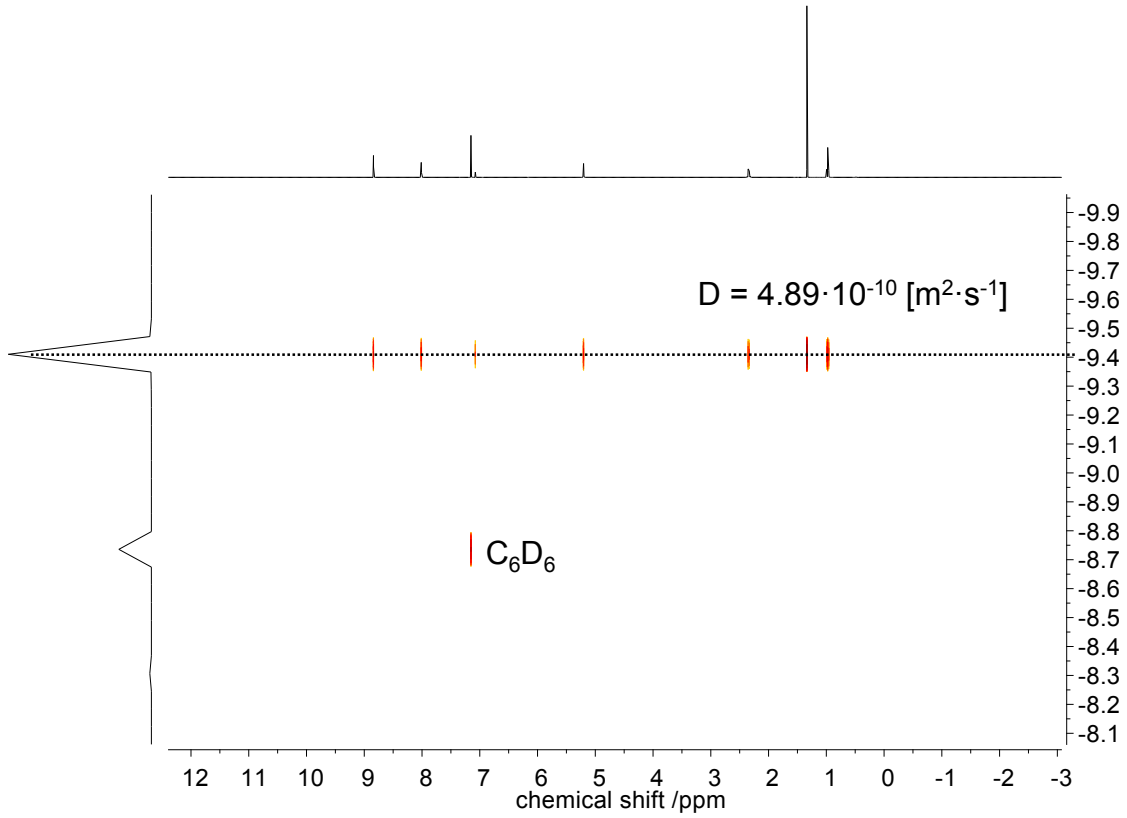


Figure S29. DOSY NMR spectrum of compound **4** (C_6D_6, 298 K, 400 MHz).

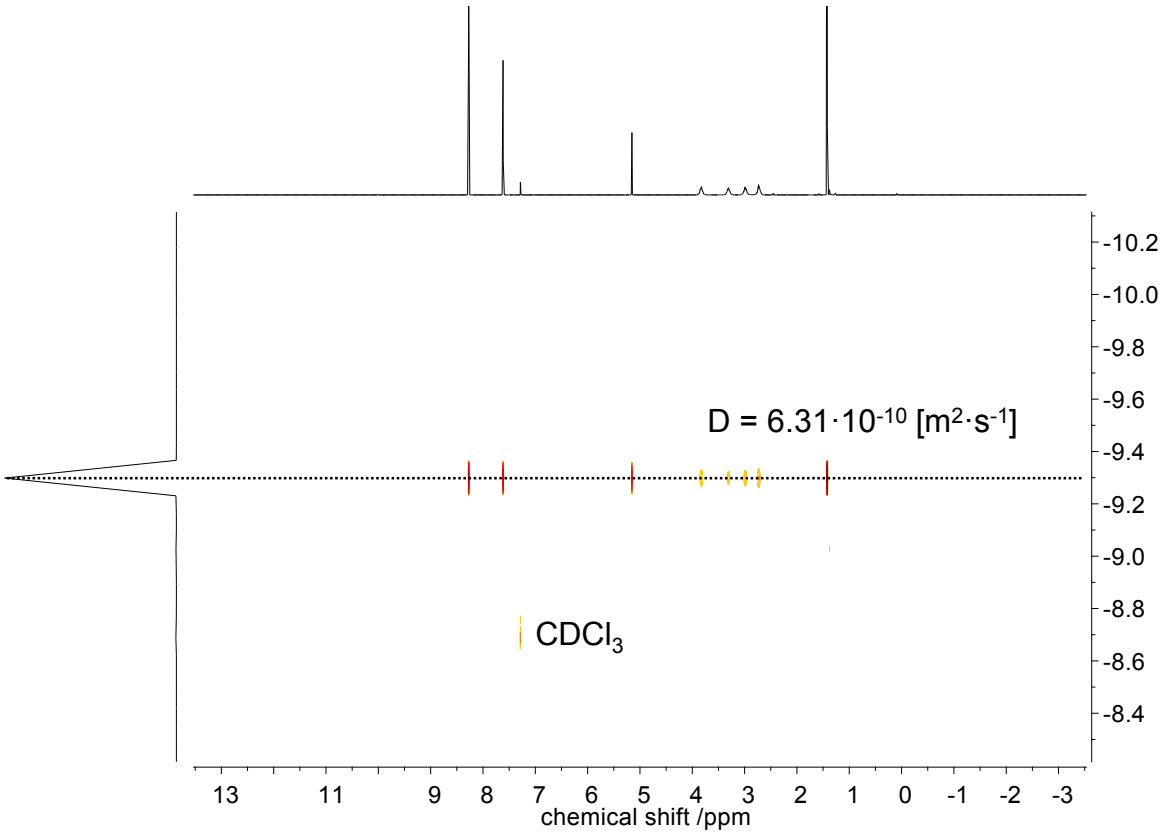


Figure S30. DOSY NMR spectrum of compound **5** ($CDCl_3$, 298 K, 400 MHz).

3. Mass Spectra

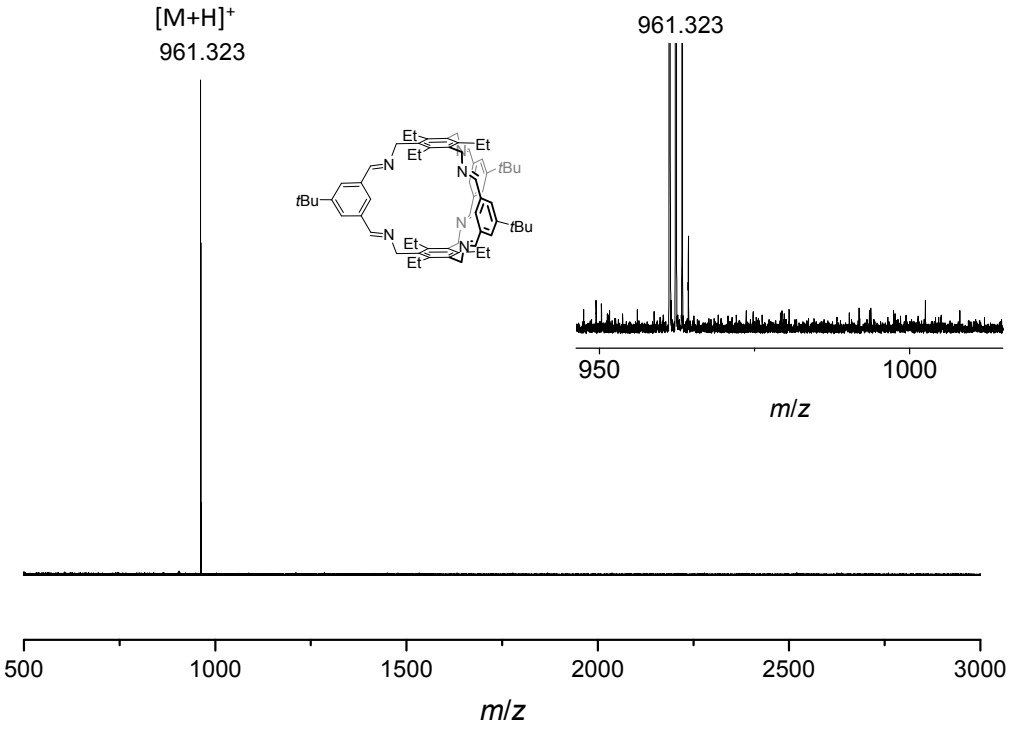


Figure S31. MALDI-TOF MS (DCTB) of cage **4**. The isotopic pattern of the signal at *m*/*z* = 961.323 in the zoomed spectrum is not visible since the signal was cut due to its high intensity.

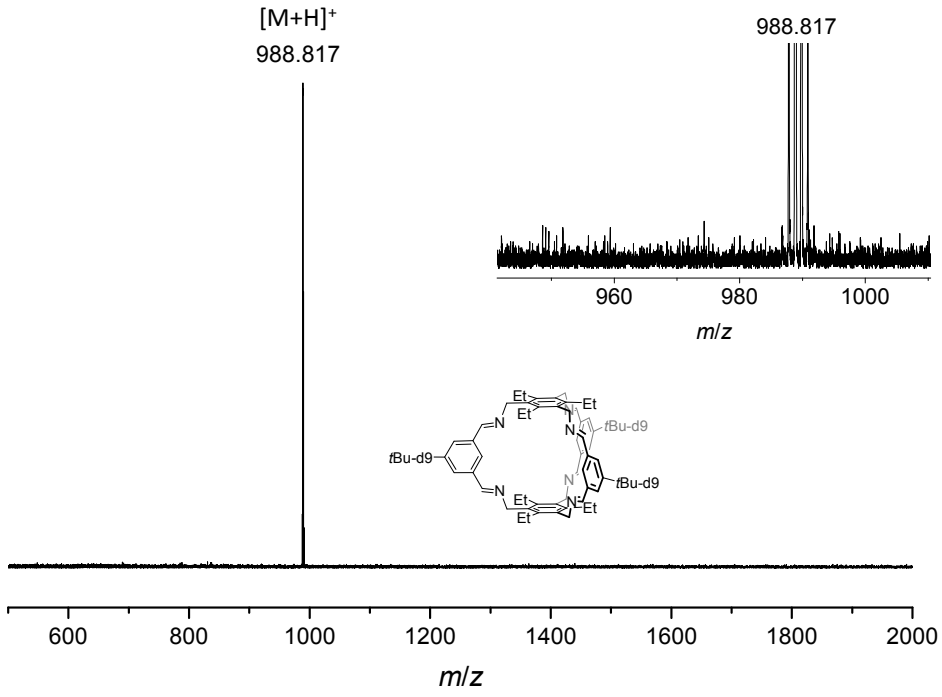


Figure S32. MALDI-TOF MS (DCTB) of cage **4-d27**. The isotopic pattern of the signal at *m*/*z* = 988.817 in the zoomed spectrum is not visible since the signal was cut due to its high intensity.

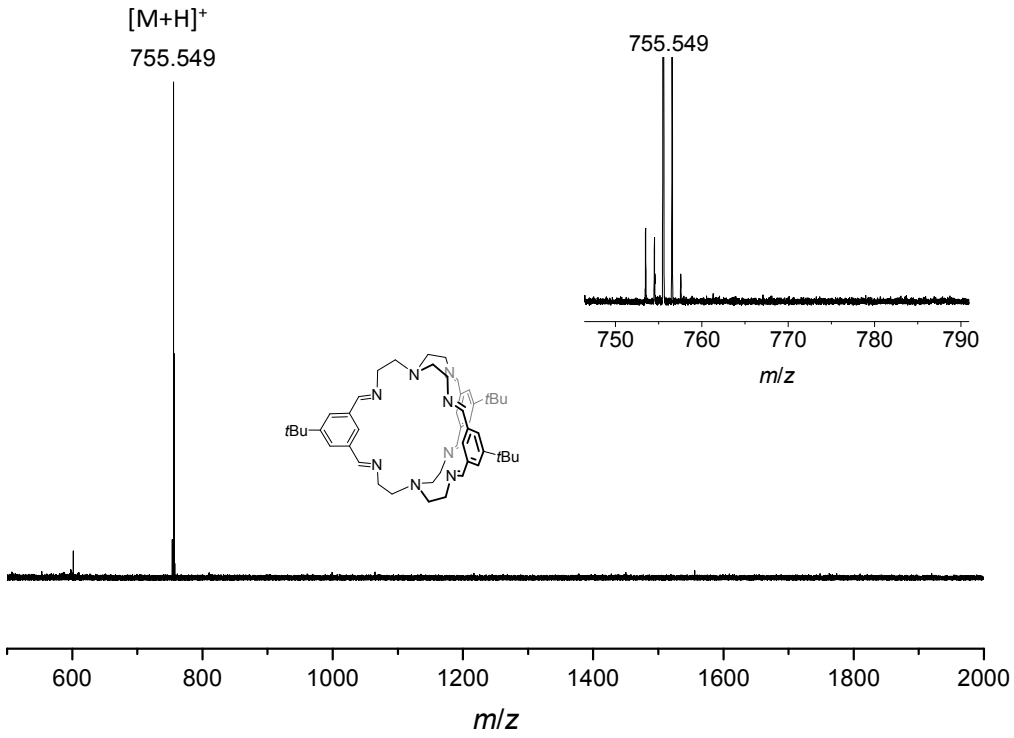


Figure S33. MALDI-TOF MS (DCTB) of cage **5**. The isotopic pattern of the signal at *m*/*z* = 755.549 in the zoomed spectrum is not visible since the signal was cut due to its high intensity.

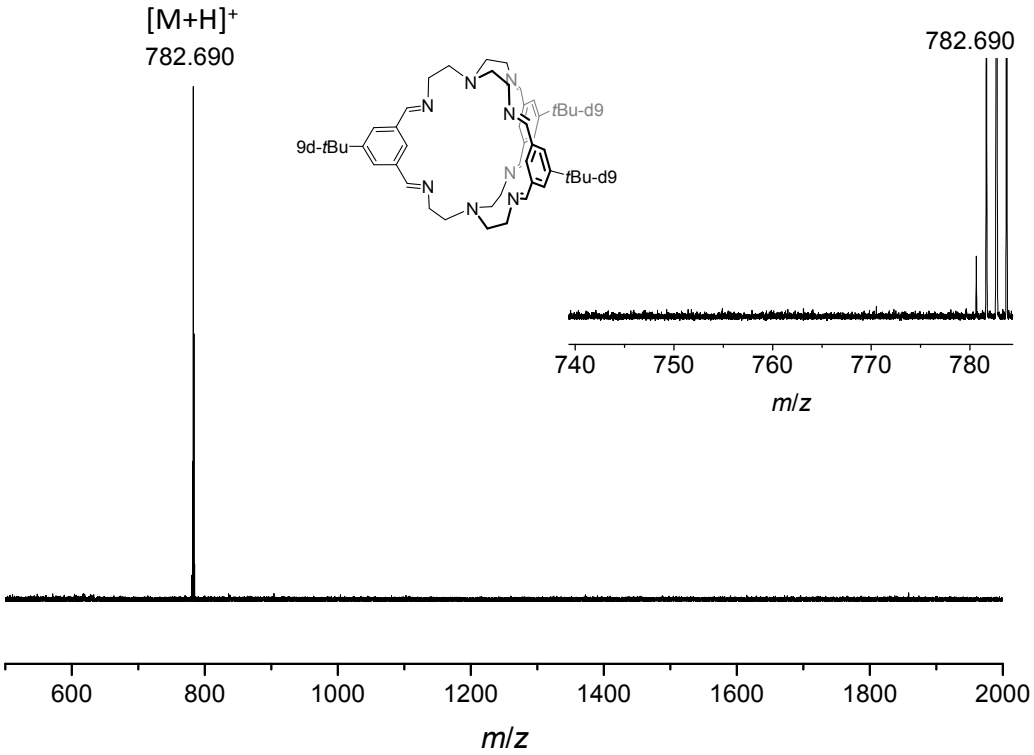


Figure S34. MALDI-TOF MS (DCTB) of cage **5-d27**. The isotopic pattern of the signal at *m*/*z* = 782.690 in the zoomed spectrum is not visible since the signal was cut due to its high intensity.

4. Infrared Spectra

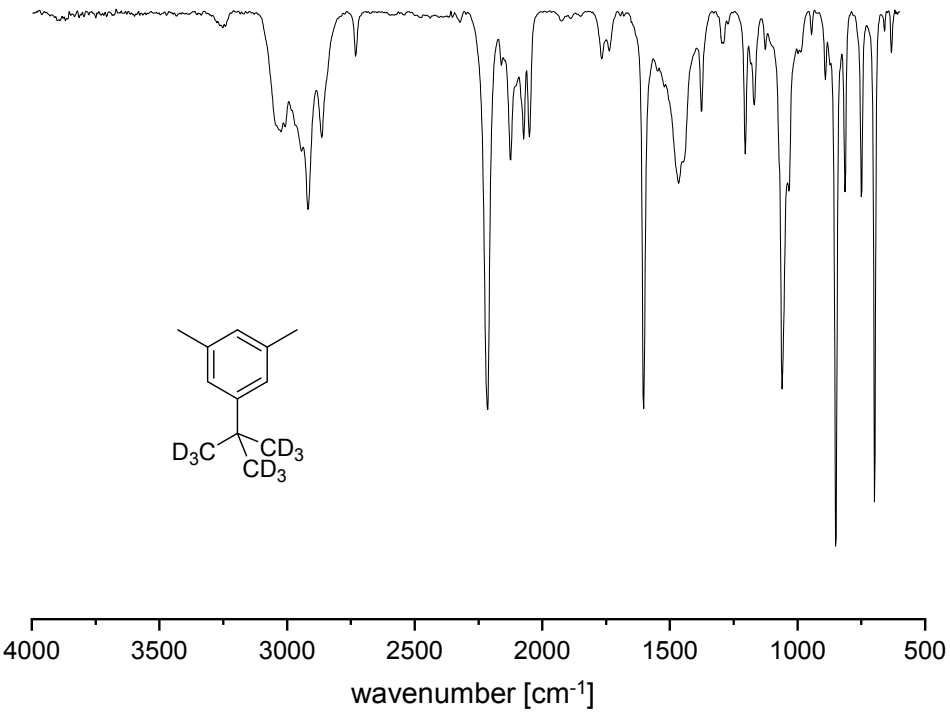


Figure S35. IR spectrum (ATR) of 1-(*tert*-butyl)-3,5-dimethyl-benzene-d9.

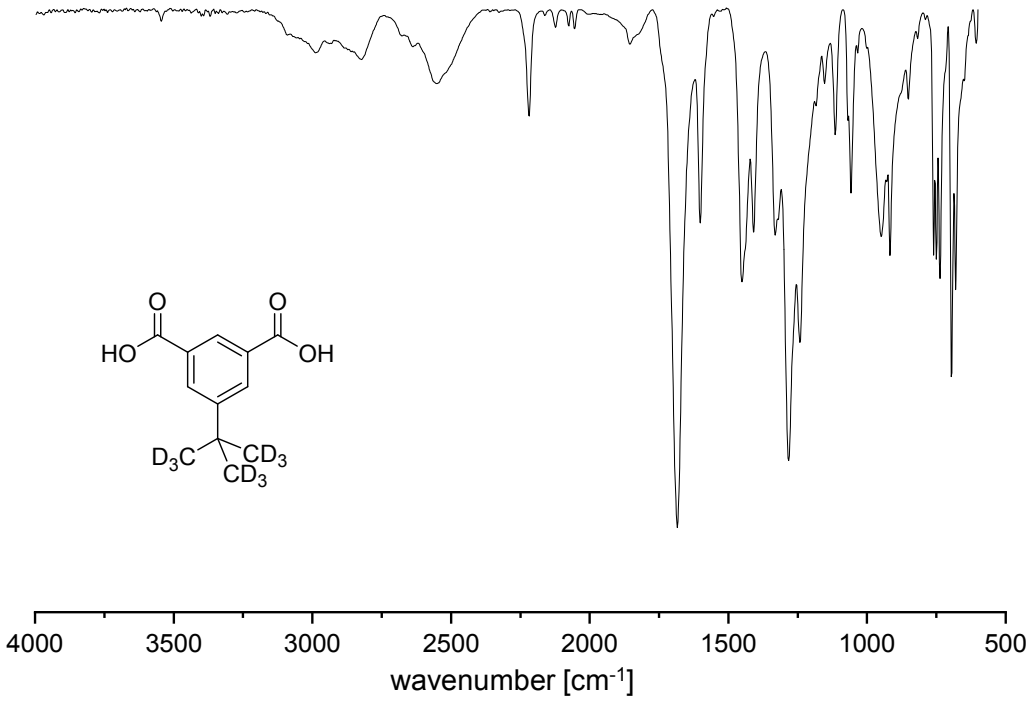


Figure S36. IR spectrum (ATR) of 5-(*tert*-butyl)isophthalic acid-d9.

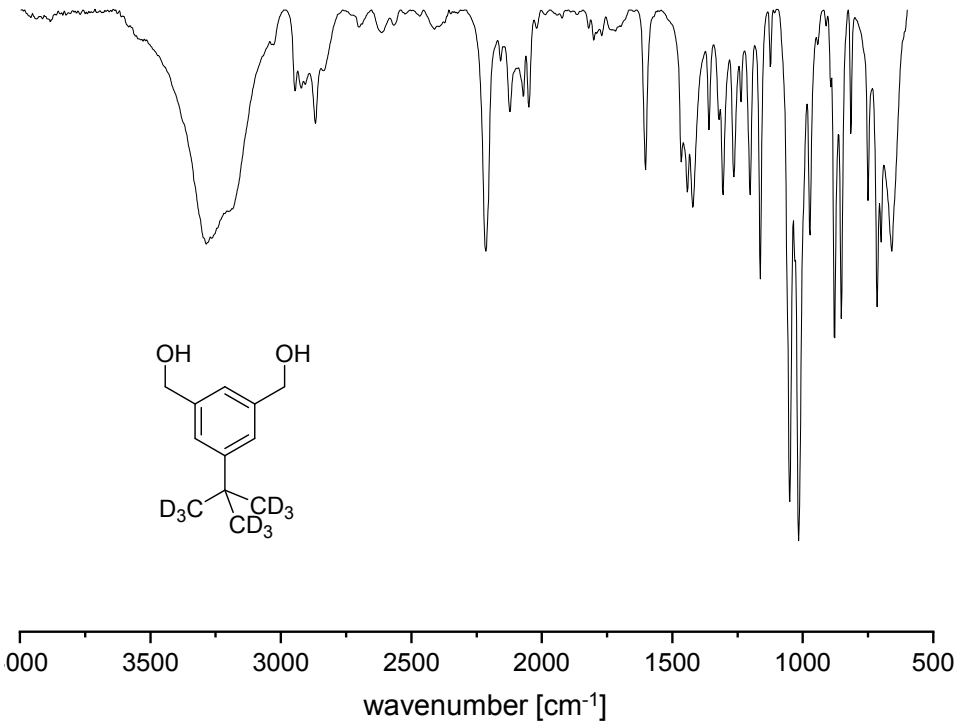


Figure S37. IR spectrum (ATR) of (5-(*tert*-butyl)-1,3-dihydroxymethylenebenzene-d9.

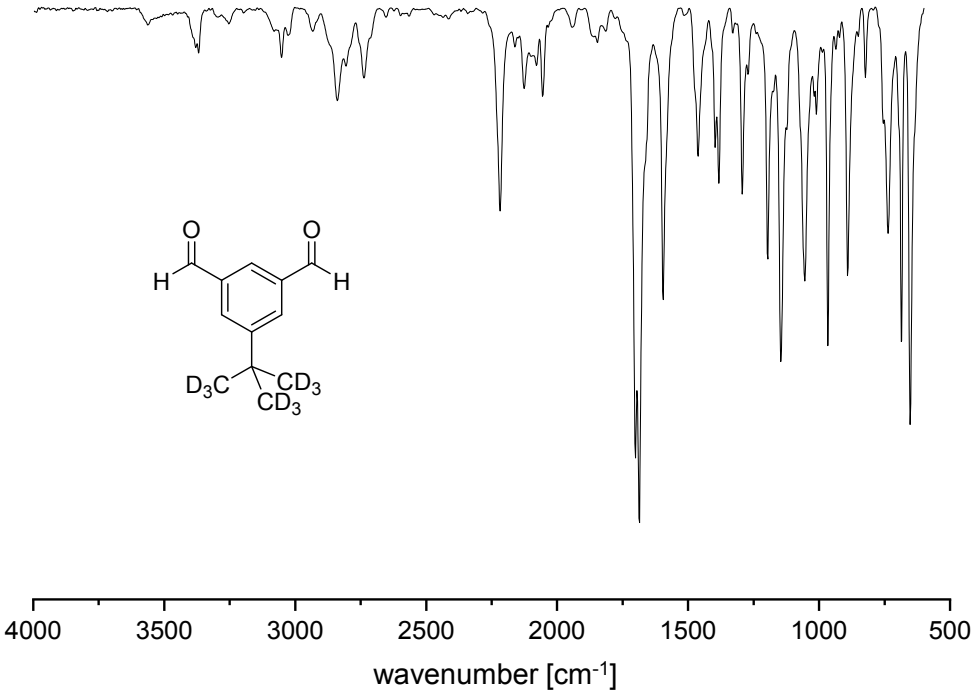


Figure S38. IR spectrum (ATR) of compound **1-d9**.

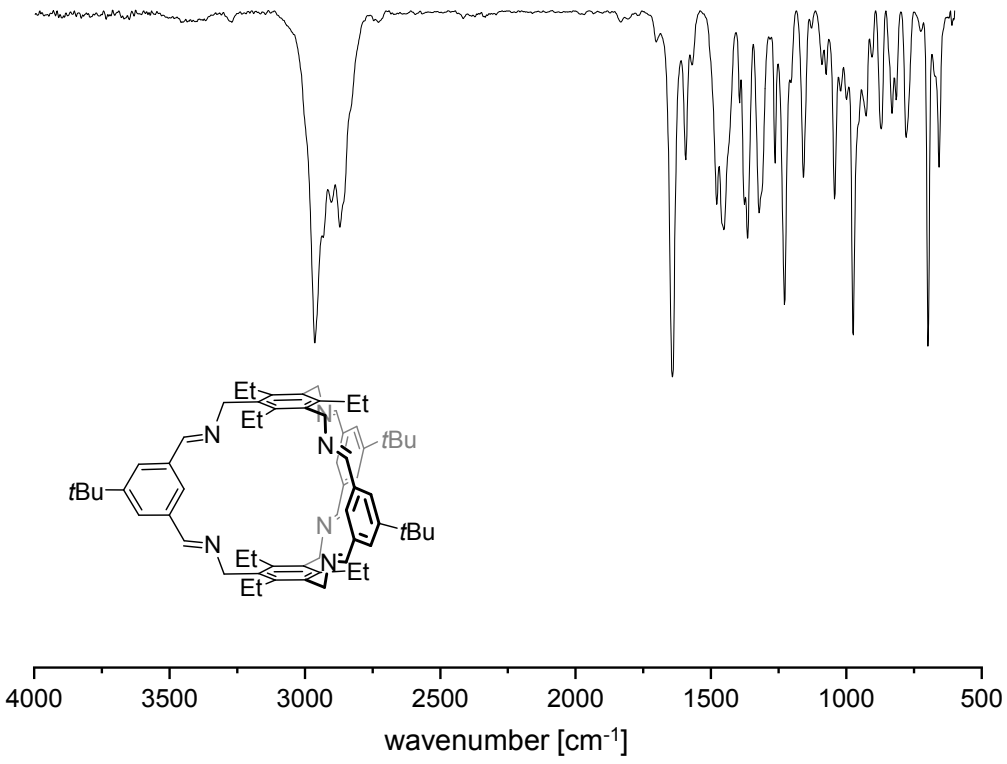


Figure S39. IR spectrum (ATR) of cage compound **4**.

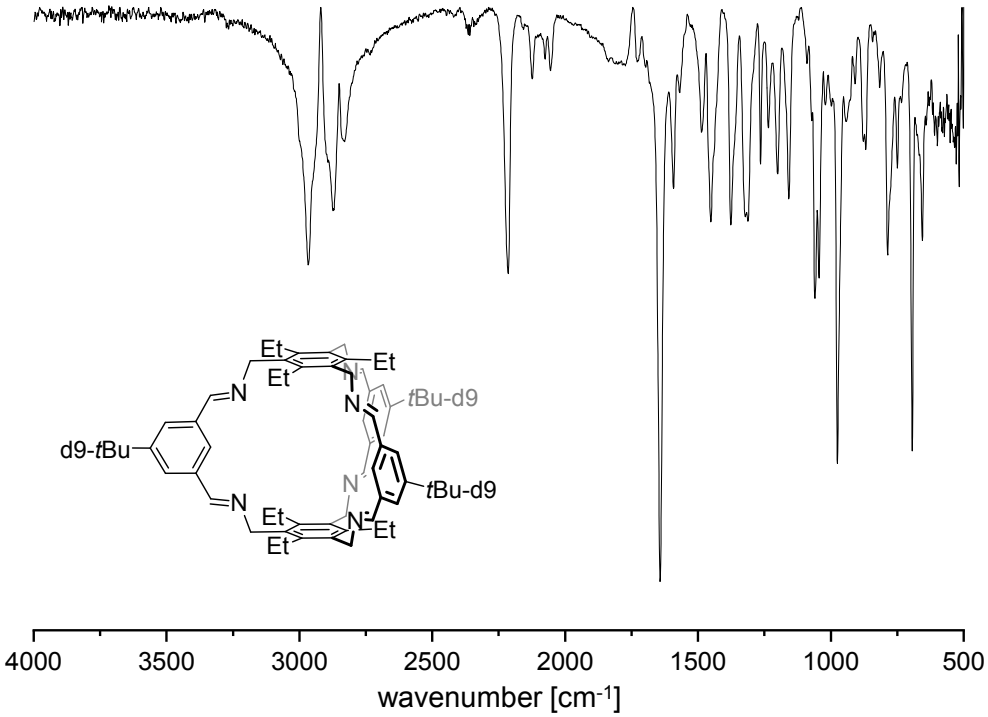


Figure S40. IR spectrum (ATR) of cage compound **4-d9**.

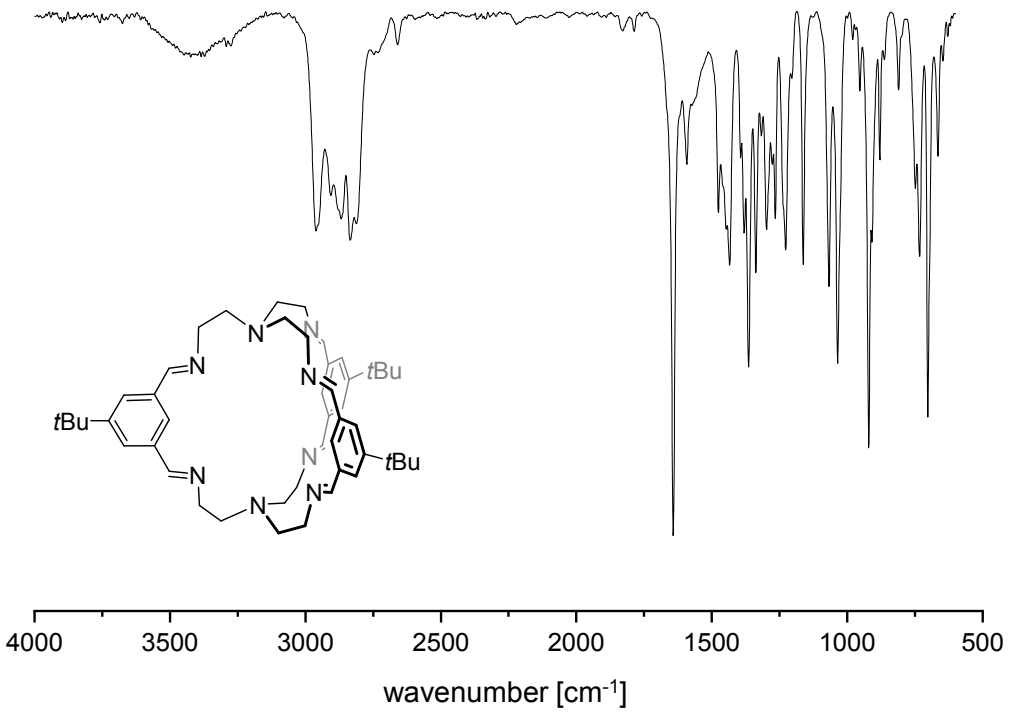


Figure S41. IR spectrum (ATR) of cage compound **5**.

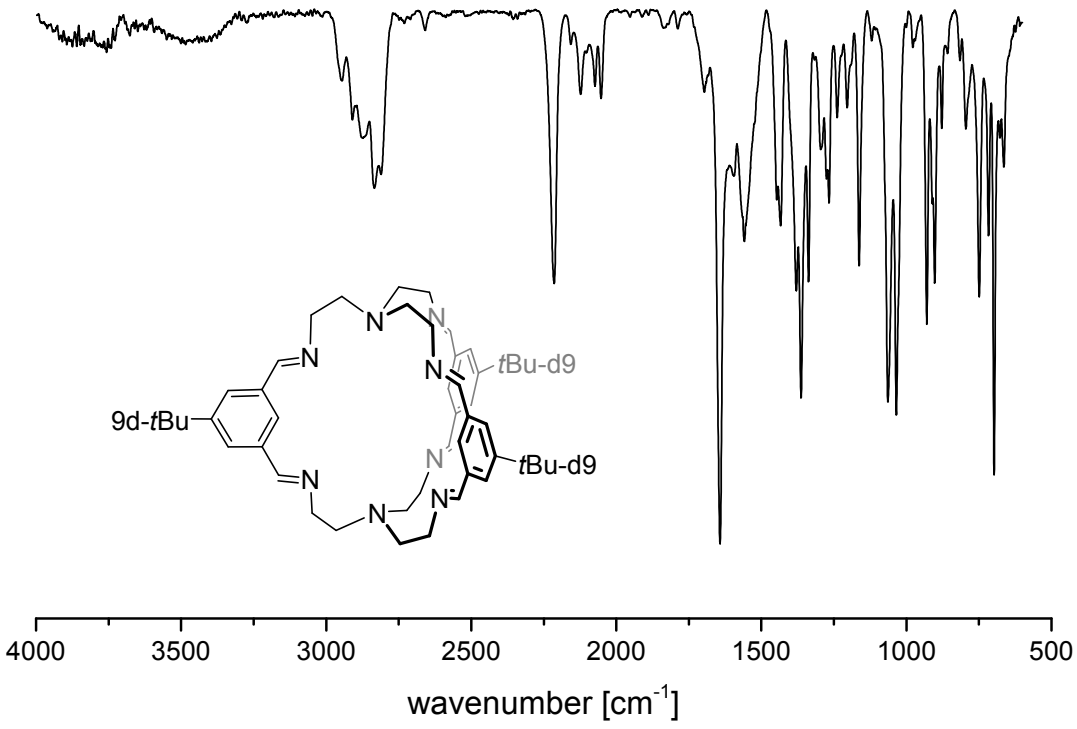


Figure S42. IR spectrum (ATR) of cage compound **5d-9**.

5. Single-crystal X-ray Diffraction Data

Crystal structure of compound 4-d27

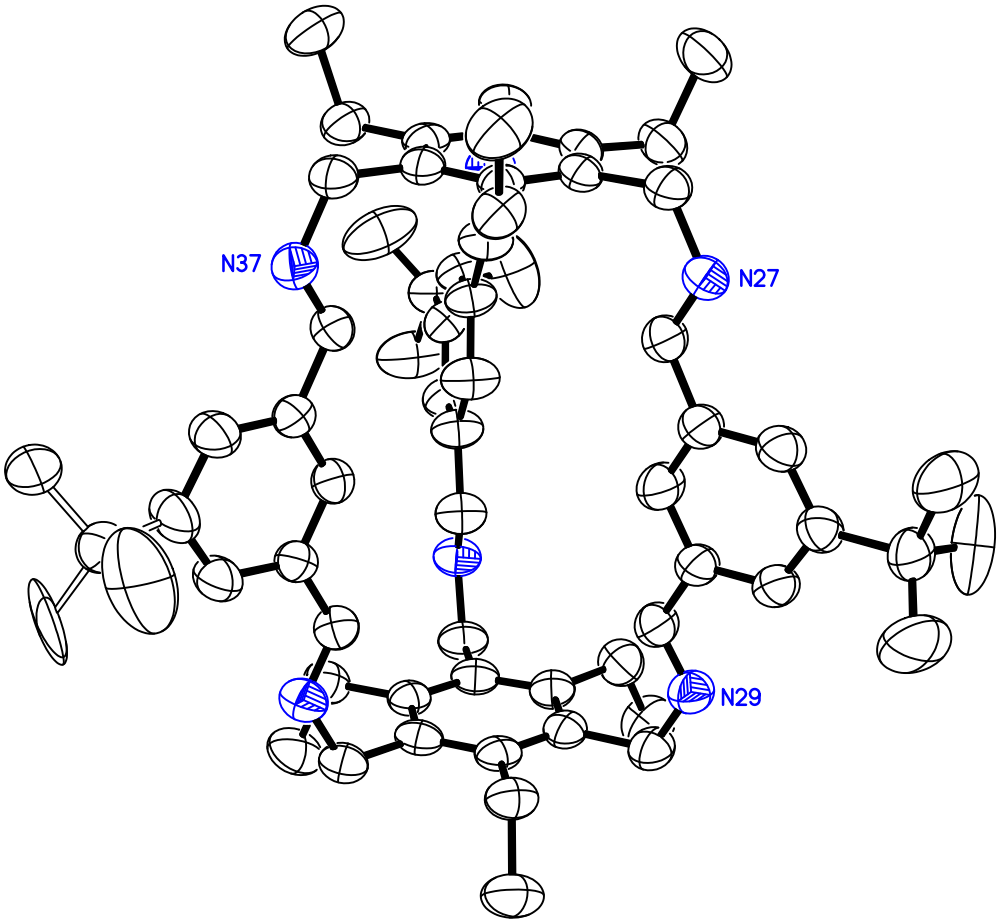


Figure S43. Crystal structure of compound **4-d27**. Atoms of carbon are depicted in white and nitrogen in blue. Ellipsoid contour plot at a 50% probability level.

Crystals were obtained by slow evaporation of Benzene.

CCDC-number : 2016234

Table S2: Crystal data and structure refinement for **4-d27**.

Empirical formula	$C_{90}H_{108}N_6$
Formula weight	1273.82
Temperature	200(2) K
Wavelength	1.54178 Å
Crystal system	orthorhombic
Space group	Pnna
Z	4
Unit cell dimensions	a = 29.9197(13) Å α = 90 deg.
	b = 21.7163(8) Å β = 90 deg.
	c = 12.1918(4) Å γ = 90 deg.
Volume	7921.6(5) $Å^3$
Density (calculated)	1.07 g/cm^3
Absorption coefficient	0.47 mm^{-1}
Crystal shape	plate
Crystal size	0.089 x 0.066 x 0.019 mm^3
Crystal colour	colourless
Theta range for data collection	3.0 to 52.6 deg.
Index ranges	$-28 \le h \le 30$, $-22 \le k \le 11$, $-12 \le l \le 9$
Reflections collected	19298
Independent reflections	4513 (R(int) = 0.0720)
Observed reflections	2610 ($I > 2\sigma(I)$)
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	1.39 and 0.79
Refinement method	Full-matrix least-squares on F^2
Data/restraints/parameters	4513 / 79 / 493
Goodness-of-fit on F^2	1.06
Final R indices (I>2sigma(I))	R1 = 0.061, wR2 = 0.126
Largest diff. peak and hole	0.14 and -0.15 $eÅ^{-3}$

Crystal structure of compound 4

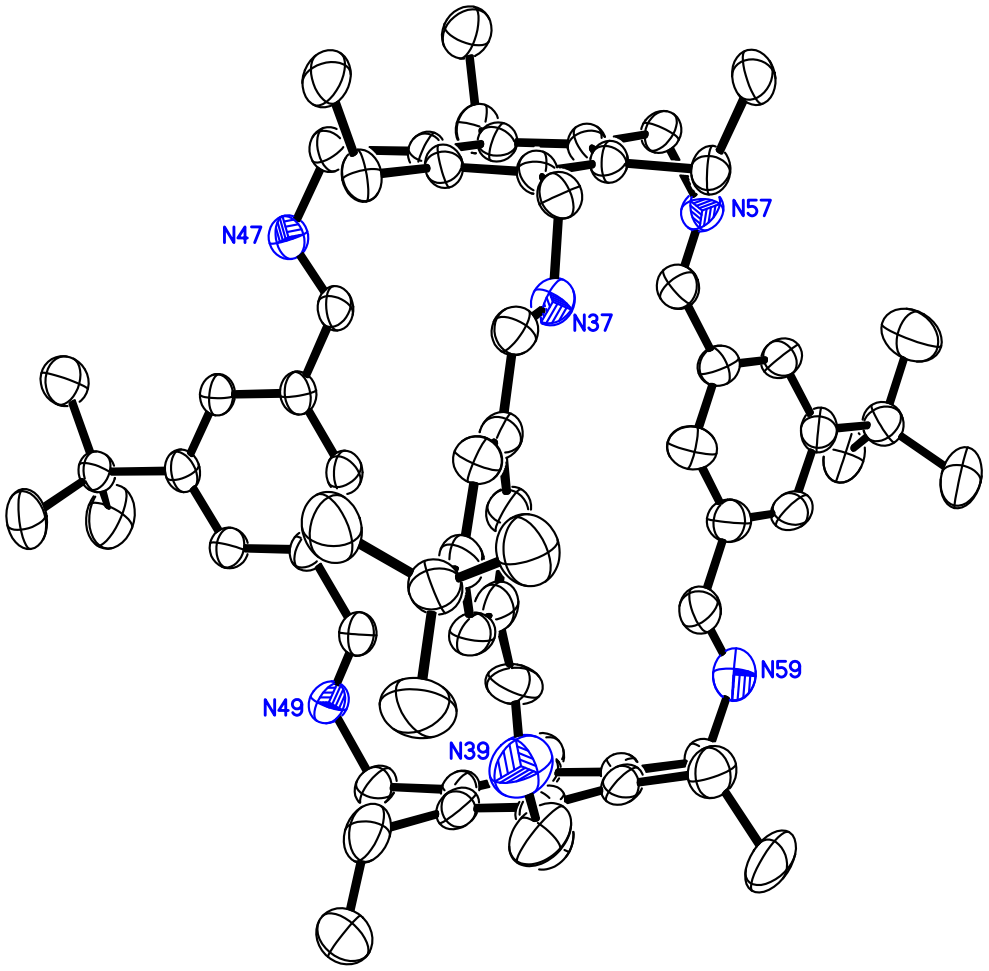


Figure S44 Crystal structure of compound **4**. Atoms of carbon are depicted in white and nitrogen in blue. Ellipsoid contour plots at a 50% probability level.

Crystals were obtained by diffusion of methanol into a chloroform solution of cage **4**.

CCDC-number : 2016637

Table S3: Crystal data and structure refinement for **4**.

Empirical formula	$C_{66}H_{84}N_6$
Formula weight	961.39
Temperature	200(2) K
Wavelength	1.54178 Å
Crystal system	triclinic
Space group	$P\bar{1}$
Z	2
Unit cell dimensions	a = 13.1663(8) Å α = 71.914(4) deg.
	b = 14.0425(8) Å β = 88.948(5) deg.
	c = 18.3518(10) Å γ = 85.804(5) deg.
Volume	3216.7(3) $Å^3$
Density (calculated)	0.99 g/cm^3
Absorption coefficient	0.44 mm^{-1}
Crystal shape	brick
Crystal size	0.106 x 0.105 x 0.068 mm^3
Crystal colour	colourless
Theta range for data collection	2.5 to 67.2 deg.
Index ranges	$-14 \le h \le 15$, $-16 \le k \le 16$, $-21 \le l \le 12$
Reflections collected	29468
Independent reflections	11058 (R(int) = 0.0539)
Observed reflections	6567 ($I > 2\sigma(I)$)
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	1.82 and 0.65
Refinement method	Full-matrix least-squares on F^2
Data/restraints/parameters	11058 / 0 / 664
Goodness-of-fit on F^2	1.04
Final R indices (I>2sigma(I))	R1 = 0.075, wR2 = 0.191
Largest diff. peak and hole	0.62 and -0.31 $eÅ^{-3}$

Crystal structure of compound 5

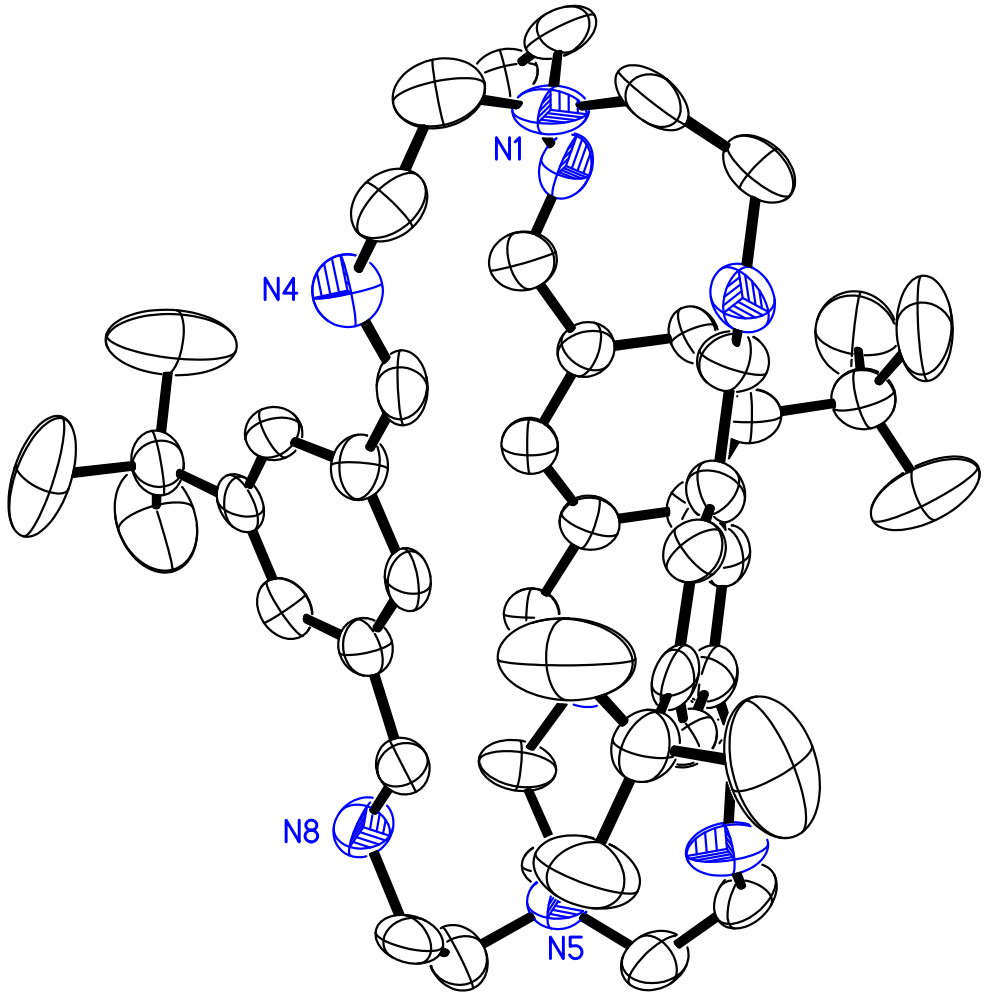


Figure S45 Crystal structure of compound **5**. Atoms of carbon are depicted in white and nitrogen in blue. Ellipsoid contour plots at a 50% probability level.

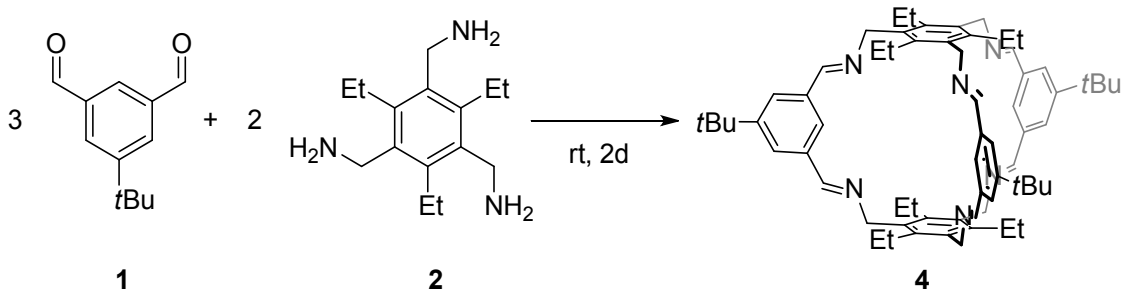
Crystals were obtained by slow evaporation of chloroform.

CCDC-number : 2016235

Table S4: Crystal data and structure refinement for **5**.

Empirical formula	$C_{48}H_{66}N_8$
Formula weight	755.08
Temperature	200(2) K
Wavelength	1.54178 Å
Crystal system	trigonal
Space group	P_{ii}
Z	4
Unit cell dimensions	a = 11.9345(3) Å α = 90 deg.
	b = 11.9345(3) Å β = 90 deg.
	c = 40.593(2) Å γ =120 deg.
Volume	5007.2(4) $Å^3$
Density (calculated)	1.00 g/cm^3
Absorption coefficient	0.46 mm^{-1}
Crystal shape	plank
Crystal size	0.142 x 0.082 x 0.055 mm^3
Crystal colour	colourless
Theta range for data collection	2.2 to 63.7 deg.
Index ranges	$-12 \le h \le 13$, $-13 \le k \le 13$, $-47 \le l \le 28$
Reflections collected	30462
Independent reflections	4294 (R(int) = 0.0803)
Observed reflections	2623 ($I > 2\sigma(I)$)
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	1.48 and 0.73
Refinement method	Full-matrix least-squares on F^2
Data/restraints/parameters	4294 / 667 / 338
Goodness-of-fit on F^2	1.72
Final R indices (I>2sigma(I))	R1 = 0.175, wR2 = 0.391
Absolute structure parameter	0.7(3)
Largest diff. peak and hole	1.14 and -0.69 $eÅ^{-3}$

6. Cage Formation Experiments



Without TFA

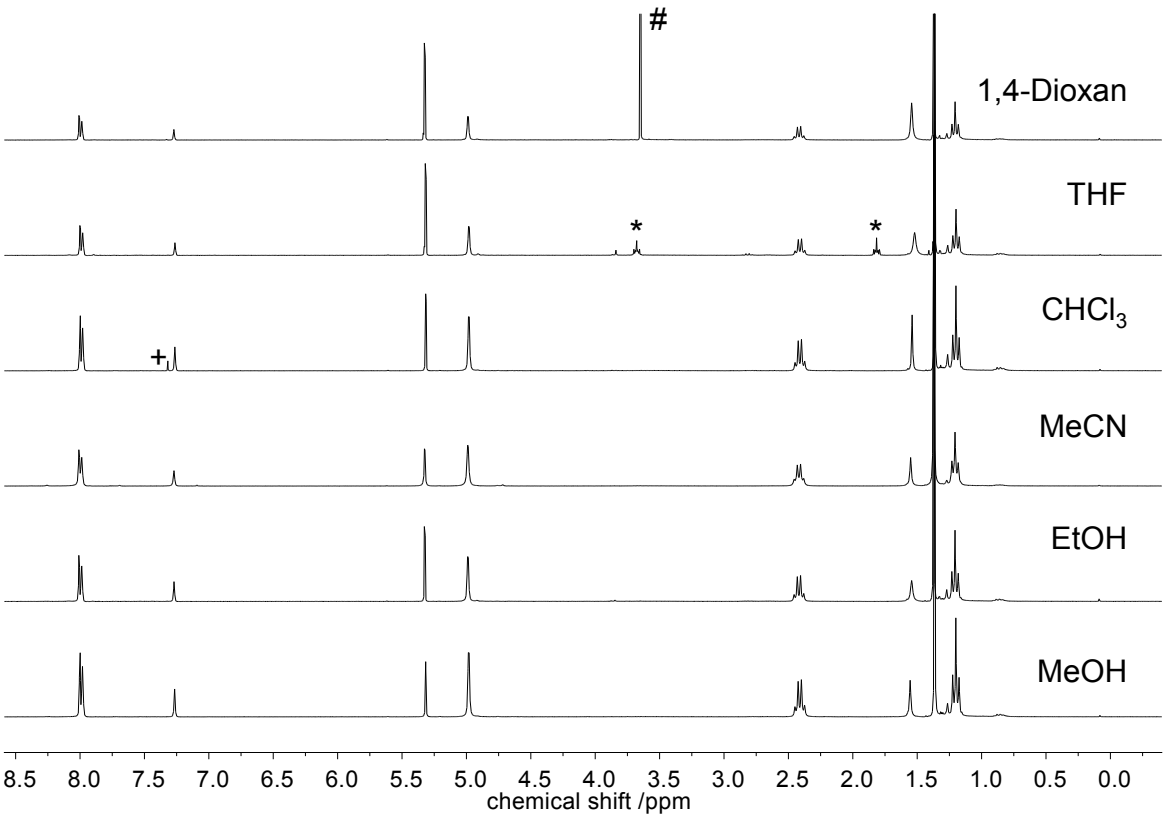


Figure S46. Stacked ^{1}H NMR spectra (CD_2Cl_2, 300 MHz) from the isolated precipitates (reaction a, b, c, e, f, g). $^{+}CHCl_3$, $^{\#}$1,4-Dioxane, *THF.

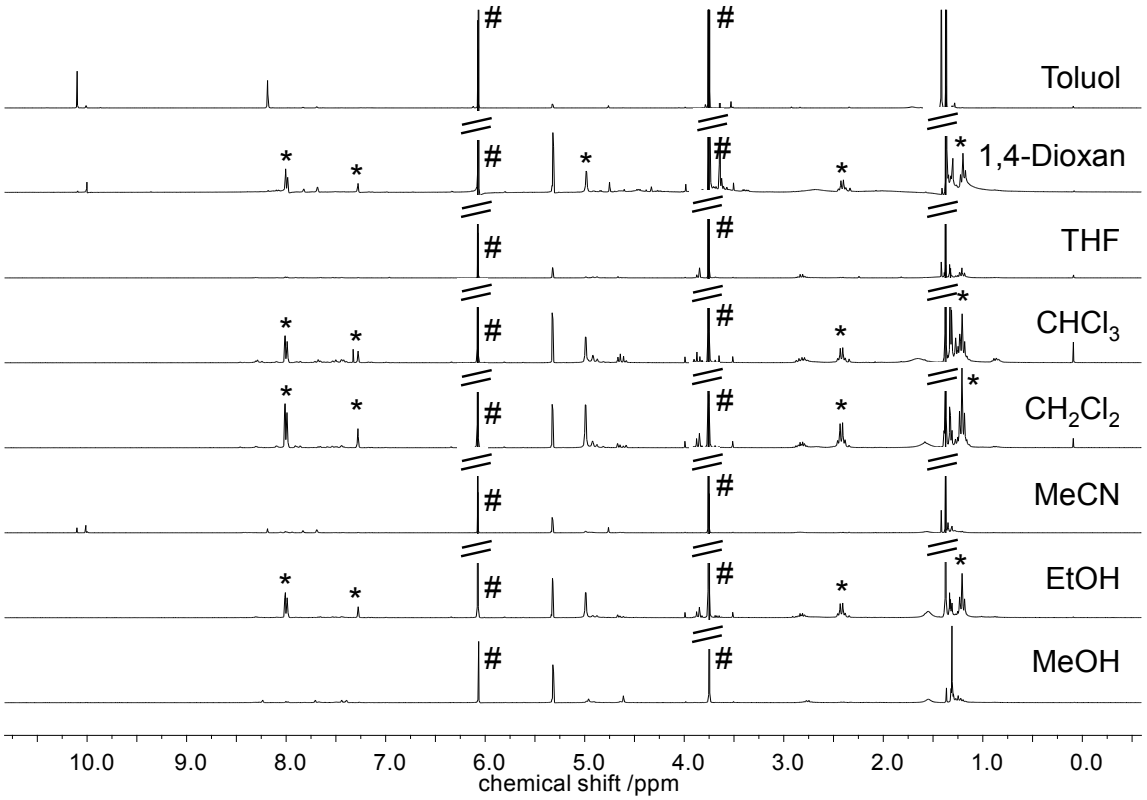


Figure S47. Stacked ^{1}H NMR spectra (CD_2Cl_2, 300 MHz) from the mother liquor (reaction a, b, c, d, e, f, g, h). *Cage compound **4**, $^{\#}$1,3,5-trimethoxybenzene as standard.

With 2 mol% of TFA

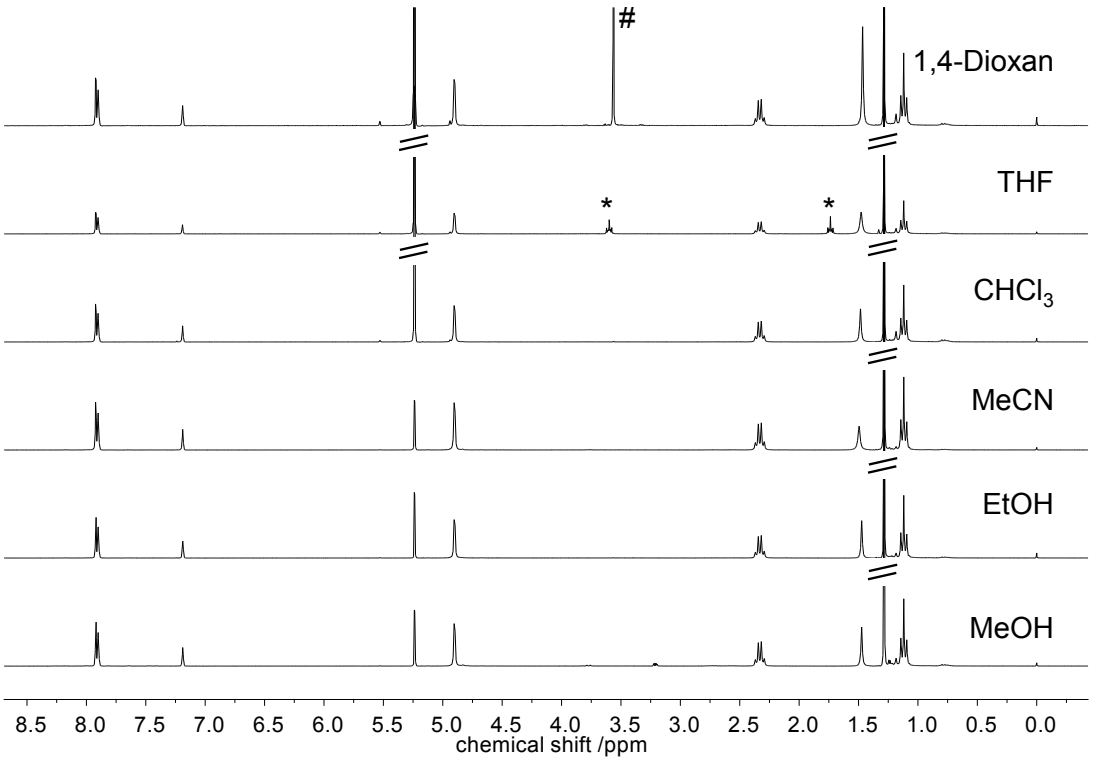


Figure S48. Stacked ^{1}H NMR spectra (CD_2Cl_2, 300 MHz) from the isolated precipitate (reaction a, b, c, e, f, g). $^{\#}$1,4-Dioxane, $^{+}$THF.

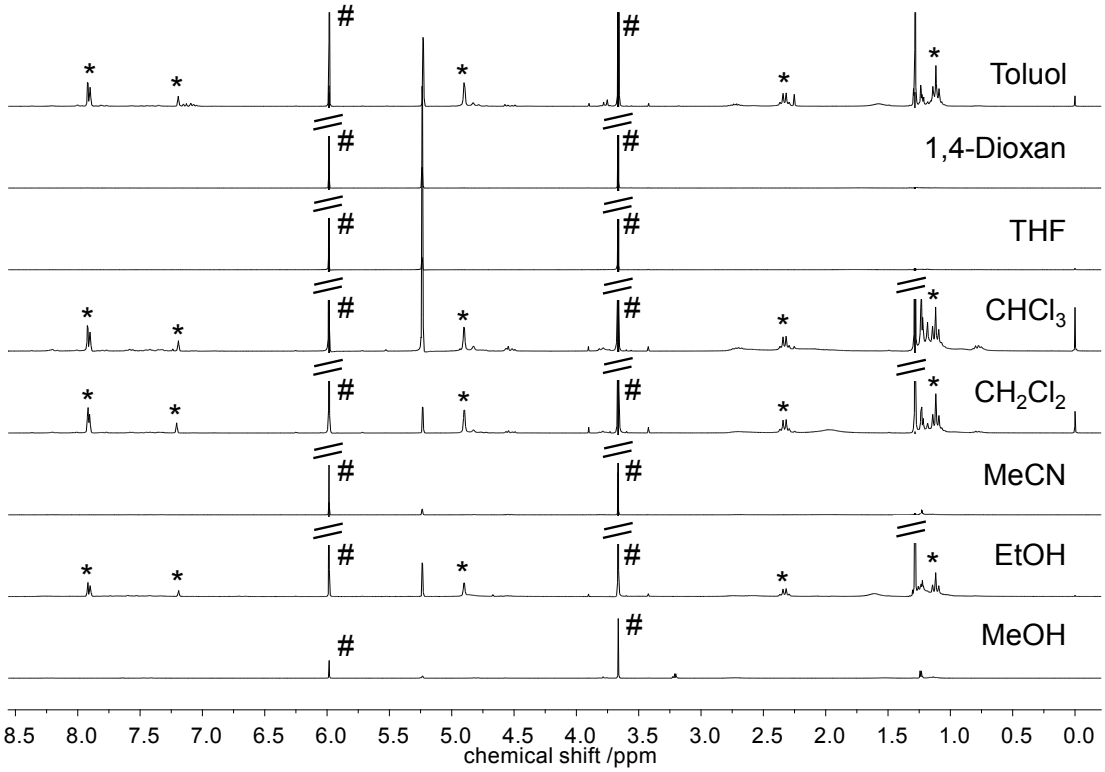
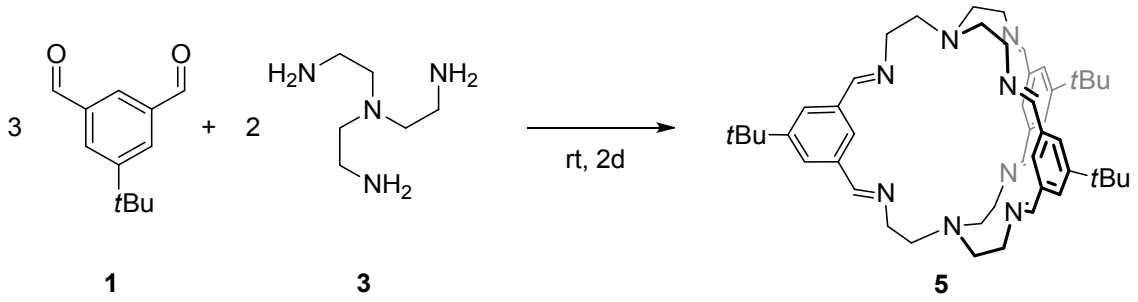


Figure S49. Stacked ^{1}H NMR spectra (CD_2Cl_2, 300 MHz) from the isolated solid form the mother liquor (reaction a, b, c, d e, f, g, h). *Cage compound **4**, $^{\#}$1,3,5-Trimethoxybenzene as standard.



1 **3** **5**

Without TFA

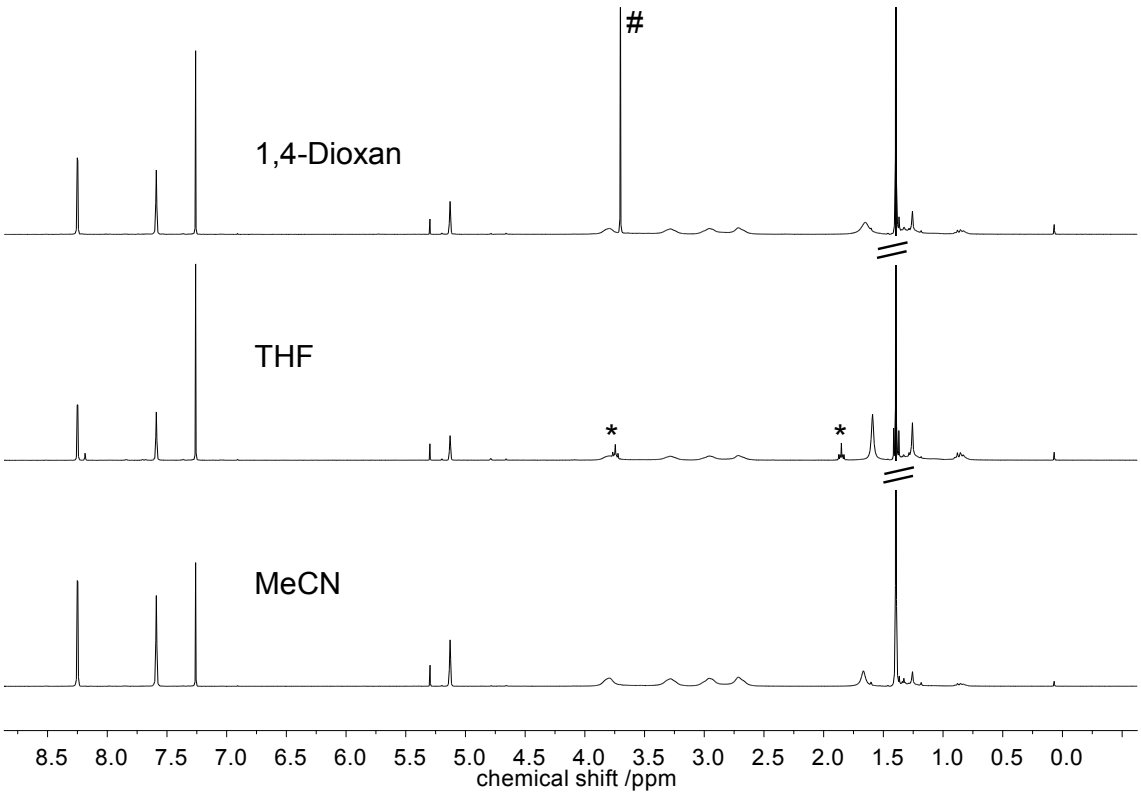


Figure S50. Stacked ^{1}H NMR spectra (CD_2Cl_2, 300 MHz) from the isolated precipitates (reaction c, f, g). $^{\#}$1,4-Dioxane, $^{+}$THF.

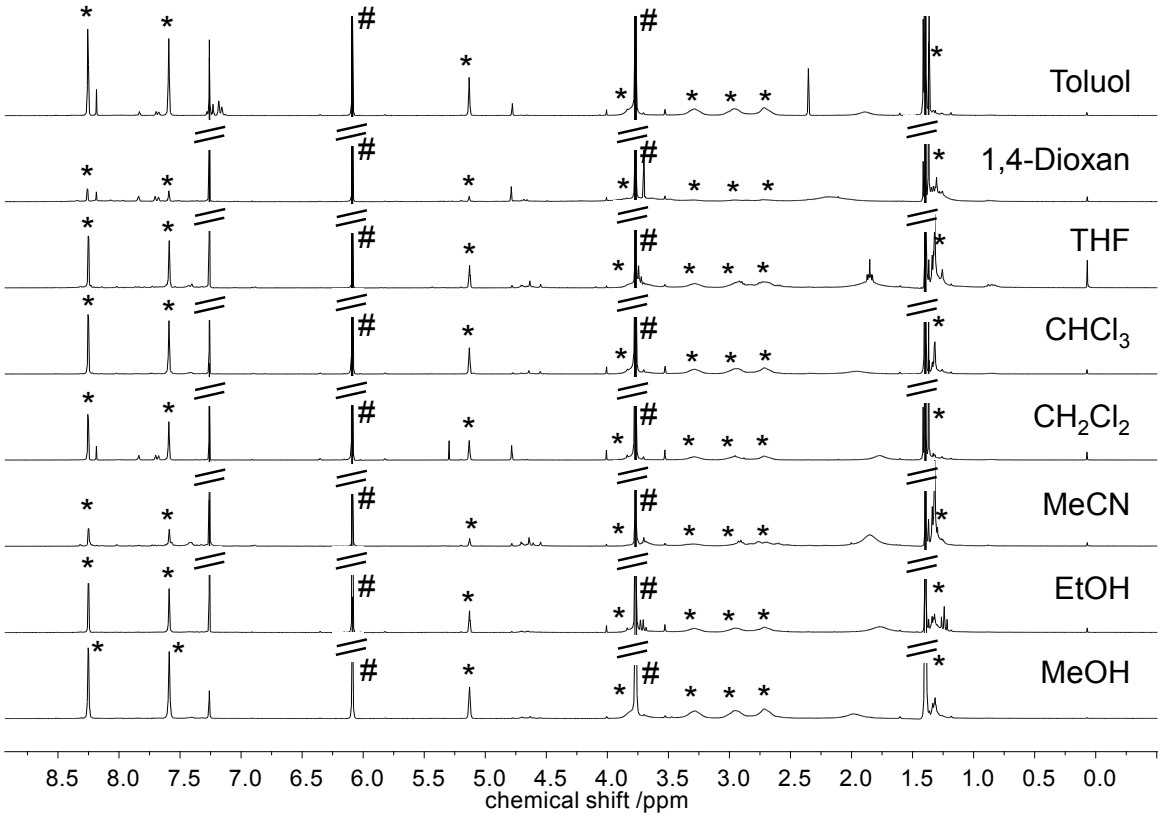


Figure S51. Stacked ^{1}H NMR spectra (CD_2Cl_2, 300 MHz) from the isolated solid form the mother liquor (reaction a, b, c, d e, f, g, h). *Cage compound **5**, $^{\#}$1,3,5-Trimethoxybenzene as standard.

with 2 mol% of TFA

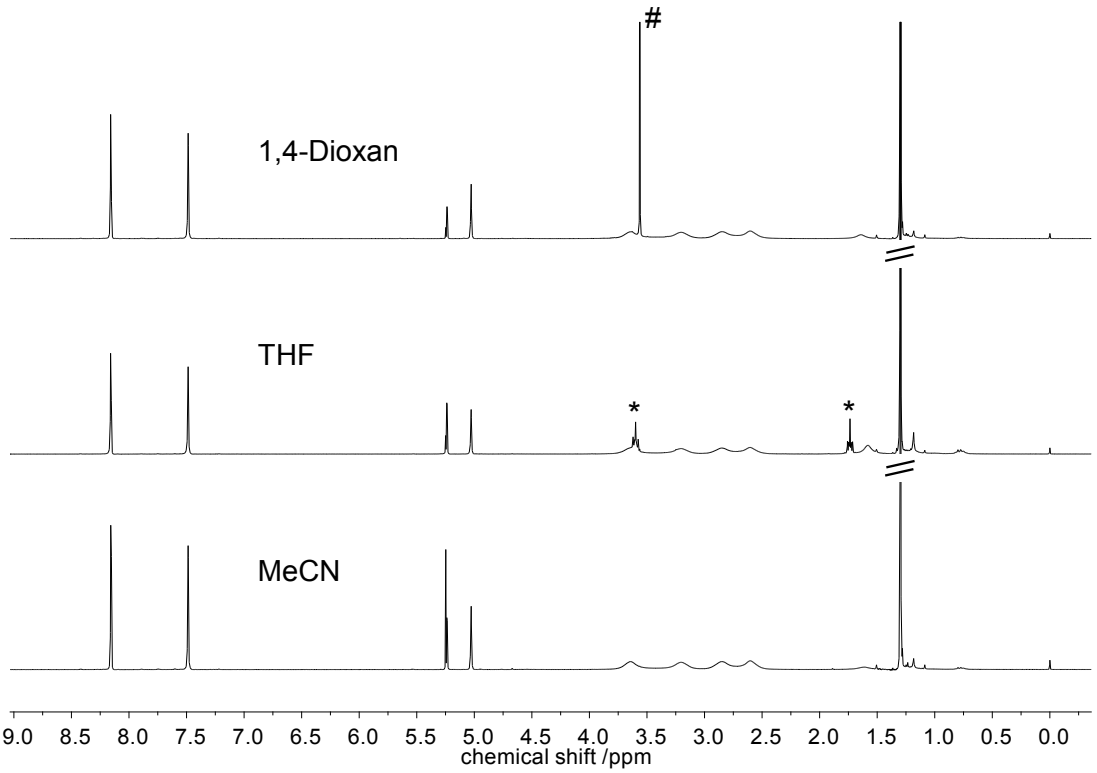


Figure S52. Stacked ^{1}H NMR spectra (CD_2Cl_2, 300 MHz) from the isolated precipitate (reaction c, f, g). $^{\#}$1,4-Dioxane, *THF.

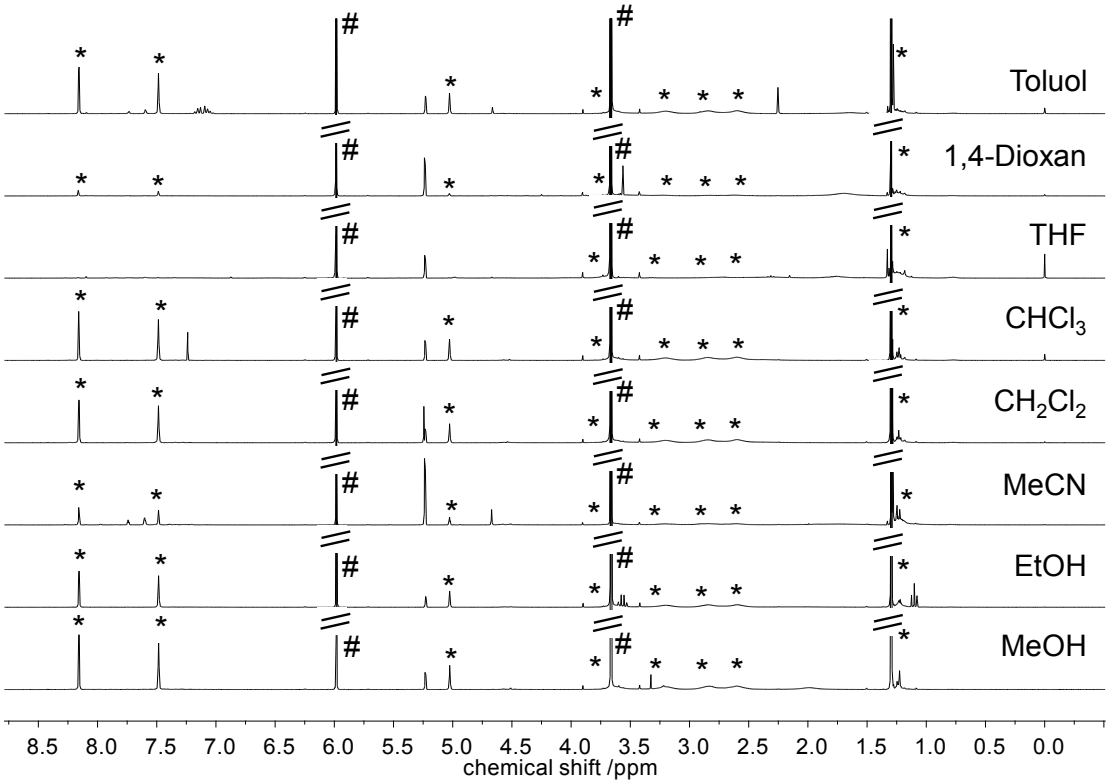
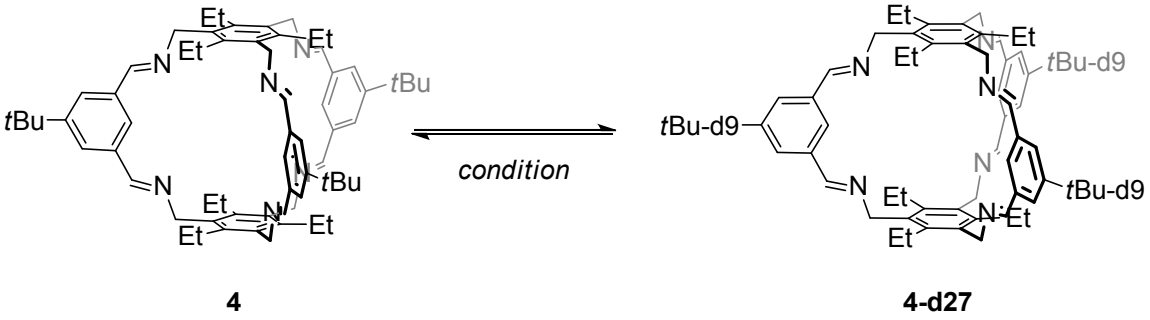


Figure S53. ^{1}H NMR spectra (CD_2Cl_2, 300 MHz) from the isolated solid form the mother liquor (reaction a, b, c, d, e, f, g, h). *Cage compound **5**, $^{\#}$1,3,5-Trimethoxybenzene as standard.

7. Cage-to-Cage Scrambling



4 **4-d27**

Without TFA

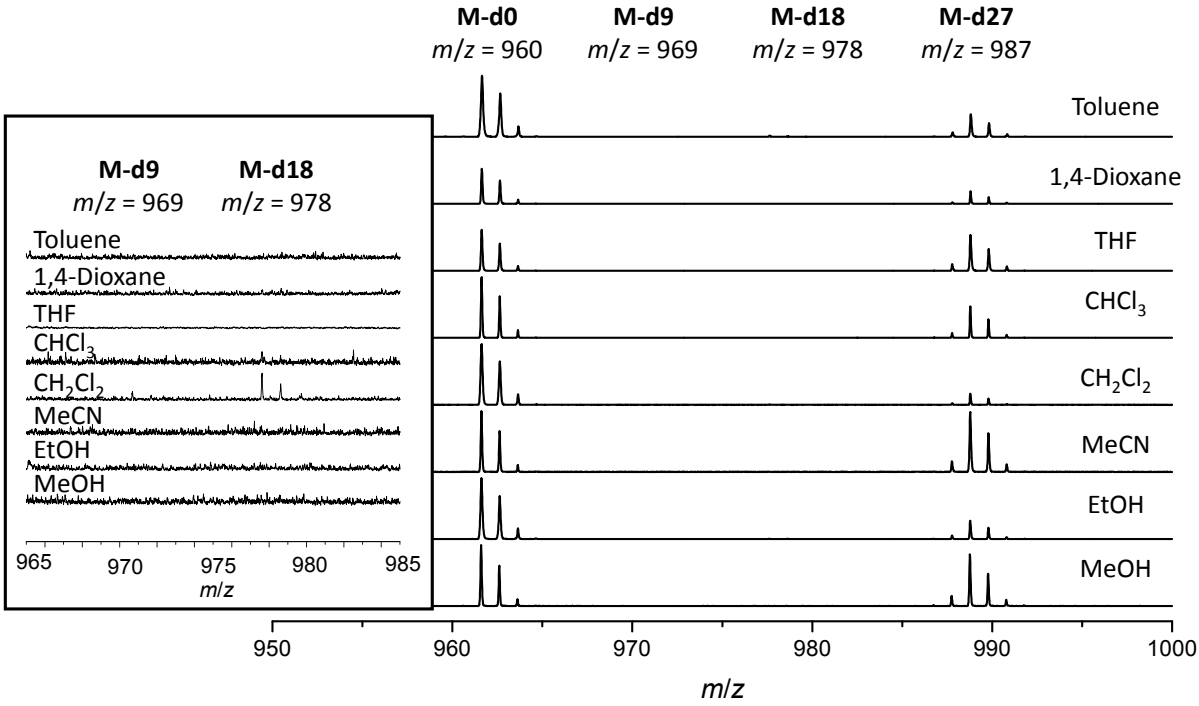


Figure S54. MS MALDI (TOF, DCTB) spectra of the reactions a, b, c, d, e, f, g, h taken out of the homogeneous reaction mixture after 7d before addition of water.

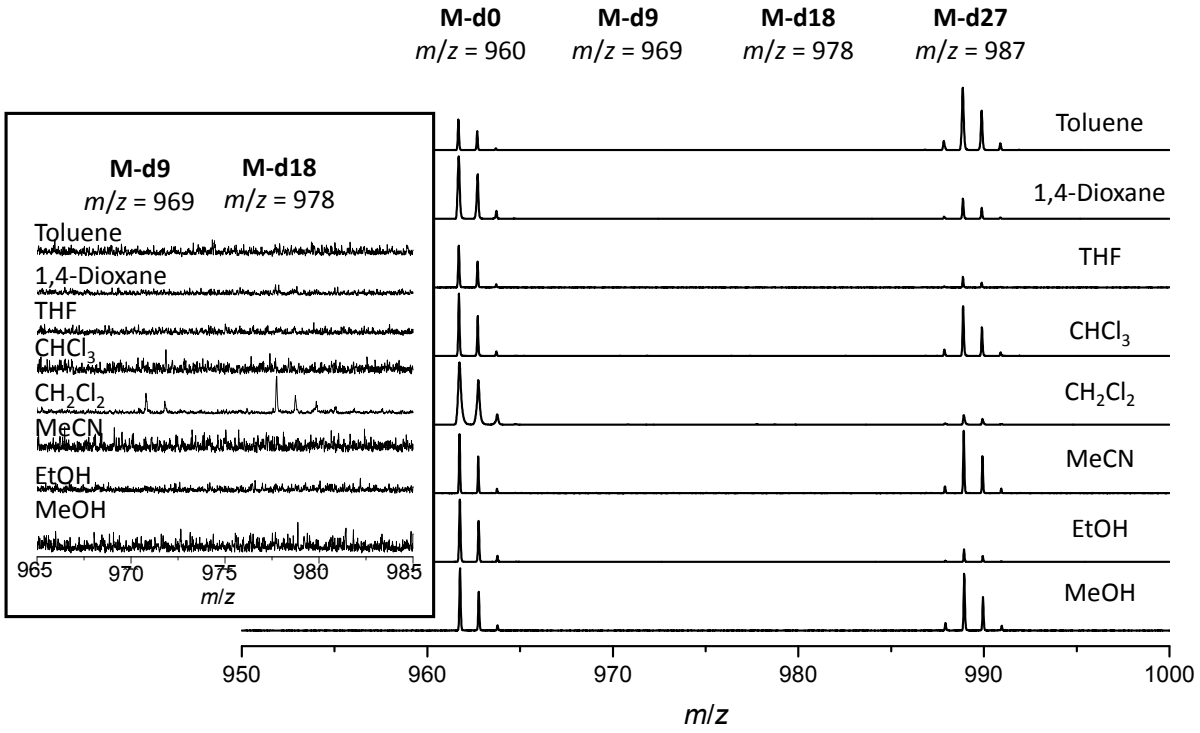


Figure S55. MS MALDI (TOF, DCTB) spectra of the reactions a, b, c, d, e, f, g, h taken out of the homogeneous reaction mixture after 7days after addition of water.

With TFA

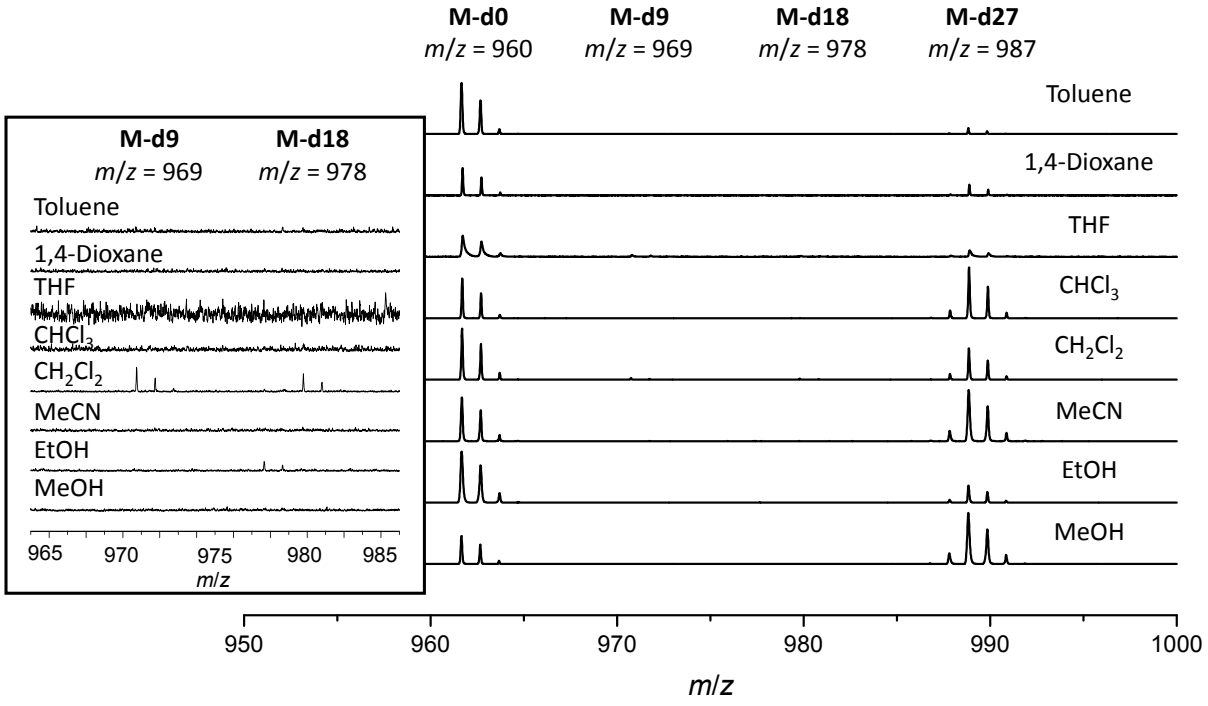


Figure S56. MS MALDI (TOF, DCTB) spectra of the reaction a, b, c, d, e, f, g, h taken out of the homogeneous reaction mixture after 7d.

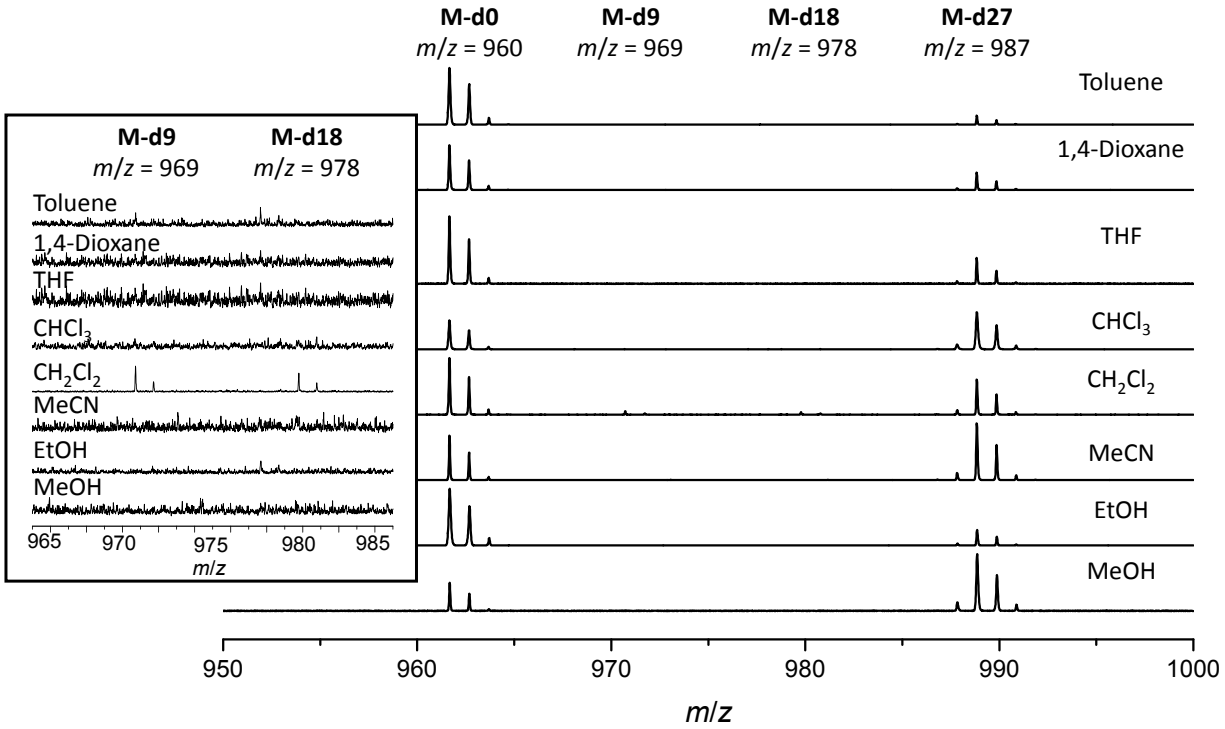
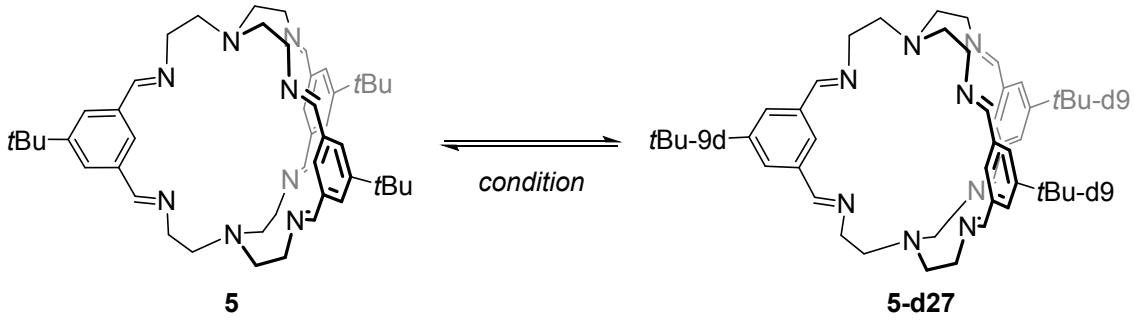


Figure S57. MS MALDI (TOF, DCTB) spectra of the reaction a, b, c, d, e, f, g, h taken out of the homogeneous reaction mixture after 7d.



5 **5-d27**

Without TFA

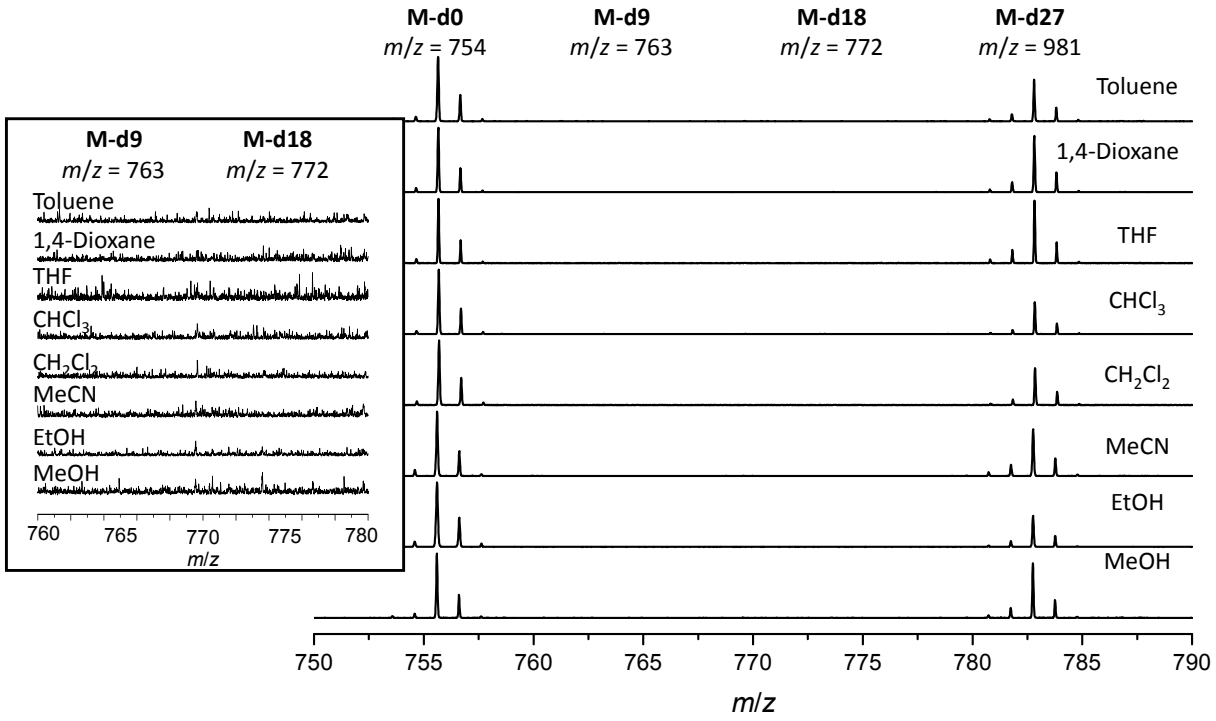


Figure S58. MS MALDI (TOF, DCTB) spectra of the reaction a, b, c, d, e, f, g, h taken out of the homogeneous reaction mixture after 7d.

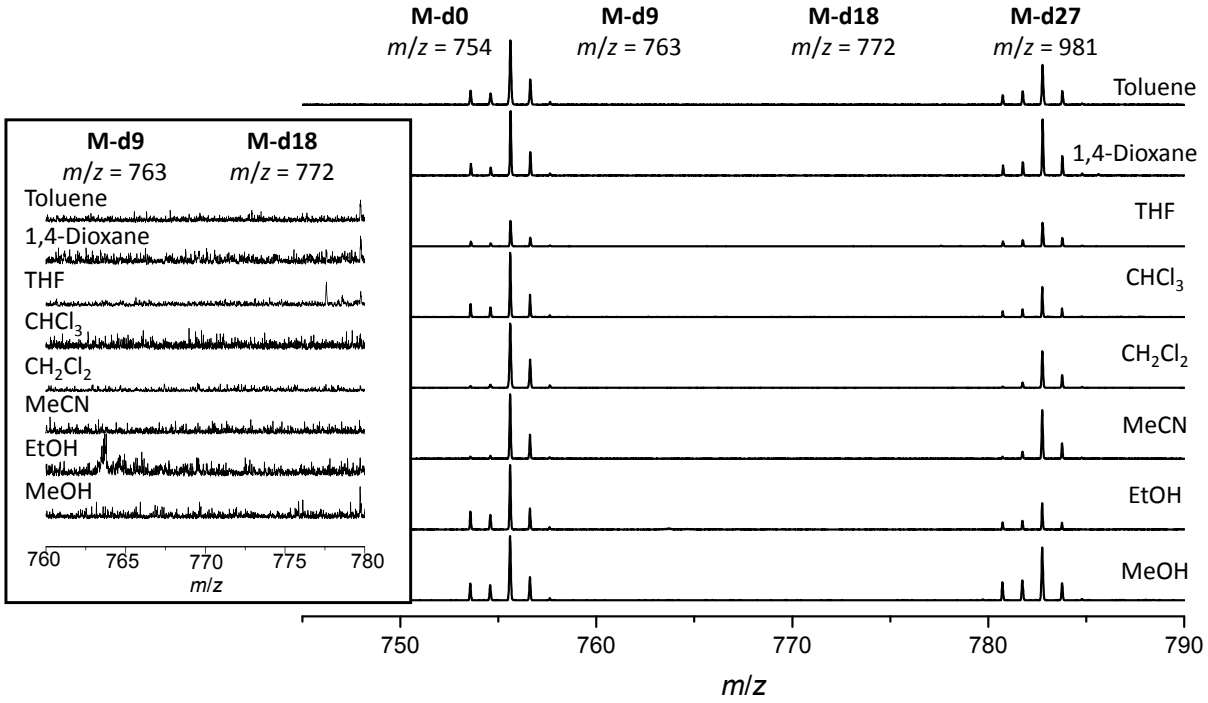


Figure S59. MS MALDI (TOF, DCTB) spectra of the reaction a, b, c, d, e, f, g, h taken out of the homogeneous reaction mixture after 7d.

With TFA

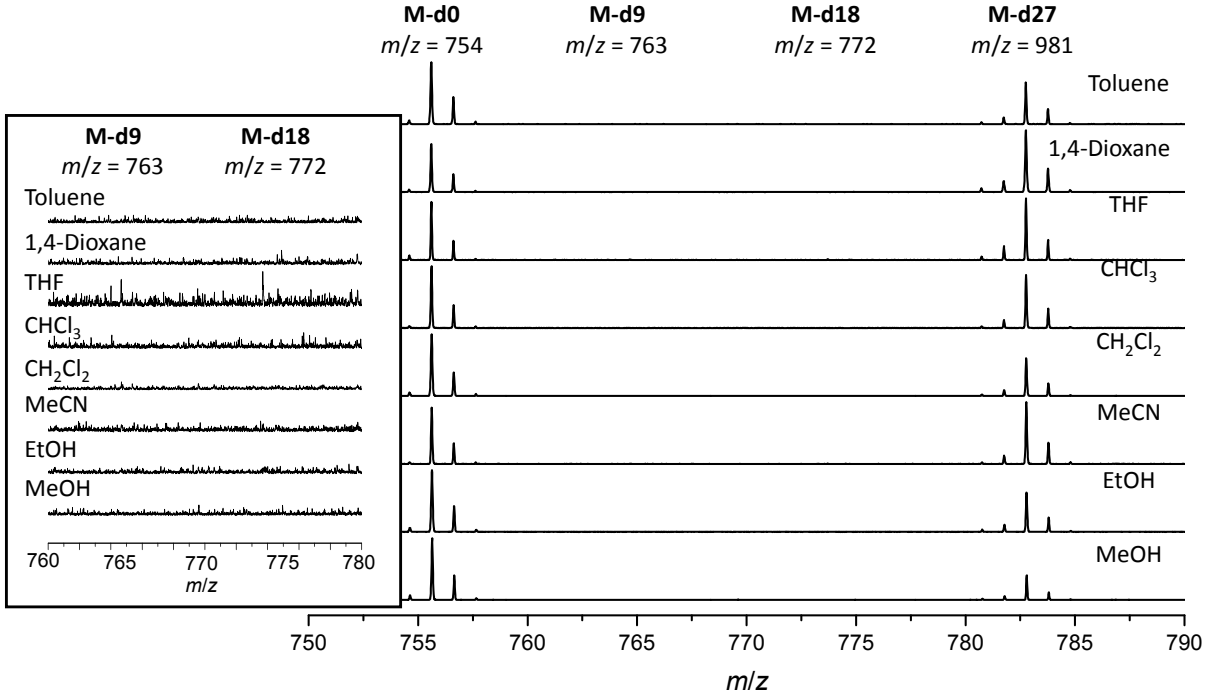


Figure S60. MS MALDI (TOF, DCTB) spectra of the reaction a, b, c, d, e, f, g, h taken out of the homogeneous reaction mixture after 7d.

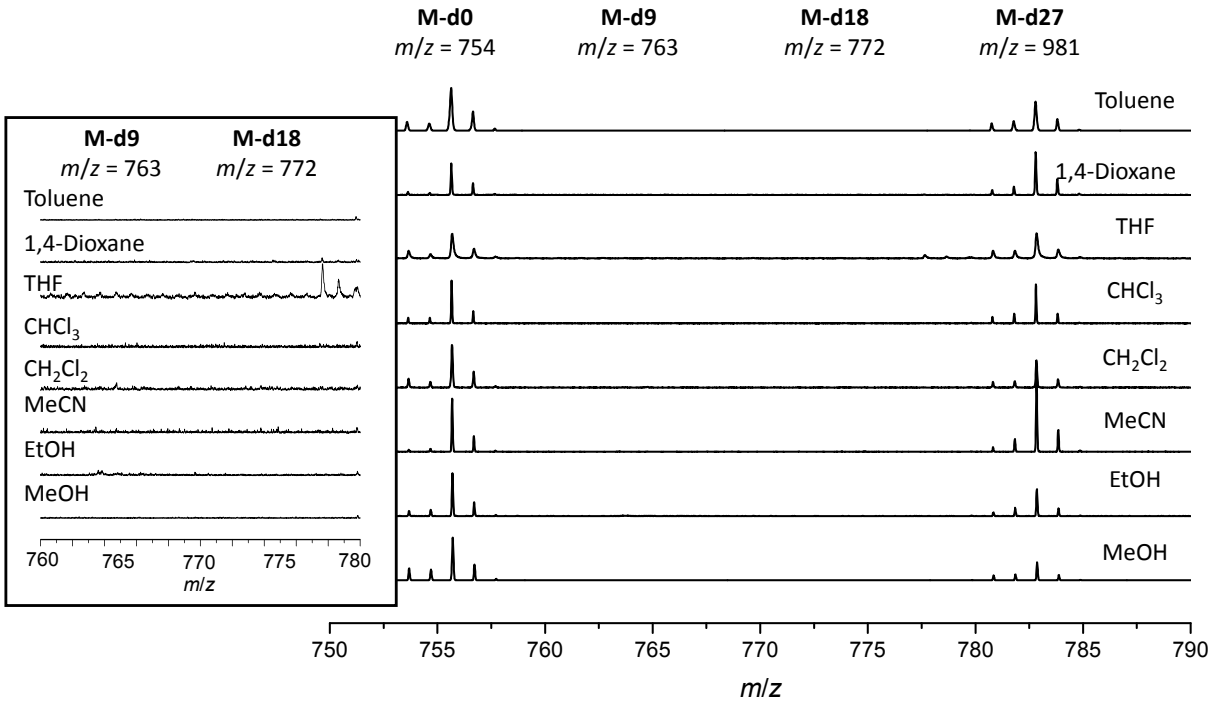
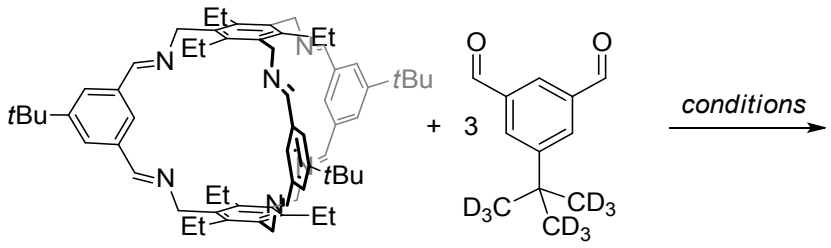


Figure S61. MS MALDI (TOF, DCTB) spectra of the reaction a, b, c, d, e, f, g, h taken out of the homogeneous reaction mixture after 7d.

8. Aldehyde Exchange



4 **1-d9**

Without TFA

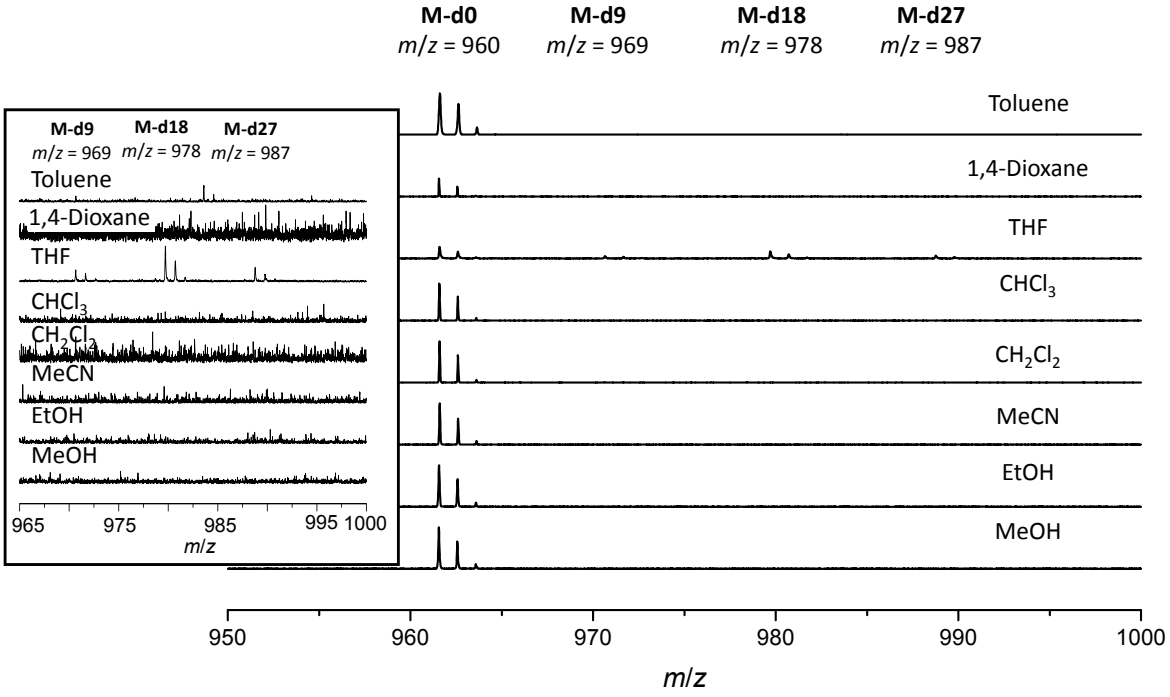


Figure S62. MS MALDI (TOF, DCTB) spectra of the reaction a, b, c, d, e, f, g, h taken out of the homogeneous reaction solution after 7d.

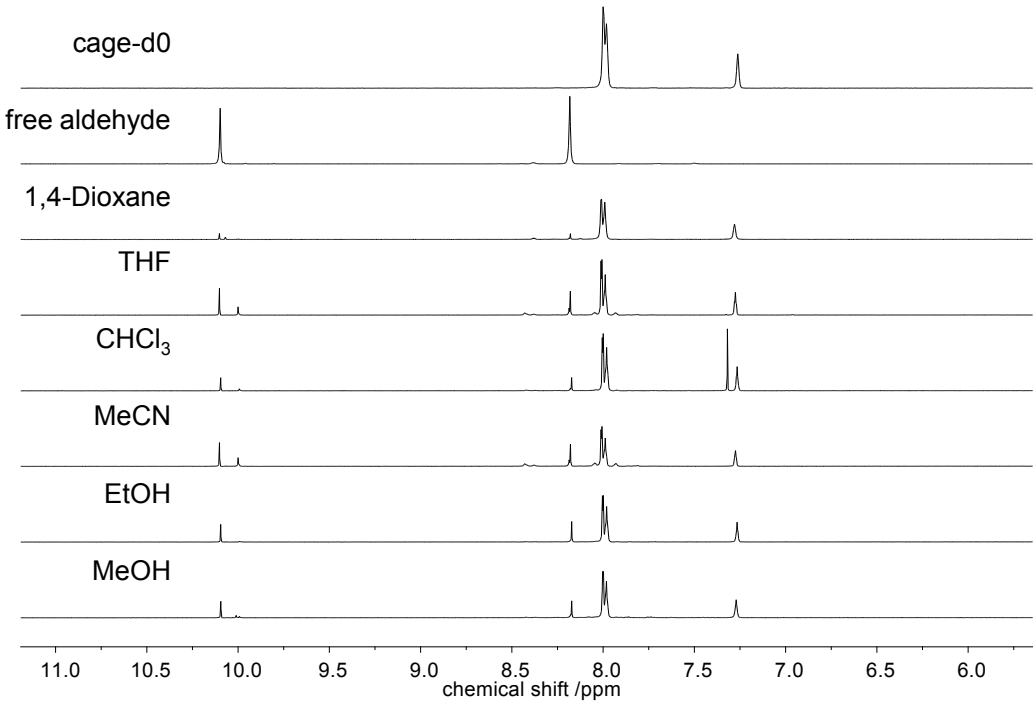


Figure S63. ^{1}H NMR spectra (CD_2Cl_2, 300 MHz; region δ=11.0 ppm – 6.00 ppm) from the isolated precipitates (reaction a, b, c, e, f, g; reaction time: 7d).

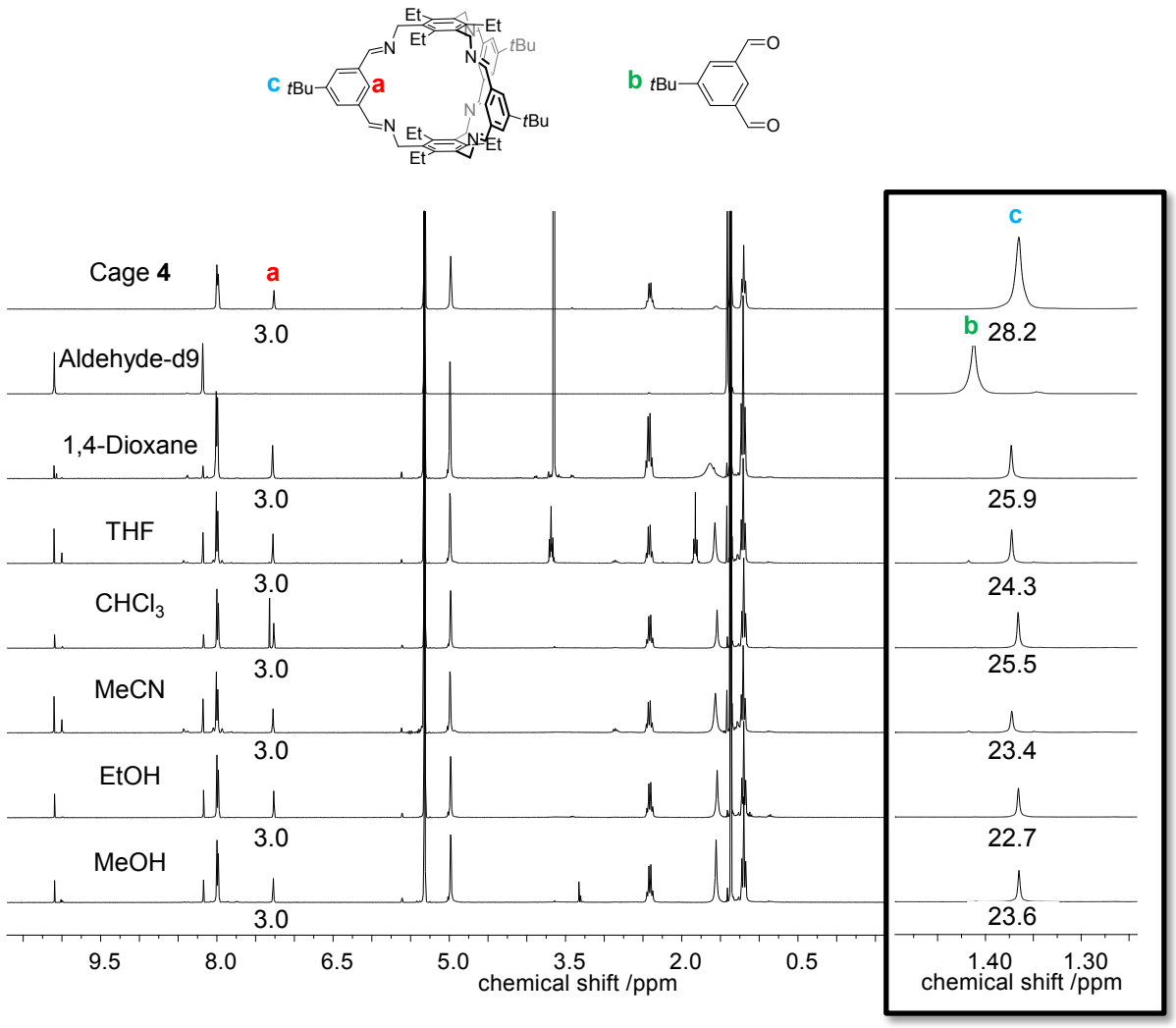


Figure S64. ^{1}H NMR spectra (CD_2Cl_2, 300 MHz from the isolated precipitates (reaction a, b, c, e, f, g; reaction time: 7d). Integrals of Signals at δ = 7.27 ppm and δ = 1.37 ppm are given.

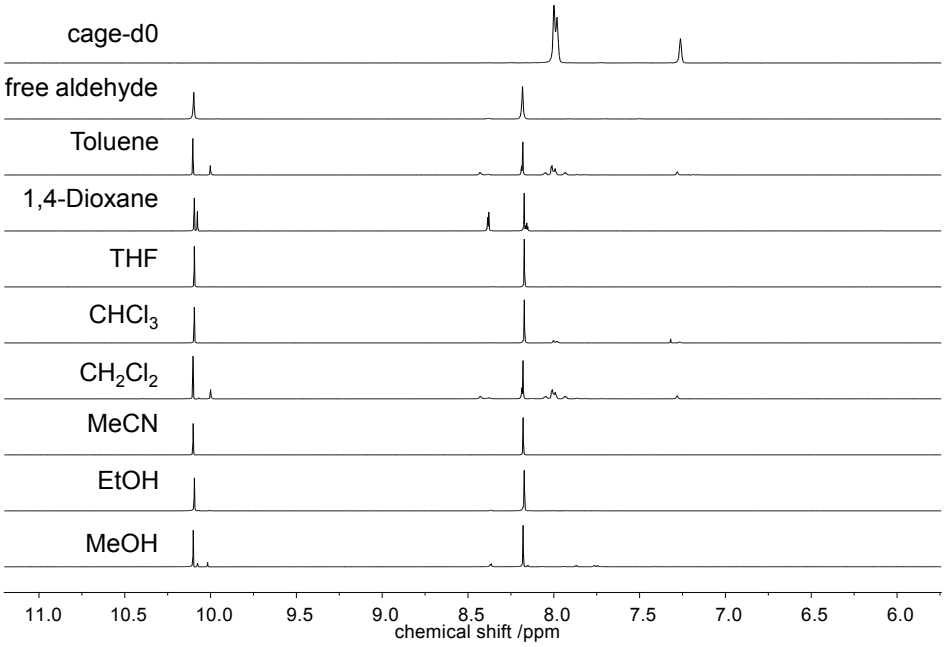


Figure S65. ^{1}H NMR spectra (CD_2Cl_2, 300 MHz; region δ=11.0 ppm – 6.00 ppm) from the isolated solid from the mother liquor (reaction a, b, c, d, e, f, g, h; reaction time: 7d)..

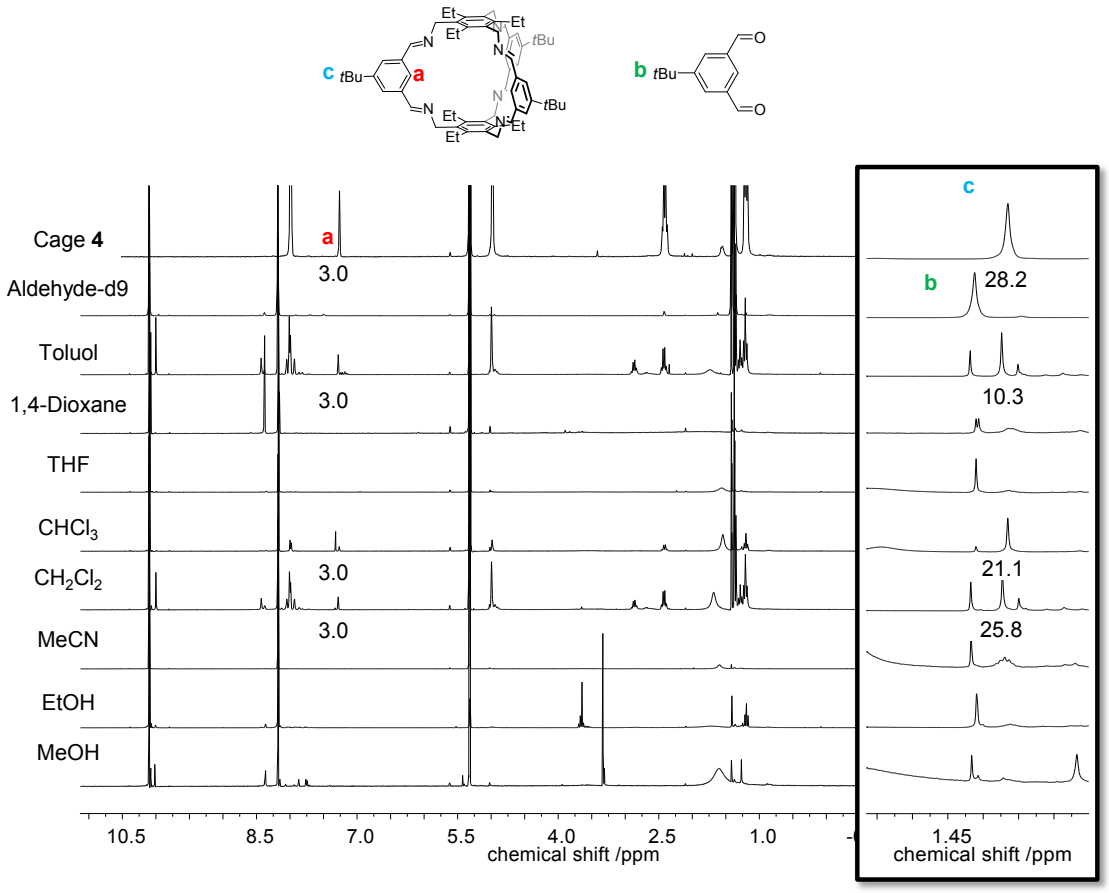


Figure S66. ^{1}H NMR spectra (CD_2Cl_2, 300 MHz;) from the mother liquor (reaction a, b, c, e, f, g; reaction time: 7d). Integrals for signals at δ = 7.27 ppm and δ = 1.37 ppm are given.

With TFA

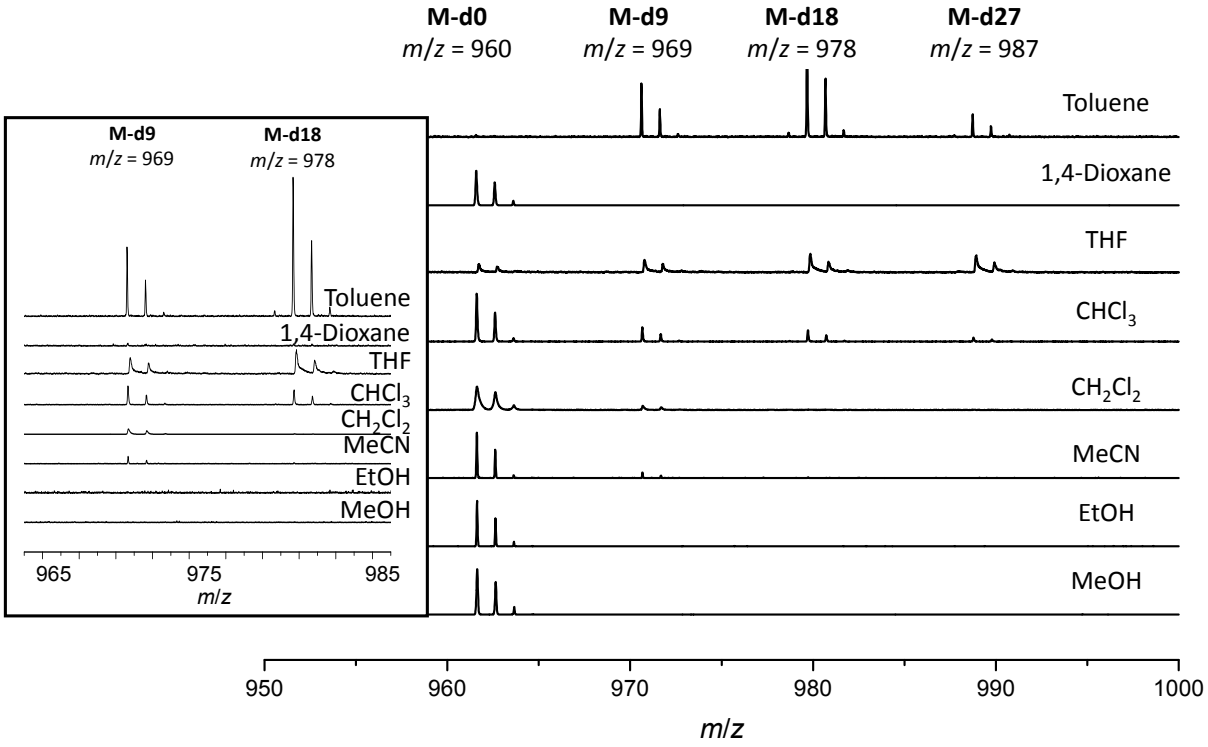


Figure S67. MS MALDI (TOF, DCTB) spectra of the reaction a, b, c, d, e, f, g, h taken out of the homogeneous reaction solution after 7d.

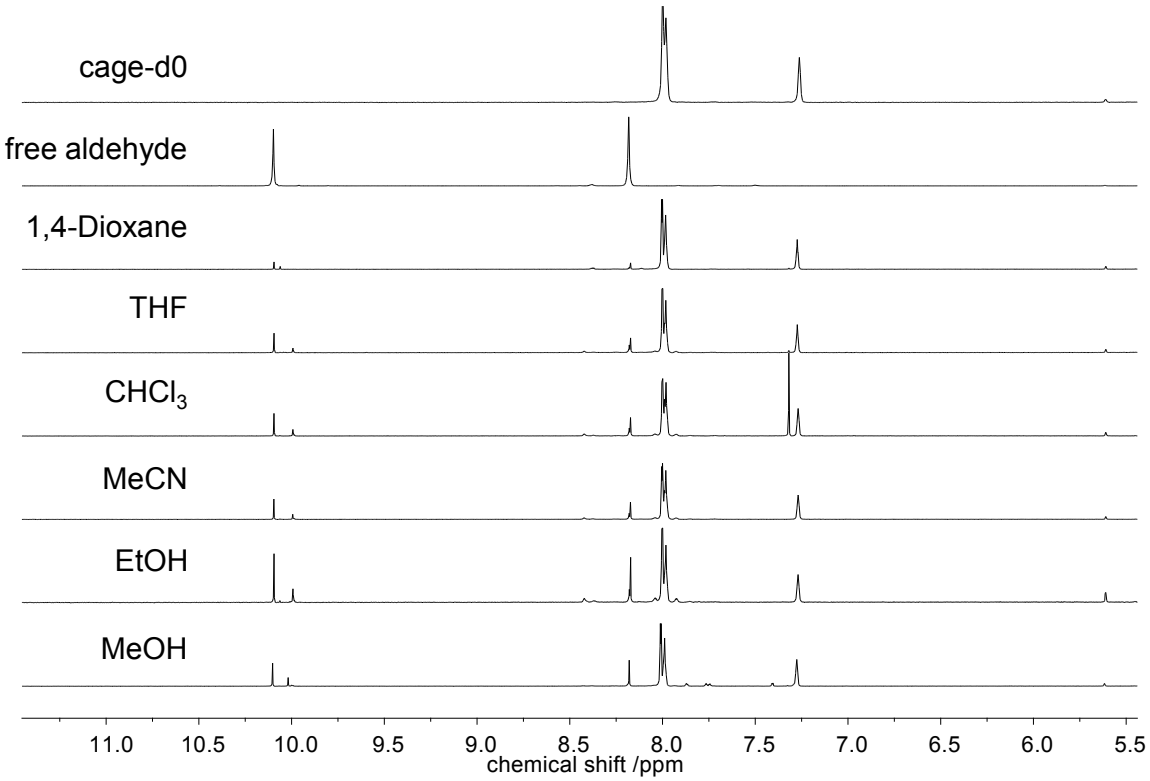


Figure S68. ^{1}H NMR spectra (CD_2Cl_2, 300 MHz; region δ=11.0 ppm – 6.00 ppm) from the isolated precipitate (reaction a, b, c, e, f, g; reaction time: 7d).

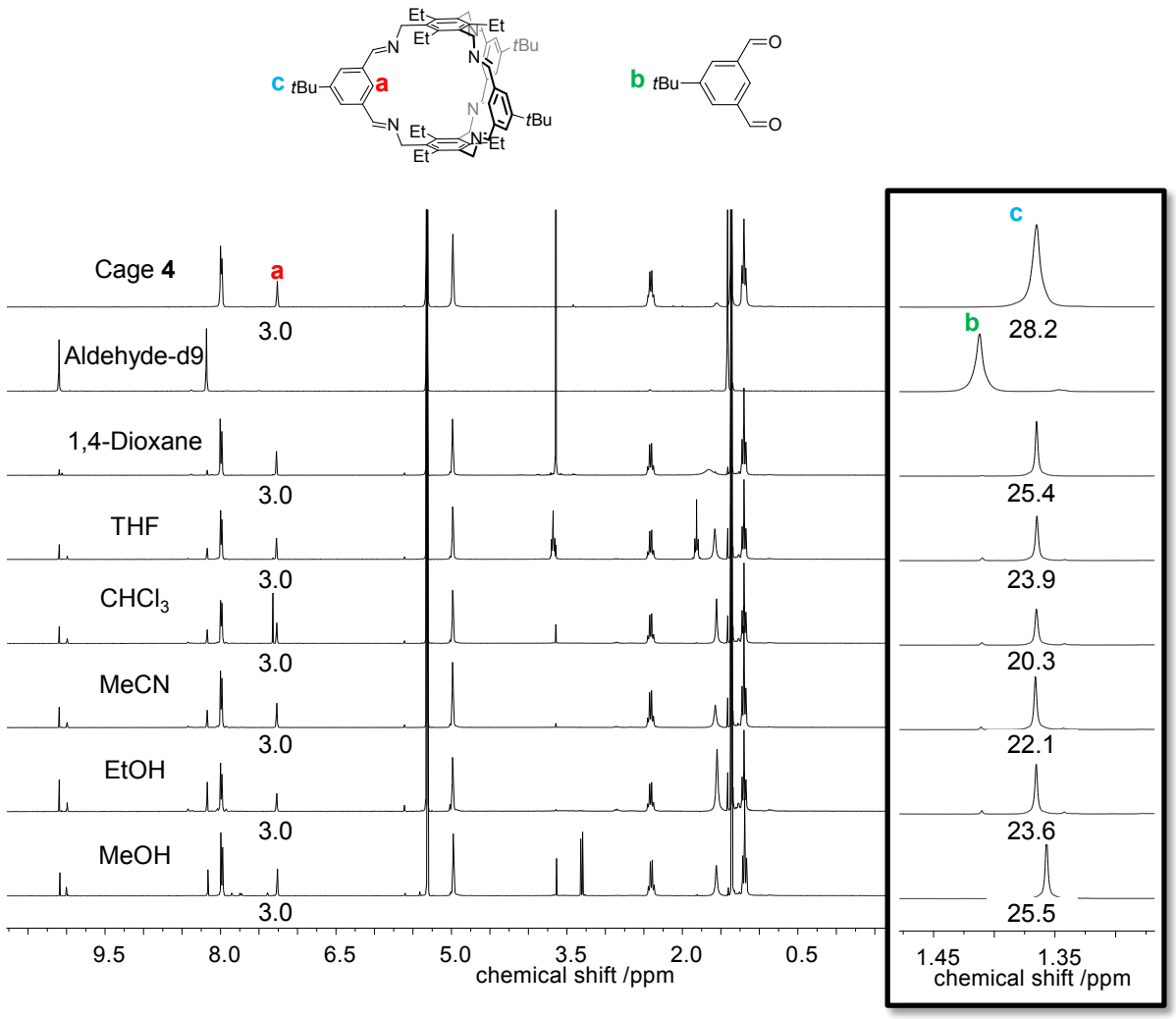


Figure S69. ^{1}H NMR spectra (CD_2Cl_2, 300 MHz) from the isolated precipitates (reaction a, b, c, e, f, g; reaction time: 7d). Integrals of signals at δ = 7.27 ppm and δ = 1.37 ppm are given.

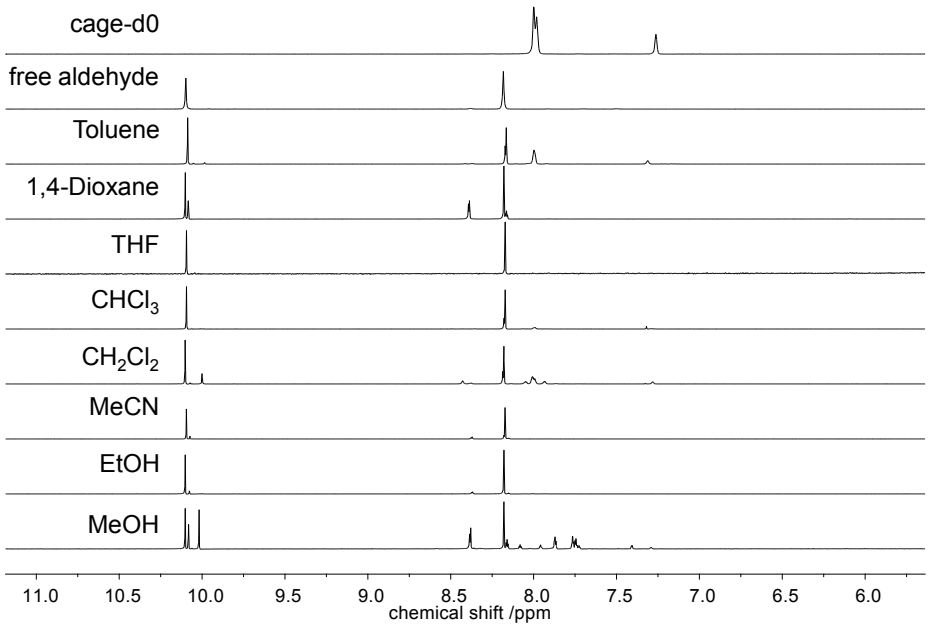


Figure S70. ^{1}H NMR spectra (CD_2Cl_2, 300 MHz; region δ=11.0 ppm – 6.00 ppm) from the isolated solid from the mother liquor (reaction a, b, c, d, e, f, g, h; reaction time: 7d)..

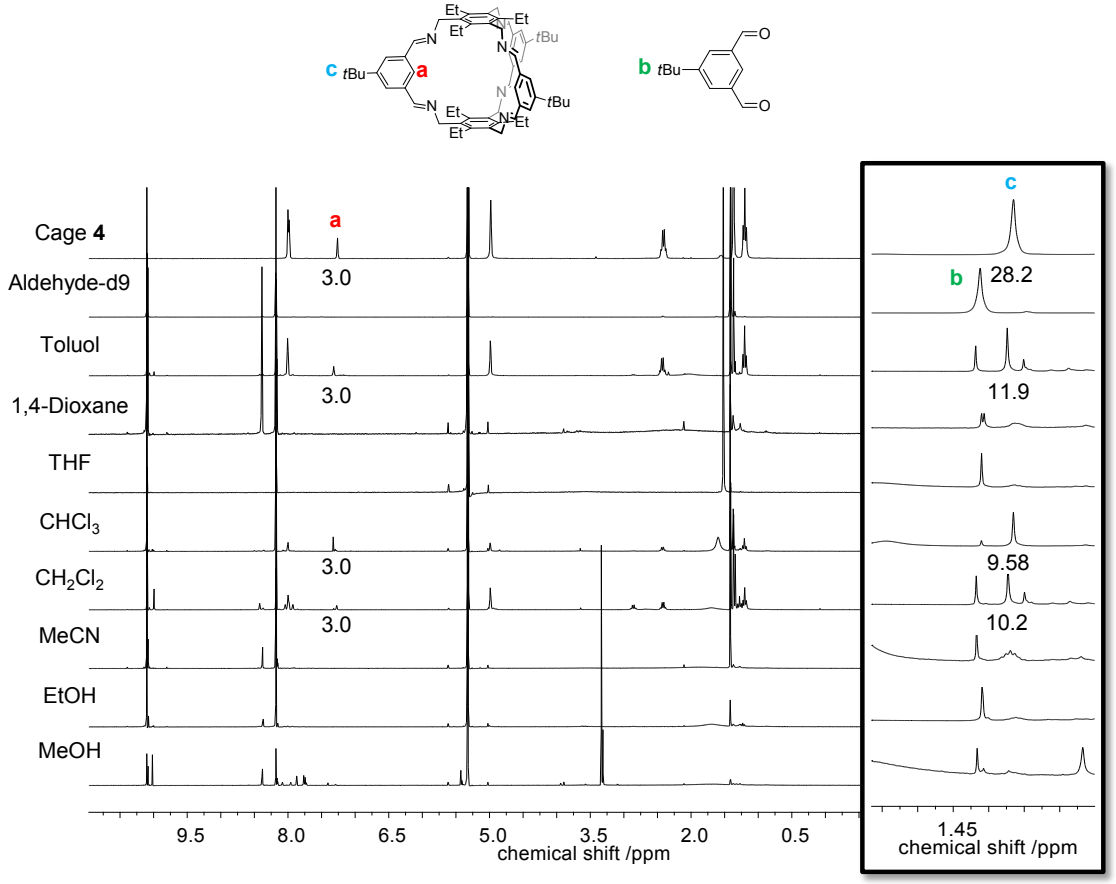
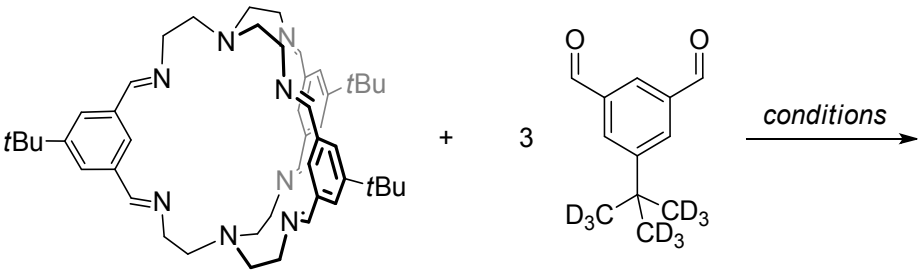


Figure S71. ^{1}H NMR spectra (CD_2Cl_2, 300 MHz) from the mother liquor (reaction a, b, c, e, f, g; reaction time: 7d). Integrals for signals at δ = 7.27 ppm and δ = 1.37 ppm are given.



5 **1-d9**

Without TFA

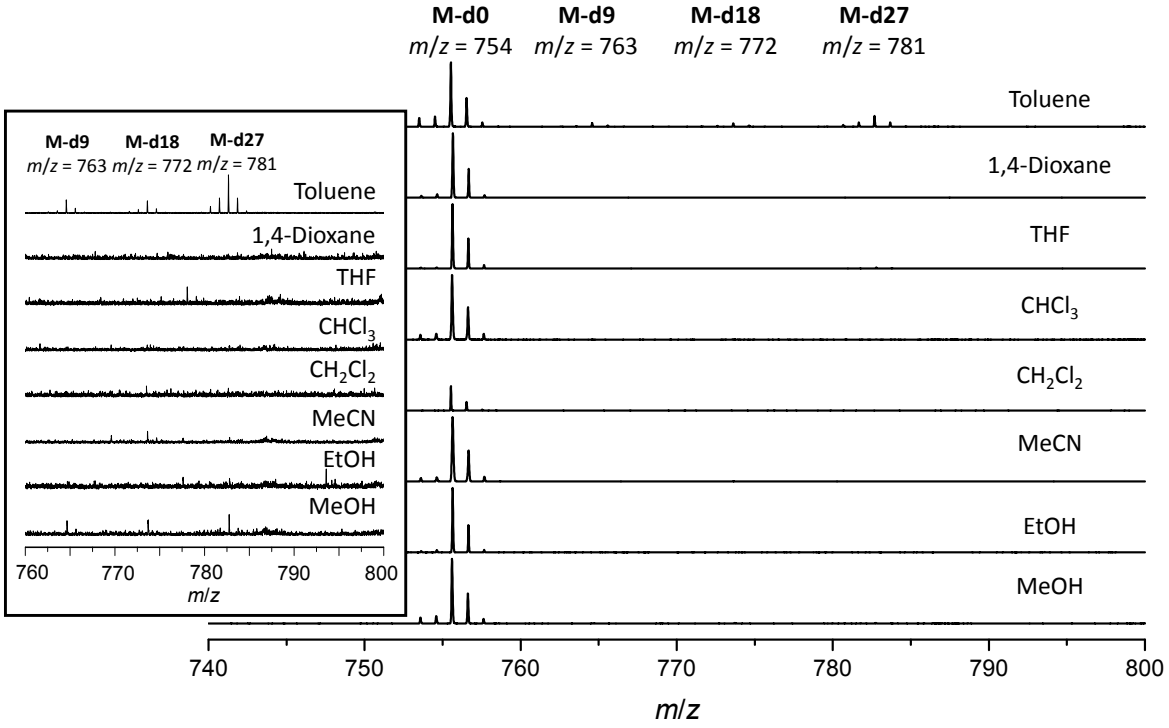


Figure S72. MS MALDI (TOF, DCTB) spectra of the reaction a, b, c, d, e, f, g, h taken out of the homogeneous reaction solution after 7d.

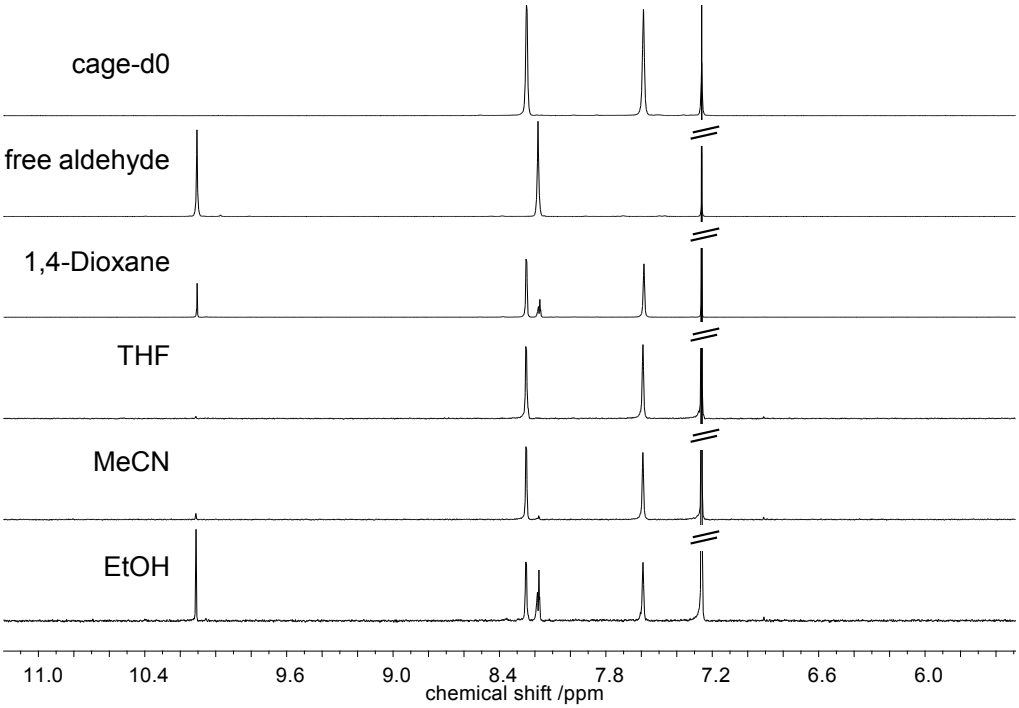


Figure S73. ^{1}H NMR spectra ($CDCl_3$, 300 MHz; region δ=11.0 ppm – 6.00 ppm) from the isolated precipitate (reaction b, c, f, g; reaction time: 7d).

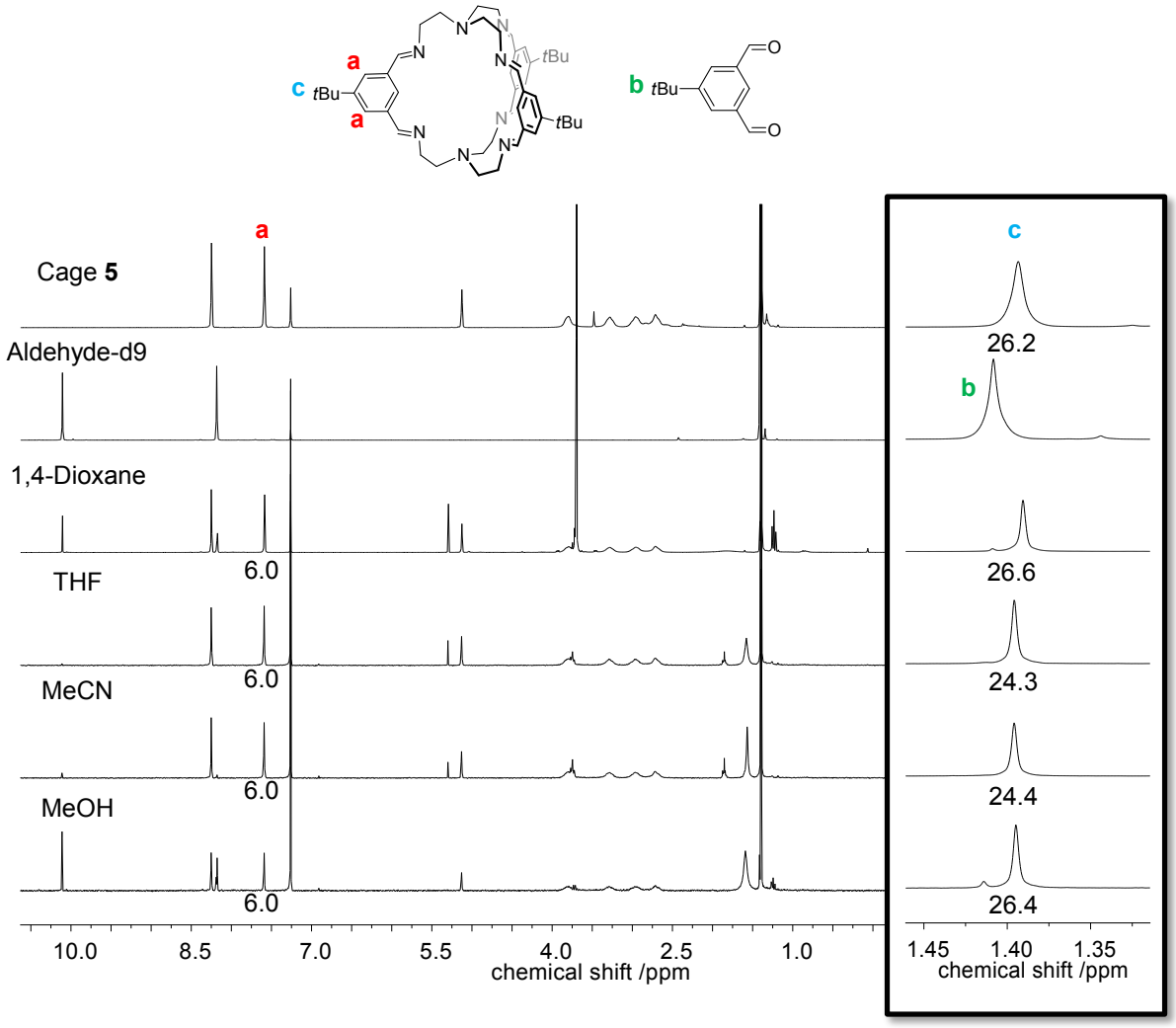


Figure S74. ^{1}H NMR spectra ($CDCl_3$, 300 MHz) from the isolated precipitates (reaction a, b, c, e, f, g; reaction time: 7d). Integrals of signals at δ = 7.59 ppm and δ = 1.40 ppm are given.

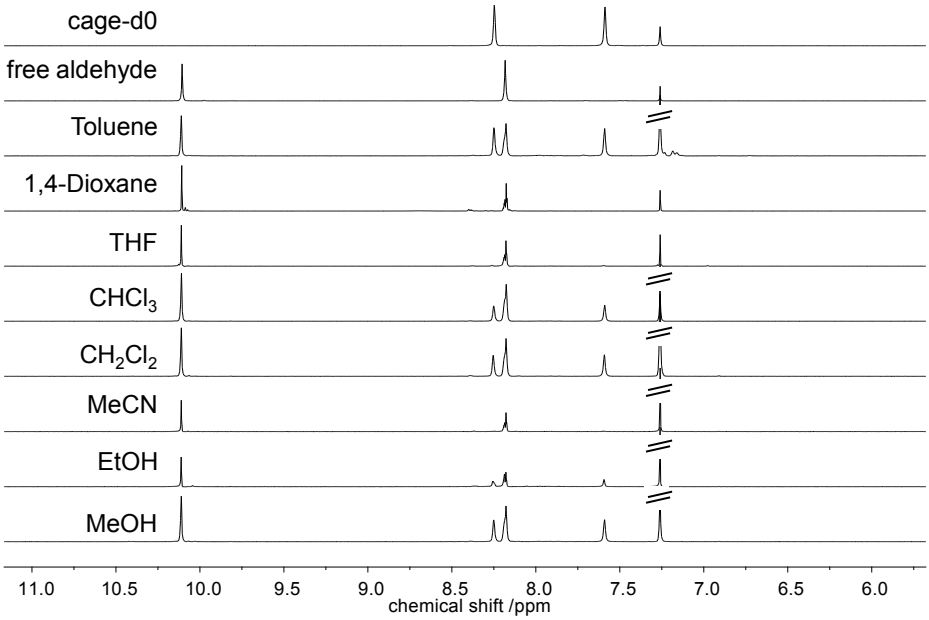


Figure S75. ^{1}H NMR spectra ($CDCl_3$, 300 MHz; region δ=11.0 ppm – 6.00 ppm) from the solid from the mother liquor (reaction a, b, c, d, e, f, g, h; reaction time: 7d).

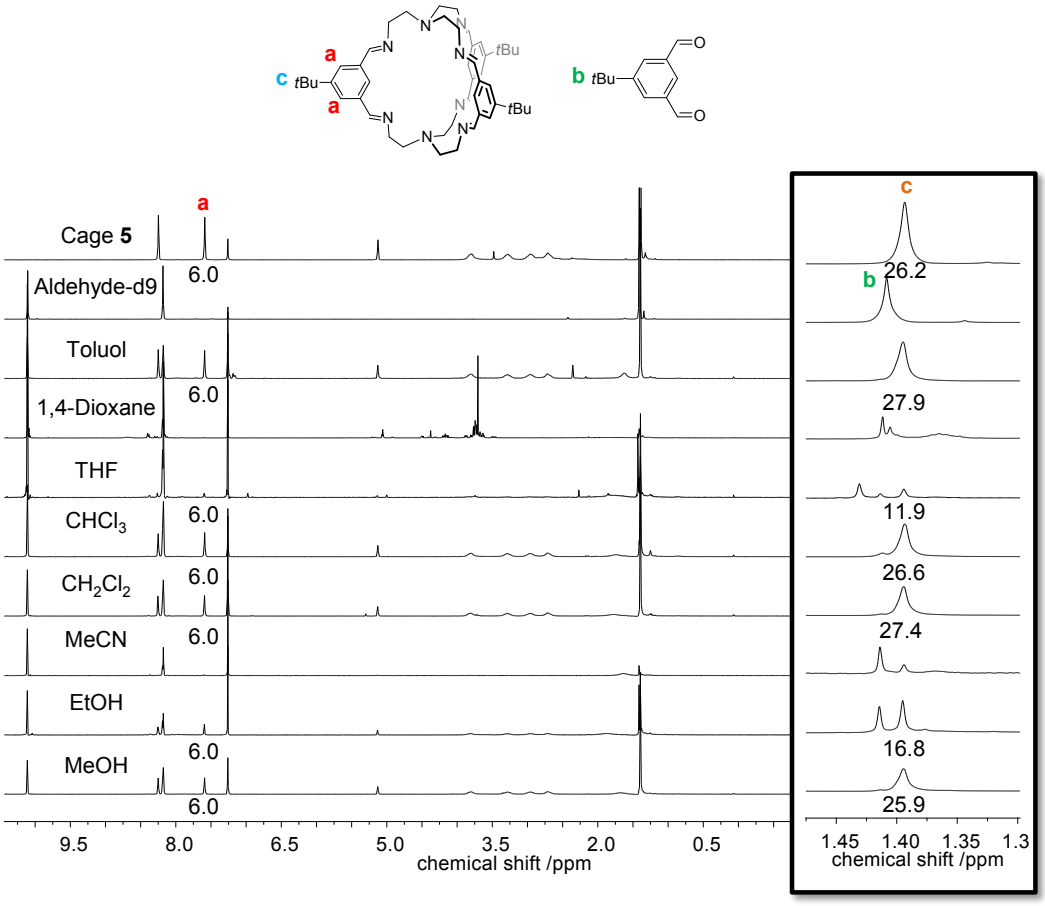


Figure S76. ^{1}H NMR spectra ($CDCl_3$, 300 MHz) from the mother liquor (reaction a, b, c, e, f, g; reaction time: 7d). Integrals of signals at δ = 7.59 ppm and δ = 1.40 ppm are given.

With TFA

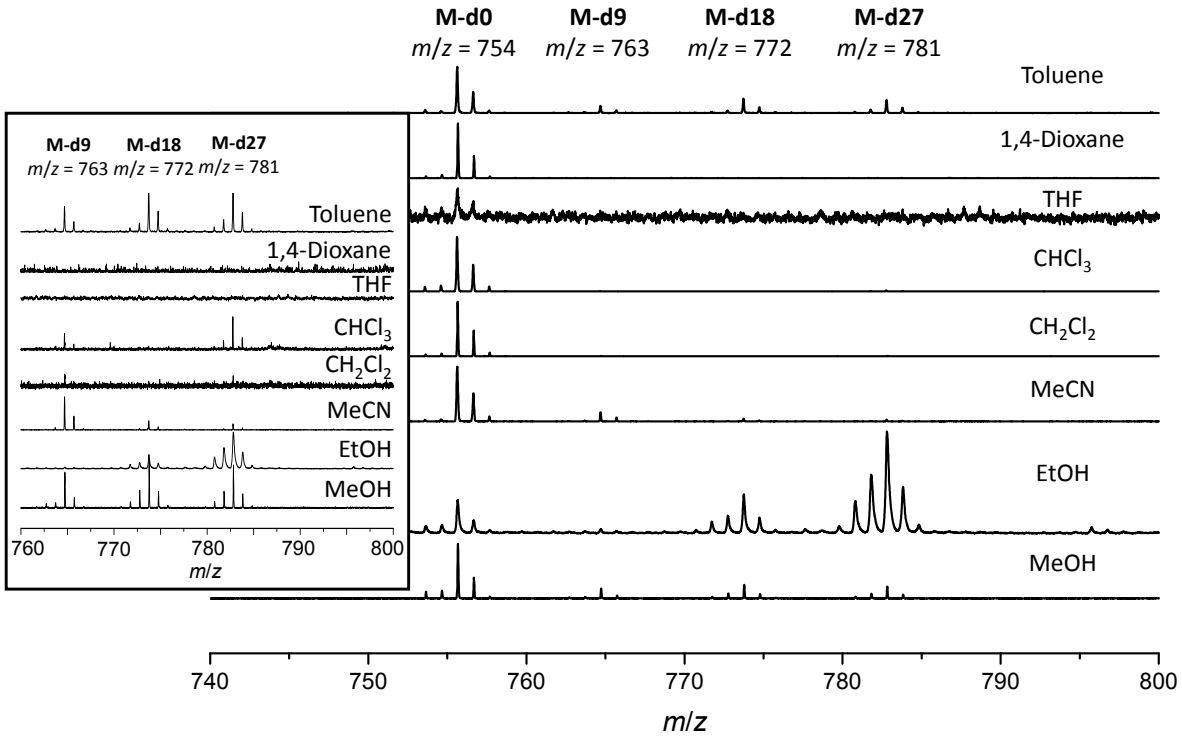


Figure S77. MS MALDI (TOF, DCTB) spectra of the reaction a, b, c, d, e, f, g, h taken out of the homogeneous reaction solution after 7d.

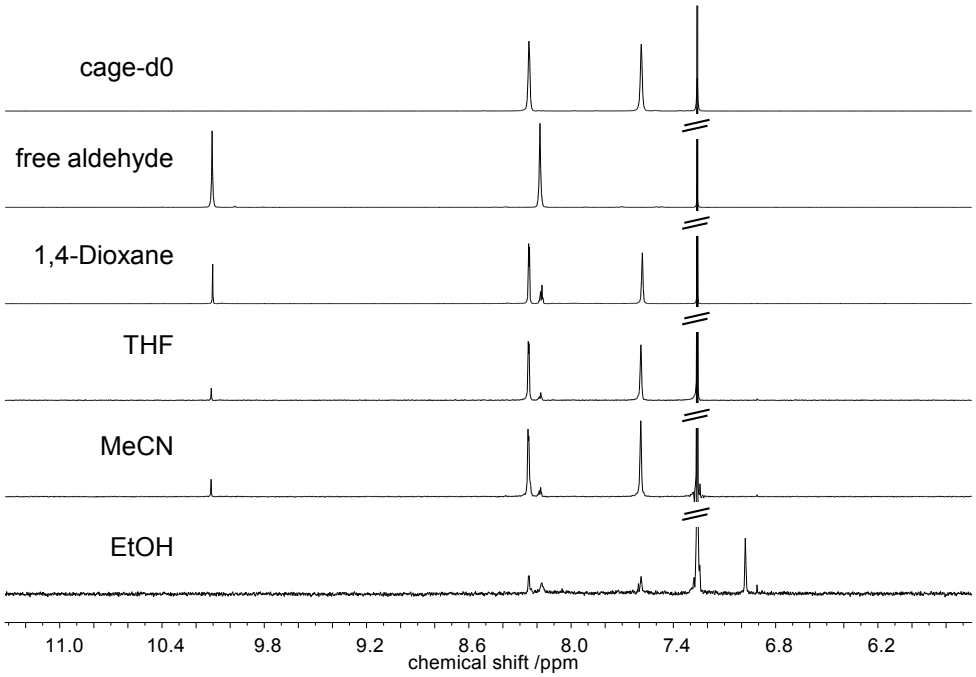


Figure S78. ^{1}H NMR spectra ($CDCl_3$, 300 MHz; region δ=11.0 ppm – 6.00 ppm) from the isolated precipitate (reaction b, c, f, g; reaction time: 7d).

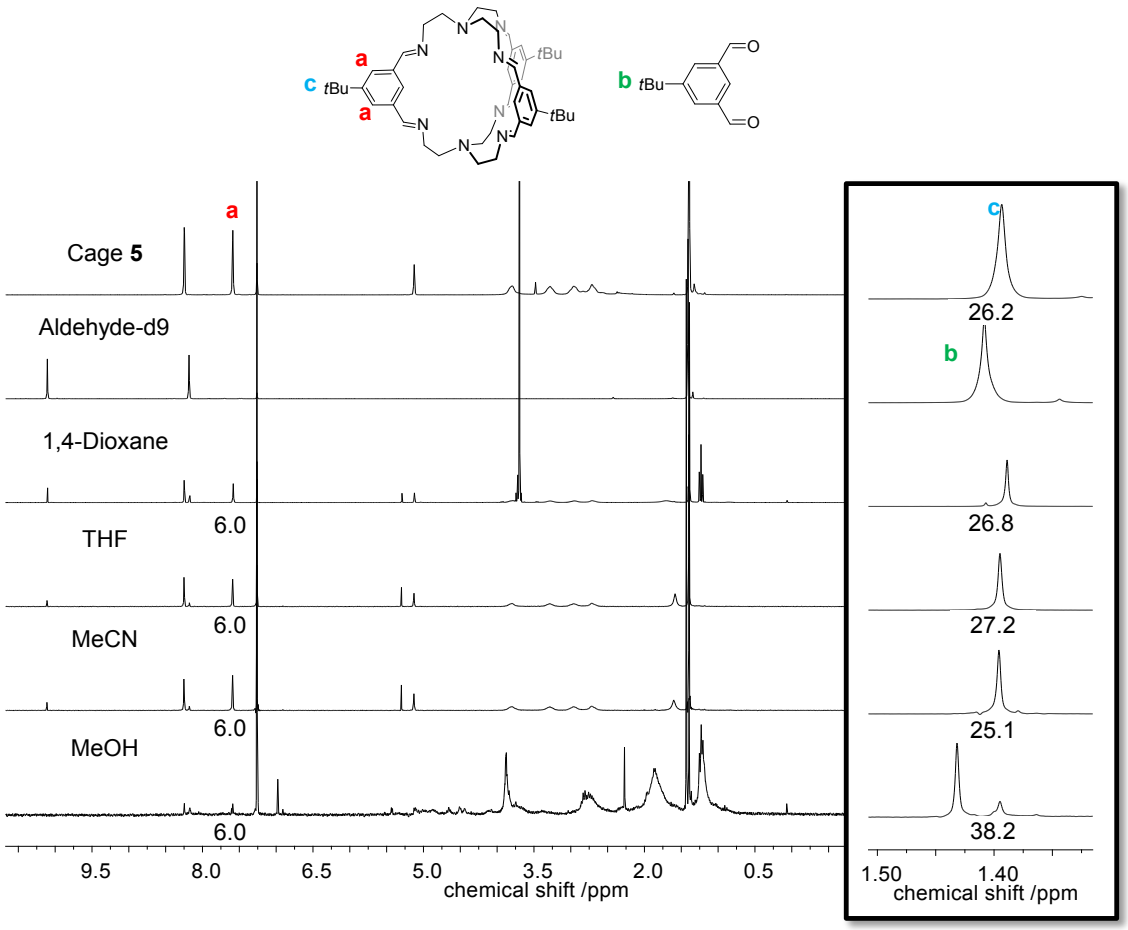


Figure S79. ^{1}H NMR spectra ($CDCl_3$, 300 MHz) from the isolated precipitates (reaction a, b, c, e, f, g; reaction time: 7d). Integrals of signals at δ = 7.59 ppm and δ = 1.40 ppm are given.

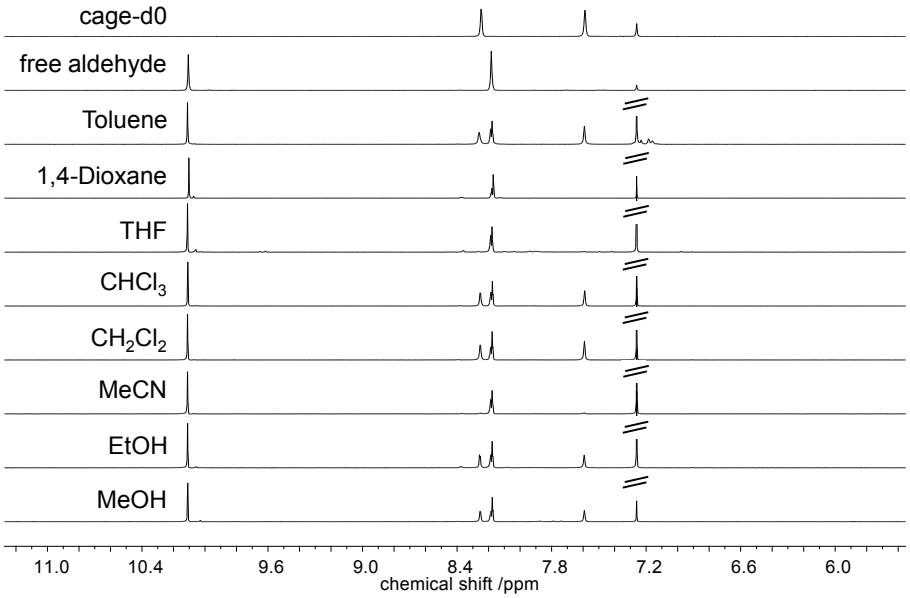


Figure S80. ^{1}H NMR spectra ($CDCl_3$, 300 MHz; region δ=11.0 ppm – 6.00 ppm) from the solid from the mother liquor (reaction a, b, c, d, e, f, g, h; reaction time: 7d).

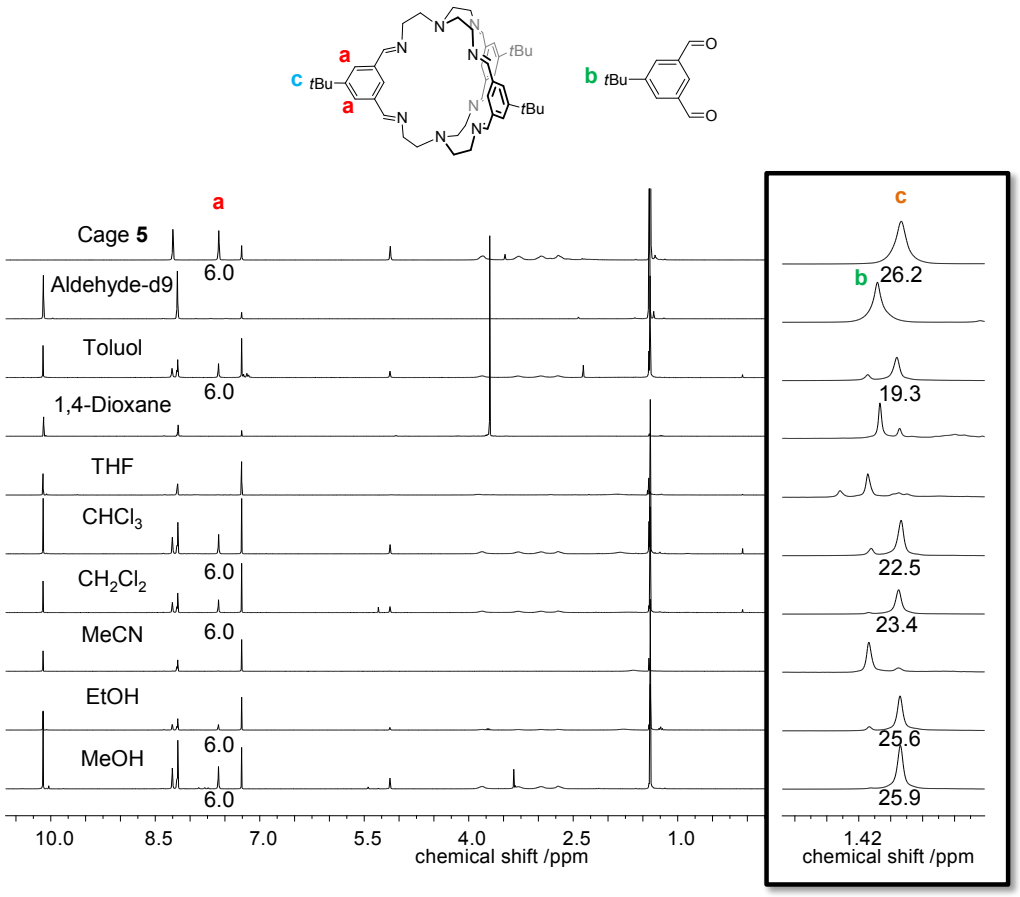
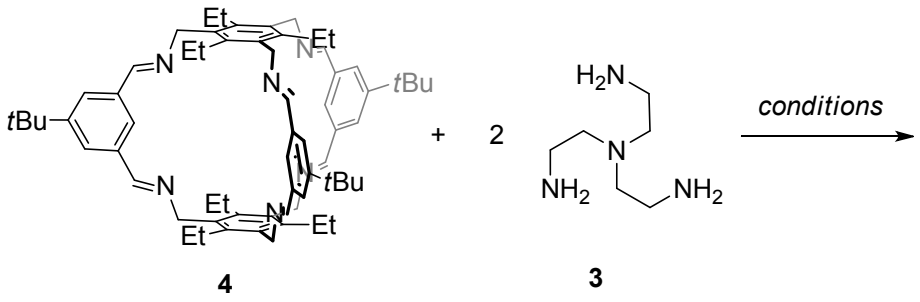


Figure S81. ^{1}H NMR spectra ($CDCl_3$, 300 MHz) from the mother liquor (reaction a, b, c, e, f, g; reaction time: 7d). Integrals of signals at δ = 7.59 ppm and δ = 1.40 ppm are given.

9. Amine Exchange



Without TFA

Table S5. Summary where scrambling was detected from the recorded data.

entry	solvent	Exchange of amine observed in MALDI MS	Cage found in		Exchange of amine observed in ^{1}H NMR	
			mother liquor	solid	mother liquor	solid
a	MeOH	✔	✔	✔	✔ (11%)	✘
b	EtOH	✔	✘	✔	✘	✘
c	MeCN	✔	✘	✔	✘	✘
d	CH_2Cl_2	✔	✔	–[1]	✔ (36%)	✘
e	$CHCl_3$	✔	✔	✔	✘	✘
f	THF	✔	✘	✔	✘	✘
g	1,4-Dioxane	✔	✘	✔	✘	✘
h	Toluene	✔	✔	–[1]	✘	✘

[1] cage stayed in solution.

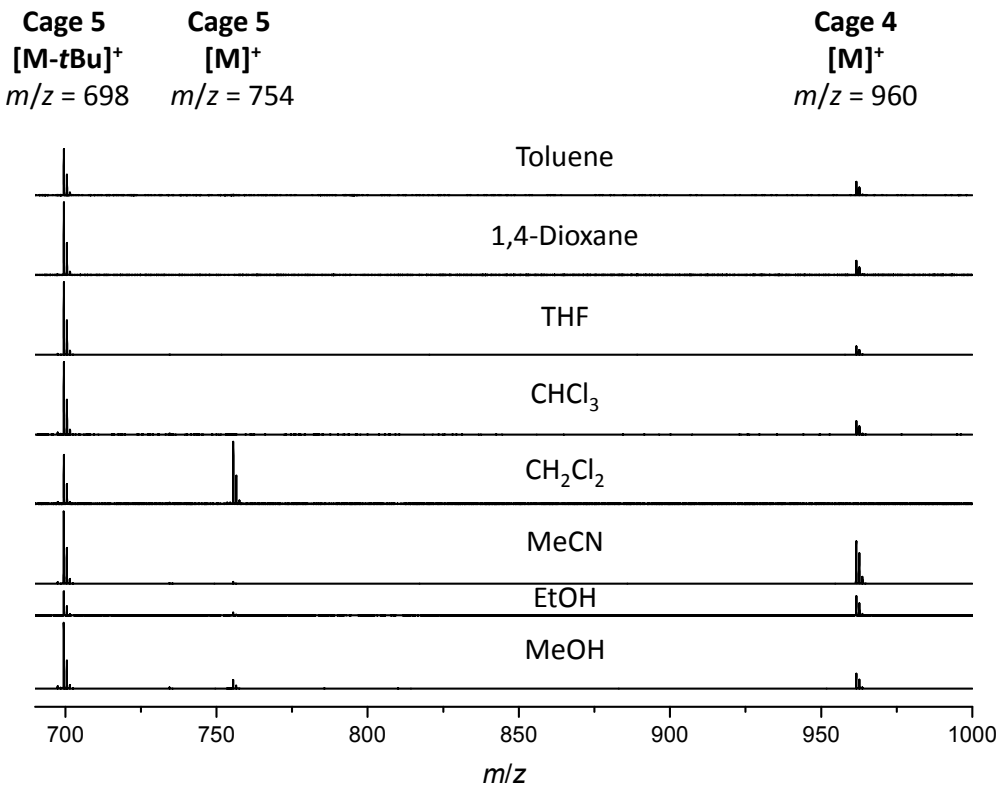


Figure S82. MS MALDI (TOF, DCTB) spectra of the reactions a, b, c, d, e, f, g, h taken out of the reaction mixture after 7d. An exchange of amines can be observed with all solvents.

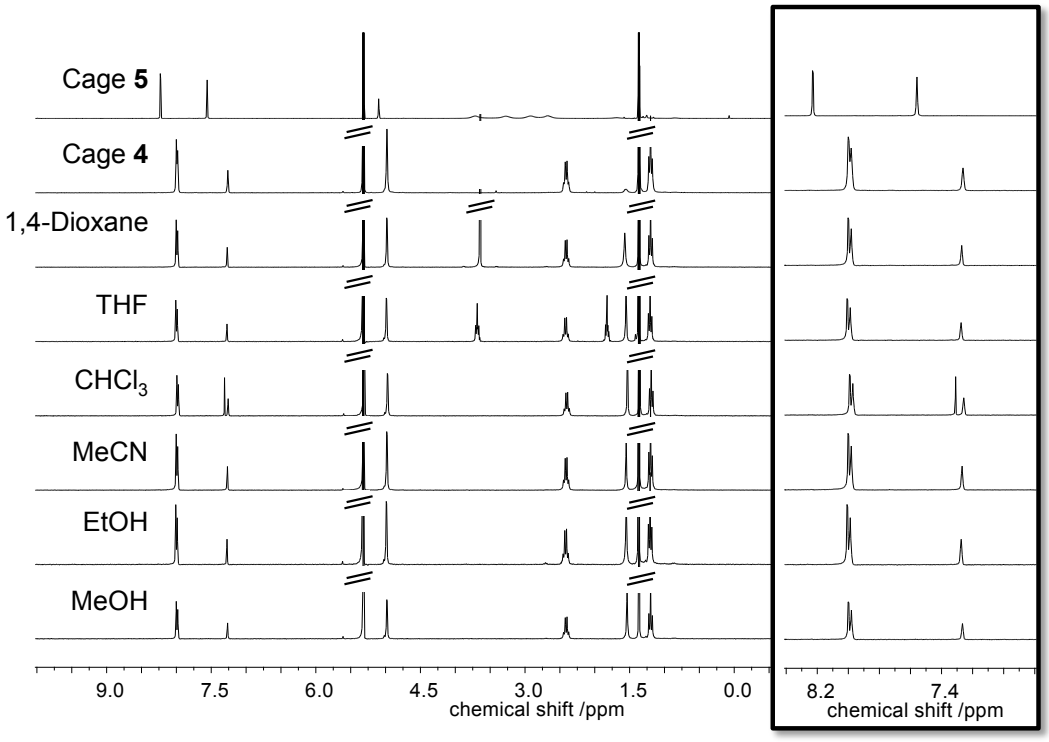


Figure S83. ^{1}H NMR spectra (CD_2Cl_2, 300 MHz) from the isolated precipitate (reaction a, b, c, e, f, g; reaction time: 7d).

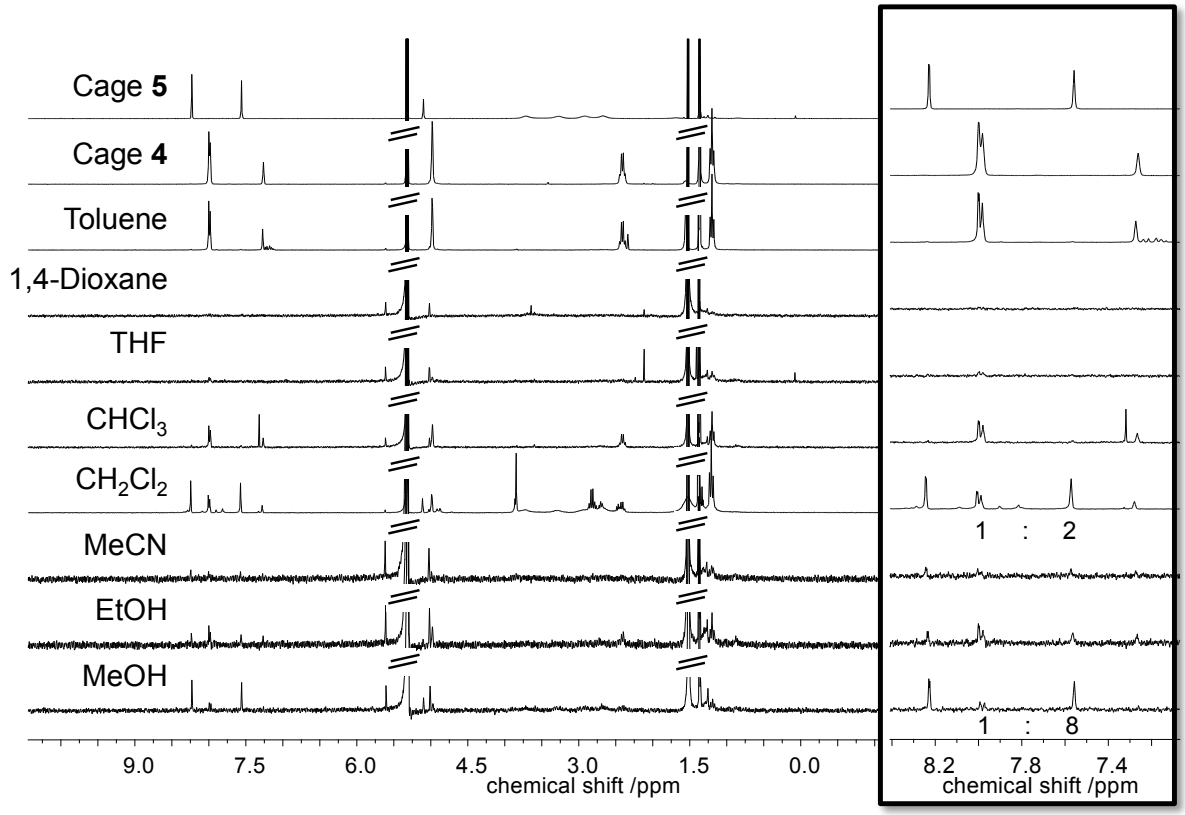


Figure S84. ^{1}H NMR spectra (CD_2Cl_2, 300 MHz) from the mother liquor residue (reaction a, b, c, d, e, f, g, h; reaction time: 7d). Relative integrals are given.

with TFA

Table S6. Summary where scrambling was detected from the recorded data.

entry	solvent	Exchange of aldehydes observed in MALDI MS	Cage found in		Exchange of aldehydes observed in ^{1}H NMR	
			mother liquor	solid	mother liquor	solid
a	MeOH	✔	✔[2]	✔	✔	✘
b	EtOH	✔	✔	✔	✘	✘
c	MeCN	✔	✔[2]	✔	✔ (71%)	✔ (17%)
d	CH_2Cl_2	✔	✔	✔	✔ (55%)	✔ (59%)
e	$CHCl_3$	✔	✔	✔	✔ (29%)	✘
f	THF	✔[3]	✘	✔	✘	✘
g	1,4-Dioxane	✔	✘	✔	✘	✘
h	Toluene	✔	✔	–[1]	✔ (33%)	–[1]

[1] cage stayed in solution. [2] in traces. [3] very unclean.

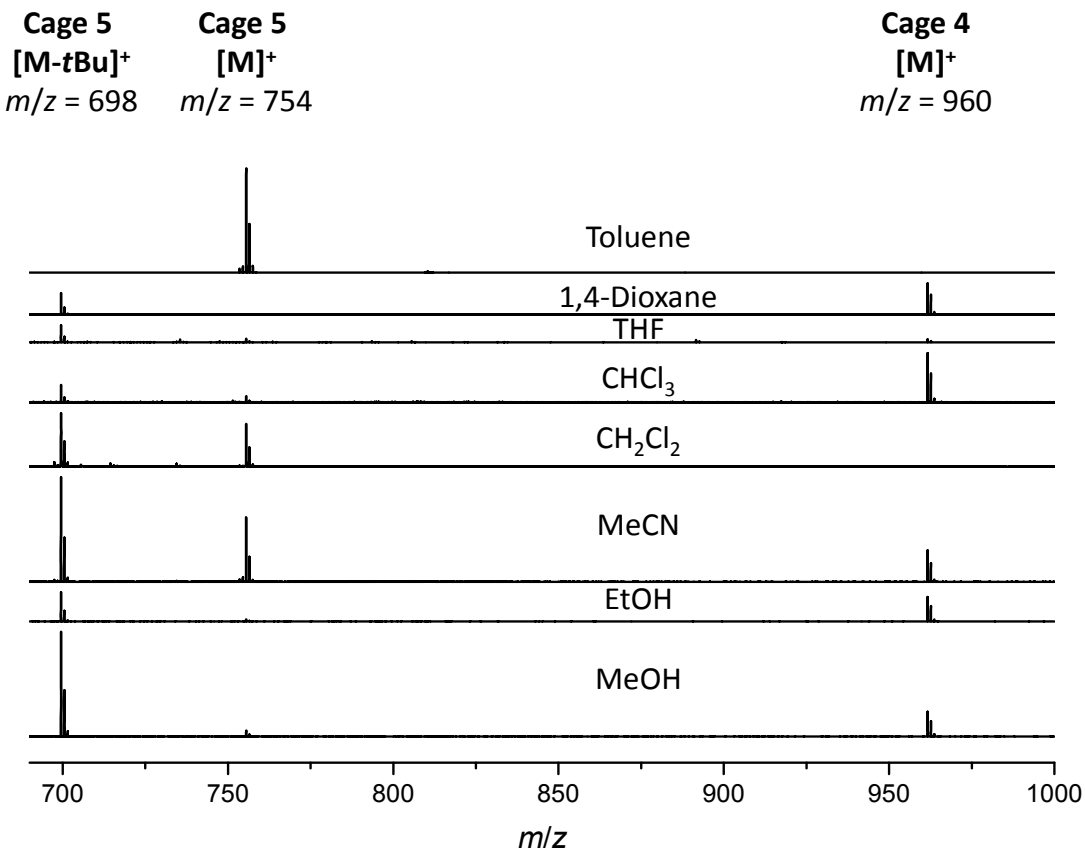


Figure S85. MS MALDI (TOF, DCTB) spectra of the reactions a, b, c, d, e, f, g, h taken out of the homogeneous reaction mixture after 7d.

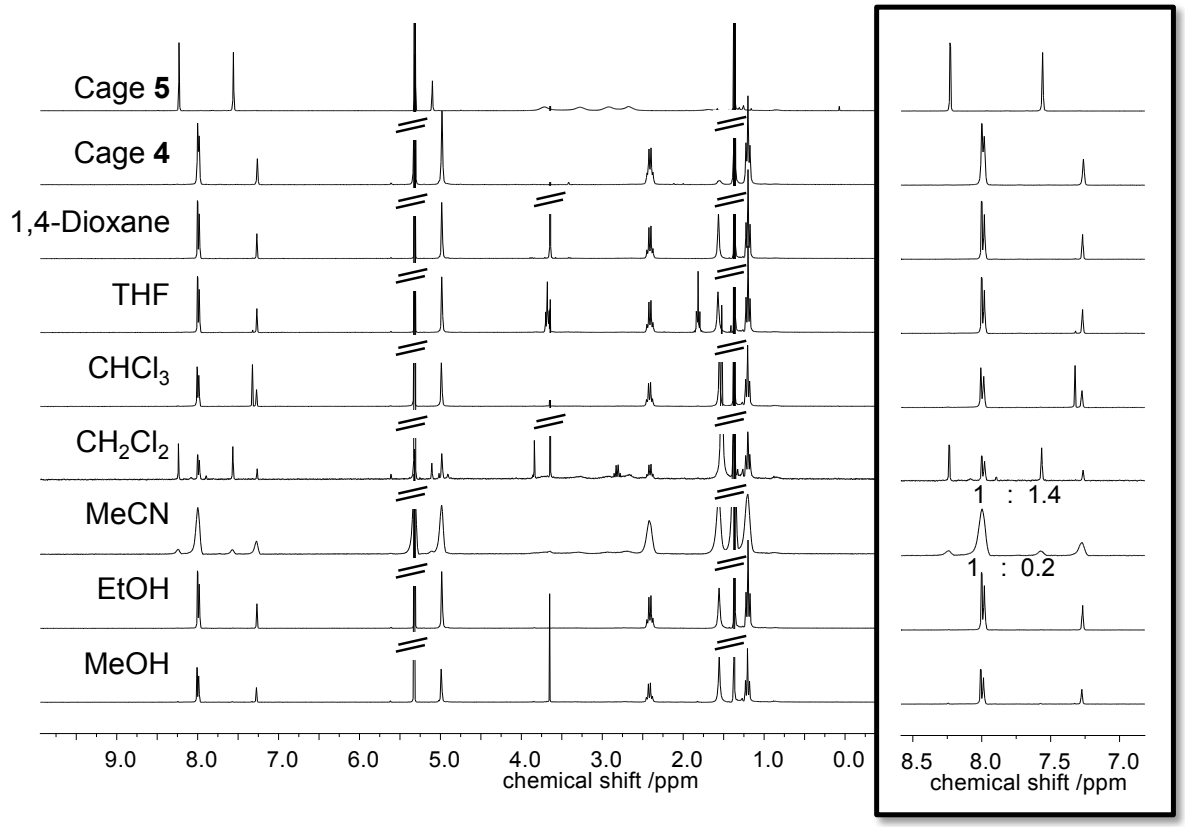


Figure S86. ^{1}H NMR spectra (CD_2Cl_2, 300 MHz) from the isolated precipitate (reaction a, b, c, d, e, f, g; reaction time: 7d.

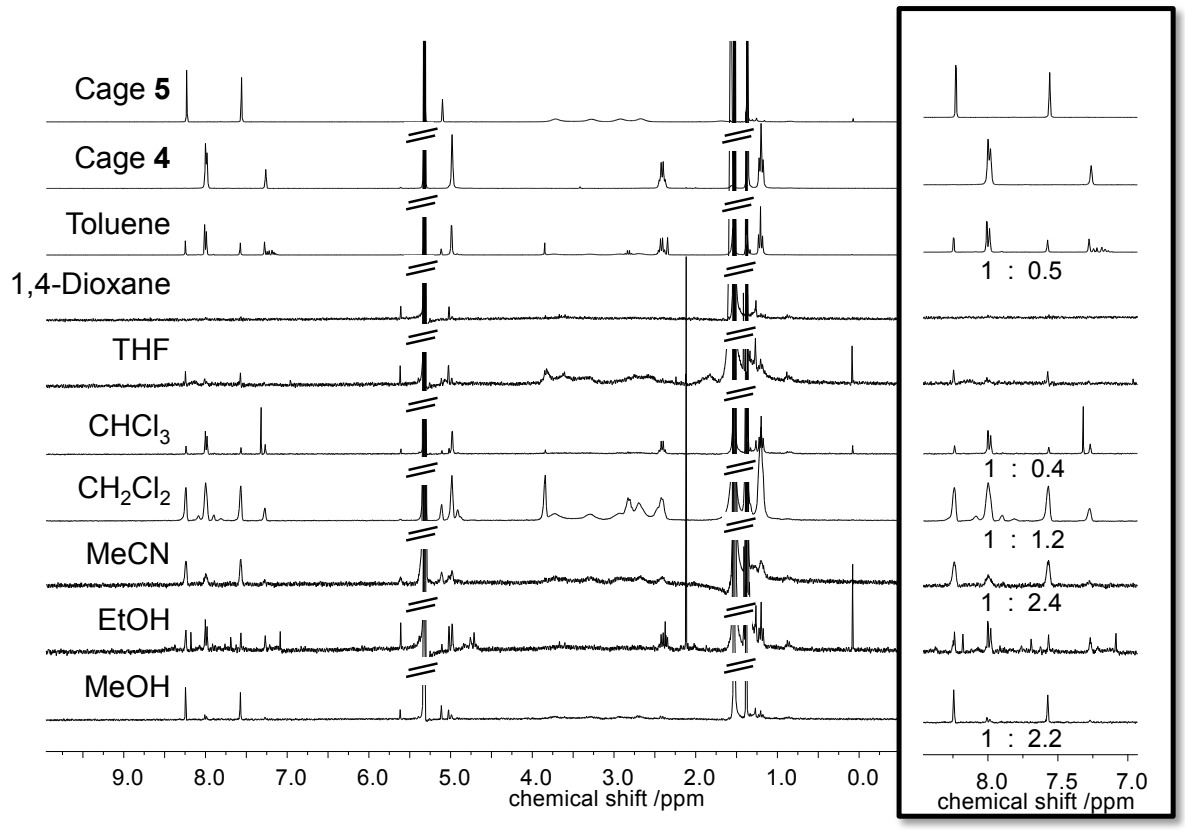
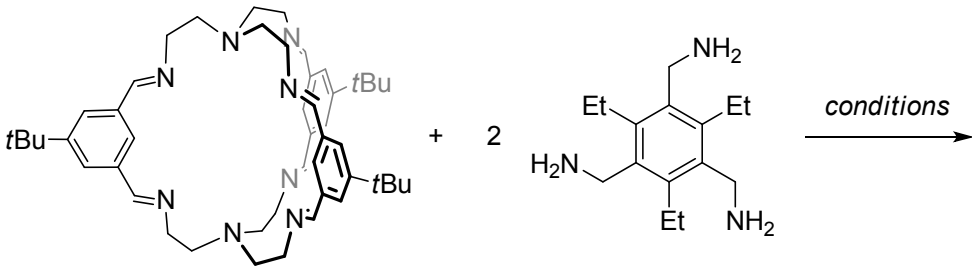


Figure S87. ^{1}H NMR spectra (CD_2Cl_2, 300 MHz) from the solid from the mother liquor (reaction a, b, c, d, e, f, g, h; reaction time: 7d). Relative integrals are given.



5 **2**

Without TFA

Table S7. Summary where scrambling was detected from the recorded data.

entry	solvent	Exchange of amines observed in MALDI MS	Cage found in		Exchange of amines observed in ^{1}H NMR	
			mother liquor	solid	mother liquor	solid
a	MeOH	✔	✔	✔	✘	✔ (47%)
b	EtOH	✘	✔	–[1]	✘	–[1]
c	MeCN	✘	✔	✔	✘	✔ (7%)
d	CH_2Cl_2	✘	✔	–[1]	✘	–[1]
e	$CHCl_3$	✘	✔	–[1]	✘	–[1]
f	THF	✘	✔	✔	✘	✘
g	1,4-Dioxane	✘	✔	✘	✘	✘
h	Toluene	✘	✔	–[1]	✘	–[1]

[1] cage stayed in solution.

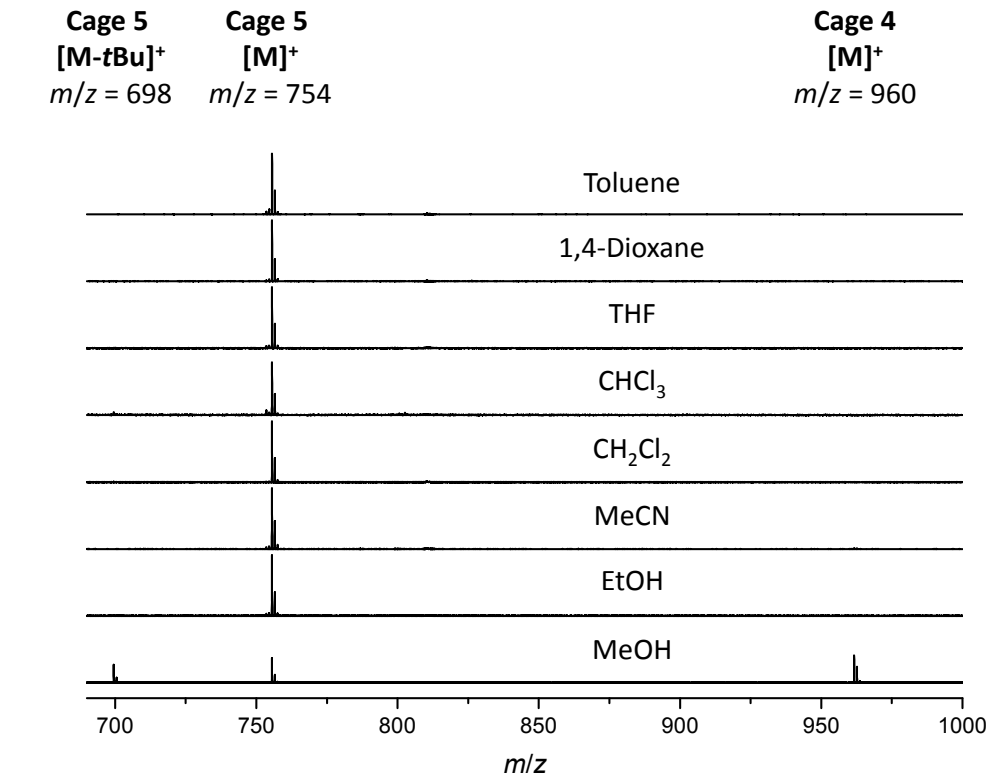


Figure S88. MS MALDI (TOF, DCTB) spectra of the reaction a, b, c, d, e, f, g, h taken out of the homogeneous reaction solution after 7d. An exchange of amines can be observed with methanol.

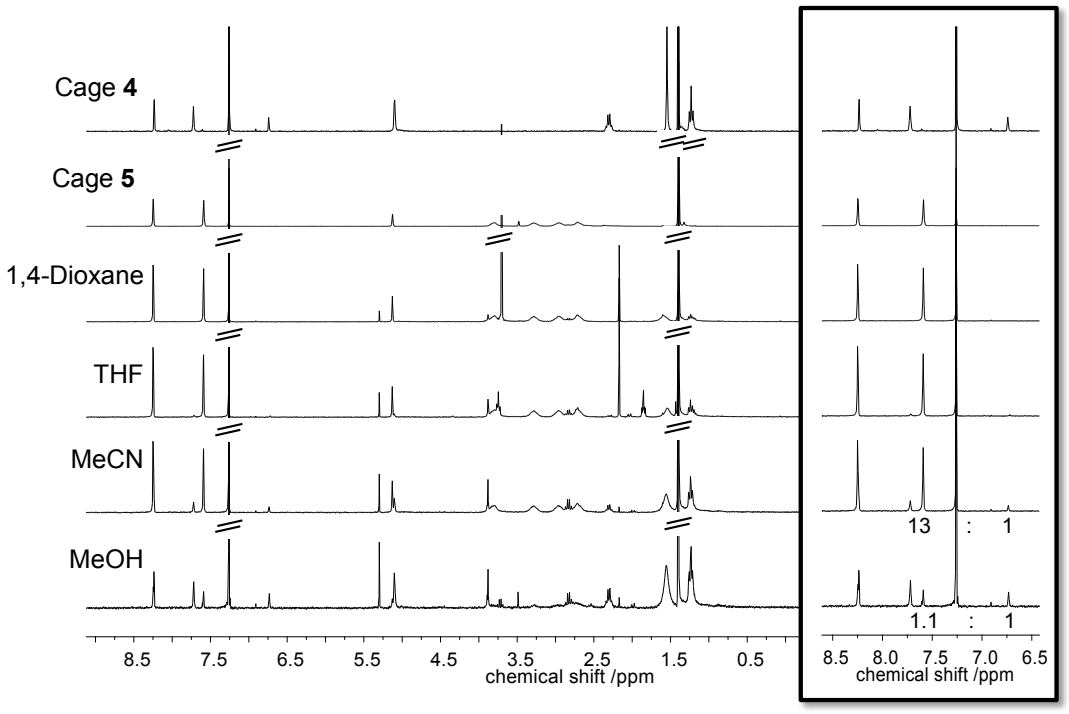


Figure S89. ^{1}H NMR spectra ($CDCl_3$, 300 MHz). from the isolated precipitate (reaction a, c, f, g; reaction time: 7d).

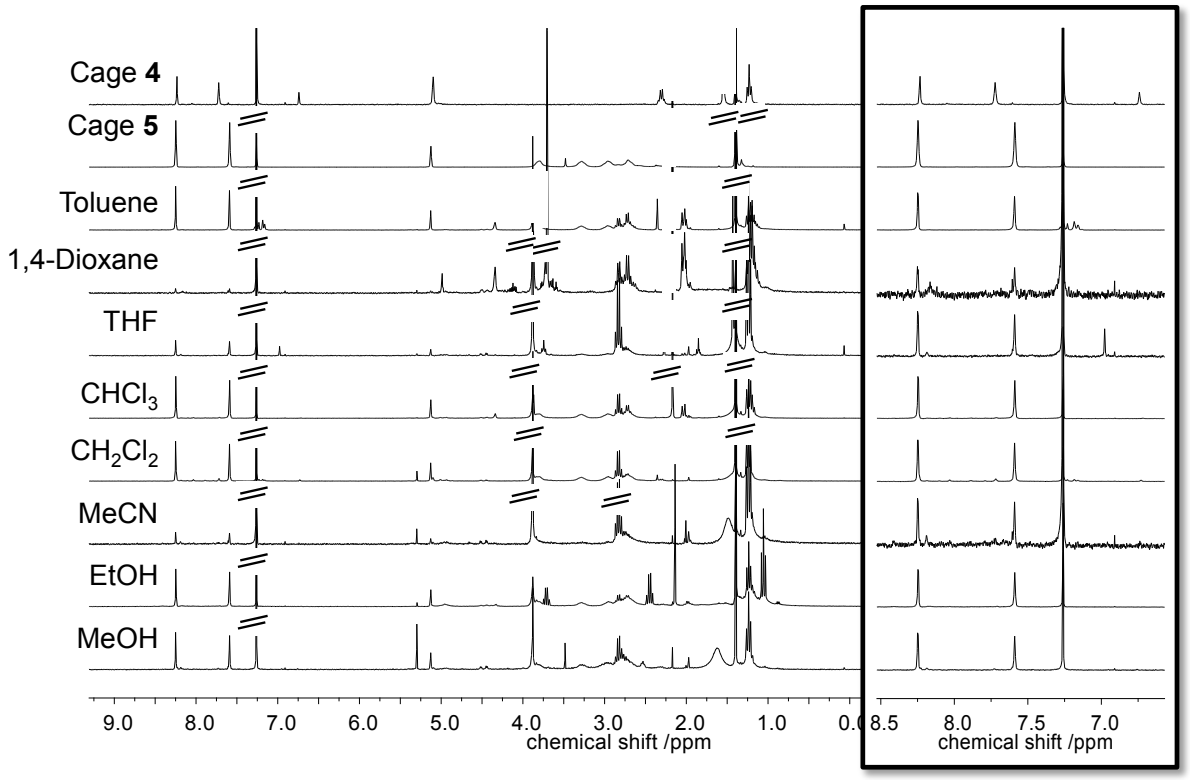


Figure S90. ^{1}H NMR spectra ($CDCl_3$, 300 MHz) from the isolated solid from the mother liquor (reaction a, b, c, d, e, f, g, h; reaction time: 7d).

with TFA

Table S8. Summary where scrambling was detected from the recorded data.

entry	solvent	Exchange of amines observed in MALDI MS	Cage found in		Exchange of amines observed in ^{1}H NMR	
			Mother liquor	solid	Mother liquor	solid
a	MeOH	✔	✔	✔	✘	✔ (100%)
b	EtOH	✘	✔	–[1]	✘	–[1]
c	MeCN	✘	✔	✔	✘	✔(13%)
d	CH_2Cl_2	✘	✔	–[1]	✘	–[1]
e	$CHCl_3$	✘	✔	–[1]	✘	–[1]
f	THF	✘	✔	✔	✘	✘
g	1,4-Dioxane	✘	✔	✘	✘	–[1]
h	Toluene	✘	✔	–[1]	✘	–[1]

[1] cage stayed in solution.

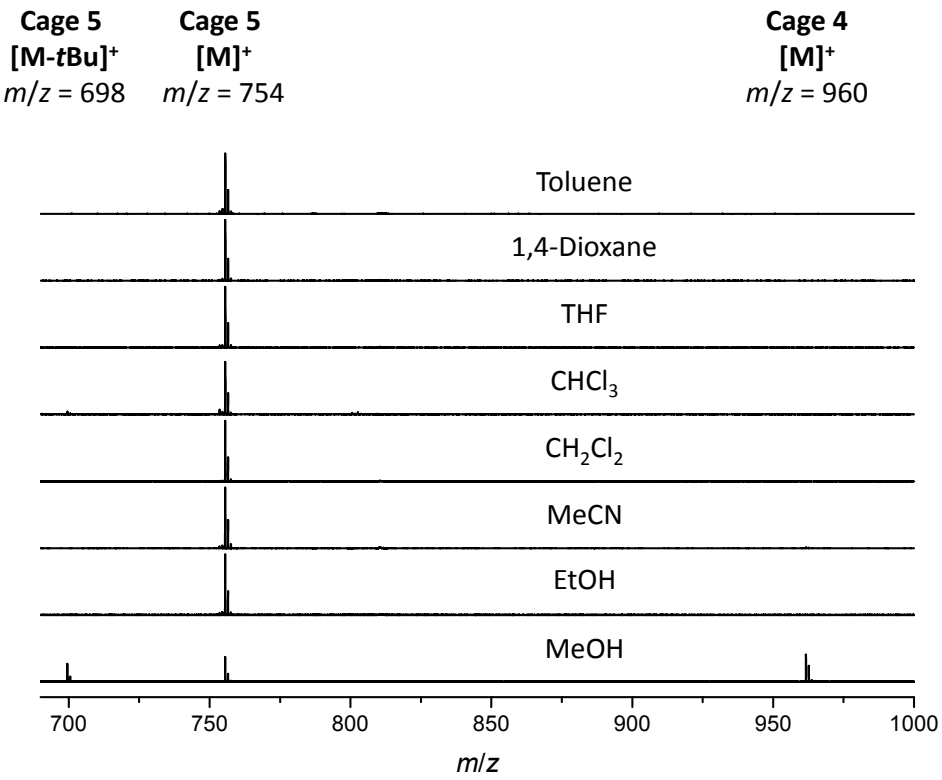


Figure S91. MS MALDI (TOF, DCTB) spectra of the reaction a, b, c, d, e, f, g, h taken out of the homogeneous reaction solution after 7d. An exchange of amines can be observed in methanol.

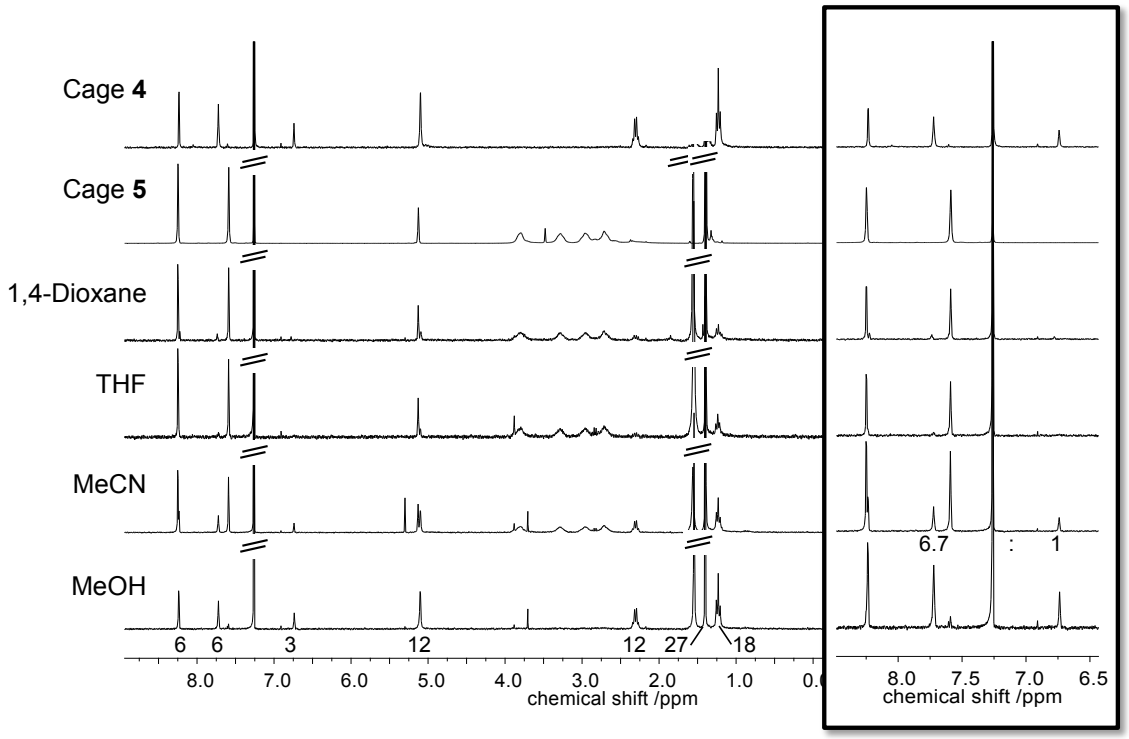


Figure S92. ^{1}H NMR spectra ($CDCl_3$, 300 MHz) from the isolated precipitate (reaction a, c, f, g; reaction time: 7d).

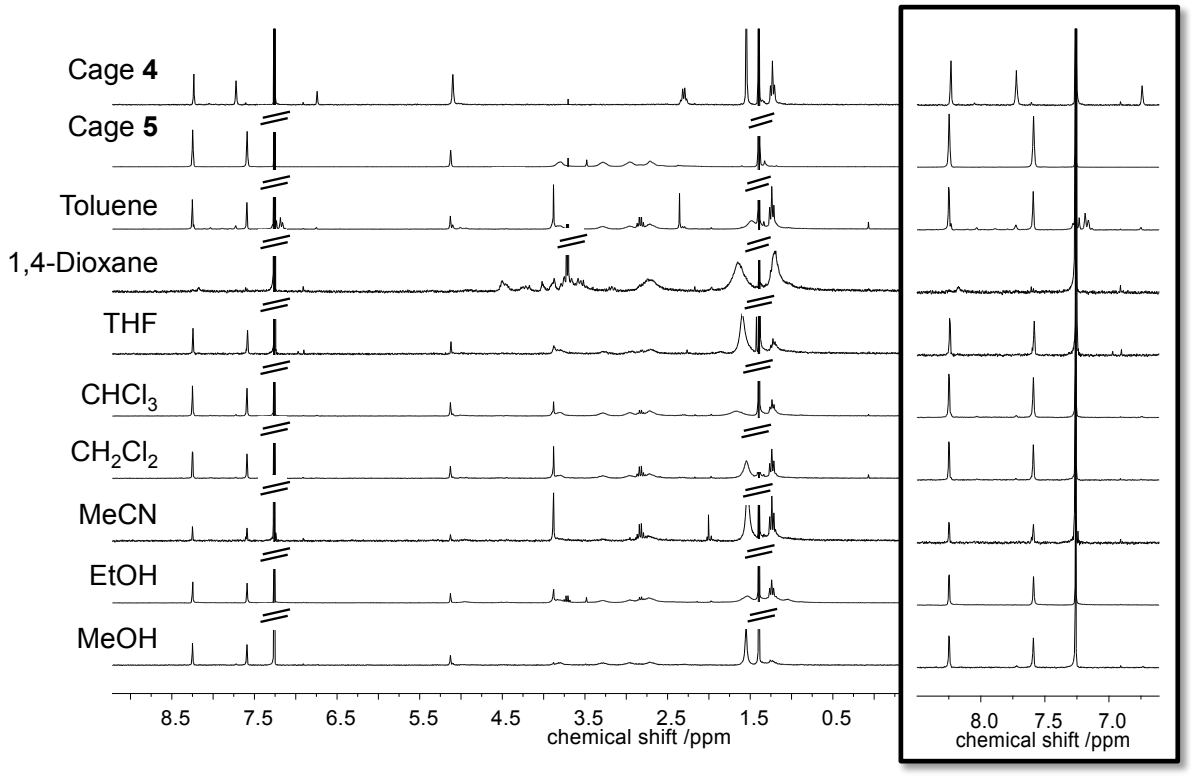
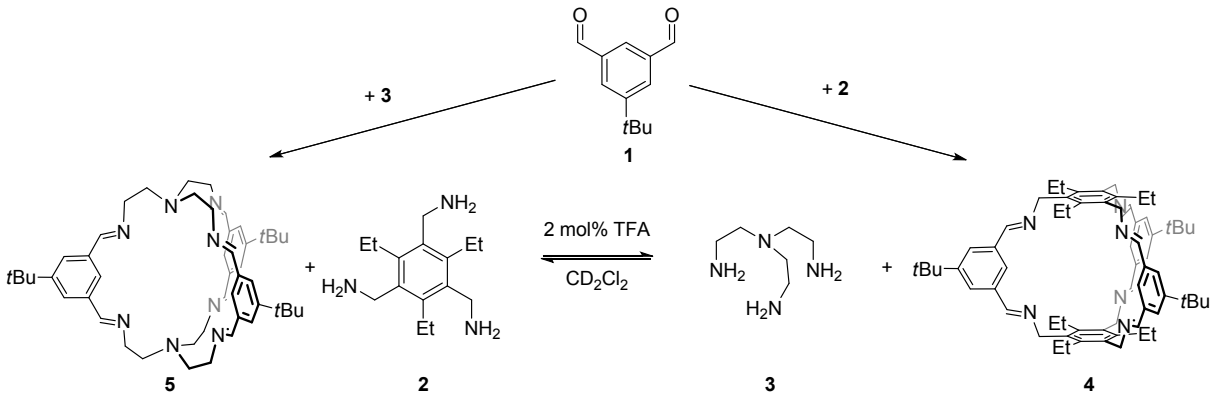


Figure S93. ^{1}H NMR spectra ($CDCl_3$, 300 MHz) from the mother liquor residue (reaction a, b, c, d, e, f, g, h; reaction time: 7d).

10. Estimating Thermodynamic Data for Amine Exchange

In dichloromethane-d_2



Scheme S1 Dynamic transformation of cage **5** to **4** and vice versa with TFA as a catalyst.

Table S9. Integrals of diagnostic signals of compound **2**, **3**, **4**, **5** found in the reaction solution.

	¹H NMR integrals				Normed integrals			
	Cage **4**	Cage **5**	Amine **2**	Amine **3**	Cage **4**	Cage **5**	Amine **2**	Amine **3**
entry	δ = 7.28 ppm (3H)	δ = 7.58 ppm (6H)	δ = 3.84 ppm (6H)	δ = 2.71 ppm (6H)	δ = 7.28 ppm (1H)	δ = 7.58 ppm (1H)	δ = 3.84 ppm (1H)	δ = 2.71 ppm (1H)
A	0.25	1.00	1.21	0.77	0.08	0.17	0.20	0.13
B	0.29	1.00	1.71	0.84	0.10	0.17	0.29	0.14
C	0.47	1.00	4.32	1.87	0.16	0.17	0.72	0.31
D	0.46	1.00	5.70	2.18	0.15	0.17	0.95	0.36
E	0.48	1.00	8.82	4.36	0.16	0.17	1.47	0.73
F	0.91	1.00	1.73	0.77	0.30	0.17	0.29	0.13
G	0.20	1.00	1.48	1.17	0.07	0.17	0.25	0.20
H	0.14	1.00	1.21	1.16	0.05	0.17	0.20	0.19

Table S10. Calculation of equilibrium concentration of compounds **4**, **3**, **5**, **2** in the reactions solution.

	used molar amounts for synthesis			Calculated molar amounts from ¹H NMR spectrum			
entry	Aldehyde **1** µmol	Amine **2** µmol	Amine **3** µmol	Cage **4** µmol	Amine **3** µmol	Cage **5** µmol	Amine **2** µmol
A	13.6	8.40	8.90	1.51	2.86	3.02	5.38
B	13.6	11.6	8.90	1.66	3.16	2.87	8.27
C	13.6	17.3	8.90	2.20	4.23	2.34	12.9
D	13.6	20.1	8.90	2.17	4.18	2.36	15.8
E	13.6	25.7	8.90	2.22	4.27	2.31	21.3
F	11.2	4.80	12.6	2.71	1.82	1.49	5.78
G	9.00	9.60	12.1	1.15	3.84	2.88	6.90
H	4.80	9.60	13.2	0.96	2.73	3.44	2.88

$$K = \frac{[cage\ \mathbf{5}] * [amine\ \mathbf{2}]^2}{[cage\ \mathbf{4}] * [amine\ \mathbf{3}]^2} \quad \textbf{(I)}$$

$$\Delta G_{eq} = -RT * \ln(K_{eq}) \quad \textbf{(II)}$$

Table S11. Calculated equilibrium constants ($K_{eq.}$) and Gibbs free energy (ΔG_{eq}) using equation **I** and **II** and the concentration of compound **2**, **3**, **4**, **5**.

Cage **4** -> Cage **5**

entry	K_{eq}	ΔG_{eq} kJ·mol^{-1}
A	7.09	-4.77
B	11.8	-6.02
C	9.92	-5.59
D	15.5	-6.67
E	25,8	-7.92
F	5.53	-4.17
G	8.07	-5.09
H	3.98	-3.36

The average equilibrium constant for transformation of cage **4** to cage **5** is K_{eq} = 11.0 and thus ΔG_{eq} = -5.83 kJ·mol^{-1}.

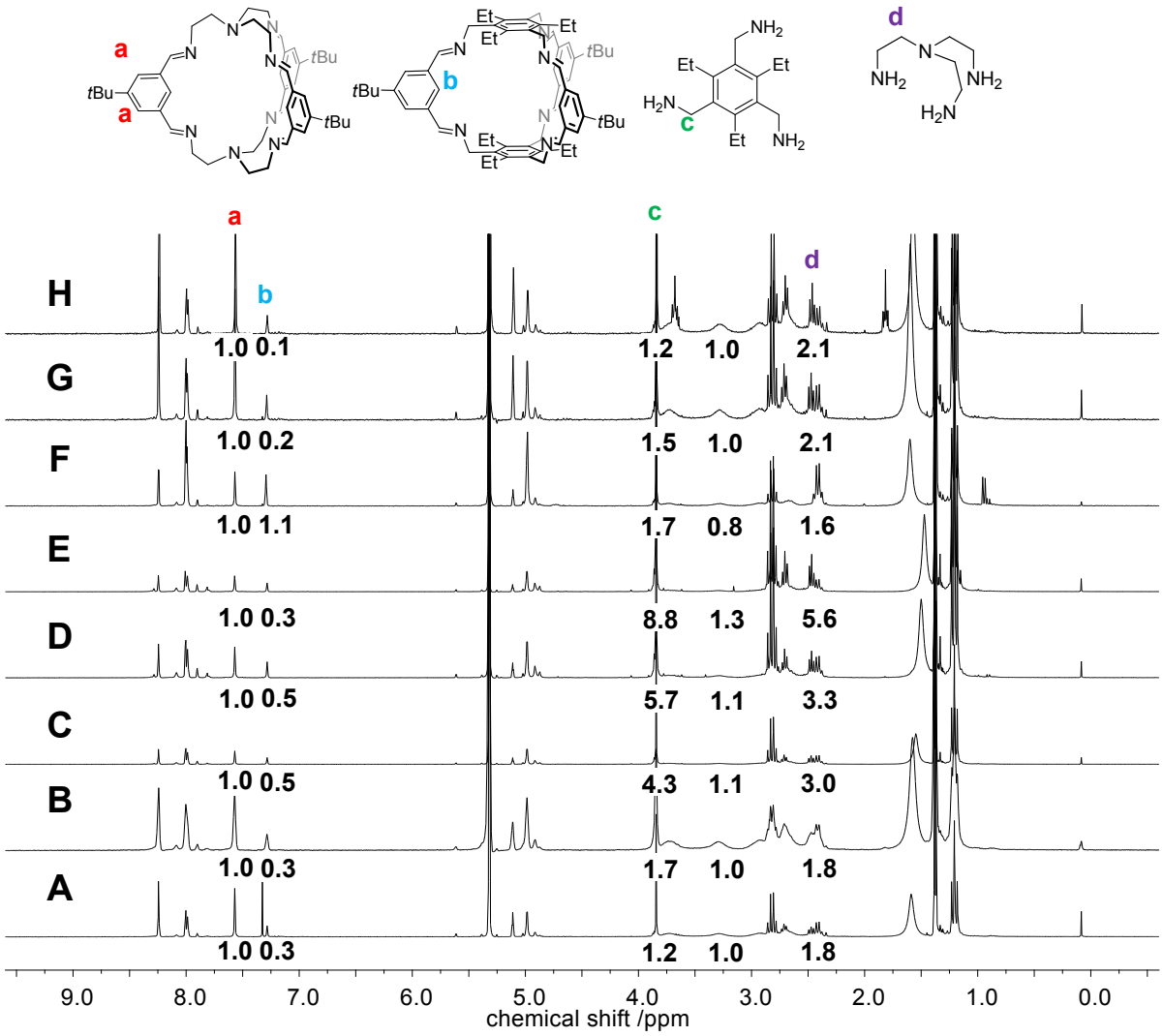
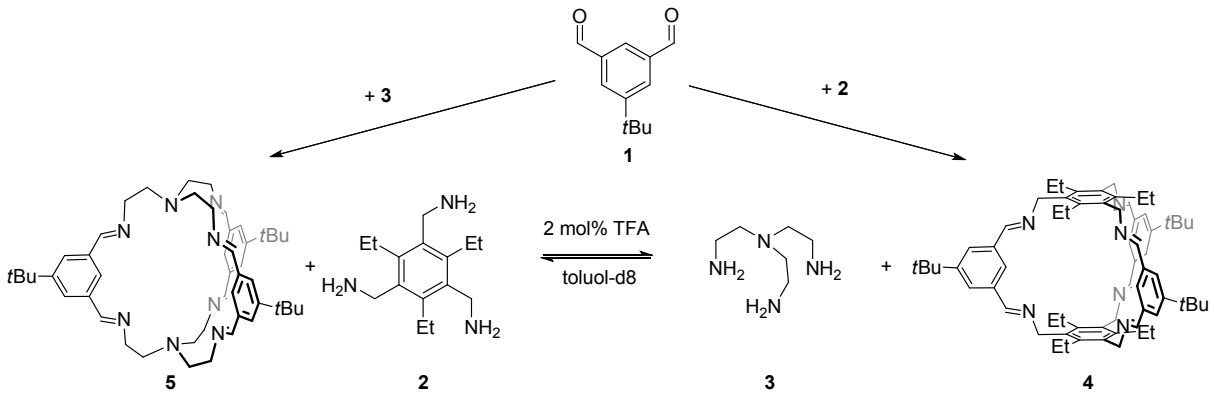


Figure S94. ^{1}H NMR spectra (CD_2Cl_2, 300 MHz) for reactions A–H with integrated signals.

In toluene$_{-d8}$



Scheme S2 Dynamic transformation of cage **5** to **4** and vice versa with TFA as a catalyst.

Table S12. Integrals of diagnostic signals of compound **2**, **3**, **4**, **5** found in the reaction solution. [1]calculated as leftover after the reaction from the formation of cage **5**.

	^{1}H NMR integrals				**Normed integrals**			
	Cage **4**	Cage **5**	Amine **2**	Amine **3**	Cage **4**	Cage **5**	Amine **2**	Amine **3**
entry	δ = 8.71 ppm (3H)	δ = 7.86 ppm (6H)	δ = 3.74 ppm (6H)	δ = 2.18 ppm (6H)	δ = 8.71 ppm (1H)	δ = 7.86 ppm (1H)	δ = 3.74 ppm (1H)	δ = 2.18 ppm (1H)
A	1.00	1.04	0.31	0.00[1]	0.17	0.17	0.05	0.00[1]
B	1.00	0.84	0.98	0.00[1]	0.17	0.14	0.16	0.00[1]
C	1.00	4.41	1.81	0.00[1]	0.17	0.74	0.30	0.00[1]

Table S13. Calculation of equilibrium concentration of compounds **4**, **3**, **5**, **2** in the reactions solution. [1]calculated as leftover after the reaction from the formation of cage **5**.

	used molar amounts for synthesis			**Calculated molar amounts from ^{1}H NMR spectrum**			
entry	Aldehyde **1** µmol	Amine **2** µmol	Amine **3** µmol	Cage **4** µmol	Amine **3** µmol	Cage **5** µmol	Amine **2** µmol
A	13.6	25.7	8.90	2.22	4.28[1]	2.31	21.3
B	11.2	4.80	12.6	2.28	0.97[1]	1.92	6.63
H	9.20	9.60	12.1	0.75	3.02[1]	3.29	7.71

$$K = \frac{[cage\ \mathbf{5}] * [amine\ \mathbf{2}]^2}{[cage\ \mathbf{4}] * [amine\ \mathbf{3}]^2} \qquad \textbf{(I)}$$

$$\Delta G_{eq} = \ -RT * \ln\left(K_{eq}\right) \qquad \textbf{(II)}$$

Table S14. Calculated equilibrium constants ($K_{eq.}$) and Gibbs free energy (ΔG_{eq}) using equation **I** and **II** and the concentration of compound **2**, **3**, **4**, **5**.

Cage **5** -> Cage **4**

entry	K_{eq}	ΔG_{eq} kJ·mol^{-1}
A	25.7	-7.91
B	39.7	-8.97
H	28.7	-8.18

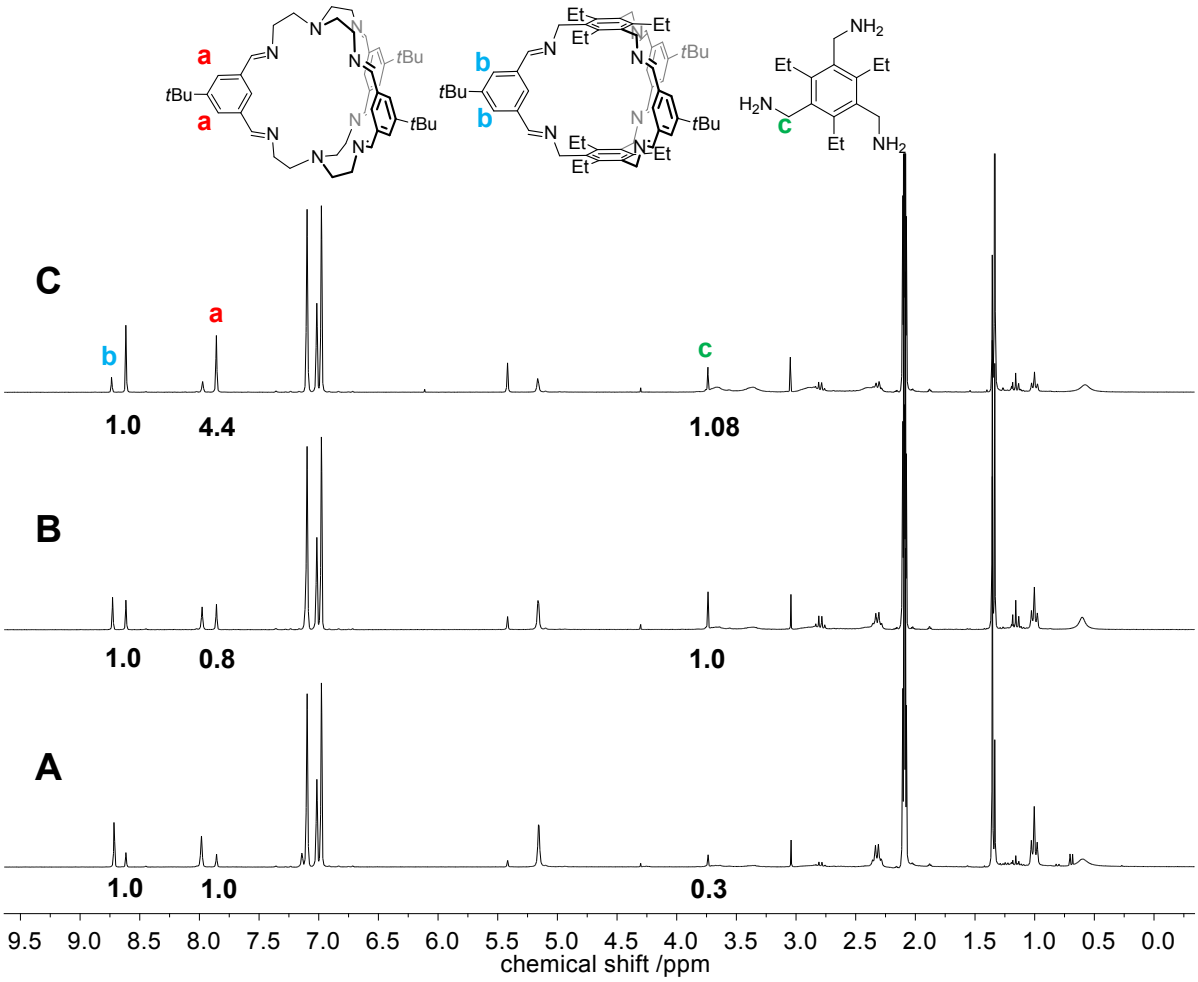


Figure S95. ^{1}H NMR spectra (Toluol-d8, 300 MHz) for reactions A–C with integrated signals.

Solubility of cage 4 and 5

The solubility was determined by suspending a defined amount (ca. 8 mg) of the pure cages in a defined volume (ca. 2 mL) of the corresponding solvents and sonicate the slurry. Not dissolved cages was removed by filtration via a syringe filter and the solvent of the filtrate was removed in vacuum The weight of the remaining residue was used to estimate the solubility in $mg \cdot mL^{-1}$.

Table S15: Solubility of cage compounds 4 and 5 in various solvents.

Solvent	Solubility of Cage **4**[1]	Soluvility of Cage **5**[1]
MeOH	<1	2
EtOH	<1	3
MeCN	<1	<1
CH2Cl2	5	>15
CHCl3	<1	6
THF	<1	1
1,4-Dioxane	<1	<1
Toluene	>12	9

[1]in $mg \cdot mL^{-1}$