Supporting Information

One-Step Synthesis of Chiral Cages

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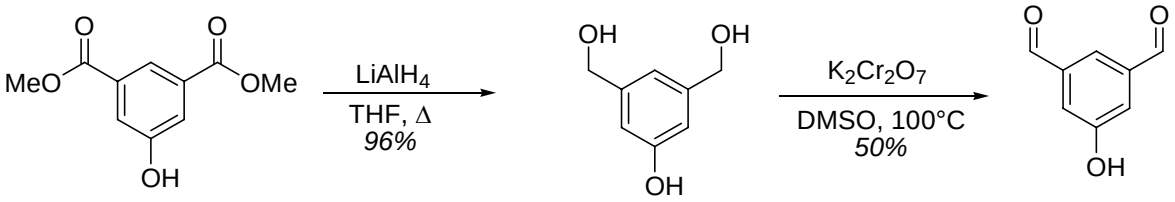
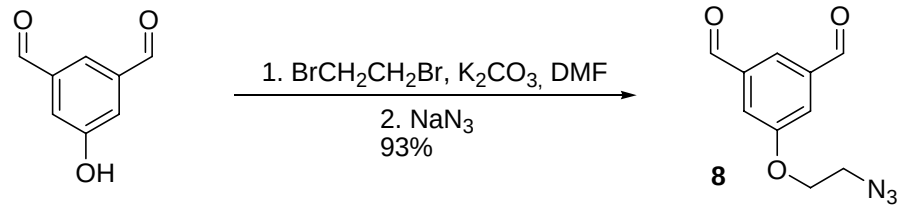
General comments

^{1}H and ^{13}C spectra were recorded at 300 and 75 MHz respectively; chemical shifts are reported in ppm from TMS. All reactions were carried out under argon. Columns chromatography were performed on a silica gel 230-400 mesh by using various mixtures of diethyl ether (Et_2O), ethyl acetate (AcOEt) and petroleum ether (PE). TLCs were run on Kieselgel $60F_{254}$ plates. Melting points are uncorrected. THF and ether were distilled from sodium/benzophenone ketyl. Dichloromethane was distilled from calcium hydride.

Phenol-3,5-dicarboxaldehyde or hydroxyisophthalaldehyde was prepared in two steps according to a known procedure: A. Star, Y. Liu, K. Grant, L. Ridvan, J. F. Stoddart, D. W. Steuerman, M. R. Diehl, A. Boukai and J. R. Heath, *Macromolecules* **2003**, *36*, 553-560





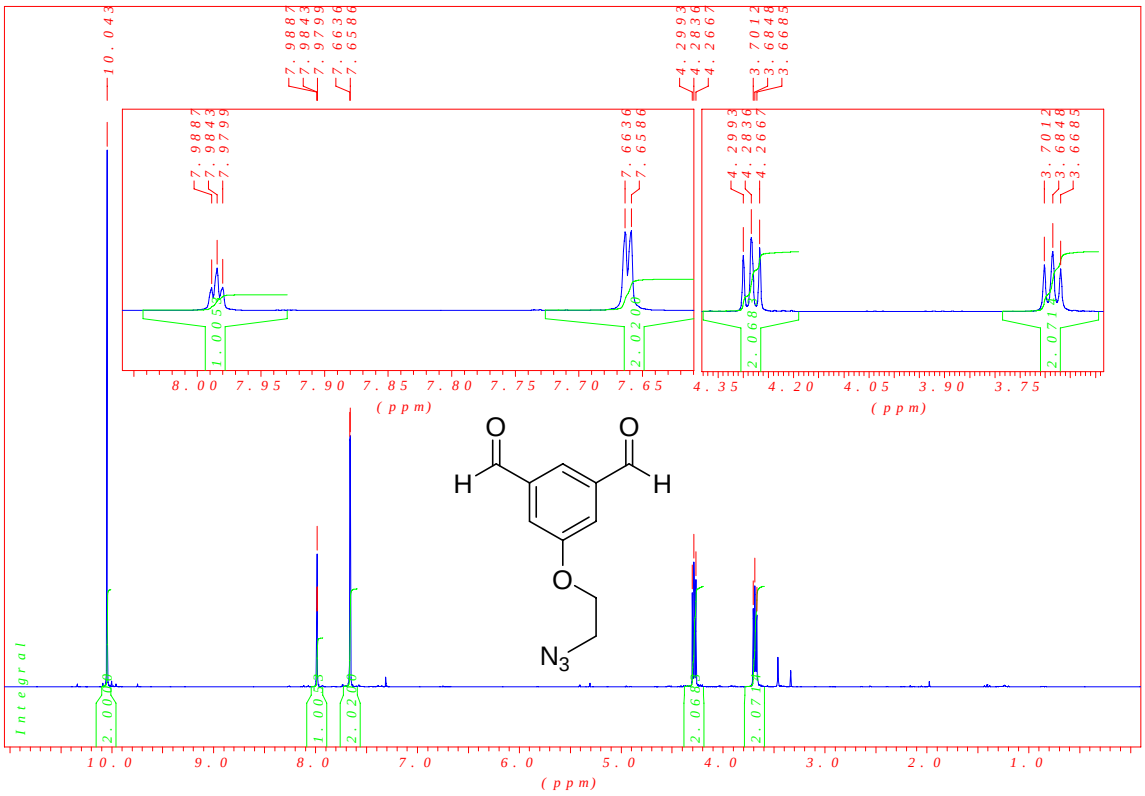
5-(2-Azido-ethoxy)-benzene-1,3-dicarbaldehyde **8**

Phenol-3,5-dicarboxaldehyde 811 mg (5.4 mmol) was dissolved in 30 mL of DMF, finely grounded K_2CO_3 (3.7 g, 5 equiv., M = 138.21) was added followed by dibromoethane (4.6 mL, 10 equiv., M = 187.86, d = 2.18). The resulting suspension was vigorously stirred for three days, after which, it was poured into water and extracted with Et_2O (4x50 mL). The combined organic layers were washed with water (2x50 mL), with brine, and finally dried over $MgSO_4$. Evaporation under vacuum gave the crude bromide. This was redissolved in 20 mL of DMF, sodium azide was added (1 g, 3 equiv., M = 65.01) and the suspension was stirred overnight. The mixture was diluted with water and extracted with Et_2O (4x50 mL). The combined organic layers were washed with water (2x50 mL), with brine and finally dried over $MgSO_4$. Evaporation under vacuum gave the crude compound which was purified by column chromatography over silica gel using pure Et_2O as eluent (R_f = 0.55) to give 1.1 g of azide **8**. Yield: 93%

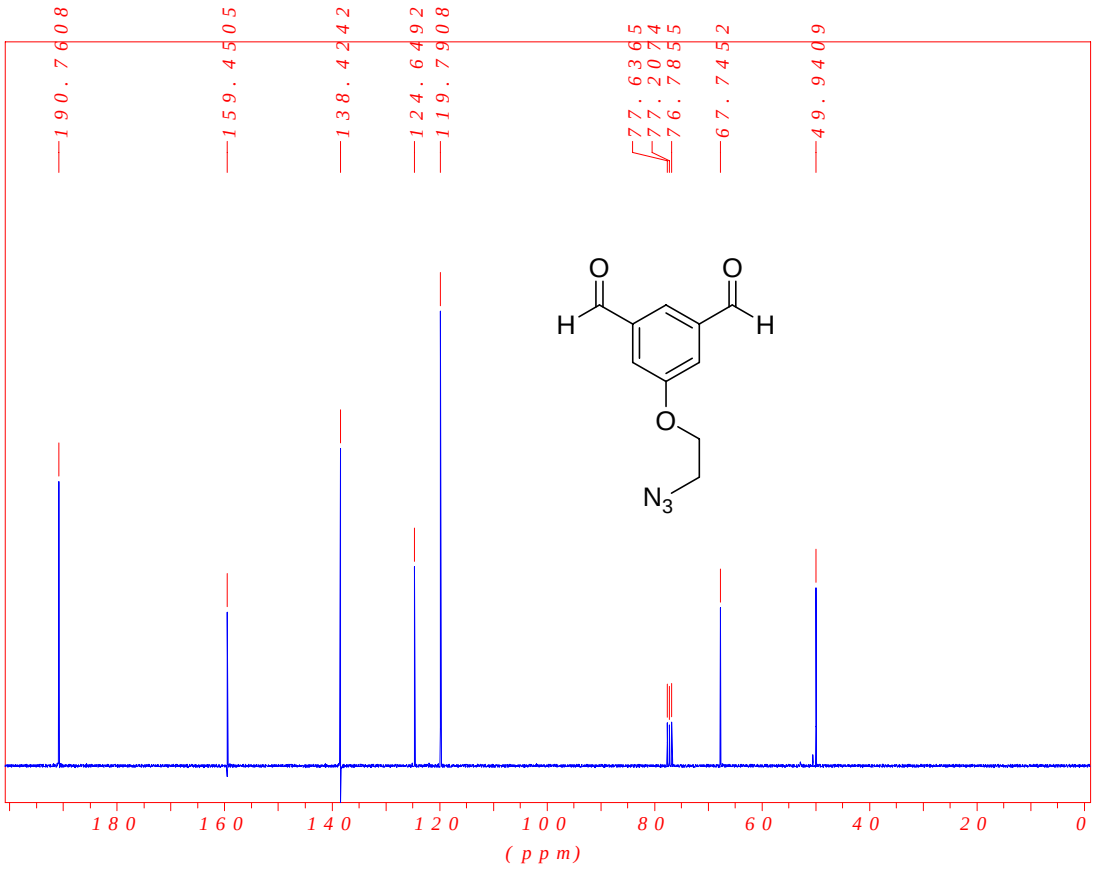
^{1}H NMR (300 MHz, $CDCl_3$) δ: 3.63 (t, 2H, *J* = 4.9 Hz), 4.23 (t, 2H, *J* = 4.9 Hz), 7.61 (d, 2H, *J* = 1.4 Hz), 7.93 (t, 1H, *J* = 1.4 Hz), 9.99 (s, 2H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ: 190.7 (CH), 159.4 (Cq), 138.4 (Cq), 124.6 (CH), 119.7 (CH), 67.7 (CH_2), 49.9 (CH_2). **IR** (KBr, cm^{-1}) ν: 2120, 1700, 1603. **HRMS** (ESI, TOF MS) m/z: calcd for [MNa^+.MeOH] 274.0804, found 274.0794.

T_f: decomposition above 100°C

Proton NMR spectrum of azide **8** in $CDCl_3$, 300 MHz



Carbon[13] NMR spectrum of azide **8** in $CDCl_3$, 75 MHz

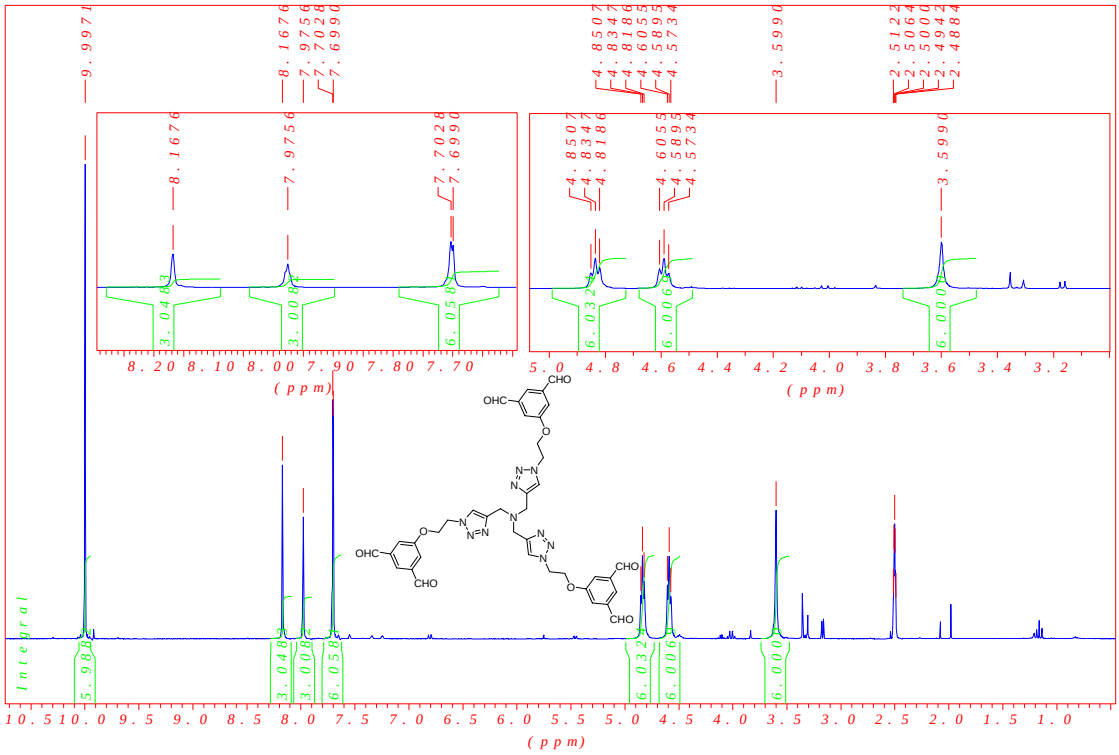


Tristriazole 9

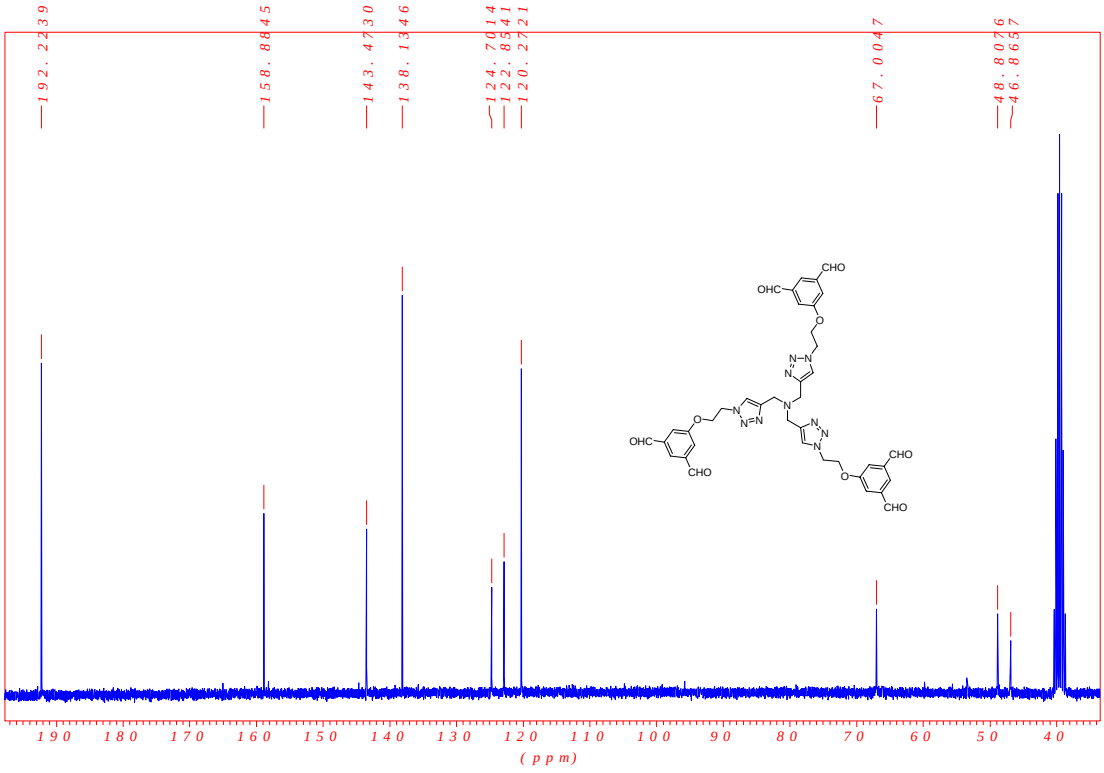
Azide **8** (1.08 g, 4.93 mmol, 3 equiv., M = 219.19) was dissolved in a mixture of DMSO (50 mL) and water (10 mL) and tripropargylamine is added (232 µL, 1.64 mmol, M = 131.18, d = 0.927) followed by $CuSO_4.5H_2O$ (11 mg, M = 249.69) and sodium ascorbate (10 mg, M = 198.11). The mixture was stirred for 5 days at 45°C and then was poured into one liter of a water/ice mixture. The solid formed was collected by filtration and thoroughly washed with water and then dried under vacuum. The white solid obtained was used without further purification, but could be purified by column chromatography over silica gel using (CH_2Cl_2/MeOH : 9/1, R_f = 0.5) as eluent. Yield = 75%.

^{1}H NMR (300 MHz, DMSO) δ: 3.60 (s, 6H), 4.59 (t, 6H, *J* = 4.8 Hz), 4.83 (t, 6H, *J* = 4.8 Hz), 7.70 (d, 6H, *J* = 1.1 Hz), 7.97 (t, 3H, *J* = 1.1 Hz), 8.16 (S, 3H), 9.99 (S, 6H).
^{13}C NMR (75 MHz, DMSO) δ: 46.8 (CH_2), 48.8 (CH_2), 67.0 (CH_2), 120.3 (CH), 122.8 (CH), 124.7 (CH), 138.1 (Cq), 143.5 (Cq), 158.9 (Cq), 192.2 (CH). **IR** (KBr, cm^{-1}) ν: 1690, 1603. **HRMS** (ESI, TOF MS) m/z: calcd for [MH^+] 789.2745, found 789.2766
T_f: decomposition above 200°C

Proton NMR spectrum of crude compound **9** in DMSO-d6, 300 MHz



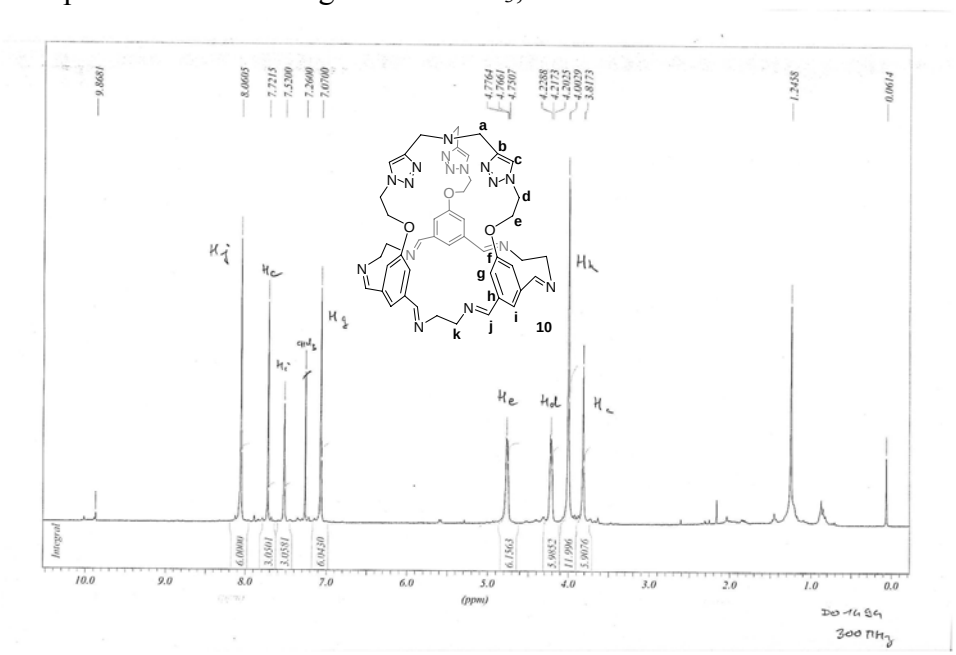
Carbon[13] NMR spectrum of ccompound **9** in DMSO-d6, 75 MHz



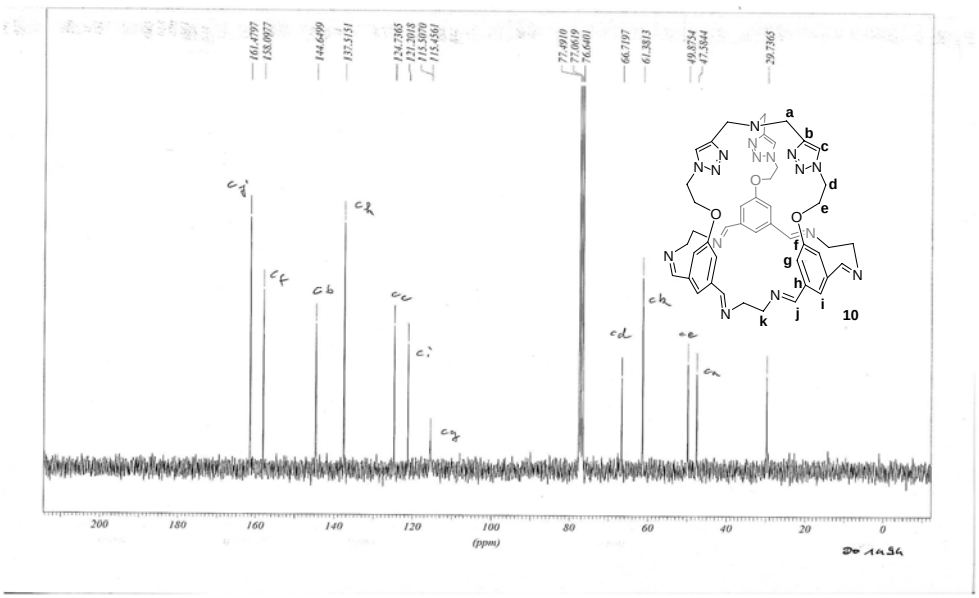
Synthesis of Cage **10**

Tristriazole **9**, 34.1 mg (4.3 μmol, M = 788.76) was introduced into a 5 mL flask, dissolved in a mixture of 2 mL of dichloromethane. Ethylenediamine (8.7 μL, 120 μmol, 3 equiv., M = 60.10) was added, the mixture was stirred at room temperature for three weeks, at which time the starting suspension was completely dissolved indicating the completion of the reaction. The crude cage was obtained after careful evaporation to dryness (heating is to be avoided to prevent the formation of polymeric insoluble material) 38 mg of an off-white solid. 99% yield. **^{1}H NMR** (300 MHz, $CDCl_3$) δ: 8.06 (s, 6H, Hj), 7.72 (s, 3H, Hc), 7.52 (s, 3H, Hi), 4.75-4.77 (m, 6H, He), 4.20-4.22 (m, 6H, Hd), 4.00 (s, 12H, Hk), 3.81 (s, 6H, Ha). **^{13}C NMR** (75 MHz, $CDCl_3$) δ: 161.4 (Cj), 158.1 (Cf), 144.6 (Cb), 137.5 (Ch), 124.7 (Cc), 121.2 (Ci), 115.5 (Cg), 66.7 (Cd), 61.4 (Ck), 49.8 (Ce), 47.5 (Ca). MS (ESI) m/e calculated for [MNa+] 883.4, measured: 883.5, high resolution could not be efficiently performed due to the formation of polymeric material. **IR** (KBr, cm^{-1}) ν: 1700, 1639, 1582.

Proton NMR spectrum of crude cage **10** in $CDCl_3$, 300 MHz



Carbon[13] NMR spectrum of crude cage **10** in $CDCl_3$, 75 MHz



Syntheses of Cage **11**

1. Tristriazole **9**, 473.8 mg (0.6 mmol, M = 788.76) was introduced into a 10 mL flask, dissolved in a mixture of 5 mL of dichloromethane and 1 mL of methanol. Chiral diamine (205.8 mg, 1.8 mmol, 3 equiv., M = 114.9) was quickly added to avoid carbonatation, the mixture was stirred at room temperature overnight and then evaporated to dryness at room temperature. Chromatography over silica gel, eluting with (CH_2Cl_2/MeOH : 9/1, R_f = 0.2) gave pure title compound as an off-white resin in 98% yield.

2. (1*R*,2*R*)-1,2-diaminocyclohexane (89.2 mg, 0.781 mmol, 3.05 equiv./alkyne, M = 114.19) was weighed in a 50 mL flask purged with argon and was then diluted with 10 mL of dry dichloromethane. Azide **8** (168.4 mg, 0.768 mmol, 3 equiv./alkyne, M = 219.19) was added. Argon was bubbled through the solution to eliminate traces of oxygen before tripropargylamine addition (36.2 µL, 33.6 mg, 0.256 mmol, M = 131.18, d = 0.927). A catalytic amount (3 mg) of copper (I) iodide was added and after sonication for five minutes the solution was allowed to stir overnight at room temperature. After this period of time, TLC indicated complete disappearance of the reactants and formation of a unique spot slightly colored blue-green. The mixture was exposed to air to oxidize copper (I) into copper (II), and 20 mg of sodium diethyldithiocarbamate was added in 2 mL of MeOH. The solution turned dark brown indicating the formation of the copper complex. After concentration to dryness, the residue was purified by column chromatography over silica gel eluting with (CH_2Cl_2/MeOH : 9/1, R_f = 0.2). The copper complex eluted first (R_f = 0.9) followed by the title compound which was isolated in 70% yield (180 mg).

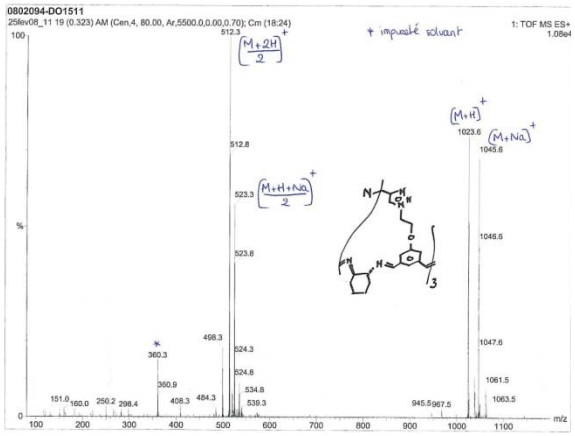
$[\alpha]^{20}_{578nm}$ = + 128 (c 0.49, $CHCl_3$)

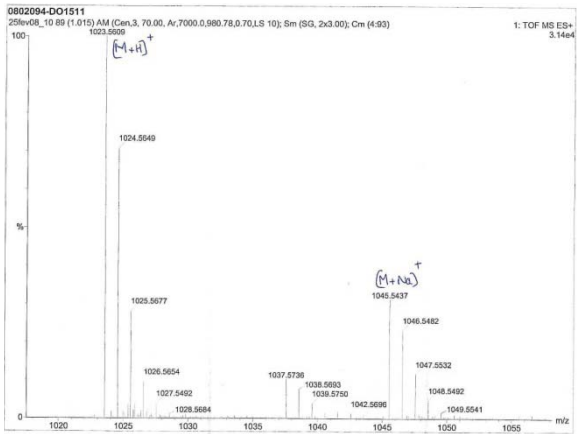
^{1}H NMR (300 MHz, $CDCl_3$) δ: 1.1-1.2 (m, 6H, Hm), 1.4-1.8 (m, 18H, Hm', Hl), 3.17-3.32 (m, 6H, Hk and Hk'), 3.45 (d, *J* = 13.6 Hz, 3H, Ha), 4.08-4.20 (m, 9H, Ha' and Hd), 4.47-4.55 (m, 3H, He), 4.85-4.90 (m, 3H, He'), 6.73 (s, 3H, Hg), 7.17 (s, 3H, Hg'), 7.45 (s, 3H, Hi), 7.63 (s, 3H, Hc), 7.92 (s, 3H, Hj), 8.03 (s, 3H, Hj').

^{13}C NMR (75 MHz, $CDCl_3$) δ: 24.3 (Cm), 24.4 (Cm'), 32.7 (Cl), 32.9 (Cl'), 47.9 (Ca), 49.8 (Ce), 66.7 (Cd), 74.2 (Ck), 74.8 (Ck'), 107.9 (Cg), 121.2 (Ci), 122.4 (Cg'), 124.5 (Cc), 137.7 (Ch), 137.8 (Ch'), 144.8 (Cb), 157.9 (Cf), 158.7 (Cj), 159.5 (Cj'). **IR** (KBr, cm^{-1}) ν: 2924, 2847, 1644, 1593. T_f: decomposition above 100°C

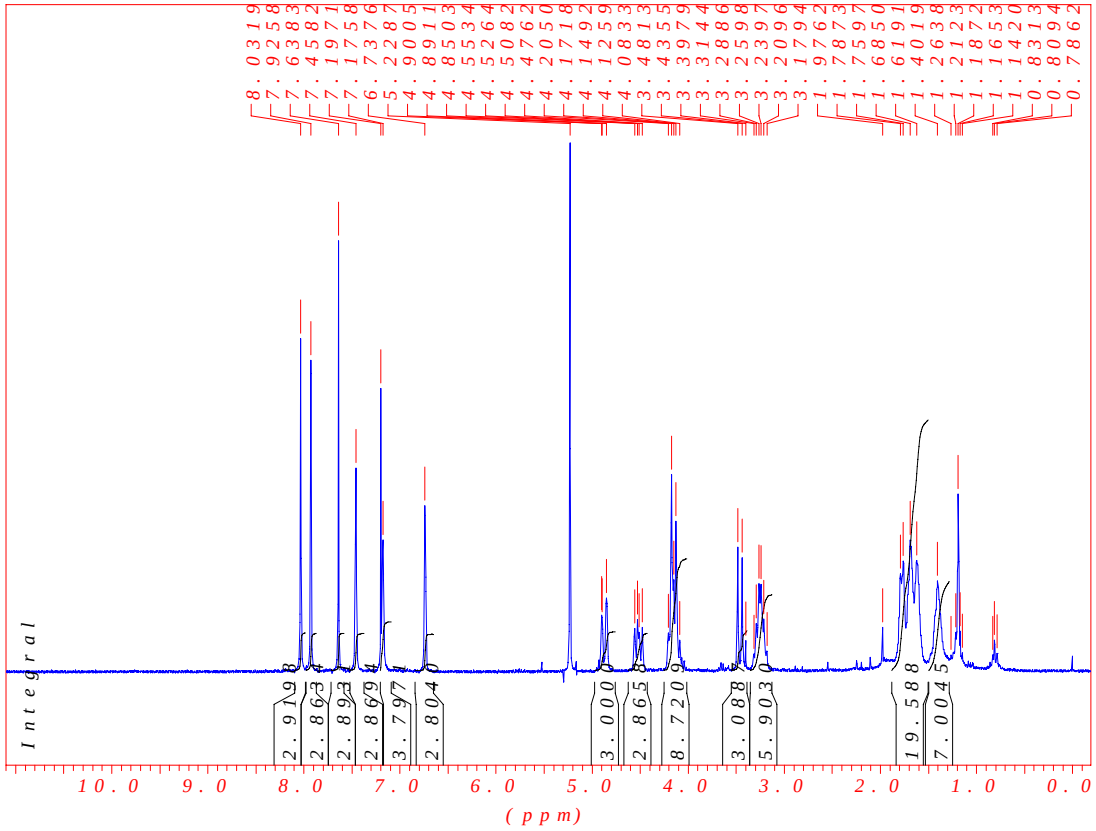
HRMS (ESI, TOF MS) m/z: calcd for [MH^+] 1023.5582, found 1023.5609

HRMS (ESI, TOF MS) m/z: calcd for [MNa^+] 1045.5401, found 1045.5437

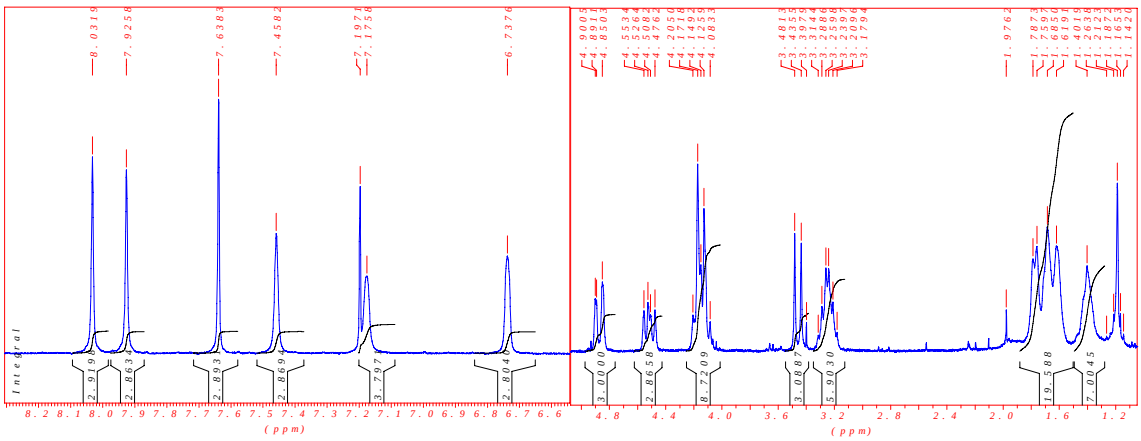




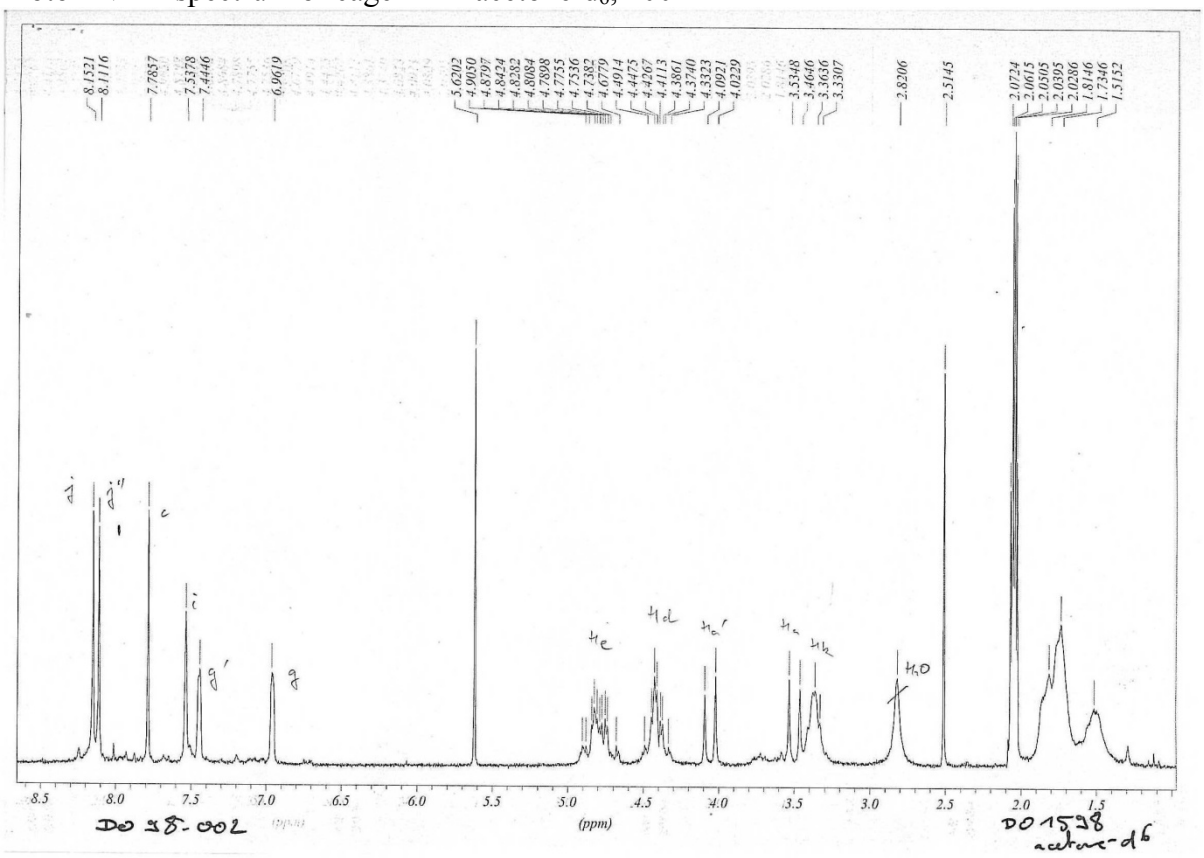
Proton NMR spectrum of cage **11** in $CDCl_3$, 300 MHz



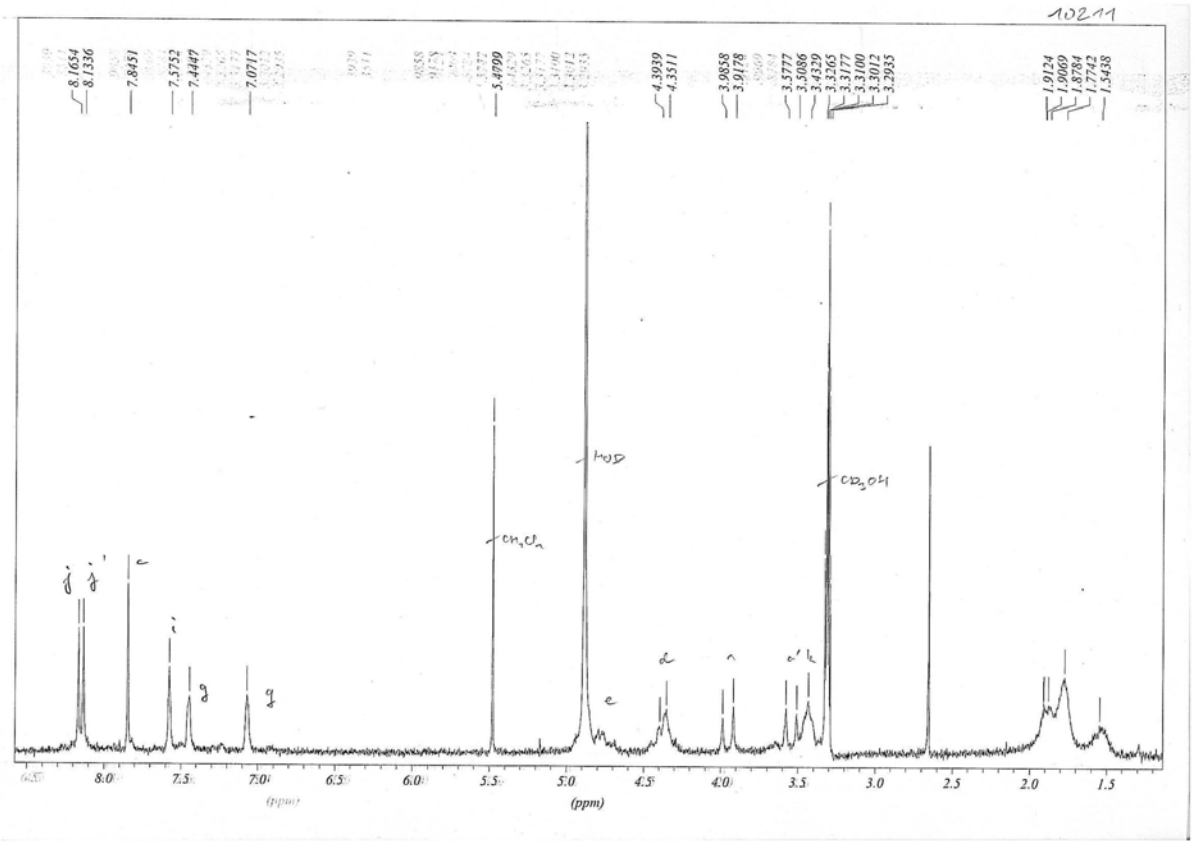
Proton NMR spectrum of cage **11** in $CDCl_3$, 300 MHz, 6 to 8 ppm and 1 to 5 ppm region



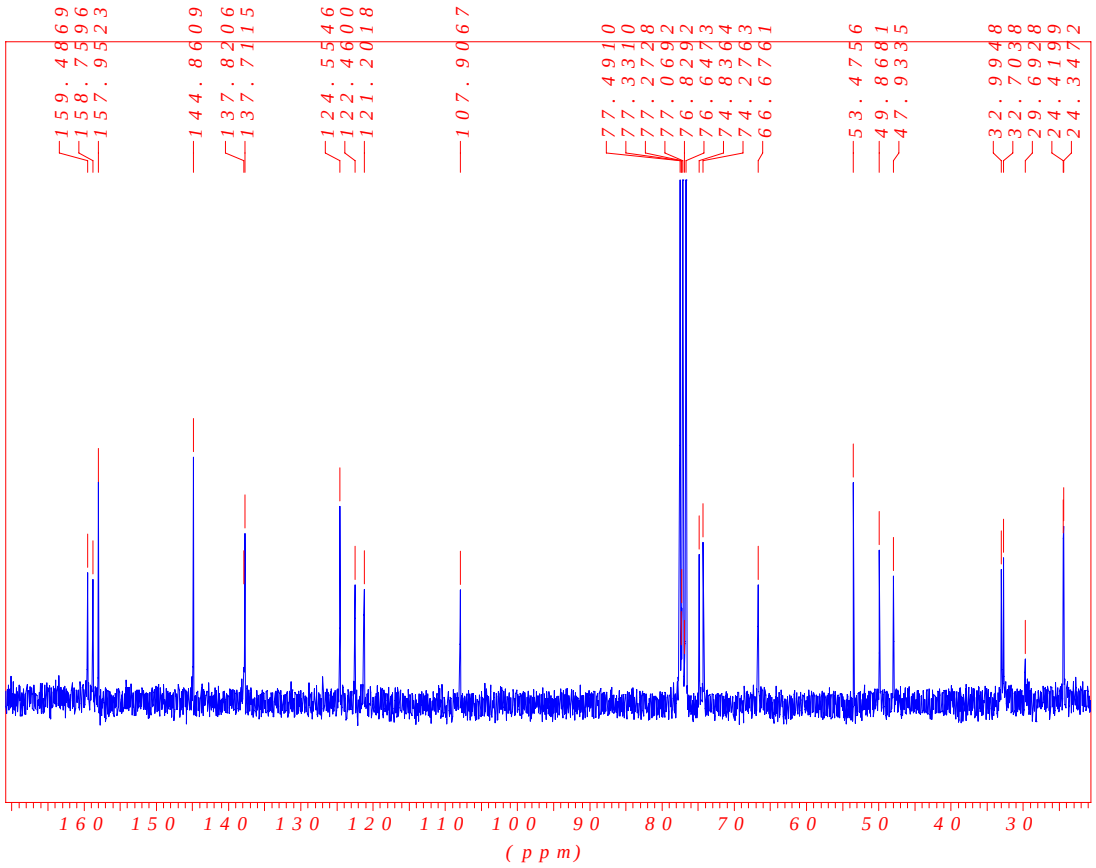
Proton NMR spectrum of cage **11** in acetone-d_6, 200 MHz



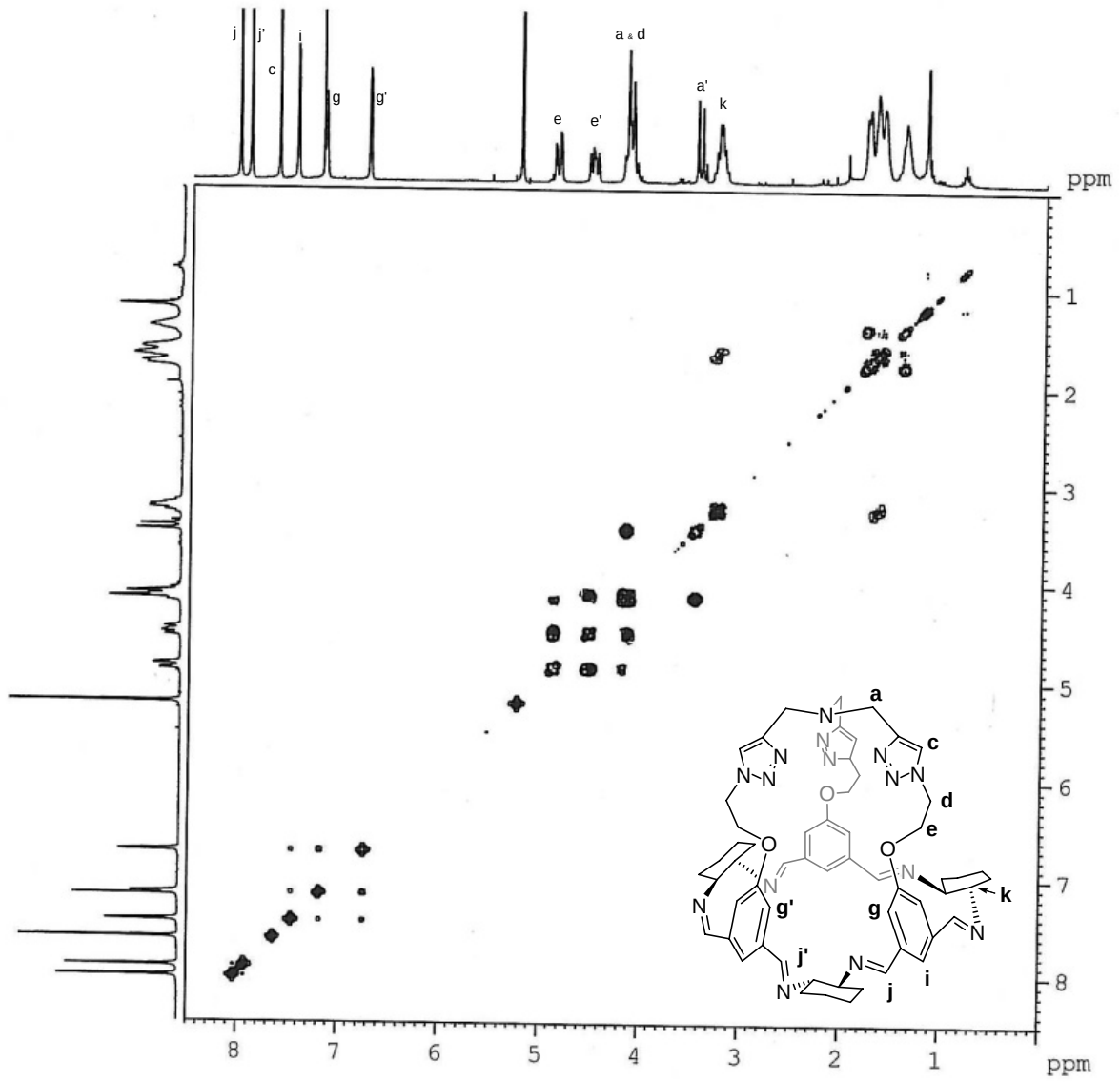
Proton NMR spectrum of cage **11** in CD_3OD, 200 MHz



Carbon[13] NMR spectrum of cage **11** in $CDCl_3$, 75 MHz

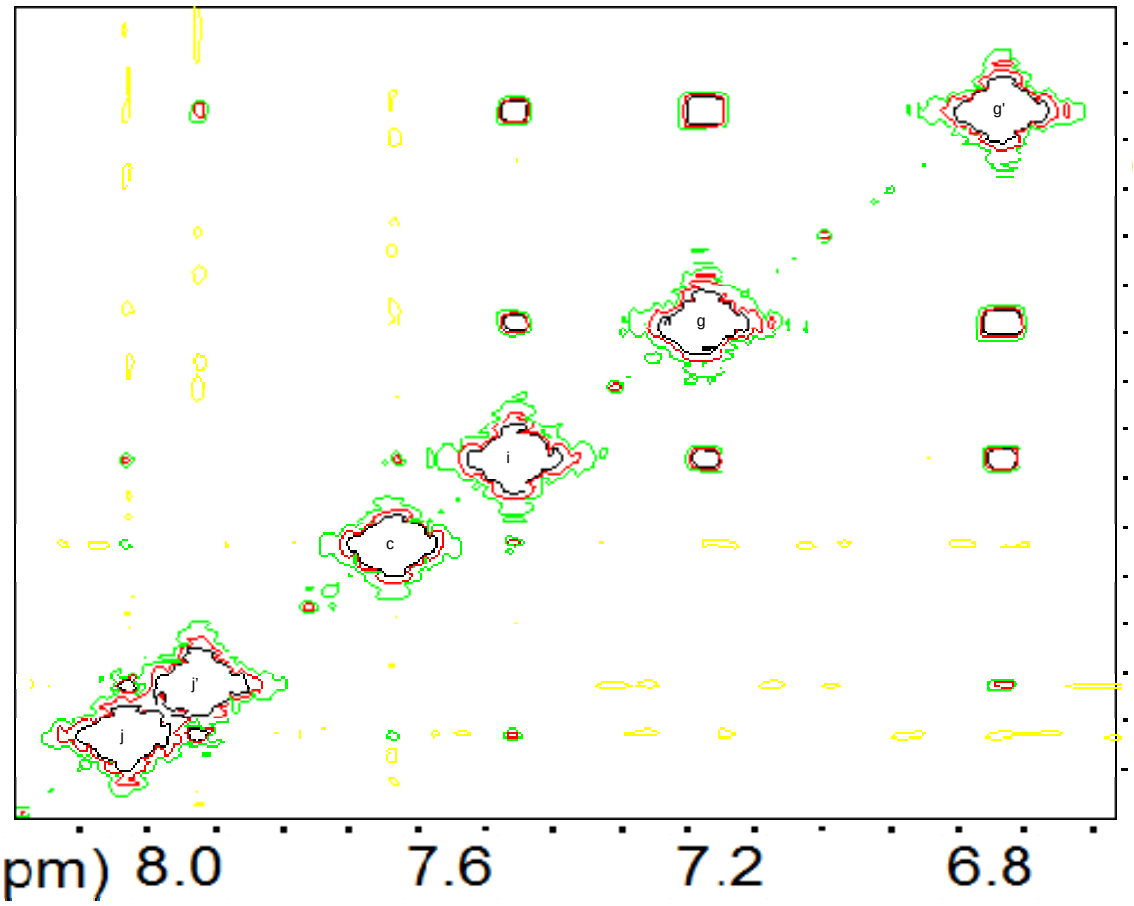


Cosy H-H correlation for cage **11** in $CDCl_3$

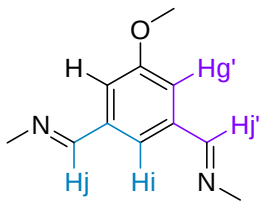


Attribution:
Hk is the only proton to couple with cyclohexyl signals.
Ha and **Ha'** are strongly correlated and are located on the same carbon (see H-C)
Hd is coupling with both He and He'.
He and **He'** are strongly correlated and are bears by the same carbon (see H-C)
Hg and **Hg'** are magnetically non-equivalents (which is also true for the ^{13}C signals) due to the twisted shape induced by the chiral diamine. A correlation is present between them and both are coupling with Hi (through a $^{4}J_{H\text{-}H}$)
Hi is coupling with Hg and Hg'
Hj and **Hj'** are also non-equivalents (which is also true for the ^{13}C signals).

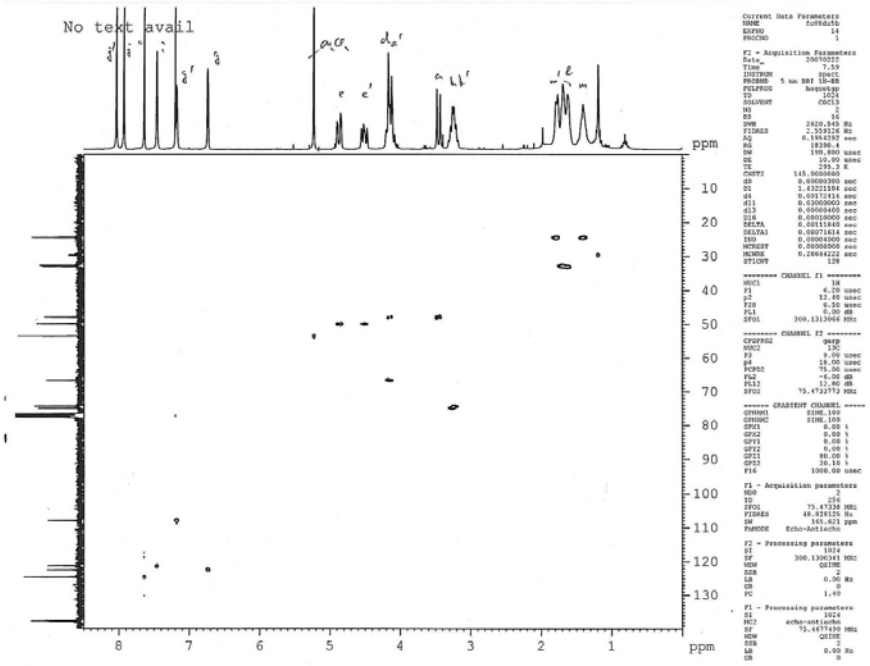
Cosy H-H correlation for cage **11** in $CDCl_3$, 6.6-8.2 ppm region



Magnifying the aromatic region renders apparent a weak ^4J coupling of Hg' with Hj' as well as a correlation between Hi and Hj. This is in favour of an alternate conformation of the imines as depicted below:

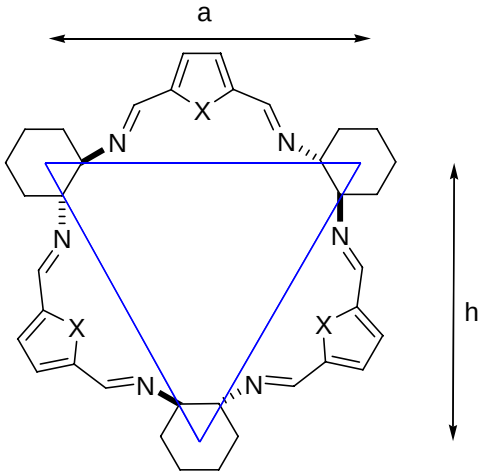


Proton-Carbon correlation for cage **11** in $CDCl_3$,



The dimensions of cage **11** deserve some comments. Although several examples of polyimine crowns are reported in the literature, none is reporting the crystallographic data for a trianglimine incorporating a 1,3-disubstituted benzene. However, two examples including a furane and a thiophene, are fairly close to our structure. For these, optimal conformation calculation allowed the estimation of the size to approximately 10-11 angstroms: N. Kuhnert, N. Burzlaff, C. Patel an A. Lopez-Periago, *Org. Biomol. Chem.* **2005**, *3*, 1911-1921.

With X = O, a = 10.4 Å and h = 9.0 Å
With X = S, a = 11.4 Å and h = 9.9 Å



Therefore, we can estimate the central opening of cage **11** to be in the range of these dimensions. The conformation of the apical part is still to be determined. So far, all our attempts to crystallize cage **11** only met with failure. Moreover, a rough estimation by calculation proved unsuccessful because of the very flexible nature of the tripodal cap. This can even be experimentally observed from the important shifts of the proton NMR signals of cage **11** in solvents of different polarities. Hence, comparison of the spectra in $CDCl_3$, acetone-d^6 and CD_3OD (see pages S7-S8) shows appreciable shifts:

	$CDCl_3$	acetone-d^6	CD_3OD
Ha/Ha’	4.15/3.45	4.06/3.35	3.95/3.53
Hj/Hj’	8.03/7.92	8.15/8.11	8.16/8.13
Hg/Hg’	7.17/6.73	7.44/6.96	7.44/7.07
Hc	7.63	7.78	7.84

This can be indicative of a conformational adaptation depending of the polarity of the medium.

Complexation study with cage **11**

A stock solution of cage **11** (c = 10^{-4} mol.L^{-1}) in methanol was mixed with increasing amounts of cation salts (the nitrate in each case) dissolved in water (c = 10^{-2} mol.L^{-1}). The resulting solution was diluted tenfold with MeOH to reach a final concentration of 10^{-5} mol.L^{-1}. The resulting solution was injected into the mass spectrometer source. Spectra were measured in positive ESI with an MS Engin HP5989B using an electrospray module HP59987A. Source is of Brandford type. Samples were introduced by infusion with a flow of 5 µL.min^{-1}, with a desolvatation gas heated at 120°C. The potentials of the capillary and the skimmer were respectively 180V and 36V.

Salts used: $Mn(NO_3)_2.xH_2O$, x = 4-6; $Fe(NO_3)_3.9H_2O$; $Co(NO_3)_2.6H_2O$; $Ni(NO_3)_2.6H_2O$; $Cu(NO_3)_2.xH_2O$, x = 2-3; $Zn(NO_3)_2.6H_2O$; $Cs(NO_3)$; $Ag(NO_3)$; $Hg(NO_3)_2.H_2O$.

The spectrogram showed several peaks:
"L" denotes cage **11** as the ligand, "M" the metal studied.
- LH^+, LNa^+, LK^+ counted as free ligand
- LM^{2+}, $(LMNO_3)^+$ counted as simply complexed metal
- L_2M^+ counted as doubly complexed metal

Integration of all these species allowed determination of:
- x_L fraction of free ligand
- x_{LM} fraction of simple complex
- x_{L2M} fraction of double complex

Assuming that all species have the same response coefficient and that integration of a given species is linearly correlated to its concentration in solution, one can postulate that:

$$\frac{xLM}{xL} = \frac{[LM]}{[L]}$$

This assumption mainly suffers from the difference of sensitivity between a non ionic species (the free ligand L) that have to be protonated or sodated and a positively charged complex (LM). This is leading to an under-estimation of the quantity of free ligand, thus affecting the value of K. Nevertheless, this still allows comparison of K values between several metals. For that reason K values are given relative to nickel which, as the most efficiently complexe, represents 100%.

The complexation equilibrium

$$L + M \overset{K}{\Leftrightarrow} LM$$

With $K = \frac{[LM]}{[L][M]} \Rightarrow \frac{[LM]}{[L]} = \frac{xLM}{xL} = K[M]$ thus, the plot $\frac{[LM]}{[L]} = f([M])$ should be a linear curve with *K* as directing coefficient and 0 as origin.

[M] is deduced from the initial concentration of metal minus the fractions of simple and double complexes. [M] = 10^{-5} (n – x_{LM} – x_{L2M}) with n being the number of equivalents of

metal introduced, in the experiments, n had the following values 0 / 0.2 / 0.5 / 1.0 / 2.0 / 6.0 / 10.0

The values of $\frac{[LM]}{[L]} = \frac{xLM}{xL}$ are then plotted versus the corresponding values of [M] to obtain the curves showed. Linear regression extracted the best value of *K* for each curve.
In every measurement, R^2 was > 0.99

Plots for the different titrations, with $\frac{[LM]}{[L]} = f([M])$

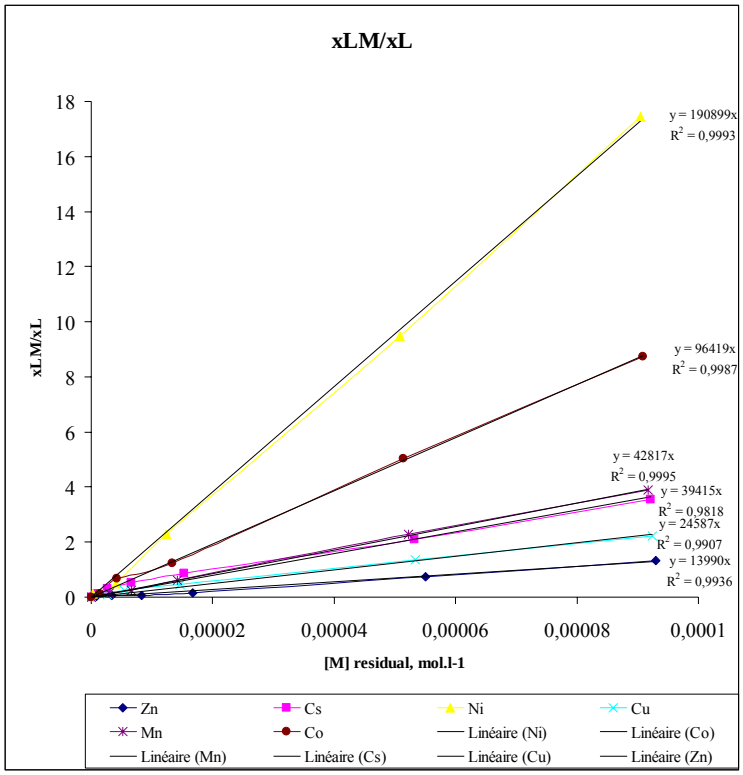
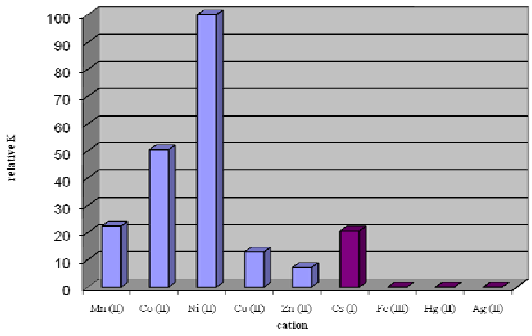


Table of *K* versus the cation

	K	relative K (%)
Mn	42817	22,4291379
Co	96419	50,5078602
Ni	190899	100
Cu	24587	12,8795855
Zn	13990	7,3284826
Cs	39415	20,6470437

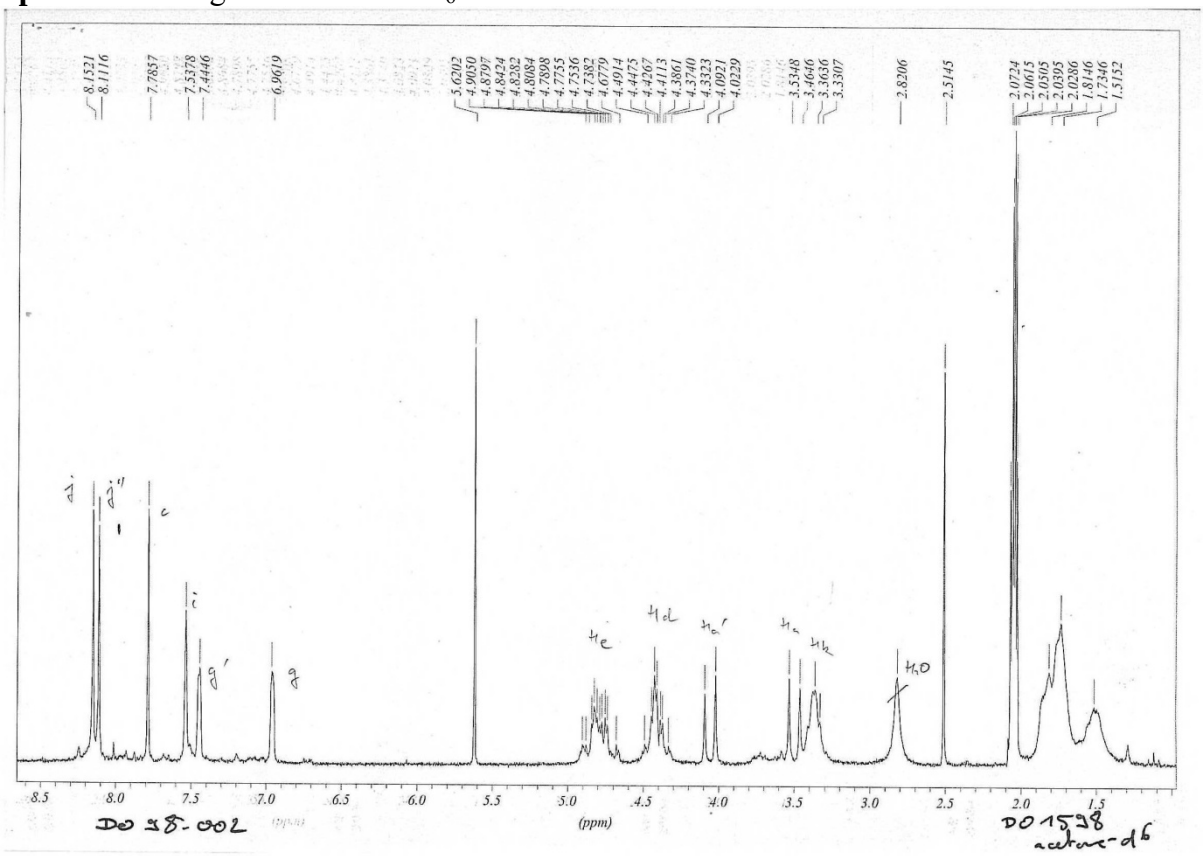
Plot of relative *K* versus the cation



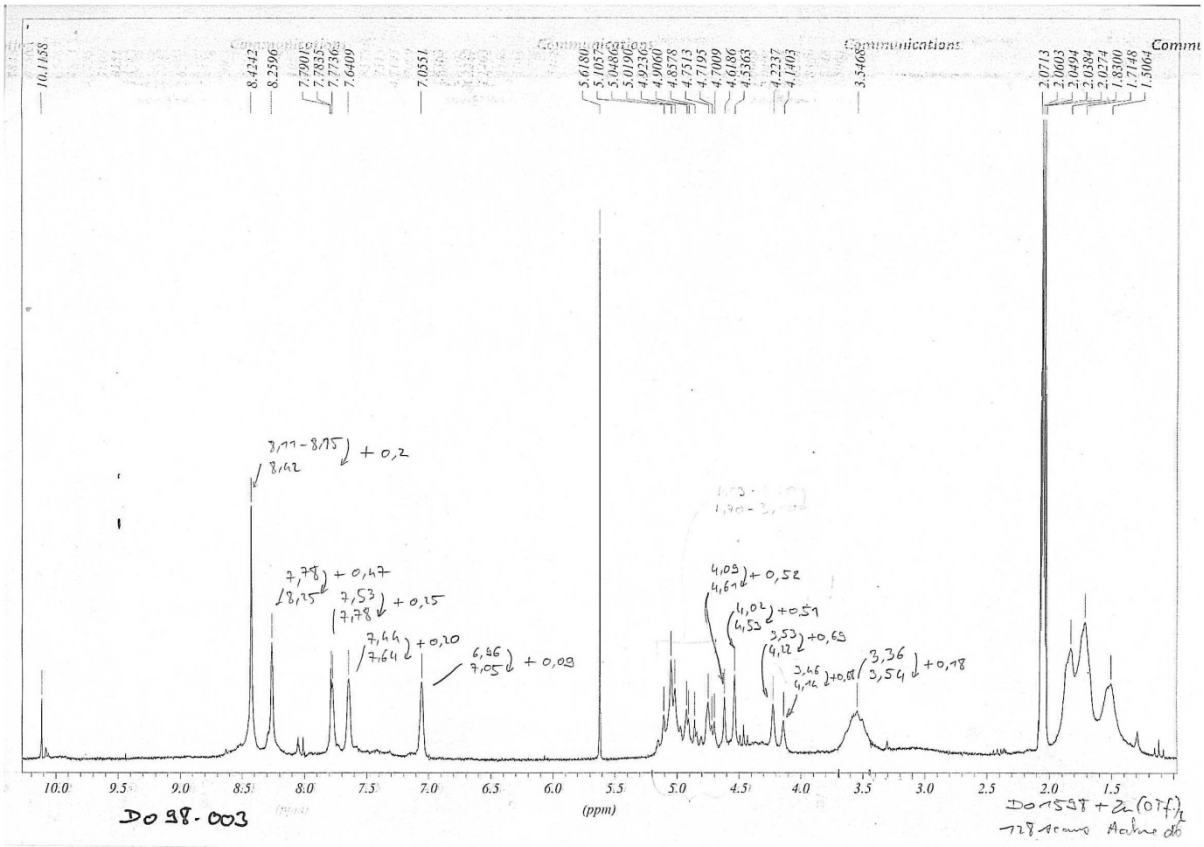
Complexation of zinc (II) triflate
In an NMR tube, 10.7 mg (10.45 µmol, M = 1023.24) of cage **11** was introduced followed by 0.6 ml of acetone-d_6. The suspension was sonicated for a few minutes, resulting in partial dissolution of the compound, and a proton NMR spectrum was recorded with 128 scans giving **spectrum 1**. To this suspension was added zinc (II). Zinc (II) triflate, 3.8 mg (10.45

µmol, M = 363.21) was weighed in an NMR tube cap, which was fitted onto the previously prepared tube. The whole was vigorously shaken, resulting in a clear solution after few seconds. A proton NMR spectrum was recorded with 128 scans giving **spectrum 2**.

Spectrum 1. Cage **11** in acetone-d_6



Spectrum 2. Complexe **12**: cage **11** + Zn^{2+} in acetone-d_6



Proposed structures for complexe **12**