Electronic Supplementary Material (ESI) for ChemComm.
This journal is © The Royal Society of Chemistry 2015

Experimental

Contents

1 Synthesis and NMR spectra 1

2 Acetal deprotection screen 11

3 ESI-MS 13

4 Preparation of Samples 14

5 2D NMR spectra 18

6 Isomers of the grid leading to complexity in the NMR spectrum 20

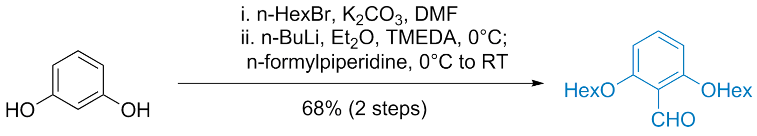
1 Synthesis and NMR spectra

Chemicals were purchased from Sigma-Aldrich, Acros, Lancaster, Alfa-Aesar or TCI and were used as received. All solvents were distilled before use from the appropriate drying agents. Merck silica gel 9385 (230 - 400 mesh) was used for chromatography. TLC was performed on Kiesel silica gel 60 PF254 (Merck) 0.2 mm glass plates.

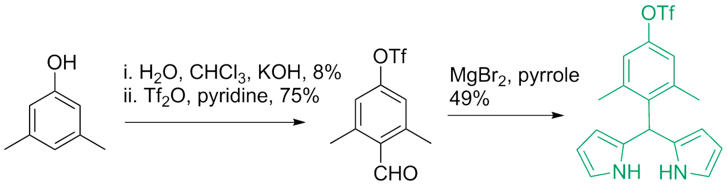
NMR spectra were recorded on Bruker 400 MHz AVIII HD Smart Probe or Bruker 500 MHz DCH Cryoprobe Spectrometers. Chemical shifts (δ) are quoted in ppm and shifts are referenced to the residual solvent peak. Abbreviations: s = singlet, d = doublet, t = triplet, br s = broad singlet, m = multiplet.

LDI-MS data was collected on a 4700 Proteomics Analyser (Applied Biosystems) with TOF/TOF optics. The spectra were acquired in reflector mode and averaged over 2500 shots. HR-MS was collected using an LTQ Orbitrap analyser.

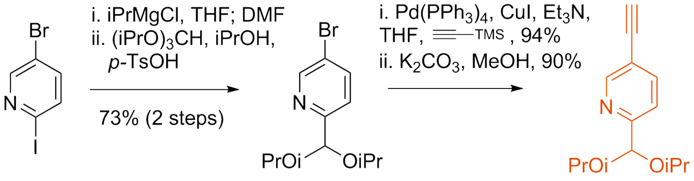
The following compounds were previously reported: 2,6-dimethyl-4-triflyloxybenzaldehyde,[1] 2,6-dihexyloxybenzaldehyde,[2] linear porphyrinic bisphenanthroline **6**.[3] Crude 5-bromo-2-picolinaldehyde obtained from commercial 2-iodo-5-bromopyridine was used according to a literature procedure.[4]



HO
OH
i. n-HexBr, K2CO3, DMF
ii. n-BuLi, Et2O, TMEDA, 0°C; n-formylpiperidine, 0°C to RT
68% (2 steps)
HexO
OHex
CHO



OH
i. H2O, CHCl3, KOH, 8%
ii. Tf2O, pyridine, 75%
OTf
CHO
MgBr2, pyrrole
49%
OTf
NH
HN



Br
N
I
i. iPrMgCl, THF; DMF
ii. (iPrO)3CH, iPrOH, p-TsOH
73% (2 steps)
Br
N
PrOi
OiPr
i. Pd(PPh3)4, CuI, Et3N, THF, TMS, 94%
ii. K2CO3, MeOH, 90%
N
PrOi
OiPr

5-(2,6-dimethyl-4-triflyloxyphenyl)dipyrromethane:

4-Triflyloxy-2,6-dimethylbenzaldehyde (5.61 g, 20 mmol) was dissolved in freshly-distilled pyrrole (39.2 mL) and sparged with nitrogen for 15 minutes. TFA (0.1 mL, 1.3 mmol) was added and the mixture stirred for 30 minutes. The reaction mixture was worked up (dilution with DCM, washed with aq. NaOH) and chromatographed on silica, eluting with DCM:PE 8:2 + 1% Et_3N. The dipyrromethane fraction that eluted from the column was still contaminated with pyrrole, which was removed by heating the sample to 100 °C under vacuum for 2 h. Brown oil (5.27 mg, 13.25 mmol, 67%).

An alternative synthesis[5] from 1.02 g of the starting material in 25 mL of pyrrole with 333 mg $MgBr_2$ (2 hours) afforded, after silica chromatography, 706 mg (49%) of the title compound as a clear yellow resin. The reaction catalysed by $InCl_3$ proceeded very slowly, and significant starting material was still seen by TLC after 2 h.

^{1}**H-NMR** (400 MHz, $CDCl_3$): δ 7.96 (br s, 2H), 6.95 (s, 2H), 6.71 (dd, J = 2.5 Hz, 4.0 Hz, 2H), 6.17 (dd, J = 2.5 Hz, 6 Hz, 2H), 5.93 (s, 1H), 5.91 (m, 2H), 2.13 (s, 6H).

^{13}**C-NMR** (101 MHz, $CDCl_3$): δ 147.82, 140.55, 138.38, 129.91, 121.64, 116.86, 108.84, 107.02, 38.47, 20.91.

2-(diisopropoxymethyl)-5-bromopyridine:

Crude 5-bromopyridine-2-picolinaldehyde prepared via formylation of the Grignard reagent (1050 mg, 5.65 mmol) was dissolved in iPrOH (8 mL) and triisopropyl orthoformate (5 mL). Catalytic p-TsOH was added and the reaction was heated to reflux for 6 hours under a calcium chloride guard tube. Conversion was incomplete by TLC so additional orthoformate (2 mL) was added. The reflux was continued overnight, and conversion was still not complete the following day (TLC). The reaction mixture was poured into dilute sodium bicarbonate and the product was extracted into Et_2O, which was washed with 3 × water and 1 × brine. Drying (Na_2SO_4) and evaporation of the organics afforded the product dissolved in triisopropyl orthoformate. This was loaded directly onto a silica column and eluted with

PE:EtOAc 1:0 → 7:1. The product co-eluted with unconsumed starting material. NMR of this mixture showed 97% conversion to the acetal and this material was carried forward to the Sonogashira reaction with no further purification. Colourless oil (1430 mg, approx. 88%).

^{1}**H-NMR** (400 MHz, $CDCl_3$): δ 8.62 (d, J = 2.3 Hz, 1H), 7.86 (dd, J = 8.4, 2.3 Hz, 1H), 7.55 (d, J = 8.4 Hz, 1H), 5.51 (s, 1H), 3.96 (sept, J = 6 Hz, 2H), 1.25 (d, J = 6.0 Hz, 6H), 1.16 (d, J = 6.0 Hz, 6H).

2-(diisopropoxymethyl)-5-(trimethylsilylethynyl)pyridine:

2-(diisopropoxymethyl)-5-bromopyridine (700 mg, 2.43 mmol), $Pd(PPh_3)_4$ (60 mg, 0.05 mmol) and CuI (10 mg, 0.05 mmol) were dissolved in Et_3N:THF 1:1 (15 mL) and the reaction was degassed by 4 × vacuum-N_2 cycles. Ethynyltrimethylsilane (360 μL, 2.5 mmol) was added and the mixture was stirred at 60 °C for 3 hours under N_2 atmosphere. The mixture was cooled to room temperature and poured into dilute sodium bicarbonate and extracted with DCM (3 x). The combined organics were washed once with water, dried (Na_2SO_4), filtered and evaporated to afford an orange oil that was chromatographed on silica (PE:EtOAc 95:1 + 1% Et_3N) to afford the title compound as a white solid (698 mg, 94%).

^{1}**H-NMR** (400 MHz, $CDCl_3$): δ 8.62 (d, J = 2.1 Hz, 1H), 7.78 (dd, J = 8.1, 2.1 Hz, 1H), 7.58 (d, J = 8.1 Hz, 1H), 5.53 (s, 1H), 3.96 (sept, J = 6 Hz, 2H), 1.23 (d, J = 6.0 Hz, 6H), 1.15 (d, J = 6.0 Hz, 6H), 0.28 (s, 9H).

2-(diisopropoxymethyl)-5-ethynylpyridine:

2-(diisopropoxymethyl)-5-(trimethylsilylethynyl)pyridine (698 mg, 2.28 mmol) was dissolved in 1:1 MeOH:THF (80 mL) and K_2CO_3 (3 g) was added. The mixture was stirred for 5 hours at room temperature until TLC indicated the starting material was consumed. Enough water was added to dissolve the K_2CO_3, and the mixture was diluted with brine and the organic layer separated. The aqueous phase was extracted with 3 × Et_2O and the combined organics were washed once with brine, dried (Na_2SO_4), filtered and evaporated. The pale yellow filtrate took on a dark colour on evaporation. The dark oil that was obtained was chromatographed on silica (PE:EtOAc 9:1 + 0.1% Et_3N) to afford a pale yellow oil that crystallized in the freezer and remained solid after drying under vacuum (480 mg, 90%).

^{1}**H-NMR** (400 MHz, $CDCl_3$): δ 8.73 (d, J = 2.1 Hz, 1H), 7.53 (d, J = 8.1 Hz, 1H), 7.35 (dd, J = 8.1, 2.1 Hz, 1H), 5.69 (s, 1H), 3.87 (sept, J = 6.1 Hz, 2H), 2.67 (s, 1H), 1.15 (d, J = 6.1 Hz, 6H), 1.03 (d, J = 6.1 Hz, 6H).

^{13}**C-NMR** (101 MHz, $CDCl_3$): δ 160.31, 151.42, 139.29, 120.50, 118.72, 100.66, 80.50, 80.42, 68.63, 22.93, 22.35.

Bis((diisopropoxymethyl)pyridyl porphyrin:

The porphyrin (208 mg), the diisopropyl acetal (85 mg, 2.5 eq.), $Pd(PPh_3)_4$ (17 mg) and a catalytic amount of CuI were heated to 90 °C overnight in 1:1 Et_3N:DMF (6 mL), in a sealed tube. The reaction mixture was cooled to room temperature and evaporated to dryness. The purple residue obtained was chromatographed on silica. Elution with hexane:DCM 1:1 + 1% Et_3N afforded a very pale pink fore-running band and a pale yellow band. The polarity was increased to 2:1 DCM:hexane, and eventually to 2:1 DCM:hexane + 2% MeOH, which caused the elution of a purple fraction that could easily be visually identified on the column. Evaporation of this fraction afforded a residue (216 mg) with the expected LDI-MS and NMR (with minor contaminants). The residue was dissolved in minimal $CHCl_3$ and recrystallised by the layered addition of MeOH, resulting in the formation of purple needles (125 mg). The combined yield from these crystals and evaporation of the liqor (40 mg) was 79%.

^{1}**H-NMR** (400 MHz, CD_2Cl_2): δ 8.89 (d, J = 4.7 Hz, 4H), 8.85 (d, J = 2.1 Hz, 2H), 8.70 (d, J = 4.7 Hz, 4H), 8.03 (dd, J = 8.0, 2.1 Hz, 2H), 7.74 (s, 4H), 7.73 (t, J = 8.5 Hz, 2H), 7.68 (d, J = 8.0 Hz, 4H), 7.06 (d, J = 8.5 Hz, 4H), 5.61 (s, 2H), 4.03 (sept, J = 6.1 Hz, 4H), 3.92 (t, J = 6.5 Hz, 8H), 1.94 (s, 12H), 1.29 (d, J = 6.1 Hz, 12H), 1.22 (d, J = 6.1 Hz, 12H), 0.97 (m, 8H), 0.63 - 0.54 (m, 16H), 0.53 - 0.42 (m, 8H), 0.28 (t, J = 6.8 Hz, 12H).

LDI-MS: 1597.13

Note: The liqor was evaporated to obtain about 40 mg of impure material that was subjected to the deacetalization conditions. The resulting dialdehyde could be chromatographed on silica (DCM:hexane 1:3 → 1:1 → 1:0 + 1-2% MeOH), but the purity (by NMR) was inferior to material derived from the recrystallised acetal.

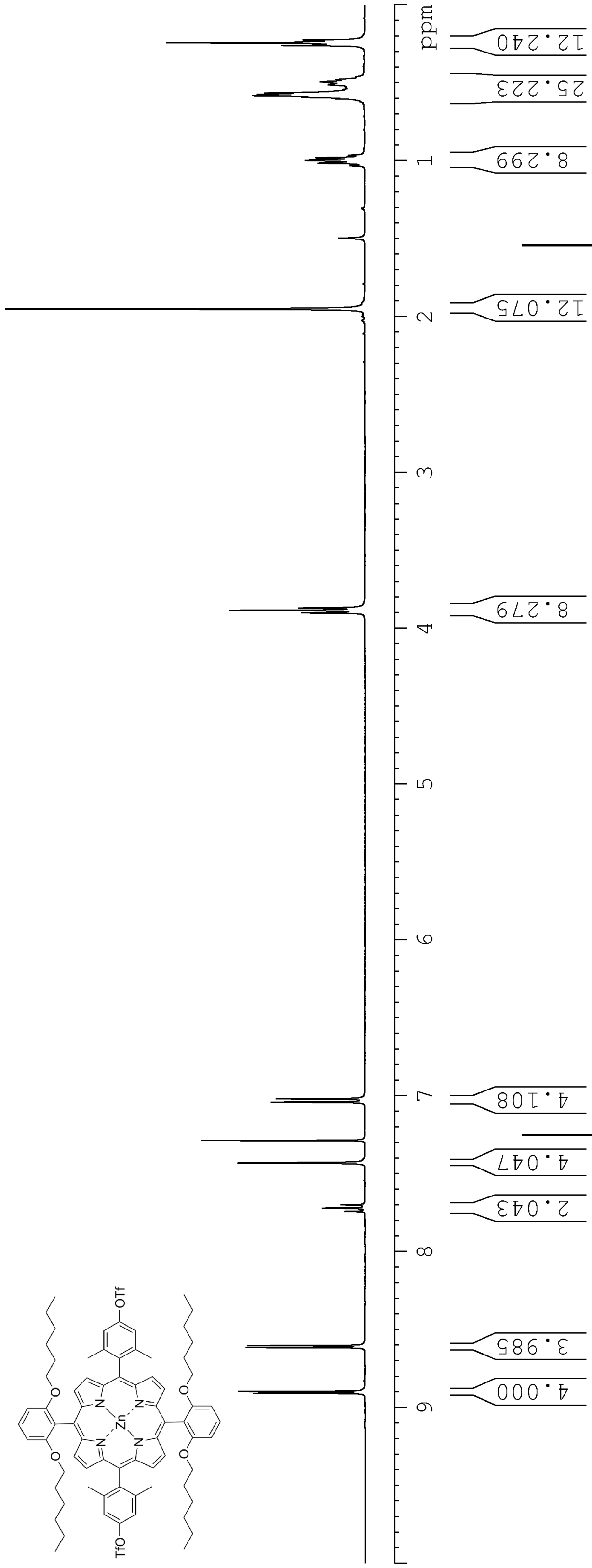
Dialdehyde porphyrin 1:

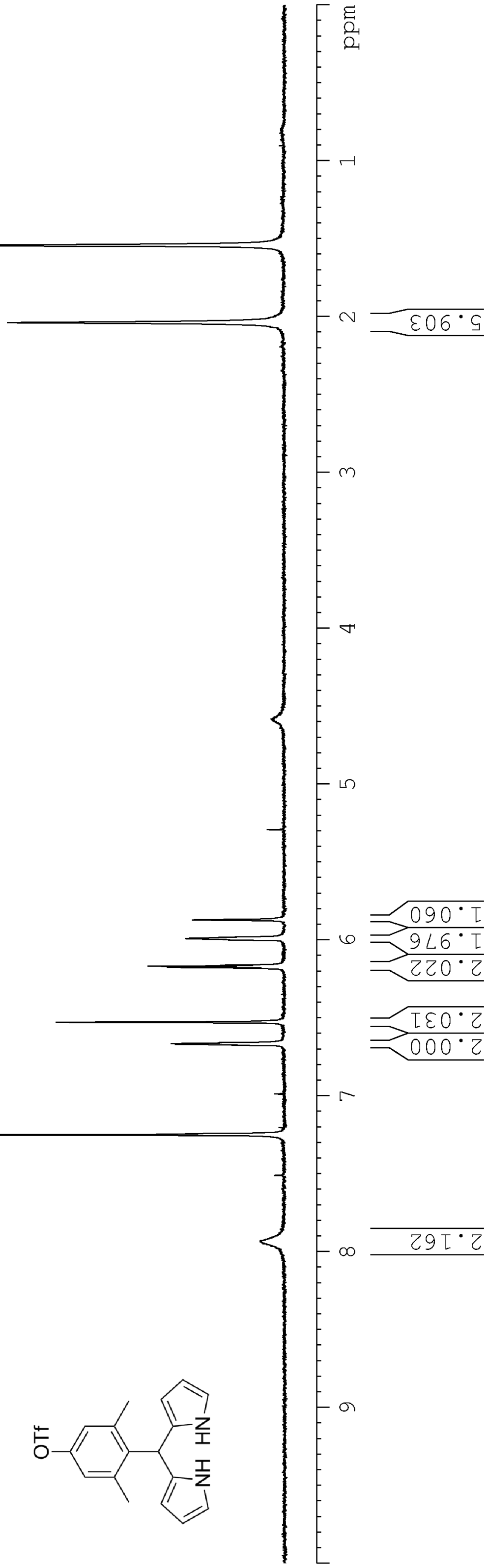
The porphyrin (119 mg, 75 μmol) was dissolved in THF:acetone:water 5:4:1 and PPTS was added (small spatula tip, about 40 mg = 2 eq.). The mixture was heated to reflux for 1 hour and then diluted with water, and extracted with DCM. The organics were washed with water, dried ($MgSO_4$), filtered and evaporated to obtain a purple solid (110 mg). This material was the deprotected porphyrin, but by NMR it was found to have retained pyridine from the deprotection. The material was dissolved in cold $CHCl_3$ (from the freezer), and washed with 3 × 30 mL ice cold 20% aqueous AcOH followed by 2 × aqueous $NaHCO_3$. Drying ($MgSO_4$), filtration and evaporation gave a residue that was chromatographed on silica. DCM caused the elution of a pale pink, very dilute band. Increasing the polarity to 0.75% MeOH in DCM caused the elution of the product as a dark purple band. This was evaporated to obtain the title compound as a purple solid (99 mg, 96%).

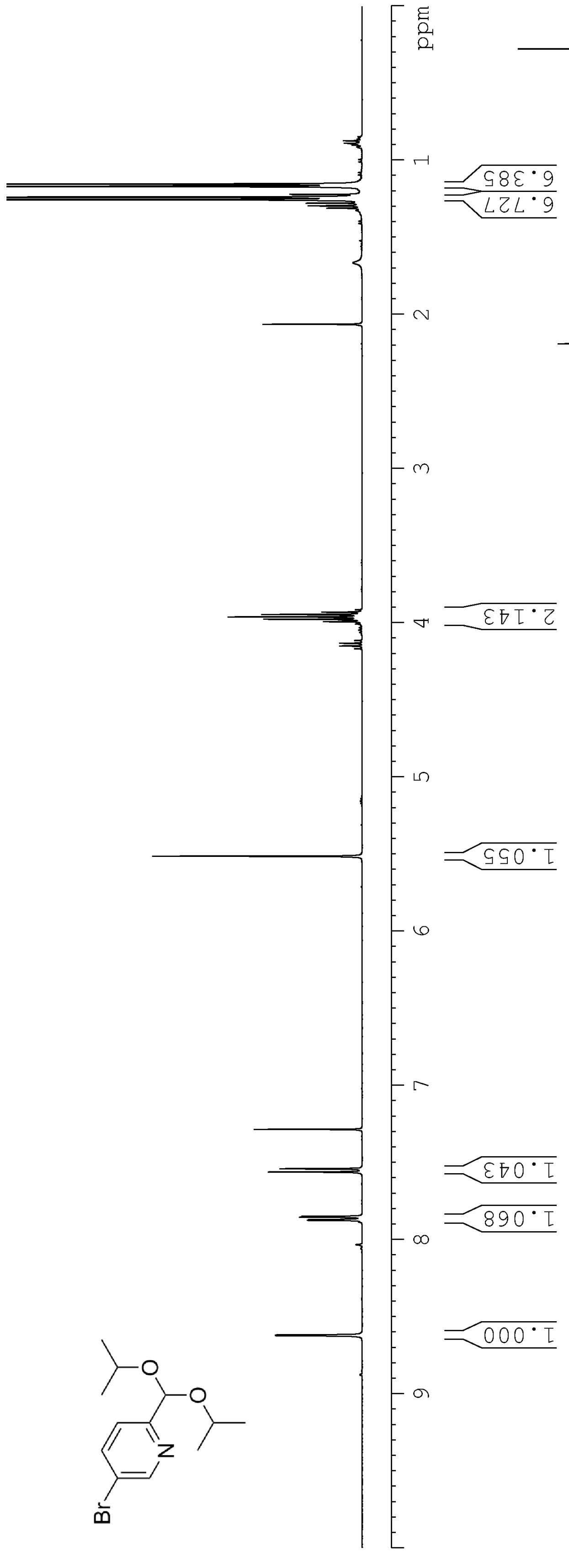
^{1}**H-NMR** (500 MHz, CD_2Cl_2): δ 9.45 (s, 2H), 8.91 (d, J = 4.5 Hz, 4H), 8.71 (d, J = 4.5 Hz, 4H), 8.36 (s, 2H), 8.01 (dd, J = 7.9, 2.0 Hz, 2H), 7.84 (d, J = 7.9 Hz, 2H), 7.75 (s, 4H), 7.72 (t, J = 8.6 Hz, 2H), 7.06 (d, J = 8.6 Hz, 4H), 3.92 (t, J = 6.4 Hz, 8H), 1.96 (s, 12H), 1.00 - 0.92 (m, 8H), 0.63 - 0.56 (m, 16H), 0.51 - 0.44 (m, 8H), 0.33 - 0.29 (m, 12H). These peaks are reported for one particular experiment, but the peak positions tend to wander due to self-coordination.

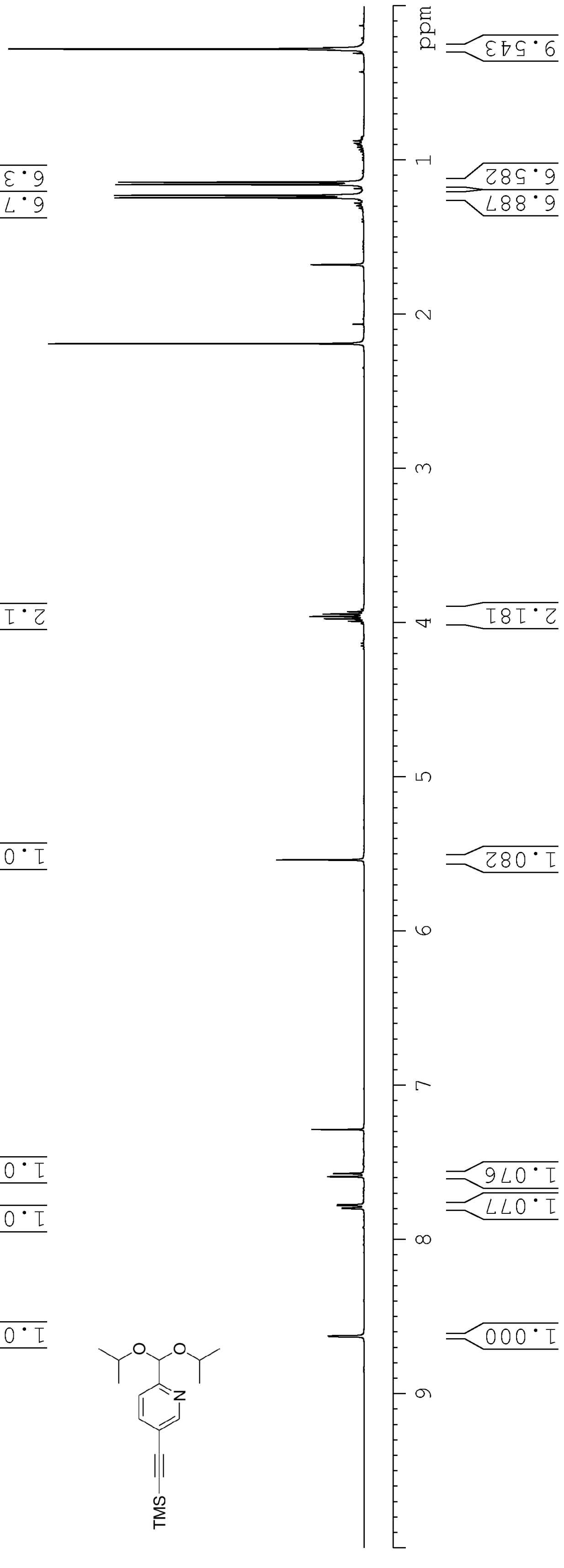
^{13}**C-NMR** (126 MHz, CD_2Cl_2): δ 192.49, 160.23, 152.50, 150.94, 150.77, 148.88, 144.65, 140.55, 139.44, 132.37, 130.48, 130.20, 129.97, 125.24, 121.50, 121.14, 121.01, 116.77, 113.58, 105.53, 97.22, 85.61, 68.82, 31.01, 28.71, 24.95, 22.18, 21.70, 13.63.

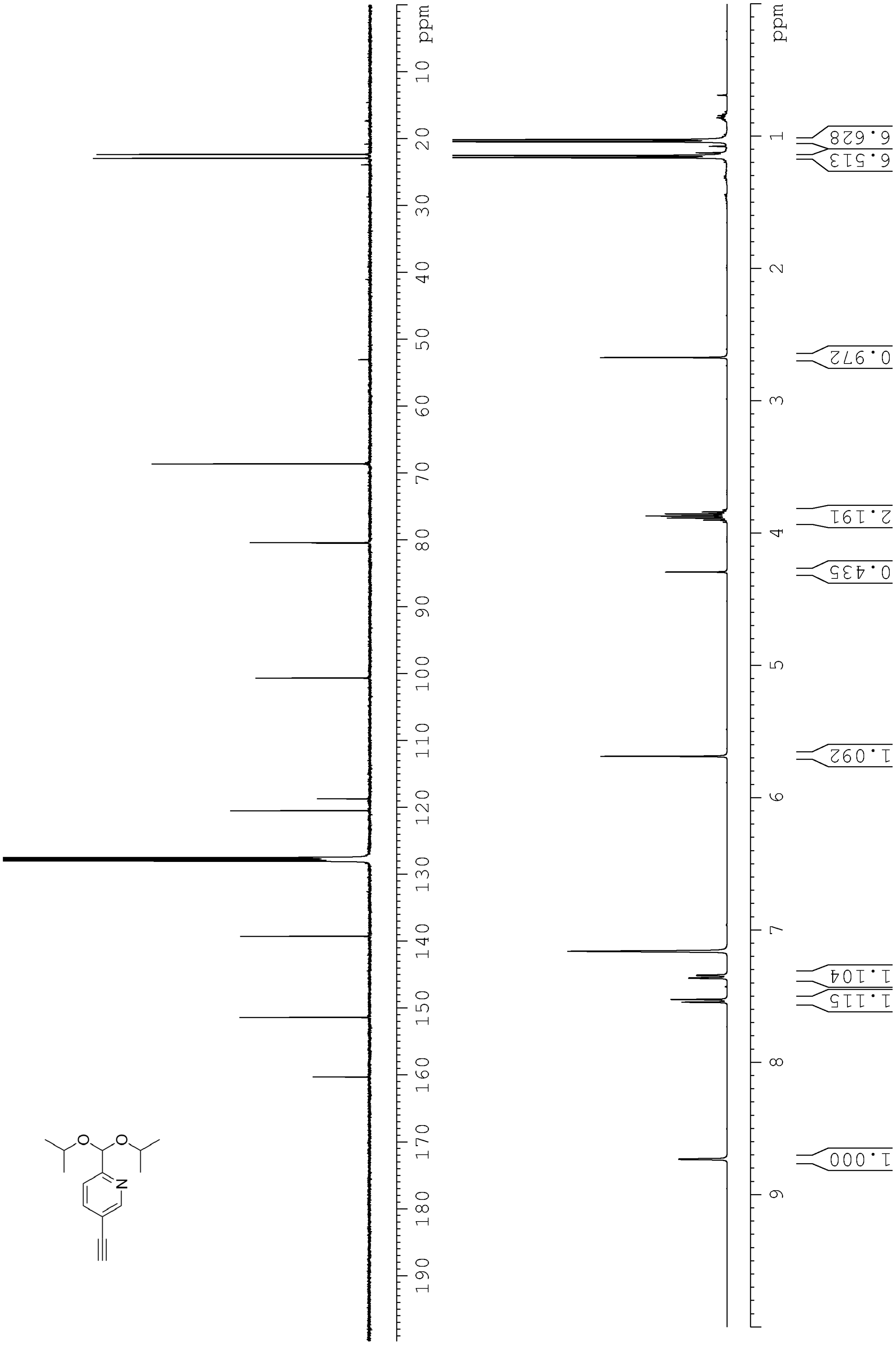
LDI-MS: 1393.04


ppm
1
2
3
4
5
6
7
8
9
12.240
25.223
8.299
12.075
8.279
4.108
4.047
2.043
3.985
4.000
OTf
TfO
N
Zn

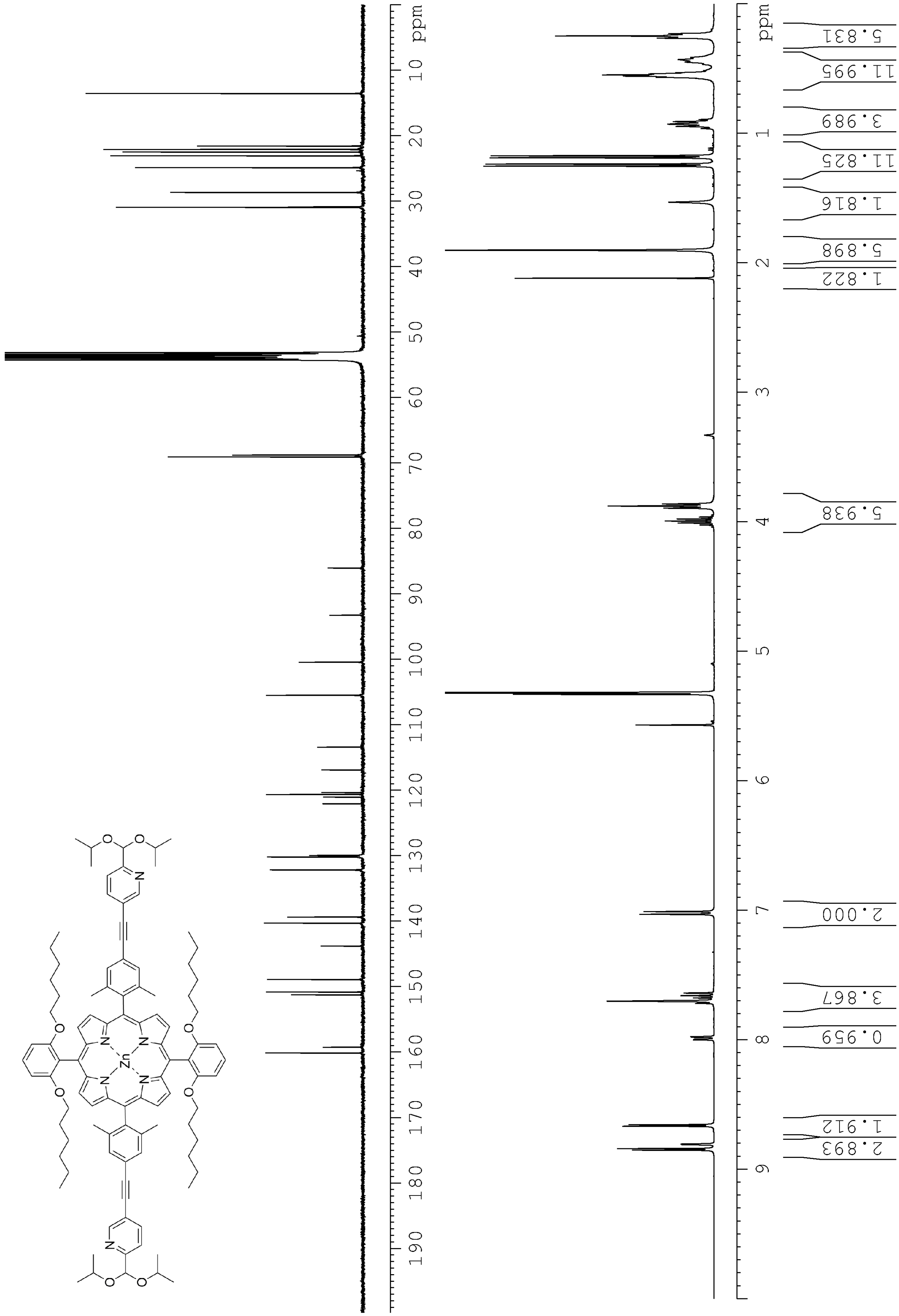

ppm
1
2
3
4
5
6
7
8
9
5.903
1.060
1.976
2.022
2.031
2.000
2.162
OTf
NH HN

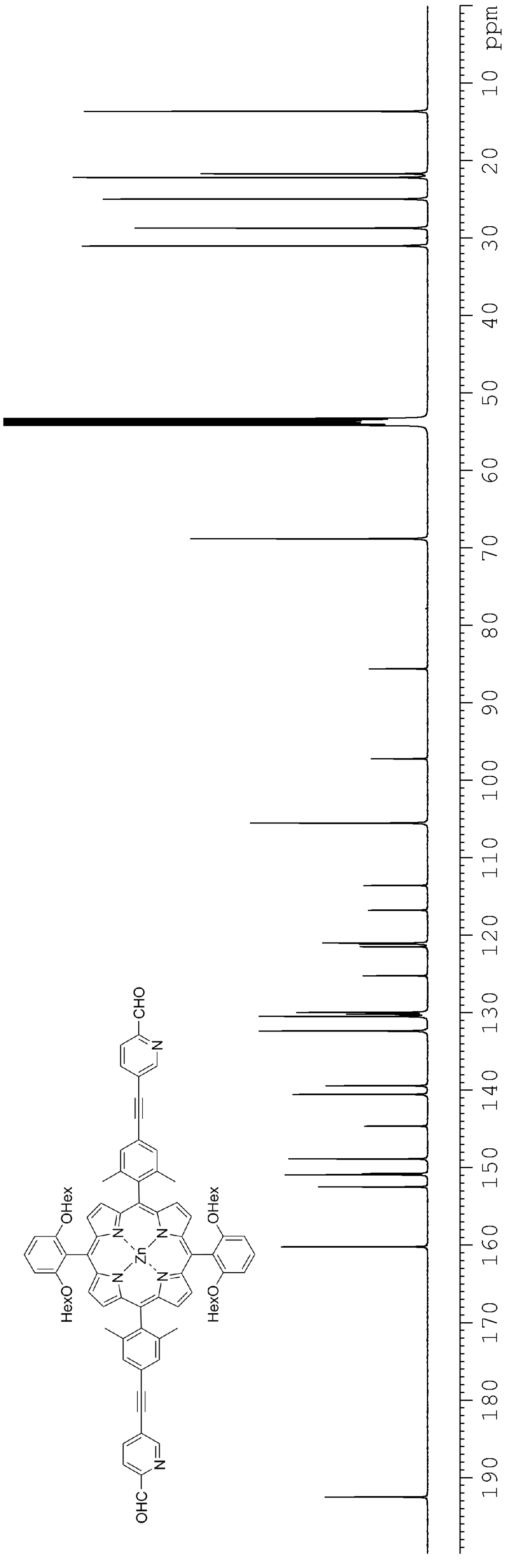

Br
N
O
O
ppm
1
2
3
4
5
6
7
8
9
6.385
6.727
2.143
1.055
1.043
1.068
1.000

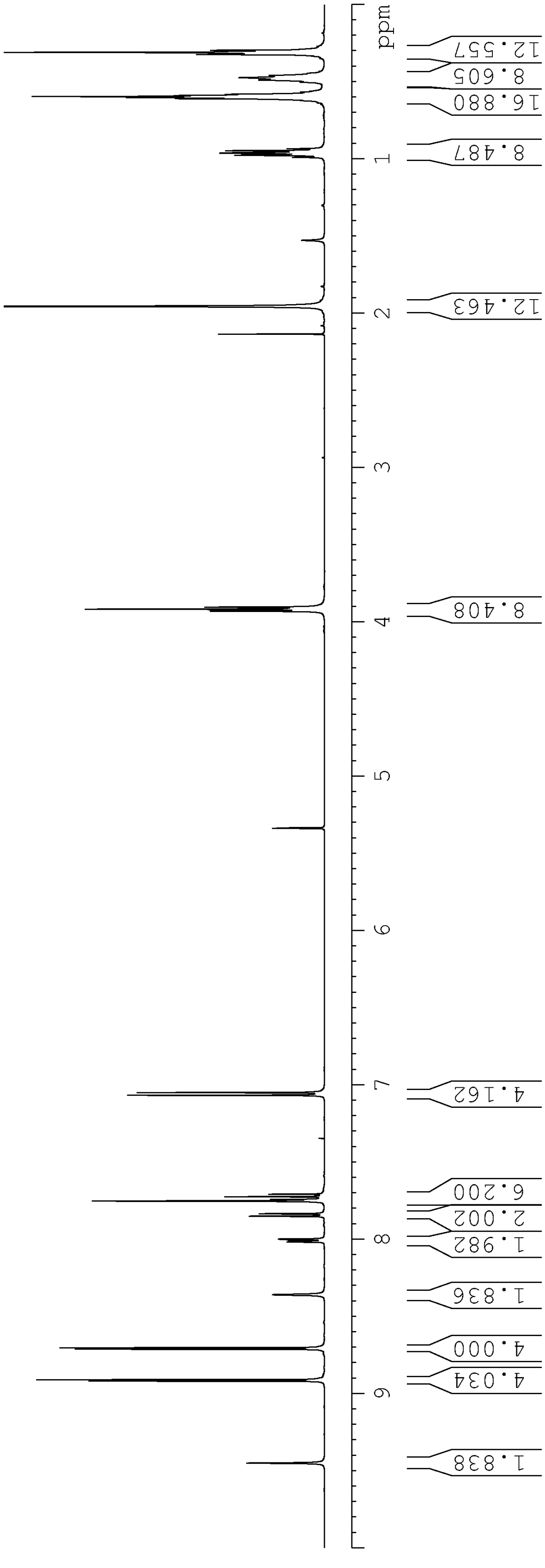

TMS
N
O
O
ppm
1
2
3
4
5
6
7
8
9
9.543
6.582
6.887
2.181
1.082
1.076
1.077
1.000



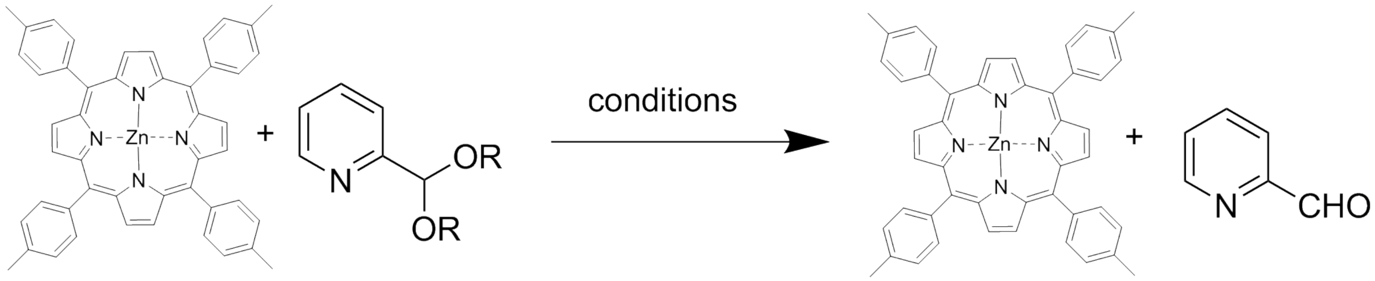
O
O
N
ppm
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160
170
180
190
ppm
1
2
3
4
5
6
7
8
9
6.628
6.513
0.972
2.191
0.435
1.092
1.104
1.115
1.000


ppm
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160
170
180
190
ppm
1
2
3
4
5
6
7
8
9
5.831
11.995
3.989
11.825
1.816
5.898
1.822
5.938
2.000
3.867
0.959
1.912
2.893
N
Zn
O


ppm
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160
170
180
190
OHC
N
CHO
OHex
HexO
Zn


ppm
1
2
3
4
5
6
7
8
9
12.557
8.605
16.880
8.487
12.463
8.408
4.162
6.200
2.002
1.982
1.836
4.000
4.034
1.838

2 Acetal deprotection screen



The initial synthesis proceeded *via* the dimethyl acetal, however, we encountered problems in deprotecting this penultimate product to afford the target compound. In order to study the deprotection conditions, 2-(dimethoxymethyl)pyridine was subjected to various procedures (see table) in the presence of a small amount of zinc *meso*-tetratolyl porphyrin. The acetal breakdown was followed by TLC. Demetallation of the porphyrin was assessed by LDI-MS. Once it was established that the dimethyl acetal would be a challenging substrate, the same screening was repeated with a smaller set of conditions using 2-(diisopropoxymethyl)pyridine.

Conditions	Deprotection	Demetallation
10% HCl/THF, 40 °C	✓	✓
80% AcOH/THF, rt	✕	✓
80% AcOH/THF, 0 °C[6]	✕	✕
SiO_2, 10 wt% H_2O, DCM, rt[7]	✕	✓
SiO_2, 10 wt% oxalic acid$_{(aq.)}$, DCM, rt	(✓)	✓
SiO_2, 10 wt% $H_2SO_{4(aq.)}$, DCM, rt	✓	✓
Ph_3PBr_2, DCM, −40 °C → rt[8]	✕	✓
PPTS, Me_2CO/H_2O, 60 °C	✕	✕
LiCl, DMSO/H_2O/THF, 90 °C[9]	✕	✕
Bu_4NI, $BF_3 \cdot Et_2O$, $CHCl_3$, 65 °C[10]	✕	✓
Amberlyst® 15, THF/Me_2CO/H_2O, rt	✕	✕
DOWEX® 50WX8, THF/Me_2CO/H_2O, rt	✕	✕
$In(OTf)_3$, Me_2CO, rt[11]	✕	✕
$In(OTf)_3$, Me_2CO, μW	†	✕
$In(OTf)_3$, Me_2CO, 60 °C	†	✕
$PdCl_2(MeCN)_2$, Me_2CO, rt	✕	✕

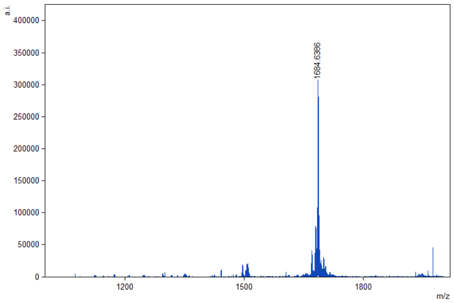
Table 1 Conditions survey for deprotection of the dimethyl acetal. † = decomposition of product, (✓) = partial conversion.

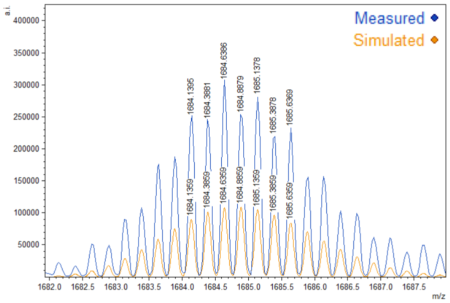
Conditions	Deprotection	Demetallation
$In(OTf)_3$, Me_2CO, rt	✕	✕
$PdCl_2(MeCN)_2$, Me_2CO, rt	✕	✕
PPTS, Me_2CO/H_2O, rt	(✓)	✕
PPTS, Me_2CO/H_2O, 40°C	✓	✕
80% AcOH/THF, 0 °C	✕	✕
SiO_2, 10 wt% oxalic acid$_{(aq.)}$, DCM, 0 °C	✕	✕

Table 2 Conditions survey for deprotection of the diisopropyl acetal. (✓) = partial conversion.

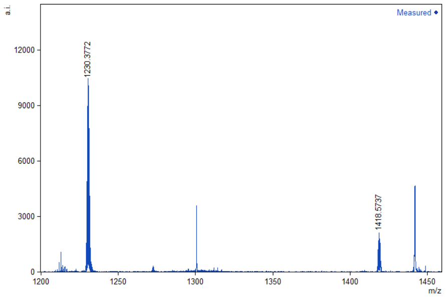
3 ESI-MS

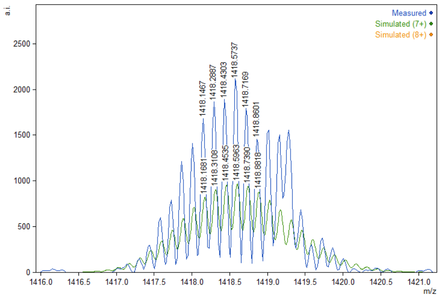
Square grid, $C_{432}H_{392}Cu_4N_{32}O_{12}Zn_4$

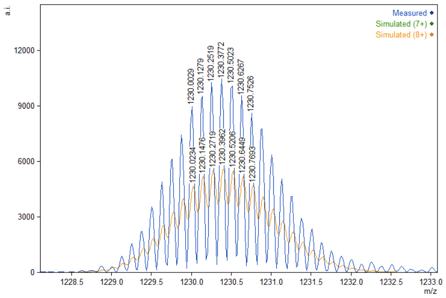




Tetrahedral cage, $C_{612}H_{624}Fe_4N_{48}O_{36}Zn_6$







4 Preparation of Samples

Square Grid

A 2:1 complex of $\mathrm{Cu(MeCN)_4 \cdot PF_6}$ and the porphyrin bisphenanthroline **6** was prepared by adding a solution of $\mathrm{Cu(MeCN)_4 \cdot PF_6}$ in $\mathrm{CD_2Cl_2}$ (2 equiv.) to **6** in $\mathrm{CD_2Cl_2}$. In an NMR tube, the porphyrin dialdehyde **1** was combined with 2 equiv. of *p*-anisidine in $\mathrm{CD_2Cl_2}$ and allowed to stand for 2 days before addition of 1 equiv. of the previously prepared copper-bisphenanthroline complex. The mixture was allowed to stand for two days and then characterised by NMR and ESI-MS.

Tetrahedral cage

In an NMR tube, the porphyrin dialdehyde **1** was combined with 2 equiv. of *p*-anisidine in $\mathrm{CD_3CN}$, resulting in a suspension of the insoluble porphyrin. A solution of $\mathrm{Fe(BF_4)_2 \cdot 6\,H_2O}$ in $\mathrm{CD_3CN}$ was added so that the relative proportion of **1** to Fe(II) was 6:4. The mixture was heated to 70 °C overnight in a sealed NMR tube, after which time a homogenous, deep red solution resulted. This was characterised by NMR and ESI-MS.

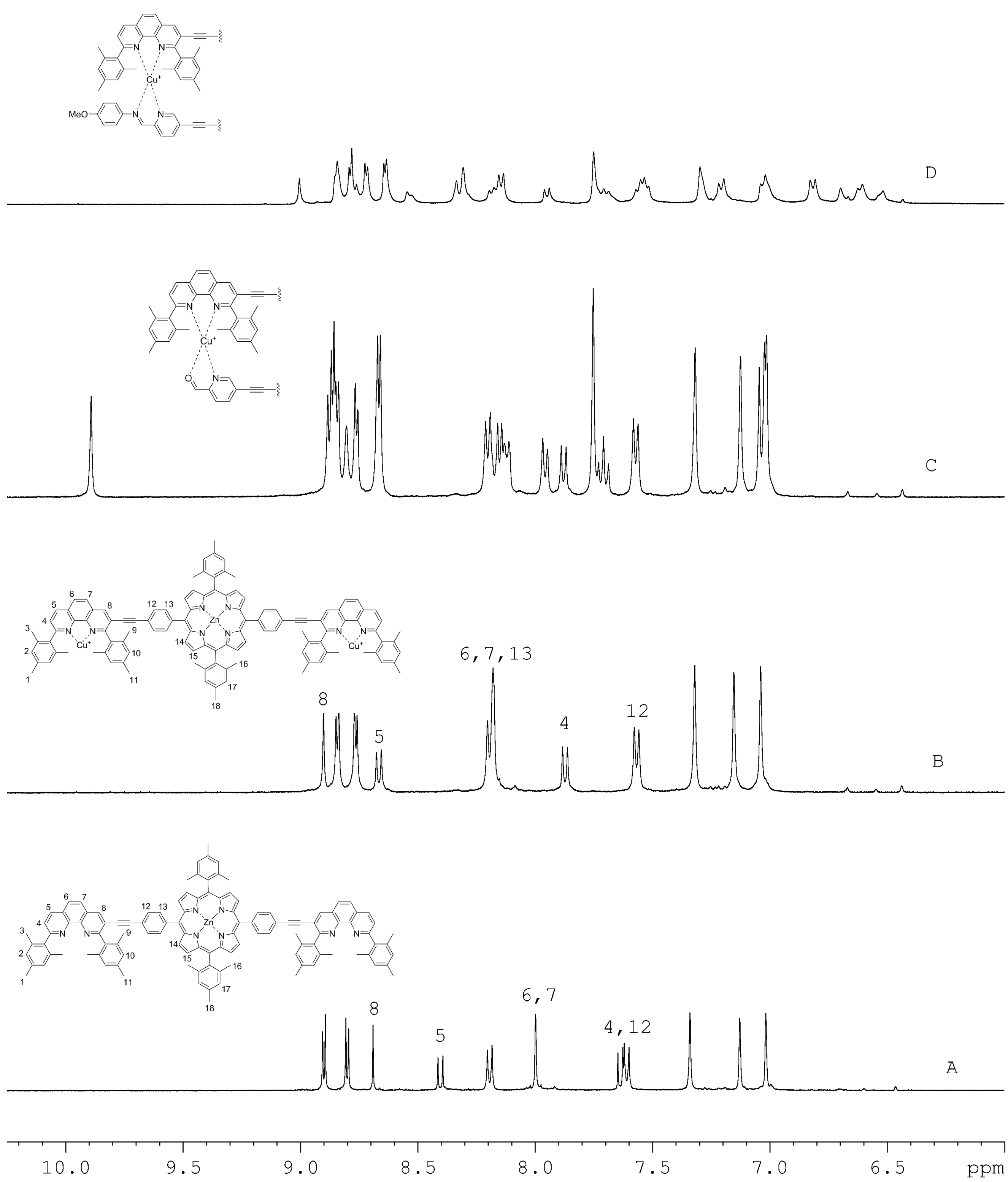
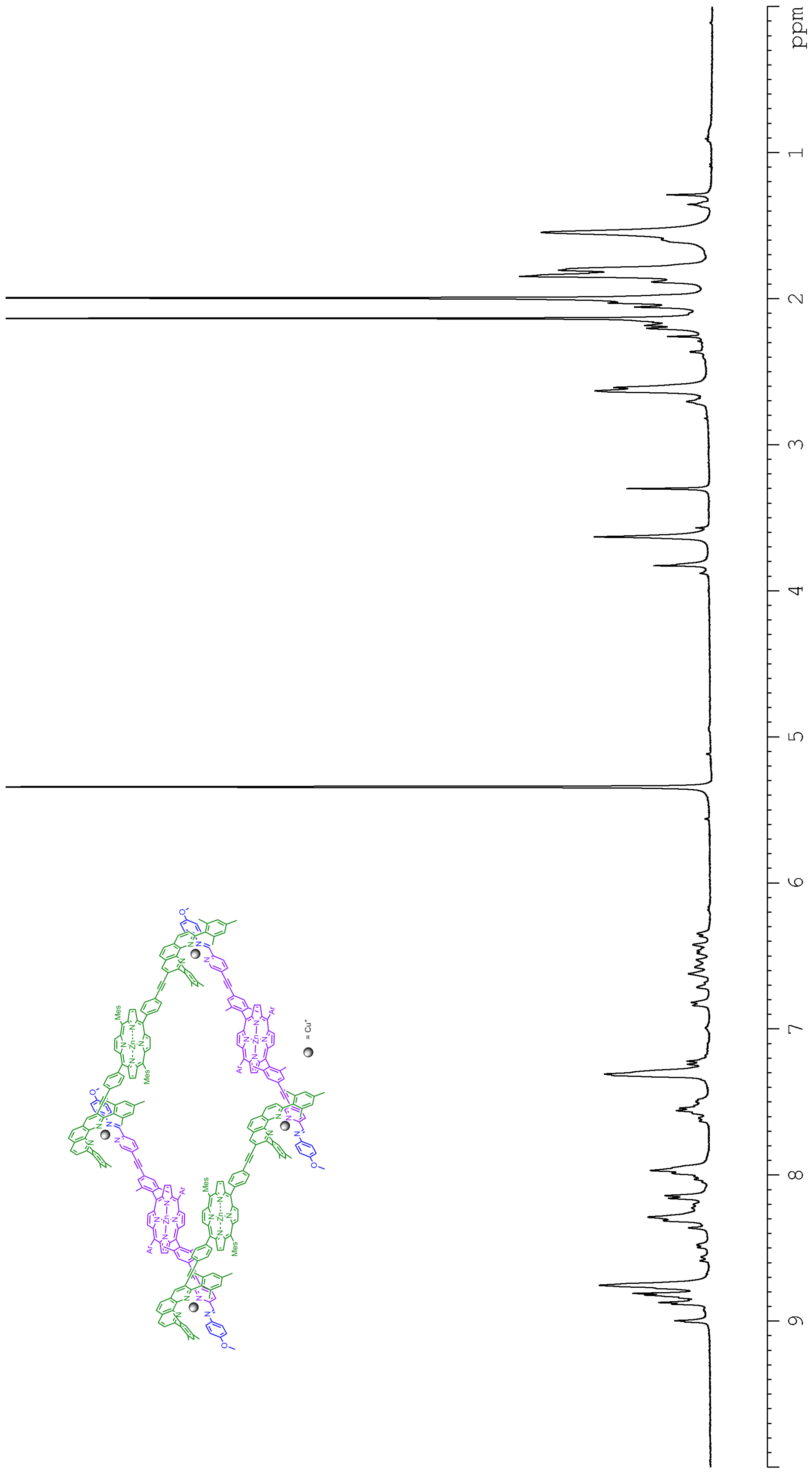
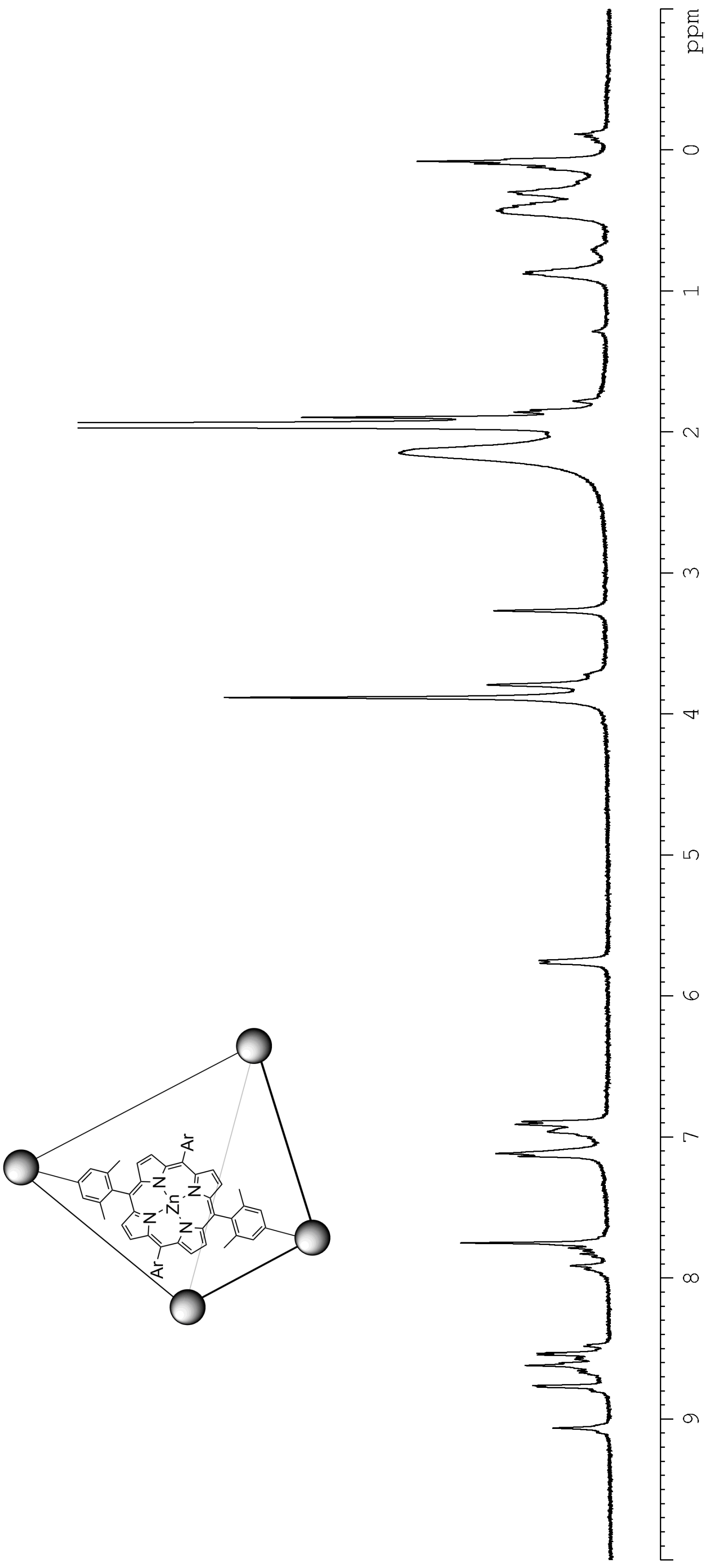


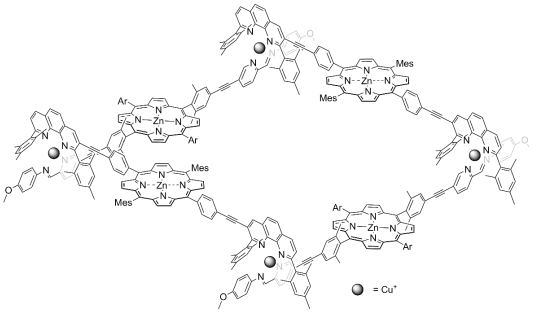
Figure 1 ^{1}**H-NMR** spectra (400 MHz, CD_2Cl_2) of porphyrin bisphenanthroline **6** (A), **6** + 2 eq. Cu(I) (B), + 1 eq. porphyrin bis(pyridyl aldehyde) **1** (C), and + 2 eq. *p*-anisidine (D). Notable features are the disappearance of the *p*-anisidine aldehyde peak at around 9.8 ppm, and the appearance of peaks at 6.5 ppm corresponding to mesityl aromatic protons (2 and 10) experiencing loss of symmetry due to Cu(I)-pyridyl imine complexation.


ppm
1
2
3
4
5
6
7
8
9
Mes
Zn
N
Ar
= Cu+

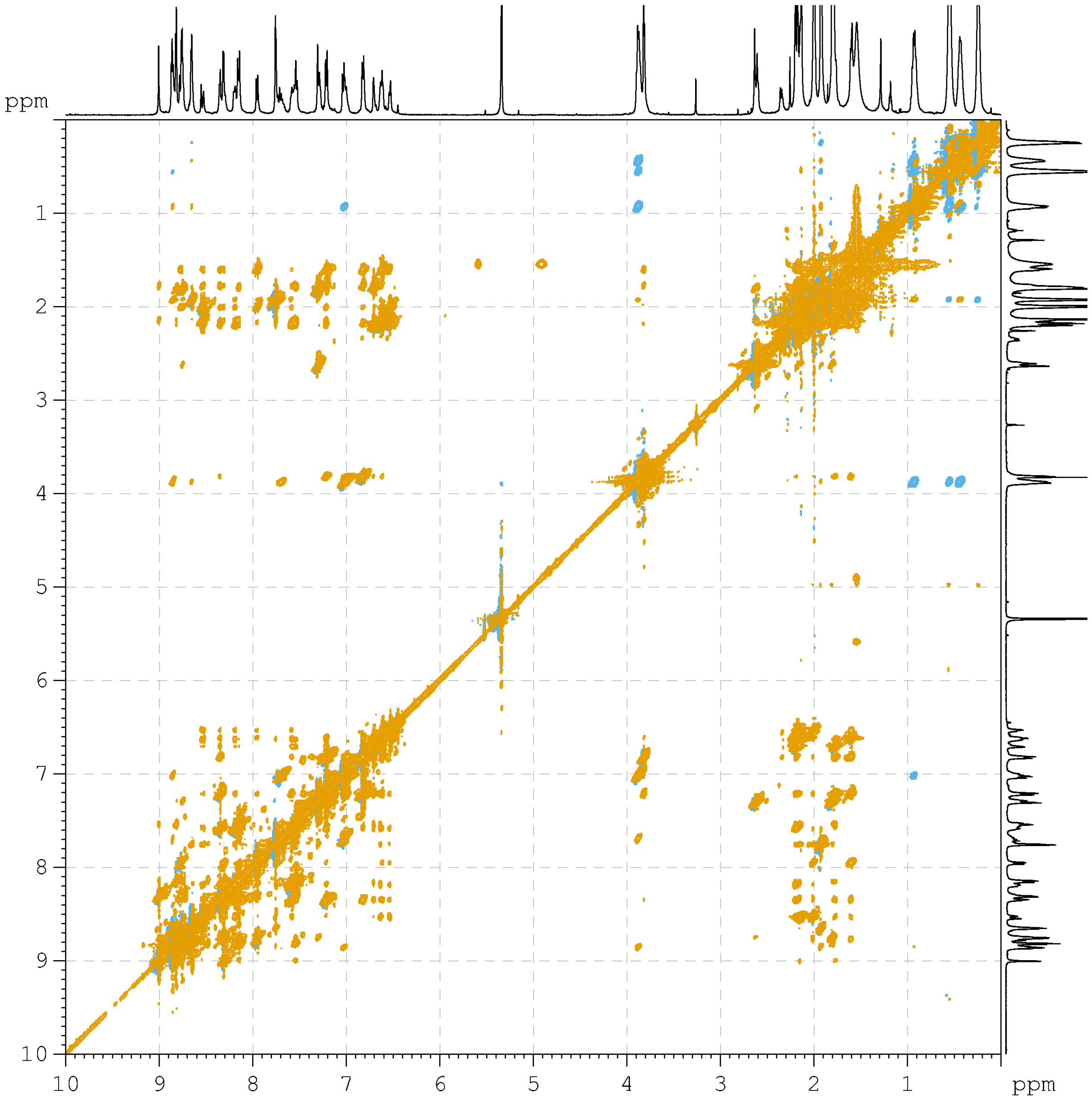


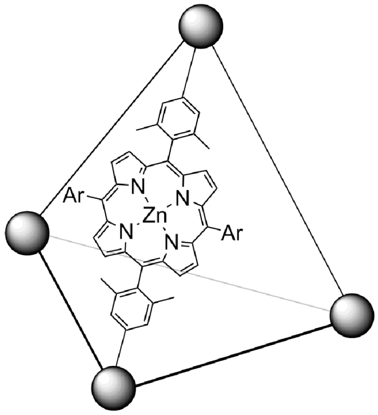
ppm
0
1
2
3
4
5
6
7
8
9
Ar
Ar
N
N
N
N
Zn

5 2D NMR spectra

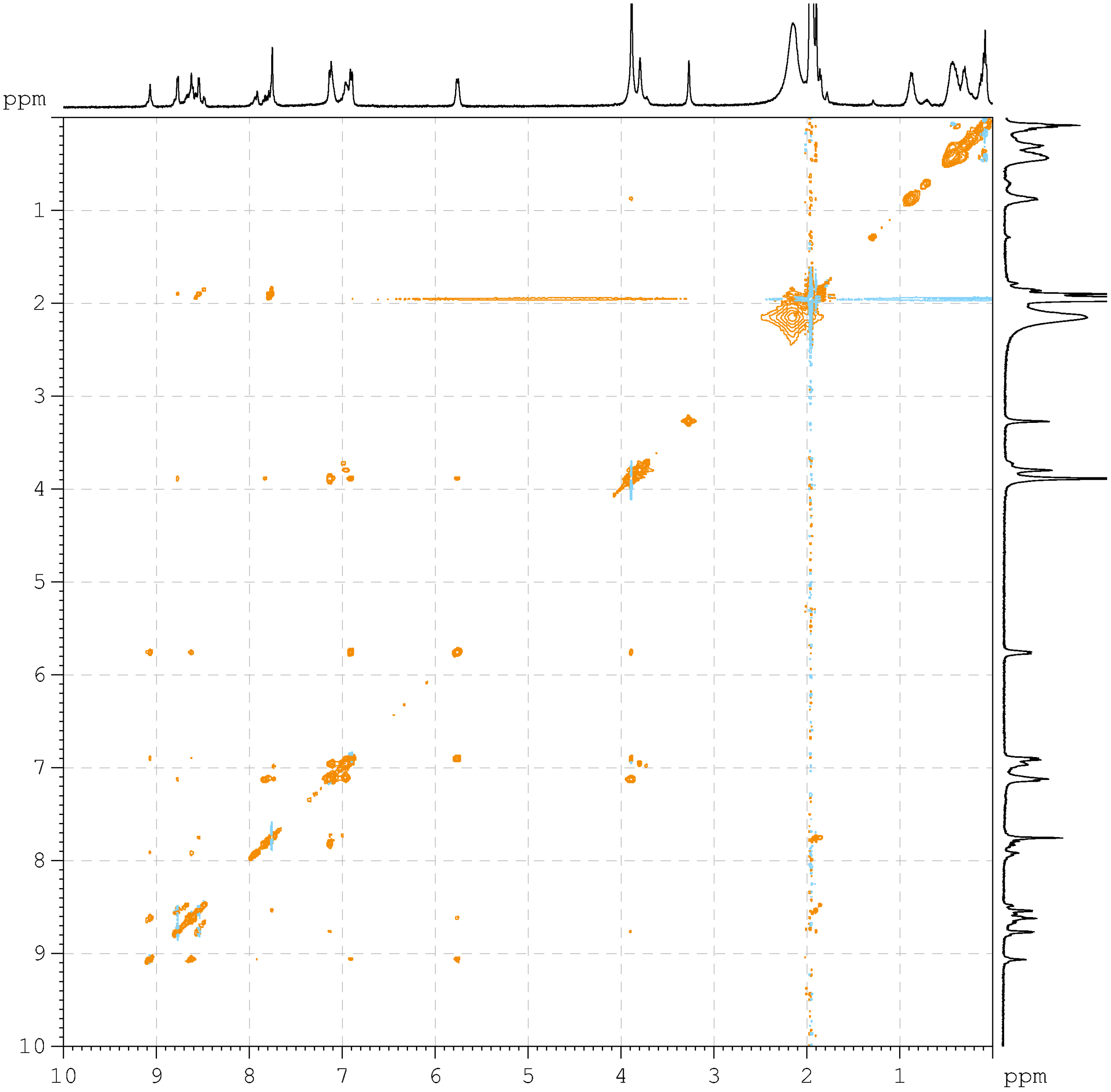

N
Zn
Mes
Ar
O
= Cu+

Dialdehyde square full NOESY spectrum (500 MHz, CD_2Cl_2)

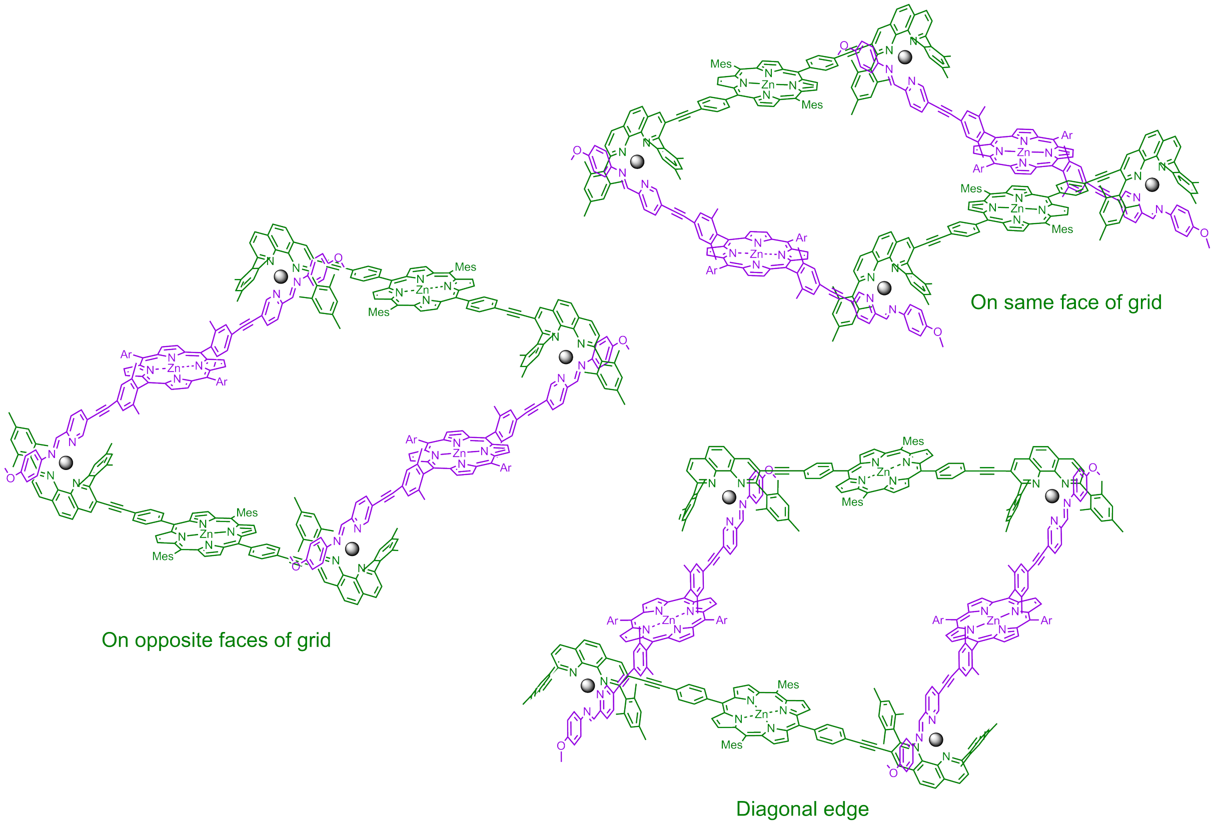



Ar
N
Zn
N
N
N
Ar

Tetrahedral cage full NOESY spectrum (400 MHz, CD_3CN)



6 Isomers of the grid leading to complexity in the NMR spectrum



On same face of grid

On opposite faces of grid

Diagonal edge

Figure 2 Representation of some of the possible isomers of the grid: subcomponents of the same type may be on the same or opposite faces of the grid, and one or more edges may be "diagonal" through the plane of the grid.

References

[1] J. Taesch, T. T. Dang and V. Heitz, *Tetrahedron Letters*, 2012, **53**, 333–337.

[2] K. E. Splan and J. T. Hupp, *Langmuir*, 2004, **20**, 10560–10566.

[3] M. A. Alemàn-García, *Porphyrin-based Multicomponent Supramolecular Assemblies*, PhD thesis, University of Cambridge, 2011.

[4] J.-F. Ayme, J. E. Beves, D. A. Leigh, R. T. McBurney, K. Rissanen and D. Schultz, *Nat Chem*, 2011, **4**, 15–20.

[5] J. K. Laha, S. Dhanalekshmi, M. Taniguchi, A. Ambroise and J. S. Lindsey, *Organic Process Research & Development*, 2003, **7**, 799–812.

[6] Y. Kuramochi, S. Sandanayaka, Atula, A. Satake, Y. Araki, K. Ogawa, O. Ito and Y. Kobuke, *Chemistry - A European Journal*, 2009, **15**, 2317–2327.

[7] F. Huet, A. Lechevallier, M. Pellet and J. M. Conia, *Synthesis*, 1978, **1978**, 63–65.

[8] A. Wagner, M.-P. Heitz and C. Mioskowski, *Journal of the Chemical Society, Chemical Communications*, 1989, 1619–1620.

[9] P. K. Mandal, P. Dutta and S. C. Roy, *Tetrahedron Letters*, 1997, **38**, 7271–7274.

[10] A. K. Mandal, P. Y. Shrotri and A. D. Ghogare, *Synthesis*, 1986, **1986**, 221–222.

[11] B. T. Gregg, K. C. Golden and J. F. Quinn, *The Journal of Organic Chemistry*, 2007, **72**, 5890–5893.