Supporting Information

Aromatic oligoamide β-sheet foldamers

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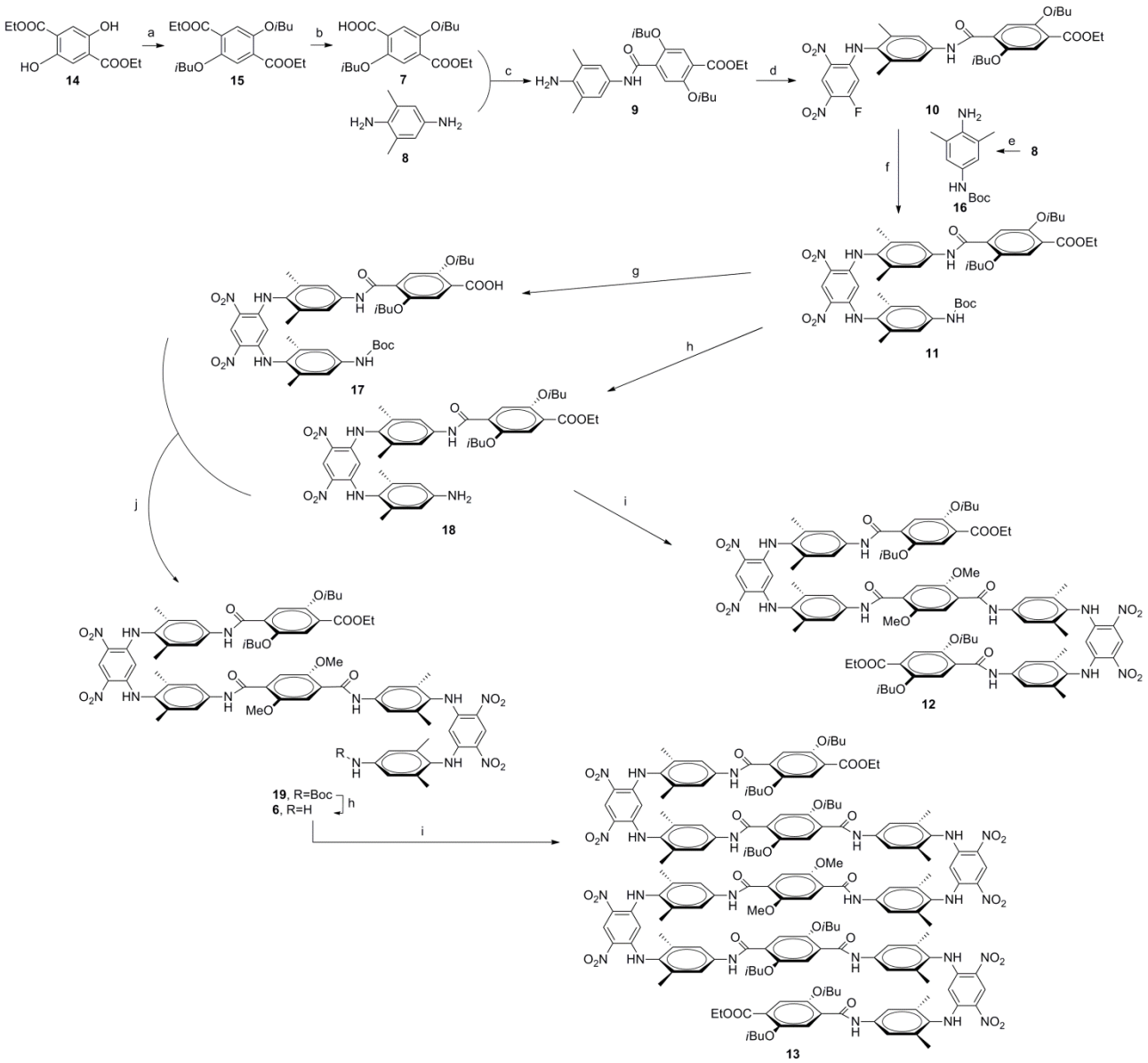
Synthetic schemes for multi-turn structures



Reagents and conditions: a) 3.5 equiv PPh_3, 3.5 equiv isobutanol, 3.5 equiv DIAD, THF, rt, 16h, 86%. b) 1 equiv KOH, dioxane/H_2O 3:1, rt, 16h, 49% c) 1,2 equiv EDCI, CH_2Cl_2, 24h, rt, 82%. d) 1 equiv 1,5-difluoro-2,4-dinitrobenzene, DMSO, 4h, rt, 95%. e) 1 equiv Boc_2O, THF, rt, 16h, 80%. f) 1 equiv DIEA, DMSO, +80 °C, 3 days, 50%. g) 5 equiv KOH, THF/MeOH 2:1, rt, 24h, 80%. h) 20% TFA/CH_2Cl_2, rt, 4h, 99%. i) 0.5 equiv 2,5-dimethoxyterephtalic acid chloride, 2.5 equiv DIEA, $CHCl_3$, 16h, rt, 90% for **12**, 93% for **13**. j) 1.5 equiv DIEA, 1.5 equiv PyBOP, $CHCl_3$, +45 °C, 3 days, 69%.

NMR experiments

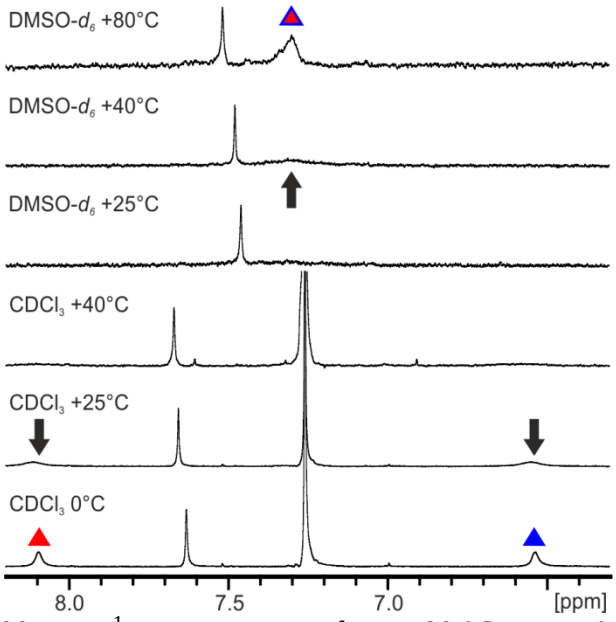


Figure S1. Part of the 400 MHz ^{1}H NMR spectra from +80 °C to +25 °C in DMSO-d_6 and from +40°C to 0°C in $CDCl_3$ for OiBu macrocycle **5a**. H_3 and H_5 signals are marked with red and blue triangles, respectively. H_3+H_5 fast exchange average signal is marked by a red-in-blue triangle.

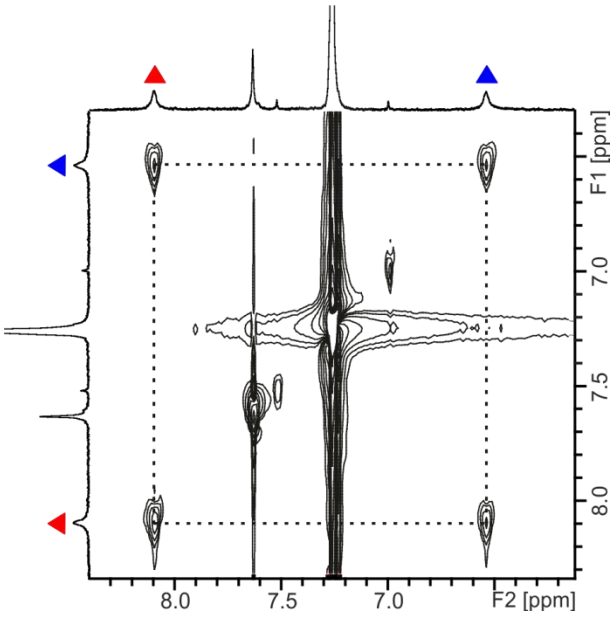
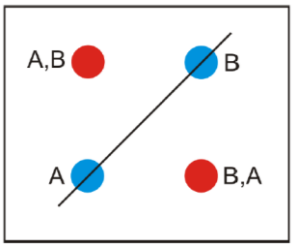


Figure S2. Excerpt of the 2D ROESY plot (τ_m = 300 ms) at +25 °C showing chemical exchange between protons H_3 and H_5 of macrocycle **5a**. H_3 and H_5 signals are marked with red and blue triangles, respectively.

2D-EXSY experiment were used to quantify the rate of the chemical exchange process between H_3 and H_5. EXSY experiments were made on a a DPX-400 NMR spectrometer (Bruker Biospin) at 273K at different mixing time (τ_m). The use of the following equation and the integration of the different cross-peaks (as presented in the scheme below), allowed us to determine a value for k (constant for rate exchange) which correspond to the sum of forward (k_1) and backward (k_{-1}) of the pseudo-first order rate constants for the chemical exchange process.



$$r = \frac{(I_{AA} + I_{BB})}{(I_{AB} + I_{AB})}$$

$$k = \frac{1}{\tau_m} \times \ln \frac{r+1}{r-1}$$

$$k = k_1 + k_{-1} \qquad (k_1 = k_{-1} = k_{obs})$$

I_A and I_B in blue, I_{AB} and I_{BA} in red are the raw volume intensities of diagonal and cross peaks observed in the EXSY experiments. The magnetization exchange rate constants k_1 and k_{-1} correspond to the off-diagonal values (A, B and B,A in red) and are expressed in s^{-1}.

The value of $\Delta G^{\#}$ can be determined using Eyring equation: $\Delta G^{\neq} = -RT ln \frac{k_{obs} h}{k_B T}$, with R = 1,9872 $cal.K^{-1}.mol^{-1}$, h= 1,58 x 10^{-34} cal.s, k_B = 3,30 x 10^{-24} $cal.K^{-1}$ and $k_{obs}=k_1=k_{-1}$.

The results of the Exchange Rate Matrix are presented in the table below :

Table S1. Kinetic parameters for chemical exchange process between H_3 and H_5 in macrocycle **5a**.

τ_m	I_A	I_B	I_{AB}	I_{BA}	k_{obs} (s^{-1})	$\Delta G^{\ddagger}$ ($kJ.mol^{-1}$)
300 ms	-3,107	-3,534	5,576	5,519	5,5475	62.8
250 ms	-4,641	-4,810	7,477	7,415	7,446	62.4
200 ms	-4,496	-4,823	8,228	7,819	8,0235	62
150 ms	-4,670	-5,195	9,325	9,273	9,302	61.5
50 ms	-1,856	-1,903	9,176	8,556	8,866	62
1 ms	0,9545	1				

Then k_m=7,8367 s^{-1} and $\Delta G^{\ddagger}_m$ = 62 $kcal.mol^{-1}$

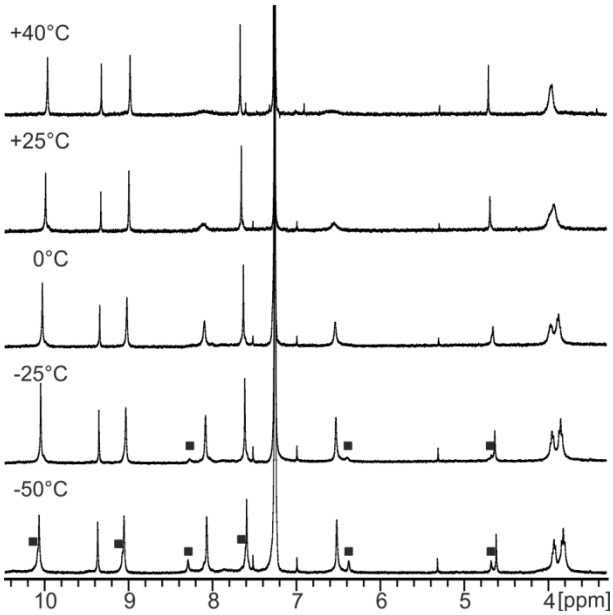


Figure S3. Part of the 400 MHz ^{1}H NMR spectra from +40 °C to -50 °C in $CDCl_3$ for OiBu macrocycle **5a**. Signals belonging to a second conformer are marked with squares.

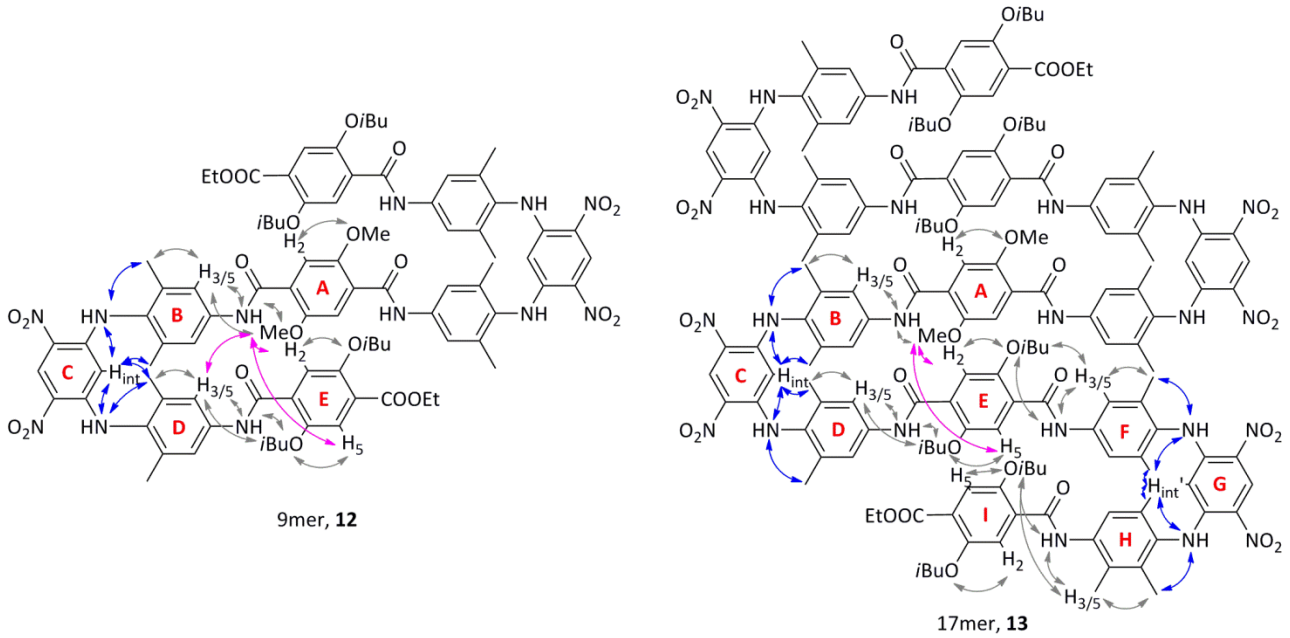


Figure S4. Schematic representation of all the ROESY-2D 1H-1H correlations on 400 MHz at +25 °C in $CDCl_3$ for nonamer **12** (left) and heptadecamer **13** (right). Blue arrows represent correlation in the hairpin turn, pink arrows represent interstrand correlations and others correlations are represented by grey arrows.

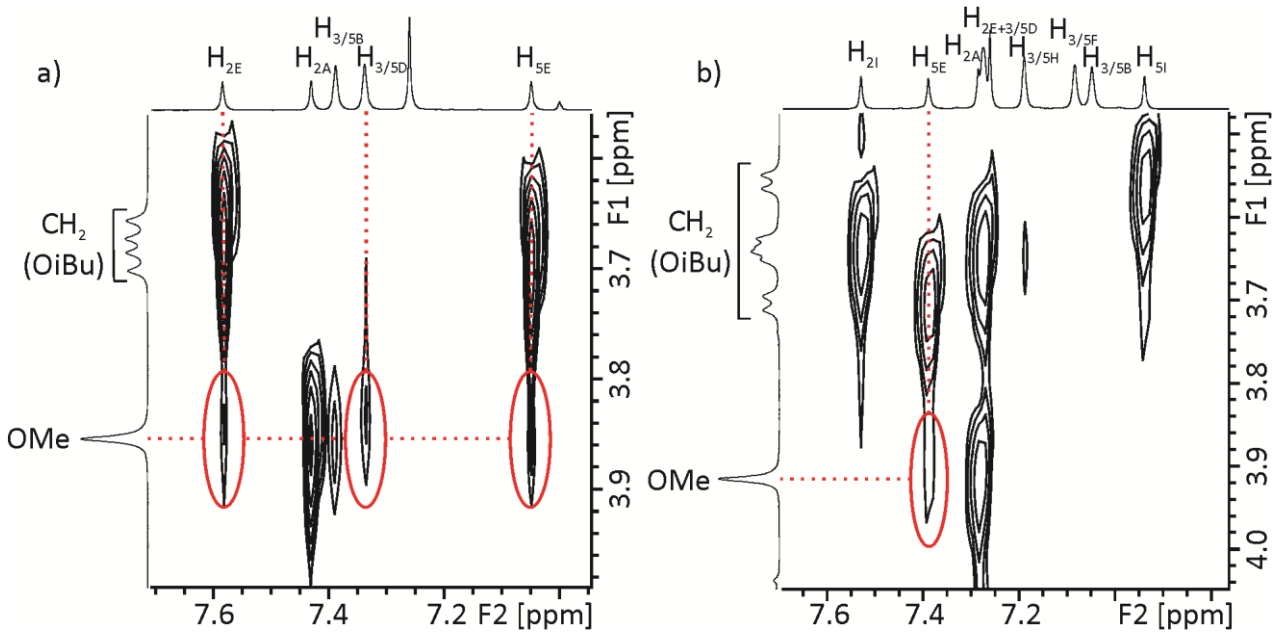


Figure S5. Excerpt of the 2D ROESY plot on 400MHz (τ_m = 300 ms) at +25 °C in $CDCl_3$ for (a) nonamer **12** and (b) heptadecamer **13**. Details on –OMe and aromatic protons region.

Solution structure determination

Multi-dimentionnal NMR experiences (HSQC, HMBC, TOCSY et ROESY) allow complete structural assignment of three oligomers.[1]

- *Experimental conditions:*

NMR spectra were recorded on 3 different NMR spectrometers: (1) an Avance II NMR spectrometer (Bruker Biospin) with a vertical 7.05T narrow-bore/ultrashield magnet operating at 300 MHz for ^{1}H observation and 75 MHz for ^{13}C observation by means of a 5-mm direct BBO H/X probe with Z gradient capabilities; (2) a DPX-400 NMR spectrometer (Bruker Biospin) with a vertical 9.4T narrow-bore/ultrashield magnet operating at 400 MHz for ^{1}H observation by means of a 5-mm direct QNP $^{1}H/^{13}C/^{31}P/^{19}F$ probe with gradient capabilities; (3) an Avance III NMR spectrometer (Bruker Biospin) with a vertical 16.45T narrow-bore/ultrashield magnet operating at 700 MHz for ^{1}H observation by means of a 5-mm TXI $^{1}H/^{13}C/^{15}N$ probe with Z gradient capabilities. Chemical shifts are reported in parts per million (ppm, δ) relative to the ^{1}H residual signal of the deuterated solvent used. ^{1}H NMR splitting patterns with observed first-order coupling are designated as singlet (s), doublet (d), triplet (t), or quartet (q). Coupling constants (*J*) are reported in hertz. Samples were not degassed. Data processing was performed with Topspin 2.0 software.

TOCSY. Total Correlation Spectroscopy (TOCSY) experiments were recorded at 400 MHz or at 700 MHz. They were used to identify protons of oligomer that belong to the same whole spin system regardless of the exact topology with the following acquisition parameters: the acquisition was performed with 2048(t_2) × 256(t_1) data points, relaxation delay of 2 s, and 32 scans per increment. Processing was done after a sine-bell multiplication in both dimensions and Fourier transformation in 1K x 1K real points.

HSQC. Heteronuclear Single-Quantum Correlation spectroscopy (HSQC) experiments were recorded at 400 MHz or at 700 MHz. They were used to observe correlations between nuclei of two different types which are separated by one bond with the following acquisition parameters: the acquisition was performed with 2048(t_2) × 256(t_1) data points, relaxation delay of 2 s, and 64 scans per increment. Processing was done after a sine-bell multiplication in both dimensions and Fourier transformation in 1K x 1K real points.

HMBC. Heteronuclear Multiple Bond Correlation spectroscopy (HMBC) experiments were recorded at 400 MHz or 700 MHz. They were used to detect heteronuclear correlations over longer ranges of about 2–4 bonds with the following acquisition parameters: the acquisition was performed with 2048(t_2) × 256(t_1) data points, relaxation delay of 2 s, and 64 scans per increment. Processing was done after a sine-bell multiplication in both dimensions and Fourier transformation in 1K x 1K real points.

ROESY. Rotating-frame Overhauser Spectroscopy (ROESY) experiments were recorded at 400 or 700 MHz and were used to observe dipolar interactions between protons with the following acquisition parameters: the acquisition was performed with 2048(t_2) × 256(t_1) data points, in States-TPPI mode with CW-spinlock for mixing, relaxation delay of 1.5 s, and 90 scans per increment, mixing time of 300 ms. Processing was done after a sine-bell multiplication in both dimensions and Fourier transformation in 1K x 1K real points.

- *OiBu Macrocycle, **5a**:*

No recorded ^{13}C spectrum due to low solubility.

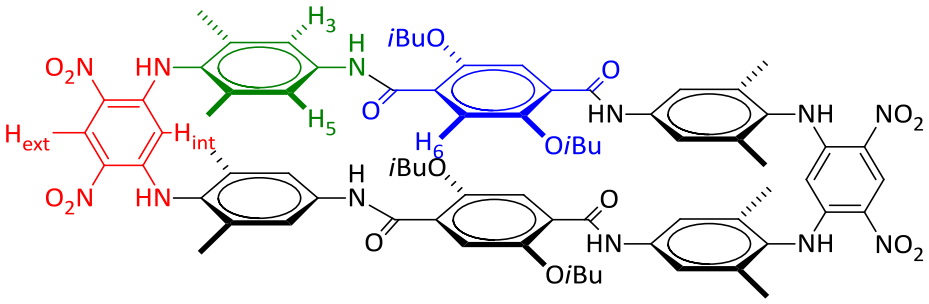


Table S2: ^{1}H chemical shifts for OiBu macrocycle **5a** in $CDCl_3$, 300 MHz, 0°C.

Proton	^{1}H Chemical Shift (ppm)
H_{ext}	9.30
H_{int}	4.62
NH	8.98
H_5	8.05
H_3	6.49
NHCO	9.98
CH_3	2.00
H_6	7.59
OiBu CH_2	3.93-3.83
OiBu CH	2.37-2.26
OiBu CH_3	1.15

Table S3: TOCSY and ROESY correlations for OiBu macrocycle **5a** in $CDCl_3$, 300 MHz, 0°C.

TOCSY correlation ROESY correlation TOCSY + ROESY correlation		**Hext**	**Hint**	**NH**	**H5**	**H3**	**NHCO**	**CH_3**	**H6**	**OiBu CH_2**	**OiBu CH**	**OiBu CH_3**
		9.30	4.62	8.98	8.05	6.49	9.98	2.00	7.59	3.93-3.83	2.37-2.26	1.15
Hext	9.30		TOCSY									
Hint	4.62	TOCSY						ROESY				
NH	8.98				TOCSY	TOCSY		ROESY + TOCSY				
H5	8.05			TOCSY		TOCSY	ROESY	ROESY + TOCSY				
H3	6.49			TOCSY	TOCSY		ROESY	ROESY + TOCSY				
NHCO	9.98				ROESY	ROESY						
CH_3	2.00		ROESY	ROESY + TOCSY	ROESY + TOCSY	ROESY + TOCSY						
H6	7.59									ROESY		
OiBu CH_2	3.93-3.83								ROESY		TOCSY	TOCSY
OiBu CH	2.37-2.26									TOCSY		TOCSY
OiBu CH_3	1.15									TOCSY	TOCSY	

- *Nonamer, **12**:*

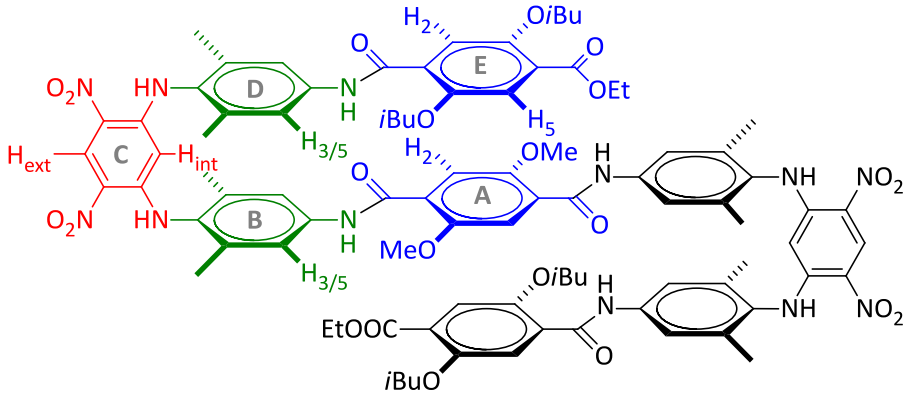


Table S4: ^{1}H and ^{13}C chemical shifts for nonamer **12** in $CDCl_3$, 400 MHz, +25°C.

Proton	^{1}H Chemical Shift (ppm)	^{13}C Chemical Shift (ppm)
H_{2A}	7.43	114.81
A-OCH_3	3.85	56.63
B-NHCO	9.76	
$H_{3/5B}$	7.39	119.90
B-CH_3	2.07	18.09
B-NH	9.12	
C-H_{int}	4.85	94.05
C-H_{ext}	9.36	129.57
D-NH	9.11	
D-CH_3	2.06	18.19
$H_{3/5D}$	7.34	119.71
D-NHCO	9.96	
H_{2E}	7.58	116.56
H_{5E}	7.05	115.52
E-OiBu α H_{2E} CH_2	3.66	75.87
E-OiBu α H_{5E} CH_2	3.69	76.48
E-OiBu α H_{2E} CH	2.03-2.00	28.45
E-OiBu α H_{5E} CH	2.25-2.18	28.57
E-OiBu α H_{2E} CH_3	0.98	19.32
E-OiBu α H_{5E} CH_3	1.11	19.56
E-COOEt CH_2	4.13	61.45
E-COOEt CH_3	1.23	14.32

Table S5: HSQC and HMBC correlation for nonamer **12** in $CDCl_3$, 400 MHz, +25°C.

HSQC correlation / HMBC correlation	A		B			C				D			E									
	H2	OCH_3	NHCO	H3/5	CH_3	B-NH	Hint	Hext	D-NH	CH_3	H3/5	NHCO	H2	H5	OiBu α H2E CH_2	OiBu α H5E CH_2	OiBu α H2E CH	OiBu α H5E CH	OiBu α H2E CH_3	OiBu α H5E CH_3	COOEt CH_2	COOEt CH_3
	7.43	3.85	9.76	7.39	2.07	9.12	4.85	9.36	9.11	2.06	7.34	9.96	7.58	7.05	3.66	3.69	2.03-2.00	2.25-2.18	0.98	1.11	4.13	1.23
166.03													■	■							■	
162.06												■	■	■								
161.41	■		■																			
152.48													■	■	■							
150.75	■	■																				
149.66													■	■		■						
148.37						■	■	■	■													
138.11				■							■	■										
137.03																						
136.82					■	■			■	■												
130.81																						
130.29																						
130.18					■	■			■	■												
129.57								■														
125.01																						
124.87	■												■	■								
123.85						■	■	■	■													
119.90			■	■	■																	
119.71										■	■	■										
118.79																						
116.56													■									
115.52														■								
114.81	■																					
94.05						■	■		■													
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19.32															■		■		■			
18.19										■	■											
18.09				■	■																	
14.32																					■	■

Table S6: TOCSY and ROESY correlation for nonamer **12** in $CDCl_3$, 400 MHz, +25°C.

TOCSY correlation
ROESY correlation
TOCSY + ROESY correlation

			A		B			C				D			E										
			H2	OCH_3	NHCO	H3/5	CH_3	B-NH	Hint	Hext	D-NH	CH_3	H3/5	NHCO	H2	H5	OiBu α H2E CH_2	OiBu α H5E CH_2	OiBu α H2E CH	OiBu α H5E CH	OiBu α H2E CH_3	OiBu α H5E CH_3	COOEt CH_2	COOEt CH_3
			7.43	3.85	9.76	7.39	2.07	9.12	4.85	9.36	9.11	2.06	7.34	9.96	7.58	7.05	3.66	3.69	2.03-2.00	2.25-2.18	0.98	1.11	4.13	1.23
A	H2	7.43																						
	OCH_3	3.85																						
B	NHCO	9.76																						
	H3/5	7.39																						
	CH_3	2.07																						
C	B-NH	9.12																						
	Hint	4.85																						
	Hext	9.36																						
	D-NH	9.11																						
D	CH_3	2.06																						
	H3/5	7.34																						
	NHCO	9.96																						
E	H2	7.58																						
	H5	7.05																						
	OiBu α H2E CH_2	3.66																						
	OiBu α H5E CH_2	3.69																						
	OiBu α H2E CH	2.03-2.00																						
	OiBu α H5E CH	2.25-2.18																						
	OiBu α H2E CH_3	0.98																						
	OiBu α H5E CH_3	1.11																						
	COOEt CH_2	4.13																						
	COOEt CH_3	1.23																						

- *Heptadecamer, **13** :*

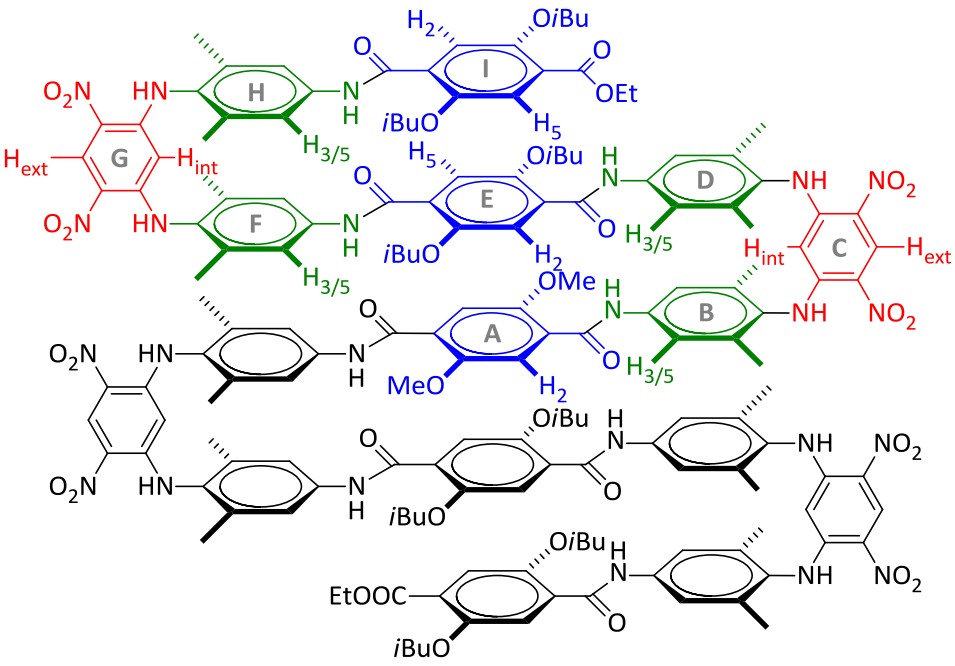


Table S7: ^{1}H and ^{13}C chemical shifts for heptadecamer **13** in $CDCl_3$, 400 MHz, +25°C.

Proton	^{1}H Chemical Shift (ppm)	^{13}C Chemical Shift (ppm)
H_{2A}	7.28	114.64
A-OCH_3	3.92	56.76
B-NHCO	9.44	
$H_{3/5B}$	7.05	119.14
B-CH_3	1.90	17.97
B-NH	8.83	
C-H_{int}	4.63	93.74
C-H_{ext}	9.34	129.53
D-NH	9.07	
D-CH_3	2.01	17.97
$H_{3/5D}$	7.27	119.37
D-NHCO	9.76	
H_{2E}	7.27	115.33
H_{5E}	7.39	115.33
E-OiBu α H_{2E} CH_2	3.64	76.21
E-OiBu α H_{5E} CH_2	3.70	76.37
E-OiBu α H_{2E} CH	2.30–2.17	28.45
E-OiBu α H_{5E} CH	2.30–2.17	28.45
E-OiBu α H_{2E} CH_3	1.14	19.67
E-OiBu α H_{5E} CH_3	1.14	19.67
F-NHCO	9.71	
$H_{3/5F}$	7.08	119.21
F-CH_3	1.91	17.97
F-NH	9.03	
G-H_{int}	4.69	93.94
G-H_{ext}	9.34	129.53
H-NH	9.09	
H-CH_3	1.97	17.97
$H_{3/5H}$	7.19	119.37
H-NHCO	9.77	
H_{2I}	7.53	116.59
H_{5I}	6.94	115.51
I-OiBu α H_{2I} CH_2	3.64	75.92
I-OiBu α H_{5I} CH_2	3.56	76.30
I-OiBu α H_{2I} CH	2.12-1.95	28.45
I-OiBu α H_{5I} CH	2.12-1.95	28.45
I-OiBu α H_{2I} CH_3	0.95	19.31
I-OiBu α H_{5I} CH_3	1.02	19.51
I-COOEt CH_2	4.06	61.36
I-COOEt CH_3	1.19	14.28

Table S8: HSQC and HMBC correlation for heptadecamer **13** in $CDCl_3$, 400 MHz, +25°C.

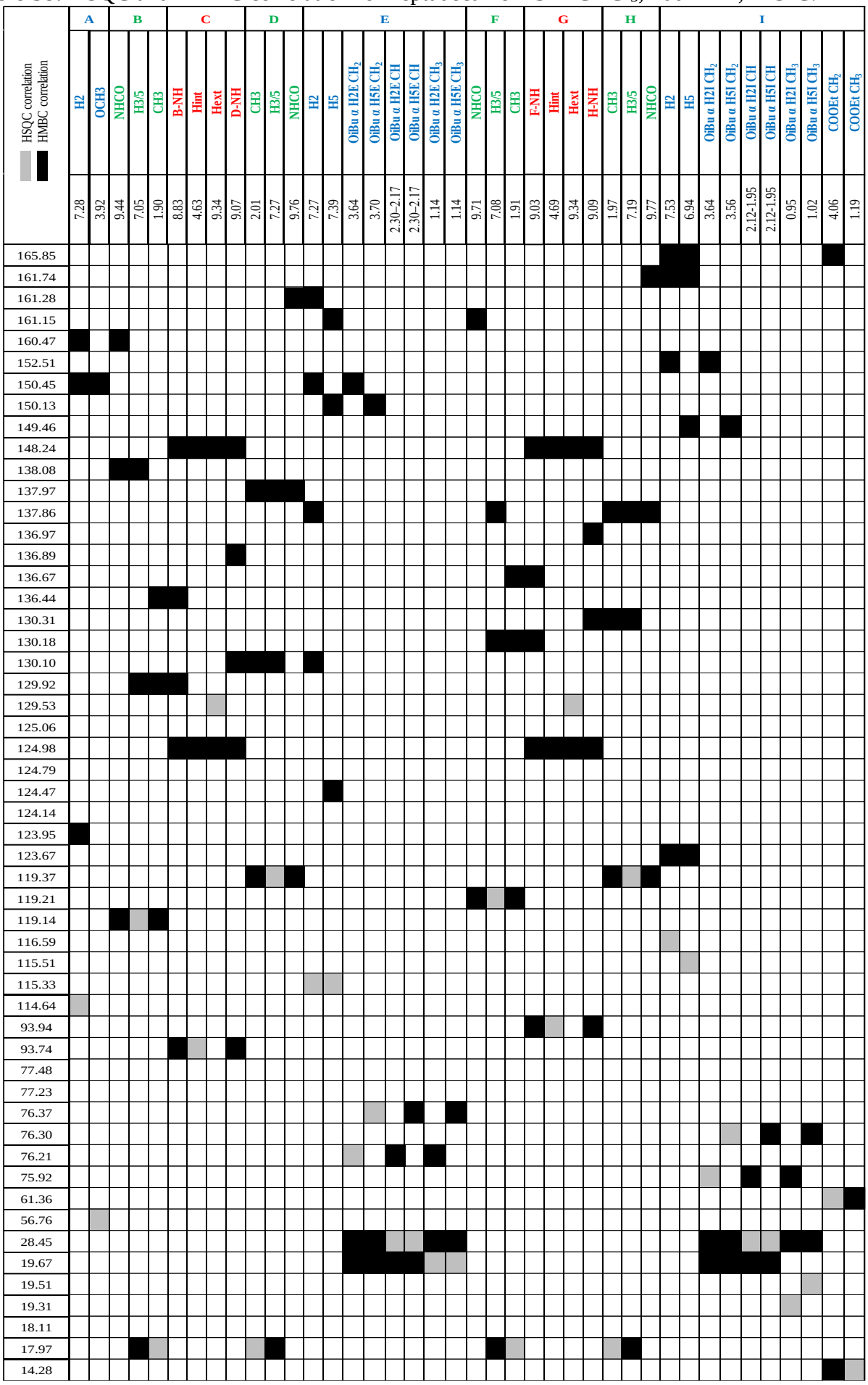
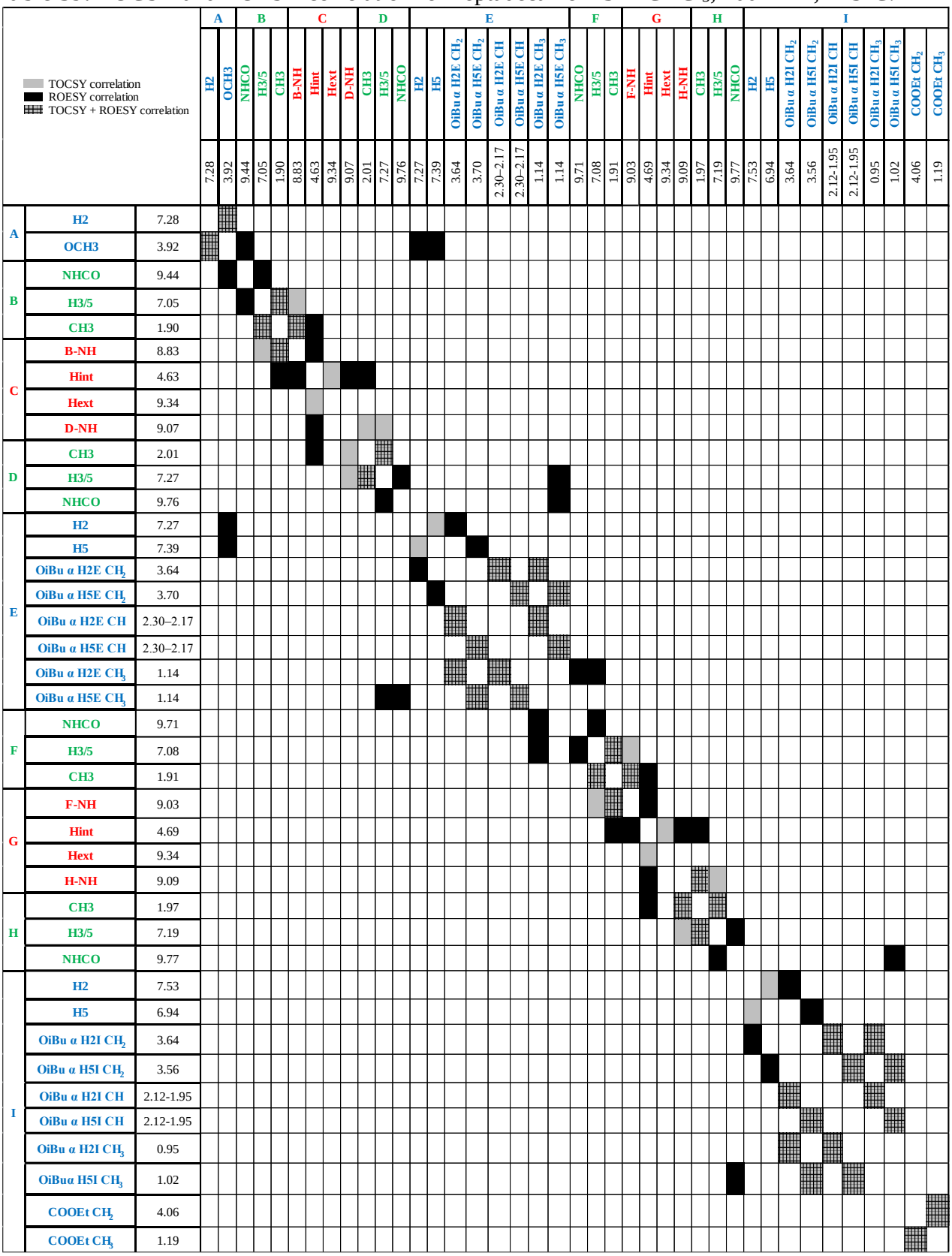


Table S9: TOCSY and ROESY correlation for heptadecamer **13** in $CDCl_3$, 400 MHz, +25°C.



Crystallography

1. Methods for X-ray crystallography

X-ray analyses were carried out at the IECB X-ray facility (UMS 3033 CNRS) on a R-Axis Rapid Rigaku MSC with a Cu Kα rotating anode and an image plate[2] as detector, a Bruker Enraf Nonius CAD4 diffractometer using the CuKalpha radiation, a Bruker Enraf Nonius Kappa CCD diffractometer using the MoKalpha radiation, both equipped with a sealed tube and a graphite monochromator, a Rigaku ultrabright FR-X rotating anode at the copper Kα wavelength and at the French CRG Beamline FIP at ESRF at the wavelength 0.81 Å. All the crystals collected at less than 200K were mounted on cryo-loops after quick soaking on Paratone—N oil from Hampton research to be flash-frozen. The unit cell determination, data reduction and collect on Kappa were performed using the supergui/EvalCCD program suite[3] on the full set of data. Except for CAD4 unit cell determination, all reflections were used for unit cell refinement. Data collected at the synchrotron were processed with the XDS software package. Data collected on Rigaku homesources were processed using the CrystalClear© suite. All the structures were solved by direct methods using SHELXS or SHELXD and refined using Shelx 97[4] in the integrated WinGX system[5]. The positions of the H atoms were deduced from coordinates of the non-H atoms and confirmed by Fourier synthesis. The non-H atoms were refined with anisotropic temperature parameters. H atoms were included for structure factor calculations but not refined. The BYPASS SQUEEZE[5b] procedure was used to take into account the electron density in the potential solvent area for the crystal structure of the compound 6 (the electron count is reported in the cif file). All the data collection and refinement statistics are reported in the tables below and in the cif files.

2. Summary of X-Ray crystallographic data

Table S10: X-ray crystallographic data.

Name	Trimer-N0$_2$ Phenyl Series **1a**, ***form 1***	Trimer-N0$_2$ Phenyl Series **1a**, ***form 2***	Trimer-NHboc Tolyl Series, **2b**	Trimer-H Tolyl Series, **2a**	Trimer-NHBoc Xylyl Series, **3b**	Trimer-H Xylyl Series, **3a**
Formula	$C_{20}H_{16}N_6O_9$	$C_{12}H_{8.50}N_{3.50}O_5$	$C_{30}H_{38}N_6O_9$	$C_{21.50}H_{21}N_4O_{4.50}$	$C_{33}H_{41}Cl_3N_6O_8$	$C_{22}H_{22}N_4O_4$
M	484.39	281.72	626.66	293(2)	756.07	406.44
Crystal system	Monoclinic	Orthorhombic	Triclinic	Triclinic	Triclinic	Triclinic
Space group	P 2_1/n	Pnma	P-1	P-1	P-1	P-1
***a*/Å**	7.434(4)	15.984(1)	7.442(1)	7.477(3)	13.057(2)	11.949(1)
***b*/Å**	21.865(6)	16.622(7)	12.755(2)	11.703(4)	16.599(2)	13.229(1)
***c*/Å**	12.827(3)	9.1600(10)	18.706(1)	12.598(4)	20.386(4)	15.912(1)
α/o	90.00	90.00	74.31(1)	73.99(3)	71.84(1)	103.066(4)
β/o	90.51(3)	90.00	82.69(1)	74.91(3)	87.53(2)	112.628(5)
γ/o	90.00	90.00	76.12(1)	77.42(3)	66.90(1)	104.644(5)
U/Å^3	2084.9(14)	2433.7(11)	1655.9(3)	1010.3(6)	3845.7(10)	2093.8(3)
T /*K*	278(2)	293(2)	293(2)	293(2)	293(2)	293(2)
Z	4	8	2	2	4	4
ρ/g cm^{-1}	1.543	1.538	1.257	1.339	1.306	1.289
Size (mm)	0.15 x 0.10 x 0.10	0.25 x 0.20 x 0.20	0.28 x 0.19 x 0.12	0.15 x 0.15 x 0.12	0.25 x 0.25 x 0.12	0.10 x 0.08 x 0.05
λ/ Å	1.5418	1.54180	0.71073	1.54180	0.71073	1.54180
μ/mm^{-1}	1.071	1.055	0.094	0.793	0.293	0.745
Absorption correction	none	Psi-scan	Semi-empirical from equivalents	none	Semi-empirical from equivalents	none
Unique data	3750	2232	6870	3748	14558	7560
Restraints/Parameters	0/317	0/194	2/422	31/292	9/933	0/550
Final R indices [I>2sigma(I)]	R1= 0.0558, wR2= 0.1223	R1 = 0.0507, wR2 = 0.1404	R1= 0.0504, wR2= 0.1252	R1= 0.0747, wR2= 0.1730	R1= 0.0788, wR2= 0.1802	R1= 0.0555, wR2= 0.1373
R indices (all data)	R1= 0.1047, wR2= 0.1520	R1 = 0.0618, wR2 = 0.1518	R1= 0.0871, wR2= 0.1464	R1= 0.0901, wR2= 0.1840	R1= 0.1130, wR2= 0.2001	R1= 0.0810, wR2= 0.1546
Goodness of fit	1.047	1.032	1.020	1.052	1.057	1.012

Table S11: X-ray crystallographic data (continued).

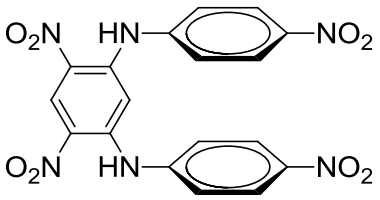
Name	Tetramer-NH_2, **18**	Octamer-NH_2, **6**	Nonamer, **12**	Heptadecamer, **13**
Formula	$C_{80}H_{92}N_{12}O_{18}$	$C_{78}H_{90}N_{12}O_{17}$	$C_{94}H_{106}Cl_{12}N_{12}O_{22}$	$C_{87}H_{101}Cl_6N_{12}O_{20}S$
M	1509.66	1467.63	2181.3	1879.55
Crystal system	Monoclinic	Monoclinic	Triclinic	Triclinic
Space group	P 2_1/c	P2_1/n	P-1	P-1
***a*/Å**	21.202(4)	13.922(3)	12.784(2)	15.248(3)
***b*/Å**	15.209(3)	22.269(5)	14.385(2)	16.890(3)
***c*/Å**	24.506(5)	30.117(6)	15.914(2)	19.555(4)
α/o	90.00	90.00	112.032(4)	85.29(3)
β/o	95.07(3)	102.16(3)	99.694(5)	67.30(3)
γ/o	90.00	90.00	98.655(3)	83.12(3)
U/Å^3	7871	9128(3)	2600.0(6)	4609.2(19)
T /*K*	296	213	123	100
Z	8	4	1	2
ρ/g cm^{-1}	1.274	1.068	1.393	1.354
Size (mm)	0.4x0.2x0.1	0.1x0.05x0.01	0.1x0.1x0.1	0.05x0.05x0.05
λ/ Å	1.54178	1.54178	1.54178	1.54178
μ/mm^{-1}	0.752	0.627	3.545	2.536
Absorption correction	Multi-scan	Multi-scan	Multi-scan	Multi-scan
Unique data	14823	6849	9161	12862
Parameters/Restraints	991/0	953/75	644/26	1136/15
R1/wR2	0.0908/0.2839	0.1732/0.4199	0.085/0.2366	0.1364/0.3537
Goodness of fit	1.061	1.755	1.084	1.337

Methods for molecular modelling

Molecular Models calculation were done using MacroModel version 8.6 (Schrödinger Inc.) with the modified MM3 force-field as implemented in this software. Energy minimized structures were obtained using 500 steps of Truncated Newton Conjugate Gradient (TNCG), chloroform as implicit solvent and the extended Cutoff option.

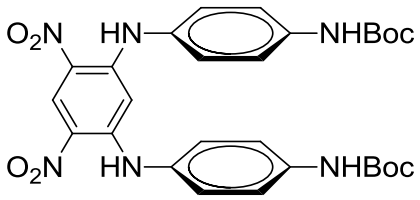
Experimental section

General. All reactions were carried out under a dry nitrogen atmosphere. Commercial reagents were purchased from Sigma-Aldrich, TCI Chemicals or Alfa-Aesar and were used without further purification unless otherwise specified. Tetrahydrofurane (THF) and dichloromethane (DCM) were dried over alumina columns; chloroform, triethylamine (Et_3N) and diisopropylethylamine (DIEA) were distilled over calcium hydride (CaH_2) prior to use. Reactions were monitored by thin layer chromatography (TLC) on Merck silica gel 60-F254 plates and observed under UV light. Column chromatography purifications were carried out on Merck GEDURAN Si60 (40-63 µm). Circular chromatography purifications were carried out on Chromatotron® with silica gel, Merck grade 7749, TLC grade with binder and fluorescent indicator. NMR spectra were recorded on Bruker 300 Avance II, Bruker 400 DPX or Bruker Avance III 700 NB US. Chemical shifts are expressed in parts per million (ppm, δ) using residual solvent protons as internal standards (chloroform: δ 7.26 ppm; DMSO: δ 2.50 ppm). Coupling constants are expressed in Hertz. ESI and MALDI mass spectra were obtained on a Waters LCT Premier and a Bruker Reflex III spectrometers respectively, from the Mass Spectrometry Laboratory at the European Institute of Chemistry and Biology (UMS 3033 - IECB), Pessac, France and a Voyager DE-STR mass spectrometer from AB Sciex, Les Ulis, France.



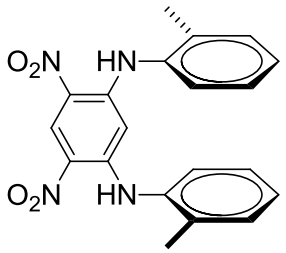
1a

Hairpin turn phenyl series 1a. To 4-nitroaniline (0.283 g, 2 mmol) dissolved in DMSO (5 mL) was added 1,5-difluoro-2,4-dinitrobenzene (0.209 g, 1 mmol). After stirring for 3h at room temperature, distilled DIEA (360 µL, 2 mmol) was added. Then the reaction mixture was allowed to proceed at +80 °C for 48h. After addition of water (30 mL), the mixture was filtered. The residue was purified by chromatography (SiO_2) eluting with CH_2Cl_2 to obtain the product **1a** as a yellow solid (0.252 g, 56% yield). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 10.06 (s, 2H), 9.38 (s, 1H), 8.28 (d, *J* = 8.9 Hz, 4H), 7.36 (d, *J* = 8.9 Hz, 4H), 6.96 (s, 1H). ^{1}H NMR (DMSO-d_6, 300 MHz): δ 10.01 (s, 2H), 9.00 (s, 1H), 8.28 (d, *J* = 9.1 Hz, 4H), 7.55 (d, *J* = 9.1 Hz, 4H), 6.86 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 145.39, 143.48, 143.20, 128.34, 127.71, 125.28, 122.25, 103.62. HRMS (ES^-): *m/z* calcd for $C_{18}H_{11}N_6O_8$ $[M-H]^-$ 439.06329 Found 439.06419.



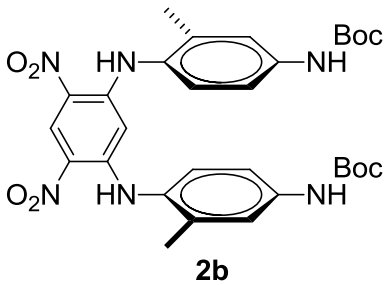
1b

Hairpin turn phenyl series 1b. Compound **1c**[6] (0.05 g, 0.13 mmol) and di-tert-butyl dicarbonate (0.086 g, 0.34 mmol) were dissolved in THF (1 mL). The mixture reaction was heated for 24h at +70 °C then evaporated. The product **1b** was purified by precipitation in Et_2O (0.071 g, 93% yield). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 9.58 (s, 2H), 9.29 (s, 1H), 7.34 (d, *J* = 8.7 Hz, 4H), 7.05 (d, *J* = 8.7 Hz, 4H), 6.65 (s, 2H), 6.39 (s, 1H), 1.54 (s, 18H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 152.97, 147.36, 136.97, 132.27, 129.41, 125.85, 125.40, 120.54, 95.55, 80.93, 28.57. HRMS (ES^-): *m/z* calcd for $C_{28}H_{31}N_6O_8$ $[M-H]^-$ 579.2198 found 579.2205.



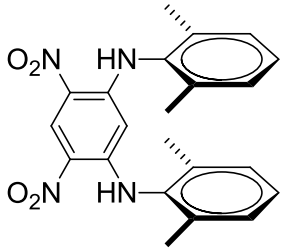
2a

Hairpin turn tolyl series 2a. To o-toluidine (0.185 g, 1.72 mmol) dissolved in DMSO (5 mL) was added 1,5-difluoro-2,4-dinitrobenzene (0.176 g, 0.86 mmol). After stirring for 3h at room temperature, distilled DIEA (150 µL, 0.86 mmol) was added. The reaction mixture was allowed to proceed at room temperature for 2 days. After addition of water (100 mL), the mixture was filtered. The precipitate was solubilized in AcOEt and washed with H_2O. After evaporation, the residue was purified by precipitation in MeOH and product **2a** was obtained as orange solid (0.258 g, 79% yield). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 9.53 (s, 2H), 9.32 (s, 1H), 7.22 – 7.01 (m, 8H), 5.78 (s, 1H), 2.16 (s, 6H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 147.47, 135.60, 134.22, 131.35, 129.36, 127.44, 126.99, 126.01, 125.16, 94.87, 17.72. HRMS (ES^-): *m/z* calcd for $C_{20}H_{17}N_4O_4$ $[M-H]^-$ 377.12491 found 377.12559.



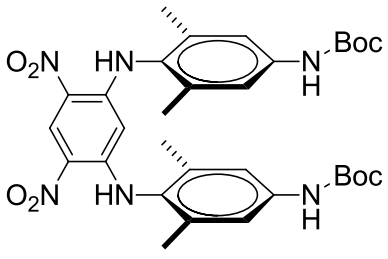
2b

Hairpin turn tolyl series 2b. Compound **20** (0.255 g, 1.1 mmol) dissolved in DMSO (10 mL) was added 1,5-difluoro-2,4-dinitrobenzene (0.078 g, 0.4 mmol). After stirring for 3h at room temperature, distilled DIEA (80 µL, 0.4 mmol) was added. The reaction mixture was allowed to proceed at room temperature for 2 days. After addition of water (150 mL), the mixture was filtered. The precipitate was solubilized in AcOEt and washed with H_2O. After evaporation, the residue was purified by chromatography (SiO_2) eluting with $CHCl_3$ to obtain the product **2b** as a purple solid (0.148 g, 64% yield). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 9.37 (s, 2H), 9.30 (s, 1H), 7.24 (d, *J* = 1.9 Hz, 2H), 7.08 (dd, *J* = 8.5, 2.3 Hz, 2H), 6.94 (d, *J* = 8.5 Hz, 2H), 6.68 (s, 2H), 5.71 (s, 1H), 2.08 (s, 6H), 1.54 (s, 18H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 153.07, 147.82, 137.41, 135.32, 130.85, 129.38, 126.98, 125.19, 121.97, 118.18, 95.25, 80.83, 28.56, 17.92. HRMS (ES^-): *m/z* calcd for $C_{36}H_{35}N_6O_8$ $[M-H]^-$ 607.2508 found 607.25325.



3a

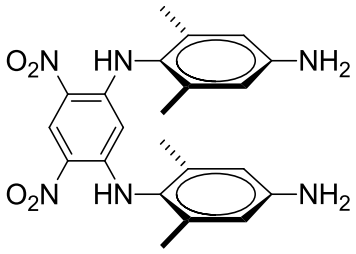
Hairpin turn xylyl series 3a. To dimethylaniline (500 µl, 4.12 mmol) dissolved in DMSO (2 mL) was added 1,5-difluoro-2,4-dinitrobenzene (210 mg, 1.03 mmol). After stirring for 3h at room temperature, distilled DIEA (0.2 mL, 1.15 mmol) was added. The reaction mixture was allowed to proceed at +60 °C for 24h. After addition of water (10 mL), the mixture was filtered. After drying, the product **3a** was obtained as a yellowish solid (253 mg, 66% yield). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 9.36 (s, 1H), 9.22 (s, 2H), 7.09 – 6.88 (m, 6H), 4.82 (s, 1H), 2.02 (s, 12H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 148.10, 135.87, 134.20, 129.55, 128.58, 128.35, 128.12, 93.64, 17.82. HRMS (ES^-): *m/z* calcd for $C_{22}H_{21}N_4O_4$ $[M-H]^-$ 405.1558 Found 405.15830.



3b

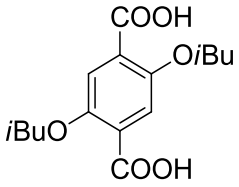
Hairpin turn xylyl series 3b. To compound **16** (2.394 g, 10 mmol) dissolved in DMSO (150 mL) was added 1,5-difluoro-2,4-dinitrobenzene (1.034 g, 5 mmol). After stirring for 3h at room temperature, distilled DIEA (1.7 mL, 10 mmol) was added. The reaction mixture was allowed to proceed at +80 °C for 10 days. After addition of water (150 mL), the mixture was filtered. The precipitate was solubilized in AcOEt and washed with H_2O. After evaporation, the residue was purified by chromatography (SiO_2) eluting with

CH_2Cl_2/petroleum ether (75:25, vol/vol) to obtain the product **3b** as a yellowish solid (2 g, 62% yield). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 9.31 (s, 1H), 9.08 (s, 2H), 6.96 (s, 4H), 6.70 (s, 2H), 4.91 (s, 1H), 1.95 (s, 12H), 1.56 (s,18H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 153.07, 148.07, 137.56, 136.53, 129.73, 129.27, 124.94, 119.46, 94.48, 80.69, 28.48, 17.89. HRMS (ES^-): *m/z* calcd for $C_{32}H_{39}N_6O_8$ $[M-H]^-$ 635.2824 Found 635.2834.



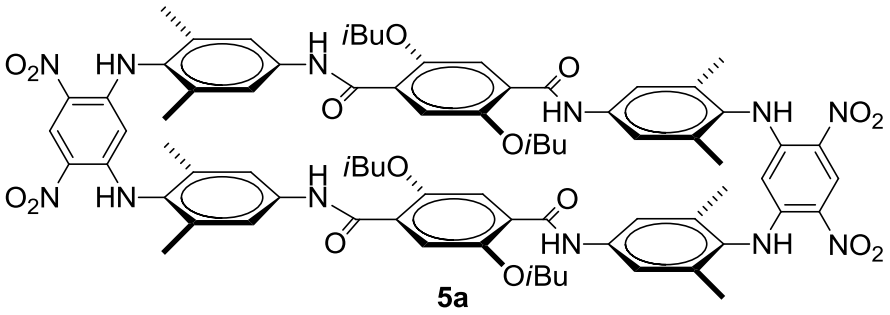
3c

Hairpin turn xylyl series 3c. Compound **3b** (0.16 g, 0.25 mmol) was dissolved in a mixture 20% TFA/CH_2Cl_2 (10 mL). The reaction mixture was allowed to proceed at room temperature for 4h. Toluene (10 mL) was added to the reaction mixture and the solution was evaporated. The residue was dissolved in AcOEt (20 mL), and washed with saturated $NaHCO_3$, dried over Na_2SO_4, filtered, and then concentrated to give compound **3c** (0.108 g, 99% yield) as a red solid which was used without further purification. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 9.31 (s, 1H), 9.00 (s, 2H), 6.31 (s, 4H), 4.90 (s, 1H), 3.58 (br, 4H), 1.92 (s, 12H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 149.02, 146.22, 137.07, 129.61, 125.47, 124.88, 114.97, 93.92, 17.96. HRMS (ES^+): *m/z* calcd for $C_{22}H_{23}N_6O_4$ $[M+H]^+$ 435.1781 Found 435.1773.



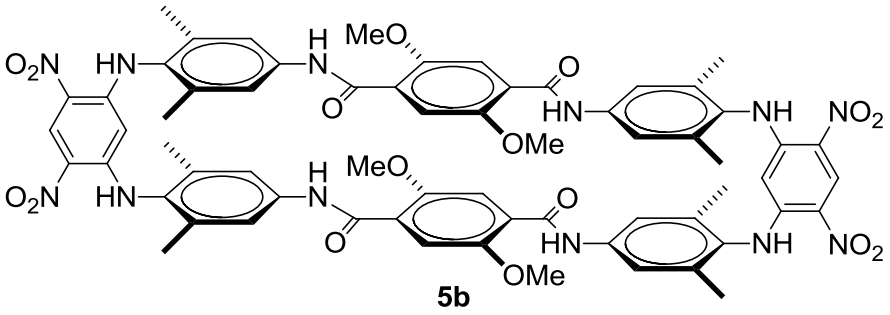
4a

2,5-diisobutoxyterephthalic acid 4a. Compound **15** (0.5 g, 1.4 mmol) and potassium hydroxyde (0.383 g, 6.8 mmol) were dissolved in a mixture dioxane/H_2O (3:1). The reaction mixture was allowed to proceed at room temperature for 16h. The dioxane was evaporated and the solution acidified to pH =1 by HCl 1N. The compound **4a** was extracted by AcOEt, washed with H_2O, dried over Na_2SO_4, filtered and then concentrated to give expected compound (0.42 g, 99% yield) as a white solid which was used without further purification. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 11.08 (br, 2H), 7.86 (s, 2H), 4.07 (d, *J* = 6.5 Hz, 4H), 2.23 (dt, *J* = 13.3, 6.7 Hz, 2H), 1.09 (d, *J* = 6.7 Hz, 12H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 164.20, 151.96, 122.73, 117.59, 77.52, 28.21, 19.24. HRMS (ES^+): *m/z* calcd for $C_{16}H_{23}O_6$ $[M+H]^+$ 311.1489 Found 311.1495.



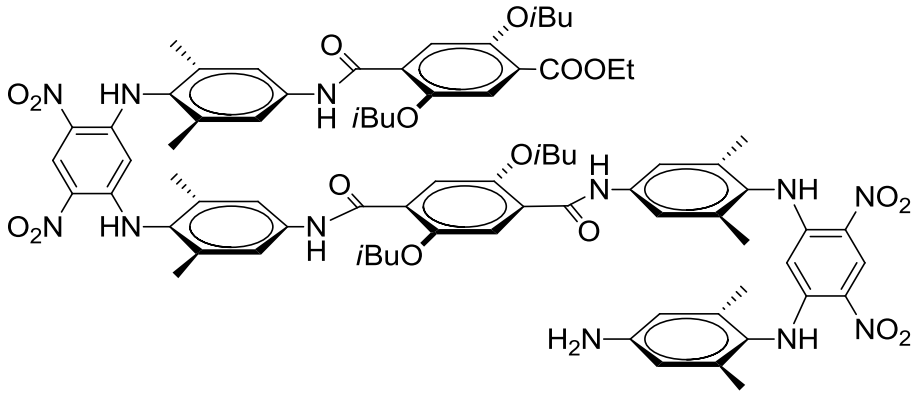
5a

Macrocycle OiBu 5a. Compound **3c** (0.052 g, 0.12 mmol) and compound **4a** (0.037 g, 0.12 mmol) were dissolved in $CHCl_3$ (170 mL), then distilled DIEA (125 μL, 0.71 mmol) and PyBOP (0.372 g, 0.71 mmol) were added. The reaction mixture was allowed to reach +45 °C and stirred for 7 days. Then the solution was washed with H_2O and evaporated. The residue was purified by flash chromatography (SiO_2) eluting with CH_2Cl_2/MeOH (95:5, vol/vol), and circular chromatography (SiO_2) eluting with CH_2Cl_2 to obtain product **5a** as a yellowish solid (0.037 g, 44% yield). ^{1}H NMR ($CDCl_3$, 300 MHz, 0°C): δ 9.98 (s, 4H), 9.30 (s, 2H), 8.98 (s, 4H), 8.05 (s, 4H), 7.59 (s, 4H), 6.49 (s, 4H), 4.62 (s, 2H), 3.93-3.83 (br, 8H), 2.00 (s, 24H), 1.20 (d, *J* = 7.8 Hz, 12H), 1.11 (d, *J* = 5.9 Hz, 12H). ^{13}C NMR ($CDCl_3$, 75 MHz): No recorded ^{13}C spectrum due to low solubility. HRMS (ES^+): m/z calcd for $C_{76}H_{85}N_{12}O_{16}$ $[M+H]^+$ 1421.6186 Found 1421.6189.



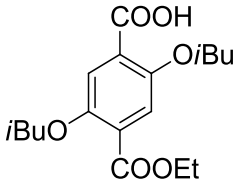
5b

Macrocycle OMe 5b. Compound **3c** (0.051 g, 0.11 mmol) and 2,5-dimethoxyterephthalic acid[7] (0.026 g, 0.11 mmol) were dissolved in $CHCl_3$ (157 mL), then distilled DIEA (122 μL, 0.7 mmol) and PyBOP (0.365 g, 0.7 mmol) were added. The reaction mixture was allowed to reach +45 °C and stirred for 7 days. Then the solution was washed with H_2O and evaporated. The residue was purified by flash chromatography (SiO_2) eluting with CH_2Cl_2/MeOH, and precipitation in MeOH and CH_2Cl_2 to obtain product **5b** as a yellowish solid (0.010 g, 7% yield). ^{1}H NMR ($CDCl_3$, 300 MHz, -25°C): δ 9.98 (s, 4H), 9.44 (s, 2H), 9.12 (s, 4H), 7.77 (s, 4H), 7.44 (s, 8H), 4.81 (s, 2H), 4.18 (s, 12H), 2.17 (s, 24H). ^{13}C NMR ($CDCl_3$, 75 MHz): No recorded ^{13}C spectrum due to low solubility. HRMS (ES^-): *m/z* calcd for $C_{64}H_{59}N_{12}O_{16}$ $[M-H]^-$ 1251.4158 Found 1251.4163.



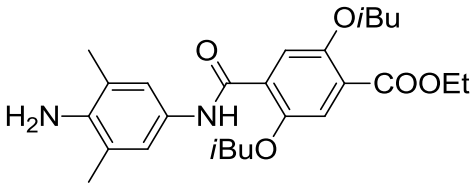
6

Octamer-amine 6. Compound **19** (0.072 g, 46 μmol) was dissolved in a solution 20% TFA/CH_2Cl_2 (10 mL) and stirred for 4h at room temperature. Then toluene (10 mL) was added to the solution and evaporated. The residue was dissolved in AcOEt (20 mL), washed with saturated $NaHCO_3$, dried over Na_2SO_4, filtered and then concentrated to give compound **6** (0.065 g, 99% yield) as a yellowish solid which was used without further purification. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 10.04 (s, 1H), 10.01 (s, 1H), 9.98 (s, 1H), 9.35 (s, 1H), 9.34 (s, 1H), 9.14 (s, 1H), 9.08 (s, 4H), 9.04 (s, 1H), 7.74 (s, 1H), 7.73 (s, 1H), 7.70 (s, 1H), 7.41 (s, 2H), 7.35 (s, 2H), 7.33 (s, 2H), 7.11 (s, 1H), 6.29 (s, 2H), 4.91 (s, 1H), 4.81 (s, 1H), 4.26 (q, *J* = 7.2 Hz, 2H), 3.90 (d, *J* = 6.7 Hz, 4H), 3.77 (d, *J* = 6.6 Hz, 2H), 3.71 (d, *J* = 6.6 Hz, 2H), 2.34-2.22 (m, 4H), 2.07 (s, 6H), 2.05 (s, 12H), 1.92 (s, 6H), 1.33 (t, *J* = 7.2 Hz, 3H), 1.16 (dd, *J* = 12.1, 6.5 Hz, 18H), 1.05 (d, *J* = 6.7 Hz, 6H).^{13}C NMR ($CDCl_3$, 75 MHz): No recorded ^{13}C spectrum due to low solubility. HRMS (ES^+): *m/z* calcd for $C_{78}H_{91}N_{12}O_{17}$ $[M+H]^+$ 1467.6620 Found 1467.6596.



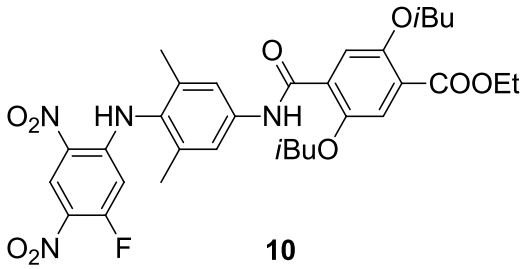
7

4-(ethoxycarbonyl)-2,5-diisobutoxybenzoic acid 7. Compound **15** (1 g, 2.7 mmol) and potassium hydroxyde (0.109 g, 2.7 mmol) were dissolved in a mixture dioxane/H_2O (3:1). The reaction mixture was allowed to proceed at room temperature for 16h. The dioxane was evaporated and the solution acidified to pH =1 by HCl 1N. Compounds were extracted by CH_2Cl_2, washed with H_2O, dried over Na_2SO_4, filtered, and then concentrated. Compound **7** was purified by flash chromatography (SiO_2) eluting with CH_2Cl_2/AcOEt (5:5, vol/vol) as a white solid (0.453 g, 49% yield). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.67 (s, 1H), 7.39 (s, 1H), 4.35 (q, *J* = 7.1 Hz, 2H), 3.97 (d, *J* = 6.5 Hz, 2H), 3.77 (d, *J* = 6.4 Hz, 2H), 2.26–1.98 (m, 4H), 1.36 (t, *J* = 7.1 Hz, 3H), 1.04 (d, *J* = 6.7 Hz, 6H), 1.00 (d, *J* = 6.7 Hz, 6H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 165.79, 164.81, 152.75, 150.69, 126.20, 120.93, 117.30, 115.83, 75.82, 61.64, 28.14, 19.12, 14.27. HRMS (ES^-): *m/z* calcd for $C_{18}H_{25}O_6$ $[M-H]^-$ 337.1646 Found 337.1652.



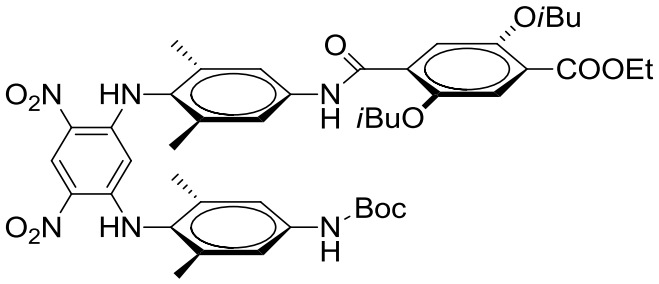
9

Dimer Xylene-Terephtalate 9. To 2,6-dimethylbenzene-1,4-diamine[8] **8** (0.4 g, 3 mmol) and compound **7** (1 g, 3 mmol) dissolved in CH_2Cl_2 (10 mL) was added EDCI (0.68 g, 3.5 mmol). The reaction mixture was allowed to proceed for 24h at room temperature. Then the solution was washed with H_2O and evaporated. The residue was purified by flash chromatography (SiO_2) eluting with CH_2Cl_2/MeOH, and then precipitation in cyclohexane to obtain after filtration product **9** as a yellowish solid (1.099 g, 82% yield). ^{1}H NMR (DMSO-d_6, 300 MHz): δ 9.85 (s, 1H), 7.90 (s, 1H), 7.40 (s, 1H), 7.26 (s, 2H), 4.37 (q, J = 7.1 Hz, 2H), 3.94 (d, J = 6.5 Hz, 2H), 3.84 (d, J = 6.5 Hz, 2H), 3.52 (br, 2H), 2.28-2.06 (m, 2H), 2.18 (s, 6H), 1.38 (t, J = 7.1 Hz, 3H), 1.11 (d, J = 6.7 Hz, 6H), 1.03 (d, J = 6.7 Hz, 6H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 166.36, 161.85, 152.77, 149.86, 139.90, 129.01, 125.88, 123.63, 122.24, 120.88, 116.80, 115.77, 76.52, 75.80, 61.40, 28.58, 28.48, 19.50, 19.26, 17.90, 14.40. HRMS (ES$^+$): *m/z* calcd for $C_{26}H_{36}N_2O_5$ $[M+H]^+$ 457.2703 Found 457.27014.



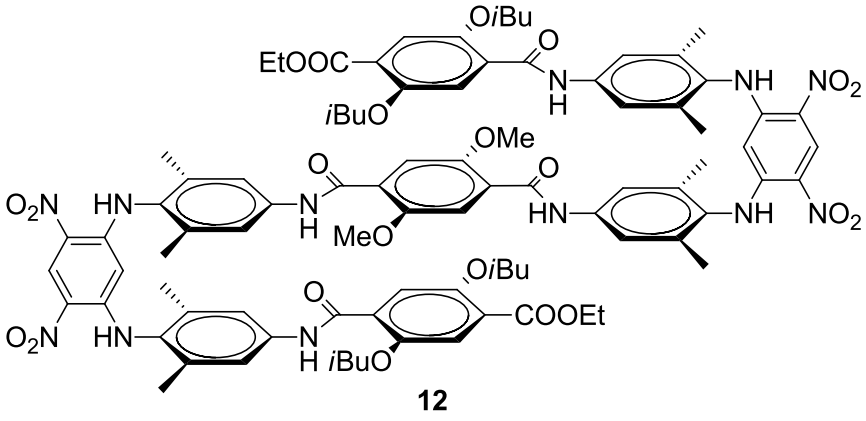
10

Trimer Turn-Xylene-Terephtalate 10. To compound **9** (1.09 g, 2.4 mmol) dissolved in DMSO (30 mL) was added 1,5-difluoro-2,4-dinitrobenzene (0.487 g, 2.4 mmol). The reaction mixture was allowed to proceed for 4h at room temperature. Then H_2O was added to the mixture. After filtration, the precipitate was redissolved in CH_2Cl_2, washed with H_2O, dried over Na_2SO_4, filtered, and then concentrated. Compound **10** (1.461 g, 95% yield) was purified by flash chromatography (SiO_2) eluting with cyclohexane/AcOEt (8:2, vol/vol) as a yellowish solid. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 10.19 (s, 1H), 9.55 (s, 1H), 9.19 (d, J = 7.7 Hz, 1H), 7.89 (s, 1H), 7.57 (s, 2H), 7.44 (s, 1H), 6.21 (d, J = 13.1 Hz, 1H), 4.40 (q, J = 7.1 Hz, 2H), 4.01 (d, J = 6.5 Hz, 2H), 3.86 (d, J = 6.4 Hz, 2H), 2.41–2.08 (m, 2H), 2.21 (s, 6H), 1.41 (t, J = 7.1 Hz, 3H), 1.16 (d, J = 6.0 Hz, 6H), 1.05 (d, J = 6.7 Hz, 6H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 166.29, 162.76, 161.62, 158.93, 152.83, 150.02, 149.23 (d, J = 12.7 Hz), 138.77, 137.10, 129.40, 128.12, 127.45, 127.08 (d, J = 9.1 Hz), 124.76 (d, J = 17.7 Hz), 120.66, 116.80, 115.95, 102.49 (d, J = 27 Hz), 76.70, 75.89, 61.64, 28.70, 28.53, 19.58, 19.30, 18.48, 14.45. HRMS (ES$^-$): *m/z* calcd for $C_{32}H_{36}N_4O_9F$ $[M-H]^-$ 639.2466 Found 639.24652.



11

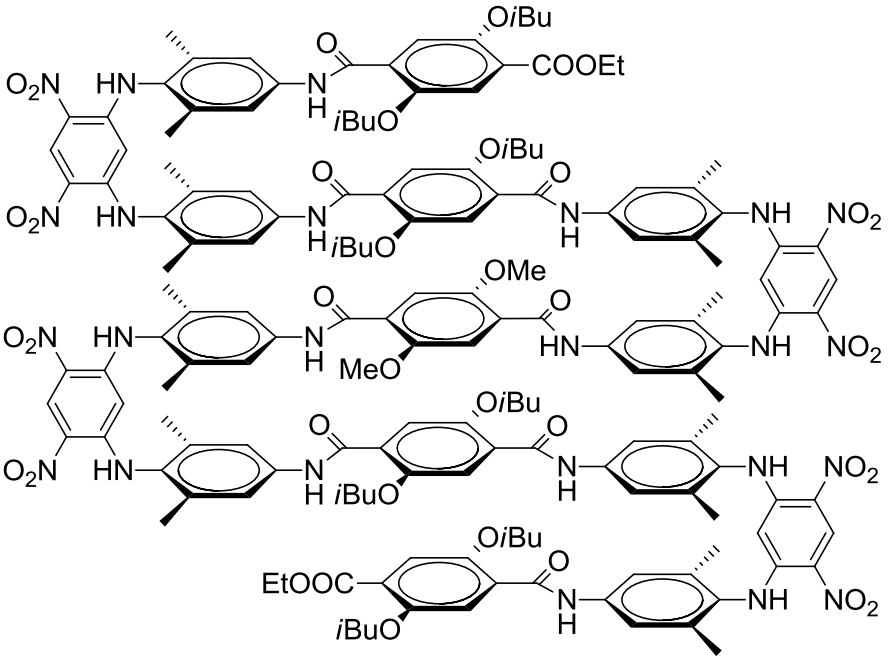
Tetramer Xylene-Turn-Xylene-Terephtalate 11. To compound **10** (1.461 g, 2.3 mmol) and compound **16** (0.538 g, 2.3 mmol) dissolved in DMSO (40 mL) was added distilled DIEA (0.4 mL, 2.3 mmol). The reaction mixture was allowed to proceed for 3 days at +80 °C. Then H_2O was added to the mixture. Products were extracted with CH_2Cl_2, washed with H_2O, dried over Na_2SO_4, filtered, and then concentrated. Compound **11** (0.979 g, 50% yield) was purified by flash chromatography (SiO_2) eluting with CH_2Cl_2 as a yellowish solid. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 10.10 (s, 1H), 9.34 (s, 1H), 9.11 (s, 2H), 7.95 (s, 1H), 7.46 (s, 1H), 7.27 (s, 2H), 7.01 (s, 2H), 6.63 (s, 1H), 4.87 (s, 1H), 4.42 (q, *J* = 7.1 Hz, 2H), 4.01 (d, J = 6.5 Hz, 2H), 3.90 (d, *J* = 6.5 Hz, 2H), 2.37–2.12 (m, 2H), 2.04 (s, 6H), 1.99 (s, 6H), 1.42 (t, *J* = 7.1 Hz, 3H), 1.29 (s, 9H) 1.16 (d, *J* = 6.7 Hz, 6H), 1.08 (d, *J* = 6.7 Hz, 6H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 166.32, 162.78, 152.94, 150.12, 148.52, 148.18, 138.11, 137.47, 137.09, 136.59, 130.77, 129.56, 129.23, 124.96, 120.68, 119.02, 116.95, 115.91, 94.02, 75.99, 61.66, 28.69, 28.62, 28.25, 19.55, 19.36, 18.19, 18.05, 14.49. HRMS (ES^+): *m/z* calcd for $C_{45}H_{57}N_6O_{11}$ $[M+H]^+$ 857.40861 Found 857.40897.



12

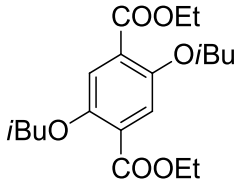
Nonamer 12. 2,5-dimethoxyterephtalic acid (0.010 g, 0.05 mmol) was suspended in anhydrous $CHCl_3$ (1 mL). 1-chloro-*N*,*N*,2-trimethyl-1-propenylamine (29 μL, 0.23 mmol) was added and the reaction was allowed to stir at room temperature for 3h. The reaction mixture solubilizes after 1h. The solvent and excess reagents were removed under vacuum and the residue was dried under vacuum for at least 2h to yield acid chloride as a white solid. To a solution of compound **19** (0.068 g, 0.09 mmol) and distilled DIEA (38 μL, 0.22 mmol) in anhydrous $CHCl_3$ (1 mL) was added dropwise a solution of the freshly prepared diacid chloride in anhydrous $CHCl_3$ (1 mL) via a syringe. The reaction was allowed to proceed at room temperature for 16h. The solution was washed with H_2O, dried over Na_2SO_4, filtered, and then concentrated. The residue was purified by precipitation in MeOH getting **12** as a yellowish solid (0.069 g, 90% yield). ^{1}H NMR ($CHCl_3$, 300 MHz): δ 9.96 (s, 2H), 9.76 (s, 2H), 9.36 (s, 2H), 9.12 (s, 2H), 9.11 (s, 2H), 7.58 (s, 2H), 7.43 (s, 2H), 7.39 (s, 4H), 7.34 (s, 4H), 7.05 (s,

2H), 4.85 (s, 2H), 4.13 (q, *J* = 7.1 Hz, 4H), 3.85 (s, 6H), 3.69 (d, *J* = 6.6 Hz, 4H), 3.66 (d, *J* = 6.5 Hz, 4H), 2.25-2.18 (m, 2H), 2.07 (s, 12H), 2.06 (s, 12H), 2.03-2.00 (m, 2H), 1.23 (t, *J* = 7.2 Hz, 6H), 1.11 (d, *J* = 6.7 Hz, 12H), 0.98 (d, *J* = 6.7 Hz, 12H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 166.03, 162.06, 161.41, 152.48, 150.75, 149.66, 148.37, 138.11, 137.03, 136.82, 130.81, 130.29, 130.18, 129.57, 125.01, 124.87, 123.85, 119.90, 119.71, 118.79, 116.56, 115.52, 114.81, 94.05, 76.48, 75.87, 61.45, 56.63, 29.85, 29.66, 28.57, 28.45, 19.56, 19.32, 18.19, 18.09, 14.32. MS(MALDI-TOF): *m/z* calcd for $C_{90}H_{103}N_{12}O_{22}$ $[M+H]^+$ 1703.72 Found 1703.70.



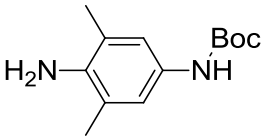
13

Heptadecamer 13. Compound **13** was obtained following the same procedure as for synthesis of compound **12** with 2,5-dimethoxyterephtalic acid (0.020 g**,** 0.09 mmol) converted to acyl chloride by 1-chloro-*N*,*N*,2-trimethyl-1-propenylamine (58 µL, 0.44 mmol) in anhydrous $CHCl_3$ (1 mL). After drying for 2h under vaccum, the freshly prepared acyl chloride solution (1 mL $CHCl_3$) was added dropwise to a solution of compound **6** (0.259 g, 0.17 mmol) and distilled DIEA (73 µL, 0.42 mmol) in anhydrous $CHCl_3$ (2 mL). Same work-up as for compound **12** leads to compound **13** (0.256 g, 93% yield) as yellowish solid. ^{1}H NMR ($CHCl_3$, 300 MHz): δ 9.77 (s, 2H), 9.76 (s, 2H), 9.71 (s, 2H), 9.44 (s, 2H), 9.34 (s, 4H), 9.09 (s, 2H), 9.07 (s, 2H), 9.03 (s, 2H), 8.83 (s, 2H), 7.53 (s, 2H), 7.39 (s, 2H), 7.28 (s, 2H), 7.27 (br, 6H), 7.19 (s, 4H), 7.08 (s, 4H), 7.05 (s, 4H), 6.94 (s, 2H), 4.69 (s, 2H), 4.63 (s, 2H), 4.06 (q, *J* = 7.1 Hz, 4H), 3.92 (s, 6H), 3.70 (d, *J* = 6.6 Hz, 4H), 3.64 (dd, 8H), 3.56 (d, *J* = 6.6 Hz, 4H), 2.30–2.17 (m, 4H), 2.12-1.95 (m, 4H), 2.01 (s, 12H), 1.97 (s, 12H), 1.91 (s, 12H), 1.90 (s, 12H), 1.19 (t, *J* = 7.2 Hz, 6H), 1.14 (dd, 24H), 1.02 (d, *J* = 6.7 Hz, 12H), 0.95 (d, *J* = 6.7 Hz, 12H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 165.85, 161.74, 161.28, 161.15, 160.47, 152.51, 150.45, 150.13, 149.46, 148.24, 138.08, 137.97, 137.86, 136.97, 136.89, 136.67, 136.44, 130.31, 130.18, 130.10, 129.92, 129.53, 125.06, 124.98, 124.79, 124.47, 124.14, 123.95, 123.67, 119.37, 119.21, 119.14, 116.59, 115.51, 115.33, 114.64, 93.94, 93.74, 77.48, 77.16, 76.37, 76.30, 76.21, 75.92, 61.36, 56.76, 28.45, 19.67, 19.51, 19.31, 18.11, 17.97, 14.28. HRMS (ES^+): m/z calcd for $C_{166}H_{186}N_{24}O_{38}$ $[M]^+$ 3125.391 Found 3125.35752.



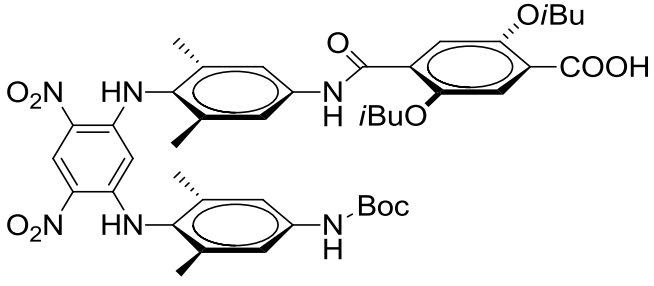
15

Diethyl 2,5-diisobutoxyterephthalate 15. Diethyl 2,5-dihydroxyterephthalate **14** (1.45 g, 5.7 mmol) was dissolved in THF (15 mL) then triphenylphosphine (5.2 g, 20 mmmol) and isobutanol (1.8 mL, 20 mmol) were added, followed by the dropwise addition of diisopropylazodicarboxylate (3.9 mL, 20 mmol). The reaction mixture was allowed to proceed at room temperature for 16h. The solution was evaporated and the residue was purified by flash chromatography (SiO_2) eluting with CH_2Cl_2 to obtain product **15** as a white solid (3.04 g, 86% yield). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.31 (s, 2H), 4.36 (q, *J* = 7.1 Hz, 4H), 3.75 (d, *J* = 6.4 Hz, 4H), 2.09 (dt, *J* = 13.2, 6.7 Hz, 2H), 1.37 (t, *J* = 7.1 Hz, 3H), 1.02 (d, *J* = 6.7 Hz, 12H).^{13}C NMR ($CDCl_3$, 75 MHz): δ 166.34, 151.79, 124.67, 116.42, 76.07, 61.36, 28.55, 19.27, 14.39. HRMS (ES$^+$): *m/z* calcd for $C_{20}H_{31}O_6$ $[M+H]^+$ 367.21214 Found 367.21224.



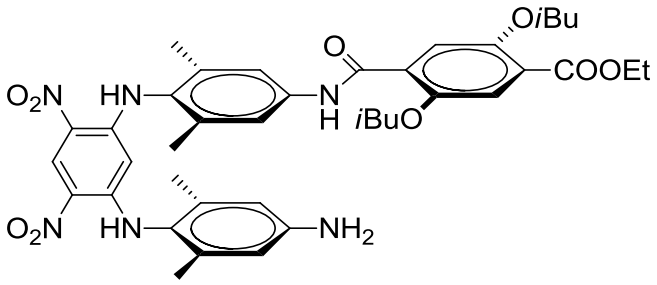
16

***Tert*-butyl 4-amino-3,5-dimethylphenylcarbamate 16.** To 2,6-dimethylbenzene-1,4-diamine[8] **8** (1.718 g, 13 mmol) dissolved in THF (25 mL) was added di-tert-butyl dicarbonate (2.75 g, 13 mmol). After stirring for 16h at room temperature, the reaction mixture was evaporated. The residue was purified by chromatography (SiO_2) eluting with cyclohexane/AcOEt (8:2, vol/vol) to obtain the product **16** as a dark green solid (2.4 g, 80% yield). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 6.93 (s, 2H), 6.29 (s, 1H), 3.43 (s, 2H), 2.14 (s, 6H), 1.50 (s, 9H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 153.53, 138.92, 128.99, 122.44, 120.00, 79.90, 28.49, 17.81. HRMS (ES$^+$): *m/z* calcd for $C_{13}H_{21}N_2O_2$ $[M+H]^+$ 237.16218 Found 237.16098.



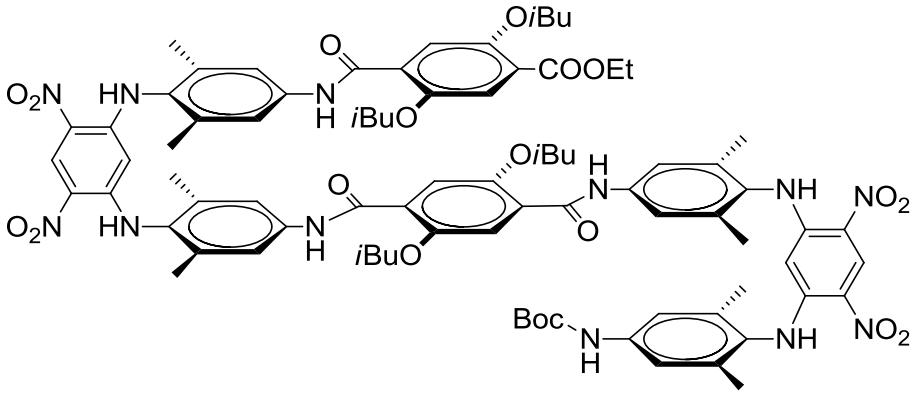
17

Tetramer-COOH 17. Compound **11** (0.088 g, 0.1 mmol) and potassium hydroxyde (0.033 g, 0.5 mmol) were dissolved in a mixture THF/MeOH (2:1). The reaction mixture was allowed to proceed at room temperature for 24h. The dioxane was evaporated and the solution acidified by a solution 5% citric acid until precipitation. Compound **17** (0.07 g, 80% yield) was obtained by filtration as a yellowish solid which was used without further purification. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 10.08 (s, 1H), 9.34 (s, 1H), 9.13 (s, 1H), 9.12 (s, 1H), 8.09 (s, 1H), 7.87 (s, 1H), 6.99 (s, 2H), 6.60 (s, 1H), 4.87 (s, 1H), 4.15 (d, *J* = 6.5 Hz, 2H), 4.07 (d, *J* = 6.5 Hz, 2H), 2.33-2.23 (m, 2H), 2.05 (s, 6H), 2.00 (s, 6H), 1.32 (s, 9H), 1.17 (d, *J* = 6.7 Hz, 6H), 1.12 (d, *J* = 6.7 Hz, 6H).



18

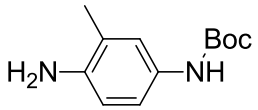
Tetramer-NH_2 18. Compound **11** (0.1 g, 0.11 mmol) was dissolved in a solution 20% TFA/CH_2Cl_2 (5 mL) and stirred for 4h at room temperature. Then toluene (10 mL) was added to the solution and evaporated. The residue was dissolved in CH_2Cl_2 (20 mL), and washed with saturated $NaHCO_3$, dried over Na_2SO_4, filtered and then concentrated to give compound **18** (0.087 g, 99% yield) as a yellowish solid which was used without further purification. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 10.09 (s, 1H), 9.32 (s, 1H), 9.09 (s, 1H), 9.01 (s, 1H), 7.91 (s, 1H), 7.46 (s, 1H), 7.33 (s, 2H), 6.24 (s, 2H), 4.88 (s, 1H), 4.42 (q, *J* = 7.1 Hz, 2H), 4.03 (d, *J* = 6.5 Hz, 2H), 3.88 (d, *J* = 6.5 Hz, 2H), 2.36-2.13 (m, 2H), 2.04 (s, 6H), 1.90 (s, 6H), 1.42 (t, *J* = 7.1 Hz, 3H), 1.18 (d, *J* = 6.7 Hz, 6H), 1.07 (d, *J* = 6.7 Hz, 6H).



19

Octamer 19. To compound **18** (0.067 g, 0.08 mmol) and compound **17** (0.051 g, 0.07 mmol) dissolved in $CHCl_3$ (1 mL) were added distilled DIEA (24 µL, 0.13 mmol) and PyBOP (0.07 g, 0.13 mmol). The reaction mixture was allowed to proceed for 3 days at +45 °C. Then the solution was washed with H_2O, dried over

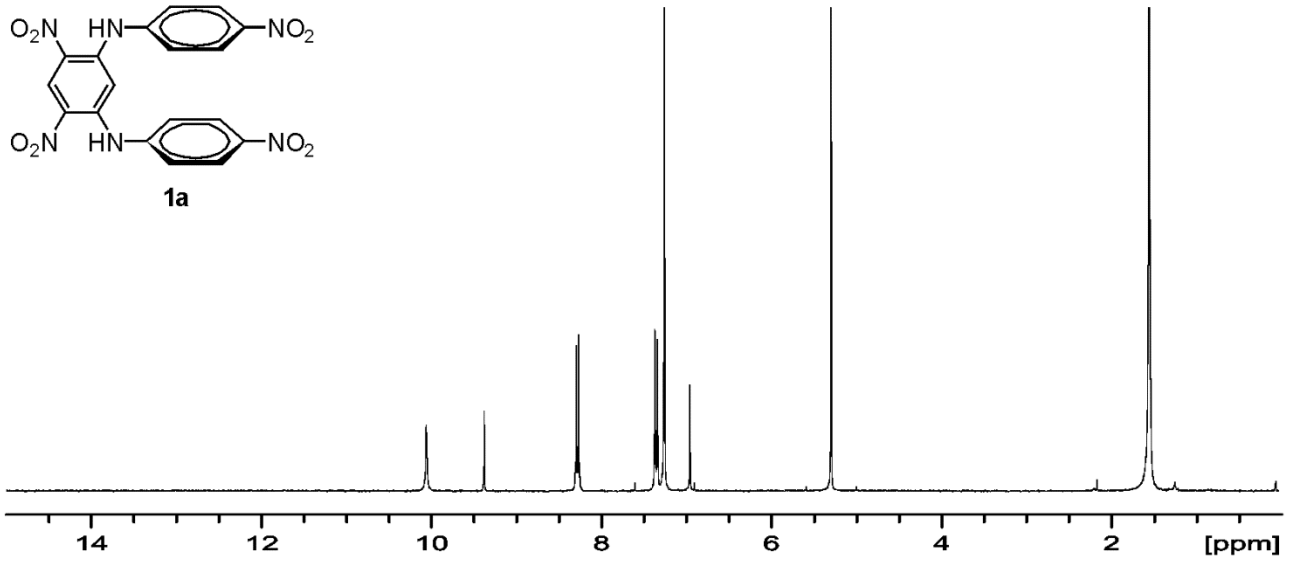
Na_2SO_4, filtered, and concentrated. The residue was purified by flash chromatography (SiO_2) eluting with CH_2Cl_2 to obtain compound **19** as a yellowish solid (0.073 g, 69% yield). ^{1}H NMR ($CHCl_3$, 300 MHz): δ 10.04 (s, 1H), 10.00 (s, 1H), 9.99 (s, 1H), 9.35 (s, 1H), 9.34 (s, 1H), 9.17 (s, 1H), 9.14 (s, 1H), 9.09 (s, 1H), 7.78 (s, 1H), 7.71 (s, 1H), 7.70 (s, 1H), 7.35 (dd, *J* = 4.6, 1.5 Hz, 6H), 7.16 (s, 1H), 7.00 (s, 2H), 4.92 (s, 1H), 4.82 (s, 1H), 4.21 (q, *J* = 7.1 Hz, 2H), 3.93 (d, *J* = 6.8 Hz, 2H), 3.90 (d, *J* = 6.9 Hz, 2H), 3.75 (d, *J* = 6.5 Hz, 4H), 2.35-2.13 (m, 4H), 2.06 (s, 6H), 2.06 (s, 12H), 2.01 (s, 6H), 1.32 (t, *J* = 7.1 Hz, 3H), 1.27 (s, 9H), 1.17-1.14 (m, 18H), 1.04 (d, *J* = 6.7 Hz, 6H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 166.26, 162.29, 162.04, 161.82, 152.92, 152.70, 150.82, 150.71, 149.75, 148.49, 148.36, 148.28, 148.21, 138.18, 138.09, 137.94, 137.71, 137.18, 137.10, 136.90, 136.51, 130.64, 130.52, 130.39, 129.61, 129.50, 129.26, 125.34, 125.10, 125.05, 125.02, 124.98, 124.67, 123.88, 120.56, 119.85, 119.80, 116.72, 116.14, 115.81, 94.17, 93.97, 80.19, 76.01, 61.58, 29.85, 28.66, 28.63, 28.57, 28.54, 28.25, 19.64, 19.59, 19.52, 19.40, 18.23, 18.16, 18.08, 14.38. HRMS (ES^+): *m/z* calcd for $C_{83}H_{99}N_{12}O_{19}$ $[M+H]^+$ 1567.715 Found 1567.71476.



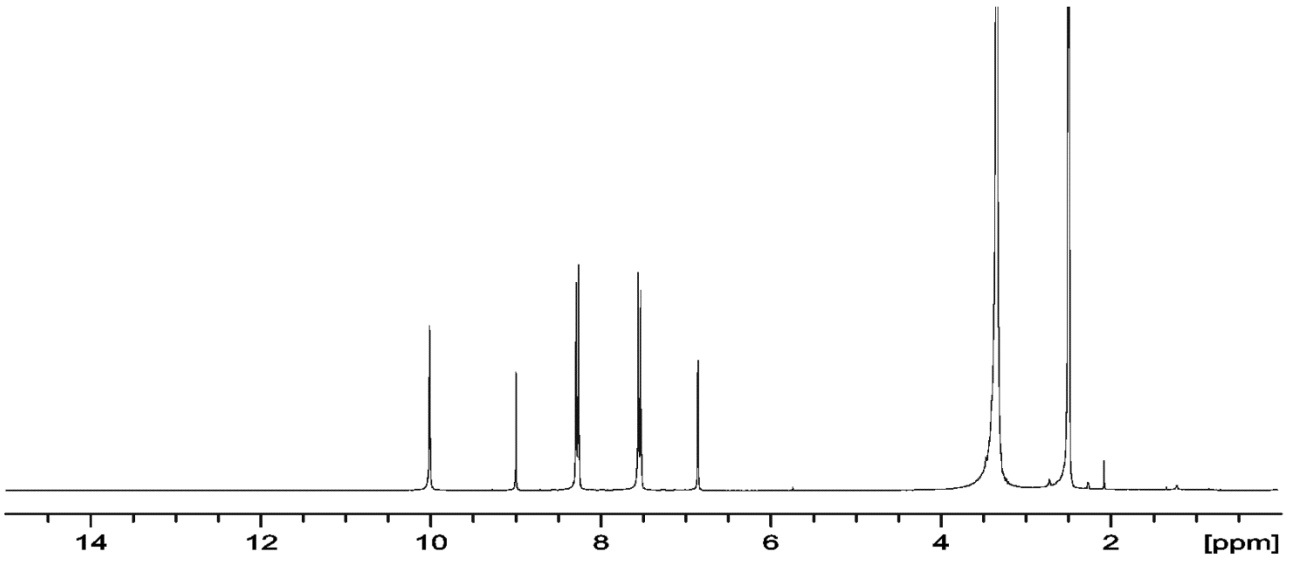
20

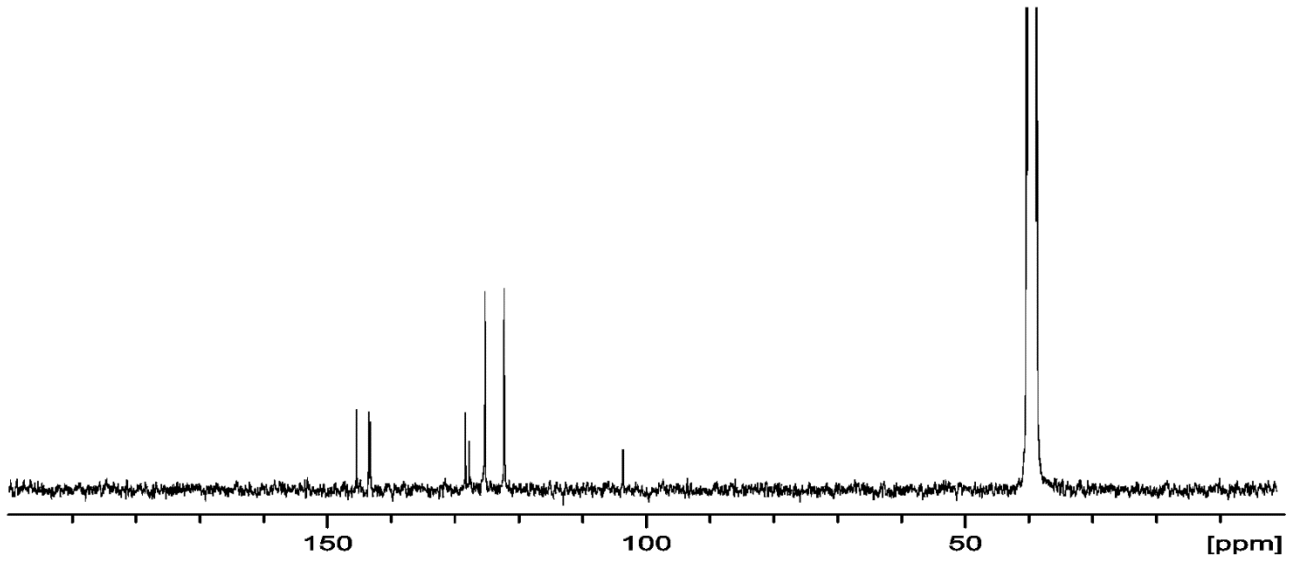
***tert*-butyl 4-amino-3-methylphenylcarbamate 20.**[9] To *tert*-butyl 3-methyl-4-nitrophenylcarbamate[10] (0.393 g, 1.6 mmol) dissolved in AcOEt (50 mL) was added 10% Pd/C (0.04 g). The reaction mixture was stirred for 48h under hydrogen at atmospheric pressure. After filtration through celite and concentration, the product **20** was obtained as purple oil (0.263 g, 76% yield) and used without further purification. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.09 (s, 1H), 6.95 (dd, *J* = 8.3, 2.2 Hz, 1H), 6.60 (d, *J* = 8.4 Hz, 1H), 6.27 (s, 1H), 3.36 (br, 2H), 2.14 (s, 3H), 1.50 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 153.48, 140.59, 129.61, 123.00, 122.15, 118.55, 115.29, 79.78, 28.38, 17.41. HRMS (ES^+): *m/z* calcd for $C_{12}H_{19}N_2O_2$ $[M+H]^+$ 223.1442 Found 223.14355.

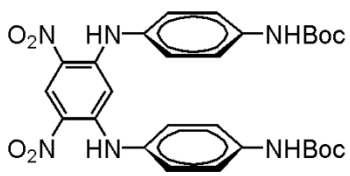
^{1}H NMR spectra of all relevant synthetic intermediates and title compounds.



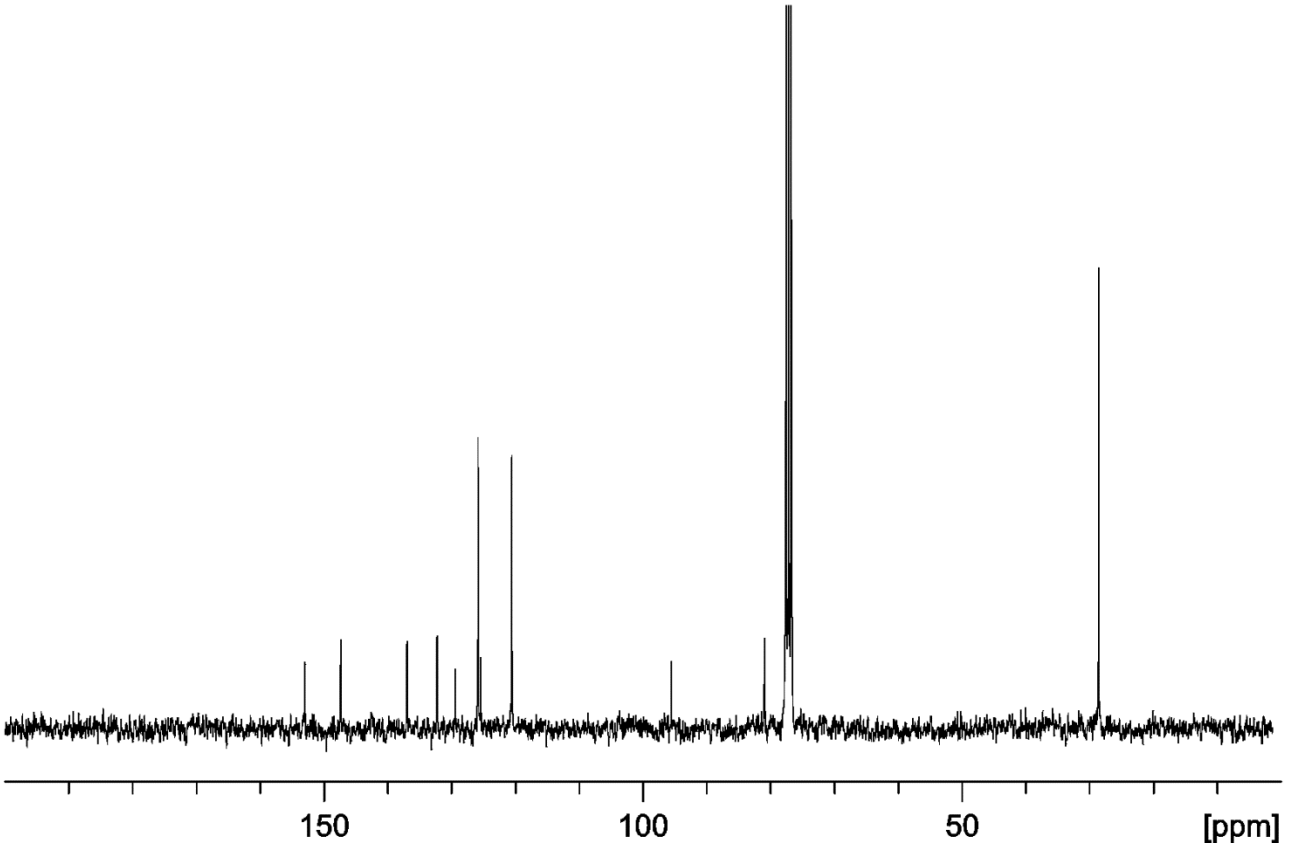
1a

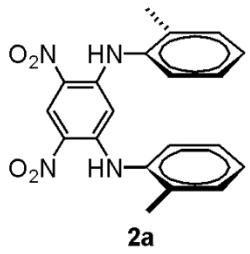




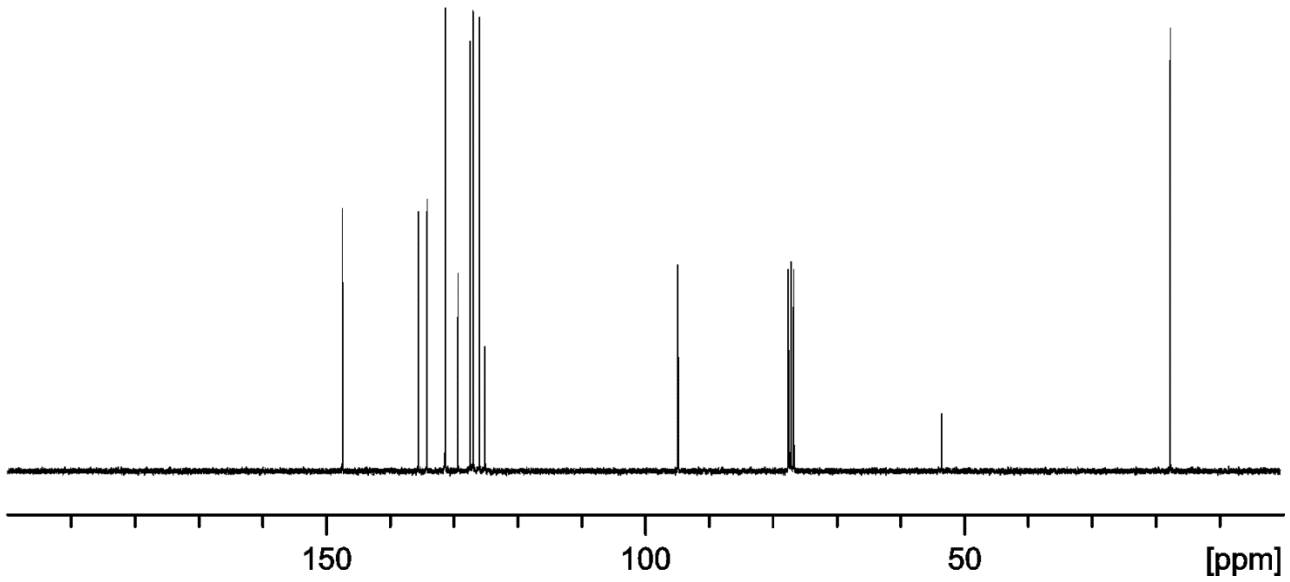


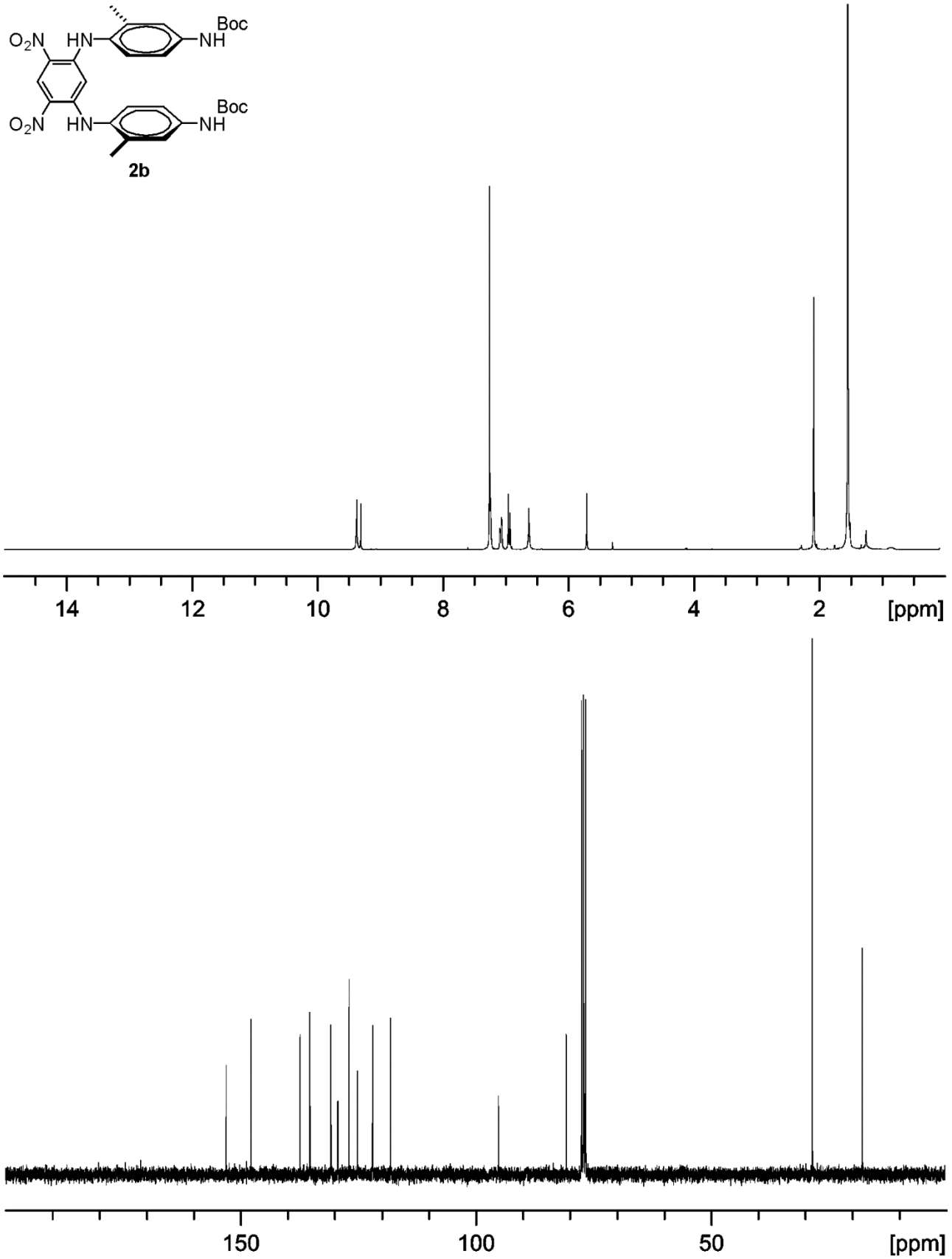
1b

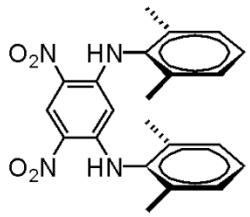




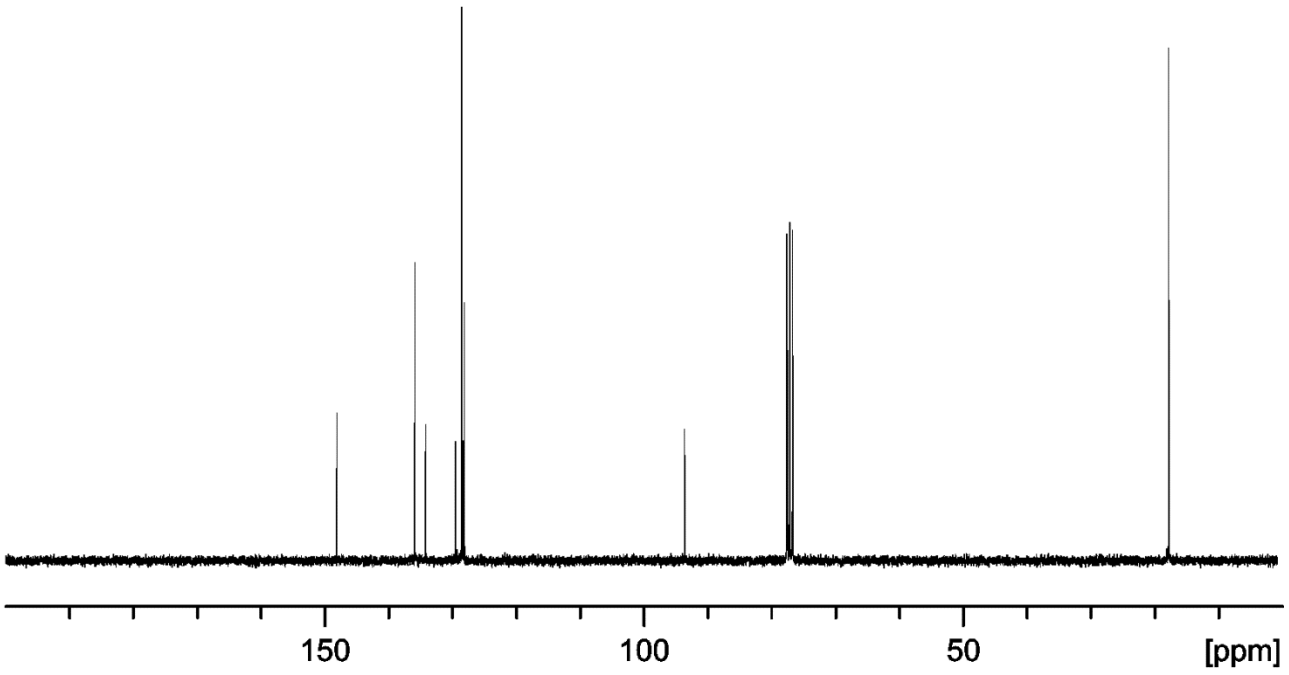
2a

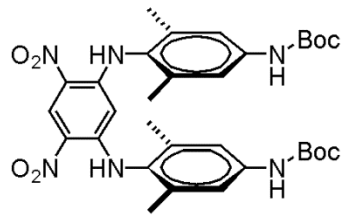



O2N
HN
Boc
NH
O2N
HN
Boc
NH
2b
14
12
10
8
6
4
2
[ppm]
150
100
50
[ppm]

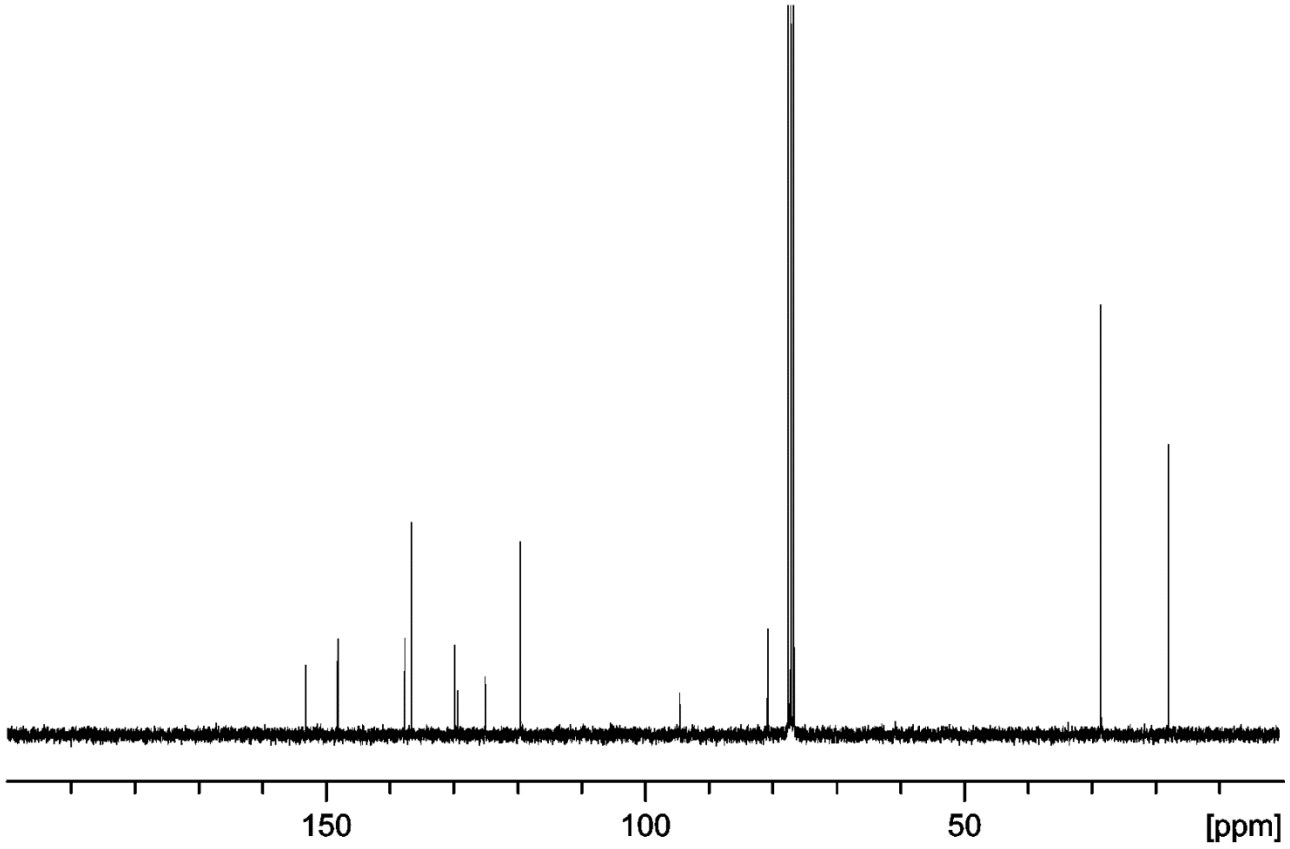


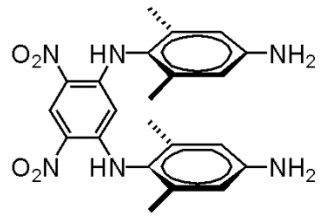
3a



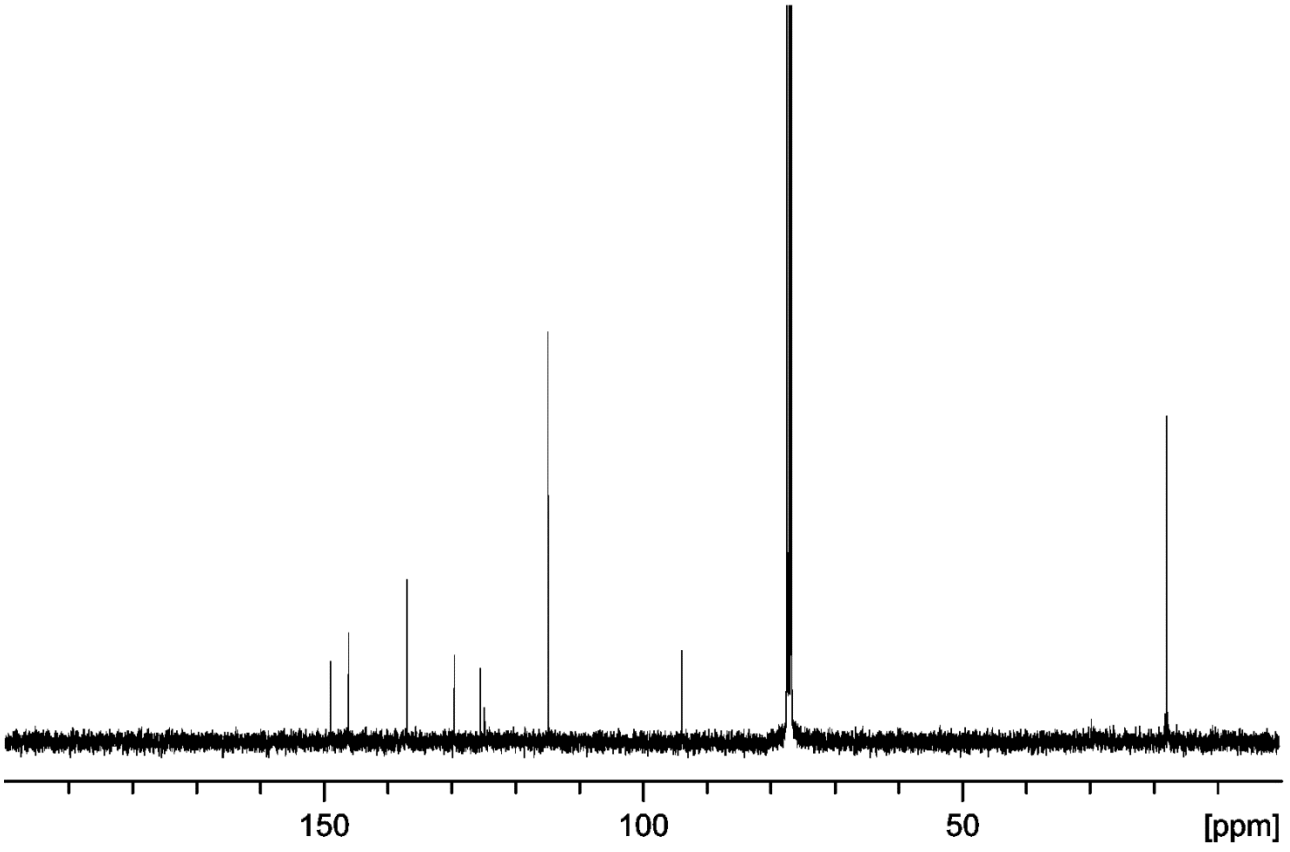


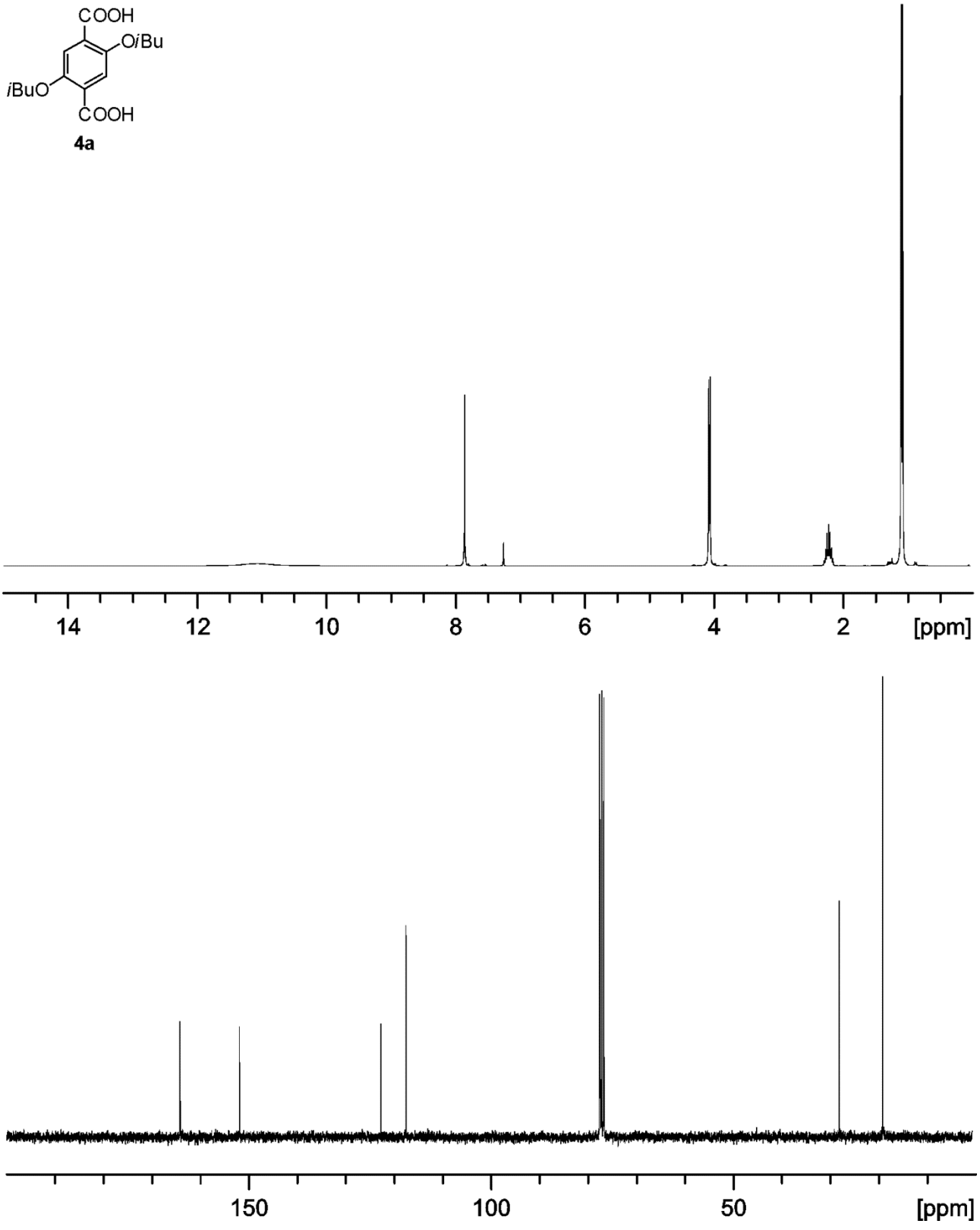
3b

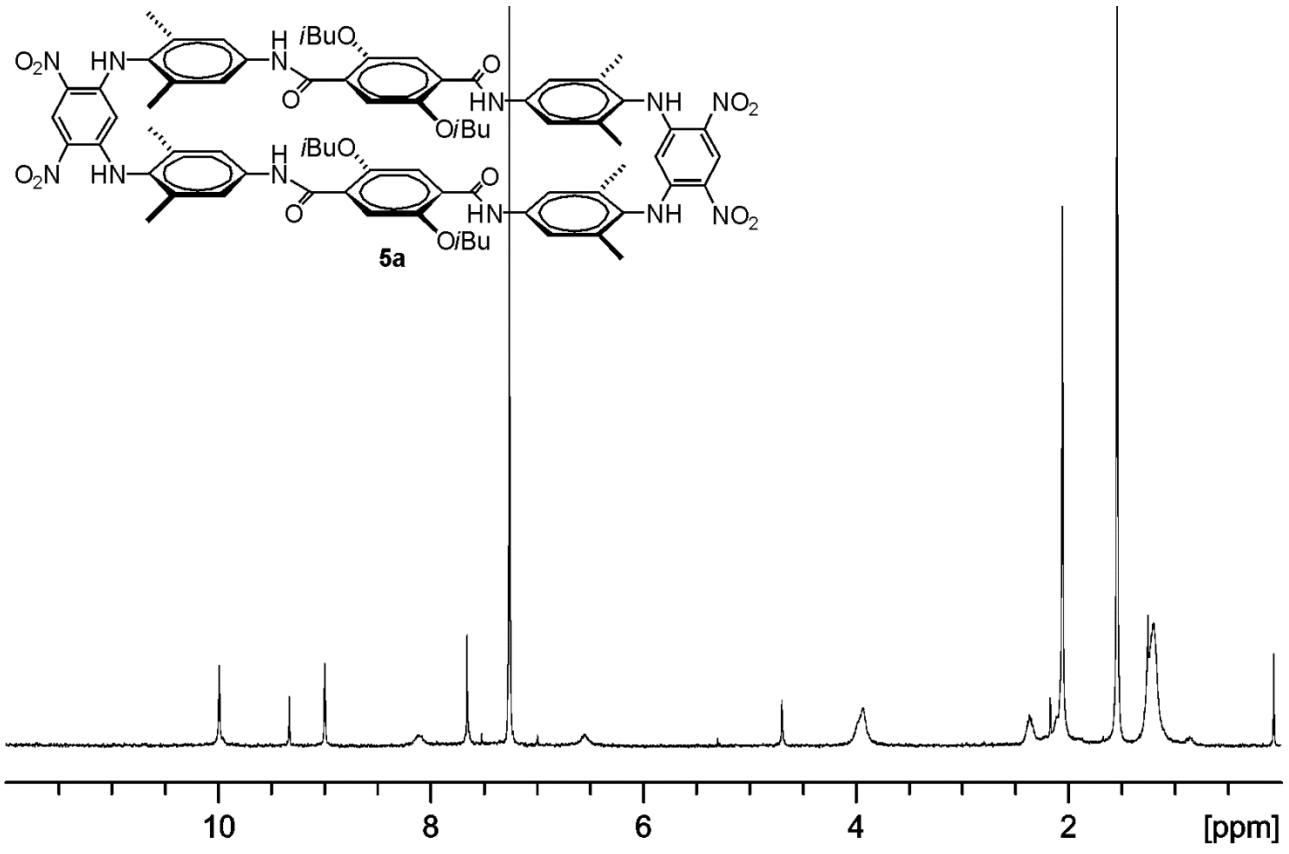




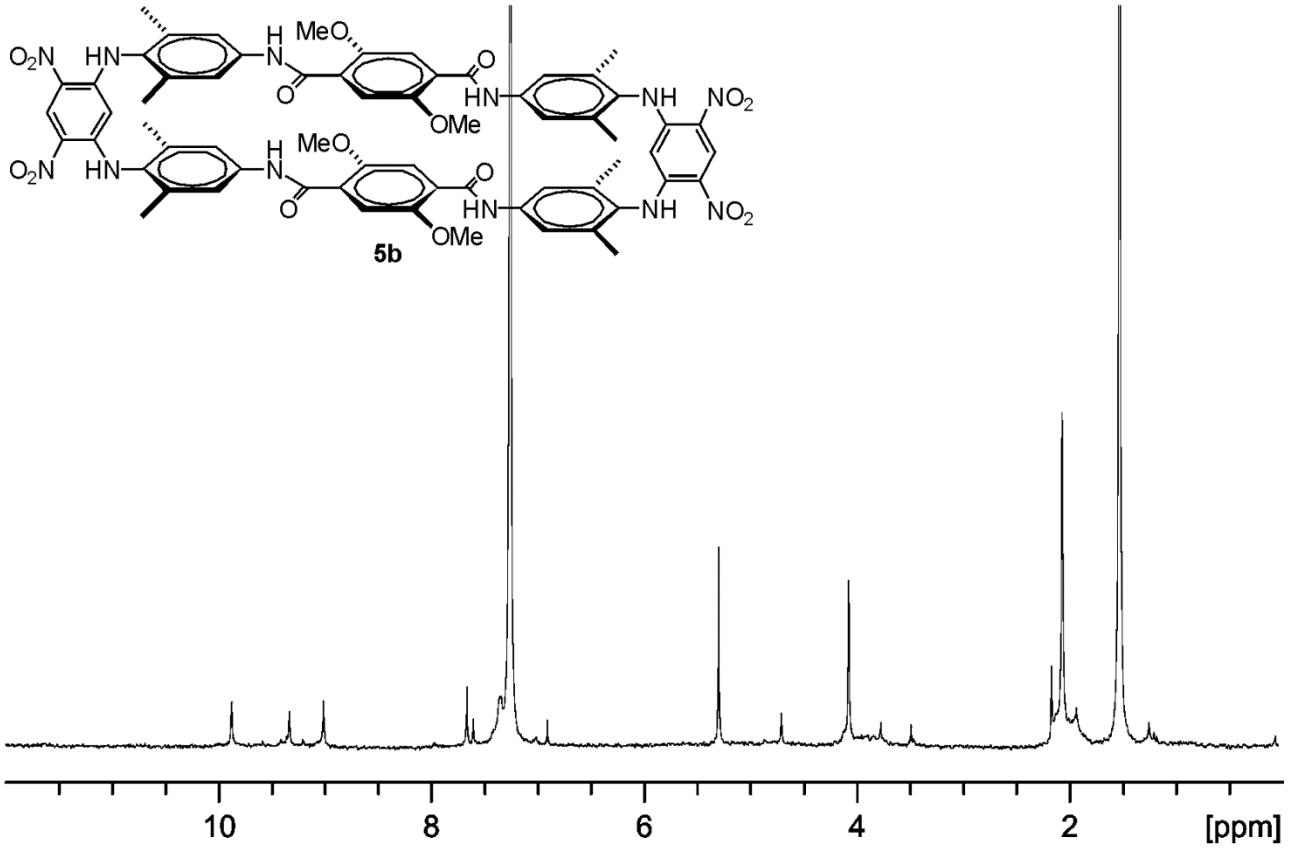
3c



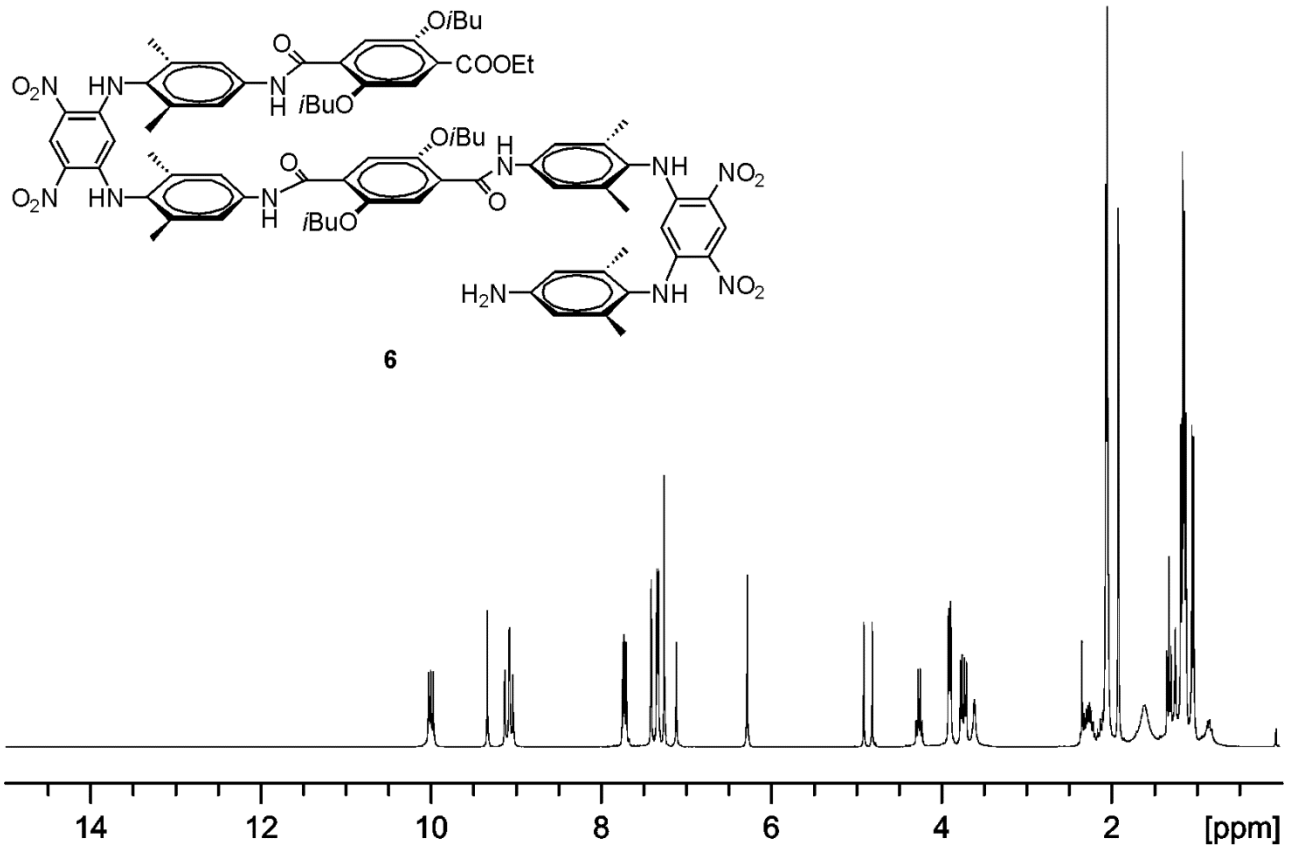

COOH
O*i*Bu
*i*BuO
COOH
4a
14
12
10
8
6
4
2
[ppm]
150
100
50
[ppm]


O2N
HN
H
N
iBuO
O
HN
NH
NO2
OiBu
10
8
6
4
2
[ppm]

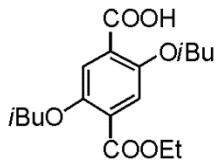
5a


O2N
HN
H
N
MeO
O
HN
NH
NO2
OMe
10
8
6
4
2
[ppm]

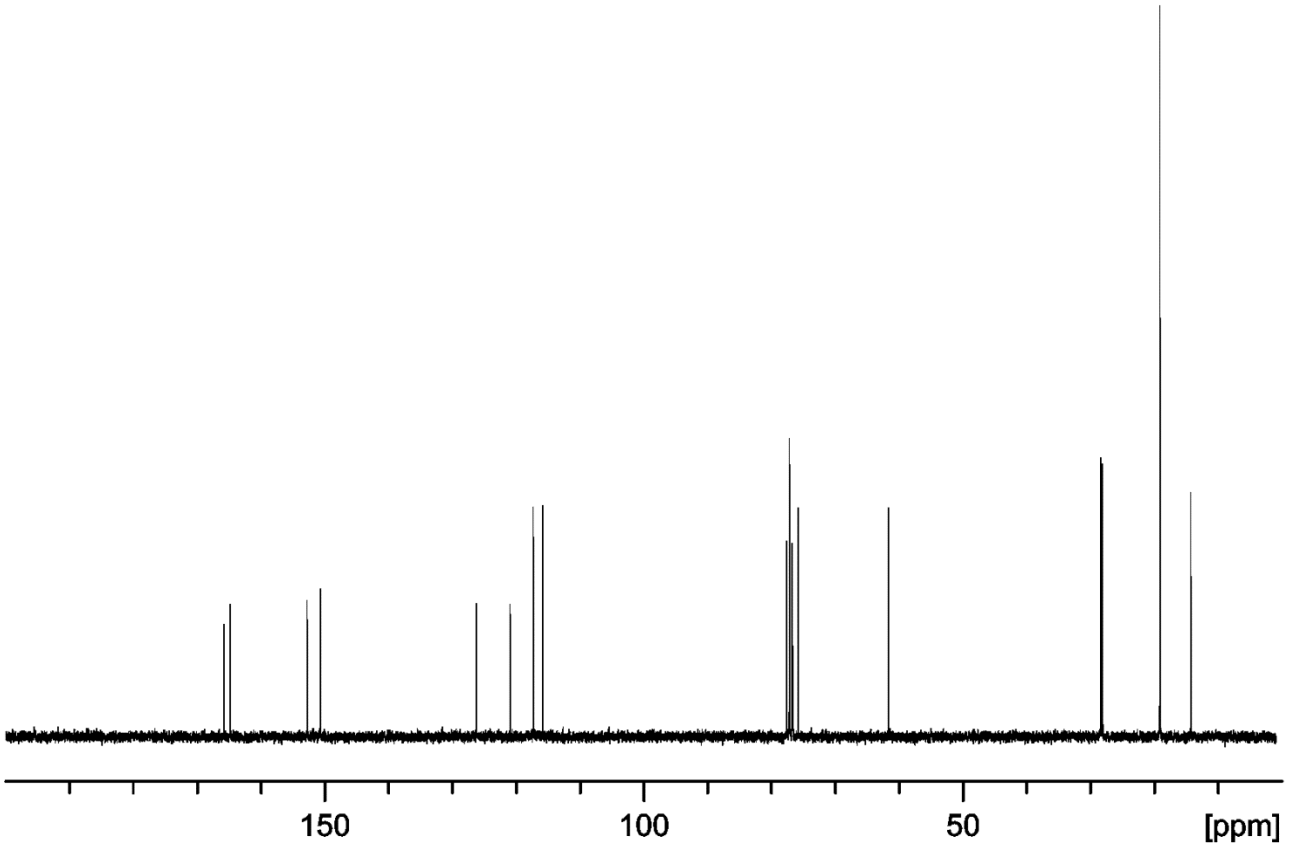
5b

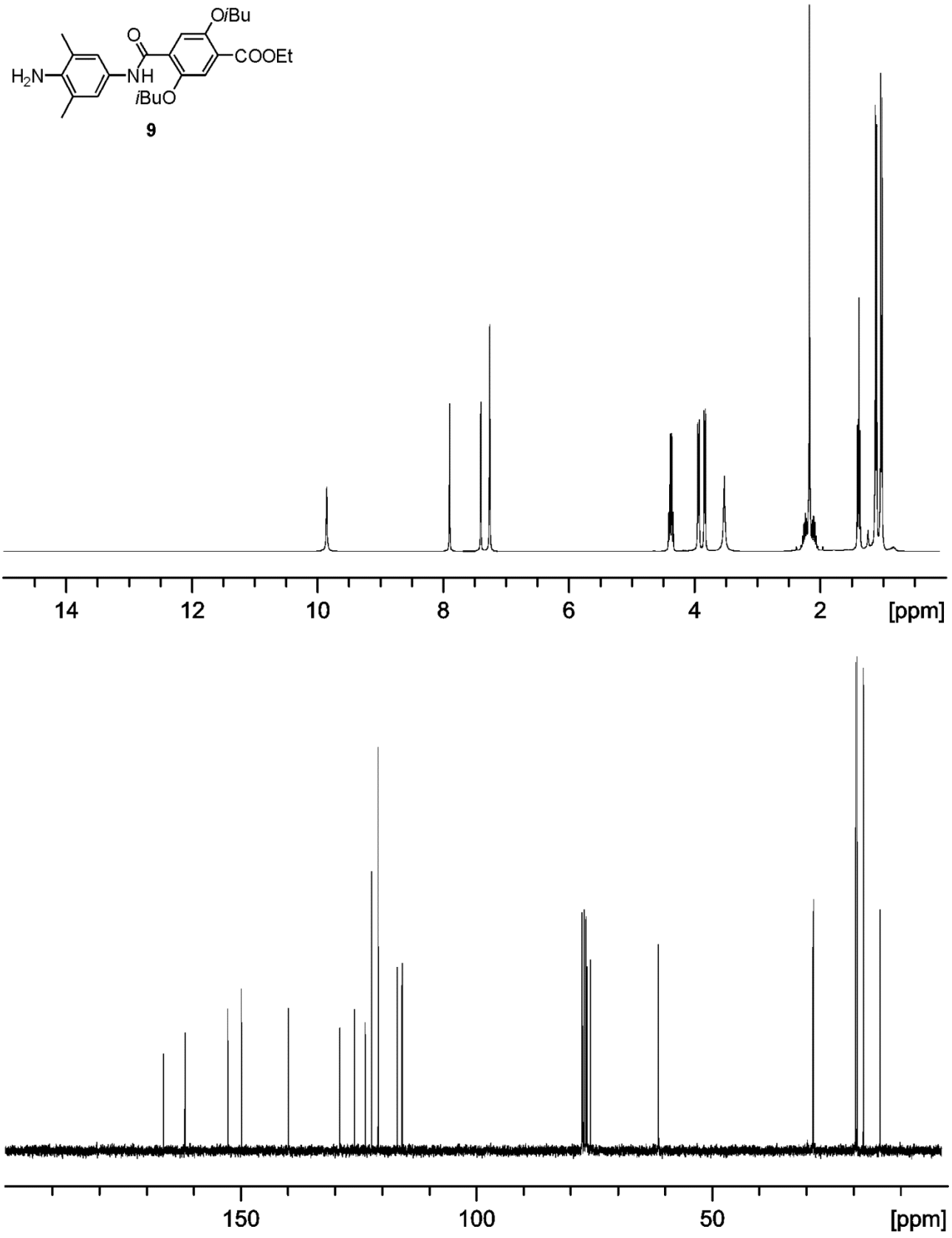

O/Bu
COOEt
O2N
HN
N
H
/BuO
O/Bu
H
N
NH
NO2
O2N
HN
N
H
/BuO
O
O
H2N
NH
NO2
14
12
10
8
6
4
2
[ppm]

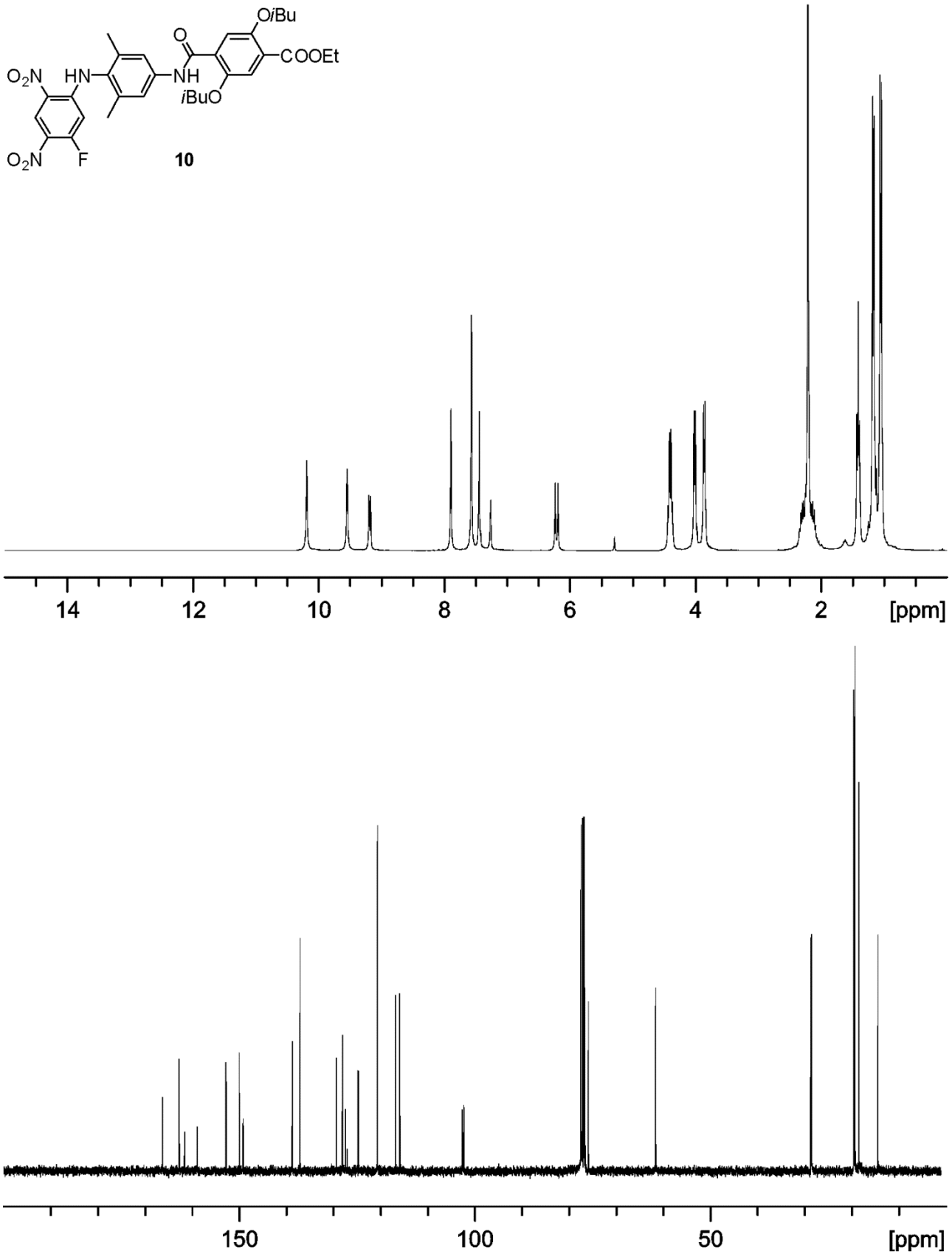
6

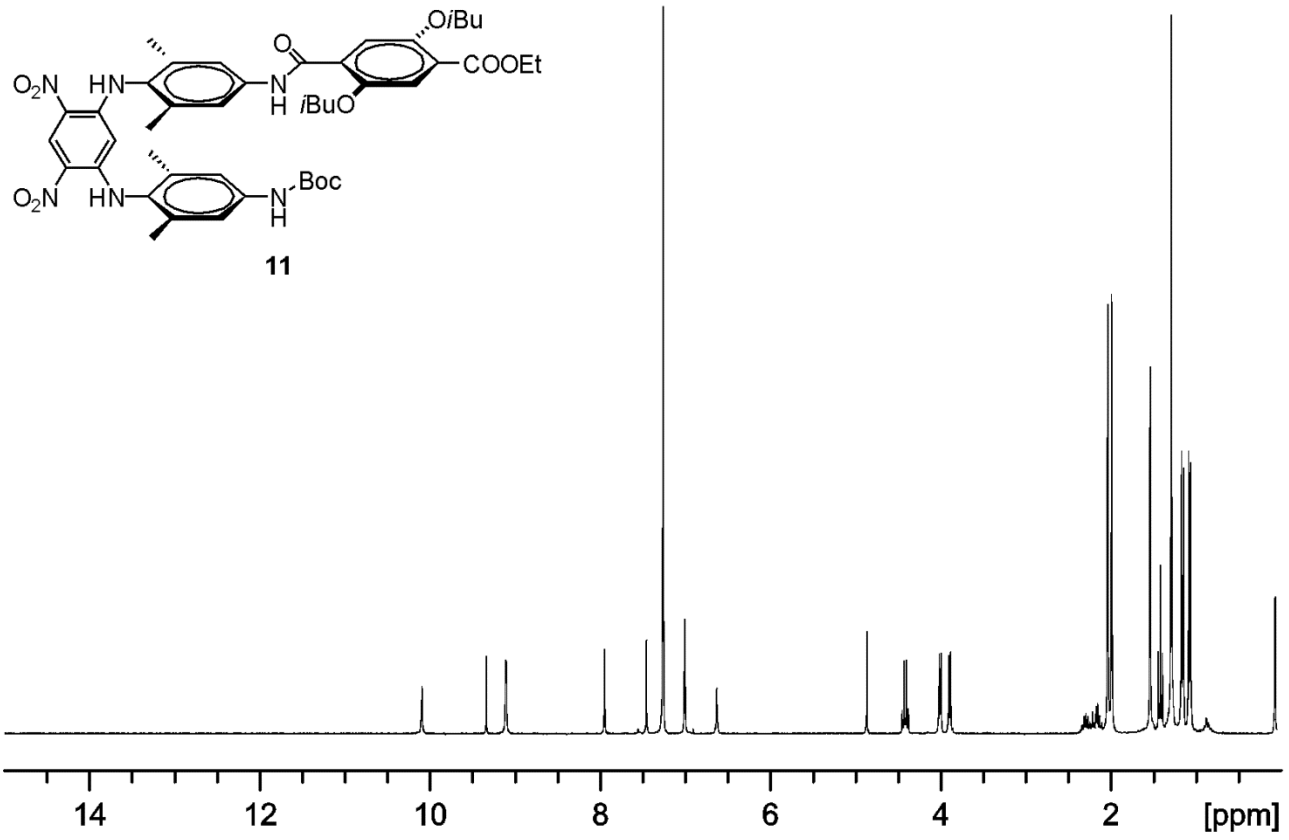


7

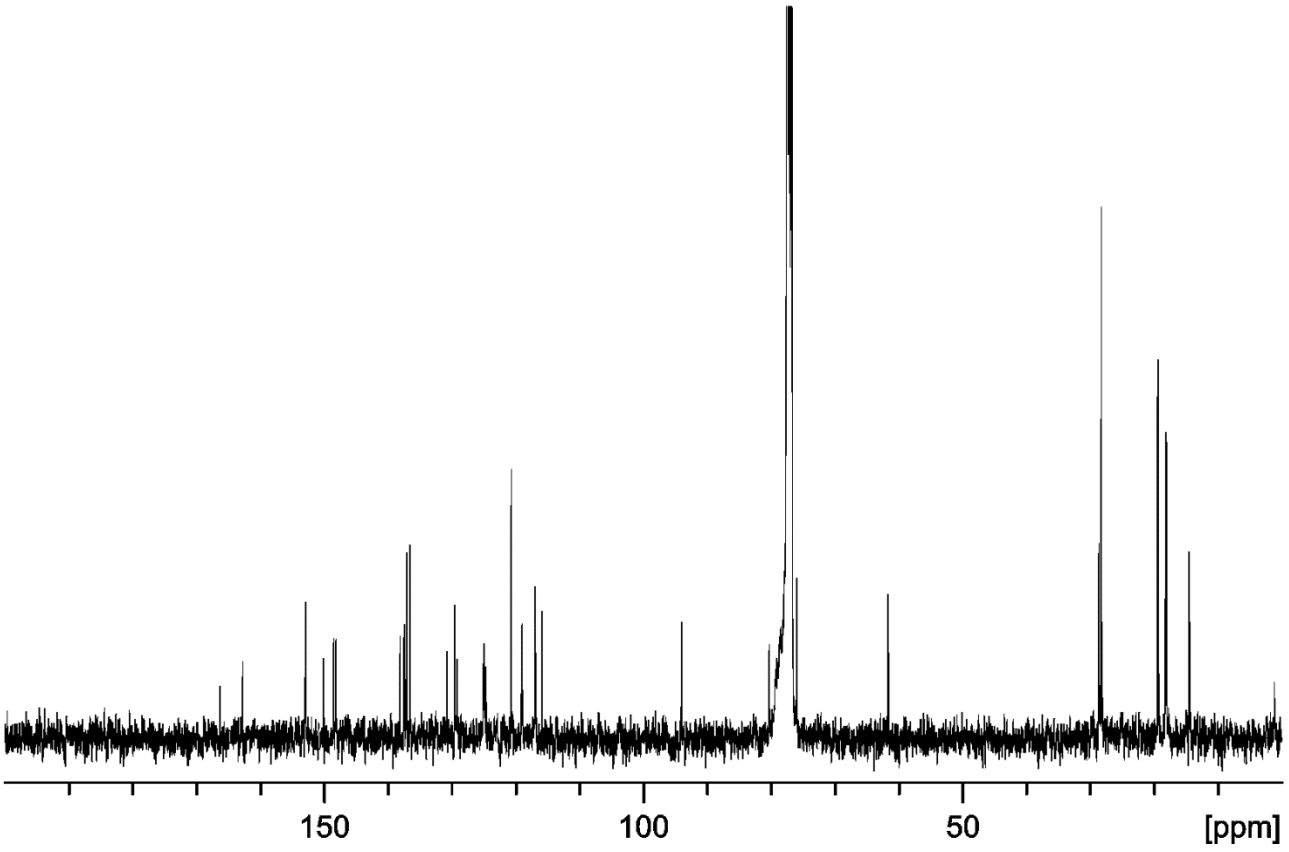


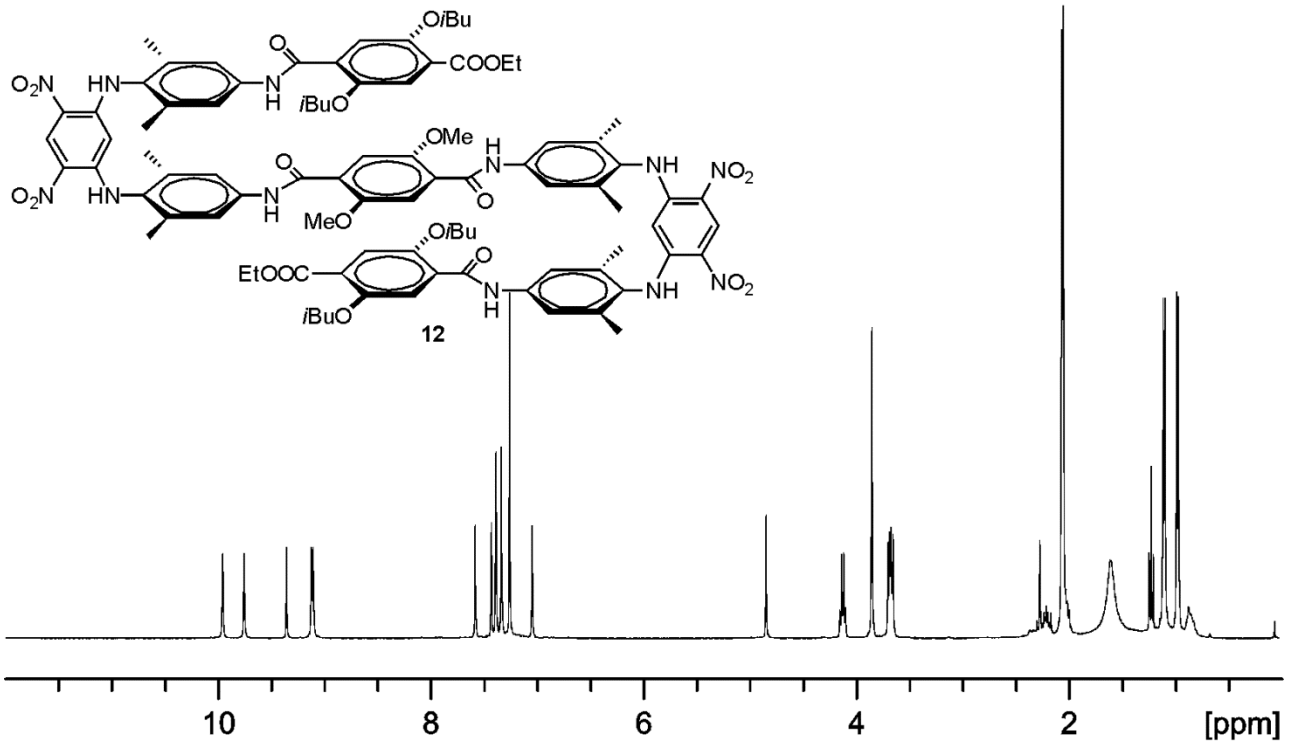

OiBu
O
COOEt
H2N
NH
iBuO
9
14
12
10
8
6
4
2
[ppm]
150
100
50
[ppm]


O2N
HN
NH
O
OiBu
COOEt
iBuO
O2N
F
10
14
12
10
8
6
4
2
[ppm]
150
100
50
[ppm]

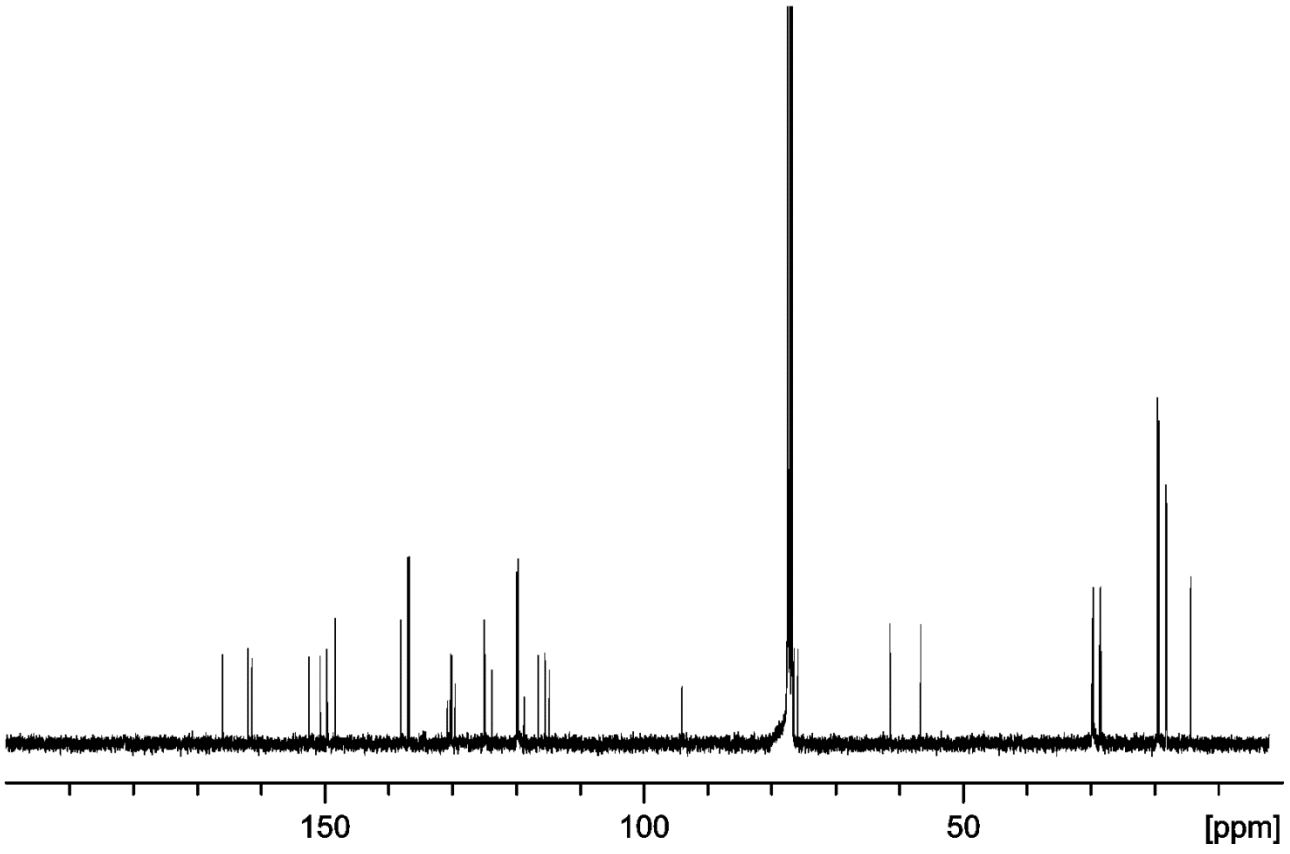

O/Bu
COOEt
O2N
HN
N
H
/BuO
O2N
HN
N
Boc
H
14
12
10
8
6
4
2
[ppm]

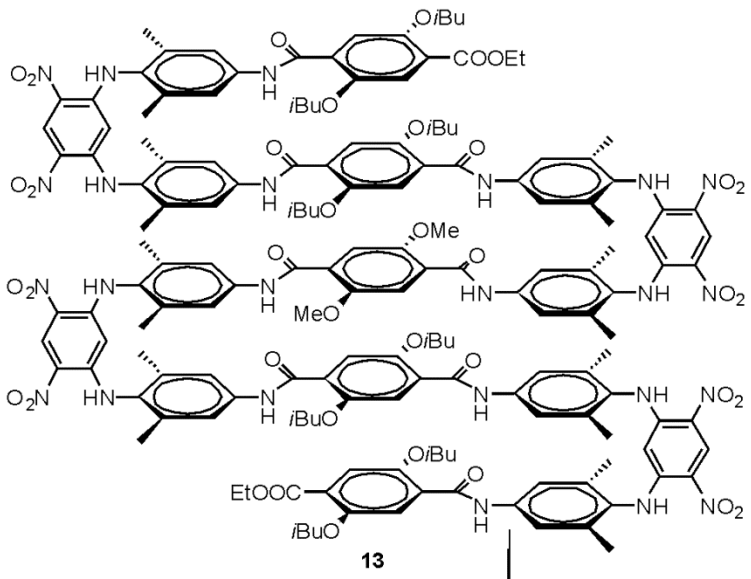
11


150
100
50
[ppm]

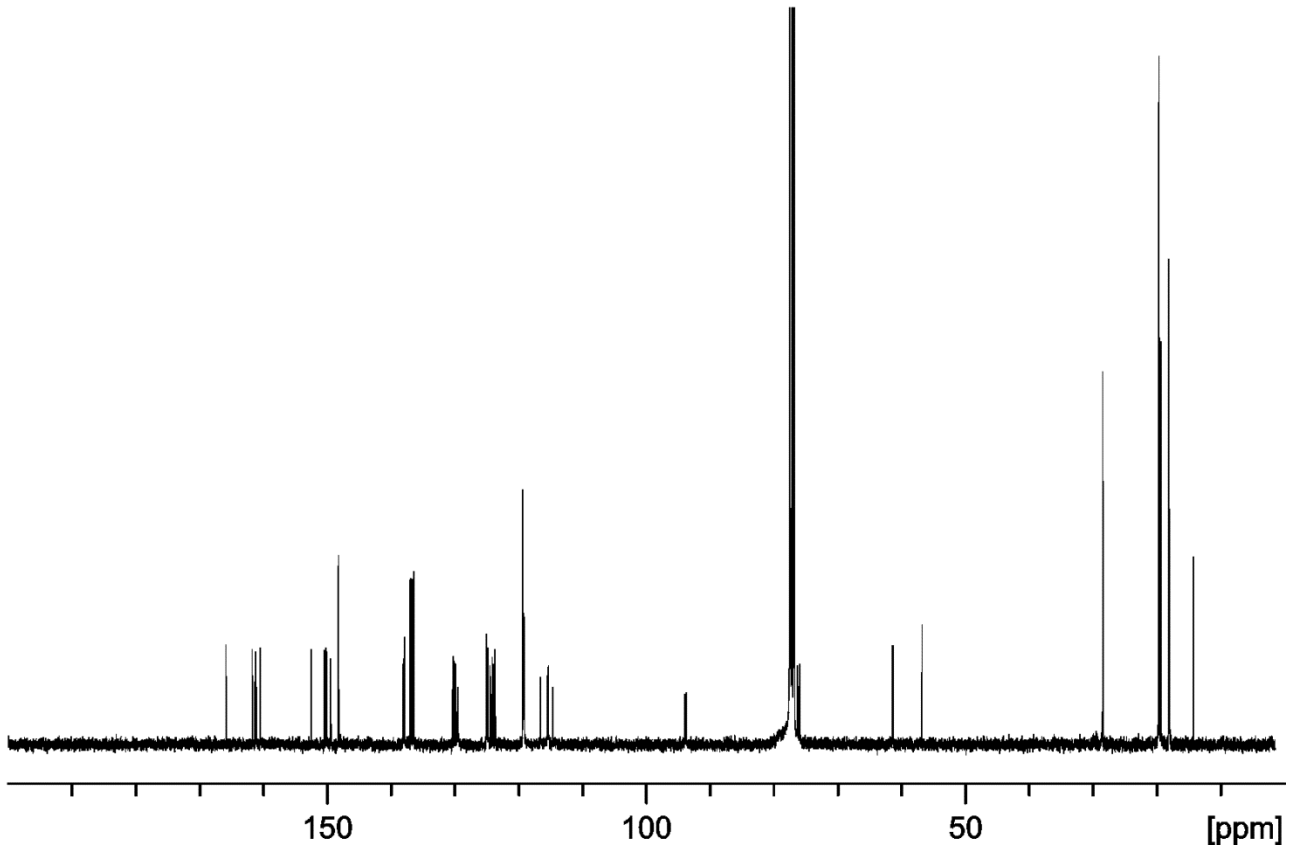


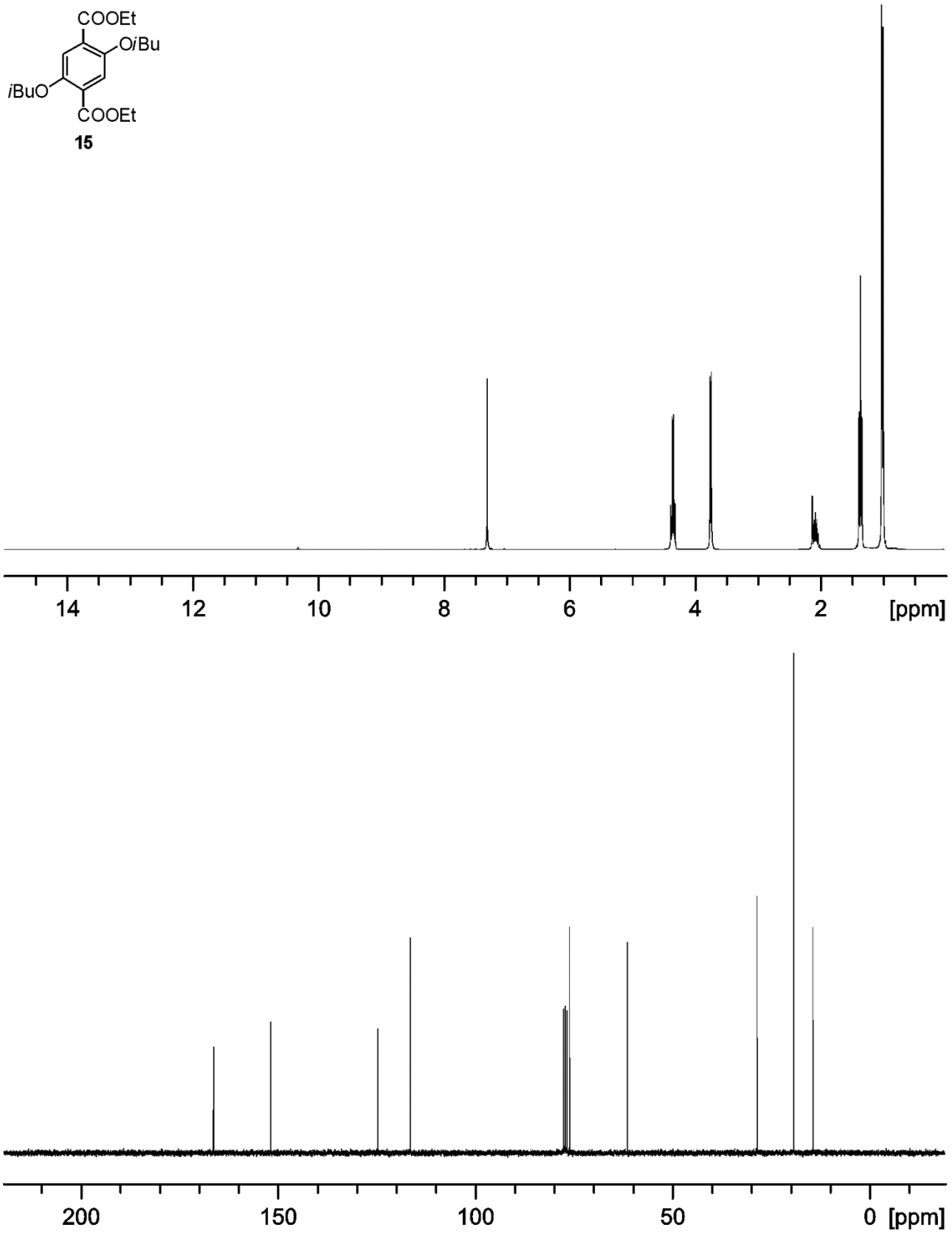
12

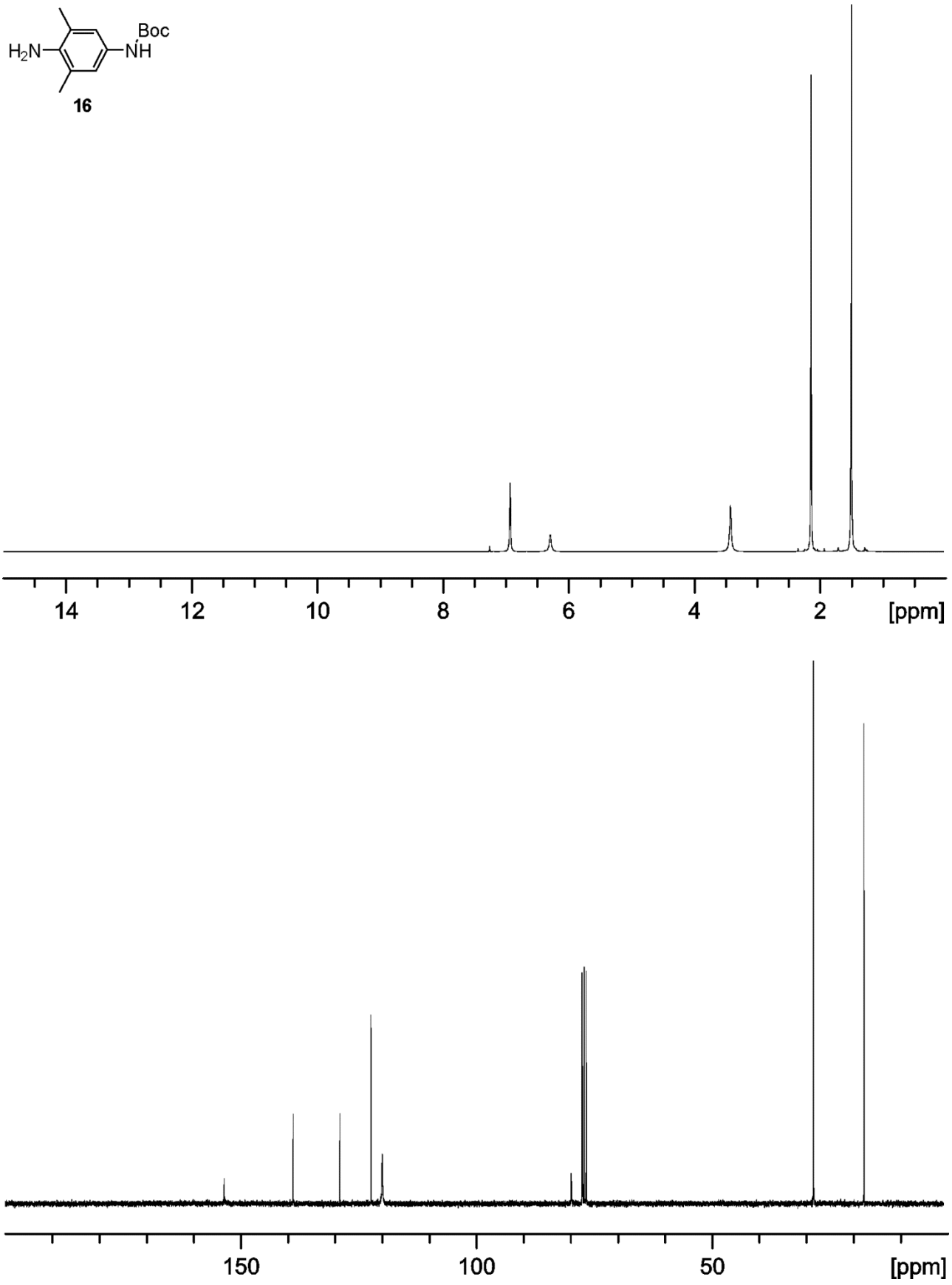


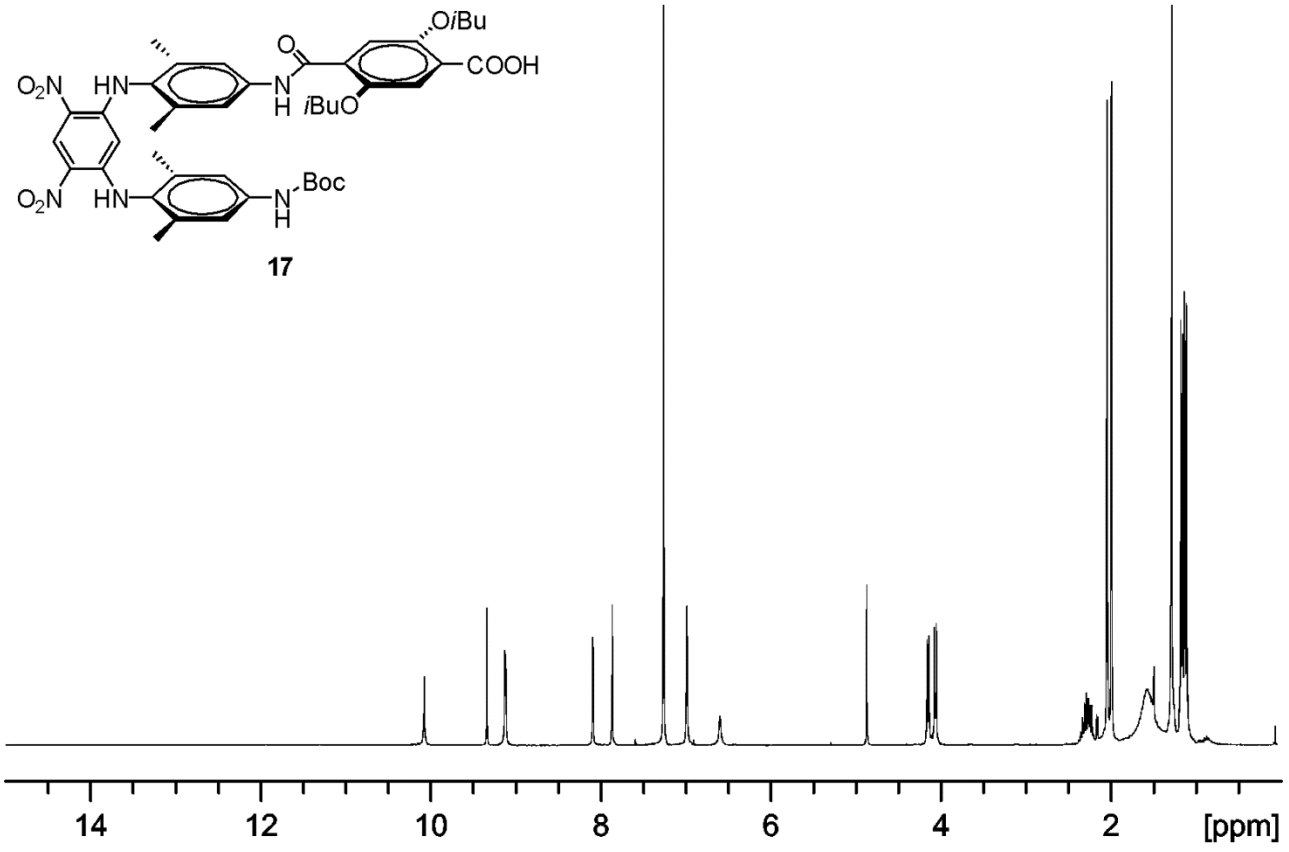

O/Bu
COOEt
/BuO
O2N
HN
NH
NO2
OMe
MeO
EtOOC
13

10
8
6
4
2
[ppm]

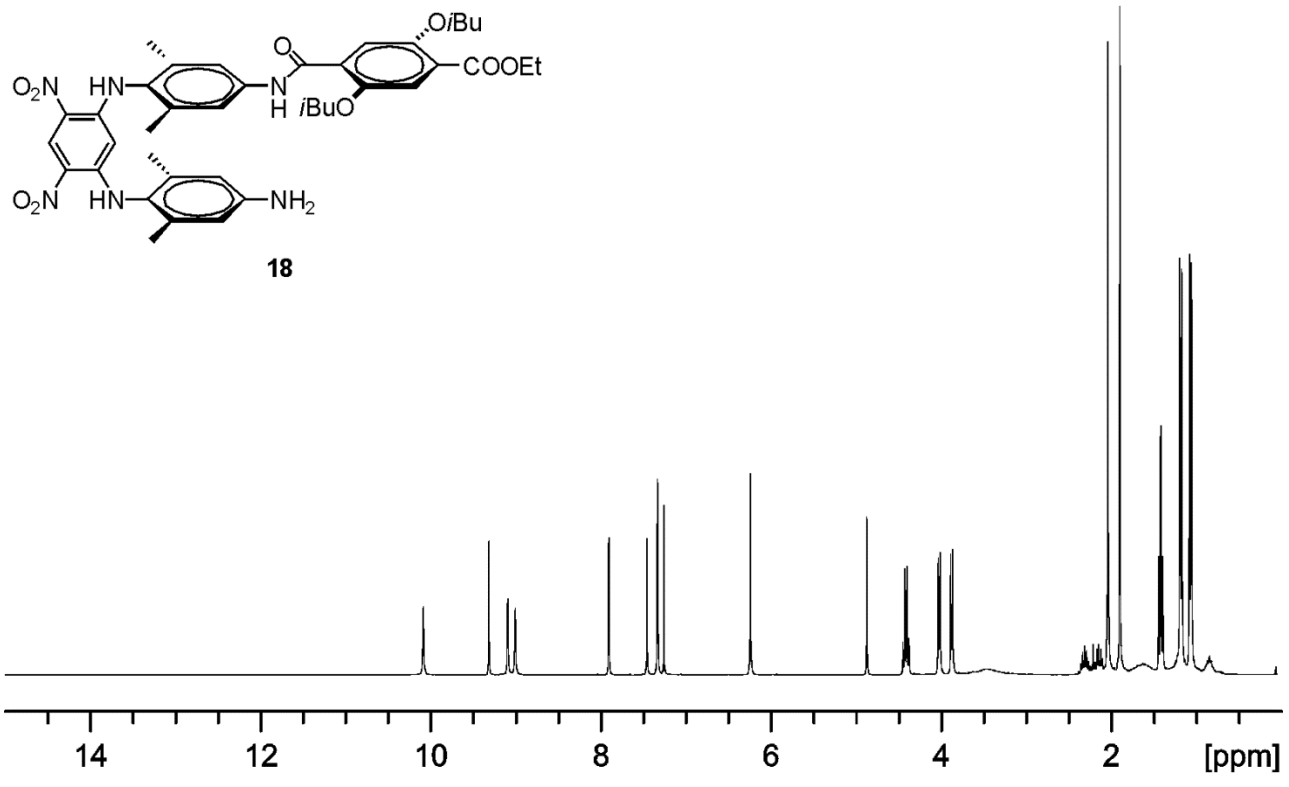

150
100
50
[ppm]


COOEt
OiBu
iBuO
COOEt
15
14
12
10
8
6
4
2
[ppm]
200
150
100
50
0
[ppm]

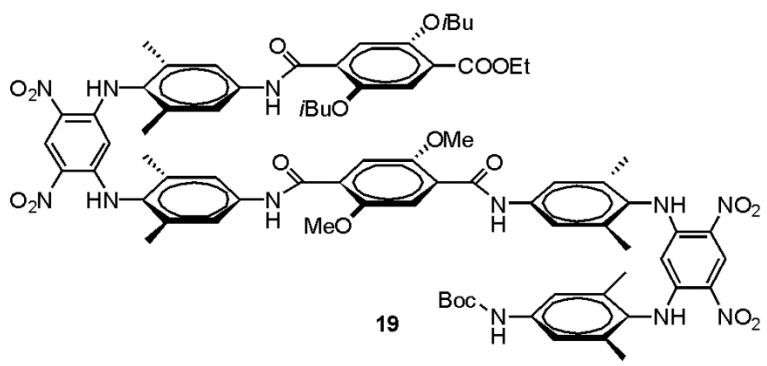

Boc
H2N
NH
16
14
12
10
8
6
4
2
[ppm]
150
100
50
[ppm]


O/Bu
COOH
O
N
H
/BuO
O2N
HN
O2N
HN
Boc
N
H
14
12
10
8
6
4
2
[ppm]

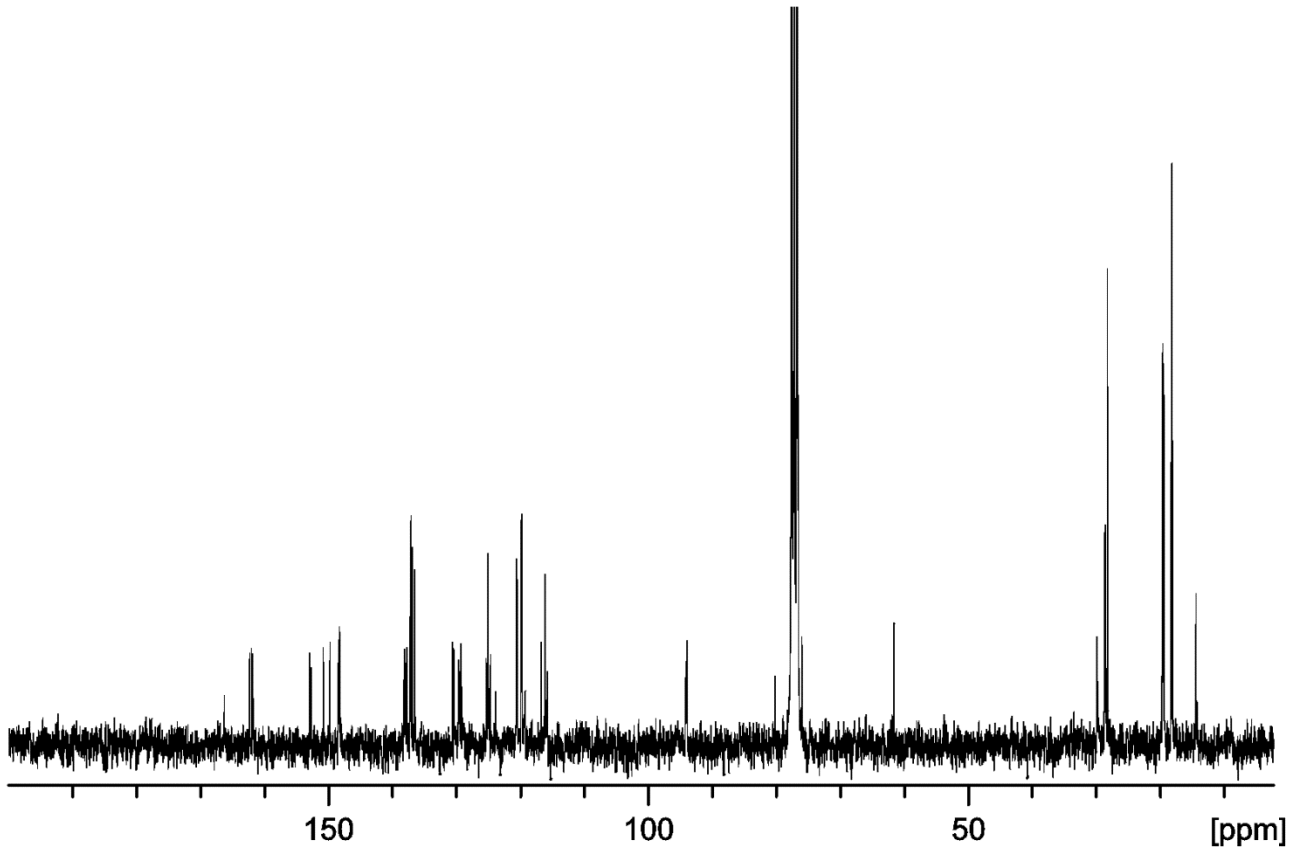
17

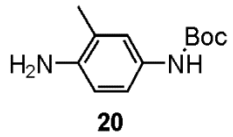

O/Bu
COOEt
O
N
H
/BuO
O2N
HN
O2N
HN
NH2
14
12
10
8
6
4
2
[ppm]

18

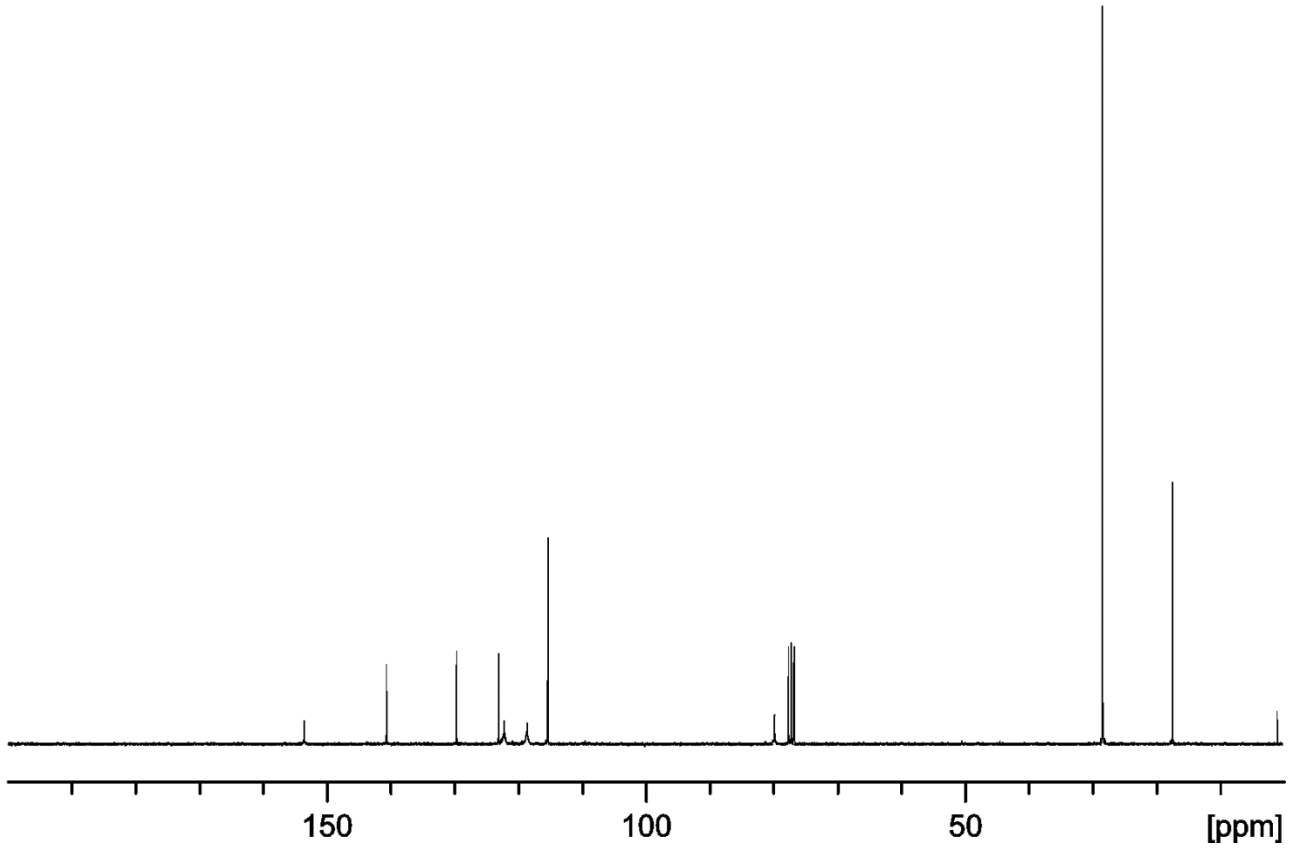

O/Bu
COOEt
O2N
HN
N
H
/BuO
OMe
MeO
NH
NO2
Boc
19

14
12
10
8
6
4
2
[ppm]


150
100
50
[ppm]



20



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