Supplementary Materials for

Conformational photoswitching of a synthetic peptide foldamer bound within a phospholipid bilayer

Matteo De Poli, Wojciech Zawodny, Ophélie Quinonero,
Mark Lorch, Simon J. Webb, Jonathan Clayden*

*Corresponding author. e-mail: j.clayden@bristol.ac.uk

This PDF file includes:

Materials and Methods

Supplementary text, images and data

Figs. S1 to S21

Tables S1 to S9

Full Reference List

Table of Contents

Materials and Methods

All reactions were carried out in flame-dried glassware under a nitrogen atmosphere unless otherwise stated. Reagents and solvents were purchased from either Sigma Aldrich, Iris Biotech GmbH, Apollo Scientific Ltd. or Fluorochem Ltd. and used without further purification. Anhydrous dichloromethane and tetrahydrofuran were obtained by distillation over calcium hydride and sodium/benzophenone respectively. Petrol refers to the fraction of light petroleum ether boiling between 40 and 65 °C. All other commercially available solvents and reagents were used as received. Nuclear Magnetic Resonance (NMR) spectra were recorded on a Bruker Ultrashield 300, 400 or 500 MHz spectrometer. ^{1}H and ^{13}C NMR spectra in solution were referenced relative to the solvent residual peaks and chemical shifts (δ) reported in ppm downfield of tetramethylsilane ($CDCl_3$ δ_H: 7.26 ppm, δ_C: 77.16 ppm; CD_3OD δ_H: 3.31 ppm, δ_C 49.05 ppm). ^{19}F spectra in solution were referenced using $CFCl_3$ as the internal standard and ^{19}F NMR chemical shifts (δ_F) are given in ppm. ^{31}P spectra were referenced using H_3PO_4 as the internal standard and ^{31}P chemical shifts (δ_P) are given in ppm. Coupling constants (*J*) are reported in Hertz. Splitting patterns are abbreviated as follows: singlet (s), doublet (d), triplet (t), quartet (q), septet (spt), multiplet (m), broad (br) or some combination of these. In ^{1}H NMR spectra, amide N*H* signals that exchange with deuterated solvent are not reported. Assignments were made using DEPT-135, 2D ^{1}H-COSY and HMQC experiments. ^{19}F solid-state NMR spectra were acquired at 293 K (unless otherwise specified) using a 4 mm MAS probe (zirconium oxide rotors used) on a Bruker Avance III 400 MHz spectrometer operating at 376.3639 MHz (^{19}F) and referenced using C_6F_6 (neat) as standard. Each experiment was carried out with a spinning rate of 10 kHz, a $\pi/2$ pulse length of 11 μs and a relaxation delay of 5s. ^{1}H solid-state NMR spectra were acquired at 293 K on a Bruker Avance II 500 MHz spectrometer using a 4 mm MAS probe operating at frequencies of 500.1013 MHz (^{1}H) with a spinning rate of 8 kHz and referenced using tetramethylsilane as standard. ^{1}H experiments were carried out with a typical $\pi/2$ pulse length of 7 μs and a relaxation delay of 4s. Electrospray (ES) spectra were recorded on a Waters Platform II and high resolution mass spectra (HRMS) were recorded on a Thermo Finnigan MAT95XP and are accurate to ±0.001 Da. Infrared spectra were recorded on a Thermo Scientific Nicolet iS5 FTIR spectrometer. Melting points were determined on a GallenKamp apparatus and are uncorrected. Thin layer chromatography (TLC) was performed using commercially available pre-coated plates (Macherey-Nagel alugram Sil G/UV254) and visualized under UV light at 254 nm and/or by staining with phosphomolybdic acid solution.

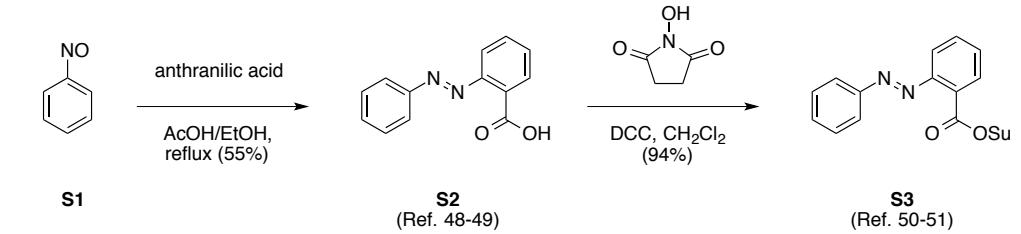
Flash column chromatography was carried out on 40-63 μm 60 Å silica (Sigma Aldrich) with the eluent quoted. Circular dichroism spectra (CD) were recorded on a Jasco J-815 spectrometer using a 1 mm cell length at 20 ^{o}C. Optical rotation measurements were taken on an AA-100 polarimeter using a cell with a pathlength of 0.25 dm at 20 °C with the solvent and concentration (g/100 mL) stated. All reactions were conducted in oven or flame-dried glassware under a nitrogen atmosphere unless otherwise stated. THF was distilled under nitrogen from sodium using a benzophenone indicator. CH_2Cl_2 and toluene were obtained by distillation over calcium hydride under a nitrogen atmosphere. Anhydrous acetonitrile and dimethylformamide were purchased from Sigma-Aldrich. All other solvents and commercially available reagents were used as received. Synthetic phospholipid bilayers were prepared using commercially available 1,2-di-(9*Z*-octadecenoyl)-*sn*-glycero-3-phosphocholine (DOPC) from Avanti Polar Lipids, Inc. (Alabaster, AL, USA), milliQ water and Dulbecco's Phosphate Buffer (pH 7.2, Sigma Aldrich). UV-visible absorption spectra were recorded using quartz cuvettes of 1 cm pathlength on an Agilent Cary 5000 UV-Vis-NIR spectrophotometer equipped with a Peltier-thermostat controlled cell holder at 25 ± 0.05 °C. Analytical irradiation experiments in solution were carried out in spectrophotometric grade MeOH using a Thorlabs DC4100 (4 channel LED driver) equipped with mounted high-power LEDs (models M365L2, M405L2 and M455L3 at 365, 405 and 455 nm, respectively). Irradiation experiments in solution were carried out in a quartz NMR tube (Wilmad Suprasil®, SP industries, Warminster, PA, USA); foldamer/lipid samples for ss-NMR were irradiated in a quartz cuvette (380 μL tot. volume, pathlength 1 mm, Hellma, Müllheim, Germany).

Abbreviations

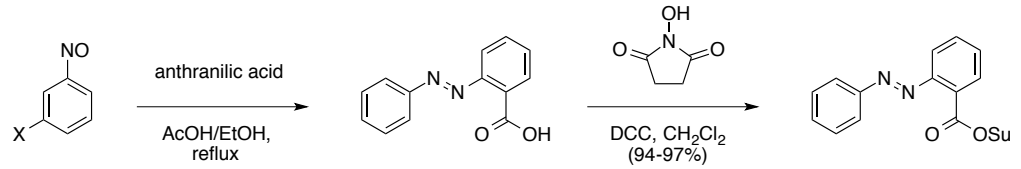
Aib, 2-aminoisobutyric acid; Fib, 2-Amino-3-fluoro-2-(fluoromethyl)propanoic acid; aMv, (S)-2-methylvaline; EDC, 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride; HOAt, 1-hydroxy-7-azabenzotriazole; TMS, trimethylsilyl; TFFH, fluoro-*N*,*N*,*N*′,*N*′-tetramethylformamidinium hexafluorophosphate; TEG, triethyleneglycol monomethyl ether; AcOH, acetic acid; Su, succinimide; THF, tetrahydrofuran; DMSO, dimethylsulfoxide; $TMSCHN_2$, trimethylsilyldiazomethane; Cbz, Carboxybenzyl; DCC *N*,*N*'-dicyclohexylcarbodiimide; DIPEA, *N*,*N*-diisopropylethylamine; MAS, magic angle spinning; PSS, photostationary state.

Synthetic schemes

1. Azobenzene precursors



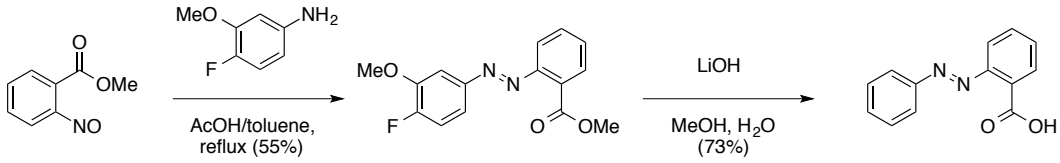
S1 **S2** (Ref. 48-49) **S3** (Ref. 50-51)



S4 (X = NO_2)
S5 (X = OMe)
(Ref. 52-53)

S6 (X = NO_2, 53%)
S7 (X = OMe, 33%)

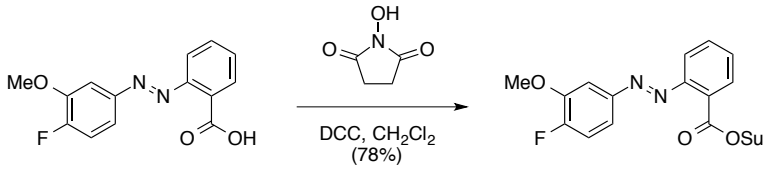
S8 (X = NO_2, 94%)
S9 (X = OMe, 97%)



S10
(Ref. 54)

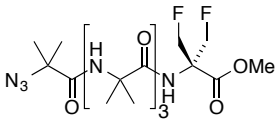
S11

S12



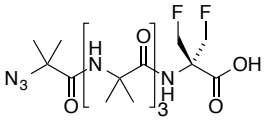
S12 **S13**

2. Fluorinated and model oligomers



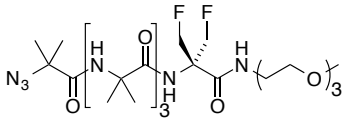
F1 (Ref. 34)

LiOH
THF/H_2O
(86%)



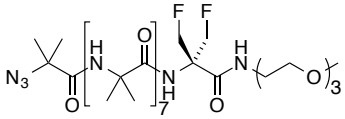
F2

$TEG\text{-}NH_2$ (Ref. 55)
EDC, HOAt, DIPEA
(83%)



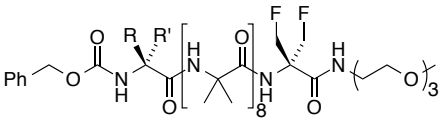
F3

1) H_2, Pd/C, EtOH (quant.);
2) azlactone from N_3Aib_4OH (Ref. 56)
CH_3CN, reflux (86%)



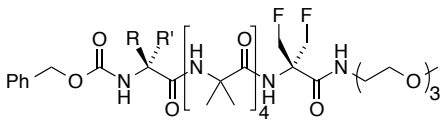
F4

1) H_2, Pd/C, EtOH (quant.);
2) Cbz-AA-OH,
EDC, HOAt, DIPEA (74-85%)
or Cbz-Aib-F (Ref. 57),
DIPEA (82%)



6a, **6c-d** (R, R': see table)

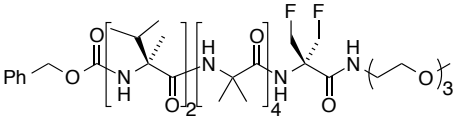
1) H_2, Pd/C, EtOH (quant.);
2) Cbz-AA-OH,
EDC, HOAt, DIPEA (64-70%)
or Cbz-AA-F (Ref. 57),
DIPEA (62-74%)



3a-e (R, R': see table)

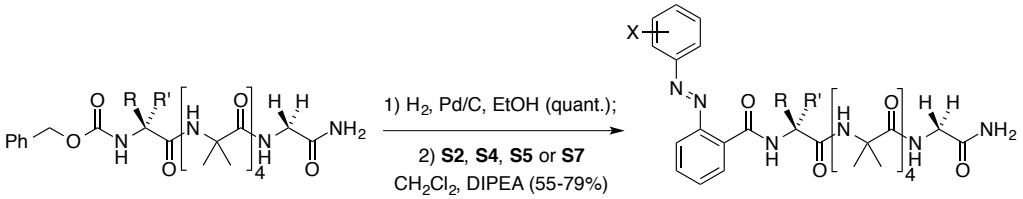
3e

1) H_2, Pd/C, EtOH (quant.);
2) Cbz-aMv-F (Ref. 57),
DIPEA (63%)



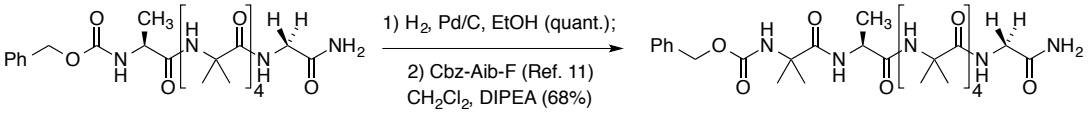
3f

amino acid (AA)	R	R'	letter code
Aib	Me	Me	a
Ala	Me	H	b
Val	*i*Pr	H	c
Phe	Bn	H	d
aMv	*i*Pr	Me	e



S14c (R = iPr, R' = H)
S14d (R = Bn, R' = H)
(Ref. 43)

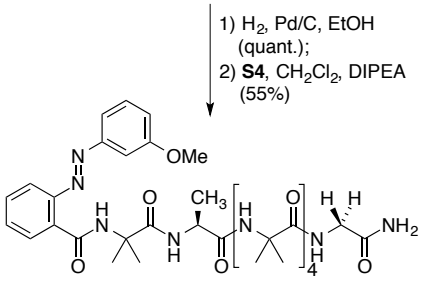
1a-h (X = H, OMe or NO_2)



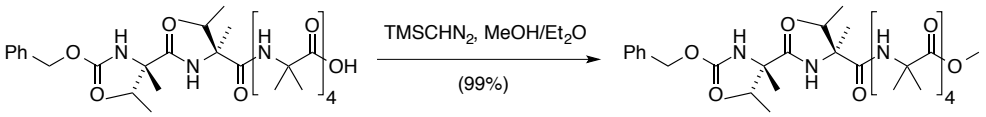
S14b (Ref. 43)

S15

amino acid (AA)	R	R'	letter code
Aib	Me	Me	a
Ala	Me	H	b
Val	*i*Pr	H	c
Phe	Bn	H	d

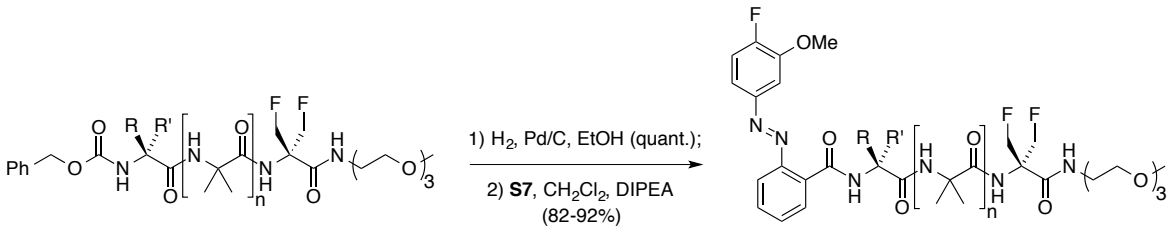


2



S16 (Ref. 57)

S17



3a (n = 4, R, R' = CH_3)
3c (n = 4, R = *i*Pr, R' = H)
3d (n = 4, R = Bn, R' = H)
6c (n = 8, R = *i*Pr, R' = H)
6d (n = 8, R = Bn, R' = H)

3g (n = 4, R, R' = CH_3)
4 (n = 4, R = *i*Pr, R' = H)
Phe-4 (n = 4, R = Bn, R' = H)
5 (n = 8, R = *i*Pr, R' = H)
Phe-5 (n = 8, R = Bn, R' = H)

General synthetic procedures

General procedure (A): Pd-catalyzed cleavage of Cbz protection and reduction of N-terminal azido-oligomers to the corresponding amines

A round-bottom flask was charged with 1.0 equiv of N-terminal Cbz-protected oligomer or azido-oligomer, 10% Pd/C in EtOH (10 mL/mmol) and the mixture was stirred at room temperature under H_2 atmosphere (balloon) until completion (TLC monitoring). Upon completion, the suspension was filtered under vacuum through a charcoal/Celite® pad and the filter cake washed several times with EtOH/CH_2Cl_2. The mixture was concentrated under reduced pressure and the residue placed under high vacuum. The resulting crude amine was used directly in the subsequent coupling step.

General procedure (B): EDC coupling of Cbz-protected amino acids and N-terminal deprotected Aib_n foldamers

To a cooled (0 °C) suspension of the appropriate Cbz-N-protected amino acid (2 eq) and HOAt (2 eq) in dry CH_2Cl_2 (10 mL/mmol) was added EDC (2.1 eq). The mixture was stirred under nitrogen until complete dissolution of the starting materials. This solution was then added to a solution of N-deprotected Aib_n fragment (1 eq) and DIPEA (2 eq) in dry CH_2Cl_2 (5 mL/mmol). Additional DIPEA was added if required to maintain basic pH. The mixture was allowed to slowly reach room temperature and stirred overnight under nitrogen. After solvent removal under vacuum, EtOAc (25 mL) was added and the organic phase washed with $KHSO_4$ 5% (3 × 5 mL), $NaHCO_3$ (saturated solution, 3 × 5 mL), brine (5 mL), dried over $MgSO_4$, filtered and concentrated under reduced pressure to yield a crude product that was purified by column chromatography (SiO_2) using the appropriate mixture of eluents.

General procedure (C): Acyl fluoride coupling of Cbz-protected amino acids and N-terminal deprotected Aib_n foldamers

1) Fluoride formation: a round bottom flask was charged with the appropriate Cbz-N protected amino acid (4 mmol), pyridine (4 mmol) and dry CH_2Cl_2 (10 mL/mmol). TFFH (6 mmol) was added and the mixture left stirring at room temperature for 3 h under nitrogen, during which the formation of a white precipitate was observed. The mixture was diluted with CH_2Cl_2 (20 mL), washed with ice-cooled water (3 × 5 mL), brine (5 mL), dried ($MgSO_4$), filtered and concentrated under vacuum (bath temperature <30 °C) to give the corresponding Cbz-AA-F, which was used immediately without further purification.

2) Coupling: a solution of the freshly prepared Cbz-protected amino acid fluoride (step 1, approximately 4 mmol) in dry CH_2Cl_2 (5 mL/mmol) was added to a solution of N-deprotected amino-oligomer (1 mmol) and DIPEA (5 mmol) in dry CH_2Cl_2 (5 mL/mmol). The solution was stirred for 4 days at room temperature under nitrogen. Additional DIPEA was added if required to maintain basic pH. After solvent removal under reduced pressure, EtOAc (25 mL) was added and the organic phase washed with $KHSO_4$ 5% (3 × 5 mL), $NaHCO_3$ (saturated solution, 3 × 5 mL), brine (5 mL), dried over $MgSO_4$, filtered and concentrated under reduced pressure to yield a crude product that was purified by column chromatography (SiO_2) using the appropriate mixture of eluents.

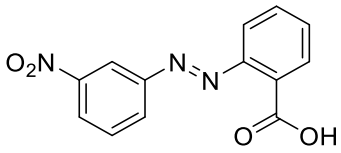
General procedure (D): Coupling of azobenzenecarboxylic acids and N-deprotected oligomers.

1) succinimidyl ester formation: A round bottom flask was charged with the appropriate azobenzene-2-carboxylic acid (1 mmol) and HOSu (1.1 mmol) in dry CH_2Cl_2 (5 mL/mmol). DCC was added in one portion (1.1 mmol) and the reaction stirred at room temperature for 1h, with protection from ambient light and under an inert atmosphere, during which a white precipitate was observed. The solids were removed by filtration and the filter cake rinsed with dry CH_2Cl_2 (5 mL). After solvent removal *in vacuo* (bath temperature <30 °C), the crude residue was purified by flash chromatography (SiO_2) using the appropriate mixture of eluents to afford a moisture-sensitive product, which was used directly in the following step.

2) Coupling: a solution of the freshly prepared azobenzene-2-carboxylic acid succynimidyl ester (step 1, 2 eq) in dry CH_2Cl_2 (5 mL/mmol) was added to a solution of N-deprotected amino-oligomer (1 eq) and DIPEA (2 eq) in dry CH_2Cl_2 (5 mL/mmol). The solution was stirred for 24 h at room temperature under nitrogen. After solvent removal *in vacuo*, EtOAc (25 mL) was added and the organic phase washed with $KHSO_4$ 5% (3 × 5 mL), $NaHCO_3$ (saturated solution, 3 × 5 mL), brine (5 mL), dried over $MgSO_4$, filtered and concentrated under reduced pressure to yield a crude product that was purified by column chromatography (SiO_2) using the appropriate mixture of eluents.

Synthetic procedures and characterization details

Methods for the synthesis of 2-((phenylazo)benzene)carboxylic acid **S2** (*48, 49*), 2-((phenylazo)benzene)carboxylate succinimidyl ester **S3** (*50, 51*), 1-nitro-3-nitrosobenzene **S4** (*52*), 1-methoxy-3-nitrosobenzene **S5** (*53*), methyl 2-nitrosobenzoate **S10** (*54*), $N_3Aib_4FibOMe$ **F1** (*34*), TEG-NH_2 (*55*), N_3Aib_4OH (*56*), Cbz-Aib-F (*57*), Cbz-aMv-F (*57*), Cbz-L-$AlaAib_4GlyNH_2$ **S14b** (*43*), Cbz-L-$ValAib_4GlyNH_2$ **S14c** (*43*), Cbz-L-$PheAib_4GlyNH_2$ **S14d** (*43*) and Cbz-L-aMv_2Aib_4OH **S16** (*57*) have been reported previously.



S6

A solution of crude 1-nitro-3-nitrosobenzene **S4** (1.58 g, 10 mmol, prepared from 1.6 g of 3-nitroaniline in 90% yield using the procedure of Tibiletti *et al.* (*52*)) and anthranilic acid (1.37 g, 1 eq) in EtOH/AcOH (16 + 4 mL) was stirred at 85 °C overnight under nitrogen. The mixture was cooled to room temperature and concentrated under vacuum. The residue was diluted with EtOAc (80 mL) and washed with $KHSO_4$ 5% (3 × 20 mL). The organic phase was extracted with NaOH (5% in H_2O, 3 × 10 mL) and filtered to remove insoluble material. The combined aqueous phases were washed with Et_2O (2 × 10 mL) then solid $KHSO_4$ was added with stirring until pH ~ 3. The aqueous phase was extracted with EtOAc (3 × 20 mL) and the combined organic fractions washed with $KHSO_4$ 5% (10 mL), H_2O (3 × 15 mL) and brine (10 mL), dried with $MgSO_4$ and filtered. After solvent removal under vacuum, the residue was purified by column chromatography (SiO_2: CH_2Cl_2 → CH_2Cl_2/MeOH, 95:5) to give **S6** as a dark yellow solid (1.45 g, 53%).

R_f 0.75 (CH_2Cl_2/MeOH, 95:5)

m.p. 153-154°C

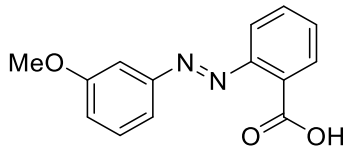
IR (ATR) ν_{max}/cm^{-1} 3088, 1731, 1594, 1525, 1399, 1349, 1243, 1216, 1082, 917, 763, 700.

^{1}H NMR (400 MHz, $CDCl_3$, observed as a 94:6 mixture of *E*/*Z* isomers) δ_H 12.03 (brs, 1H^E + 1H^Z), 8.75 (t, *J* = 2.0 Hz, 1H^E), 8.49 – 8.37 (m, 2H^E), 8.15 (dd, *J* = 8.0, 0.8 Hz, 1H^E), 8.07 (dd, *J* = 7.8, 1.1 Hz, 1H^Z), 8.04 – 7.95 (m, 1H^E), 7.89 (t, *J* = 1.9 Hz, 1H^Z), 7.79 (dd, *J* = 14.7, 6.6 Hz, 1H^E), 7.77 – 7.71 (m, 2H^E + 2H^Z), 7.44 (t, *J* = 8.1 Hz, 1H^Z), 7.38 (td, *J* = 7.7, 1.3 Hz, 1H^Z), 7.25 (dd, *J* = 19.5, 7.9 Hz, 1H^Z), 6.29 (d, *J* = 7.2 Hz, 1H^Z).

^{13}C NMR (101 MHz, $CDCl_3$, *E*/*Z* assigned only when unambiguous distinction is possible) δ_C 169.50^Z, 166.45^E, 155.41, 154.11^Z, 152.10^E, 149.63^E, 149.30^E, 148.41^Z, 134.43^Z, 134.07^E, 133.71^E, 133.28^E, 131.89^Z, 130.92^E, 130.10^Z, 127.80^E, 127.55^Z, 127.01^E, 125.70^Z, 122.58^Z, 120.14^E, 117.92^Z, 116.42^E, 116.09^Z.

MS (ES, MeOH) m/z 272 $(M+H)^+$ 50%; 294 $(M+Na)^+$ 100%; 270 $(M-H)^-$ 100%.

HRMS (ES^+, MeOH) calc. for $C_{13}H_9N_3O_3$ + K $(M+K)^+$: 310.0230, found: 310.0241.



S7

A solution of crude 1-methoxy-3-nitrosobenzene **S5** (1.55 g, 11 mmol, prepared from 2.46 g of 3-methoxyaniline in 57% yield using the method of Defoin (*53*)) and anthranilic acid (1.55 g, 11 mmol) in EtOH/AcOH (16 + 4 mL) was stirred at room temperature overnight under inert atmosphere. After solvent evaporation, the residue was diluted with Et_2O (80 mL) and washed with $KHSO_4$ 5% (3 × 20 mL). The organic phase was extracted with NaOH (5% in H_2O, 3 × 10 mL) and the combined aqueous phases washed with Et_2O (2 × 10 mL). Solid $KHSO_4$ was added with stirring until pH ~ 3, then the aqueous phase was extracted with Et_2O (3 × 20 mL). The combined organic phases were washed with $KHSO_4$ 5% (10 mL), H_2O (3 × 15 mL) and brine (10 mL), dried with $MgSO_4$ and filtered. After solvent removal under vacuum, the residue was purified by column chromatography (SiO_2: CH_2Cl_2/PE, 1:1) to give **S7** as a red-orange solid (950 mg, 33%).

R_f 0.35 (CH_2Cl_2/PE, 1:1)

m.p. 50-52 °C

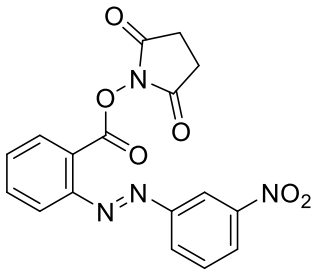
IR (ATR) ν_{max}/cm^{-1} 2962, 2772, 2360, 1735, 1595, 1447, 1251, 1240, 1035, 732, 702

^{1}H NMR (400 MHz, $CDCl_3$, observed as a 97:3 mixture of *E*/*Z* isomers) δ_H 12.96 (brs, 1H^E + 1H^Z), 8.51 – 8.41 (m, 1H^E), 8.11 – 8.00 (m, 1H^E + 1H^Z), 7.76 – 7.65 (m, 2H^E), 7.56 – 7.46 (m, 2H^E), 7.37 – 7.30 (m, 1H^E + 1H^Z), 7.20 – 7.10 (m, 1H^E + 1H^Z), 6.72 (dd, *J* = 8.2, 2.3 Hz, 1H^Z), 6.69 – 6.64 (m, 1H^Z), 6.58 (t, *J* = 2.1 Hz, 1H^Z), 6.48 (dd, *J* = 7.8, 1.0 Hz, 1H^Z), 6.32 (d, *J* = 8.4 Hz, 1H^Z), 3.91 (s, 3H^E), 3.69 (s, 3H^Z).

^{13}C NMR (126 MHz, $CDCl_3$) δ_C 166.27, 160.83, 152.81, 149.43, 133.96, 133.31, 132.93, 130.67, 127.24, 120.38, 117.50, 115.93, 106.98, 55.71.

MS (ES, MeOH) m/z 257 $(M+H)^+$ 100%; 279 $(M+Na)^+$ 45%; 255 $(M-H)^-$ 100%.

HRMS (ES^+, MeOH) calc. for $C_{14}H_{13}N_2O_3$ $(M+H)^+$: 257.0926, found: 257.0916.



S8

Compound **S8** was prepared according to general method (D, step 1) using azobenzene acid **S6** (100 mg, 0.37 mmol), HOSu (47 mg, 0.40 mmol) and DCC (84 mg, 0.40 mmol). After workup, the pure product was isolated by column chromatography (SiO_2: CH_2Cl_2) as a moisture-sensitive, dark red waxy solid (129 mg, 94%).

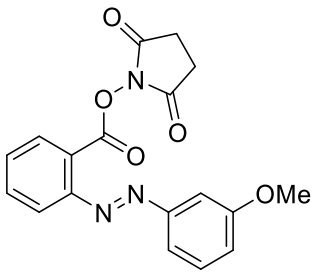
R_f 0.45 (CH_2Cl_2)

IR (ATR) ν_{max}/cm^{-1} 3079, 1734, 1527, 1351, 1199, 1061, 994

^{1}H NMR (400 MHz, $CDCl_3$, observed as a 94:6 mixture of *E*/*Z* isomers) δ_H 8.82 (t, *J* = 2.0 Hz, 1H^E), 8.37 (dddd, *J* = 14.7, 8.2, 2.0, 1.1 Hz, 2H^E), 8.14 (dd, *J* = 7.9, 1.2 Hz, 1H^Z), 8.07 (dd, *J* = 7.7, 1.2 Hz, 1H^E), 8.02 (ddd, *J* = 8.2, 2.2, 0.9 Hz, 1H^Z), 7.91 (t, *J* = 2.0 Hz, 1H^Z), 7.83 (dd, *J* = 8.1, 1.0 Hz, 1H^E), 7.76 (td, *J* = 7.7, 1.4 Hz, 1H^E), 7.71 (t, *J* = 8.1 Hz, 1H^E), 7.65 (td, *J* = 7.5, 1.3 Hz, 1H^E), 7.53 – 7.46 (m, 1H^Z), 7.41 (t, *J* = 8.1 Hz, 1H^Z), 7.30 (td, *J* = 7.9, 1.1 Hz, 1H^Z), 7.04 (ddd, *J* = 7.9, 1.9, 1.0 Hz, 1H^Z), 6.46 (dd, *J* = 8.0, 0.8 Hz, 1H^Z), 2.93 (s, 4H^E + 4H^Z).

^{13}C NMR (126 MHz, $CDCl_3$) δ_C 169.15, 162.50, 152.79, 151.33, 149.13, 134.04, 131.38, 131.19, 130.22, 129.17, 125.92, 124.78, 119.12, 118.92, 25.86.

MS (ES^+, MeOH) m/z 369 $(M+H)^+$ 100%; 386 $(M+Na)^+$ 50%.



S9

Compound **S9** was prepared according to general method (D, step 1) using azobenzene acid **S7** (193 mg, 0.75 mmol), HOSu (95 mg, 0.83 mmol) and DCC (178 mg, 0.83 mmol). After workup, the pure product was isolated by column chromatography (SiO_2: EtOAc/CH_2Cl_2 5:95) as a moisture-sensitive, viscous red liquid (255 mg, 97%).

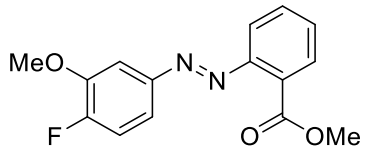
R_f 0.55 (EtOAc/CH_2Cl_2 1:9)

IR (ATR) ν_{max}/cm^{-1} 2943, 1735, 1594, 1479, 1255, 1200, 1061, 992

^{1}H NMR (500 MHz, $CDCl_3$) δ_H 8.05 (d, *J* = 7.6 Hz, 1H), 7.77 – 7.66 (m, 3H), 7.60 – 7.54 (m, 2H), 7.43 (t, *J* = 8.0 Hz, 1H), 7.07 (dd, *J* = 8.2, 2.5 Hz, 1H), 3.90 (s, 3H), 2.89 (brs, 4H).

^{13}C NMR (126 MHz, $CDCl_3$) δ_C 169.15, 162.58, 160.50, 153.75, 152.28, 134.00, 131.00, 130.20, 129.92, 124.16, 119.38, 118.82, 118.73, 105.91, 55.72, 25.86.

MS (ES^+, CH_2Cl_2) m/z 354 $(M+H)^+$ 100%; 376 $(M+Na)^+$ 30%.



S11

A solution of 2-nitrosobenzoic acid methyl ester **S10** (1.288 g, 8 mmol, prepared from 1.43 g methyl anthranilate in 83% yield using the procedure of Jurok *et al.* (*54*)), 3-methoxy-4-fluoroaniline (1.10 g, 7.8 mmol), AcOH (0.46 mL) and toluene (10 mL) was heated (60 °C) with stirring overnight under nitrogen. The mixture was cooled to room temperature and concentrated under vacuum. The residue was diluted with EtOAc (50 mL) and washed with $KHSO_4$ 5% (3 × 10 mL), $NaHCO_3$ (saturated solution, 3 × 10 mL), brine (5 mL), dried over $MgSO_4$, filtered and concentrated under reduced pressure. The crude product was purified by column chromatography (SiO_2:CH_2Cl_2/PE, 1:1) to afford methyl ester **S11** as a bright orange solid (1.17 g, 55%).

R_f 0.60 (CH_2Cl_2/PE, 1:1)

m.p. 64-65 °C

IR (ATR) ν_{max}/cm^{-1} 2949, 2960, 1723, 1594, 1505, 1409, 1267, 1209, 1109, 1050, 1029, 862, 768

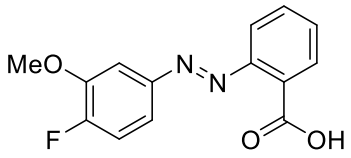
^{1}H NMR (400 MHz, $CDCl_3$) δ_H 7.86 – 7.82 (m, 1H), 7.62 – 7.46 (m, 5H), 7.26 – 7.20 (m, 1H), 3.98 (s, 3H), 3.91 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ_C 168.00, 154.72 (d, J = 253.7 Hz), 151.84, 149.43 (d, J = 3.2 Hz), 148.54 (d, J = 11.9 Hz), 132.21, 130.00 (d, J = 3.6 Hz), 128.63, 119.28 (d, J = 7.4 Hz), 118.93, 116.31 (d, J = 19.8 Hz), 105.53 (d, J = 2.9 Hz), 56.31, 52.53.

^{19}F NMR (376 MHz, $CDCl_3$) δ_F -129.4 (ddd, J = 10.9, 7.9, 4.6 Hz, 1F).

MS (ES^+, MeOH) m/z 289 $(M+H)^+$ 50%; 312 $(M+H)^+$ 90%.

HRMS (ES^+, MeOH) calc. for $C_{15}H_{13}N_2O_3F$ $(M+H)^+$: 289.0988, found: 289.1002.



S12

To a solution of methyl ester **S11** (1.18 g, 4 mmol) in MeOH/H_2O (30 + 6 mL) was added LiOH (690 mg, 29 mmol) and the mixture heated to reflux for 5 h (TLC monitoring). Upon reaction completion the mixture was cooled down to room temperature and concentrated under vacuum. The residue was diluted with EtOAc (20 mL) and the organic phase extracted with NaOH 2M (3 × 10 mL). The combined aqueous phases were washed with Et_2O (2 × 10 mL) then HCl (20% in H_2O) was added with external cooling and stirring until pH ~ 3. The aqueous phase was extracted with EtOAc (2 × 20 mL), dried with $MgSO_4$ and filtered. After solvent removal under vacuum, the residue was purified by column chromatography (SiO_2:CH_2Cl_2/EtOAc, 98:2 → 95:5) to give **S12** as an orange solid (819 mg, 73%)

R_f 0.40 (CH_2Cl_2/PE, 2:1)

m.p. 139-141 °C

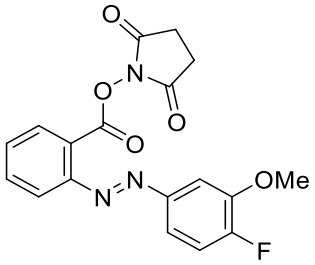
IR (ATR) ν_{max}/cm^{-1} 3070, 1737, 1593, 1507, 1483, 1273, 1106, 1026, 667

^{1}H NMR (400 MHz, $CDCl_3$, observed as a 94:6 mixture of *E*/*Z* isomers) δ_H 13.13 (brs, 1H^E + 1H^Z), 8.46 (dd, J = 7.0, 2.3 Hz, 1H^E), 8.09 (d, J = 8.2 Hz, 1H^Z), 8.03 (dd, J = 6.0, 3.2 Hz, 1H^E), 7.75 – 7.66 (m, 2H^E + 1H^Z), 7.60 (ddd, J = 8.3, 4.1, 2.4 Hz, 1H^E), 7.41 (dd, J = 7.7, 2.1 Hz, 1H^E), 7.31 (dd, J = 10.1, 8.8 Hz, 1H^E), 6.98 (d, J = 10.4 Hz, 1H^Z), 6.93 (d, J = 10.4 Hz, 1H^Z), 6.69 (dd, J = 7.2, 2.0 Hz, 1H^Z), 6.55 – 6.48 (m, 1H^Z), 6.29 (d, J = 7.5 Hz, 1H^Z), 4.00 (s, 3H^E), 3.70 (s, 3H^Z).

^{13}C NMR (101 MHz, $CDCl_3$) δ_C 166.25, 155.85 (d, *J* = 258.7 Hz), 149.31, 149.14 (d, *J* = 12.1 Hz), 148.27 (d, *J* = 3.4 Hz), 134.00, 133.27, 132.87, 127.02, 120.12 (d, *J* = 7.6 Hz), 117.05 (d, *J* = 20.1 Hz), 115.91, 105.60 (d, *J* = 3.4 Hz), 56.37.

^{19}F NMR (376 MHz, $CDCl_3$, observed as a 94:6 mixture of *E*/*Z* isomers) δ_F -124.49 – -124.59 (m, $1F^E$), -133.65 – -133.79 (m, $1F^Z$).

MS: (ES, MeOH) m/z 273 $(M-H)^-$ 100%; 275 $(M+H)^+$ 100%; **HRMS:** (ES^+, MeOH) calc. for $C_{14}H_{11}N_2O_3F$ + Na $(M+Na)^+$: 297.0651, found: 297.0664.



S13

Compound **S13** was prepared according to general method (D, step 1) using azobenzene acid **S12** (200 mg, 0.73 mmol), HOSu (92 mg, 0.80 mmol) and DCC (165 mg, 0.80 mmol). After workup, the pure product was isolated by column chromatography (SiO_2: CH_2Cl_2 → CH_2Cl_2/EtOAc 95:5) as a moisture-sensitive, bright red waxy solid (210 mg, 78%).

R_f 0.5 (CH_2Cl_2)

m.p. 179-181 °C

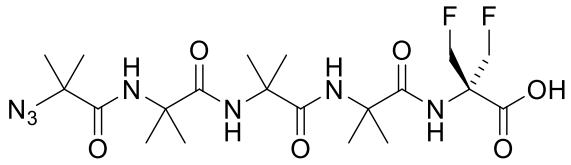
IR (ATR) ν_{max}/cm^{-1} 2944, 1735, 1593, 1495, 1270, 1200, 1059, 992, 909, 797

^{1}H NMR (500 MHz, $CDCl_3$) δ_H 8.03 (d, *J* = 7.5 Hz, 1H), 7.76 – 7.72 (m, 2H), 7.71 – 7.66 (m, 2H), 7.58 (ddd, *J* = 14.2, 7.1, 4.3 Hz, 1H), 7.27 – 7.20 (m, 1H), 3.99 (s, 3H), 2.91 (qt, *J* = 6.8, 4.8 Hz, 4H).

^{13}C NMR (126 MHz, $CDCl_3$) δ_C 169.14, 162.90, 155.05 (d, *J* = 254.4 Hz), 151.87, 149.25 (d, *J* = 3.2 Hz), 148.67 (d, *J* = 11.9 Hz), 133.88, 130.92, 130.25, 124.43, 120.74 (d, *J* = 7.4 Hz), 118.80, 116.16 (d, *J* = 19.7 Hz), 105.38 (d, *J* = 2.9 Hz), 56.49, 25.85.

^{19}F NMR (471 MHz, $CDCl_3$) δ_F -128.53 (ddd, *J* = 10.6, 8.0, 4.5 Hz, 1F).

MS: (ES^+, CH_2Cl_2) m/z 372 $(M+H)^+$ 100%; 394 $(M+Na)^+$ 30%.



F2

A round bottom flask was charged with $N_3Aib_4FibOMe$ **F1** (1.05 g, 2 mmol, prepared using the procedure of Pike *et al.* (*34*)) and THF/H_2O (3:1, 30 mL). LiOH (840 mg, 35 mmol) was added in one portion and the mixture stirred at room temperature for 7 h (TLC monitoring). Upon reaction completion, HCl 1M was added dropwise with stirring until pH < 2 and the mixture extracted with EtOAc (2 × 30 mL). The combined organic phases were washed with brine (10 mL), dried with $MgSO_4$, filtered and evaporated under vacuum to give azido acid **F2** as a white solid (862 mg, 86%).

R_f 0.15 (EtOAc/PE, 7:3)

m.p. 183-185 °C

IR (ATR) ν_{max}/cm^{-1} 3305, 2965, 2113, 1656, 1519, 1364, 1224, 1023

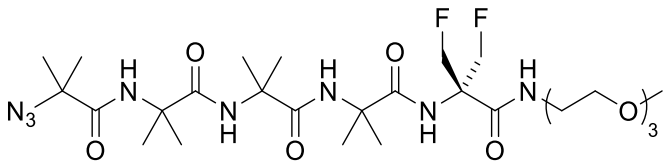
^{1}H NMR (500 MHz, $CDCl_3$) δ_H 7.87 (s, 1H), 7.84 (s, 1H), 7.77 (s, 1H), 7.67 (s, 1H), 4.96 – 4.67 (m, 4H), 1.52 (s, 6H), 1.48 (s, 6H), 1.45 (s, 6H), 1.37 (s, 6H).

^{13}C NMR (126 MHz, $CDCl_3$) δ_C 177.65, 176.52, 176.18, 174.76, 171.66, 81.43 (d, J = 168 Hz), 64.77, 62.76 (t, J = 19.7 Hz), 58.16, 58.08, 57.97, 25.60, 25.36, 24.81, 24.49.

^{19}F NMR (376 MHz, MeOD) δ_F -235.7 (t, J = 47.0 Hz).

MS (ES^-, MeOH) m/z 504 $(M-H)^-$ 100%; (ES^+, MeOH) m/z 506 $(M+H)^+$ 50%.

HRMS (ES^+, MeOH) calc. for $C_{20}H_{34}N_7O_6F_2$ $(M+H)^+$: 506.2538, found: 506.2541.



F3

EDC (282 mg, 1.47 mmol) was added with stirring to a cooled (0 °C) suspension of azido acid **F2** (720 mg, 1.40 mmol) and HOAt (200 mg, 1.47 mmol) in dry CH_2Cl_2 (5 mL). After complete dissolution of the starting materials, a solution of TEG-NH_2 (430 mg, 2.66 mmol, prepared according to the method of Dan *et al.* (*55*)) in dry CH_2Cl_2 (1 mL) was added, followed by DIPEA (0.415 mL, 2.3 mmol). The mixture was allowed to slowly reach room temperature and stirred for 48 hs under nitrogen. After solvent evaporation, the residue was

taken up in EtOAc (10 mL) and the organic phase washed with $KHSO_4$ 5% (3 × 5 mL), $NaHCO_3$ (saturated solution, 3 × 5 mL), brine (5 mL), dried over $MgSO_4$, filtered and concentrated under reduced pressure. The crude residue was purified by column chromatography (SiO_2:EtOAc → EtOAc/MeOH, 95:5) to afford **F3** as a white solid (753 mg, 83%).

R_f 0.45 (EtOAc/MeOH, 95:5)

m.p. 94-96 °C

IR (ATR) ν_{max}/cm^{-1} 3305, 2938, 2113, 1657, 1530, 1463, 1364, 1224, 1107

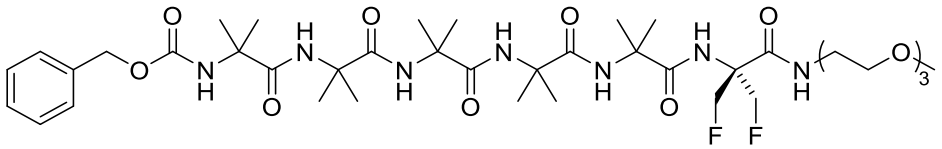
^{1}H NMR (500 MHz, $CDCl_3$) δ_H 7.54 (s, 1H), 7.49 (t, *J* = 5.6 Hz, 1H), 7.44 (s, 1H), 6.85 (s, 1H), 6.09 (s, 1H), 5.02 (A of AB, dd, *J* = 9.4, 2.2 Hz, 1H), 4.92 (B of AB, dd, *J* = 9.4, 2.2 Hz, 1H), 4.86 (A of AB, d, *J* = 9.4 Hz, 1H), 4.76 (B of AB, d, *J* = 9.4 Hz, 1H), 3.65 – 3.60 (m, 6H), 3.58 (t, *J* = 6.4 Hz, 2H), 3.53 (dd, *J* = 5.7, 3.8 Hz, 2H), 3.47 (dd, *J* = 12.3, 6.2 Hz, 2H), 3.37 (s, 3H), 1.53 (s, 6H), 1.48 (s, 12H), 1.43 (s, 6H).

^{13}C NMR (126 MHz, $CDCl_3$) δ_C 174.82, 174.26, 173.24, 173.22, 168.96 (t, *J* = 4.5 Hz), 82.34 (dd, *J* = 176 Hz, *J* = 5.2 Hz), 72.05, 70.65, 70.57, 70.34, 69.40, 64.08, 62.92 (t, *J* = 18 Hz), 59.11, 57.29, 56.98, 56.96, 39.37, 25.27, 25.13, 24.92, 24.38.

^{19}F NMR (471 MHz, $CDCl_3$) δ_F -233.5 (t, *J* = 45.9 Hz).

MS (ES^+, MeOH) m/z 651 $(M+H)^+$ 60%; 673 $(M+Na)^+$ 100%.

HRMS (ES^+, MeOH) calc. for $C_{27}H_{48}N_8O_8F_2$ + Na $(M+Na)^+$: 673.3461, found: 673.3430.



3a

Oligomer **3a** was prepared according to general method (C). Crude Cbz-Aib-F, obtained from Cbz-Aib-OH (30 mg, 0.128 mmol) using the procedure of Byrne *et al.* (*57*), amino-oligomer H-Aib$_4$FibTEG (obtained from the Pd-catalyzed hydrogenolysis of the corresponding azido-oligomer **F3** following general method (A)) and DIPEA (28 μL, 0.16 mmol) in dry CH_2Cl_2 were used (reaction time: 4 days). After workup, the product was purified by column chromatography (SiO_2: EtOAc/PE, 9:1) to give a white solid (20 mg, 74%).

R_f 0.55 (CH_2Cl_2/MeOH, 95:5)

m.p. 163-164 °C

IR (ATR) ν_{max}/cm^{-1} 3294, 2984, 1664, 1529, 1263, 1089, 731

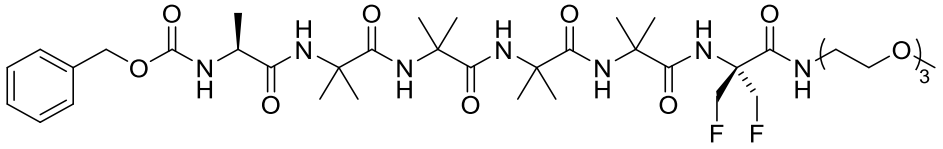
^{1}H NMR (500 MHz, $CDCl_3$) δ_H 7.72 (s, 1H), 7.61 (t, *J* = 5.8 Hz, 1H), 7.60 – 7.58 (m, 5H), 7.57 (s, 1H), 6.38 (s, 1H), 5.34 (s, 1H), 5.12 (s, 2H), 5.05 (d, *J* = 8.8 Hz, 1H), 4.94 (t, *J* = 10.0 Hz, 2H), 4.84 (d, *J* = 9.3 Hz, 1H), 3.66 – 3.61 (m, 6H), 3.59 (t, *J* = 6.6 Hz, 2H), 3.54 (dd, *J* = 5.7, 3.8 Hz, 2H), 3.48 (dd, *J* = 12.5, 6.3 Hz, 2H), 3.37 (s, 3H), 1.49 (s, 6H), 1.46 (s, 12H), 1.42 (s, 6H), 1.30 (s, 6H).

^{13}C NMR (101 MHz, $CDCl_3$) δ_C 176.01, 175.44, 175.39, 174.20, 174.11, 169.47 (t, *J* = 5 Hz), 156.01, 136.14, 128.89, 128.82, 128.30, 82.26 (d, *J* = 176 Hz), 72.06, 70.65, 70.57, 70.36, 69.44, 67.65, 62.77 (t, *J* = 18 Hz), 59.15, 57.33, 57.10, 56.86, 56.59, 39.32, 25.28, 25.25, 25.22, 25.19, 25.15, 25.08, 25.07, 25.03, 24.98, 24.95, 24.90, 24.84.

^{19}F NMR (471 MHz, $CDCl_3$) δ_F -233.58 (brs, 2F); (376 MHz, MeOD) δ_F -235.59 (brs, 2F).

MS (ES, CH_2Cl_2) m/z 866 $(M+Na)^+$ 60%; 842 $(M-H)^-$ 80%.

HRMS (ES^+, MeOH) calc. for $C_{39}H_{63}N_7O_{11}F_2$ + Na $(M+Na)^+$: 866.4451, found: 866.4470.



3b

Oligomer **3b** was prepared according to general method (B) using Cbz-Ala-OH (33 mg, 0.15 mmol), HOAt (20 mg, 0.13 mmol), EDC (30 mg, 0.16 mmol), amino-oligomer H-Aib$_4$FibTEG (40 mg, 0.074 mmol, obtained from the Pd-catalyzed hydrogenolysis of the corresponding azido-oligomer **F3** following general method (A)) and DIPEA (26 μL, 0.15 mmol) in dry CH_2Cl_2 (reaction time: 24 hs). After workup, the product was purified by column chromatography (SiO_2: CH_2Cl_2/MeOH, 95:5) to give a white solid (45 mg, 74%).

R_f 0.45 (CH_2Cl_2/MeOH, 95:5)

m.p. 91-93 °C

IR (ATR) ν_{max}/cm^{-1} 3292, 2985, 1653, 1530, 1421, 1384, 1229, 1025, 735

$[\alpha]_D^{25}$ –3.4 (c = 1, $CHCl_3$)

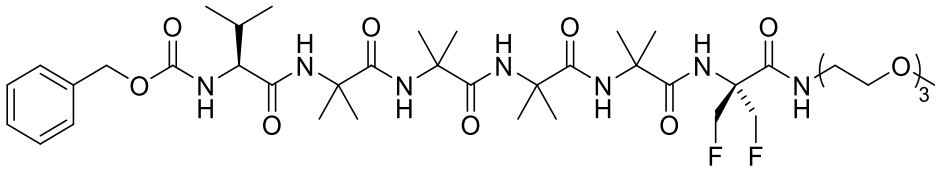
^{1}H NMR (400 MHz, $CDCl_3$) δ_H 7.75 (s, 1H), 7.64 (t, *J* = 5.8 Hz, 1H), 7.61 (s, 1H), 7.56 (s, 1H), 7.39 – 7.31 (m, 5H), 7.15 (s, 1H), 6.66 (s, 1H), 5.73 (d, *J* = 3.8 Hz, 1H), 5.14 (A of AB, *J* = 12.3 Hz, 1H), 5.10 (B of AB, *J* = 12.3 Hz, 1H), 5.08 – 4.76 (m, 4H), 3.99 – 3.90 (m, 1H), 3.66 – 3.61 (m, 6H), 3.58 (t, *J* = 6.6 Hz, 2H), 3.55 – 3.51 (m, 2H), 3.47 (dd, *J* = 12.4, 6.3 Hz, 2H), 3.37 (s, 3H), 1.48 (s, 6H), 1.45 (s, 3H), 1.44 (s, 3H), 1.41 (s, 9H), 1.40 (s, 3H), 1.31 (brs, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ_C 175.95, 175.48, 175.16, 173.96, 173.00, 169.57 (t, J = 4.4 Hz), 156.94, 136.07, 128.87, 128.76, 128.22, 72.04, 70.63, 70.55, 70.36, 69.42, 67.66, 62.72 (t, J = 18.8 Hz), 59.14, 57.09, 56.90, 56.70, 39.34, 25.40 (brs), 24.65 (brs), 16.94.

^{19}F NMR (376 MHz, $CDCl_3$) δ_F -233.0 (brs, 1F), -233.9 (brs, 1F); (376 MHz, MeOD) δ_F -234.8 (brs, 1F), -236.2 (brs, 1F).

MS: (ES, MeOH) m/z 853 $(M+Na)^+$ 100%.

HRMS: (ES^+, MeOH) calc. for $C_{38}H_{61}N_7O_{11}F_2$ + Na $(M+Na)^+$: 852.4295, found: 852.4262.



3c

Oligomer **3c** was prepared according to general method (B) using Cbz-Val-OH (32 mg, 0.128 mmol), HOAt (17 mg, 0.128 mmol), EDC (26 mg, 0.134 mmol), amino-oligomer H-Aib$_4$FibTEG (40 mg, 0.064 mmol, obtained from the Pd-catalyzed hydrogenolysis of the corresponding azido-oligomer **F3** following general method (A)) and DIPEA (23 μL, 0.128 mmol) in dry CH_2Cl_2 (reaction time: 48 hs). After workup, the product was purified by column chromatography (SiO_2: EtOAc/PE, 95:5 → EtOAc, 100%) to give a white solid (38 mg, 70%).

R_f 0.4 (EtOAc/PE, 9:1)

m.p. 149-150 °C

IR (ATR) ν_{max}/cm^{-1} 3293, 2963, 1652, 1529, 1384, 1229, 1105, 1018

$[\alpha]_D^{25}$ −12.8 (c = 1, MeOH)

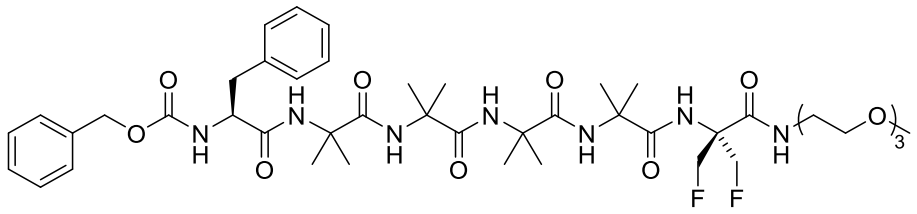
^{1}H NMR (500 MHz, $CDCl_3$) δ_H 7.70 (s, 1H), 7.60 (t, J = 5.7 Hz, 1H), 7.58 (s, 1H), 7.55 (s, 1H), 7.41 – 7.33 (m, 5H), 7.02 (s, 1H), 6.29 (s, 1H), 5.21 (d, J = 3.7 Hz, 1H), 5.15 (A of AB, d, J = 12.1 Hz, 1H), 5.09 (B of AB, d, J = 12.1 Hz, 1H), 5.09 – 4.77 (m, 4H), 3.70 – 3.66 (m, 1H), 3.66 – 3.61 (m, 6H), 3.59 (t, J = 6.6 Hz, 2H), 3.54 (dd, J = 5.7, 3.8 Hz, 2H), 3.51 – 3.44 (m, 2H), 3.37 (s, 3H), 2.09 (dt, J = 13.4, 6.8 Hz, 1H), 1.49 (s, 6H), 1.46 (s, 3H), 1.45 (s, 3H), 1.44 (s, 3H), 1.43 (s, 3H), 1.40 (s, 3H), 1.31 (s, 3H), 1.02 (t, J = 6.5 Hz, 6H).

^{13}C NMR (126 MHz, $CDCl_3$) δ_C 175.79, 175.31, 174.90, 173.60, 171.60, 169.38, 169.34, 169.30 (t, J = 5.0 Hz), 157.26, 135.77, 128.93, 128.37, 82.62 (d, J = 173 Hz), 82.03 (d, J = 176 Hz), 72.06, 70.67, 70.59, 70.36, 69.41, 67.88, 62.82 (t, J = 18 Hz), 62.44, 59.17, 57.10, 56.94, 56.85, 39.30, 29.81, 25.53, 24.72, 24.55, 19.31, 18.69.

^{19}F NMR (471 MHz, $CDCl_3$) δ_F -232.9 (brs, 1F), -234.2 (brs, 1F); (376 MHz, MeOD) δ_F -234.6 (brs, 1F), -236.6 (brs, 1F).

MS (ES^+, MeOH) m/z 880 $(M+Na)^+$ 100%.

HRMS (ES^+, MeOH) calc. for $C_{40}H_{64}N_7O_{11}F_2$ + Na $(M+Na)^+$ 880.4608, found: 880.4606.



3d

Oligomer **3b** was prepared according to general method (B) using Cbz-Phe-OH (29 mg, 0.32 mmol), HOAt (44 mg, 0.32 mmol), EDC (64 mg, 0.33 mmol), amino-oligomer H-Aib$_4$FibTEG (105 mg, 0.17 mmol, obtained from the Pd-catalyzed hydrogenolysis of the corresponding azido-oligomer **F3** following general method (A)) and DIPEA (56 μL, 0.32 mmol) in dry CH_2Cl_2 (reaction time: 24 hs). After workup, the product was purified by column chromatography (SiO_2: CH_2Cl_2/MeOH, 95:5) to give a white solid (98 mg, 64%).

R_f 0.6 (CH_2Cl_2/MeOH, 95:5)

m.p. 78-80 °C

IR (ATR) ν_{max}/cm^{-1} 3297, 2933, 1651, 1530, 1421, 1381, 1226, 1041, 699

$[\alpha]_D^{25}$ −16.9 (c = 1, MeOH)

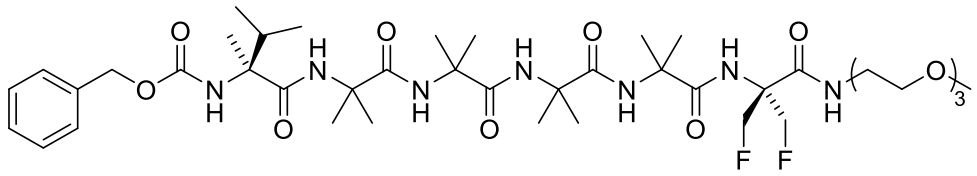
^{1}H NMR (500 MHz, $CDCl_3$) δ_H 7.82 (s, 1H), 7.70 (s, 3H), 7.44 – 7.20 (m, 6H), 6.81 (s, 1H), 5.88 (brs, 1H), 5.18 – 5.11 (m, 2H), 5.10 – 5.02 (m, 1H), 4.98 (t, *J* = 9.3 Hz, 2H), 4.88 (t, *J* = 9.4 Hz, 1H), 4.19 – 4.12 (m, 1H), 3.69 – 3.64 (m, 6H), 3.62 (t, *J* = 6.4 Hz, 2H), 3.58 (dd, *J* = 5.6, 3.7 Hz, 2H), 3.50 (dd, *J* = 11.8, 5.7 Hz, 2H), 3.41 (s, 3H), 3.23 (dd, *J* = 13.9, 5.8 Hz, 1H), 3.04 (dd, *J* = 13.9, 8.8 Hz, 1H), 1.54 (s, *J* = 6.5 Hz, 9H), 1.51 (s, 3H), 1.46 (s, *J* = 2.6 Hz, 3H), 1.45 (s, *J* = 15.0 Hz, 3H), 1.40 (s, 3H), 1.33 (s, 3H).

^{13}C NMR (101 MHz, MeOD) δ_C 177.93, 177.56, 177.34, 176.65, 171.43 (t, *J* = 4.0 Hz), 158.59, 138.20, 138.04, 130.56, 129.59, 129.54, 129.12, 128.62, 127.95, 83.48 (d, *J* = 177 Hz), 81.86 (d, *J* = 168 Hz), 72.98, 71.55, 71.41, 70.18, 67.67, 63.72 (t, *J* = 18.9 Hz), 59.12, 58.22, 58.01, 57.86, 57.59, 40.49, 38.28, 26.46, 26.37, 26.15, 24.59, 24.51, 24.16, 23.98.

^{19}F NMR (471 MHz, $CDCl_3$) δ_F -233.4 (brs, 2F); (376 MHz, MeOD) δ_F -234.2 (brs, 1F), -236.8 (brs, 1F).

MS (ES, MeOH) m/z 906 $(M+H)^+$ 100%; 928 $(M+Na)^+$ 80%; 904 $(M-H)^-$ 20%; 940 $(M+Cl)^-$ 100%.

HRMS (ES^+, MeOH) calc. for $C_{44}H_{66}N_7O_{11}F_2$ $(M+H)^+$: 906.4788, found: 906.4814.



3e

Oligomer **3e** was prepared according to general method (C) from crude Cbz-aMv-F (obtained from Cbz-aMv-OH, 94 mg, 0.35 mmol, using the method of Byrne *et al.* (*57*)) amino-oligomer H-Aib$_4$FibTEG (54 mg, 0.087 mmol, obtained from the Pd-catalyzed hydrogenolysis of the corresponding azido-oligomer **F3** following general method (A)) and DIPEA (76 µL, 0.44 mmol) in dry CH_2Cl_2 (reaction time: 5 days). After workup, the product was purified by column chromatography (SiO_2: EtOAc/PE, 9:1) to give a white solid (40 mg, 62%).

R_f 0.5 (EtOAc/PE, 9:1)

m.p. 167-168 °C

IR (ATR) ν_{max}/cm^{-1} 3290, 2962, 1652, 1530, 1259, 1227, 1103, 1029

$[\alpha]_D^{25}$ +39.5 (c = 1, MeOH)

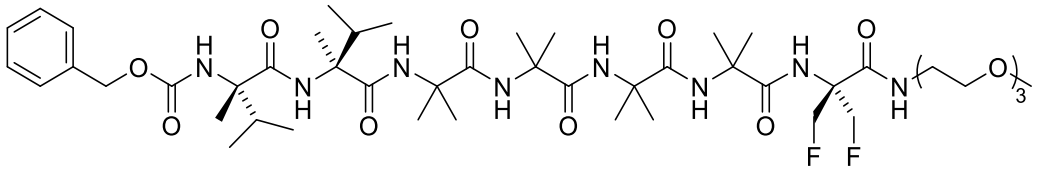
^{1}H NMR (400 MHz, $CDCl_3$) δ_H 7.73 (s, 1H), 7.67 (s, 1H), 7.61 (t, *J* = 5.6 Hz, 1H), 7.60 (s, 1H), 7.52 (s, 1H), 7.43 – 7.32 (m, 5H), 6.29 (s, 1H), 5.24 (s, 1H), 5.19 (A of AB, d, *J* = 12.2 Hz, 1H), 5.14 (ddd, *J* = 47.2, 9.4, 2.5 Hz, 1H), 5.04 (B of AB, d, *J* = 12.0 Hz, 1H), 4.98 (dd, *J* = 48.0, 10.8 Hz, 1H), 4.88 (dd, *J* = 27.8, 9.1 Hz, 1H), 4.76 (dd, *J* = 27.4, 9.0 Hz, 1H), 3.66 – 3.40 (m, 12H), 3.37 (s, 3H), 1.92 (dt, *J* = 13.7, 6.6 Hz, 1H), 1.49 (s, 6H), 1.47 (s, 3H), 1.45 (s, 3H), 1.44 (s, 6H), 1.42 (s, 6H), 1.19 (s, 3H), 0.97 (dd, *J* = 13.8, 6.8 Hz, 6H).

^{13}C NMR (126 MHz, 1:1 MeOD/$CDCl_3$) δ_C 175.95, 175.35, 175.32, 173.93, 172.77, 169.33 (t, *J* = 5.0 Hz), 156.18, 135.94, 128.94, 128.42, 83.41 (d, *J* = 176 Hz), 81.29 (d, *J* = 176 Hz), 72.07, 70.68, 70.59, 70.37, 69.42, 67.78, 63.18, 62.83 (t, *J* = 18 Hz), 59.18, 57.10, 56.92, 56.90, 56.73, 39.28, 35.81, 26.93, 26.87, 26.83, 26.71, 23.61, 23.43, 23.34, 23.28, 17.74, 17.41, 17.27.

^{19}F NMR (376 MHz, $CDCl_3$) δ_F -231.3 (brs, 1F), -235.8 (brs, 1F); (376 MHz, MeOD) δ_F -233.9 (brs, 1F), -237.3 (brs, 1F).

MS (ES^+, MeOH) m/z 872 $(M+H)^+$ 70%; 895 $(M+Na)^+$ 100%.

HRMS (ES^+, MeOH) calc. for $C_{41}H_{67}N_7O_{11}$ + H $(M+H)^+$: 872.4945, found: 879.4913.



3f

Oligomer **3f** was prepared according to general method (C) from crude Cbz-aMv-F (obtained from Cbz-aMv-OH, 71 mg, 0.27 mmol using the method of Byrne *et al.* (*57*)) amino-oligomer H-aMvAib$_4$FibTEG (50 mg, 0.067 mmol, obtained from the Pd-catalyzed hydrogenolysis of the corresponding Cbz-protected oligomer **4e** following general method (A)) and DIPEA (58 μL, 0.335 mmol) in dry CH_2Cl_2 (reaction time: 5 days). After workup, the product was purified by column chromatography (SiO_2: EtOAc → EtOAc/MeOH, 95:5) to give a white solid (43 mg, 63%).

R_f 0.3 (EtOAc/PE, 95:5)

m.p. 141-145 °C

IR (ATR) ν_{max}/cm^{-1} 3304, 2981, 1651, 1529, 1415, 1361, 1107

$[\alpha]_D^{25}$ +53.2 (c = 1, $CHCl_3$)

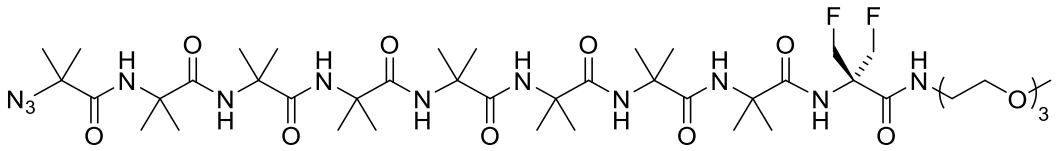
^{1}H NMR (400 MHz, MeOD) δ_H 8.07 (s, 1H), 8.03 (s, 1H), 8.02 (s, 1H), 8.00 (s, 1H), 7.99 (s, 1H), 7.78 (s, 1H), 7.46 – 7.29 (m, 5H), 5.21 (A of AB, d, *J* = 12.4 Hz, 1H), 5.06 (B of AB, d, *J* = 12.4 Hz, 1H), 5.05 – 4.66 (m, 4H), 3.64 – 3.57 (m, 8H), 3.53 (dd, *J* = 5.7, 3.5 Hz, 2H), 3.51 – 3.38 (m, 2H), 3.35 (s, 3H), 1.94 (dt, *J* = 13.6, 6.8 Hz, 1H), 1.60 (dt, *J* = 13.8, 7.0 Hz, 1H), 1.52 – 1.44 (m, 24H), 1.41 (s, 3H), 1.40 (s, 3H), 0.98 (dd, *J* = 22.1, 6.8 Hz, 6H), 0.83 (dd, *J* = 23.7, 6.8 Hz, 6H).

^{13}C NMR (101 MHz, $CDCl_3$) δ_C 176.27, 175.87, 175.52, 175.23, 172.48, 169.44 (t, *J* = 5.0 Hz), 165.58, 156.29, 135.74, 129.87, 128.89, 128.85, 128.72, 83.57 (dd, *J* = 180 Hz, *J* = 5.3 Hz), 80.88 (dd, *J* = 172 Hz, *J* = 4.5 Hz), 72.02, 70.63, 70.55, 70.32, 69.40, 67.87, 63.52, 62.73 (t, *J* = 18.1 Hz), 62.40, 59.17, 57.07, 56.97, 56.92, 56.82, 56.78, 56.72, 39.23, 36.14, 35.82, 29.84, 27.29, 27.26, 27.14, 27.08, 23.10, 22.97, 22.82, 22.79, 18.14, 18.07, 17.42, 17.28, 17.15, 17.07, 14.29, 8.79.

^{19}F NMR (376 MHz, $CDCl_3$) δ_F -230.8 (t, *J* = 46.6 Hz, 1F), -236.3 (t, *J* = 47.2 Hz, 1F); (471 MHz, MeOD) δ_F -233.2 (t, *J* = 45.9 Hz), -237.9 (t, *J* = 46.8 Hz).

MS (ES, MeOH) m/z 1007 $(M+Na)^+$ 100%; 983 $(M-H)^-$ 30%; 1019 $(M+Cl)^-$ 100%.

HRMS (ES^+, MeOH) calc. for $C_{47}H_{78}N_8O_{12}F_2$ + Na $(M+Na)^+$: 1007.5599, found: 1007.5621.



F4

1) Azlactone formation: a round bottom flask was charged with N_3Aib_4OH (683 mg, 1.78 mmol, obtained using the method of Clayden *et al.* (*56*)) and dry CH_2Cl_2 (5 mL). After cooling with an external ice bath, EDC (358 mg, 1.87 mmol) was added. After 5 minutes, the ice bath was removed and the mixture stirred at room temperature for 3 h. The solvents were removed under reduced pressure and the residue diluted with EtOAc (25 mL) and $KHSO_4$ 5% (5 mL). The phases were separated and the organic layer washed again with $KHSO_4$ 5% (2 × 5 mL), $NaHCO_3$ 5% (2 × 3 mL) and brine. After drying ($MgSO_4$) and solvent removal under vacuum, the residue was placed under high vacuum for 2 h to give the pure azlactone (590 mg, 90%) as confirmed by NMR, which was used directly in the next step.

2) Coupling: the freshly prepared azlactone was dissolved in dry CH_3CN (5 mL) and added via syringe under nitrogen to H-Aib_4FibTEG (370 mg, 0.59 mmol, obtained from the Pd-catalyzed hydrogenolysis of the corresponding azido-oligomer **F3** following general method (A)) and DIPEA (465 μL, 2.67 mmol) in CH_3CN (2 mL). The mixture was stirred at reflux (90 °C) under nitrogen for 5 days, after which it was cooled down to ambient temperature and the solvent removed under vacuum. EtOAc (25 mL) was added and the organic phase washed with $KHSO_4$ 5% (3 × 5 mL), NaOH 5% (3 × 5 mL), brine (5 mL), dried over $MgSO_4$, filtered and concentrated under reduced pressure. The crude residue was purified by column chromatography (SiO_2: EtOAc/MeOH, 95:5) to give a white solid (505 mg, 86%).

R_f 0.45 (EtOAc/MeOH, 95:5)

m.p. 225-226 °C

IR (ATR) ν_{max}/cm^{-1} 3295, 2985, 2116, 1650, 1534, 1415, 1382, 1227

^{1}H NMR (400 MHz, $CDCl_3$) δ_H 7.81 (s, 1H), 7.73 (s, 1H), 7.65 (t, *J* = 5.7 Hz, 1H), 7.62 (s, 1H), 7.61 (s, 2H), 7.53 (s, 1H), 6.98 (s, 1H), 6.22 (s, 1H), 5.06 (d, *J* = 8.7 Hz, 1H), 5.00 – 4.88 (m, 2H), 4.83 (d, *J* = 9.2 Hz, 1H), 3.66 – 3.61 (m, 6H), 3.59 (t, *J* = 6.6 Hz, 2H), 3.54 (dd, *J* = 5.8, 3.6 Hz, 2H), 3.48 (dd, *J* = 12.3, 6.2 Hz, 2H), 3.37 (s, 3H), 1.56 (s, 6H), 1.51 (s, 6H), 1.49 (s, 6H), 1.48 (s, 6H), 1.46 (s, 12H), 1.45 (s, 6H), 1.43 (s, 6H).

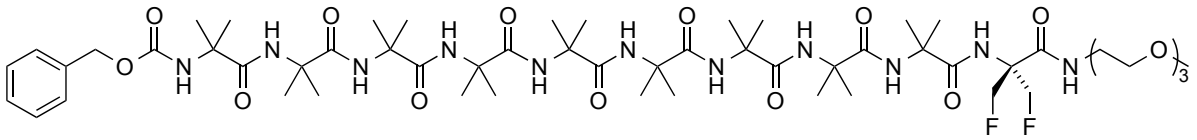
^{13}C NMR (126 MHz, $CDCl_3$) δ_C 176.31, 175.98, 175.61, 175.56, 175.46, 174.23, 173.42, 173.37, 169.50 (t, *J* = 4.3 Hz), 82.26 (d, *J* = 174 Hz), 72.05, 70.66, 70.57, 70.37, 69.41,

64.07, 62.74 (t, *J* = 18.3 Hz), 59.16, 57.08, 57.03, 56.93, 56.83, 56.77, 56.76, 56.74, 39.28, 25.51, 24.58, 24.47.

^{19}F NMR (471 MHz, $CDCl_3$) δ_F -233.6 (brs, 2F); (376 MHz, MeOD) δ_F -235.6 (brs, 2F).

MS (ES^+, MeOH) m/z 1013 $(M+Na)^+$ 100%.

HRMS (ES^+, MeOH) calc. for $C_{43}H_{76}N_{12}O_{12}F_2$ + Na $(M+Na)^+$: 1013.5571, found: 1013.5545.



6a

Oligomer **6a** was prepared according to general method (C) from crude Cbz-Aib-F (obtained from Cbz-Aib-OH, 36 mg, 0.152 mmol, using the method of Byrne *et al.* (*57*)) amino-peptide H-Aib$_8$FibTEG (40 mg, 0.038 mmol, obtained from the Pd-catalyzed hydrogenolysis of the corresponding azidopeptide **F4** following general method (A)) and DIPEA (33 mL, 0.19 mmol) in dry CH_2Cl_2 (reaction time: 4 days). After workup, the product was purified by column chromatography (SiO_2: CH_2Cl_2/MeOH, 95:5) to give a white solid (37 mg, 82%).

Rf 0.5 (CH_2Cl_2/MeOH, 95:5)

mp: 195-197 °C

IR ν_{max} (ATR)/cm^{-1} 3262, 2985, 1650, 1533, 1384, 1228, 732

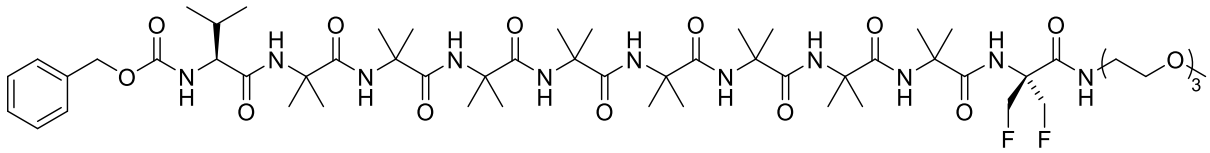
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.83 (s, 1H), 7.77 (s, 1H), 7.74 (s, 1H), 7.71 (s, 1H), 7.68 (s, 1H), 7.67 (t, *J* = 6.0 Hz, 1H), 7.64 (s, 2H), 7.53 (s, 1H), 7.42 – 7.29 (m, 5H), 6.55 (s, 1H), 5.67 (s, 1H), 5.12 (s, 2H), 5.04 (brs, 1H), 4.95 (d, *J* = 6.1 Hz, 2H), 4.85 (d, *J* = 7.1 Hz, 1H), 3.66 – 3.61 (m, 6H), 3.59 (t, *J* = 6.5 Hz, 2H), 3.56 – 3.51 (m, 2H), 3.51 – 3.44 (m, 2H), 3.37 (s, 3H), 1.54 – 1.45 (m, 48H), 1.43 (s, 6H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 176.49, 176.26, 176.13, 176.04, 175.95, 175.69, 175.54, 174.45, 174.42, 169.67 (t, *J* = 4.4 Hz), 156.09, 136.19, 128.88, 128.78, 128.26, 72.05, 70.64, 70.56, 70.38, 69.44, 67.62, 62.68 (t, *J* = 18.4 Hz), 59.16, 57.32, 57.08, 56.81, 56.80, 56.73, 56.69, 56.68, 56.60, 39.30, 26.13 – 24.06 (brs).

^{19}F NMR (471 MHz, $CDCl_3$) δ -230.9 (brs, 1F), -236.1 (brs, 1F); (376 MHz, MeOD) δ -235.6 (brs, 2F).

MS: (ES^+, MeOH) m/z 1206 $(M+Na)^+$ 100%; 1184 $(M+H)^+$ 50%.

HRMS: (ES^+, MeOH) calc. for $C_{55}H_{91}N_{11}O_{15}F_2$ + Na $(M+Na)^+$: 1206.6522, found: 1206.6556.



6c

Oligomer **6c** was prepared according to general method (B) using Cbz-Val-OH (33 mg, 0.13 mmol), HOAt (18 mg, 0.13 mmol), EDC (27 mg, 0.14 mmol), amino-oligomer H-Aib_8FibTEG (70 mg, 0.066 mmol, obtained from the Pd-catalyzed hydrogenolysis of the corresponding azido-oligomer **F4** following general method (A)) and DIPEA (13 μL, 0.058 mmol) in dry CH_2Cl_2 (reaction time: 36 hs). After workup, the product was purified by column chromatography (SiO_2: CH_2Cl_2/MeOH, 95:5) to give a white solid (61 mg, 83%).

R_f 0.5 (CH_2Cl_2/MeOH, 95:5)

m.p. 175-176 °C

IR (ATR) ν_{max}/cm^{-1} 3253, 2984, 1650, 1531, 1384, 1228, 910, 730

$[\alpha]_D^{25}$ +16.2 (c = 1, CH_2Cl_2)

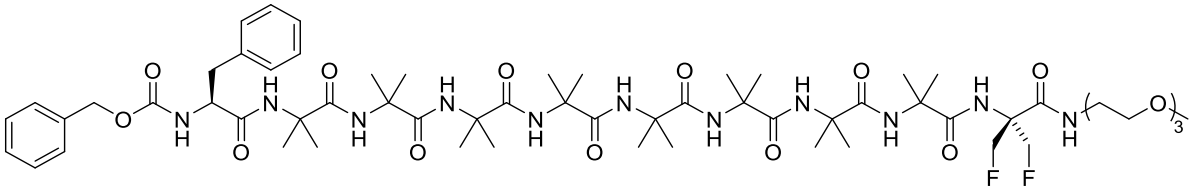
^{1}H NMR (400 MHz, $CDCl_3$) δ_C 7.84 (s, 1H), 7.78 (s, 1H), 7.74 (s, 1H), 7.72 (s, 1H), 7.70 (s, 1H), 7.69 (t, *J* = 6.1 Hz, 1H), 7.66 (s, 1H), 7.65 (s, 1H), 7.44 – 7.28 (m, 5H), 7.14 (s, 1H), 6.74 (brs, 1H), 5.64 (brs, 1H), 5.12 (dd, *J* = 19.9, 12.6 Hz, 2H), 5.05 – 4.77 (m, 4H), 3.74 – 3.67 (m, 1H), 3.65 – 3.61 (m, 6H), 3.59 (t, *J* = 6.6 Hz, 2H), 3.53 (dd, *J* = 5.7, 3.6 Hz, 2H), 3.47 (dd, *J* = 11.8, 5.9 Hz, 2H), 3.37 (s, 3H), 2.09 (dd, *J* = 13.3, 6.6 Hz, 1H), 1.56 – 1.38 (m, 48H), 1.02 (d, *J* = 6.8 Hz, 6H).

^{13}C NMR (126 MHz, $CDCl_3$) δ_C 176.53, 176.29, 176.09, 176.04, 175.85, 175.77, 175.22, 174.15, 171.96, 169.75 (t, *J* = 4.7 Hz), 157.33, 135.94, 128.89, 128.80, 128.27, 72.02, 70.61, 70.52, 70.35, 69.46, 67.73, 62.68 (t, *J* = 18.5 Hz), 59.15, 57.08, 56.86, 56.81, 56.77, 56.72, 56.69, 56.68, 39.32, 29.84, 27.19 – 22.96 (brs), 19.30, 18.83, 14.27.

^{19}F NMR (471 MHz, $CDCl_3$) δ_F -230.8 (brs, 1F), -235.9 (brs, 1F); (376 MHz, MeOD) δ_F -234.8 (brs, 1F), -236.3 (brs, 1F).

MS (ES^+, MeOH) m/z 1199 $(M+H)^+$ 100%; 1222 $(M+Na)^+$ 60%.

HRMS (ES^+, MeOH) calc. for $C_{56}H_{93}N_{11}O_{15}F_2$ + H $(M+H)^+$: 1198.6899, found: 1197.6947.



6d

Oligomer **6d** was prepared according to general method (B) using Cbz-Phe-OH (17 mg, 0.058 mmol), HOAt (8 mg, 0.058 mmol), EDC (12 mg, 0.061 mmol), amino-oligomer H-Aib_8FibTEG (30 mg, 0.029 mmol, obtained from the Pd-catalyzed hydrogenolysis of the corresponding azido-oligomer **F4** following general method (A)) and DIPEA (10 μL, 0.058 mmol) in dry CH_2Cl_2 (reaction time: 48 hs). After workup, the product was purified by column chromatography (SiO_2: CH_2Cl_2/MeOH, 95:5) to afford a white solid (31 mg, 85%).

R_f 0.45 (CH_2Cl_2/MeOH, 9:1)

m.p. 224-228 °C

IR (ATR) ν_{max}/cm^{-1} 3288, 2984, 1651, 1530, 1384, 1228, 731

$[\alpha]_D^{25}$ –8.4 (c = 1, CH_2Cl_2)

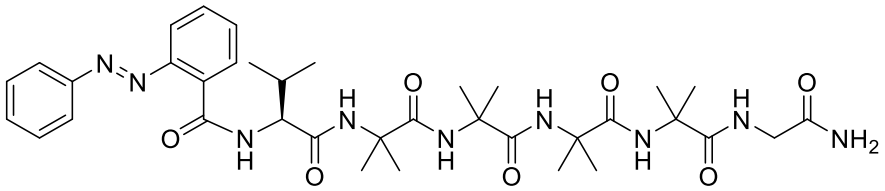
^{1}H NMR (500 MHz, $CDCl_3$) δ_H 7.83 (s, 1H), 7.76 (s, 1H), 7.73 (s, 1H), 7.71 (s, 1H), 7.68 (s, 1H), 7.66 (t, *J* = 5.6 Hz, 1H), 7.64 (s, 1H), 7.57 (s, 1H), 7.40 – 7.14 (m, 6H), 6.42 (s, 1H), 5.48 (s, 1H), 5.09 (dd, *J* = 20.3, 12.3 Hz, 2H), 5.05 – 4.80 (m, 4H), 4.10 (brs, 1H), 3.63 (m, 6H), 3.59 (t, *J* = 6.5 Hz, 2H), 3.55 – 3.51 (m, 2H), 3.47 (d, *J* = 5.9 Hz, 2H), 3.37 (s, 3H), 3.17 (A of AB, dd, *J* = 13.8, 5.7 Hz, 1H), 2.98 (B of AB, dd, *J* = 13.5, 8.7 Hz, 1H), 1.55 – 1.44 (m, 36H), 1.42 (s, 6H), 1.36 (s, 3H), 1.26 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ_C 176.59, 176.40, 176.20, 176.13, 175.96, 175.87, 175.42, 174.42, 172.00, 169.88 (t, *J* = 4.3 Hz), 136.08, 129.30, 129.02, 128.80, 128.63, 128.13, 127.45, 71.92, 70.52, 70.44, 70.25, 69.44, 67.46, 62.50 (t, *J* = 19 Hz), 59.14, 57.01, 56.78, 56.76, 56.70, 56.67, 56.64, 56.62, 39.26, 36.60, 29.83, 26.56 – 22.34 (brs).

^{19}F NMR (376 MHz, $CDCl_3$) δ_F -231.3 (brs, 1F), -235.7 (brs, 1F); (471 MHz, CD_3OH) δ_F -234.6 (brs, 1F), -236.6 (brs, 1F).

MS (ES, MeOH) m/z 1269 $(M+Na)^+$ 100%; 1244 $(M-H)^-$ 80%; 1290 $(M+Cl)^-$ 55%.

HRMS (ES^+, MeOH) calc. for $C_{60}H_{93}N_{11}O_{15}F_2$ + Na $(M+Na)^+$: 1268.6718, found: 1268.6696.



1a

Azobenzene-oligomer **1a** was prepared according to general method (D) from succinimidyl ester **S3** (62 mg, 0.194 mmol, prepared according to the method of Keiper and Vyle (*50*)), amino-oligomer H-ValAib$_4$GlyNH$_2$ (50 mg, 0.097 mmol, obtained from the Pd-catalyzed hydrogenolysis of the corresponding Cbz-protected oligomer **S14c** (*43*) following general method (A)) and DIPEA (34 μL, 0.194 mmol) in dry CH_2Cl_2 (reaction time: 24 hs). After workup, **1a** was isolated by column chromatography (SiO_2: EtOAc/MeOH, 95:5) as an orange solid (48 mg, 68%).

R_f 0.7 (EtOAc/MeOH, 95:5)

m.p. 271-272 °C

IR (ATR) ν_{max}/cm^{-1} 3306, 2983, 2467, 1642, 1420, 1290

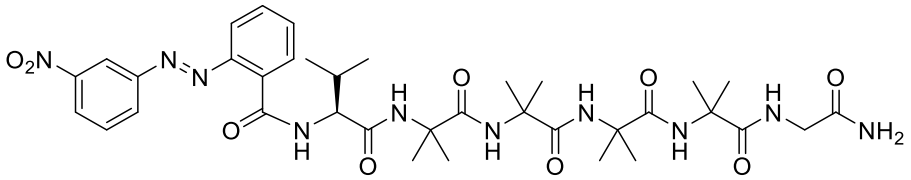
$[\alpha]_D^{25}$ −28.7 (c = 1, MeOH)

^{1}H NMR (500 MHz, MeOD, observed as a 79:21 mixture of *E*/*Z* isomers) δ_H 8.09 – 8.02 (m, 1H^E), 7.96 – 7.90 (m, 2H^E), 7.89 – 7.82 (m, 1H^E), 7.76 (dd, *J* = 7.5, 1.5 Hz, 1H^Z), 7.70 – 7.63 (m, 2H^E + 1H^Z), 7.62 – 7.57 (m, 3H^E + 2H^Z), 7.30 – 7.17 (m, 3H^Z), 7.06 – 7.02 (m, 1H^Z), 6.28 (dd, *J* = 7.6, 1.2 Hz, 1H^Z), 4.22 (d, *J* = 7.9 Hz, 1H^E), 4.14 (d, *J* = 7.4 Hz, 1H^Z), 3.91 (A of AB, d, *J* = 17.3 Hz, 1H^E), 3.89 (A of AB, d, *J* = 17.3 Hz, 1H^Z), 3.75 (B of AB, d, *J* = 17.3 Hz, 1H^Z), 3.68 (B of AB, d, *J* = 17.3 Hz, 1H^E), 2.24 – 2.07 (m, 1H^E + 1H^Z), 1.51 (s, 3H^Z), 1.50 (s, 3H^Z), 1.48 (s, 3H^Z), 1.48 – 1.44 (m, 12H^E + 6H^Z), 1.43 (s, 3H^E), 1.40 (s, 3H^Z), 1.39 (s, 1H^Z), 1.32 (s, 3H^E + 3H^Z), 1.23 (s, 3H^E), 1.19 (s, 3H^E), 1.10 (dd, *J* = 12.0, 6.8 Hz, 6H^Z), 1.02 (dd, *J* = 24.6, 6.8 Hz, 6H^E).

^{13}C NMR (126 MHz, MeOD, *E*/*Z* assigned only when unambiguous distinction is possible) δ_C 178.07^Z, 178.03^Z, 177.99^E, 177.87^Z, 177.82^E, 177.80^E, 176.73^E, 176.59^Z, 175.38^Z, 175.33^E, 174.35^E, 173.80^Z, 169.78^Z, 169.46^E, 154.81^Z, 154.58^Z, 154.05^E, 151.20^E, 133.47^E, 133.21^E, 133.17^E, 132.53^E, 131.33^E, 130.57^E, 129.91^Z, 129.75^Z, 129.37^Z, 128.28^Z, 124.35^E, 121.75^Z, 118.74^Z, 117.75^E, 62.30^E, 62.17^Z, 58.15^Z, 58.11^E, 58.01^Z, 57.83^E, 57.79^E, 57.75^Z, 43.66^E, 31.53^E, 31.23^Z, 26.50^E, 26.42^E, 26.38^E, 26.30^E, 24.62^E, 24.05^E, 23.88^E, 19.74^E, 19.63^Z.

MS (ES, MeOH) m/z 722 $(M+H)^+$ 30%; 744 $(M+Na)^+$ 100%; 720 $(M-H)^-$ 100%.

HRMS (ES^+, MeOH) calc. for $C_{30}H_{51}N_9O_7$ + Na $(M+Na)^+$: 744.3809, found: 744.3832.



1b

Azobenzene-oligomer **1b** was prepared according to general method (D) from succinimidyl ester **S8** (57 mg, 0.156 mmol), amino-oligomer H-ValAib$_4$GlyNH$_2$ (40 mg, 0.078 mmol, obtained from the Pd-catalyzed hydrogenolysis of the corresponding Cbz-protected oligomer **S14c** (*43*) following general method (A)) and DIPEA (27 μL, 0.156 mmol) in dry CH_2Cl_2 (reaction time: 24 h). After workup, **1b** was isolated by column chromatography (SiO_2: CH_2Cl_2/MeOH, 95:5) as a red-orange solid (36 mg, 61%).

R_f 0.65 (CH_2Cl_2/MeOH, 95:5)

m.p. 200-202 °C

IR (ATR) ν_{max}/cm^{-1} 299, 2963, 1642, 1531, 1418, 1352, 1226, 737

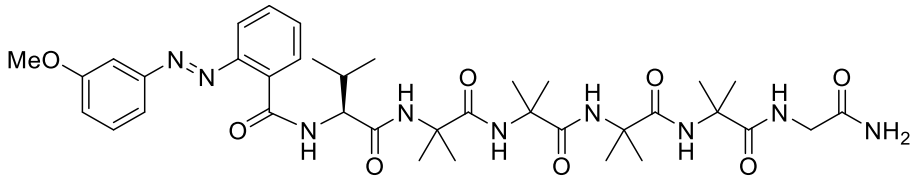
$[\alpha]_D^{25}$ −2.7 (c = 1, MeOH)

^{1}H NMR (400 MHz, MeOD, observed as a 83:17 mixture of *E*/*Z* isomers) δ_H 8.67 (t, *J* = 1.8 Hz, 1H^E), 8.48 – 8.36 (m, 2H^E), 8.06 (d, *J* = 8.0 Hz, 1H^Z), 7.98 (t, *J* = 1.7 Hz, 1H^Z), 7.95 – 7.85 (m, 3H^E), 7.76 – 7.72 (m, 1H^Z), 7.69 (dd, *J* = 5.8, 3.5 Hz, 2H^E), 7.54 (t, *J* = 8.0 Hz, 1H^Z), 7.47 (d, *J* = 7.6 Hz, 1H^Z), 7.30 (dd, *J* = 5.8, 3.3 Hz, 2H^Z), 6.43 – 6.30 (m, 1H^Z), 4.23 (d, *J* = 8.0 Hz, 1H^E), 4.11 (d, *J* = 7.4 Hz, 1H^Z), 3.93 (A of AB, d, *J* = 17.3 Hz, 1H^E), 3.88 (A of AB, d, *J* = 17.3 Hz, 1H^Z), 3.76 (B of AB, d, *J* = 17.3 Hz, 1H^Z), 3.69 (B of AB, d, *J* = 17.4 Hz, 1H^E), 2.24 – 2.10 (m, 1H^E + 1H^Z), 1.52 – 1.40 (m, 15H^E + 21H^Z), 1.39 (s, 3H^Z), 1.34 (s, 3H^E), 1.30 (s, 3H^E), 1.28 (s, 3H^E), 1.11 (dd, *J* = 9.2, 6.9 Hz, 6H^Z), 1.03 (dd, *J* = 15.7, 6.7 Hz, 6H^E).

^{13}C NMR (126 MHz, $CDCl_3$, *E*/*Z* assigned only when unambiguous distinction is possible) **δ_C** 180.24^E, 180.17^E, 180.07^Z, 179.88^E, 179.77^Z, 178.68^E, 178.58^Z, 177.88^E, 176.45^E, 176.35, 171.11^E, 171.03, 156.49^E, 153.38^E, 152.95^E, 136.73^E, 136.68^E, 135.55, 135.46, 135.00^Z, 134.71^E, 130.19, 130.09, 120.50^E, 118.85, 118.78^E, 65.45^E, 65.31^E, 60.96^E, 60.85^Z, 60.73^E, 60.56^E, 60.47^E, 60.36^Z, 46.75^E, 46.64^Z, 34.25^E, 30.28^E, 29.93^E, 29.88^E, 29.82^E, 29.76^E, 27.55^E, 27.21^E, 27.07^E, 23.25^E, 22.98^E.

MS (ES, MeOH) m/z 767 $(M+H)^+$ 60%; 790 $(M+Na)^+$ 100%; 765 $(M-H)^-$ 50%.

HRMS (ES^+, MeOH) calc. for $C_{36}H_{50}N_{10}O_0$ + K $(M+K)^+$: 805.3399, found: 805.3389.



1c

Azobenzene-oligomer **1c** was prepared according to general method (D) from succinimidyl ester **S9** (51 mg, 0.14 mmol), amino-oligomer H-ValAib$_4$GlyNH$_2$ (37 mg, 0.072 mmol, obtained from the Pd-catalyzed hydrogenolysis of the corresponding Cbz-protected oligomer **S14c** (*43*) following general method (A)) and DIPEA (25 μL, 0.14 mmol) in dry CH_2Cl_2 (reaction time: 24 hs). After workup, **1c** was isolated by column chromatography (SiO_2: CH_2Cl_2/MeOH, 95:5) as a red-orange solid (36 mg, 66%).

R_f 0.45 (CH_2Cl_2/MeOH, 9:1)

m.p. 246-247 °C

IR (ATR) ν_{max}/cm^{-1} 3303, 2985, 1642, 1530, 1421, 1251

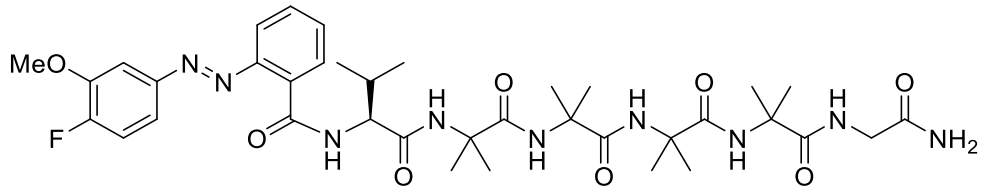
$[\alpha]_D^{25}$ −17.3 (c = 1, MeOH)

^{1}H NMR (500 MHz, MeOD, 25:75 mixture of *E*/*Z* isomers) δ_H 7.95 (dd, *J* = 7.2, 1.7 Hz, 1H^E), 7.77 – 7.70 (m, 1H^E), 7.67 – 7.63 (m, 1H^Z), 7.61 – 7.51 (m, 2H^E + 1H^Z), 7.45 (d, *J* = 7.9 Hz, 1H^E), 7.41 (t, *J* = 7.9 Hz, 1H^E), 7.45 (brs, 1H^E), 7.21 – 7.15 (m, 2H^Z), 7.10 – 7.04 (m, 1H^E + 1H^Z), 6.65 (dd, *J* = 8.3, 2.3 Hz, 1H^Z), 6.54 (s, 1H^Z), 6.50 (d, *J* = 7.9 Hz, 1H^Z), 4.11 (d, *J* = 7.9 Hz, 1H^E), 4.03 (d, *J* = 7.3 Hz, 1H^Z), 3.82 (A of AB, d, *J* = 17.4 Hz, 1H^E), 3.79 (s, 3H^E), 3.78 (A of AB, d, *J* = 17.4 Hz, 1H^Z), 3.66 (B of AB, d, *J* = 17.3 Hz, 1H^Z), 3.57 (B of AB, d, *J* = 17.4 Hz, 1H^E), 3.55 (s, 3H^Z), 2.14 – 2.06 (m, 1H^Z), 2.03 (td, *J* = 13.8, 6.8 Hz, 1H^E), 1.41 (s, 3H^Z), 1.40 (s, 3H^Z), 1.38 (s, 1H^Z), 1.38 – 1.34 (m, 12H^E + 3H^Z), 1.32 (s, 3H^E), 1.30 (s, 3H^Z), 1.29 (s, 3H^Z), 1.22 (s, 3H^Z), 1.21 (s, 3H^E + 3H^Z), 1.14 (s, 3H^E), 1.09 (s, 3H^E), 1.00 (dd, *J* = 11.3, 6.8 Hz, 6H^Z), 0.92 (dd, *J* = 20.7, 6.7 Hz, 6H^E).

^{13}C NMR (126 MHz, MeOD, *E*/*Z* assigned only when unambiguous distinction is possible) δ_C 178.07^Z, 178.04^Z, 177.99^E, 177.88^Z, 177.83^E, 177.79^E, 176.73^E, 176.58^Z, 175.38^Z, 175.34^E, 174.35^E, 173.77^Z, 169.82^Z, 169.48^E, 162.13^E, 161.50^Z, 155.99^Z, 155.23^E, 154.76^Z, 151.18^E, 133.20^E, 132.60^Z, 132.53^E, 131.34^E, 131.31^E, 130.80^Z, 129.87^Z, 129.64^Z, 128.28^Z, 119.13^E, 118.63^Z, 118.09^E, 117.82^E, 114.88^Z, 113.81^Z, 108.37^E, 107.27^Z, 62.32^E, 62.19^Z, 58.15^Z, 58.11^E, 58.01^Z, 57.83^E, 57.79^E, 57.75^Z, 56.17^E, 55.82^Z, 43.66^E, 31.57^E, 31.23^Z, 26.55^E, 26.49^E, 26.42^E, 26.34^E, 24.57^E, 24.00^E, 23.83^E, 19.79^E, 19.74^Z, 19.72^E, 19.60^Z.

MS (ES$^+$, MeOH) m/z 752 (M+H)$^+$ 15%; 774 (M+Na)$^+$ 100%.

HRMS (ES$^+$, MeOH) calc. for $C_{37}H_{53}N_9O_8$ + H (M+H)$^+$: 752.4090, found: 752.4087.



1d

Azobenzene-oligomer **1d** was prepared according to general method (D) from succinimidyl ester **S13** (41 mg, 0.11 mmol), amino-oligomer H-ValAib$_4$GlyNH$_2$ (28 mg, 0.054 mmol, obtained from the Pd-catalyzed hydrogenolysis of the corresponding Cbz-protected oligomer **S14c** (*43*) following general method (A)) and DIPEA (19 μL, 0.11 mmol) in dry CH_2Cl_2 (reaction time: 24 h). After workup, **1d** was isolated by column chromatography (SiO_2: EtOAc/MeOH, 99:1 → 95:5) as an orange solid (29 mg, 69%).

R_f 0.65 (EtOAc/MeOH, 95:5)

m.p. 213-215 °C

IR (ATR) ν_{max}/cm^{-1} (*E* isomer) 3292, 2983, 1651, 1529, 1385, 1281, 1218, 731; **IR (ATR) ν_{max}/cm^{-1}** (*Z* isomer) 3287, 2980, 2465, 2361, 1643, 1417, 1273, 1216

$[\alpha]_D^{25}$ −65.7 (c = 1, MeOH)

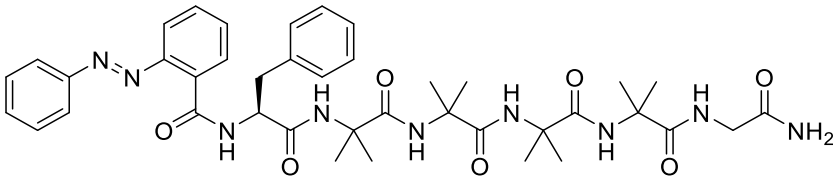
^{1}H NMR (500 MHz, MeOD) δ_H 7.99 (dd, *J* = 7.3, 1.6 Hz, 1H), 7.80 (dd, *J* = 12.0, 4.5 Hz, 1H), 7.70 – 7.56 (m, 4H), 7.34 (dd, *J* = 10.6, 8.7 Hz, 1H), 4.19 (d, *J* = 8.0 Hz, 1H), 3.97 (s, 3H), 3.93 (A of AB, d, *J* = 17.3 Hz, 1H), 3.68 (B of AB, d, *J* = 17.3 Hz, 1H), 2.10 (td, *J* = 13.7, 6.8 Hz, 1H), 1.48 (s, 3H), 1.47 (s, 6H), 1.46 (s, 3H), 1.42 (s, 3H), 1.32 (s, 3H), 1.26 (s, 3H), 1.21 (s, 3H), 1.02 (dd, *J* = 21.0, 6.7 Hz, 6H).

^{13}C NMR (126 MHz, MeOD, *E*/*Z* assigned only when unambiguous distinction is possible) δ_C 178.07^Z, 178.04^Z, 177.98^E, 177.86^Z, 177.78^E, 176.74^E, 176.56^Z, 175.38^Z, 175.33^E, 174.34^E, 173.72^Z, 169.98^Z, 169.78^E, 156.31^E (d, *J* = 254.3 Hz), 154.93^E, 152.88^Z (d, *J* = 249.2 Hz), 151.14^E, 151.06^Z, 150.83^E (d, *J* = 3.3 Hz), 150.11^E (d, *J* = 12.0 Hz), 149.28^Z (d, *J* = 11.8 Hz), 133.57^E, 133.03^E, 132.78^Z, 132.34^E, 131.06^E, 129.76^Z, 129.58, 128.26, 119.64^E (d, *J* = 7.4 Hz), 118.49^Z, 118.05^E, 117.44^E (d, *J* = 20.1 Hz), 116.88^Z (d, *J* = 19.9 Hz), 114.91^Z (d, *J* = 7.1 Hz), 108.04^Z, 107.88^E, 64.13^Z, 62.31^E, 62.21^Z, 61.54^Z, 58.16^Z, 58.13^E, 58.02^Z, 57.83^E, 57.81^E, 57.79^E, 57.75^Z, 57.04^E, 56.70^Z, 43.67^E, 31.60^E, 31.20^Z, 26.57^E, 26.46^E, 26.40, 24.56^E, 24.04^E, 23.98^E, 23.76^E, 20.86^Z, 19.90^E, 19.76^Z, 19.69^E, 19.61^Z, 14.47^E.

^{19}F NMR (376 MHz, $CDCl_3$, observed as a 92:8 mixture of *E*/*Z* isomers) δ_F -126.47 – -126.56 (m, 1F^E), -131.73 – -131.87 (m, 1F^E).

MS (ES$^+$, MeOH) m/z 792 (M+Na)$^+$ 100%.

HRMS (ES^+, MeOH) calc. for $C_{37}H_{52}N_9O_8F$ + Na $(M+Na)^+$: 792.3821, found: 792.3847.



1e

Azobenzene-oligomer **1e** was prepared according to general procedure (D) from succinimidyl ester **S3** (40 mg, 0.124 mmol prepared from acid **S2** in 94% yield using the procedure of Keiper and Vyle (*50*)), amino-oligomer H-PheAib$_4$GlyNH$_2$ (35 mg, 0.062 mmol, obtained from the Pd-catalyzed hydrogenolysis of the corresponding Cbz-protected oligomer **S14d** (*43*) following general method (A)) and DIPEA (21.6 μL, 0.124 mmol) in dry CH_2Cl_2 (reaction time: 24 h). After workup, **1e** was isolated by column chromatography (SiO_2: CH_2Cl_2/MeOH, 9:1) as an orange solid (37 mg, 79%).

R_f 0.3 (CH_2Cl_2/MeOH, 95:5)

m.p. 221-223 °C

IR (ATR) ν_{max}/cm^{-1} 3292, 2930, 1644, 1527, 1416, 1381, 730

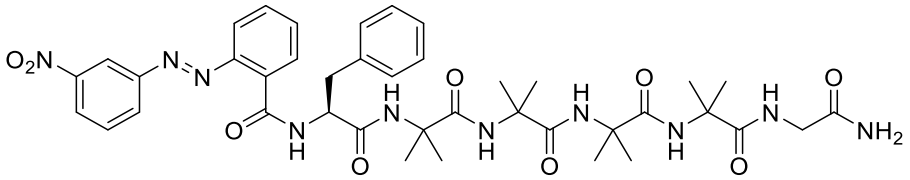
$[\alpha]_D^{25}$ +65.8 (c = 1, MeOH)

^{1}H NMR (400 MHz, MeOD, observed as a 68:32 mixture of *E*/*Z* isomers) δ_H 8.03 – 7.99 (m, 2H^Z), 7.88 – 7.82 (m, 2H^E), 7.68 – 7.54 (m, 1H^Z + 3H^E), 7.39 – 7.30 (m, 1H^E + 1H^Z), 7.30 – 7.12 (m, 4H^E + 4H^Z), 7.05 – 6.97 (m, 2H^Z), 6.29 – 6.22 (m, 1H^Z), 4.72 (t, *J* = 7.7 Hz, 1H^E), 4.54 (dd, *J* = 8.7, 6.9 Hz, 1H^Z), 3.92 (A of AB, d, *J* = 17.4 Hz, 1H^E + 1H^Z), 3.72 (B of AB, d, *J* = 17.5 Hz, 1H^Z), 3.67 (B of AB, d, *J* = 17.4 Hz, 1H^E), 3.26 – 3.06 (m, 2H^E + 2H^Z), 1.52 – 1.30 (m, 18H^E + 18H^Z), 1.26 (s, 3H^E), 1.17 (s, 3H^E).

^{13}C NMR (126 MHz, MeOD, *E*/*Z* assigned only when unambiguous distinction is possible) δ_C 178.06^Z, 178.02^Z, 177.98^E, 177.88^Z, 177.80^E, 177.79^E, 176.68^E, 176.58^Z, 175.37^Z, 175.32^E, 174.02^E, 173.58^Z, 169.58^Z, 169.15^E, 154.78^Z, 154.72^Z, 154.03^E, 151.03^E, 138.28^Z, 137.66^E, 133.40^E, 133.21^E, 133.20^E, 132.56^Z, 132.50^E, 131.28^E, 130.64^E, 130.53, 130.38^E, 129.85^Z, 129.64^Z, 129.58^E, 129.40^Z, 129.28^Z, 128.14^Z, 128.08^E, 128.01^Z, 124.42^E, 121.76, 118.79^Z, 117.54^E, 58.14^Z, 58.10^E, 57.99^E, 57.80^E, 57.78^E, 57.68^E, 57.64^E, 43.69^Z, 43.66^E, 38.34^E, 37.82^Z, 26.58^E, 26.50^E, 26.42^E, 26.36^E, 24.56^E, 24.09^Z, 23.95, 23.77^E.

MS (ES, MeOH) m/z 770 $(M+H)^+$ 20%; 792 $(M+Na)^+$ 100%; 768 $(M-H)^-$ 100%.

HRMS (ES^+, MeOH) calc. for $C_{40}H_{51}N_9O_7$ + K $(M+K)^+$: 808.3549, found: 808.3547.



1f

Azobenzene-oligomer **1f** was prepared according to general method (D) from succinimidyl ester **S8** (26 mg, 0.072 mmol), amino-oligomer H-PheAib$_4$GlyNH$_2$ (20 mg, 0.036 mmol, obtained from the Pd-catalyzed hydrogenolysis of the corresponding Cbz-protected oligomer **S14d** (*43*) following general method (A)) and DIPEA (13 μL, 0.072 mmol) in dry CH_2Cl_2 (reaction time: 24 h). After workup, **1f** was isolated by column chromatography (SiO_2: CH_2Cl_2/MeOH, 95:5) as an orange-brown solid (22 mg, 75%).

R_f 0.8 (CH_2Cl_2/MeOH, 95:5)

m.p. 241-242 °C

IR (ATR) ν_{max}/cm^{-1} 3288, 2957, 1649, 1530, 1354, 908, 728

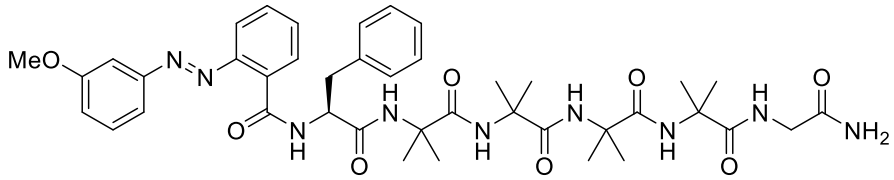
$[\alpha]_D^{25}$ +47.8 (c = 1, MeOH)

^{1}H NMR (500 MHz, MeOD) δ_H 8.63 (s, 1H), 8.44 (d, *J* = 8.1 Hz, 1H), 8.30 (d, *J* = 7.9 Hz, 1H), 7.91 (ddd, *J* = 9.1, 5.5, 3.5 Hz, 2H), 7.86 (t, *J* = 8.1 Hz, 1H), 7.68 (dd, *J* = 5.8, 3.4 Hz, 2H), 7.25 (d, *J* = 7.4 Hz, 2H), 7.18 (t, *J* = 7.5 Hz, 2H), 7.10 (t, *J* = 7.2 Hz, 1H), 4.73 (t, *J* = 7.7 Hz, 1H), 3.92 (A of AB, d, *J* = 17.4 Hz, 1H), 3.67 (B of AB, d, *J* = 17.4 Hz, 1H), 3.18 (ddd, *J* = 30.9, 13.5, 7.8 Hz, 2H), 1.47 (s, 3H), 1.46 (s, 3H), 1.40 (s, 3H), 1.32 (s, 6H), 1.31 (s, 3H), 1.29 (s, 3H), 1.23 (s, 3H).

^{13}C NMR (126 MHz, MeOD) δ_C 178.00, 177.82, 177.78, 176.73, 175.35, 173.86, 169.48, 154.17, 150.62, 150.52, 137.69, 135.14, 133.37, 132.93, 132.29, 131.98, 130.98, 130.52, 129.45, 127.94, 126.89, 117.78, 116.62, 58.13, 57.82, 57.76, 57.66, 43.66, 38.32, 26.55, 26.50, 26.43, 26.36, 24.56, 24.09, 24.00, 23.74.

MS (ES, MeOH) m/z 815 $(M+H)^+$ 30%; 837 $(M+Na)^+$ 100%; 813 $(M-H)^-$ 100%.

HRMS (ES^+, MeOH) calc. for $C_{40}H_{50}N_{10}O_9$ + K $(M+K)^+$: 853.3399, found: 853.3383.



1g

Azobenzene-oligomer **1g** was prepared according to general method (D) from succinimidyl ester **S9** (25 mg, 0.072 mmol), amino-oligomer H-PheAib$_4$GlyNH$_2$ (20 mg, 0.036 mmol, obtained from the Pd-catalyzed hydrogenolysis of the corresponding Cbz-protected oligomer **S14d** (*43*) following general method (A)) and DIPEA (13 μL, 0.072 mmol) in dry CH_2Cl_2 (reaction time: 24 hs). After workup, **1g** was isolated by column chromatography (SiO_2: CH_2Cl_2/MeOH, 9:1) as a red-orange solid (22 mg, 75%).

R_f 0.75 (CH_2Cl_2/MeOH, 9:1)

m.p. 204-205 °C

IR (ATR) ν_{max}/cm^{-1} 3305, 2985, 1645, 1417, 1258

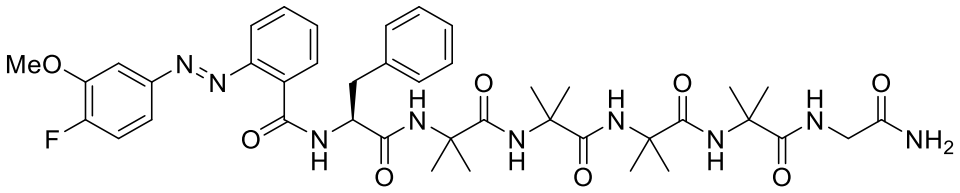
$[\alpha]_D^{25}$ +42.1 (c = 1, MeOH).

^{1}H NMR (500 MHz, MeOD, observed as a 75:25 mixture of *E*/*Z* isomers) δ_H 8.04 – 7.96 (m, 1H^E), 7.83 (d, *J* = 8.1 Hz, 1H^E), 7.65 (tt, *J* = 13.1, 6.6 Hz, 2H^E), 7.56 – 7.52 (m, 1H^E + 3H^Z), 7.46 (s, 1H^E), 7.37 – 7.31 (m, 3H^Z), 7.28 – 7.13 (m, 7H^E + 3H^Z), 6.75 (d, *J* = 8.4 Hz, 1H^Z), 6.62 (s, 1H^Z), 6.58 (d, *J* = 7.4 Hz, 1H^Z), 6.31 (d, *J* = 7.8 Hz, 1H^Z), 4.70 (t, *J* = 7.7 Hz, 1H^E), 4.53 (d, *J* = 8.2, 7.2 Hz, 1H^Z), 3.93 (A of AB, d, *J* = 17.4 Hz, 1H^E + 1H^Z), 3.90 (s, 3H^E), 3.72 (B of AB, d, *J* = 17.4 Hz, 1H^Z), 3.66 (B of AB, d, *J* = 17.4 Hz, 1H^E), 3.63 (s, 3H^Z), 3.25 – 3.06 (m, 2H^E + 2H^Z), 1.52 – 1.28 (m, 18H^E + 24H^Z), 1.26 (s, 3H^E), 1.17 (s, 3H^E).

^{13}C NMR (126 MHz, MeOD) δ_C 177.99, 177.82, 177.79, 176.69, 175.34, 174.02, 169.19, 162.15, 155.26, 150.99, 137.62, 133.28, 133.22, 132.55, 131.44, 131.29, 130.37, 129.58, 128.05, 119.12, 118.37, 117.58, 108.27, 58.11, 57.81, 57.79, 57.72, 57.67, 56.21, 43.66, 38.48, 26.63, 26.48, 26.40, 24.50, 23.88, 23.69.

MS (ES, MeOH) m/z 800 $(M+H)^+$ 50%; 822 $(M+Na)^+$ 100%; 798 $(M-H)^-$ 100%; 834 $(M+Cl)^-$ 100%.

HRMS (ES^-, MeOH) calc. for $C_{41}H_{53}N_8O_9$ + Cl $(M+Cl)^-$: 834.3711, found: 834.3717.



1h

Azobenzene-oligomer **1h** was prepared according to general method (D) from succinimidyl ester **S13** (74 mg, 0.20 mmol), amino-oligomer H-PheAib$_4$GlyNH$_2$ (55 mg, 0.10 mmol, obtained from the Pd-catalyzed hydrogenolysis of the corresponding Cbz-protected oligomer **S14d** (*43*) following general method (A)) and DIPEA (36 μL, 0.20 mmol) in dry CH_2Cl_2 (reaction time: 24 h). After workup, **1h** was isolated by column chromatography (SiO_2: CH_2Cl_2/MeOH, 95:5) as a red solid (22 mg, 75%).

R_f 0.75 (CH_2Cl_2/MeOH, 9:1)

m.p. 243-245 °C

IR (ATR) ν_{max}/cm^{-1} 3285, 2985, 1651, 1528, 1510, 1274, 734

$[\alpha]_D^{25}$ +26.7 (c = 1, MeOH)

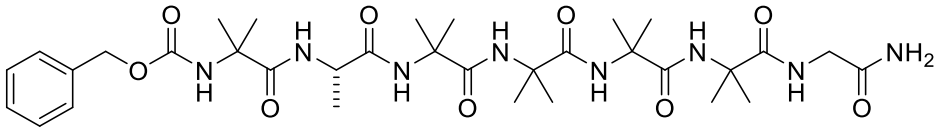
^{1}H NMR (500 MHz, MeOD, observed as a 78:22 mixture of *E*/*Z* isomers) δ_H 7.96 (dd, *J* = 7.3, 1.6 Hz, 1H^E), 7.81 (d, *J* = 7.5 Hz, 1H^E), 7.68 – 7.58 (m, 2H^E), 7.56 – 7.50 (m, 1H^E), 7.38 – 7.11 (m, 2H^E + 3H^Z), 6.99 (dd, *J* = 10.8, 8.6 Hz, 1H^Z), 6.82 (dd, *J* = 7.7, 2.0 Hz, 1H^Z), 6.67 – 6.62 (m, 1H^Z), 6.30 (d, *J* = 7.7 Hz, 1H^Z), 4.71 (t, *J* = 7.6 Hz, 1H^E), 4.54 (dd, *J* = 8.9, 6.7 Hz, 1H^Z), 3.96 (s, 3H^E), 3.93 (A of AB, d, *J* = 17.5 Hz, 1H^E), 3.91 (A of AB, d, *J* = 17.5 Hz, 1H^Z), 3.73 (d, *J* = 17.4 Hz, 1H^Z), 3.67 (d, *J* = 17.4 Hz, 1H^E), 3.61 (s, 3H^Z), 3.27 – 3.06 (m, 2H^E + 2H^Z), 1.51 (s, 3H^Z), 1.50 (s, 3H^Z), 1.47 (s, 3H^E + 3H^Z), 1.46 (s, 3H^E), 1.40 (m, 3H^E + 12H^Z), 1.33 (s, 3H^E), 1.32 (s, 6H^E + 3H^Z), 1.29 (s, 3H^E), 1.20 (s, 3H^E).

^{13}C NMR (126 MHz, MeOD, *E*/*Z* assigned only when unambiguous distinction is possible) δ_C 178.07^Z, 178.05^Z, 177.98^E, 177.86^Z, 177.77^E, 177.76^E, 176.72^E, 176.56^Z, 175.38^Z, 175.33^E, 173.95^E, 173.51^Z, 169.71^Z, 169.38^E, 156.31^E (d, *J* = 254.3 Hz), 155.17^Z, 150.97^E, 150.77^E (d, *J* = 3.2 Hz), 150.11^E (d, *J* = 11.9 Hz), 138.40^E, 137.62^E, 133.54^E, 133.08^E, 132.85^Z, 132.36^E, 131.10^E, 130.51^E, 130.38^E, 129.64^Z, 129.57^E, 129.29^Z, 128.05^E, 119.95^E (d, *J* = 7.4 Hz), 118.50^Z, 117.83^E, 117.55^E, 117.39^E, 107.69^E (d, *J* = 2.5 Hz), 58.15^Z, 58.12^E, 58.02^Z, 57.81^E, 57.78^Z, 57.71^Z, 57.67^E, 57.08^E, 56.68^Z, 43.66^E, 38.49^E, 37.79^Z, 26.59^E, 26.49^E, 26.39^E, 24.55^E, 24.00^E, 23.92^E, 23.67^E.

^{19}F NMR (471 MHz, MeOD, observed as a 68:12 mixture of *E*/*Z* isomers) δ_F -130.09 – -130.15 (m, 1F^E), -136.39 – -136.46 (m, 1F^Z).

MS (ES, MeOH) m/z 818 $(M+H)^+$ 40%; 840 $(M+Na)^+$ 80%; 856 $(M+K)^+$ 100%; 816 $(M-H)^-$ 100%; 852 $(M+Cl)^-$ 65%.

HRMS (ES^+, MeOH) calc. for $C_{41}H_{52}N_9O_8F$ + K $(M+K)^+$: 856.3560, found: 856.8574.



S15

Oligomer **S15** was prepared according to general method (C) from crude Cbz-Aib-F (obtained from Cbz-Aib-OH, 58 mg, 0.24 mmol) amino-oligomer H-ValAib$_4$GlyNH$_2$ (30 mg, 0.062 mmol, obtained from the Pd-catalyzed hydrogenolysis of Cbz-L-AlaAib$_4$GlyNH$_2$ **S14b** (*43*) following general method (A)) and DIPEA (54 μL, 0.31 mmol) in dry CH_2Cl_2. After stirring at room temperature for 48 h, a white solid precipitated out of the reaction medium and was collected by filtration to afford the pure product (29 mg, 68%).

R_f 0.35 (CH_2Cl_2/MeOH, 9:1)

m.p. 237-238 °C

IR (ATR) ν_{max}/cm^{-1} 3285, 2985, 1651, 1530, 1261, 736

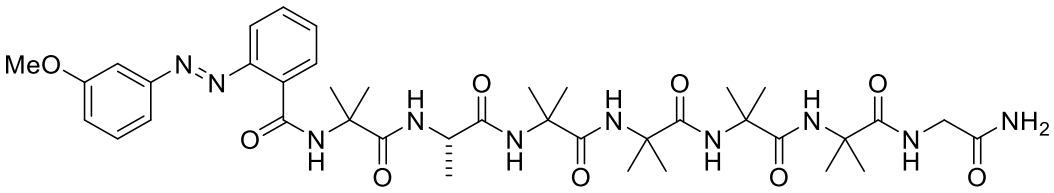
$[\alpha]_D^{25}$ +37.6 (c = 1, MeOH)

^{1}H NMR (400 MHz, MeOD) δ_H 7.48 – 7.22 (m, 5H), 5.15 (A of AB, d, *J* = 12.7 Hz, 1H), 5.11 (B of AB, d, *J* = 12.7 Hz, 1H), 3.97 (q, *J* = 7.2 Hz, 1H), 3.88 (A of AB, d, *J* = 17.3 Hz, 1H), 3.78 (B of AB, d, *J* = 17.4 Hz, 1H), 1.51 (s, 3H), 1.51 (s, 3H), 1.45 (m, 12H), 1.43 (s, 6H), 1.40 (s, 3H), 1.39 (s, 3H), 1.36 (d, *J* = 7.3 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ_C 176.54 (x2), 176.15, 176.13, 175.56, 175.16, 172.92, 156.12, 136.10, 128.89, 128.75, 128.10, 67.57, 57.23, 57.17, 56.96, 56.80, 56.77, 51.92, 43.07, 26.56, 26.26, 26.23, 26.19, 24.28, 24.26, 24.20, 24.15, 23.85, 23.81, 23.79, 23.77, 16.75.

MS (ES^+, MeOH) m/z 727 $(M+Na)^+$ 100%.

HRMS (ES^+, MeOH) calc. for $C_{33}H_{52}N_8O_9$ + H $(M+H)^+$: 705.3930, found: 705.3926.



2

Azobenzene-oligomer **2** was prepared according to general method (D) from succinimidyl ester **S9** (27 mg, 0.078 mmol), amino-oligomer H-AibAlaAib$_4$GlyNH$_2$ (14 mg, 0.039 mmol, obtained from the Pd-catalyzed hydrogenolysis of the corresponding Cbz-protected oligomer **S15** following general method (A)) and DIPEA (36 μL, 0.078 mmol) in dry CH_2Cl_2 (reaction time: 24 h). After workup, **3** was isolated by column chromatography (SiO_2: CH_2Cl_2/MeOH, 95:5 → 9:1) as a dark red solid (17 mg, 55%).

R_f 0.4 (CH_2Cl_2/MeOH, 95:5)

m.p. 262-263 °C

IR (ATR) ν_{max}/cm^{-1} 3285, 2985, 1651, 1528, 1510, 1274, 734

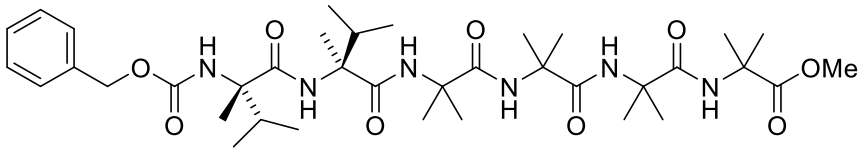
$[\alpha]_D^{25}$ +24.2 (c = 1, MeOH)

^{1}H NMR (400 MHz, MeOD) δ_H 7.98 – 7.90 (m, 1H), 7.82 (dt, *J* = 6.3, 3.5 Hz, 1H), 7.69 – 7.60 (m, 2H), 7.55 (dt, *J* = 7.8, 1.4 Hz, 2H), 7.46 – 7.44 (m, 1H), 4.03 (q, *J* = 7.2 Hz, 1H), 3.88 (s, 3H), 3.85 (d, *J* = 17.4 Hz, 1H), 3.79 (d, *J* = 17.3 Hz, 1H), 1.61 (s, 3H), 1.60 (s, 3H), 1.49 (s, 6H), 1.44 (s, 6H), 1.41 (s, 3H), 1.40 (s, 2H), 1.39 (s, 3H), 1.38 (s, 3H), 1.35 (s, 1H), 1.33 (s, 2H).

^{13}C NMR (126 MHz, MeOD) δ_C 178.07, 177.94, 177.42, 177.05, 175.41, 175.38, 169.44, 162.14, 155.39, 151.09, 135.29, 132.66, 132.41, 131.36, 130.63, 118.66, 117.87, 117.41, 108.37, 58.23, 58.16, 57.98, 57.73, 57.70, 56.17, 52.63, 25.83, 25.41, 24.95, 16.47.

MS (ES$^+$, MeOH) m/z 809 (M+H)$^+$ 70%; 831 (M+Na)$^+$ 90%.

HRMS (ES$^+$, MeOH) calc. for $C_{39}H_{56}N_{10}O_9$ + Na (M+Na)$^+$: 831.4129, found: 831.4104.



S17

A solution of Cbz-(aMv)$_2$Aib$_4$OH **S16** (11.8 mg, 0.016 mmol, obtained using the method of Byrne *et al.* (*57*)) in Et_2O/MeOH (3:1 v/v, 2 mL) was treated with $TMSCHN_2$ (2M in hexanes) dropwise under nitrogen until persistence of the yellow color (~ 15 μL). The

resulting solution was stirred for further 7 h at room temperature, after which the volatiles were removed under vacuum. The product was isolated as a white solid (12 mg, 99%).

R_f 0.75 (CH_2Cl_2/MeOH, 95:5)

m.p. 191-193 °C

IR (ATR) ν_{max}/cm^{-1} 3308, 2962, 1702, 1666, 1526, 1384, 1260, 1153, 909, 730

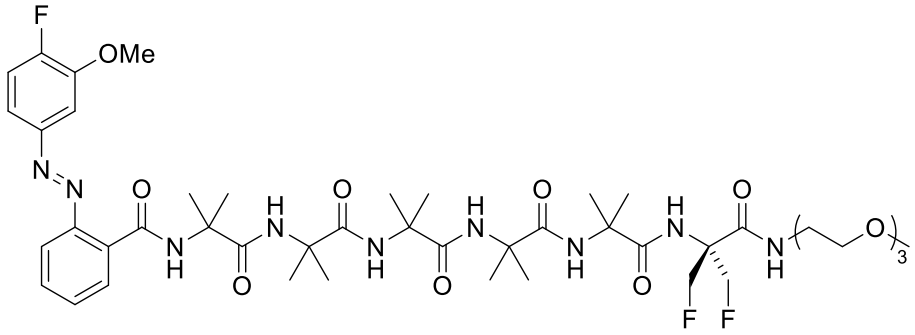
$[\alpha]_D^{25}$ +45.1 (c = 1, MeOH)

^{1}H NMR (500 MHz, $CDCl_3$) δ_H 7.67 (s, 1H), 7.51 (s, 1H), 7.46 (s, 1H), 7.39 (s, 1H), 7.38 – 7.35 (m, 5H), 6.33 (s, 1H), 5.22 (s, 1H), 5.19 (A of AB, d, *J* = 12.1 Hz, 1H), 5.02 (B of AB, d, *J* = 12.1 Hz, 1H), 3.69 (s, 3H), 1.86 (dt, *J* = 13.6, 6.8 Hz, 1H), 1.56 (s, 3H), 1.54 (s, 3H), 1.53 (m, 1H), 1.50 (s, 3H), 1.49 (s, 3H), 1.48 (s, 3H), 1.47 (s, 3H), 1.44 (s, 9H), 1.39 (s, 3H), 0.97 (dd, *J* = 11.3, 6.8 Hz, 6H), 0.78 (dd, *J* = 8.3, 7.1 Hz, 6H).

^{13}C NMR (126 MHz, $CDCl_3$) δ_C 175.78, 175.12, 175.01, 174.16, 172.27, 172.16, 156.28, 135.81, 129.18, 128.90, 128.87, 128.72, 128.37, 67.86, 63.58, 62.50, 57.04, 56.97, 56.78, 55.85, 52.07, 36.20, 35.88, 27.85, 27.53, 27.41, 25.95, 24.24, 23.15, 23.11, 23.01, 18.25, 18.20, 17.41, 17.29, 17.18, 17.09.

MS (ES, MeOH) m/z 733 $(M+H)^+$ 60%; 755 $(M+Na)^+$ 100%; 731 $(M-H)^-$ 100%.

HRMS (ES^-, MeOH) calc. for $C_{37}H_{58}N_6O_9$ - H $(M-H)^-$: 731.4349, found: 731.4349.



3g

According to general procedure (D), succinimidyl ester **S13** (37 mg, 0.1 mmol), DIPEA (18 µL, 0.1 mmol) and amino-oligomer H-Aib$_5$FibTEG (35 mg, 0.049 mmol, obtained from the Pd-catalyzed hydrogenolysis of the corresponding Cbz-protected oligomer **3a** following general method (A)) in CH_2Cl_2 were used (reaction time: 24 h). The crude product was purified by column chromatography (SiO_2: CH_2Cl_2/MeOH, 97:3) to afford **3g** as an orange-red solid (29 mg, 61%).

R_f 0.6 (CH_2Cl_2/MeOH, 95:5)

m.p. 121-123 °C

IR (ATR) ν_{max}**/cm**$^{-1}$ 3294, 2982, 1651, 1530, 1506, 1265, 1105, 1029, 730

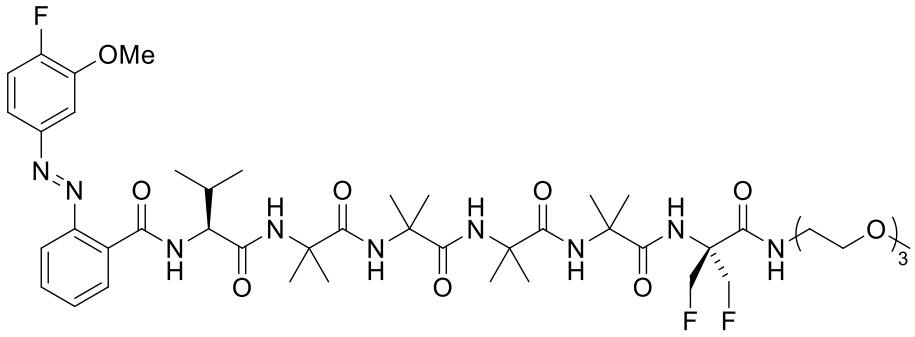
^{1}H NMR (500 MHz, $CDCl_3$, *E*/*Z* assigned only when unambiguous distinction is possible) δ_H 9.00 (s, 1H^E), 8.26 (dd, *J* = 6.1, 3.3 Hz, 1H^E), 7.83 (s, 1H^E), 7.82 – 7.77 (m, 3H^Z), 7.73 (s, 1H^E), 7.76 (s, 1H^Z), 7.69 – 7.65 (m, 2H^E), 7.65 – 7.63 (m, 1H^E + 2H^Z), 7.60 (s, 1H^Z), 7.59 – 7.57 (m, 2H^E + 1H^Z), 7.56 – 7.53 (m, 1H^E + 1H^Z), 7.44 (ddd, *J* = 8.4, 4.1, 2.3 Hz, 1H^E), 7.30 (dd, *J* = 10.2, 8.7 Hz, 2H^E), 6.96 (dd, *J* = 10.4, 8.7 Hz, 1H^Z), 6.82 (dd, *J* = 7.6, 2.0 Hz, 1H^Z), 6.74 (s, 1H^Z), 6.61 – 6.56 (m, 1H^Z), 6.46 (s, 1H^E), 6.17 (d, *J* = 7.8 Hz, 1H^Z), 5.02 – 4.99 (m, 1H^E + 1H^Z), 4.95 – 4.87 (m, 2H^E + 2H^Z), 4.83 – 4.78 (m, 1H^E + 1H^Z), 4.02 (s, 3H^E), 3.70 (s, 3H^Z), 3.65 – 3.61 (m, 6H^E + 6H^Z), 3.58 (t, *J* = 6.5 Hz, 2H^E + 2H^Z), 3.54 (dd, *J* = 5.7, 3.6 Hz, 2H^E + 2H^Z), 3.49 – 3.44 (m, 2H^E + 2H^Z), 3.37 (s, 3H^E), 3.36 (s, 3H^Z), 1.62 (s, 6H^Z), 1.59 (s, 6H^E), 1.53 (s, 6H^E), 1.49 (s, 6H^E + 6H^Z), 1.47 (s, 6H^Z), 1.46 (s, 6H^Z), 1.44 (s, 6H^E), 1.39 (s, 6H^E), 1.35 (s, 6H^Z).

^{13}C NMR (126 MHz, $CDCl_3$) δ_C 175.98, 175.49, 175.37, 174.23, 173.87, 169.39 (t, *J* = 4.6 Hz), 166.61, 155.43 (d, *J* = 256.8 Hz), 149.93, 149.38 (d, *J* = 3.4 Hz), 149.05 (d, *J* = 11.8 Hz), 133.18, 132.09, 131.42, 129.99, 117.13, 116.97, 116.72, 115.69 (d, *J* = 7.5 Hz), 109.39 (d, *J* = 3.1 Hz), 82.29 (brd, *J* = 176.0 Hz), 72.07, 70.67, 70.58, 70.37, 69.44, 62.82 (t, *J* = 18.3 Hz) 59.16, 57.49, 57.11, 57.07, 56.87, 56.86, 56.78, 39.31, 25.56, 25.06 (brs).

^{19}F NMR (471 MHz, $CDCl_3$, observed as a 81:19 mixture of *E*/*Z* isomers) δ_F -126.10 – -126.15 (m, 1F^E), -132.24 – -132.26 (m, 1F^Z), -233.5 (brs, 1F^E + 1F^Z).

MS (ES$^+$, MeOH) m/z 966 (M+H)$^+$ 20%; 988 (M+Na)$^+$ 90%.

HRMS (ES$^+$, MeOH) calc. for $C_{45}H_{66}F_3N_9O_{11}$ + Na (M+Na)$^+$: 988.4732, found: 988.4721.



4

According to general procedure (D), succinimidyl ester **S13** (26 mg, 0.07 mmol), DIPEA (12 µL, 0.07 mmol) and amino-oligomer H-ValAib$_4$FibTEG (26 mg, 0.035 mmol, obtained from the Pd-catalyzed hydrogenolysis of the corresponding Cbz-protected oligomer **3c** following general method (A)) in CH_2Cl_2 were used (reaction time: 24 h). The crude product was

purified by column chromatography (SiO_2: CH_2Cl_2/MeOH, 95:5) to afford **4** as an orange-red solid (32 mg, 92%).

R_f 0.55 (CH_2Cl_2/MeOH, 95:5)

m.p. 105-107 °C

IR (ATR) ν_{max}/cm^{-1} 3294, 2935, 1650, 1530, 1506, 1272, 1106, 1027, 910, 730

$[\alpha]_D^{25}$ +112.0 (c = 1, MeOH)

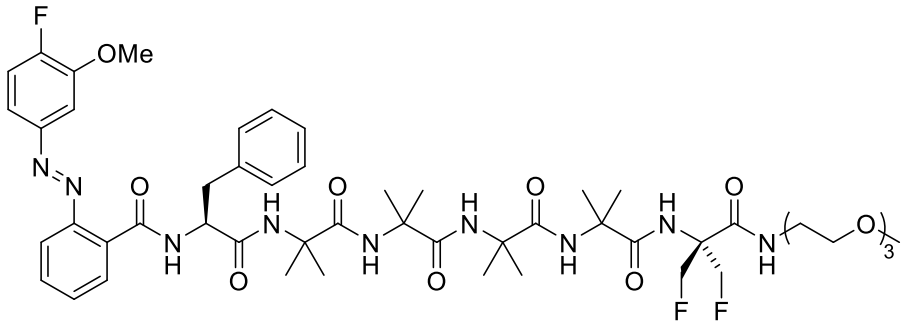
^{1}H NMR (500 MHz, $CDCl_3$, observed as a 65:35 mixture of *E*/*Z* isomers) δ_H 8.99 (d, *J* = 4.3, 1H^E), 8.26 (d, *J* = 7.0, 1H^E), 7.91 (dd, *J* = 9.3, 6.6, 1H^E), 7.76 (m, 1H^E + 1H^Z), 7.69 – 7.57 (m, 2H^E + 2H^Z), 7.53 (m, 1H^E + 2H^Z), 7.48 – 7.43 (m, 1H^E), 7.39 (s, 1H^E), 7.35 – 7.19 (m, 3H^E + 3H^Z), 6.95 (t, *J* = 9.5, 1H^Z), 6.76 (d, *J* = 7.5, 1H^Z), 6.72 (s, 1H^Z), 6.60 (s, 1H^E), 6.48 (d, *J* = 8.4, 1H^Z), 6.21 (d, *J* = 7.8, 1H^Z), 5.10 – 4.69 (m, 4H^E + 4H^Z), 4.05 – 4.01 (m, 1H^Z), 3.99 (s, 3H^E), 3.92 (dd, *J* = 7.1, 5.3, 1H^E), 3.70 (s, 1H^Z), 3.64 – 3.38 (m, 12H^E + 12H^Z), 3.36 (s, 3H^E + 3H^Z), 2.27 (dt, *J* = 13.4, 6.6, 1H^Z), 2.10 (td, *J* = 13.6, 6.8, 1H^E), 1.53 – 1.14 (m, 24H^E + 24H^Z), 1.10 (d, *J* = 6.6, 6H^Z), 1.01 (dd, *J* = 11.7, 6.7, 6H^E).

^{13}C NMR (126 MHz, $CDCl_3$, *E*/*Z* assigned only when unambiguous distinction is possible) δ_C 175.91^Z, 175.70^E, 175.39^Z, 175.26^E, 175.14^Z, 175.06^E, 173.96^Z, 173.91^E, 172.30^Z, 171.29^Z, 169.40^Z (t, *J* = 4.6 Hz), 169.32^E (t, *J* = 4.7 Hz), 167.62^E, 155.34^E (d, *J* = 256.6 Hz), 152.51^E, 152.15^Z (d, *J* = 252.5 Hz), 150.18^E, 149.43^E (d, *J* = 3.4 Hz), 148.92^E (d, *J* = 11.8 Hz), 148.30^Z (d, *J* = 11.9 Hz), 133.13^E, 132.37, 131.90^E, 131.47^E, 129.65^Z, 129.32^E, 128.24, 127.85^Z, 116.97^E, 116.83^E, 116.73^Z, 116.45^Z, 116.29, 116.23^Z, 113.68^Z (d, *J* = 7.1 Hz), 108.86^E, 107.66^Z, 82.79 (d, *J* = 177.7 Hz), 81.70 (d, *J* = 173.2 Hz), 72.03^E, 70.62^E, 70.55^E, 70.31^E, 69.42^Z, 69.38^E, 62.79 (t, *J* = 18.3 Hz), 62.20^Z, 60.55^Z, 59.15^E, 57.19^E, 57.08^Z, 57.07^Z, 57.05^E, 56.98^E, 56.96^Z, 56.89^Z 56.68^E, 56.62^E, 56.35^Z, 39.24^E, 30.15^E, 29.65^Z, 25.95 (brs), 24.05 (brs), 19.68^E, 19.61^Z, 19.41^E, 18.87^Z.

^{19}F NMR (471 MHz, $CDCl_3$, observed as a 65:35 mixture of *E*/*Z* isomers) δ_F -126.43 – -126.49 (m, 1F^E), -131.68 – -131.84 (m, 1F^Z), -232.3 (brs, 1F^E + 1F^Z), -234.8 (brs, 1F^E + 1F^Z).

MS (ES^+, MeOH) m/z 651 $(M+H)^+$ 60%; 673 $(M+Na)^+$ 100%.

HRMS (ES^+, MeOH) calc. for $C_{27}H_{48}N_8O_8F_2$ + Na $(M+Na)^+$: 673.3461, found: 673.3430.



Phe-4

Azobenzene-oligomer **Phe-4** was prepared according to general method (D) from succinimidyl ester **S13** (29 mg, 0.078 mmol), amino-oligomer H-PheAib$_4$FibTEG (30 mg, 0.039 mmol, obtained from the Pd-catalyzed hydrogenolysis of the corresponding Cbz-protected oligomer **3d** following general method (A)) and DIPEA (13.5 μL, 0.078 mmol) in dry CH_2Cl_2 (reaction time: 24 h). After workup, **Phe-4** was isolated by column chromatography (SiO_2: CH_2Cl_2/MeOH, 95:5) as an orange solid (30 mg, 82%).

R_f 0.65 (CH_2Cl_2/MeOH, 95:5)

m.p. 126-129 °C

IR (ATR) ν_{max}/cm^{-1} 3294, 2986, 1650, 1530, 1384, 1215, 1106, 1027, 751

$[\alpha]_D^{25}$ +125.9 (c = 1, $CHCl_3$)

^{1}H NMR (500 MHz, $CDCl_3$, observed as a 83:17 mixture of *E*/*Z* isomers) δ_H 9.08 (brs, 1H^E), 8.27 – 8.16 (m, 1H^E), 7.86 – 7.75 (m, 1H^E + 1H^Z), 7.70 – 7.44 (m, 7H^E + 4H^Z), 7.42 – 7.05 (m, 8H^E + 5H^Z), 6.94 (dd, *J* = 9.9, 9.2 Hz, 1H^Z), 6.73 (m, 2H^Z), 6.47 (d, *J* = 7.8 Hz, 1H^Z), 6.29 (s, 1H^E), 6.15 (d, *J* = 6.5 Hz, 1H^Z), 4.90 (m, 4H^E + 4H^Z), 4.41 (dd, *J* = 10.5, 5.2 Hz, 1H^E + 1H^Z), 3.98 (s, 3H^E), 3.68 (s, 3H^Z), 3.64 – 3.49 (m, 10H^E + 10H^Z), 3.44 (ddd, *J* = 19.4, 12.9, 6.7 Hz, 2H^E + 2H^Z), 3.36 (s, 3H^E + 3H^Z), 3.34 – 3.26 (m, 1H^Z), 3.23 – 3.08 (m, 2H^E + 1H^Z), 1.49 (s, 3H^Z), 1.46 (s, 3H^E + 3H^Z), 1.45 (s, 3H^E), 1.44 (s, 3H^Z), 1.42 (s, 3H^E), 1.39 (s, 3H^Z), 1.38 (s, 3H^Z), 1.36 (s, 3H^Z), 1.35 (s, 3H^E), 1.29 (s, 6H^E + 3H^Z), 1.27 (s, 3H^E), 1.25 (s, 3H^Z), 1.22 (s, 3H^E).

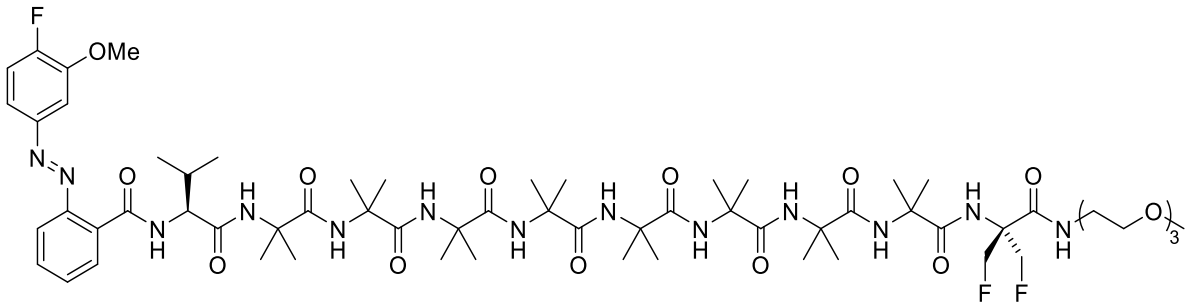
^{13}C NMR (126 MHz, $CDCl_3$, *E*/*Z* assigned only when unambiguous distinction is possible) δ_C 175.92^Z, 175.68^E, 175.42^Z, 175.26^E, 175.1^Z, 175.05^E, 174.02^Z, 173.86^E, 171.70^E, 171.07^Z, 169.32 (t, *J* = 4.6 Hz), 167.38^E, 155.30^E (d, *J* = 256.6 Hz), 151.97^Z (d, *J* = 237.5 Hz), 149.85^E, 149.35^E (d, *J* = 3.3 Hz), 148.91^E (d, *J* = 11.8 Hz), 135.78^E, 133.16^E, 132.26^Z, 131.97^E, 131.41^E, 129.55^Z, 129.33^Z, 129.10^E (d, *J* = 2.8 Hz), 127.93^Z (d, *J* = 5.7 Hz), 127.69^E, 117.00^E (d, *J* = 20.2 Hz), 116.62^E, 115.94 (d, *J* = 7.5 Hz), 109.10^E, 82.98 (d, *J* = 181.1 Hz),

81.52 (d, J = 173.9 Hz), 72.03^{E}, 70.63^{E}, 70.55^{E}, 69.38^{E}, 62.77 (t, J = 18.2 Hz), 59.15^{E}, 57.99^{E}, 57.06^{E}, 56.96^{E}, 56.71^{E}, 56.65^{E}, 39.25^{E}, 37.01^{E}, 26.34 (brs), 24.04 (brs), 23.64 (brs).

^{19}F NMR (471 MHz, $CDCl_3$, observed as a 83:17 mixture of E/Z isomers) δ_F -126.43 – -126.49 (m, 1F^{E}), -132.20 – -132.29 (m, 1F^{Z}), -231.9 (brs, 1F^{E} + 1F^{Z}), -235.2 (brs, 1F^{E} + 1F^{Z}).

MS (ES, MeOH) m/z 1026 $(M-H)^-$ 100%; 1062 $(M+Cl)^-$ 85%; 1050 $(M+Na)^+$ 100%.

HRMS (ES^+, MeOH) calc. for $C_{50}H_{68}N_9O_{11}F_3$ + Na $(M+Na)^+$: 1050.4883, found: 1050.4855.



5

Azobenzene-oligomer **5** was prepared according to general method (D) from succinimidyl ester **S13** (21 mg, 0.0.058 mmol), amino-oligomer H-ValAib$_8$FibTEG (32 mg, 0.029 mmol, obtained from the Pd-catalyzed hydrogenolysis of the corresponding Cbz-protected oligomer **6c** following general method (A)) and DIPEA (10 μL, 0.058 mmol) in dry CH_2Cl_2 (reaction time: 24 h). After workup, **5** was isolated by column chromatography (SiO_2: EtOAc/MeOH, 95:5) as an orange solid (32 mg, 84%).

R_f 0.6 (CH_2Cl_2/MeOH, 95:5)

m.p. 125-127 °C

IR (ATR) ν_{max}/cm^{-1} 3289, 2984, 1650, 1594, 1530, 1384, 1228, 910, 731

$[\alpha]_D^{25}$ -34.8 (c = 1, MeOH)

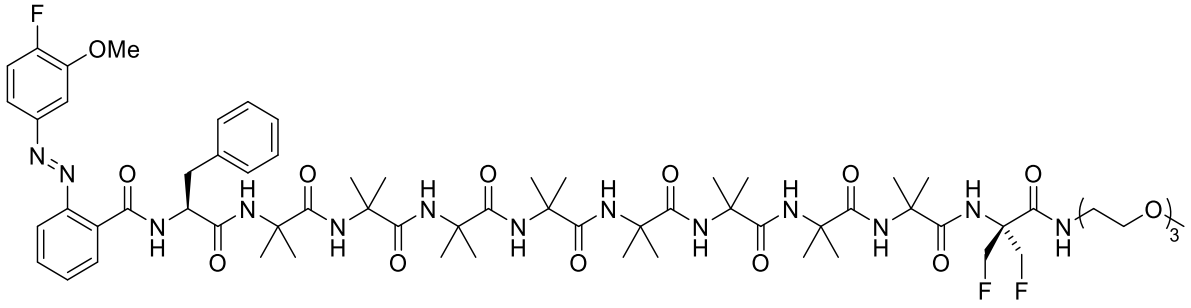
^{1}H NMR (500 MHz, $CDCl_3$, observed as a 72:28 mixture of E/Z isomers) δ_H 8.96 (brs, 1H^{E}), 8.29 – 8.21 (m, 1H^{E}), 8.11 (d, J = 4.6 Hz, 1H^{Z}), 7.92 – 7.56 (m, 11H^{E} + 8H^{Z}), 7.53 (dd, J = 7.7, 2.2 Hz, 1H^{E}), 7.49 – 7.41 (m, 1H^{E}), 7.38 – 7.21 (m, 1H^{E} + 3H^{Z}), 6.98 (s, 1H^{Z}), 6.95 (dd, J = 10.5, 8.6 Hz, 1H^{Z}), 6.84 (brs, 1H^{E}), 6.78 (d, J = 6.0 Hz, 1H^{Z}), 6.54 (brs, 1H^{Z}), 6.19 (d, J = 7.5 Hz, 1H^{Z}), 5.11 – 4.69 (m, 4H^{E} + 4H^{Z}), 4.04 – 4.00 (m, 1H^{E}), 3.99 (s, 3H^{E}), 3.98 – 3.93 (m, 1H^{Z}), 3.68 (s, 1H^{Z}), 3.62 (m, 6H^{E} + 6H^{Z}), 3.60 – 3.56 (m, 2H^{E} + 2H^{Z}), 3.54 – 3.51 (m, 2H^{E} + 2H^{Z}), 3.51 – 3.41 (m, 2H^{E} + 2H^{Z}), 3.36 (s, J = 1.3 Hz, 3H), 2.27 (dd, J = 13.6, 6.9 Hz, 1H^{Z}), 2.14 – 2.05 (m, 1H^{E}), 1.54 – 1.38 (m, 48H^{E} + 48H^{Z}), 1.11 (dd, J = 9.9, 6.8 Hz, 6H^{Z}), 1.01 (dd, J = 11.5, 6.8 Hz, 6H^{Z}).

^{13}C NMR (101 MHz, $CDCl_3$, *E*/*Z* assigned only when unambiguous distinction is possible) δ_C 176.52^Z, 176.46^E, 176.31^Z, 176.22^E, 176.11^Z, 176.01^E, 176.00^E, 175.74^E, 175.69^E, 175.51^Z, 175.35^E, 174.52^E, 174.41^E, 169.62^E (t, *J* = 4.3 Hz), 167.54^Z (brs), 155.27^E (d, *J* = 256.5 Hz), 152.95^Z, 151.95^Z (d, *J* = 251.9 Hz), 150.15^E, 149.40^E (d, *J* = 3.4 Hz), 148.87^E (d, *J* = 11.8 Hz), 148.17^Z (d, *J* = 11.8 Hz), 133.02^E, 132.17^Z, 131.84^E, 131.43^E, 129.50^E, 127.90^Z, 116.87^E (d, *J* = 16.8 Hz), 116.75^E, 116.66^Z, 116.29^Z (d, *J* = 19.8 Hz), 82.63 (d, *J* = 174 Hz), 81.60 (d, *J* = 168 Hz), 72.00^E, 70.60^E, 70.53^E, 70.33^E, 69.40^E, 62.65^E, 62.61^E (t, *J* = 18.4 Hz), 59.15^E, 57.14^E, 57.03^E, 56.98^Z, 56.88^E, 56.85^Z, 56.76^E, 56.68^Z, 56.65^E, 56.62^E, 56.58^E, 56.49^E, 56.29^Z, 39.26^E, 30.21^E, 26.03 (brs), 23.96 (brs), 19.71^Z, 19.58^Z, 19.38^E, 19.20^Z.

^{19}F NMR (471 MHz, $CDCl_3$, observed as a 72:28 mixture of *E*/*Z* isomers) δ_F -126.34 – -126.40 (m, 1F^E), -131.93 (brs, 1F^Z), -231.0 (brs, 1F^E + 1F^Z), -235.8 (1F^E + 1F^Z).

MS (ES^-, MeOH) m/z 1318 $(M-H)^-$ 100%.

HRMS (ES^-, MeOH) calc. for $C_{62}H_{95}N_{13}O_{15}F_3$ $(M-H)^-$: 1318.7023, found: 1318.7081.



Phe-5

Azobenzene-oligomer **Phe-5** was prepared according to general method (D) from succinimidyl ester **S13** (20 mg, 0.054 mmol), amino-oligomer H-PheAib$_8$FibTEG (30 mg, 0.027 mmol, obtained from the Pd-catalyzed hydrogenolysis of the corresponding Cbz-protected oligomer **6d** following general method (A)) and DIPEA (9.4 μL, 0.054 mmol) in dry CH_2Cl_2 (reaction time: 24 h). After workup, **Phe-5** was isolated by column chromatography (SiO_2: CH_2Cl_2/MeOH, 97:3 → 95:5) as an orange solid (29 mg, 85%).

R_f 0.65 (CH_2Cl_2/MeOH, 95:5)

m.p. 119-121 °C

IR (ATR) ν_{max}/cm^{-1} 3288, 2985, 1651, 1530, 1384, 1227, 753

$[\alpha]_D^{25}$ +69.4 (c = 1, $CHCl_3$)

^{1}H NMR (500 MHz, $CDCl_3$, observed as a 72:28 mixture of *E*/*Z* isomers) δ_H 9.09 (brs, 1H^E + 1H^Z), 8.24 (m, 1H^E + 1H^Z), 7.92 (brs, 1H^E), 7.72 (m, 9H^E + 9H^Z), 7.49 (d, *J* = 7.1 Hz, 1H^E),

7.43 (s, 1H^{E}), 7.37 – 7.18 (m, 7H^{E} + 8H^{Z}), 7.14 (s, 1H^{E}), 7.13 (s, 1H^{E}), 6.95 (dd, J = 10.4, 8.7 Hz, 1H^{Z}), 6.86 (s, 1H^{Z}), 6.75 (dd, J = 7.5, 2.1 Hz, 1H^{Z}), 6.50 (ddd, J = 8.4, 3.5, 2.3 Hz, 1H^{Z}), 6.33 (s, 1H^{E}), 6.19 – 6.09 (m, 1H^{Z}), 5.16 – 4.72 (m, 4H^{E} + 4H^{Z}), 4.42 (brs, 1H^{E} + 1H^{Z}), 3.98 (s, 3H^{E}), 3.68 (s, 3H^{Z}), 3.62 (m, 6H^{E} + 6H^{Z}), 3.60 – 3.56 (m, 2H^{E} + 2H^{Z}), 3.53 (m, 2H^{E} + 2H^{Z}), 3.51 – 3.39 (m, 2H^{E} + 2H^{Z}), 3.35 (s, 3H^{E} + 3H^{Z}), 3.33 (dd, J = 14.4, 5.9 Hz, 1H^{Z}), 3.24 – 3.11 (m, 2H^{E} + 1H^{Z}), 1.53 – 1.21 (m, 48H^{E} + 48H^{Z}).

^{13}C NMR (126 MHz, $CDCl_3$) δ_C 176.39, 176.14, 175.93, 175.63, 175.21, 174.16, 171.78, 169.56 (t, J = 4.6 Hz), 167.46, 155.31 (d, J = 256.9 Hz), 149.88, 149.34 (d, J = 3.4 Hz), 148.92 (d, J = 11.8 Hz), 135.78, 133.17, 131.95, 131.39, 129.12, 127.72, 117.02 (d, J = 20.1 Hz), 116.65, 109.21, 72.04, 70.64, 70.55, 70.35, 69.44, 62.73 (t, J = 18.2 Hz), 59.16, 57.08, 57.07, 56.92, 56.80, 56.70, 56.67, 56.57, 39.27, 36.98, 26.47 – 26.20 (brs), 24.04 – 23.48 (brs).

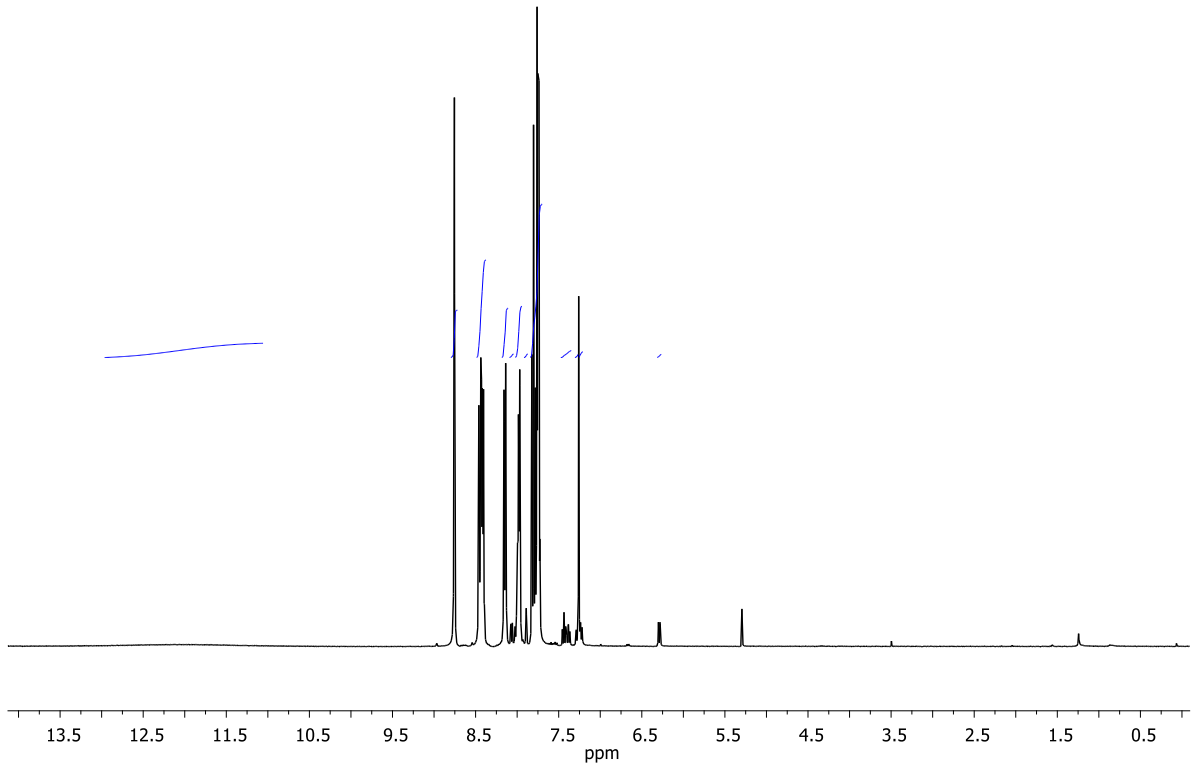
^{19}F NMR (471 MHz, $CDCl_3$, observed as a 93:7 mixture of *E*/*Z* isomers) δ_F -126.39 (dd, J = 13.6, 7.7 Hz, 1F^{E}), -132.40 (brs, 1F^{Z}), -231.04 (brs, 1F^{E} + 1F^{Z}), -236.0 (brs, 1F^{E} + 1F^{Z}).

MS (ES^+, MeOH) m/z 1390 $(M+Na)^+$ 100%.

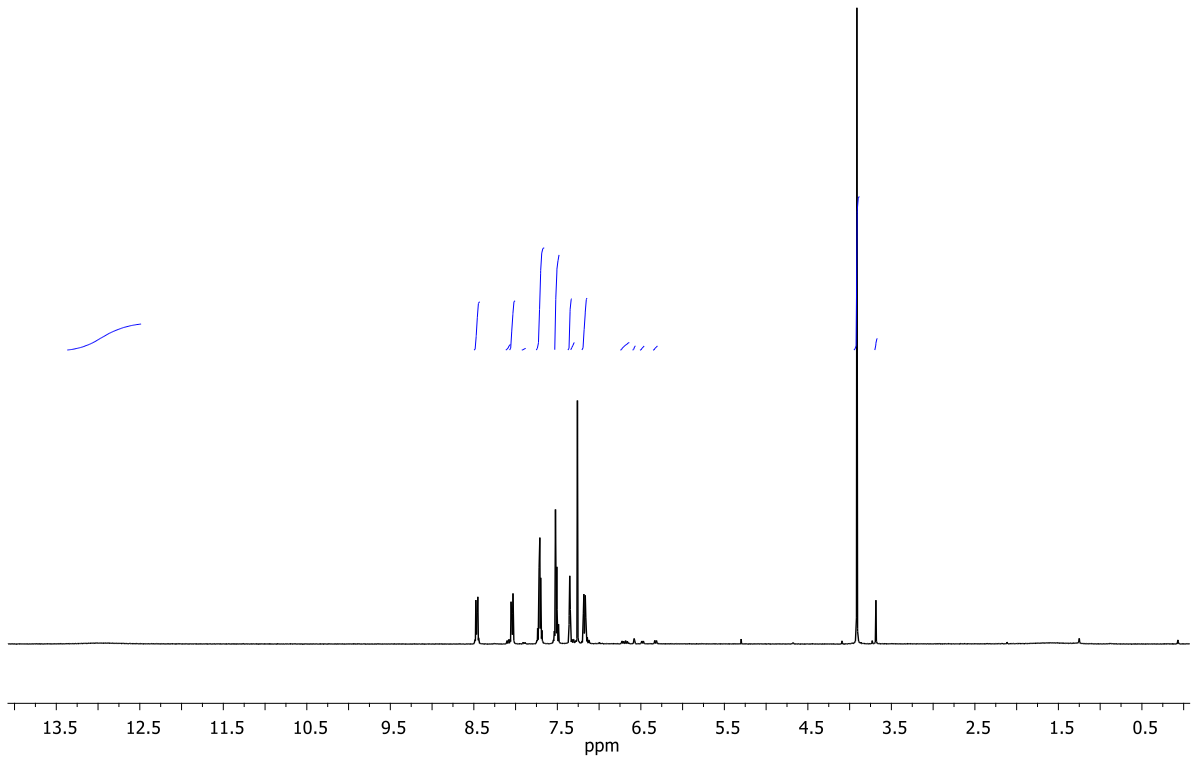
HRMS (ES^+, MeOH) calc. for $C_{66}H_{96}N_{13}O_{15}F_3$ + Na $(M+Na)^+$: 1390.6999, found: 1390.6971.

^{1}H NMR spectra

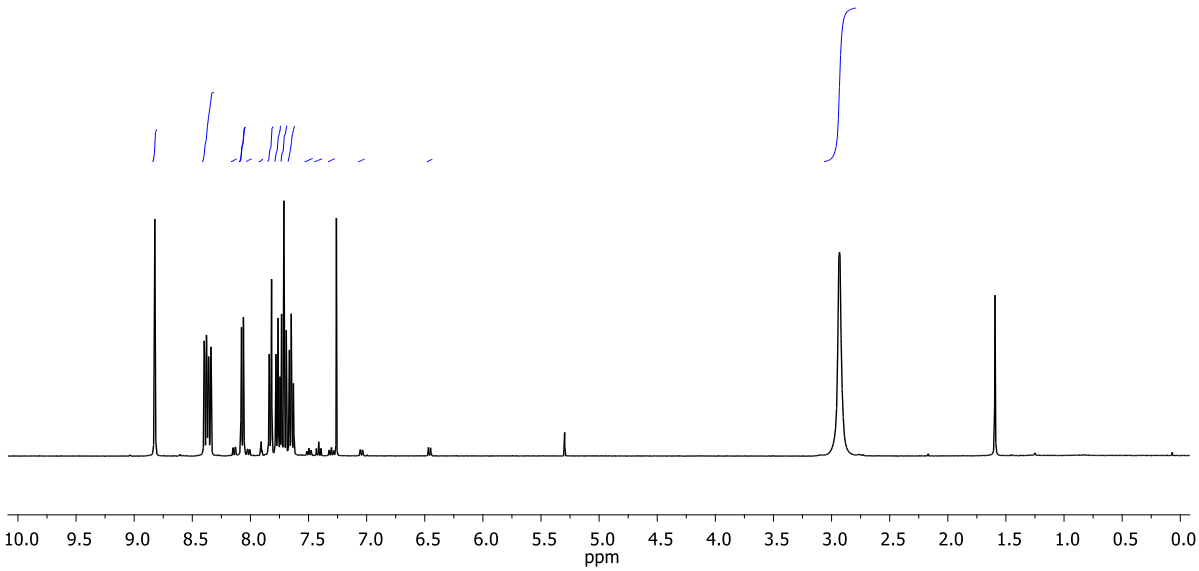
S6 ($CDCl_3$, 400 MHz)



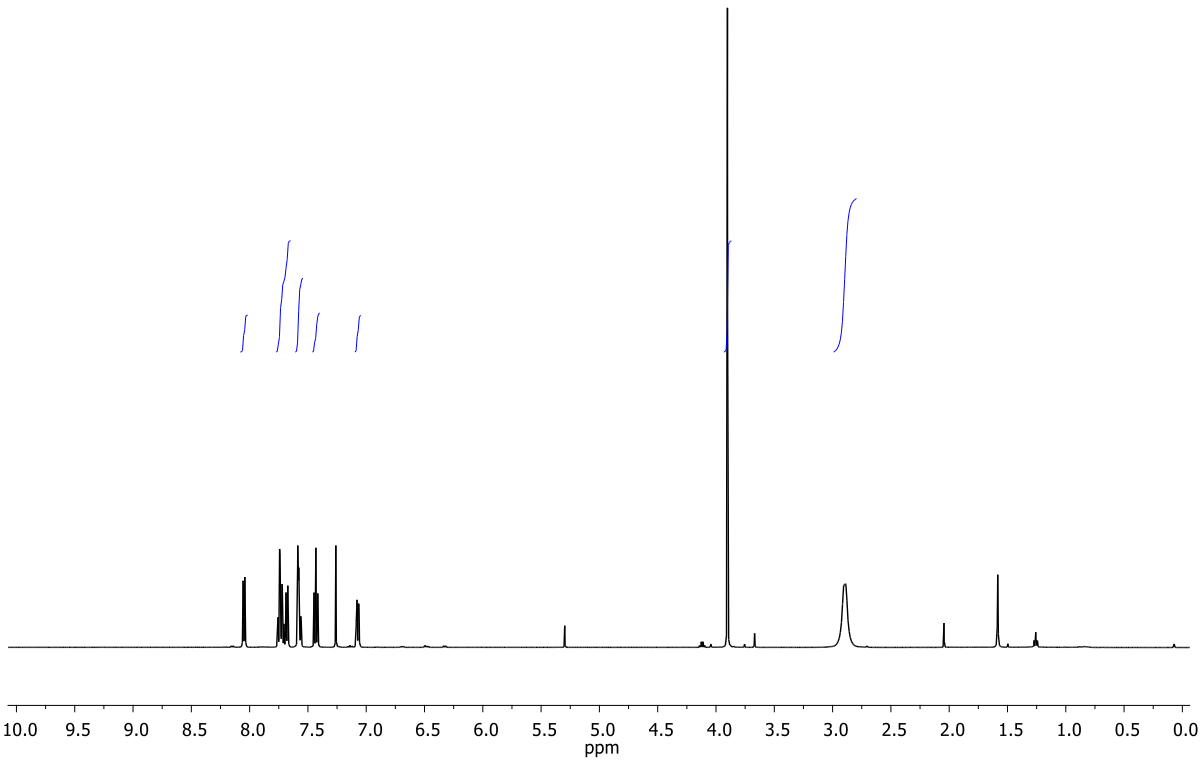
S7 ($CDCl_3$, 400 MHz)



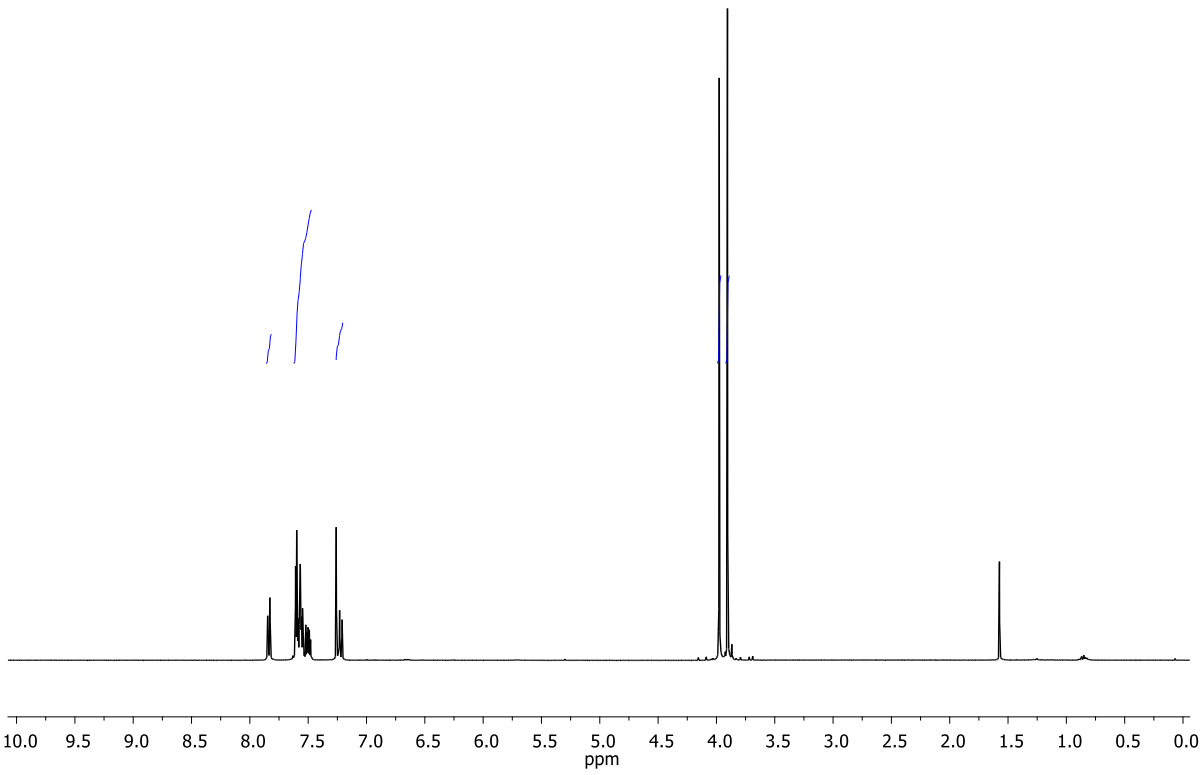
S8 ($CDCl_3$, 400 MHz)



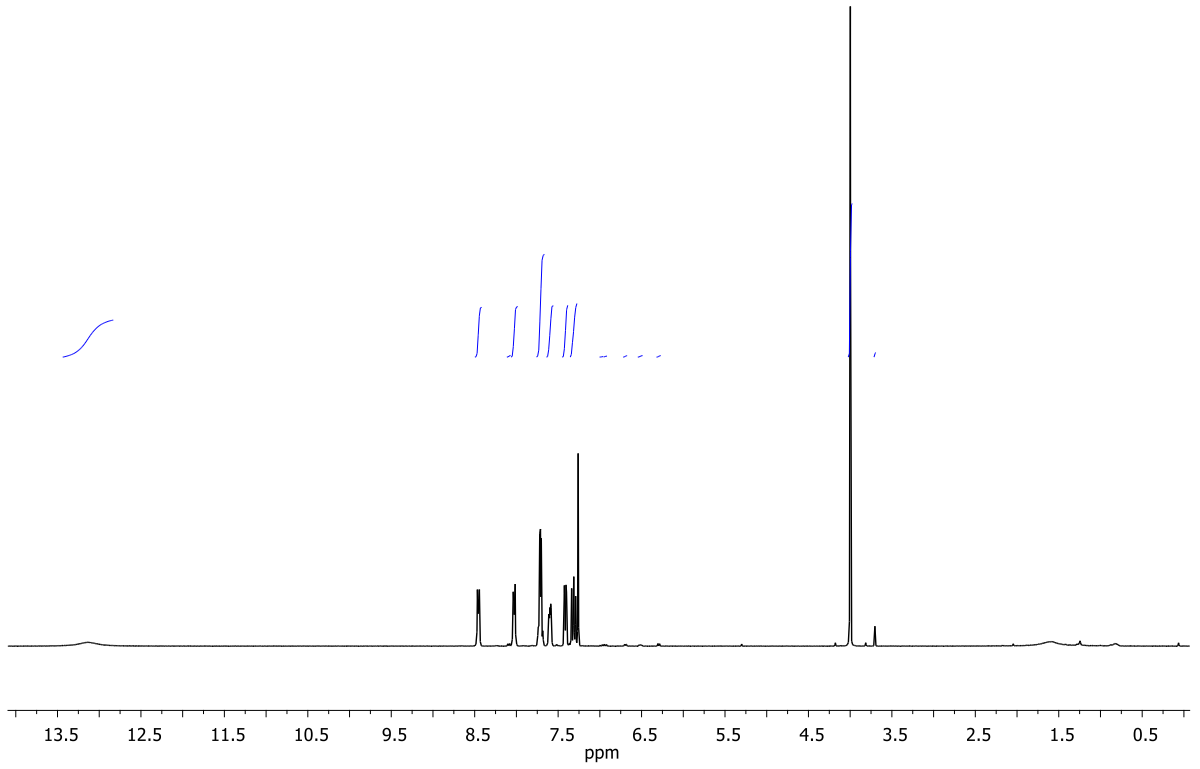
S9 ($CDCl_3$, 500 MHz)



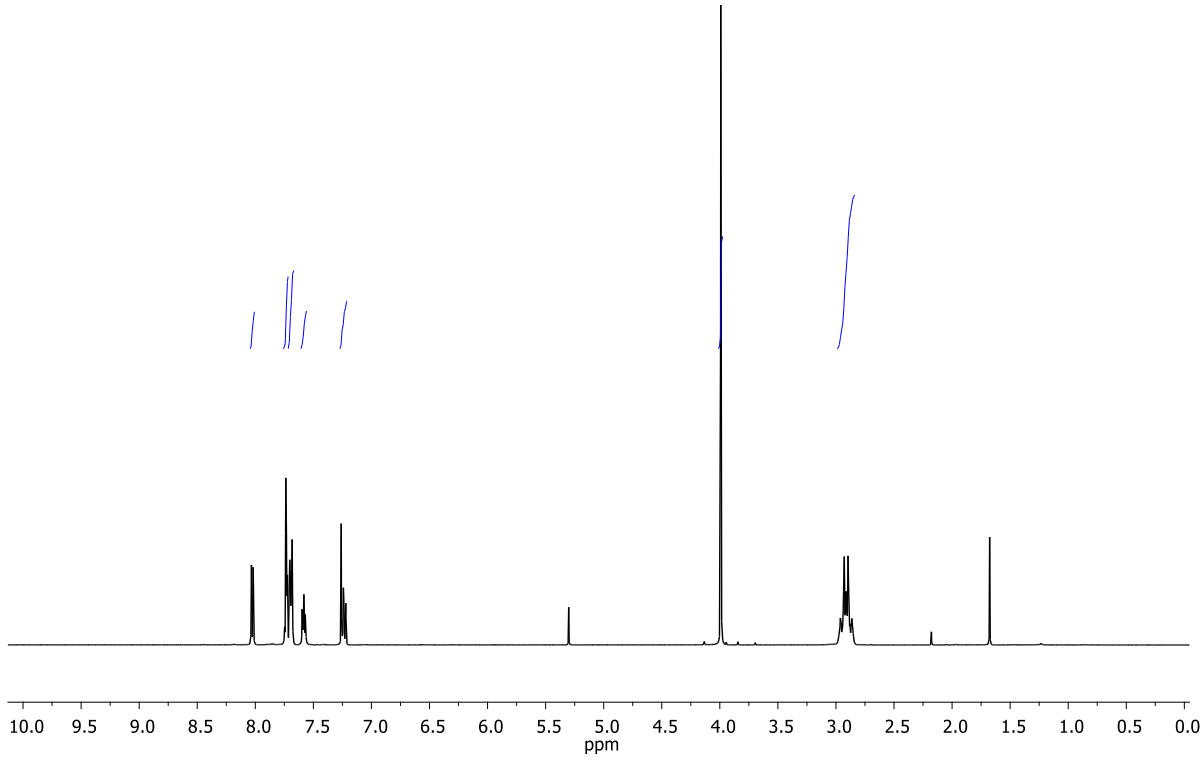
S11 ($CDCl_3$, 400 MHz)



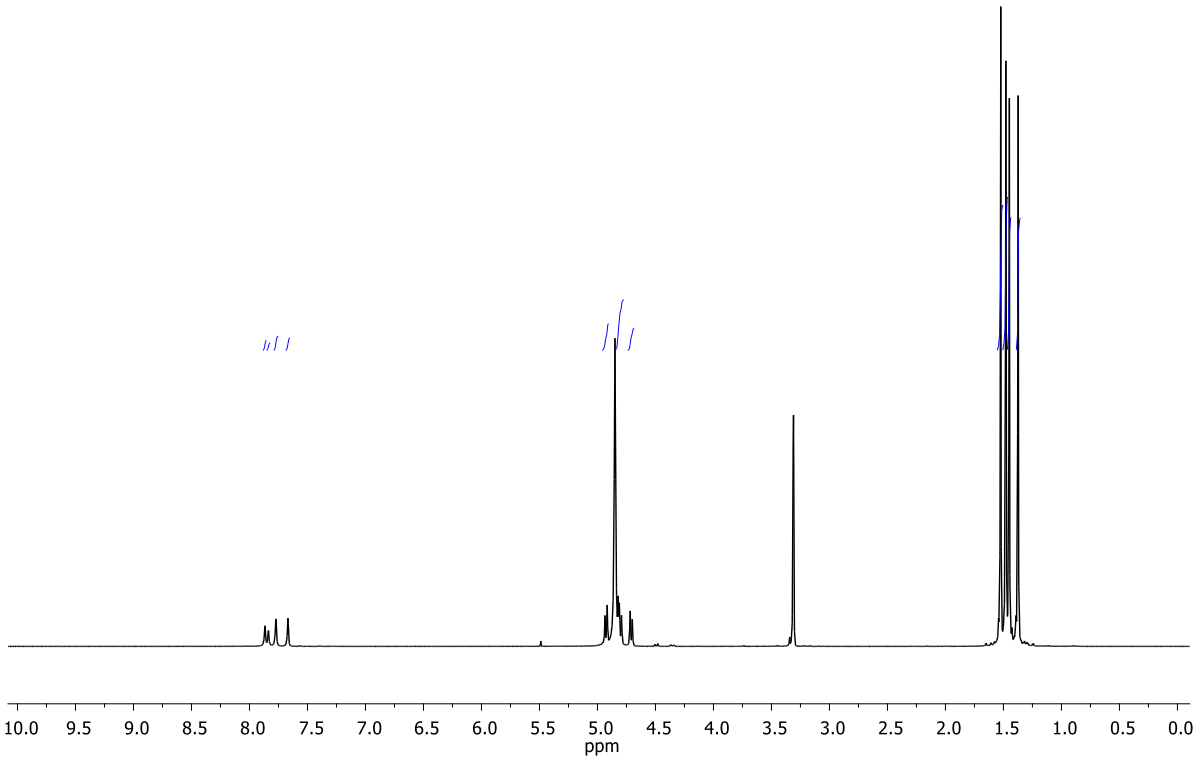
S12 ($CDCl_3$, 400 MHz)



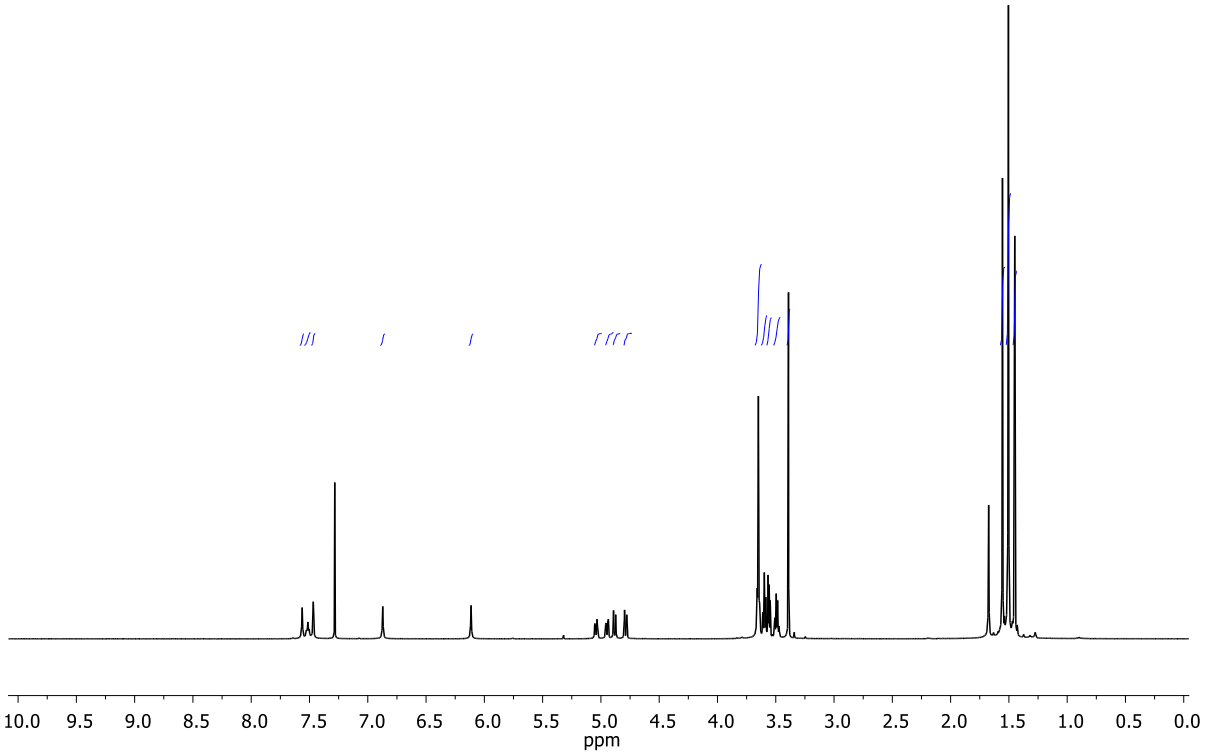
S13 ($CDCl_3$, 500 MHz)



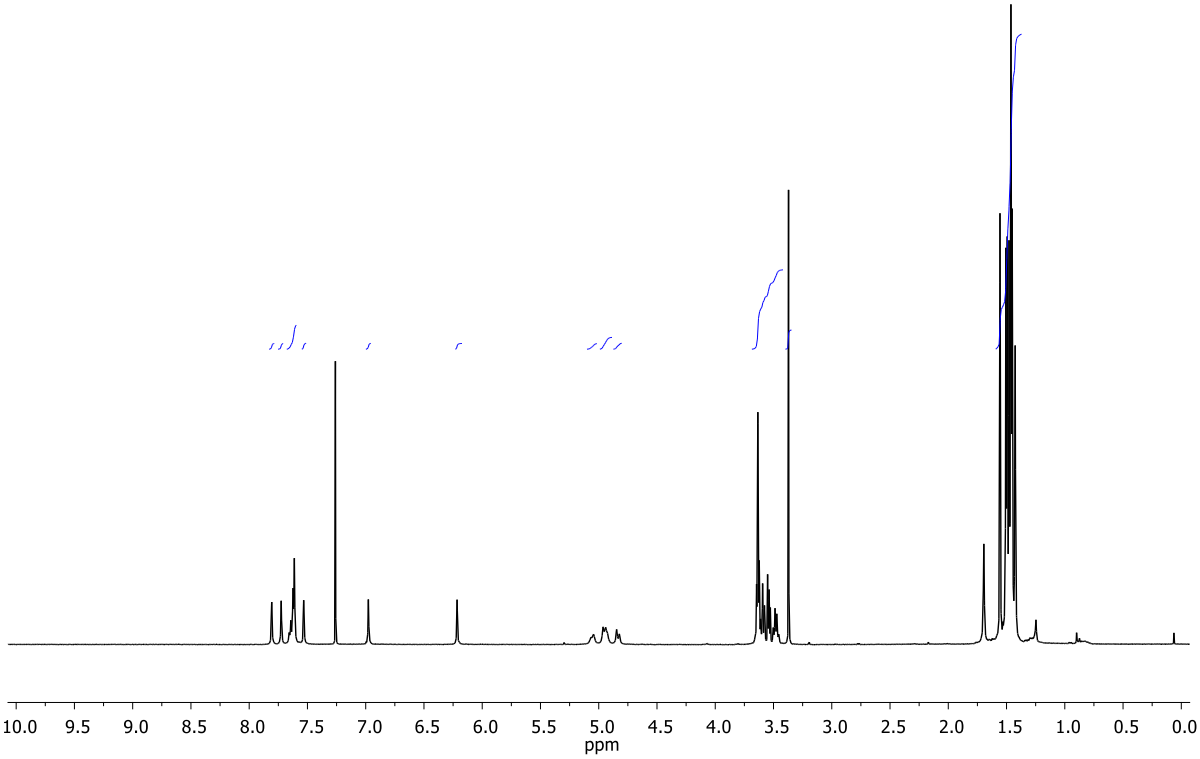
F2 ($CDCl_3$, 500 MHz)



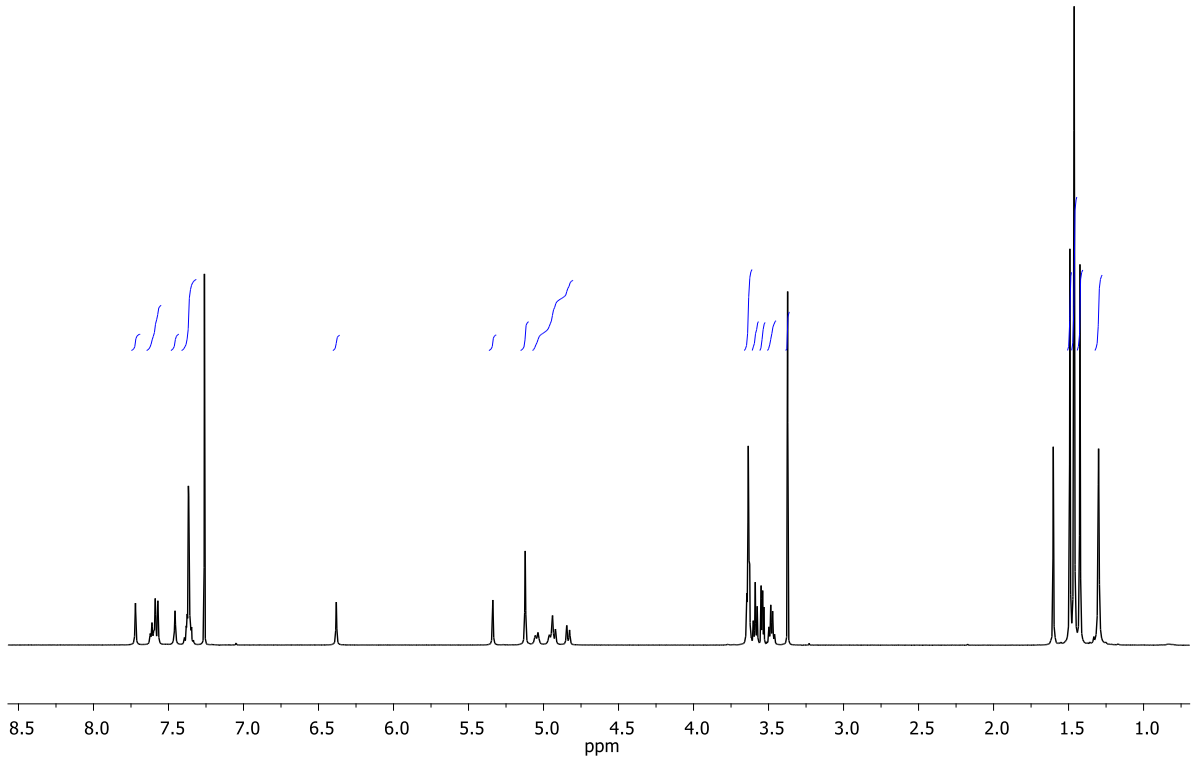
F3 ($CDCl_3$, 500 MHz)



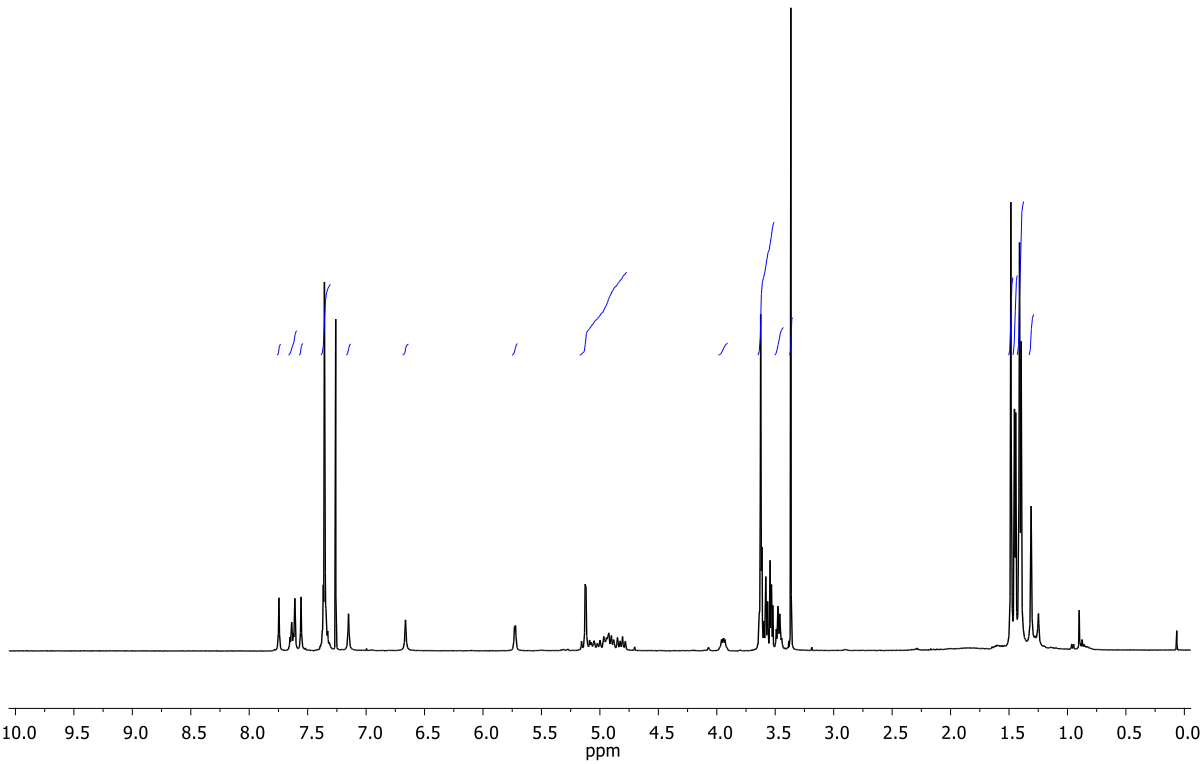
F4 ($CDCl_3$, 400 MHz)



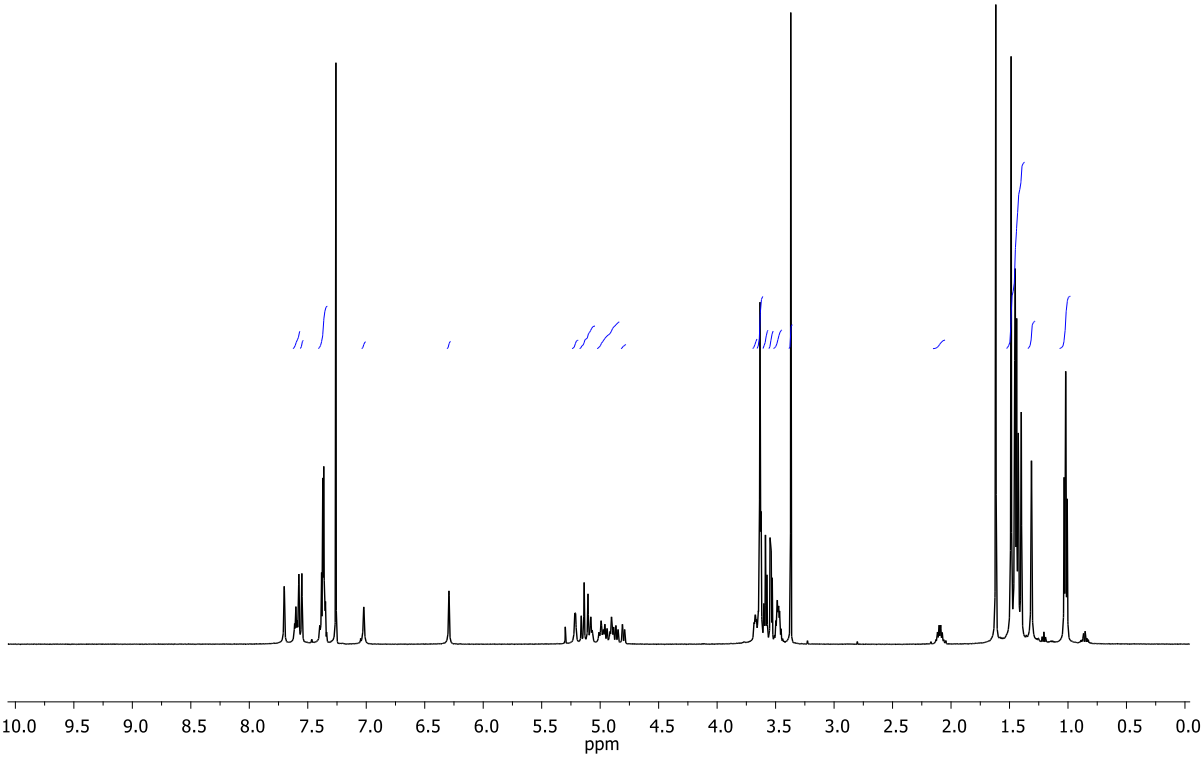
3a ($CDCl_3$, 500 MHz)



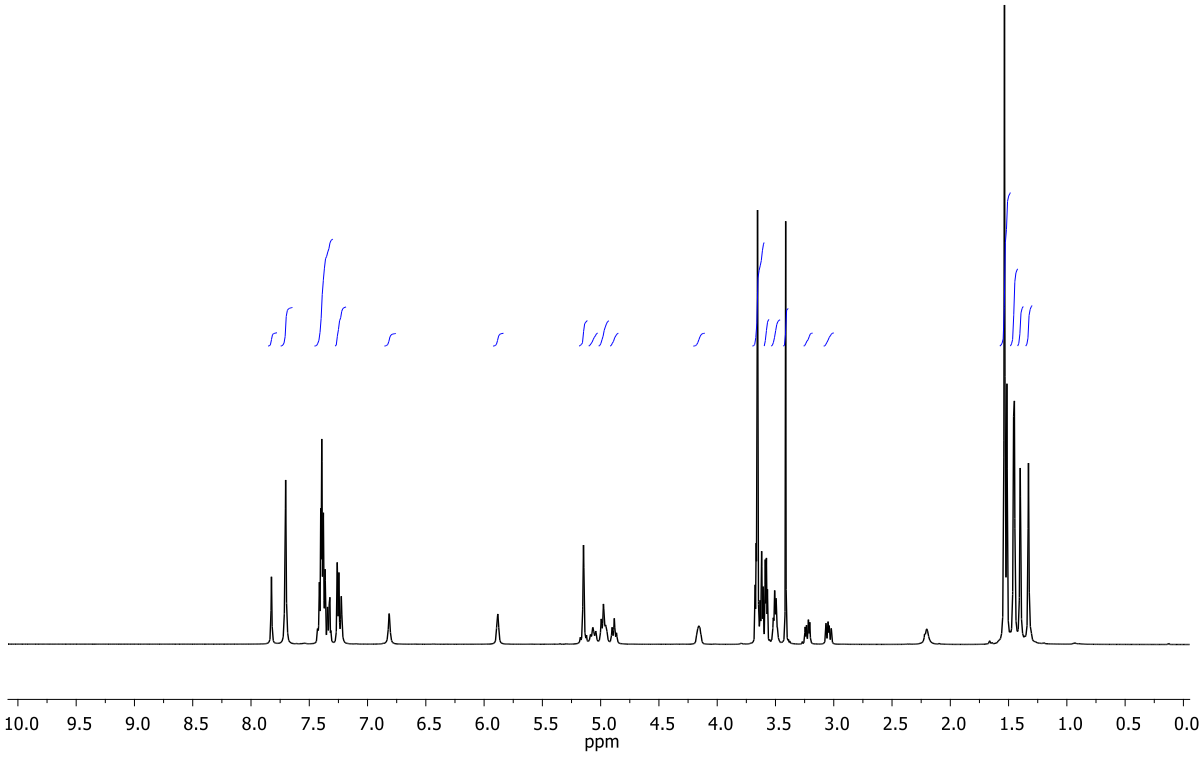
3b ($CDCl_3$, 400 MHz)



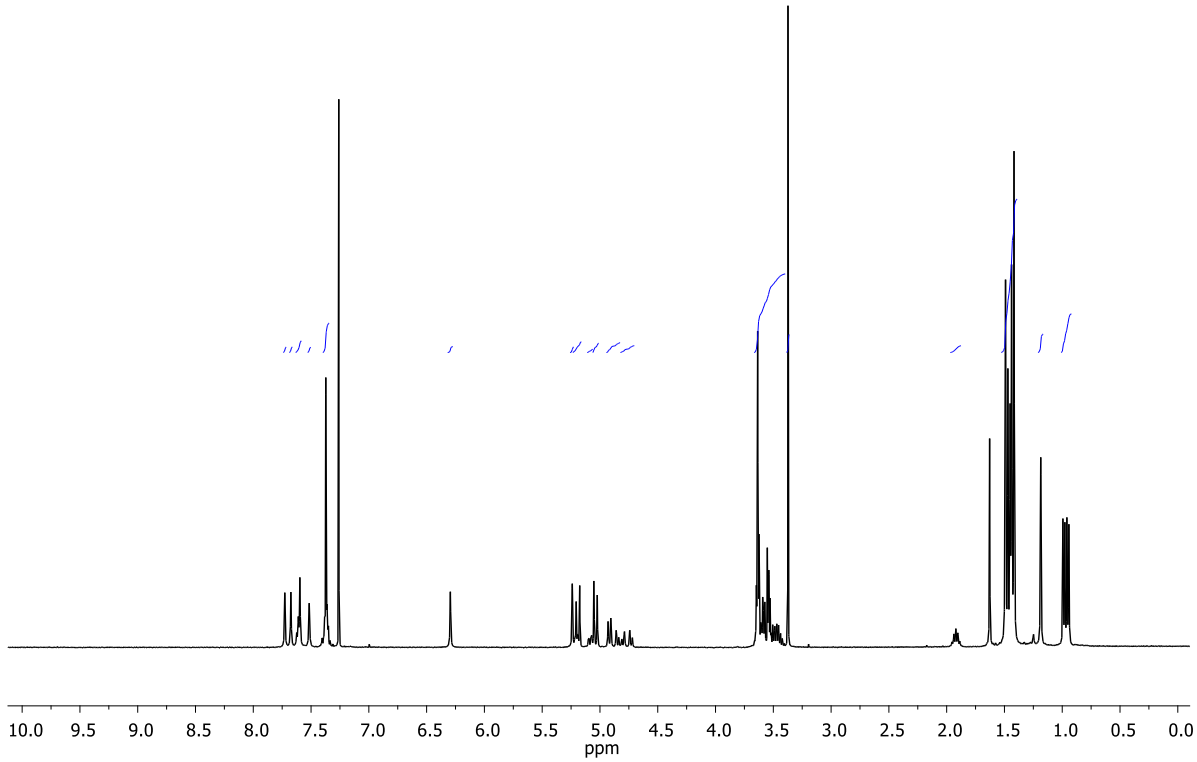
3c ($CDCl_3$, 500 MHz)



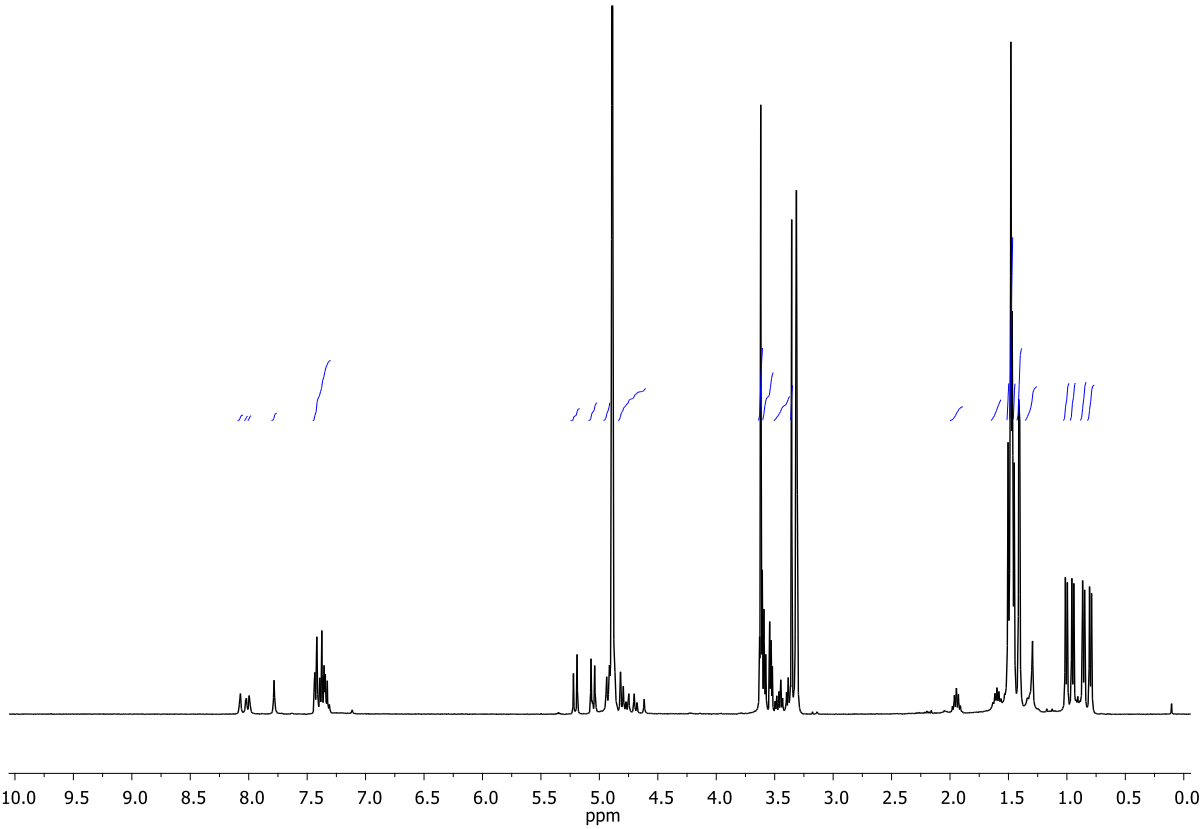
3d ($CDCl_3$, 500 MHz)



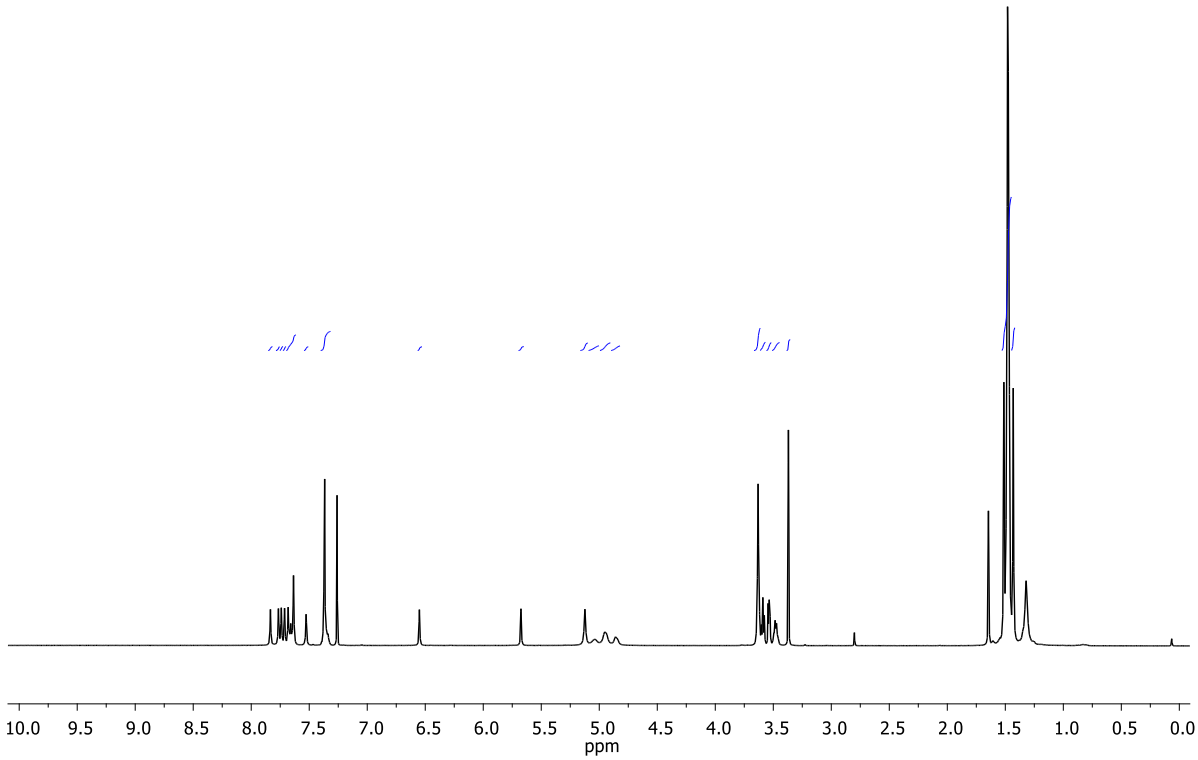
3e ($CDCl_3$, 400 MHz)



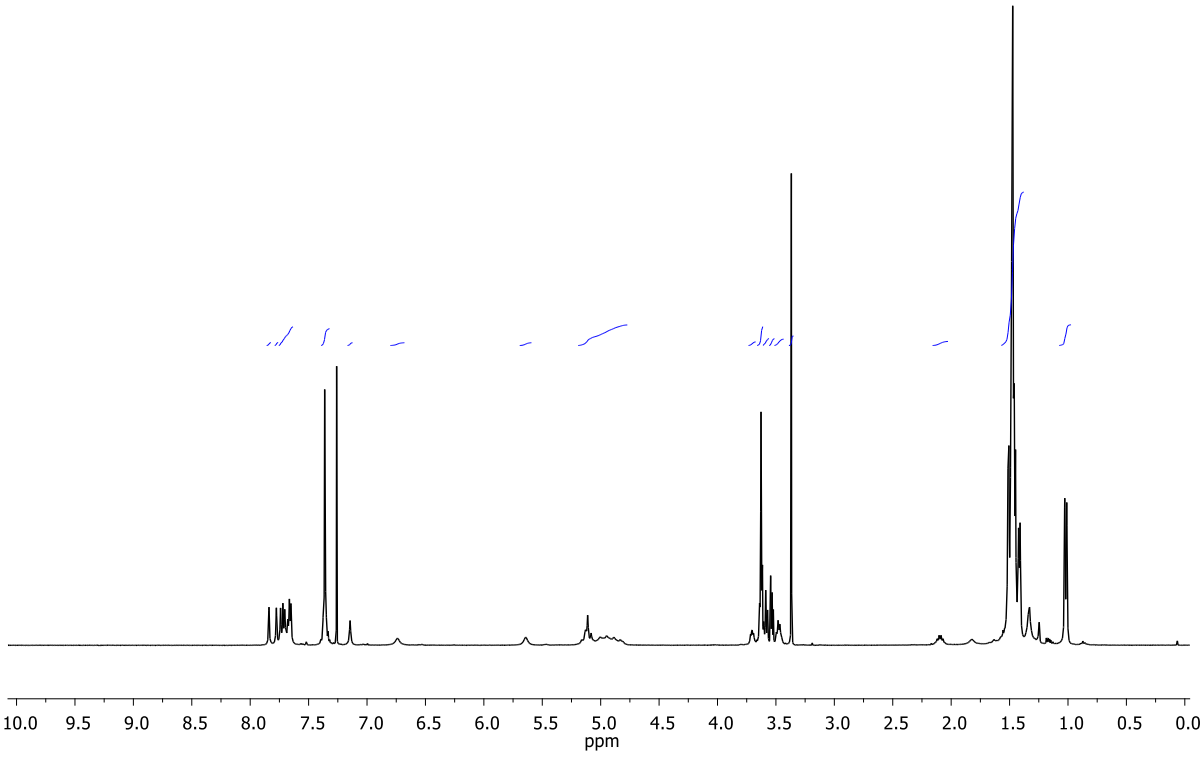
3f (CD_3OD, 400 MHz)



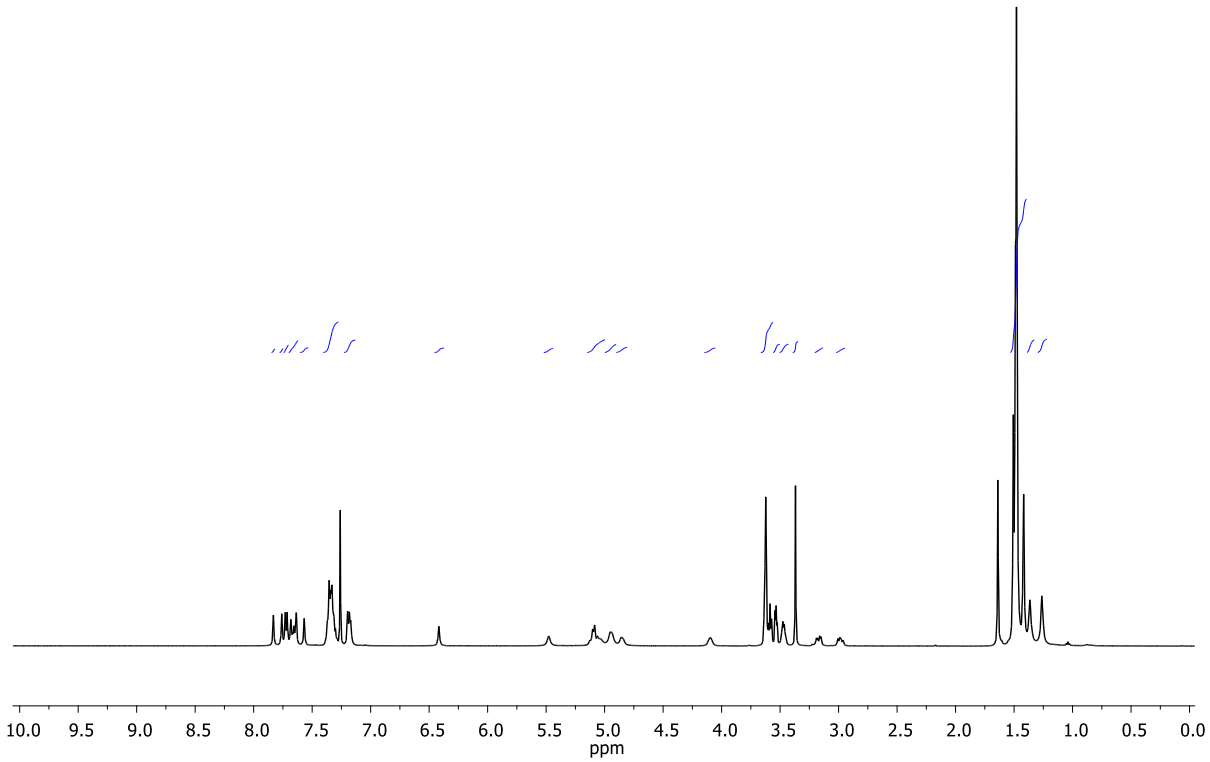
6a ($CDCl_3$, 500 MHz)



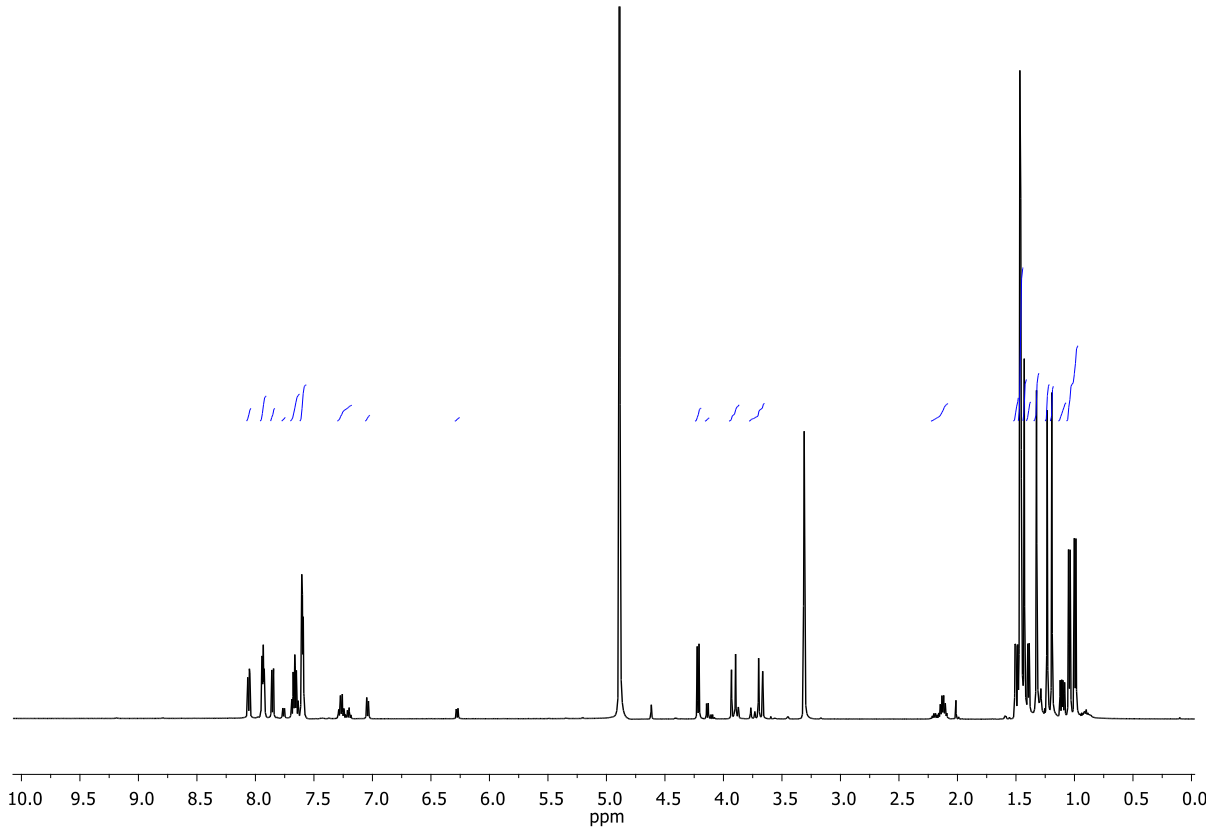
6c ($CDCl_3$, 400 MHz)



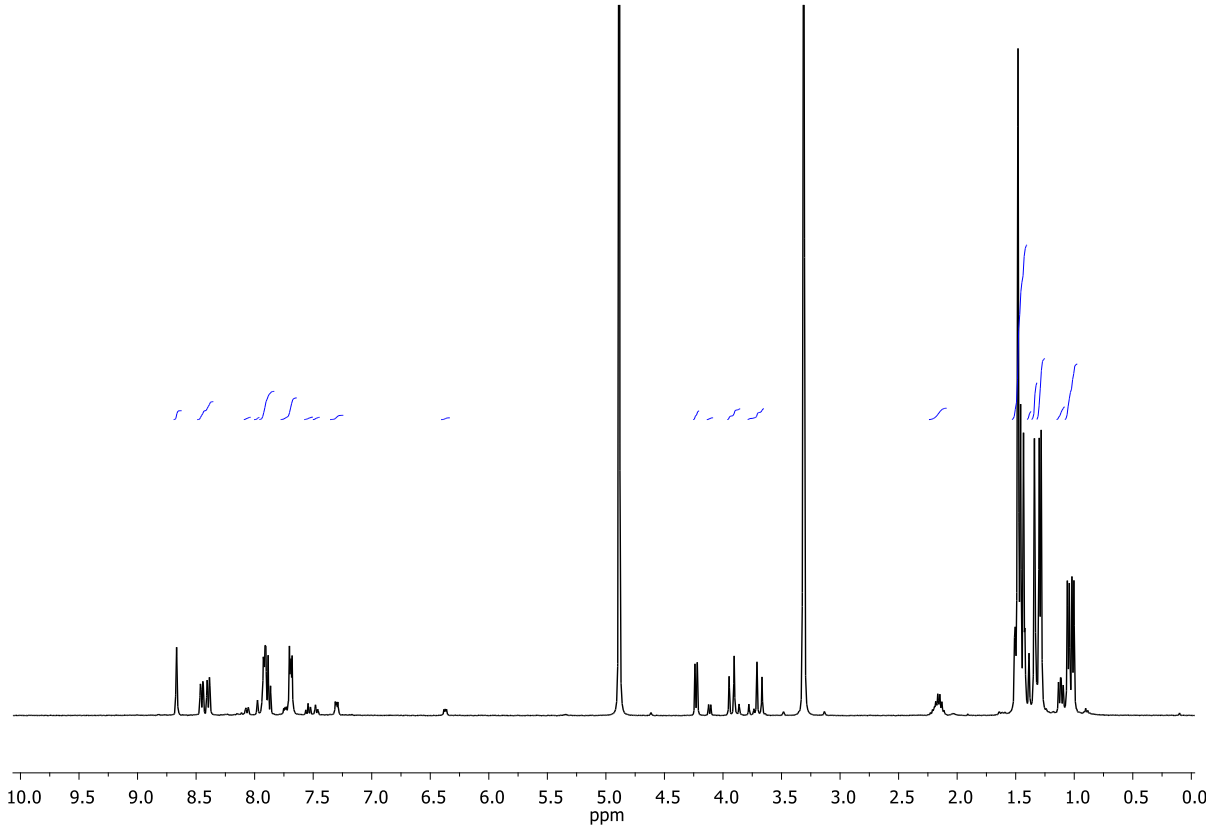
6d ($CDCl_3$, 500 MHz)



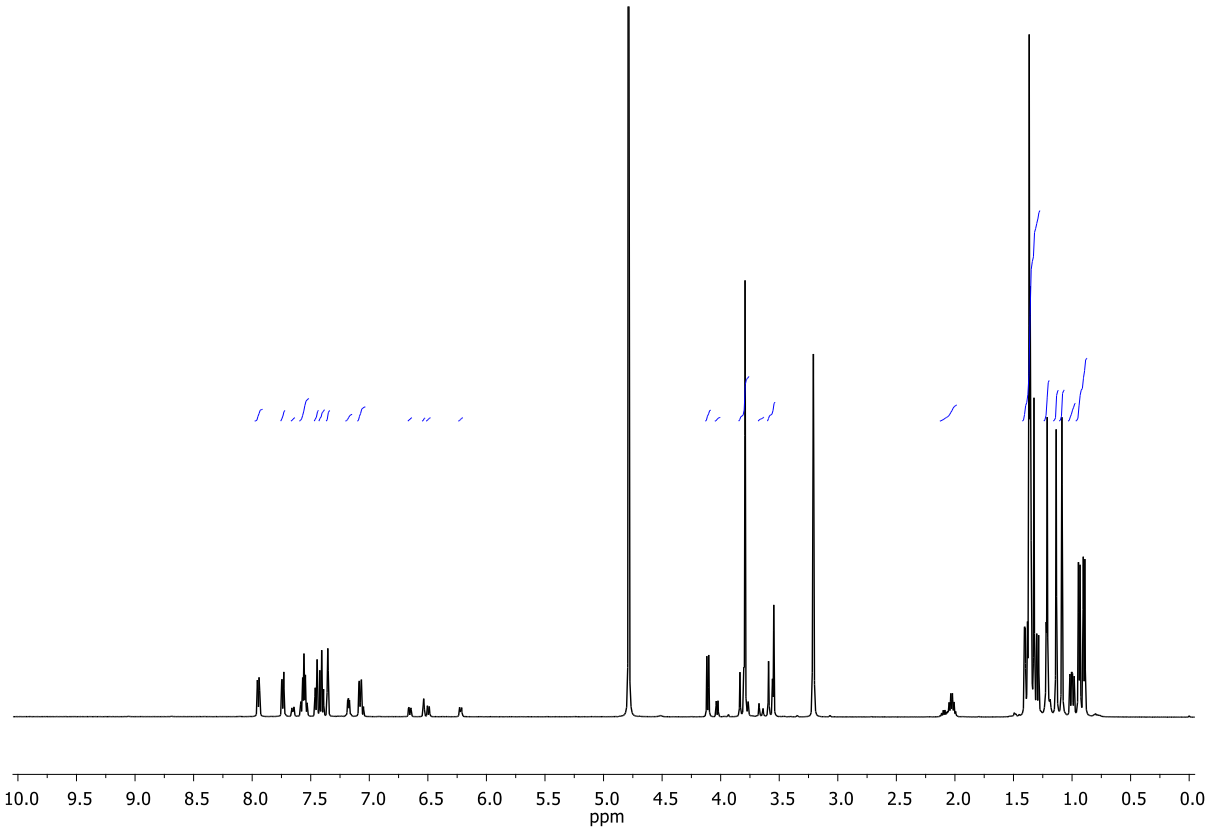
1a (CD_3OD, 500 MHz)



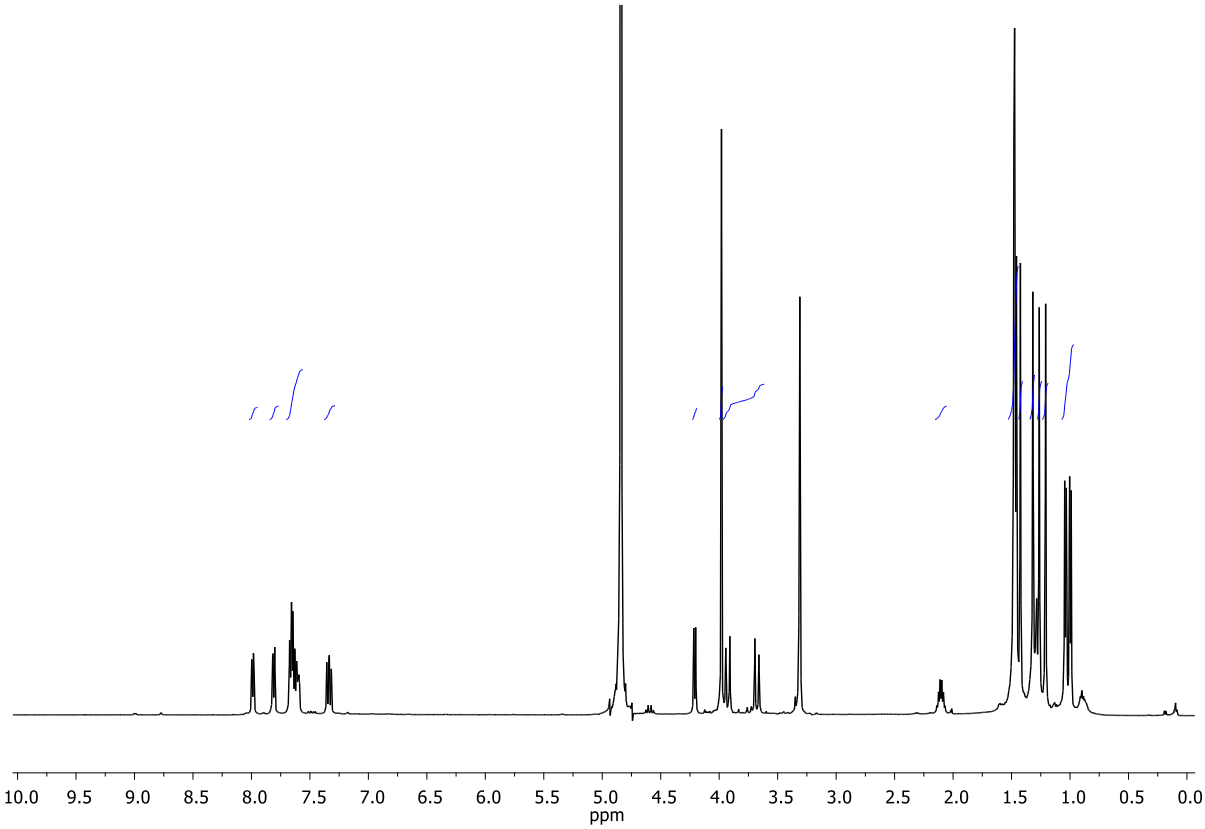
1b (CD_3OD, 400 MHz)



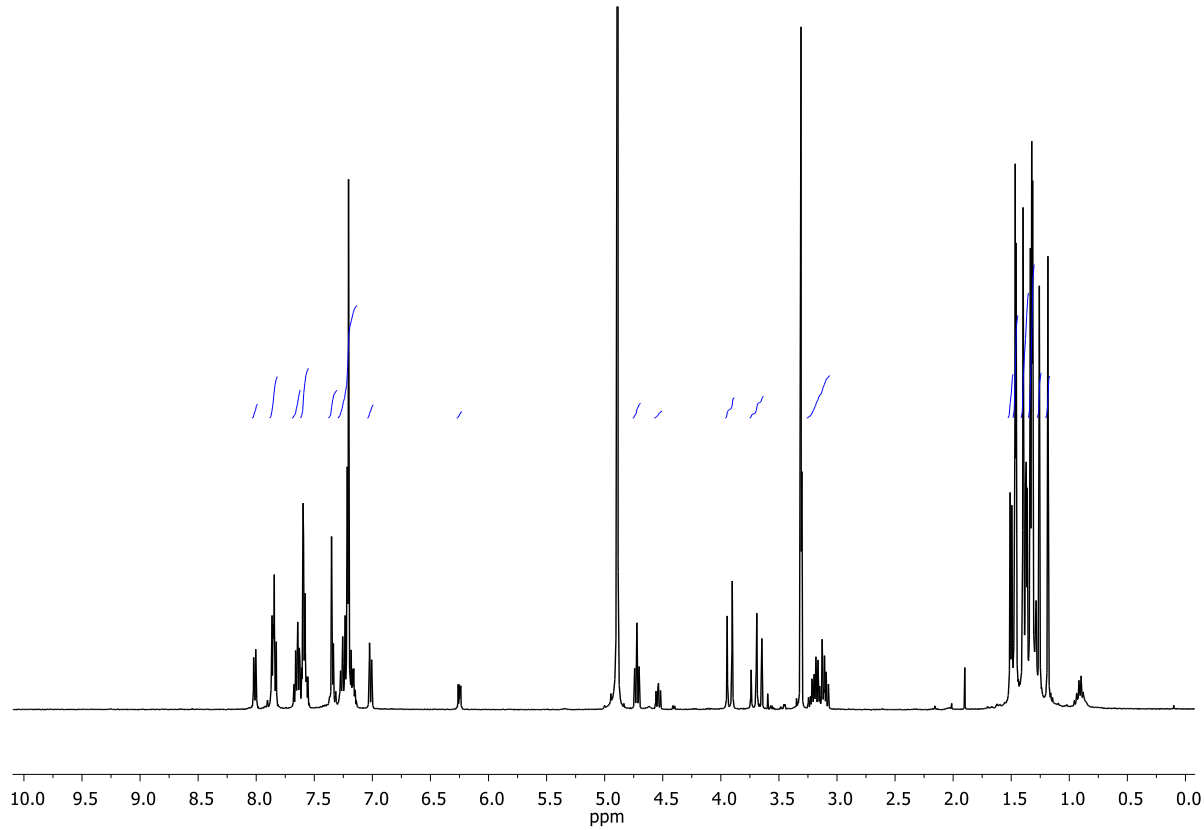
1c (CD_3OD, 500 MHz)



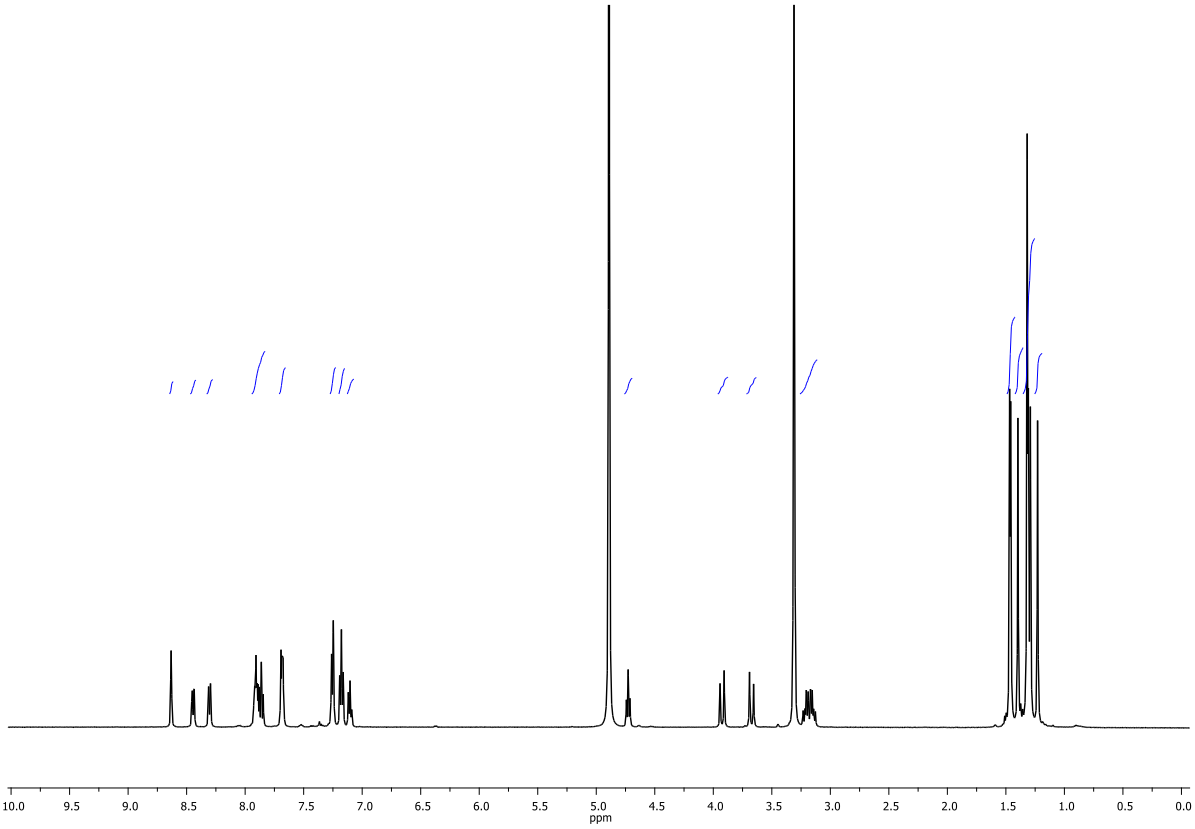
1d (CD_3OD, 500 MHz)



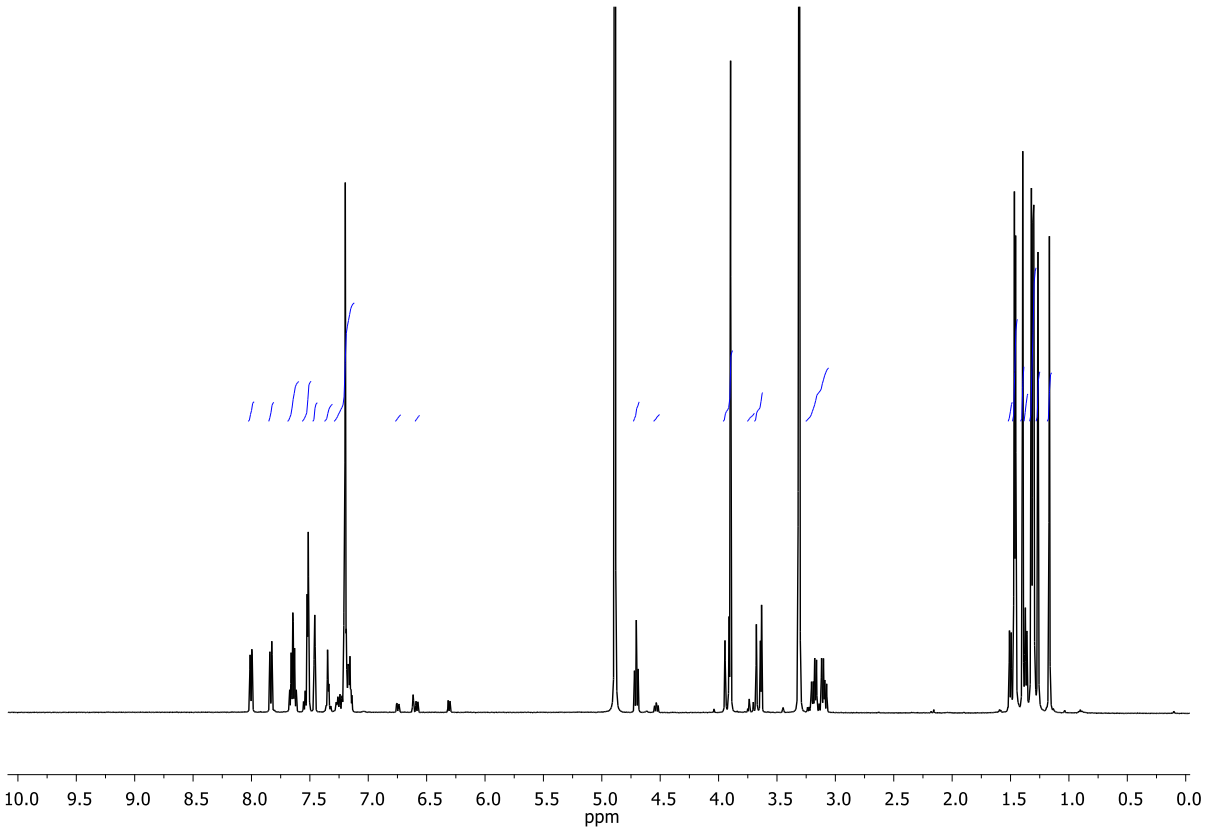
1e (CD_3OD, 500 MHz)



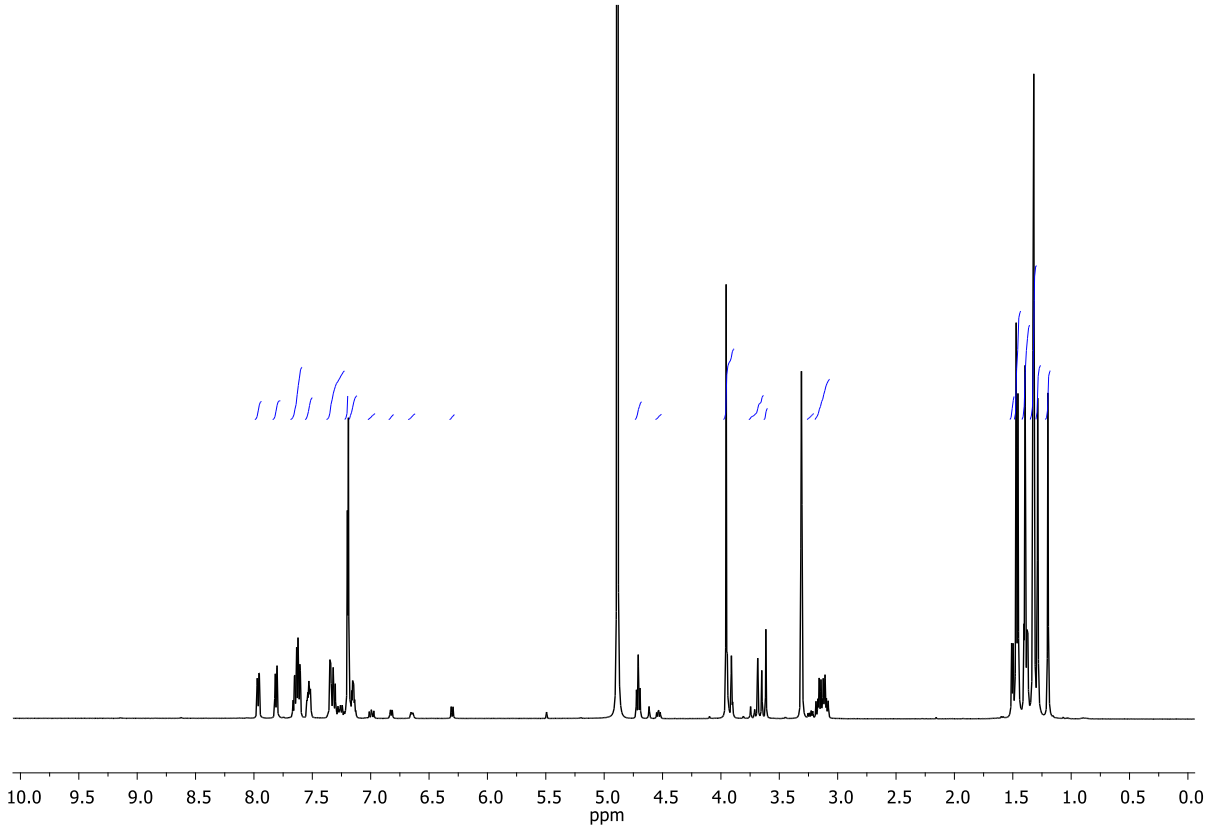
1f (CD_3OD, 500 MHz)



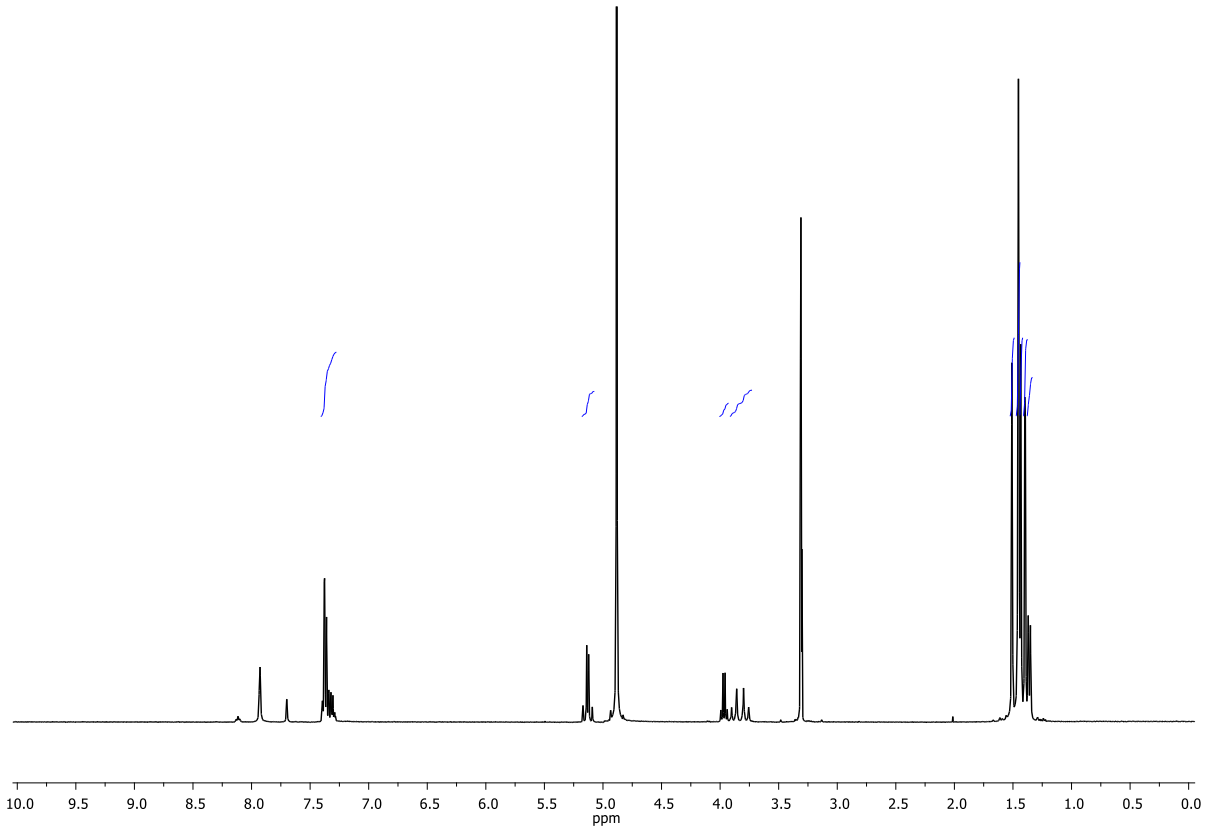
1g (CD_3OD, 500 MHz)



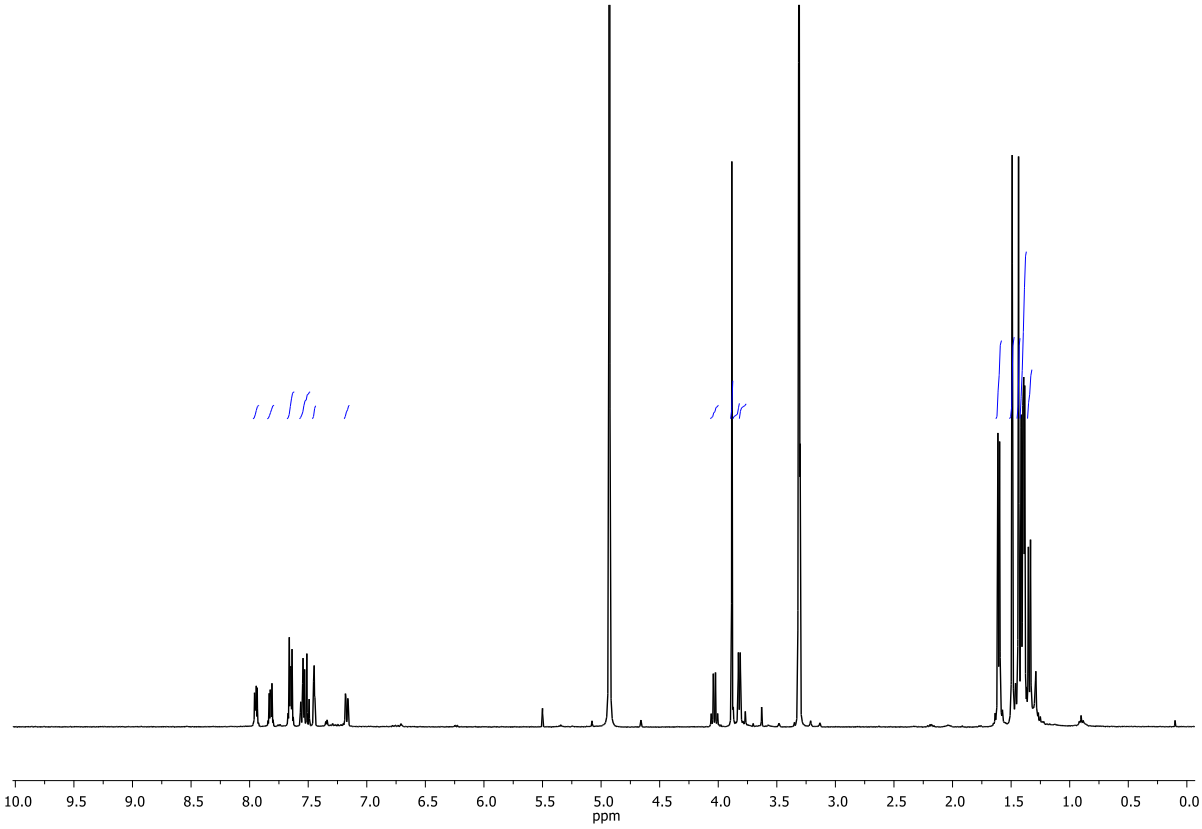
1h (CD_3OD, 500 MHz)



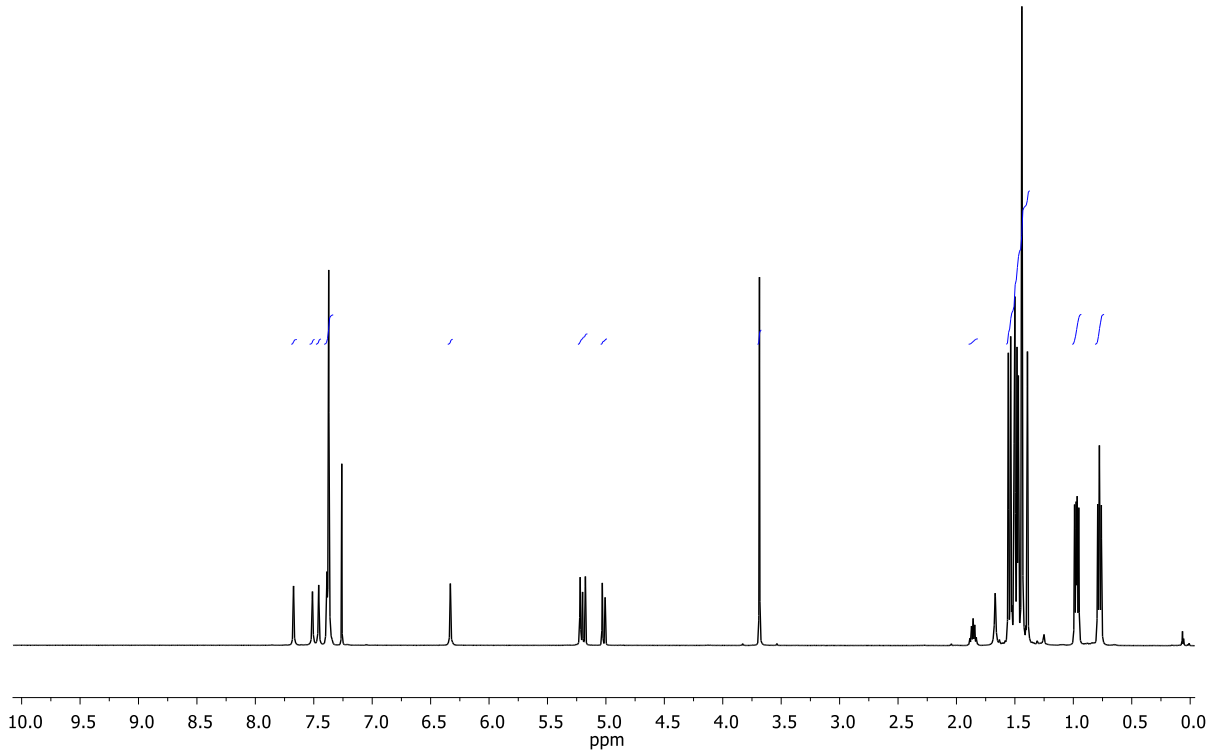
S15 (CD_3OD, 400 MHz)



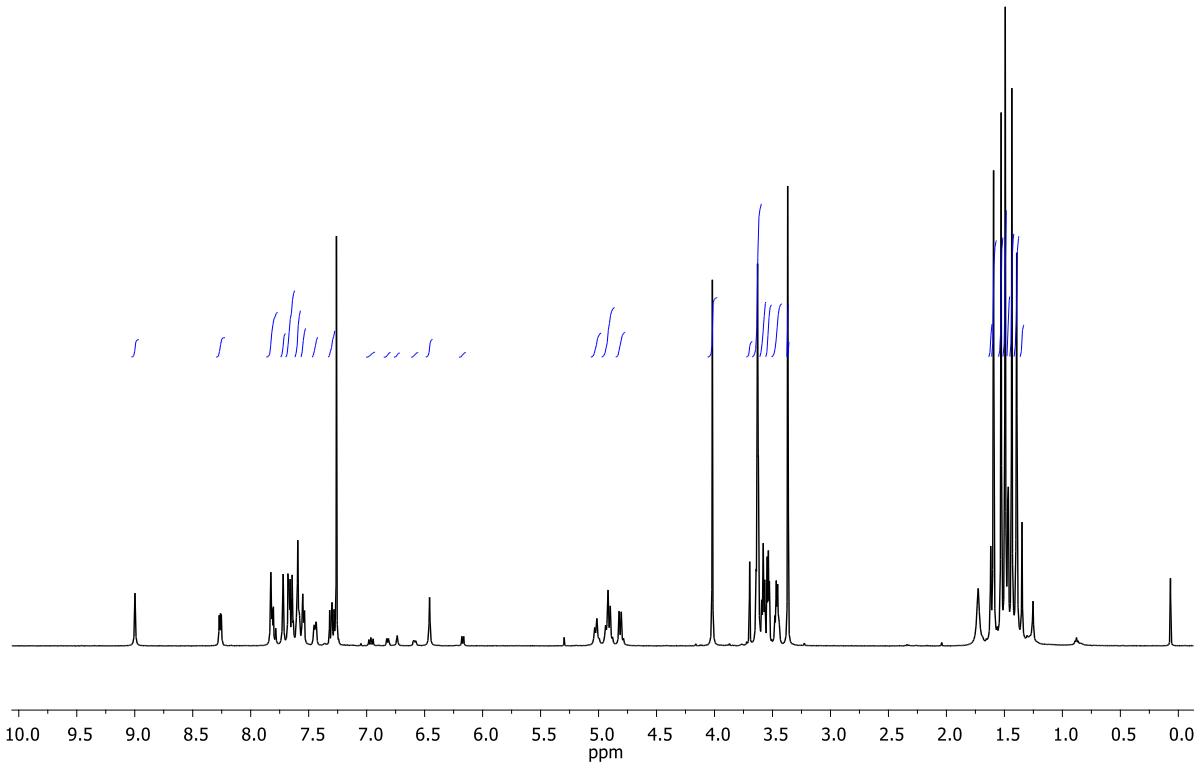
2 (CD3OD, 400 MHz)



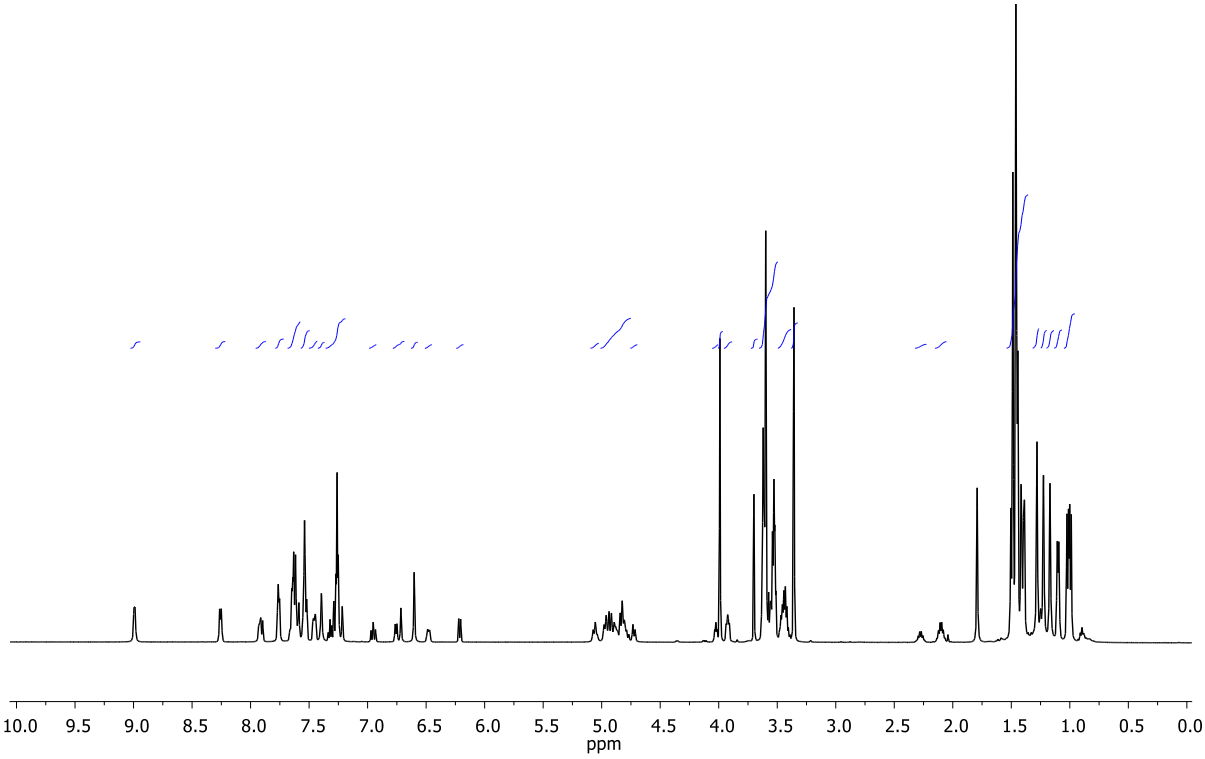
S17 ($CDCl_3$, 500 MHz)



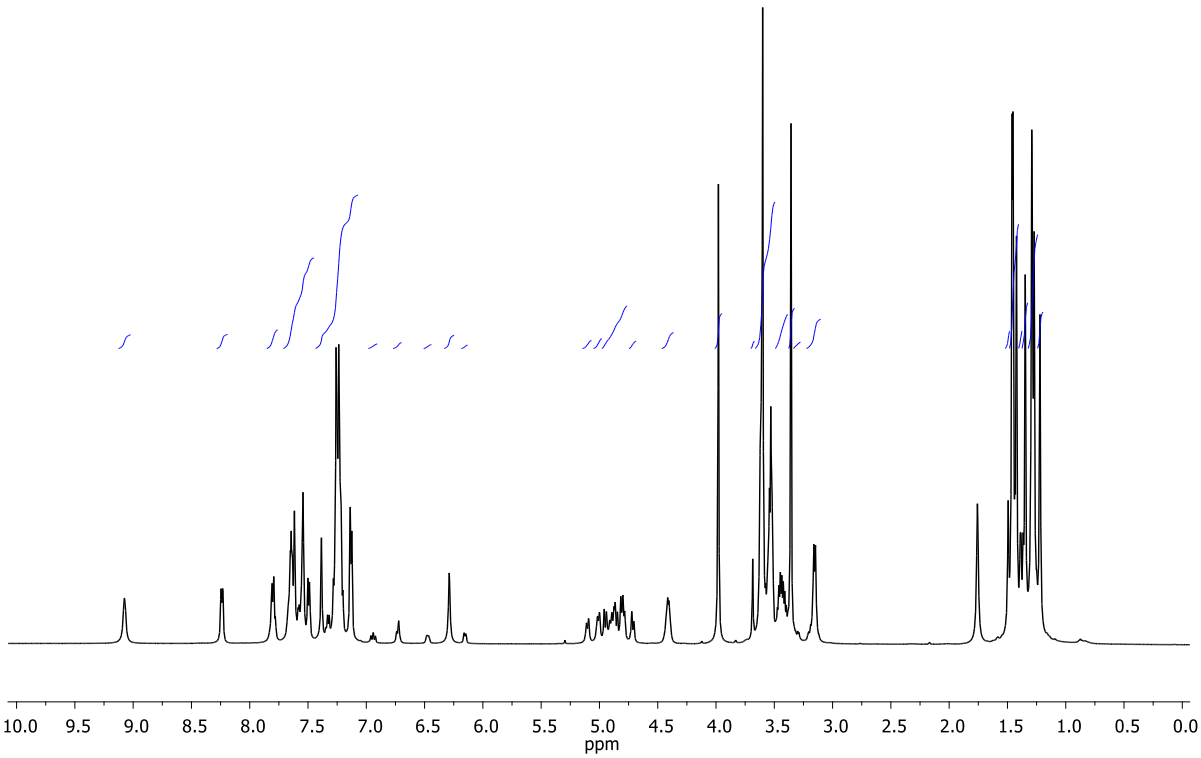
3g ($CDCl_3$, 500 MHz)



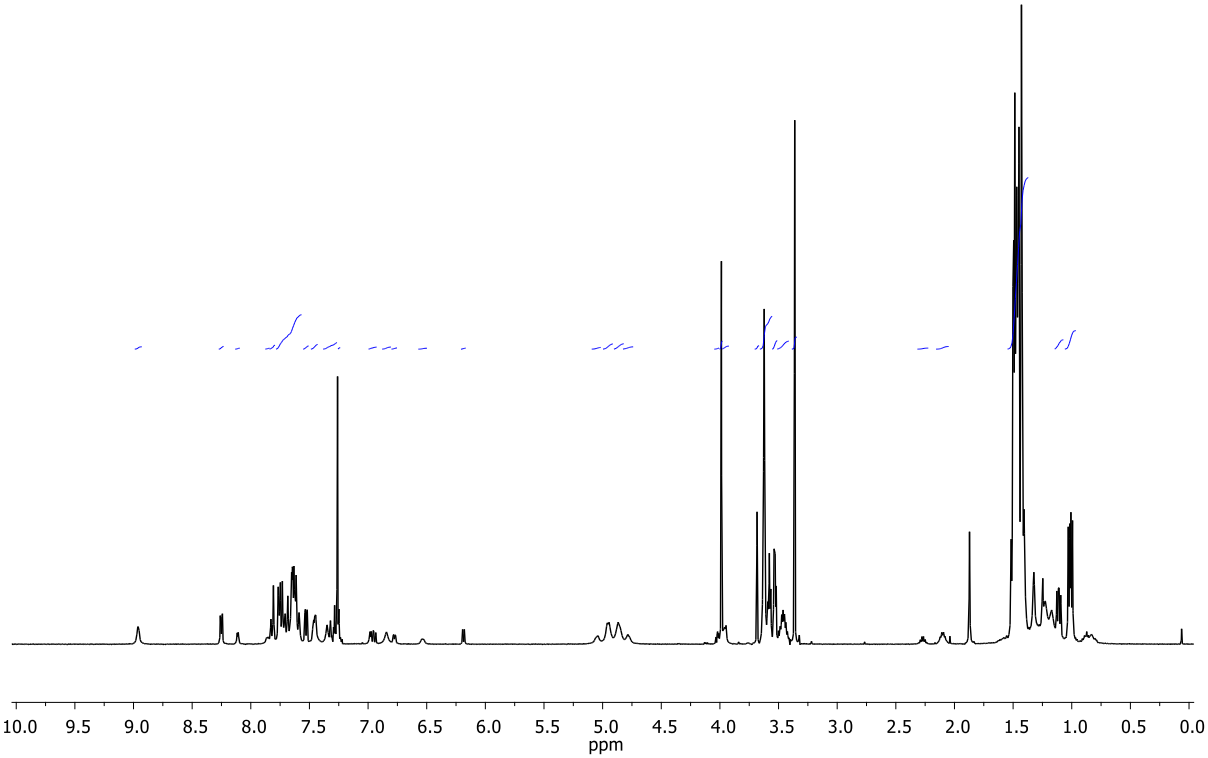
4 ($CDCl_3$, 500 MHz)



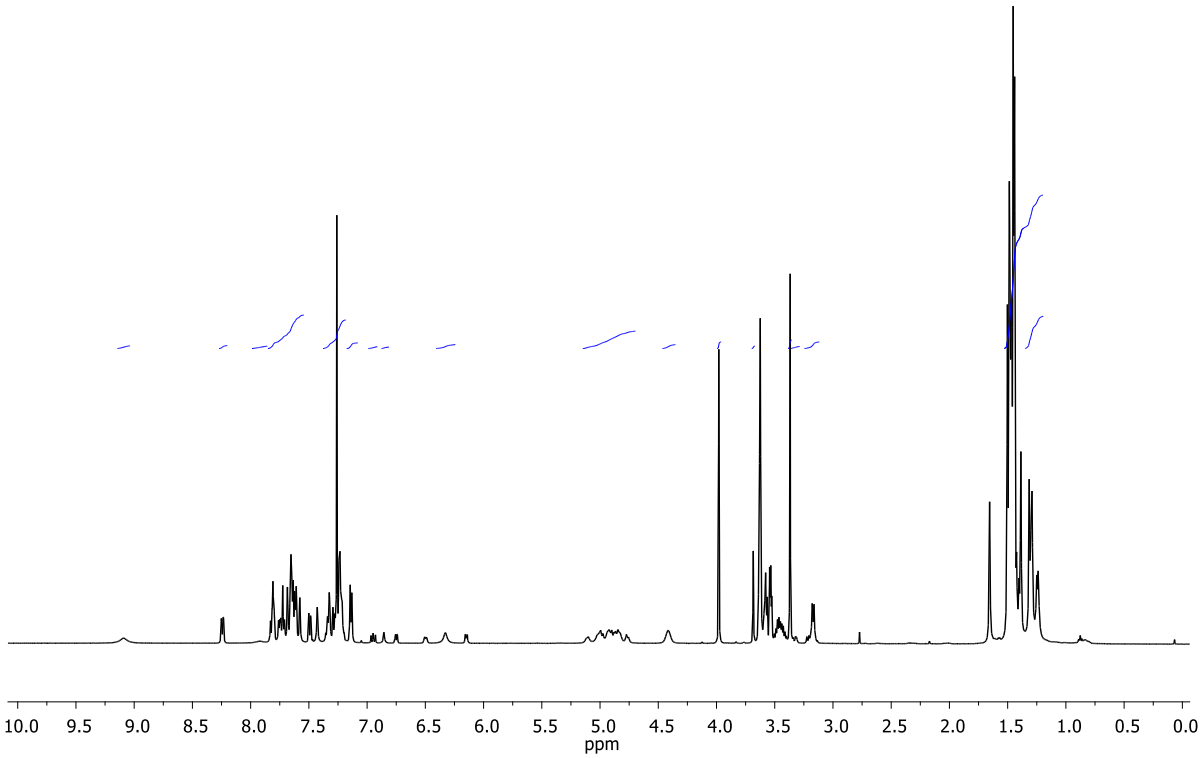
Phe-4 ($CDCl_3$, 500 MHz)



5 ($CDCl_3$, 500 MHz)

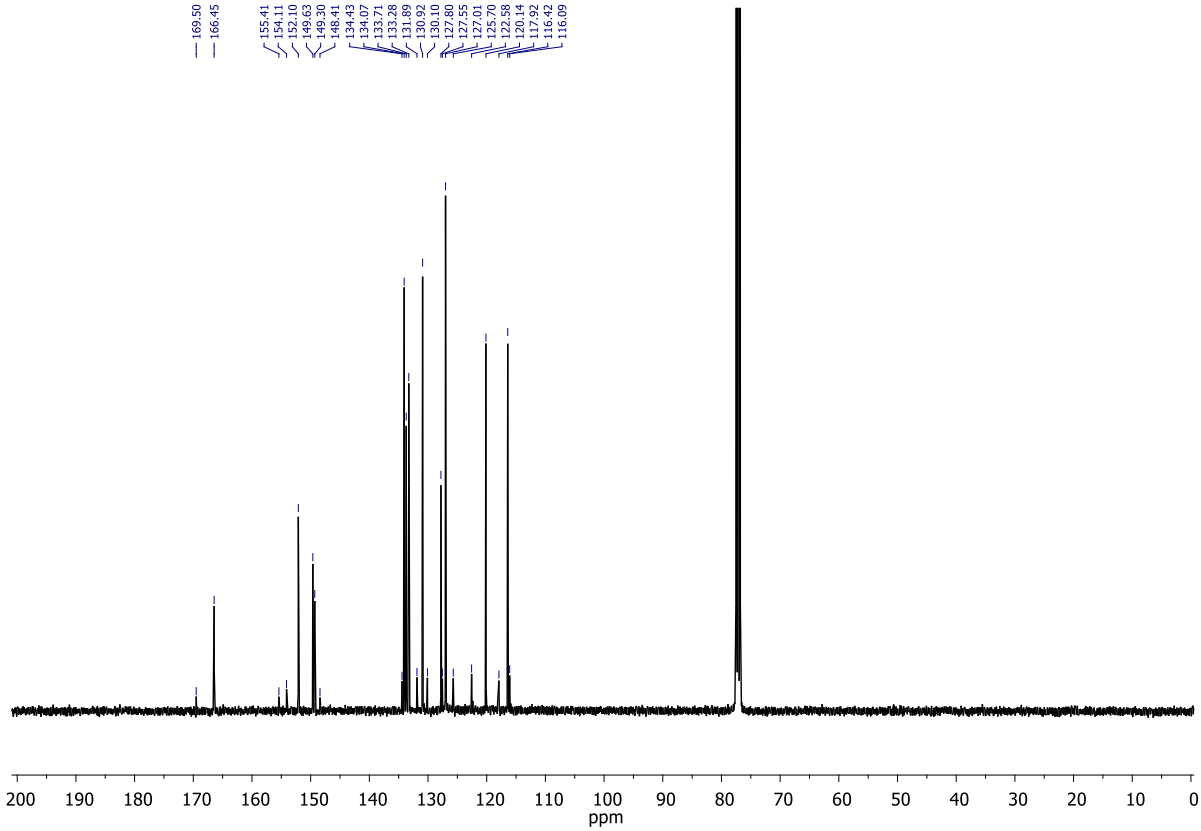


Phe-5 ($CDCl_3$, 500 MHz)

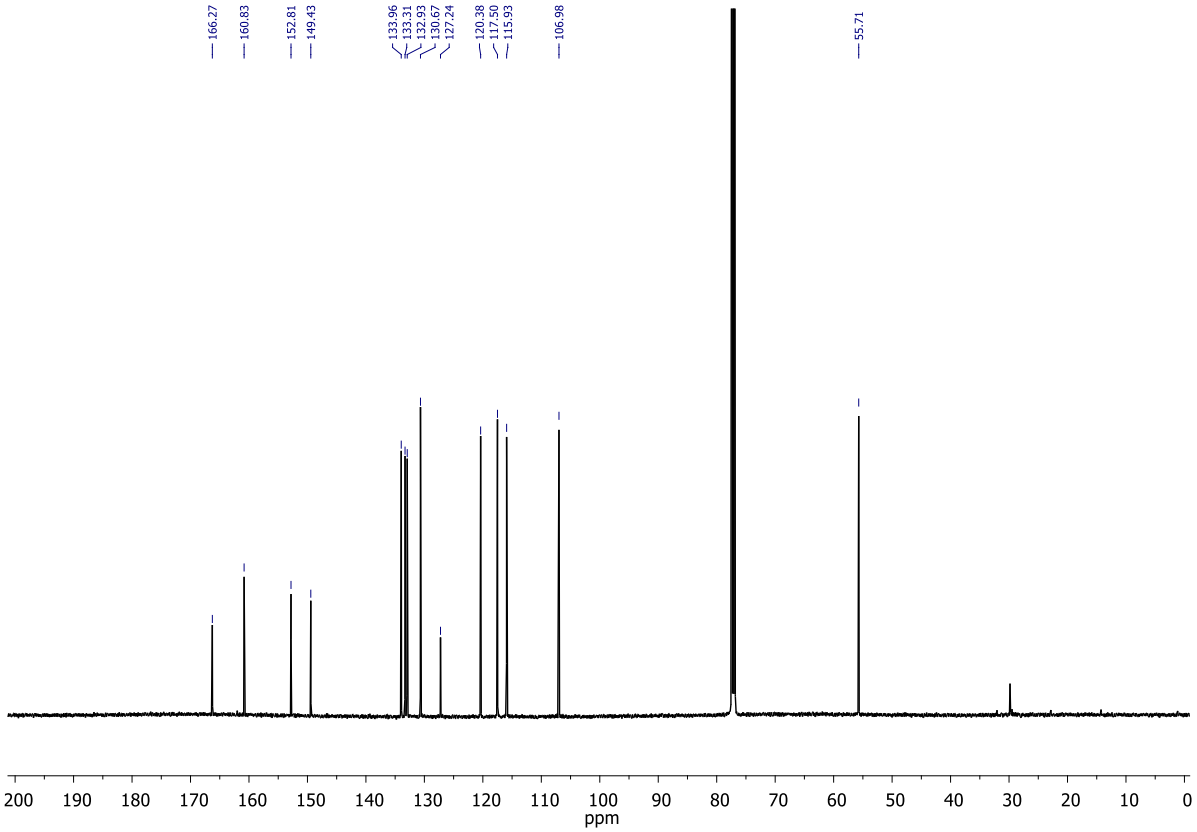


^{13}C NMR spectra

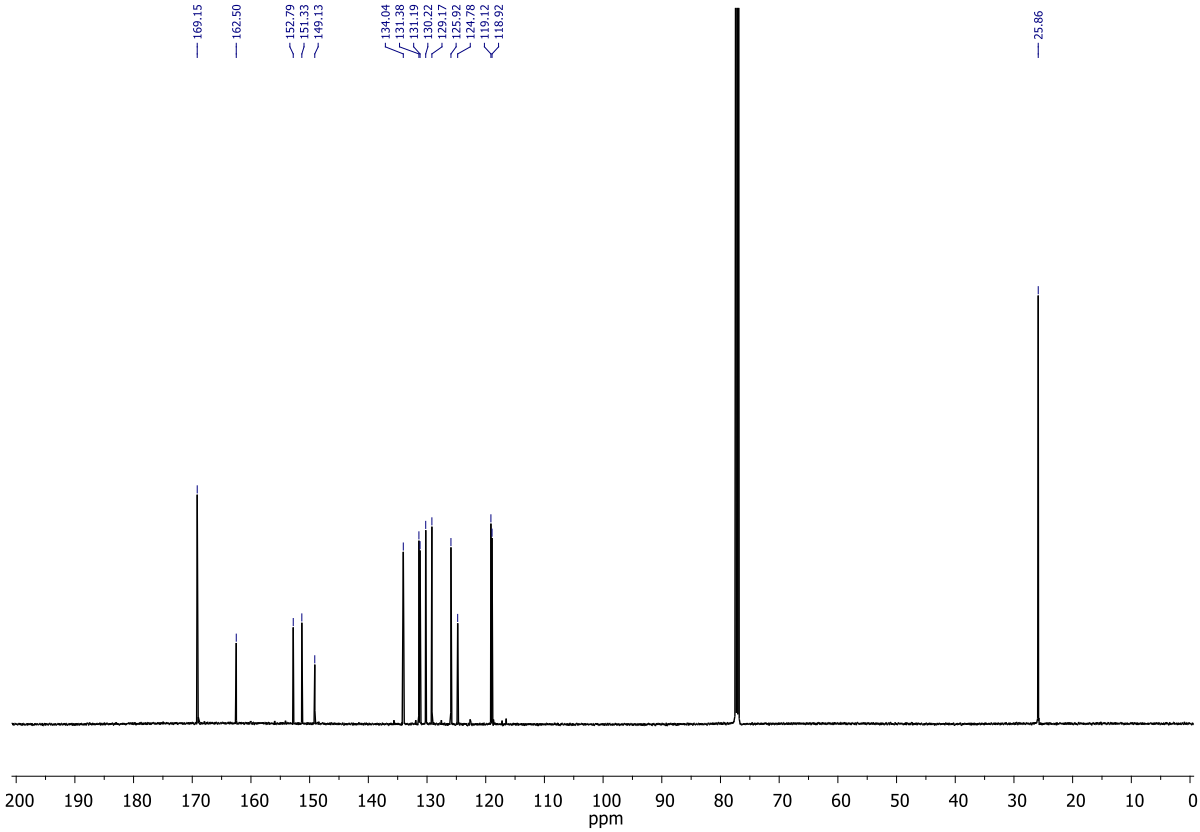
S6 ($CDCl_3$, 101 MHz)



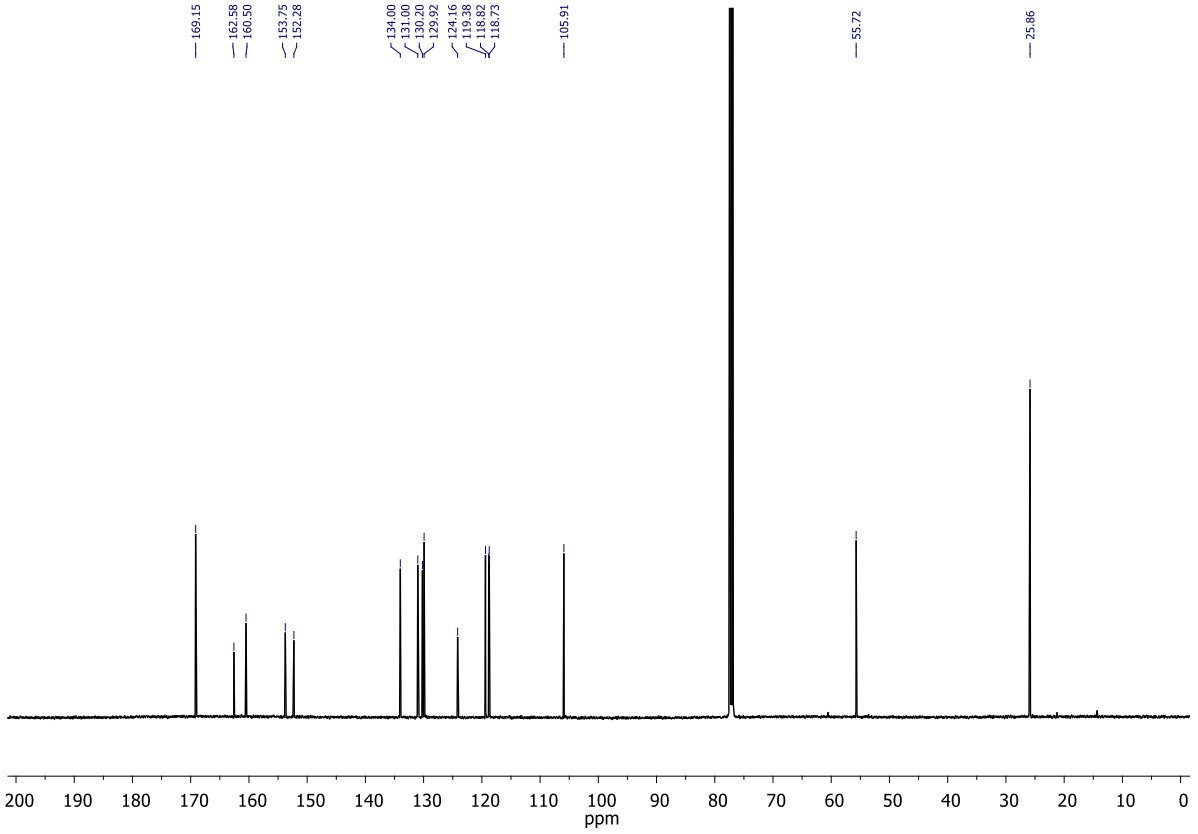
S7 ($CDCl_3$, 126 MHz)



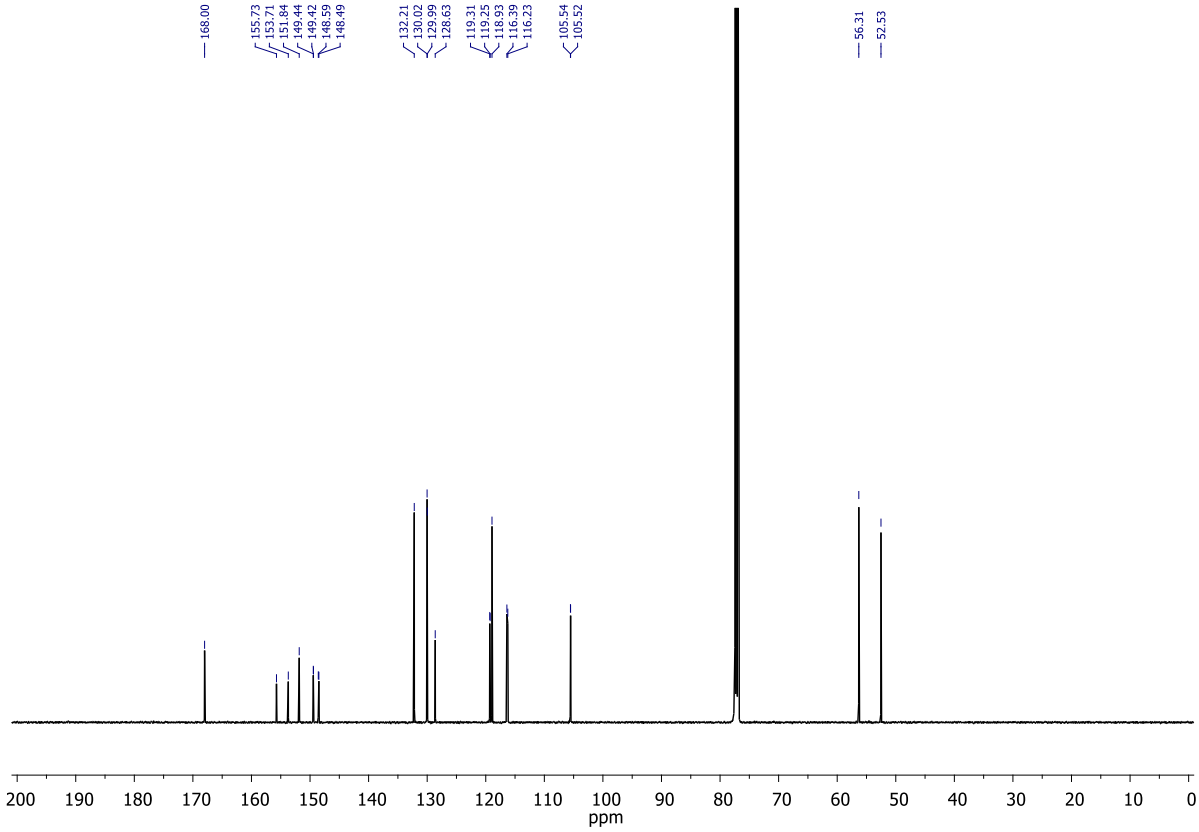
S8 ($CDCl_3$, 126 MHz)



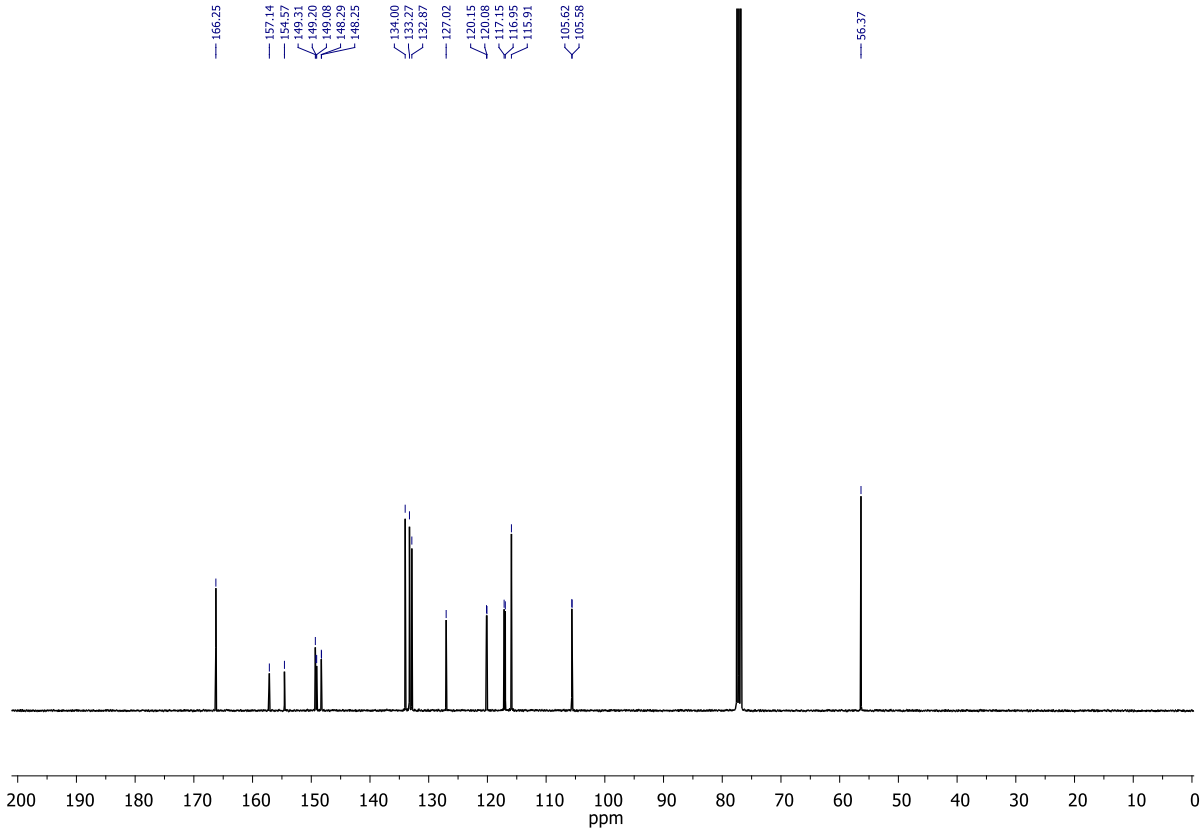
S9 ($CDCl_3$, 126 MHz)



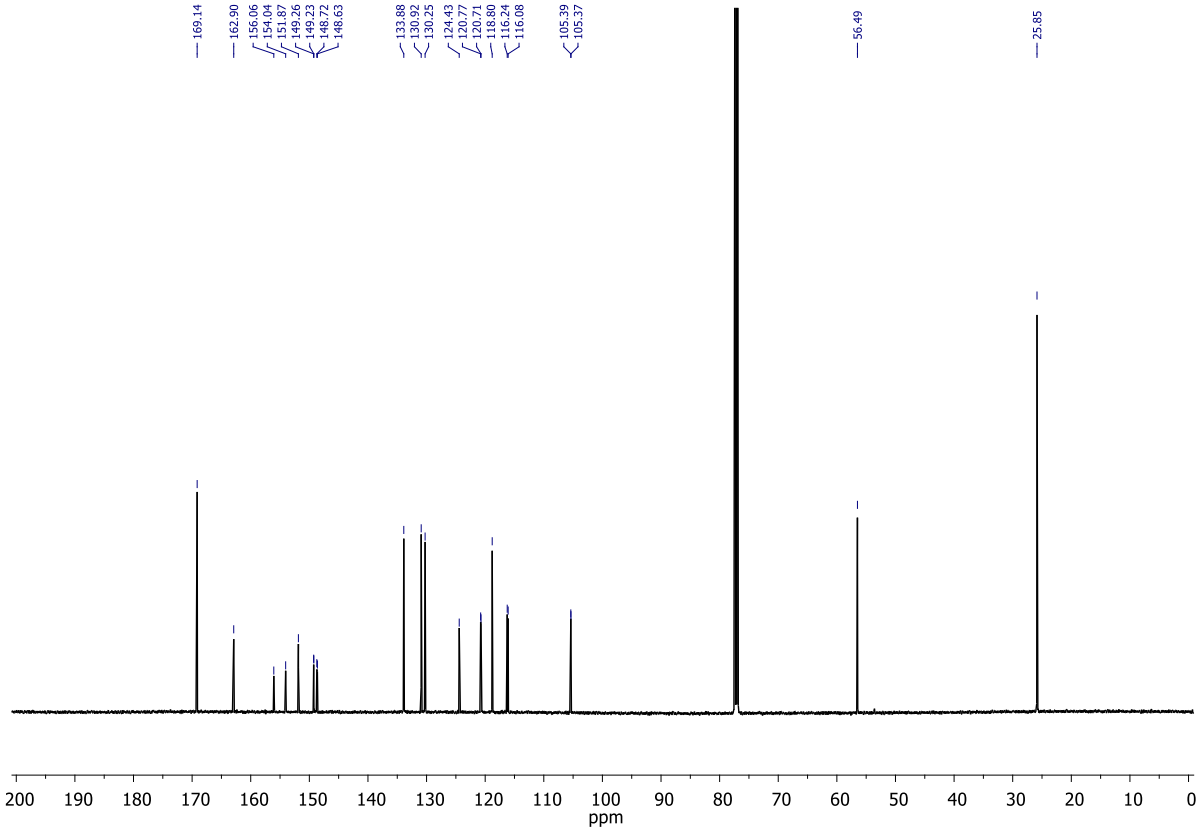
S11 ($CDCl_3$, 126 MHz)



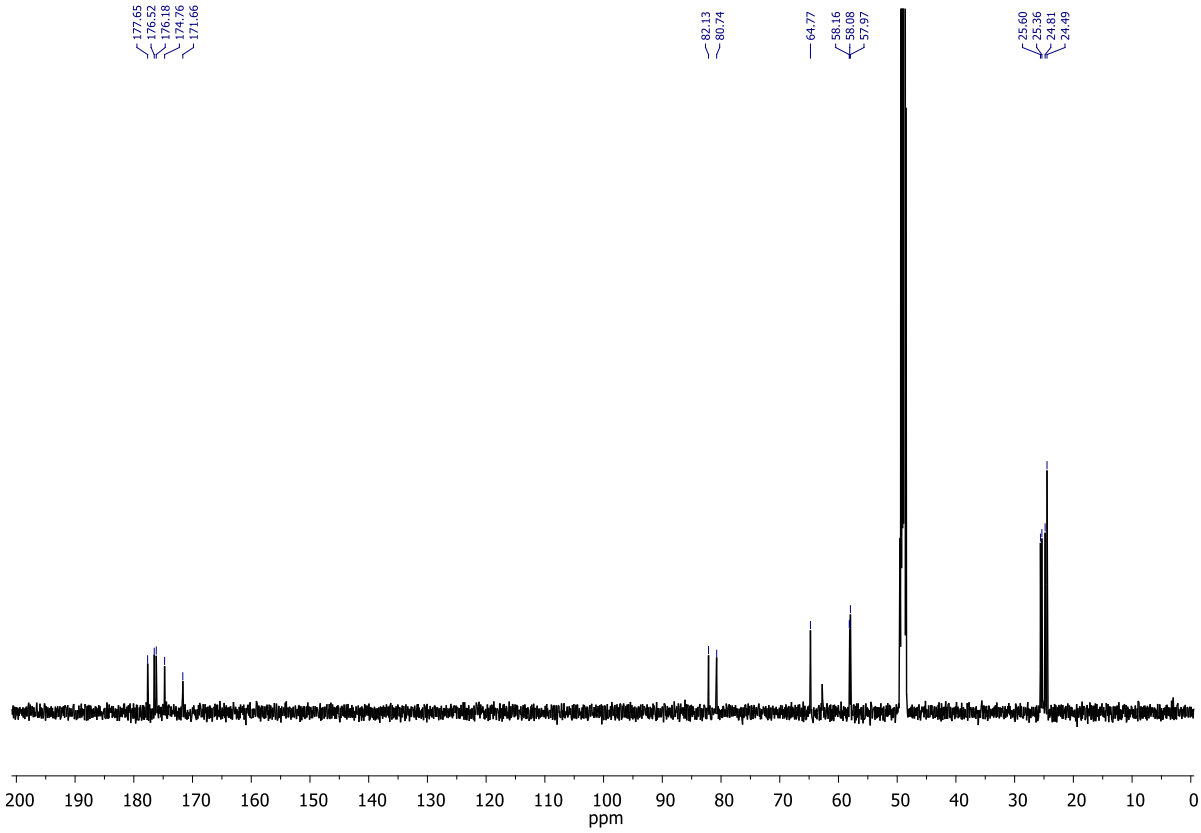
S12 ($CDCl_3$, 101 MHz)



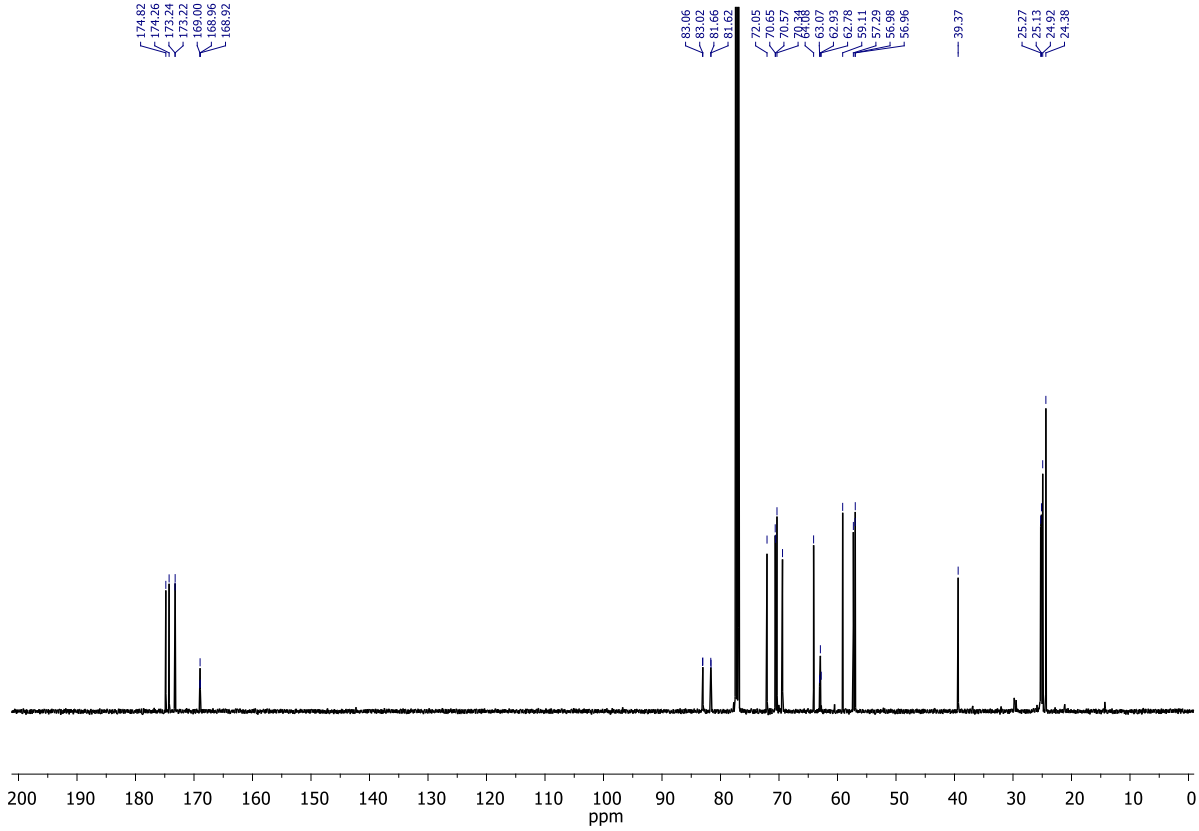
S13 ($CDCl_3$, 126 MHz)



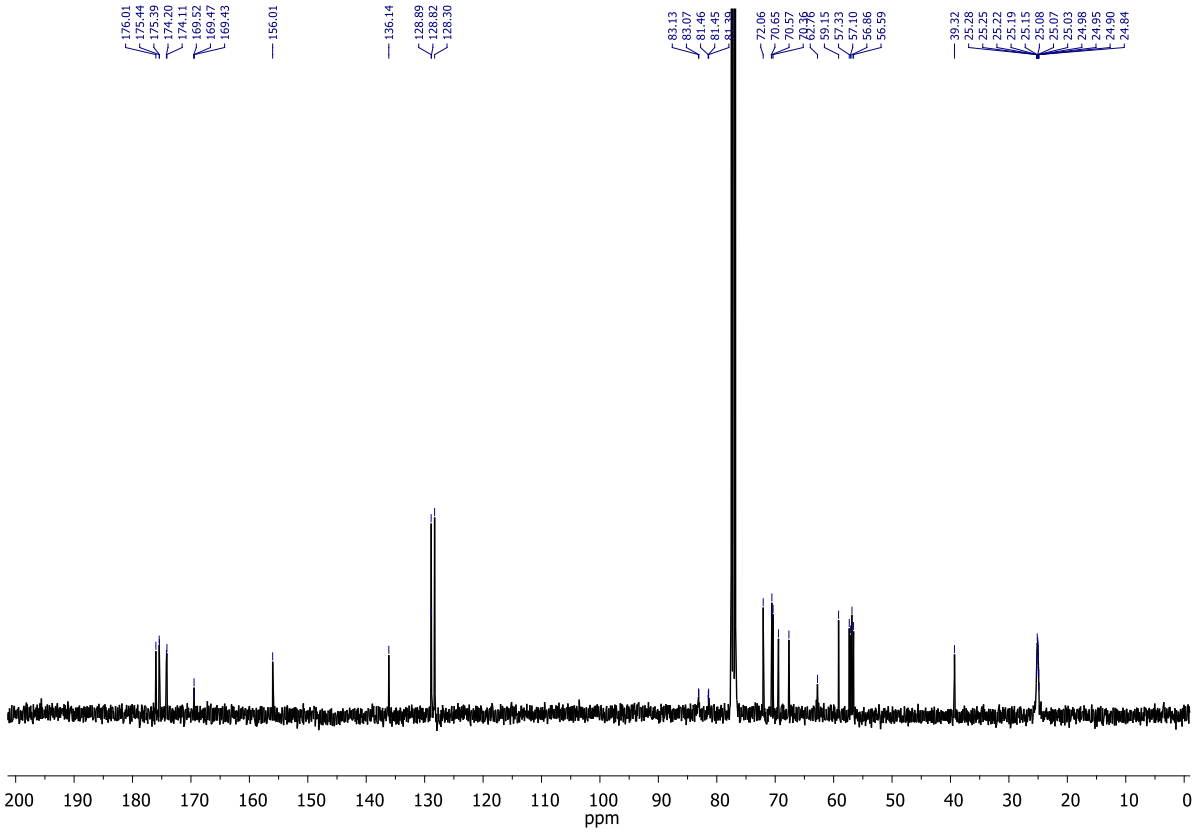
F2 (CD_3OD, 126 MHz)



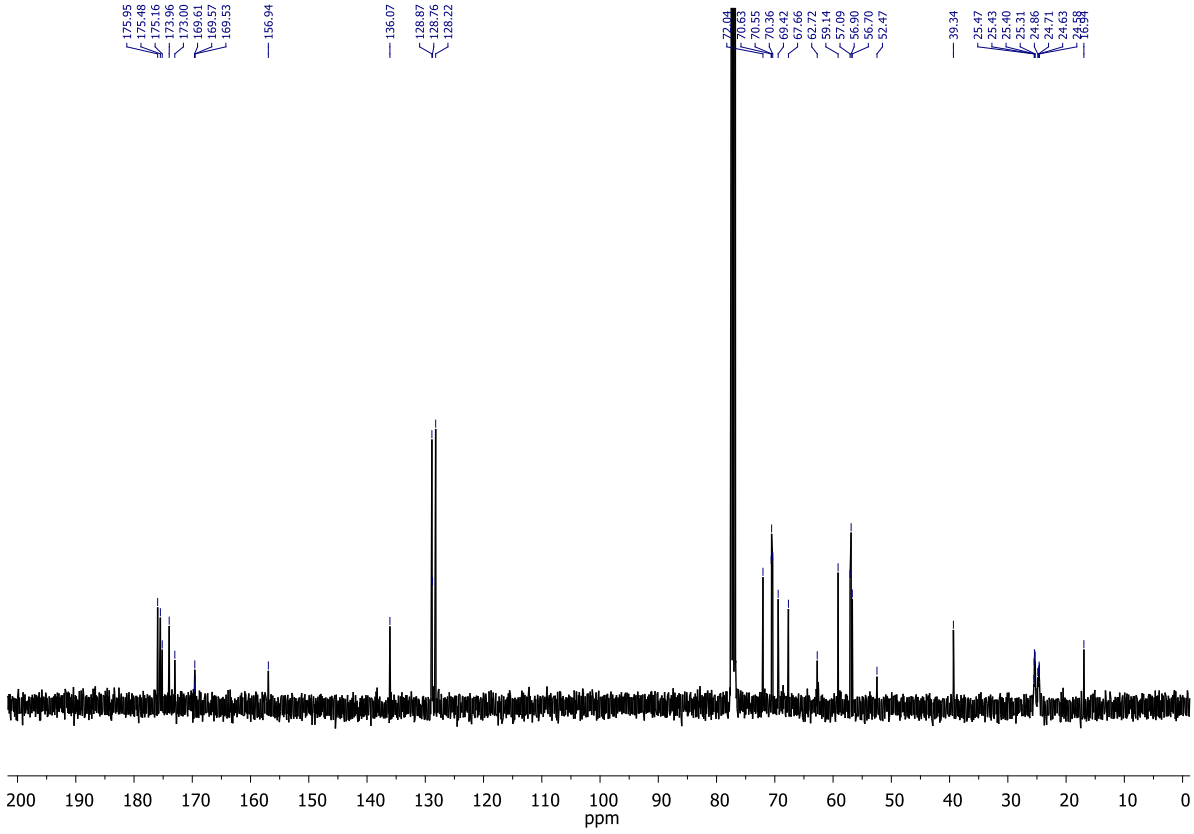
F3 ($CDCl_3$, 126 MHz)



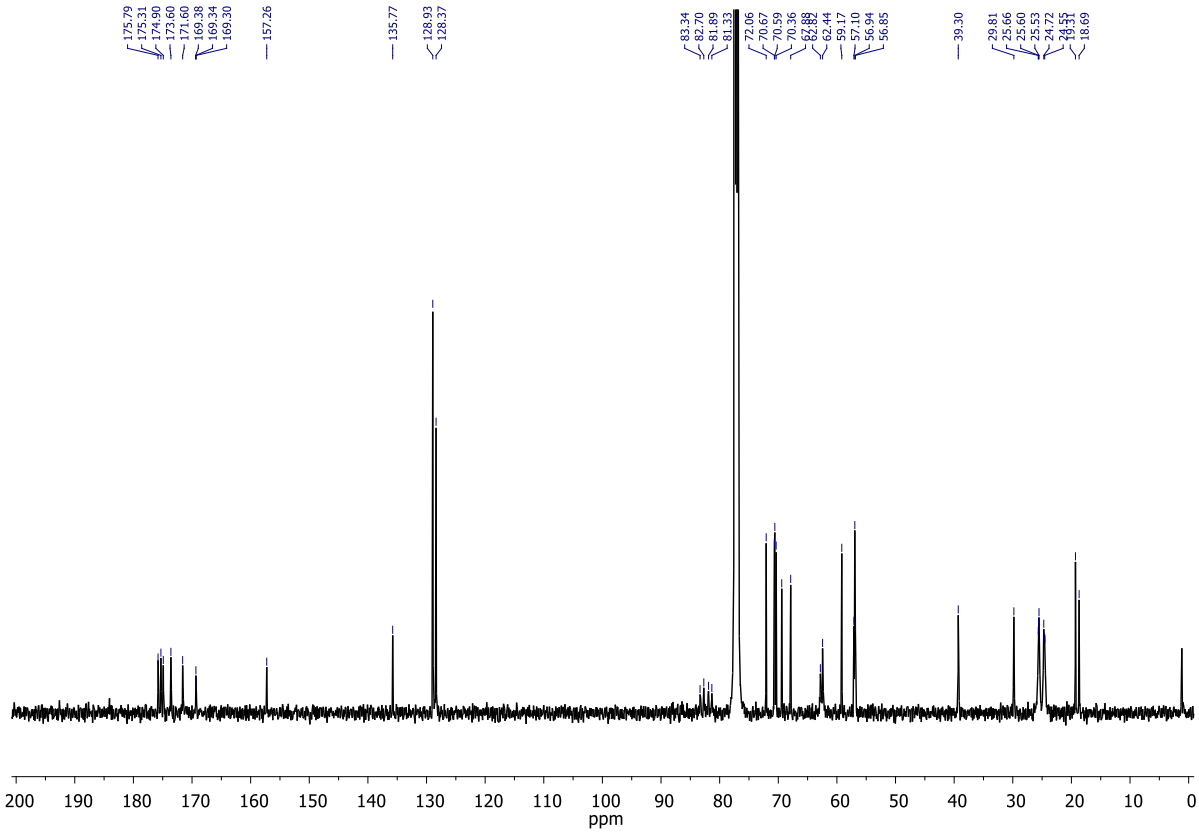
3a ($CDCl_3$, 101 MHz)



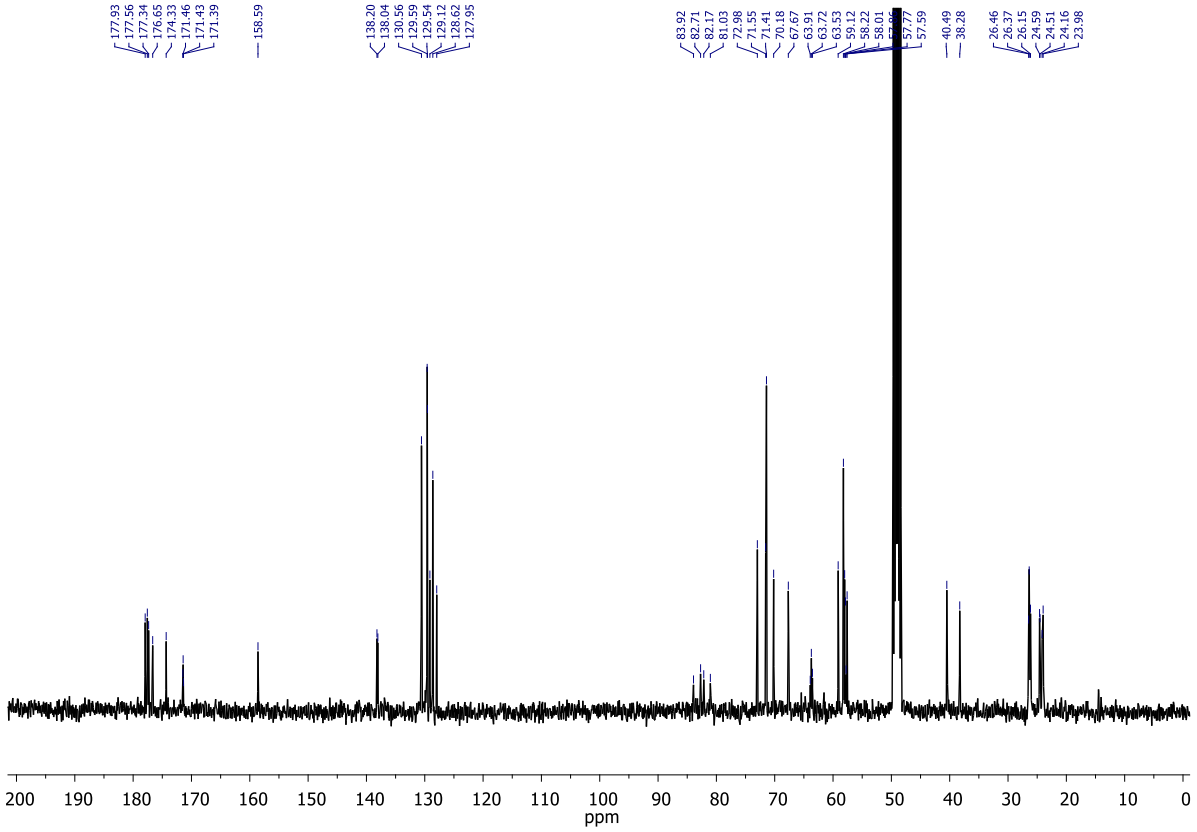
3b ($CDCl_3$, 101 MHz)



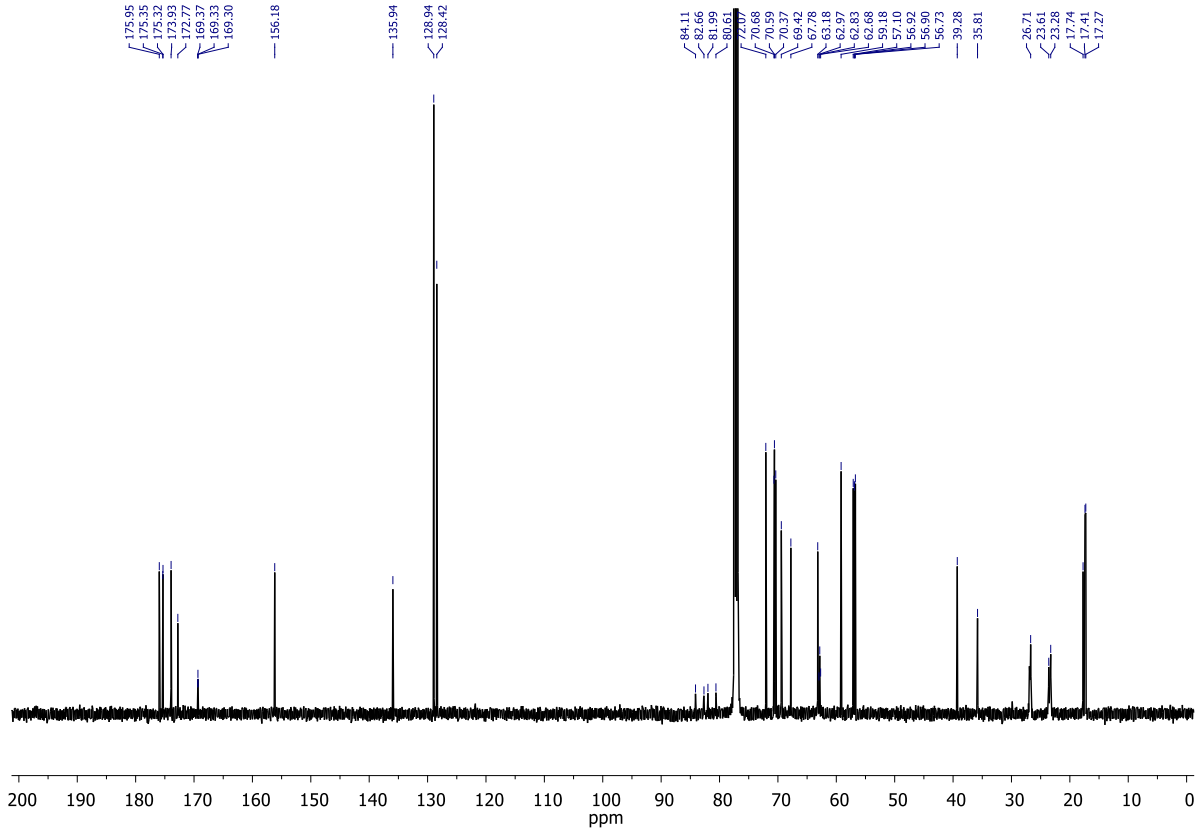
3c ($CDCl_3$, 126 MHz)



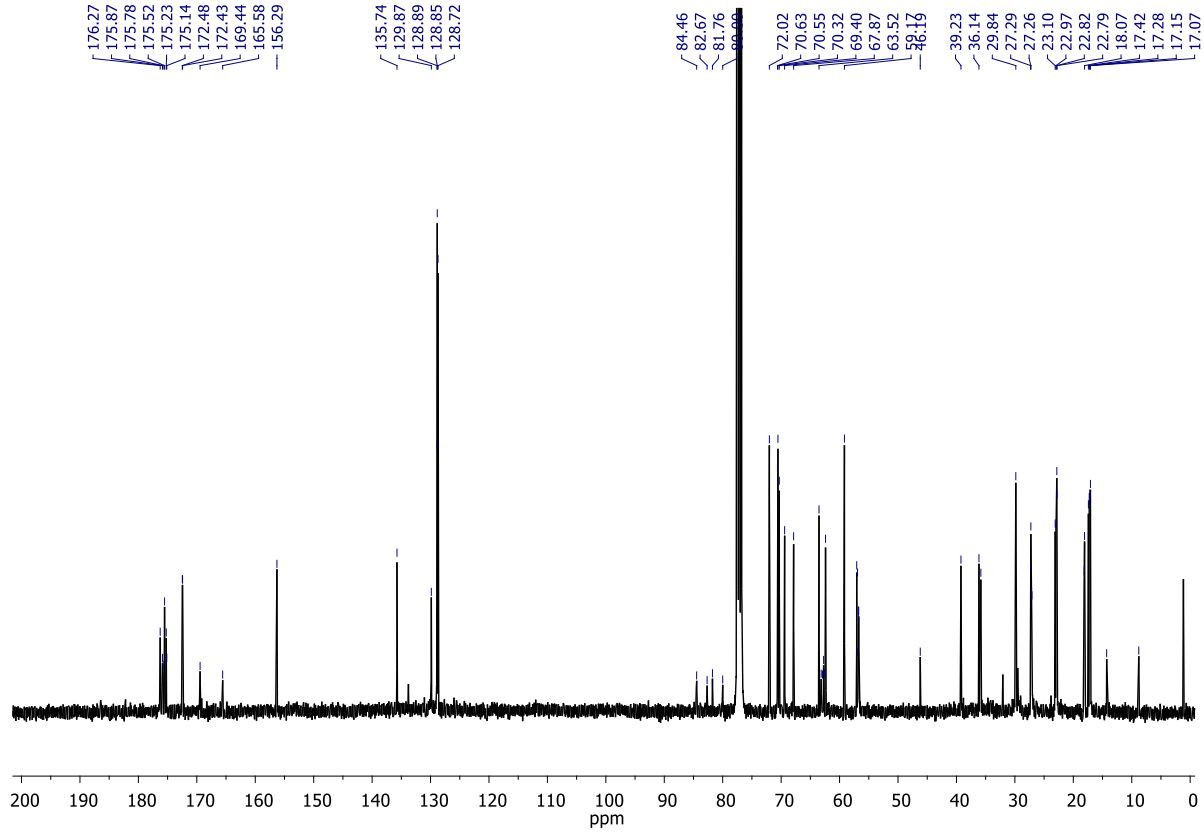
3d (CD_3OD, 126 MHz)



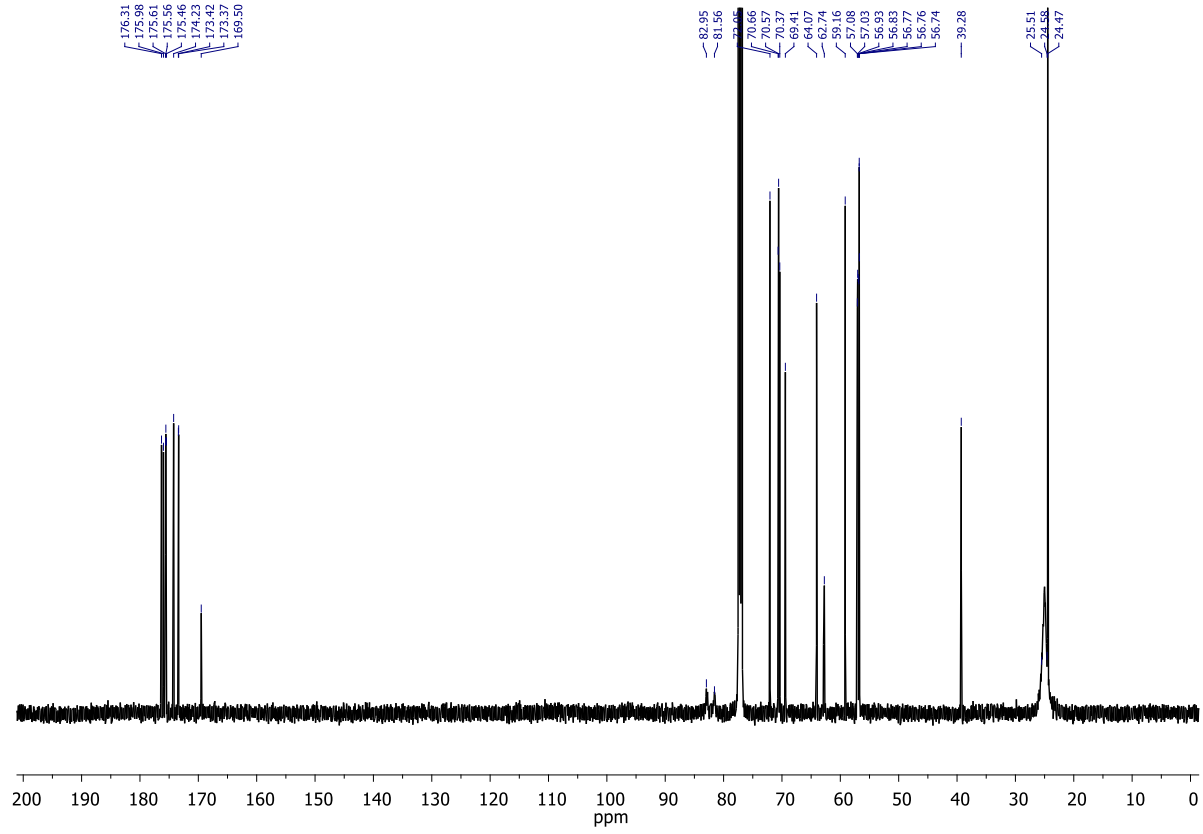
3e ($CDCl_3$, 126 MHz)



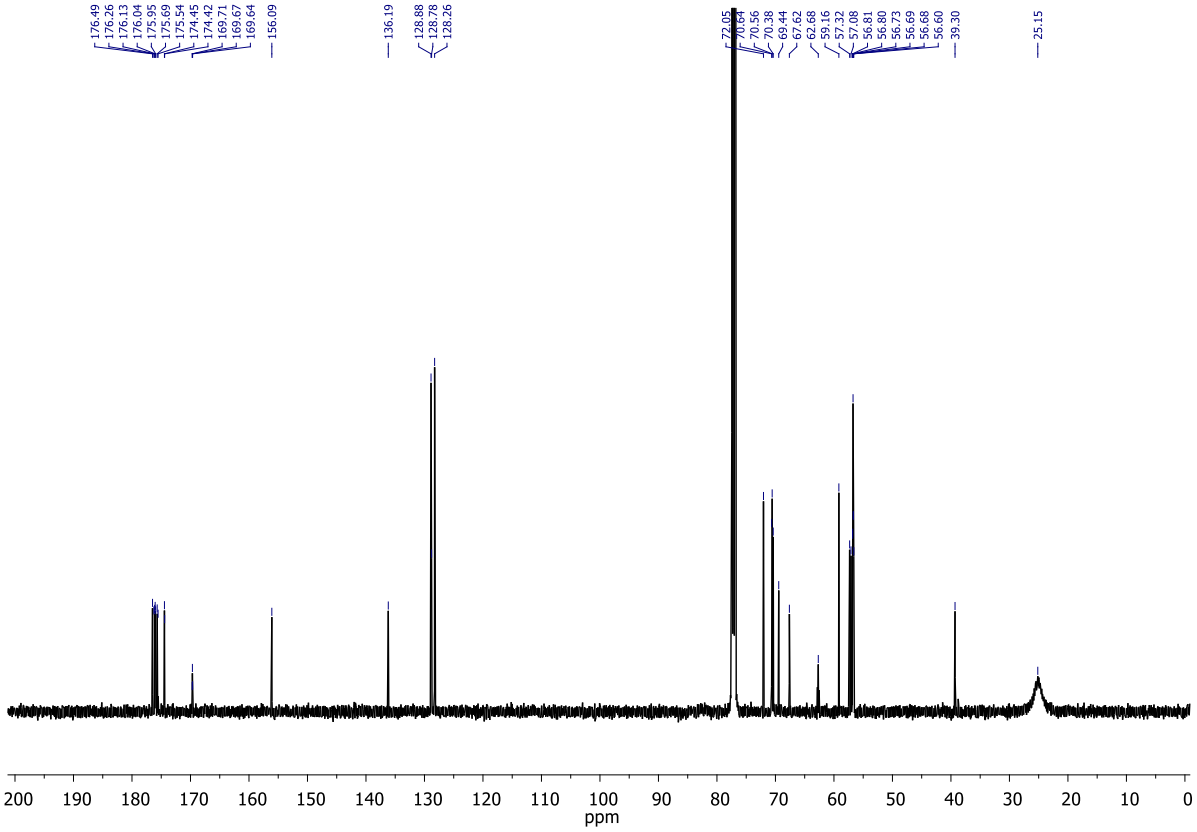
3f ($CDCl_3$, 126 MHz)



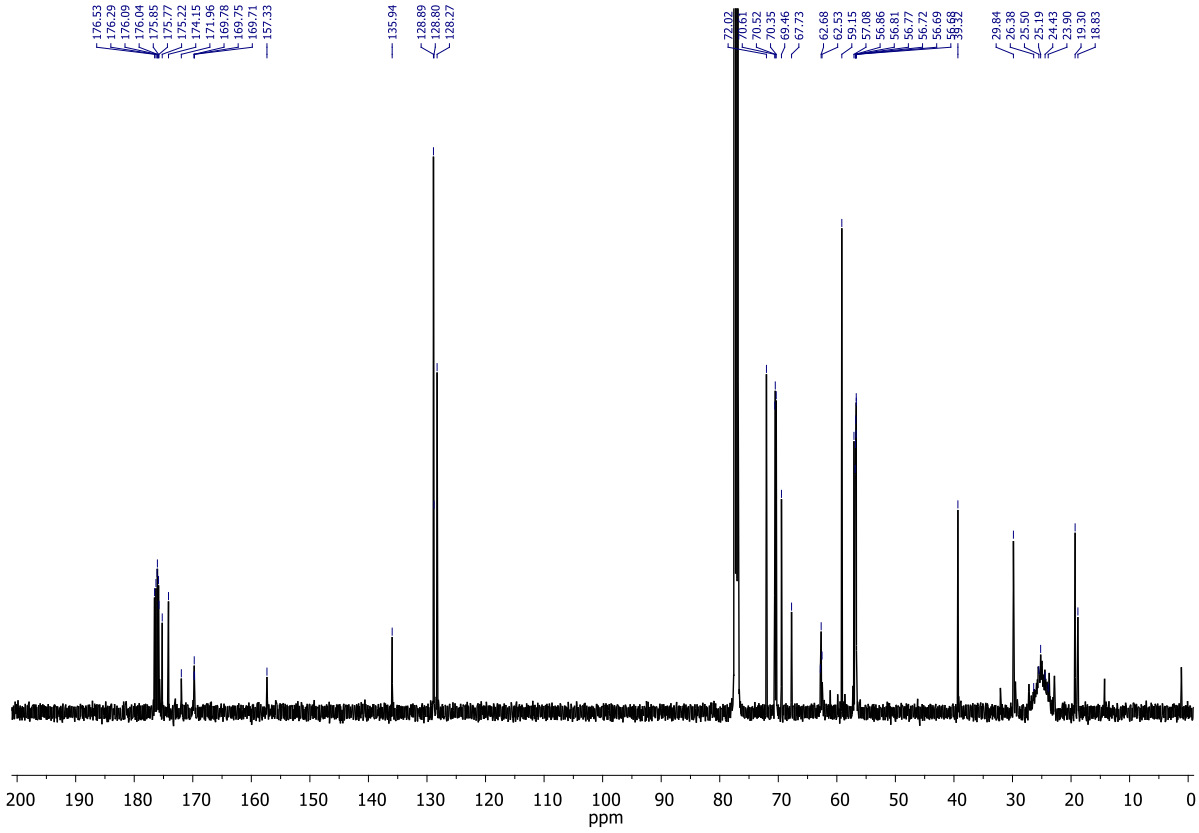
F4 ($CDCl_3$, 126 MHz)



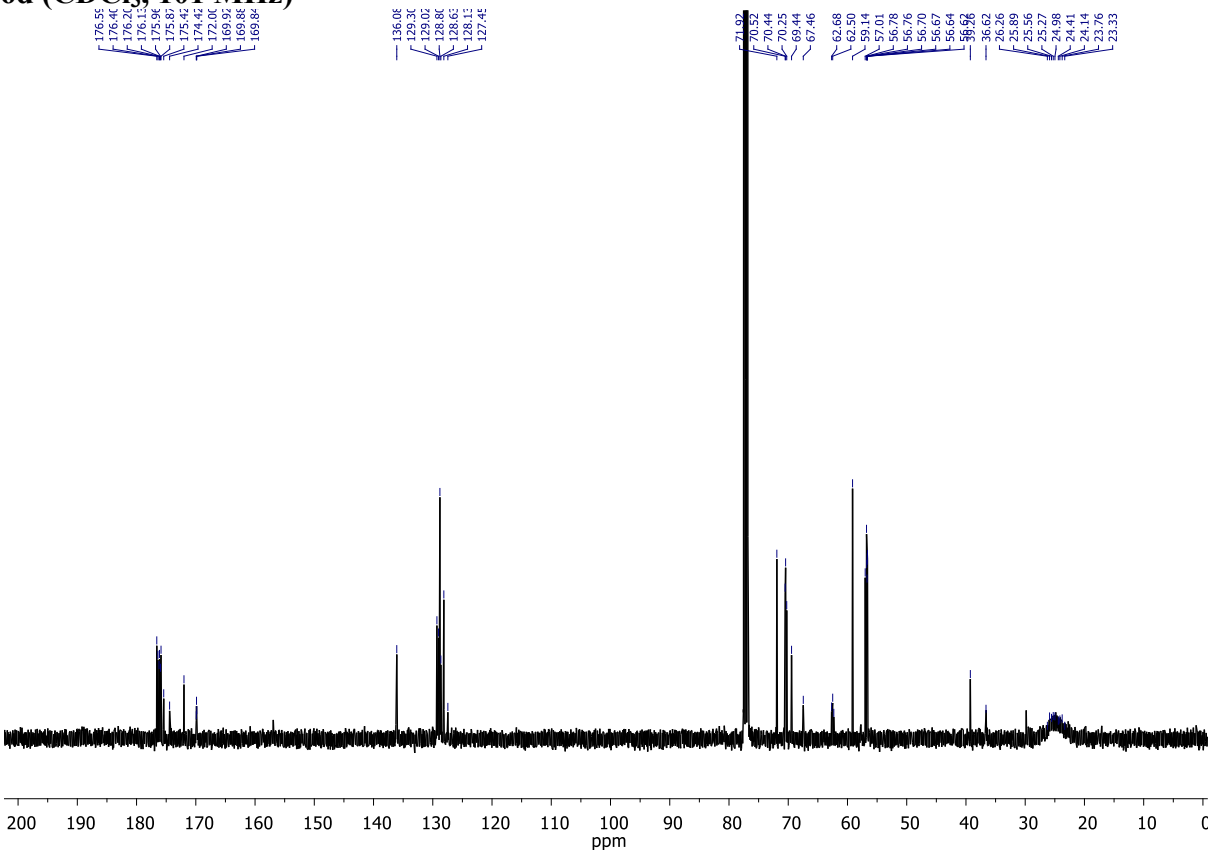
6a ($CDCl_3$, 126 MHz)



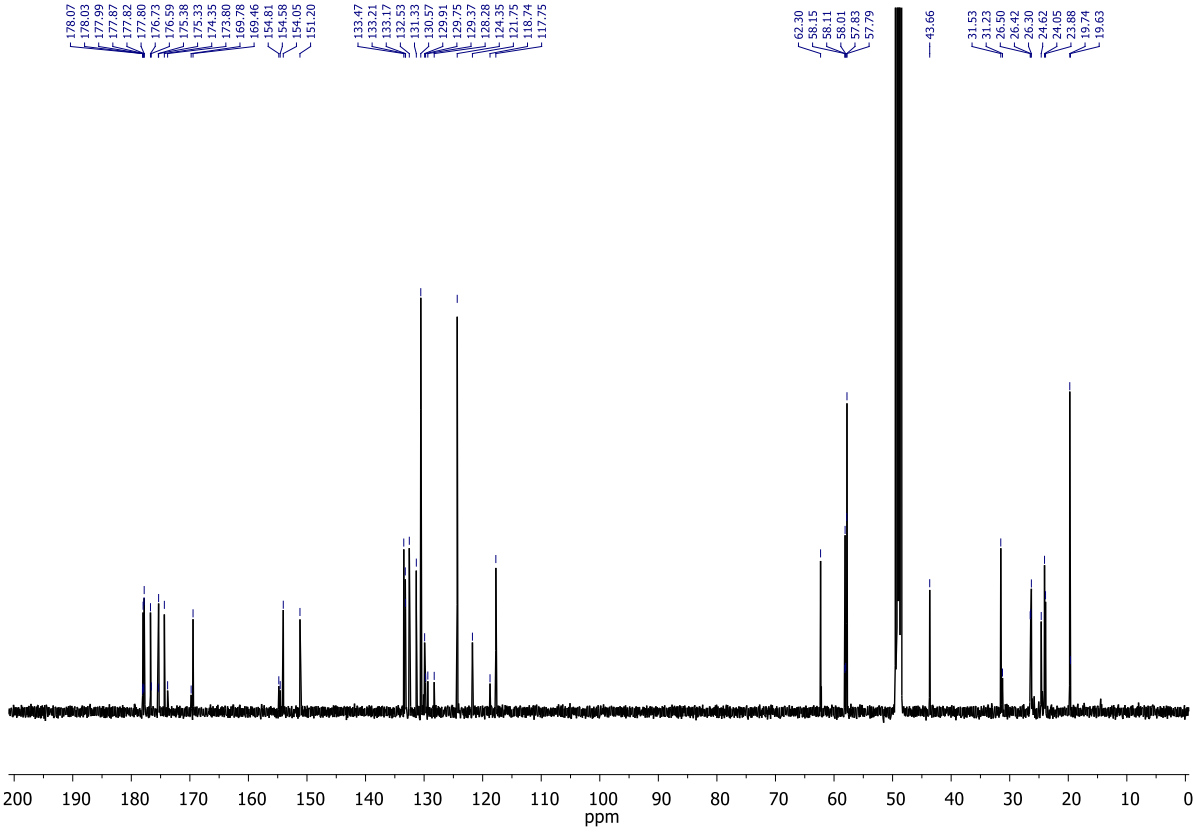
6c ($CDCl_3$, 126 MHz)



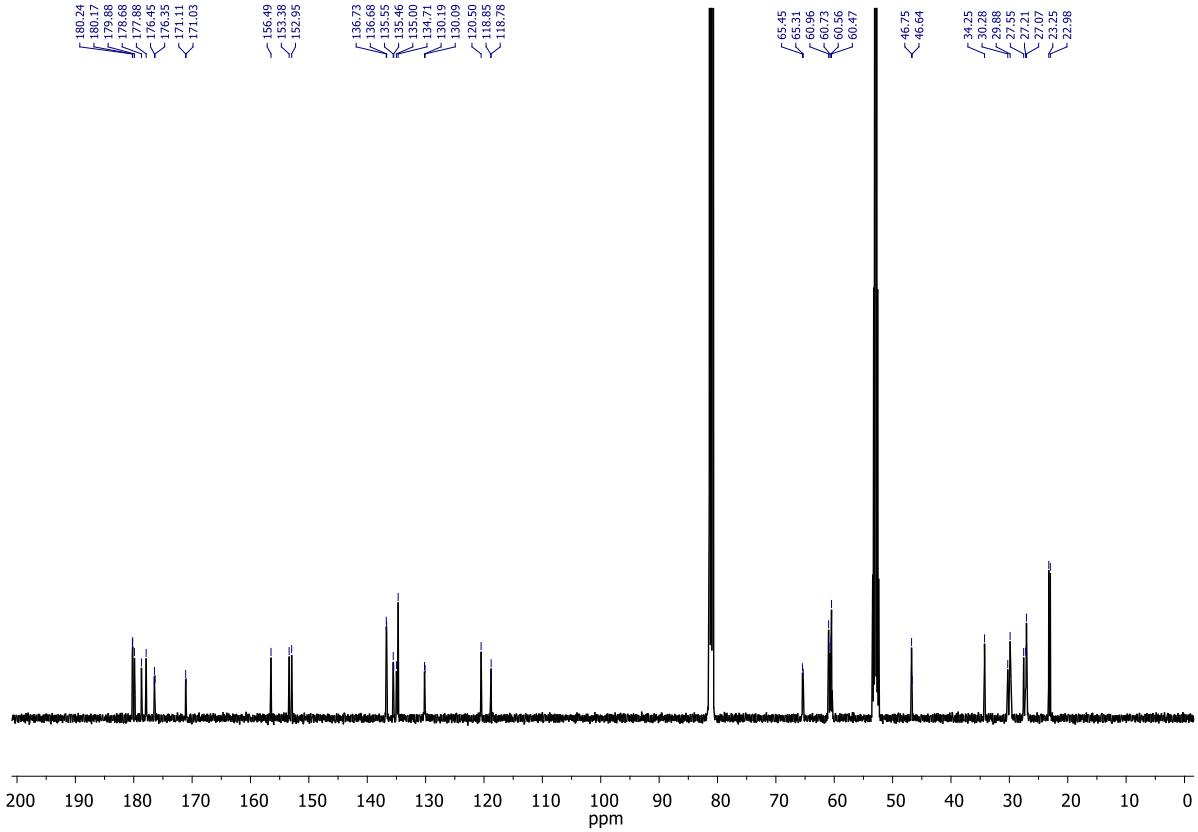
6d ($CDCl_3$, 101 MHz)



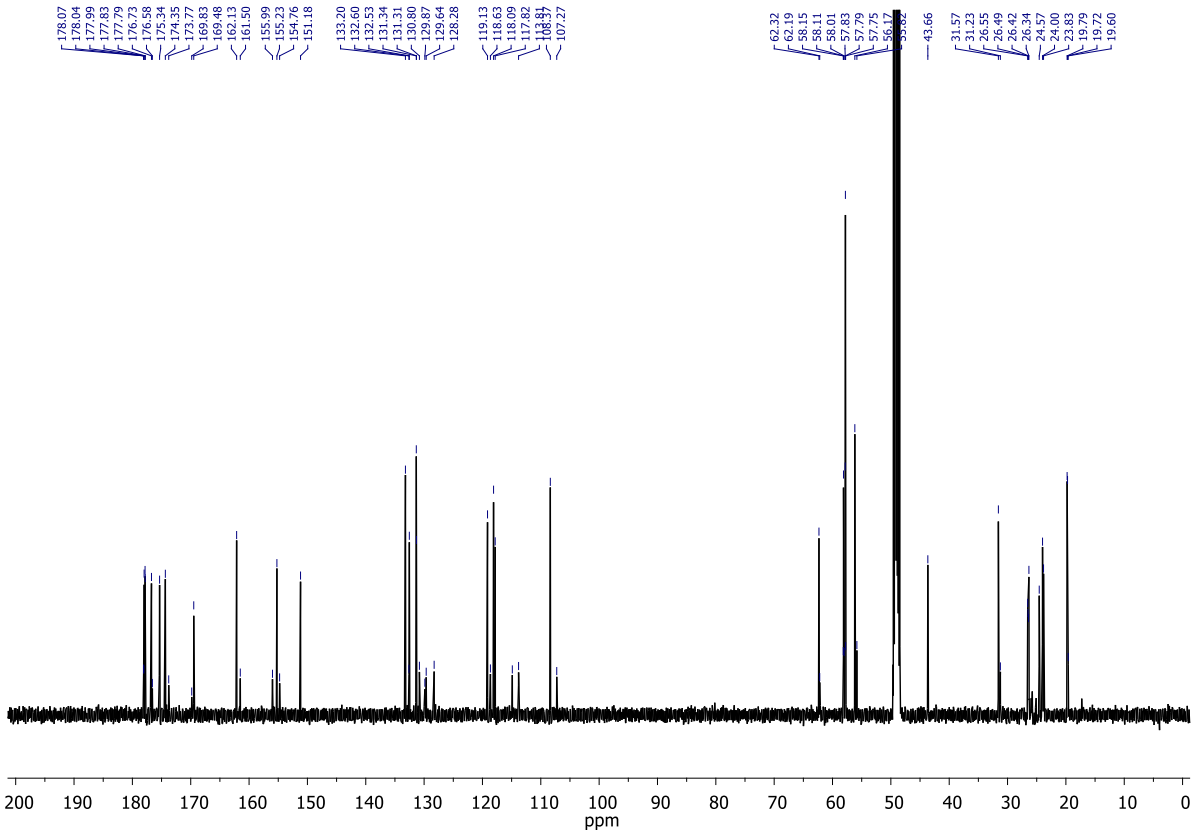
1a (CD_3OD, 126 MHz)



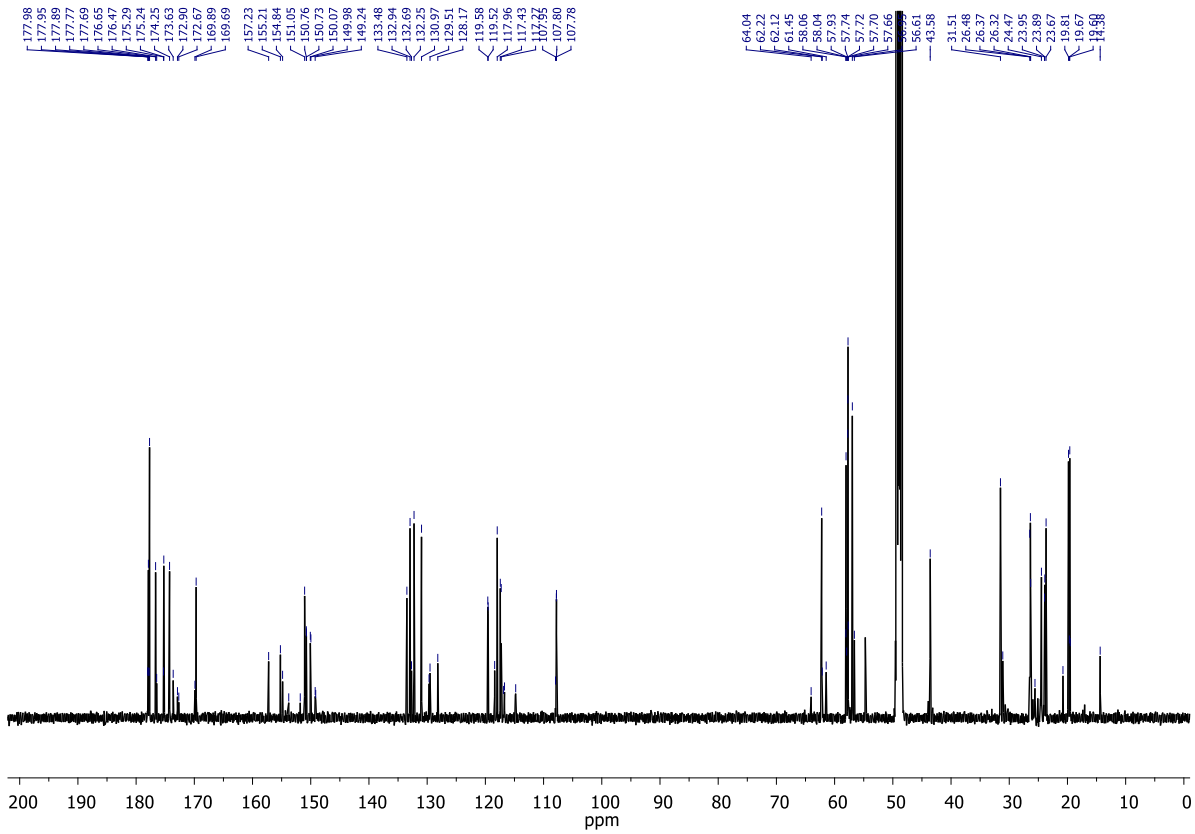
1b ($CDCl_3$, 126 MHz)



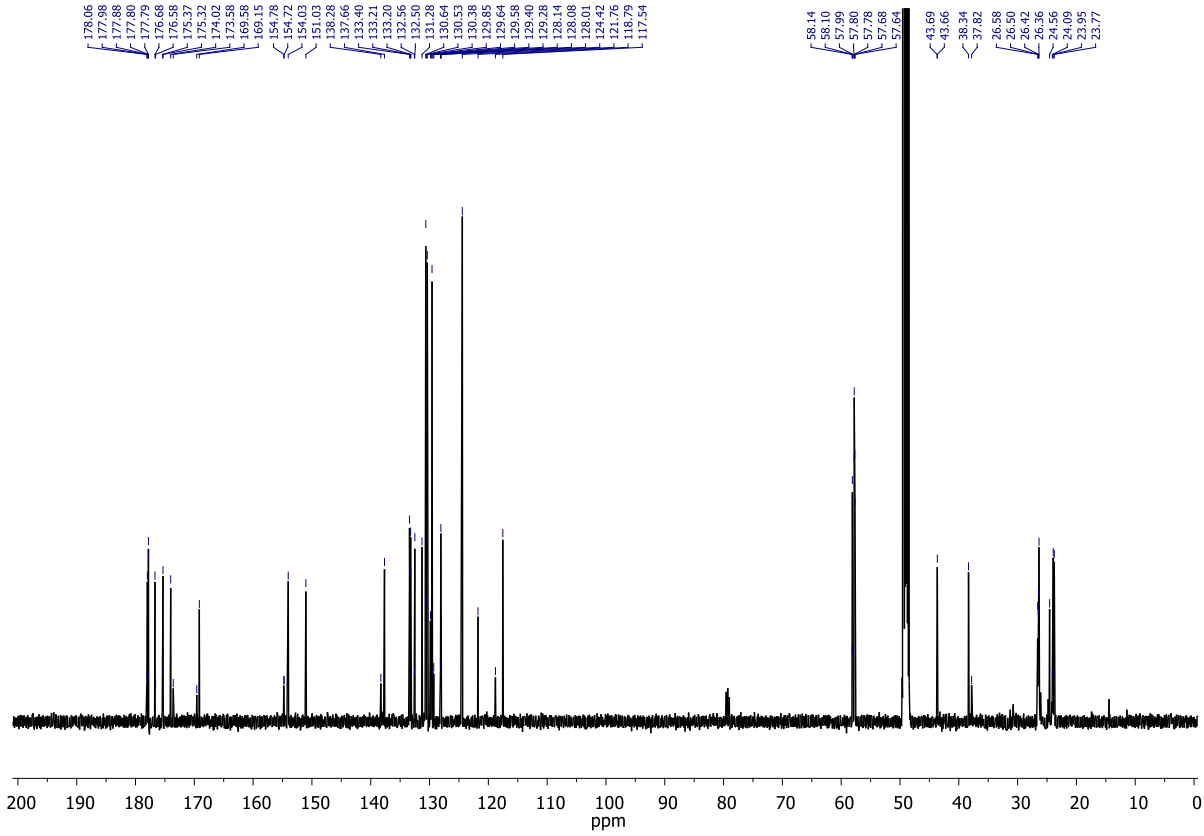
1c (CD_3OD, 126 MHz)



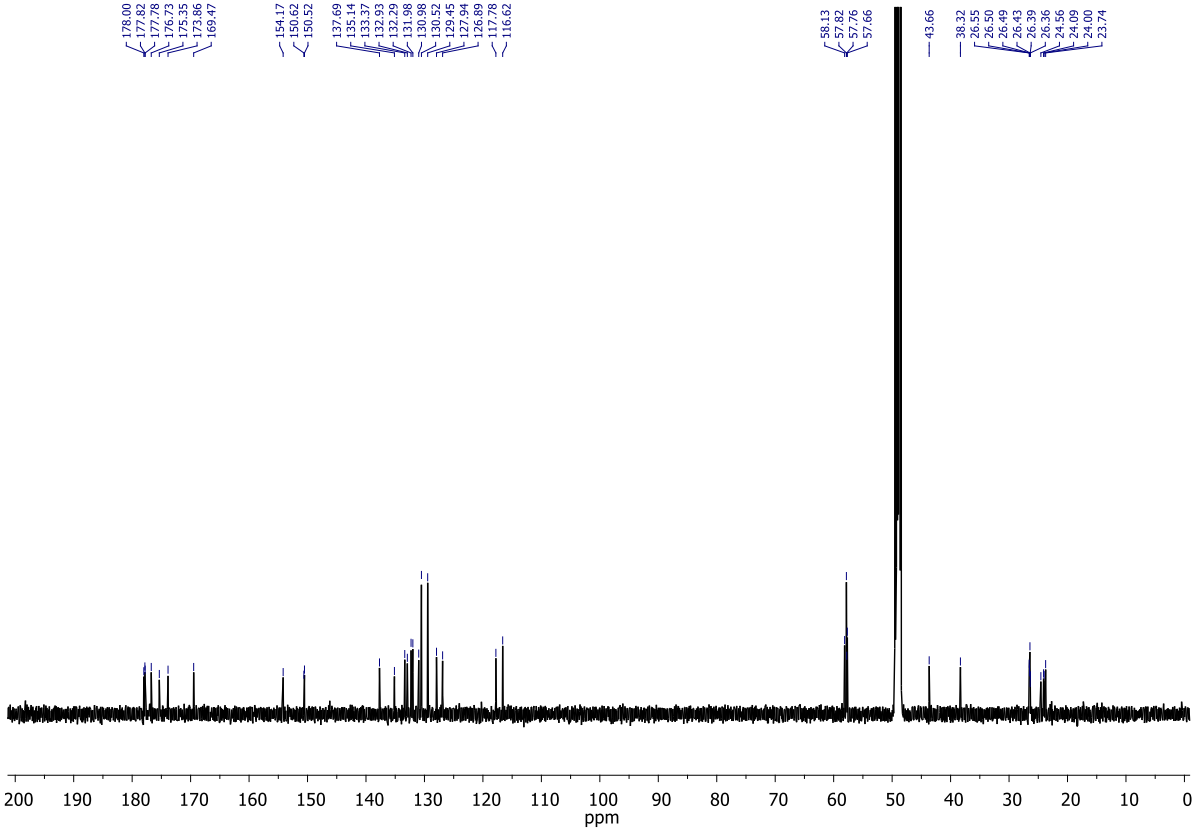
1d (CD_3OD, 126 MHz)



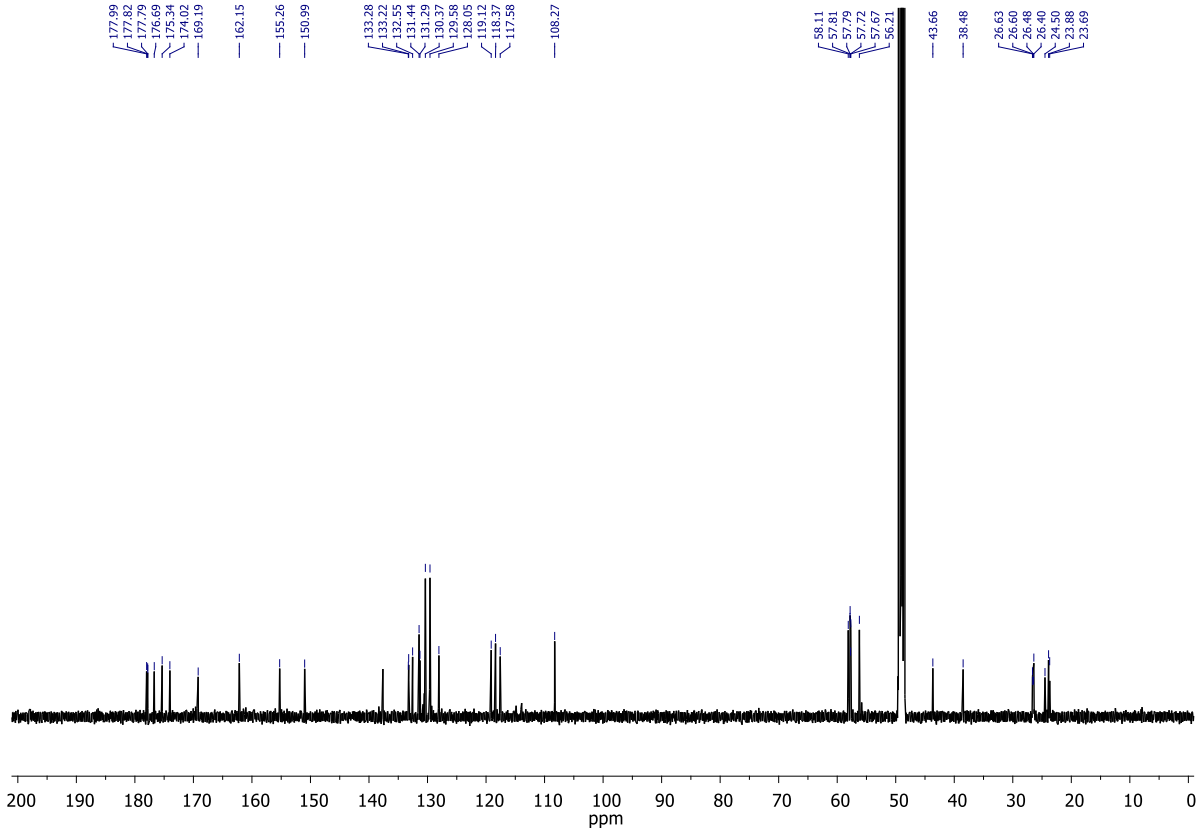
1e (CD_3OD, 126 MHz)



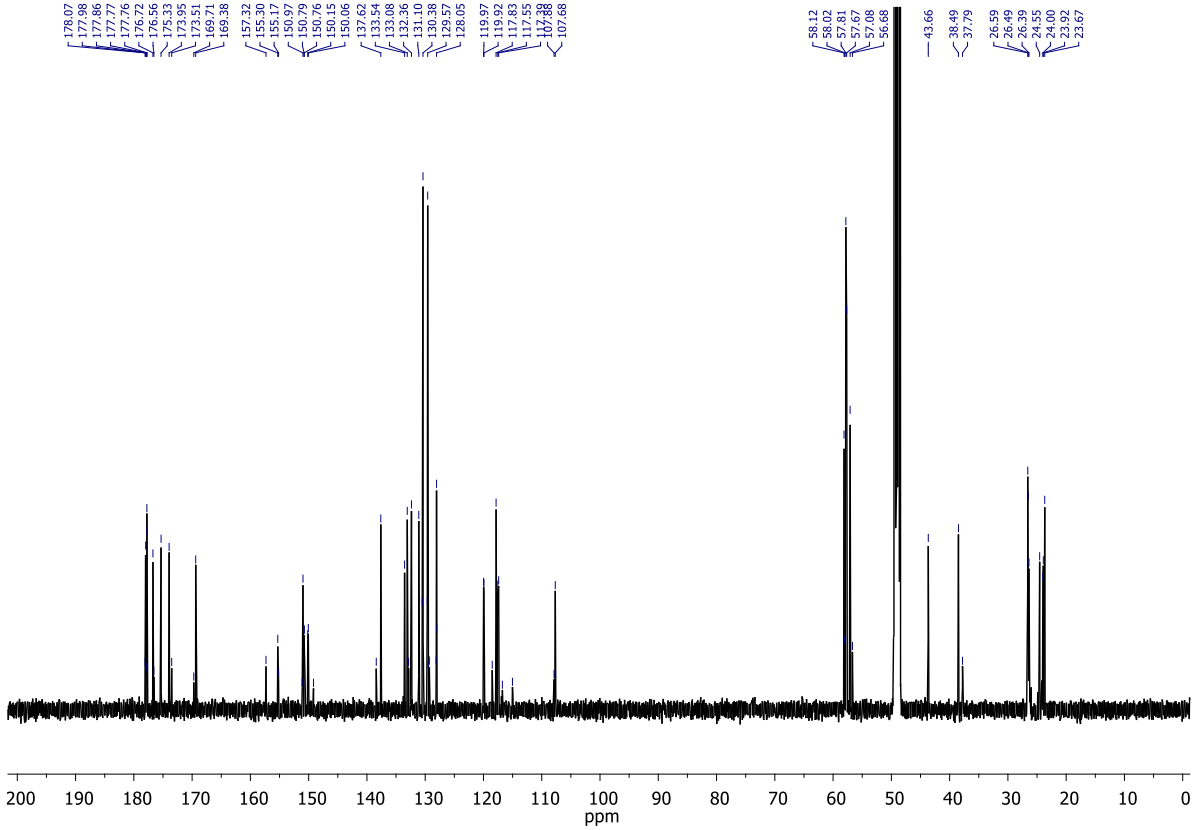
1f (CD_3OD, 126 MHz)



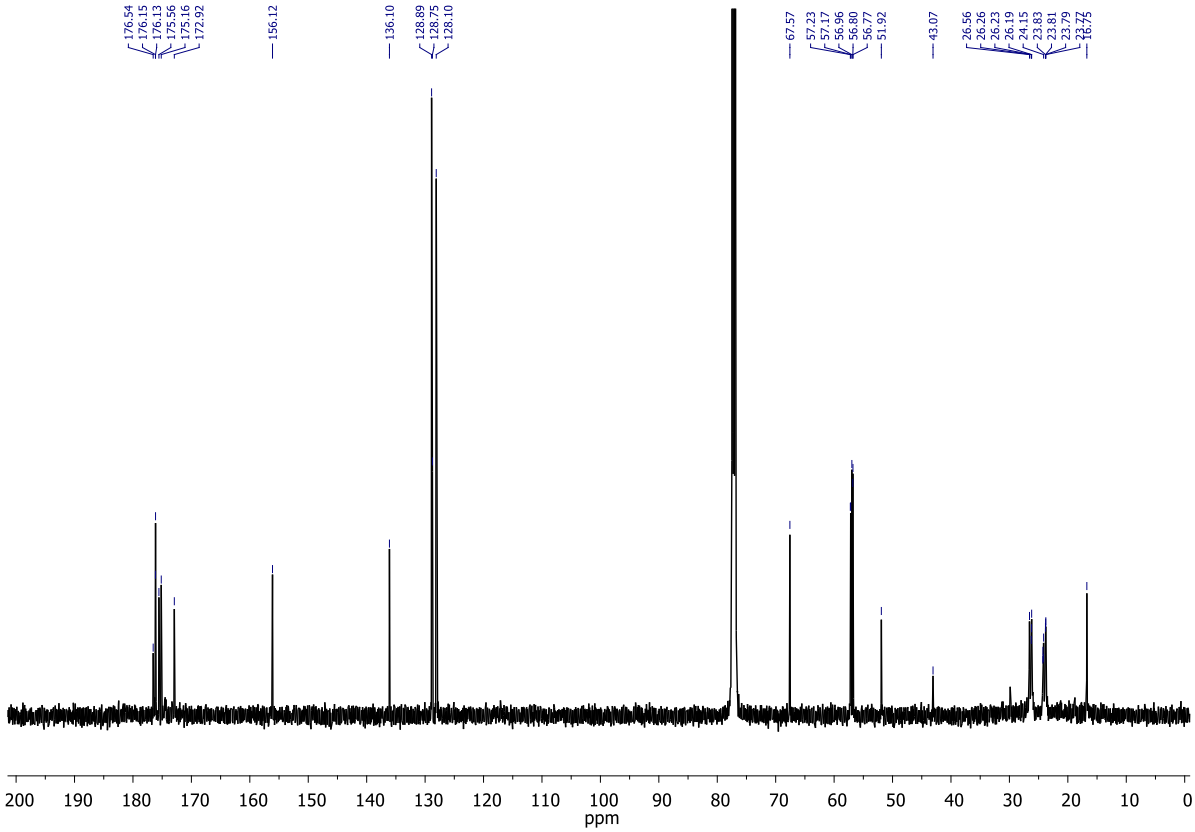
1g (CD_3OD, 126 MHz)



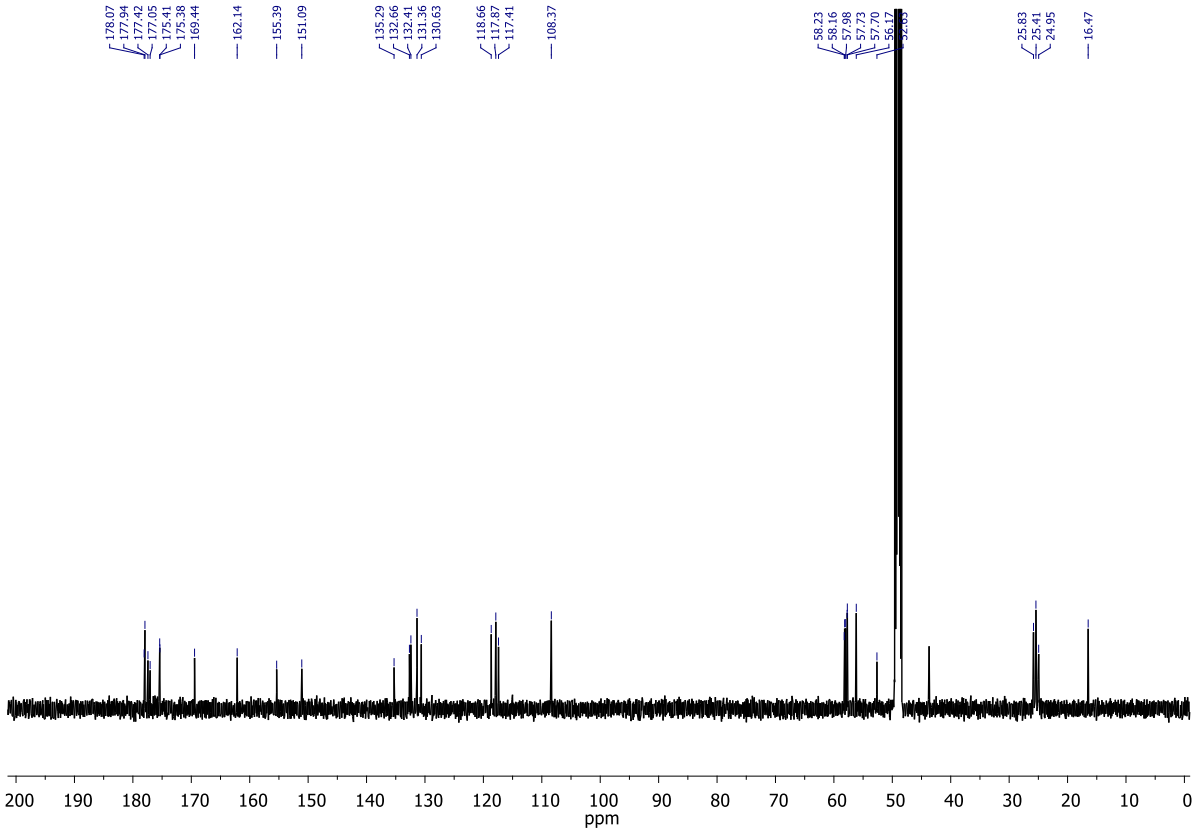
1h (CD_3OD, 126 MHz)



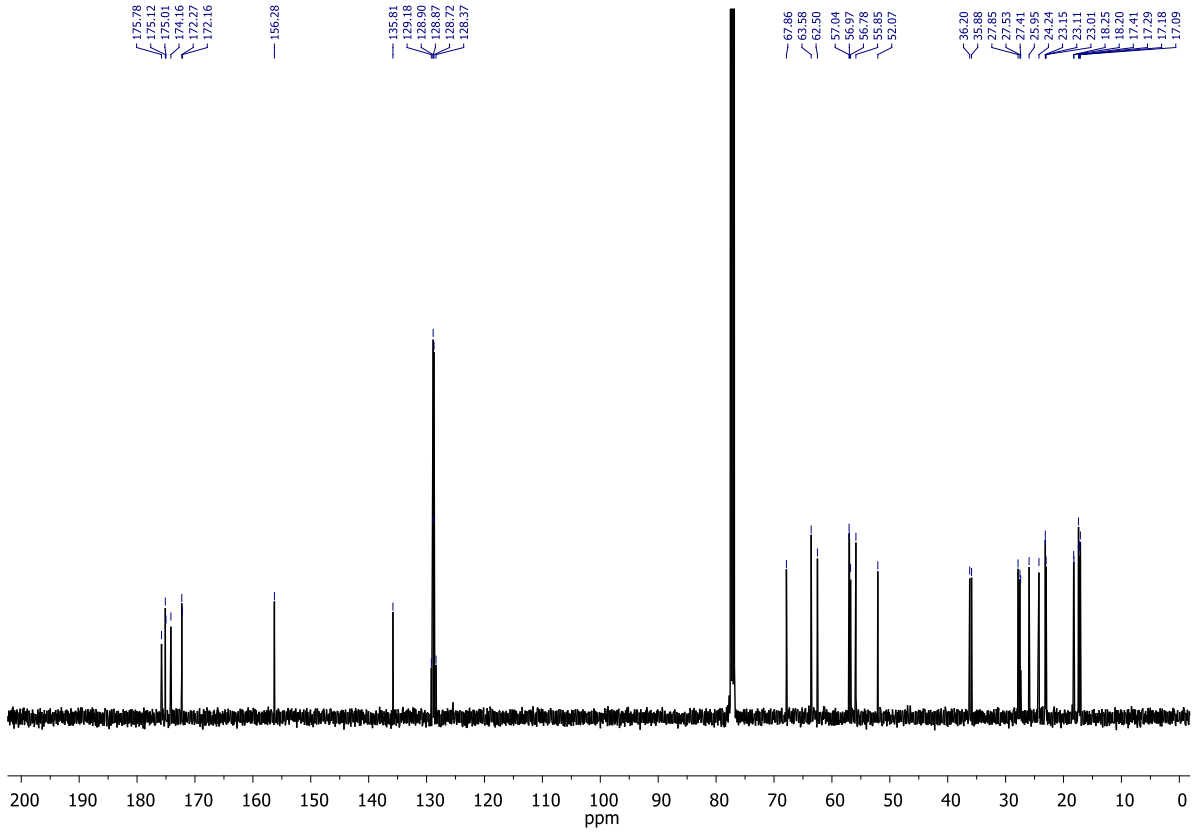
S15 ($CDCl_3$, 126 MHz)



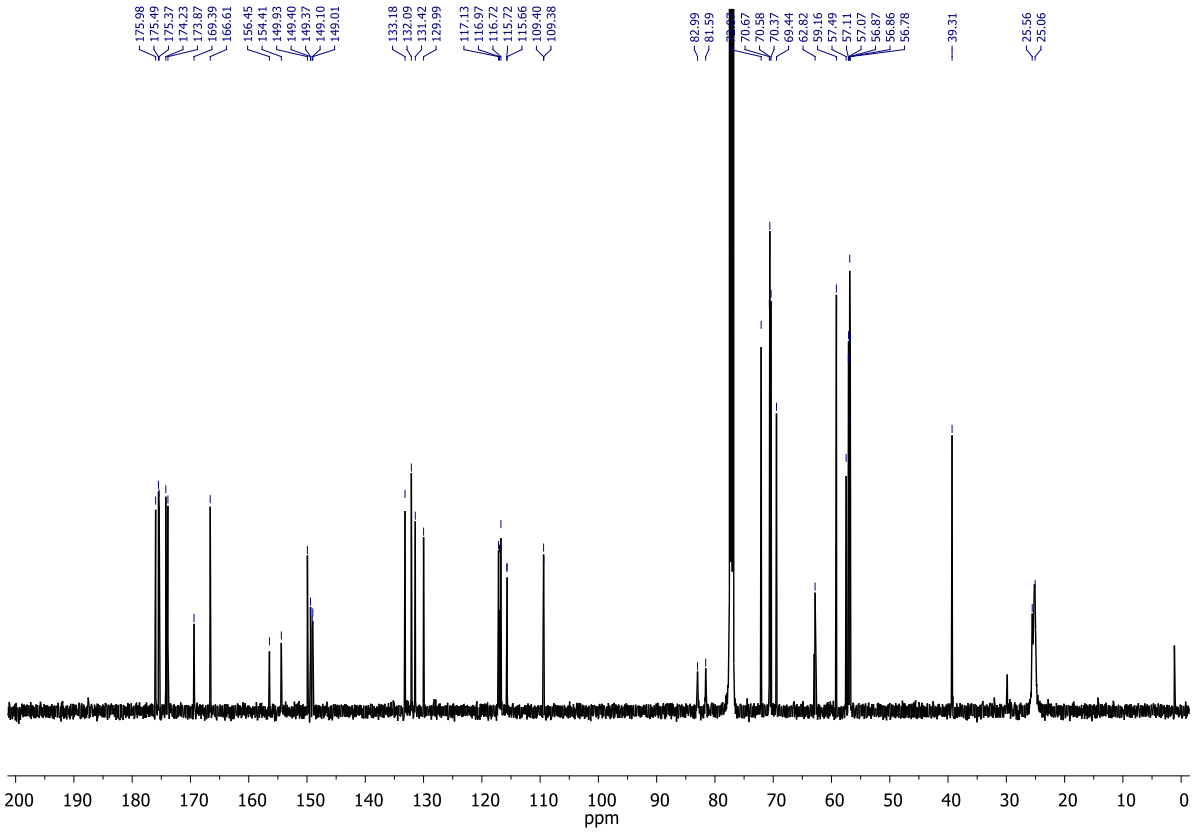
2 (CD_3OD, 126 MHz)



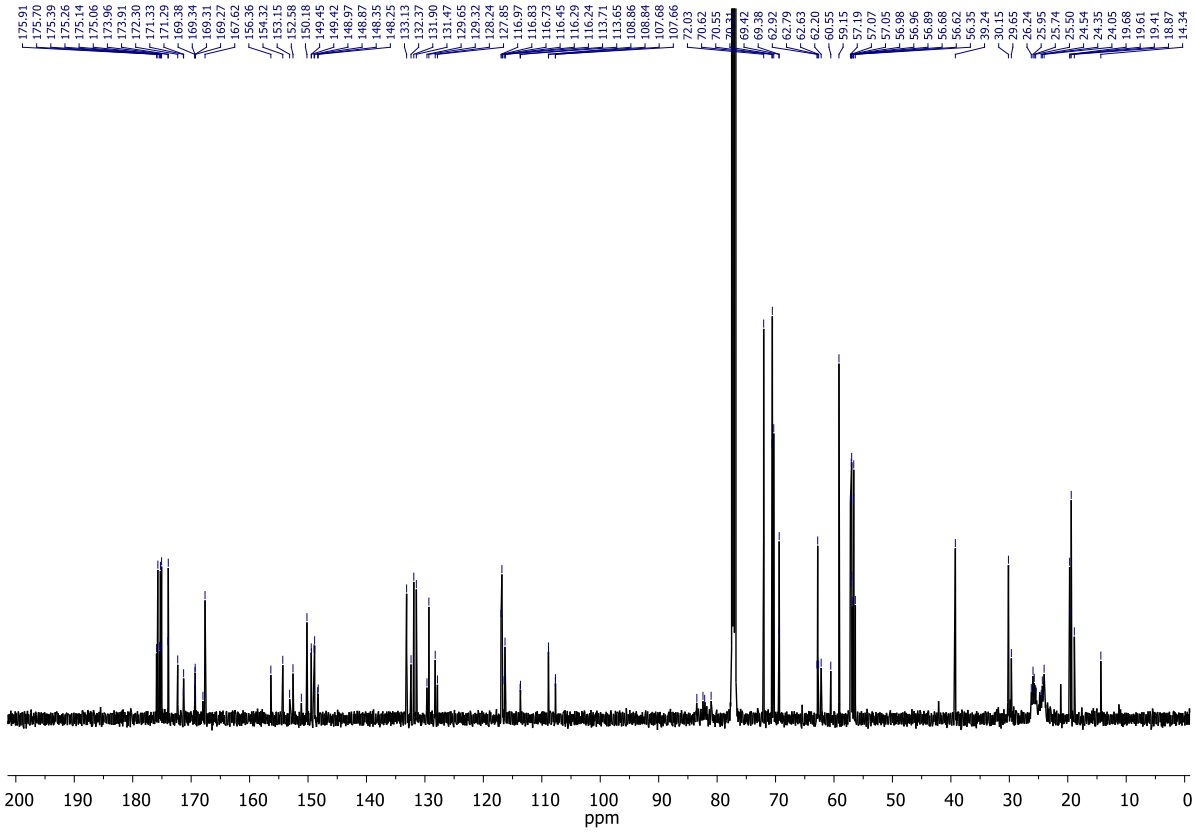
S17 ($CDCl_3$, 126 MHz)



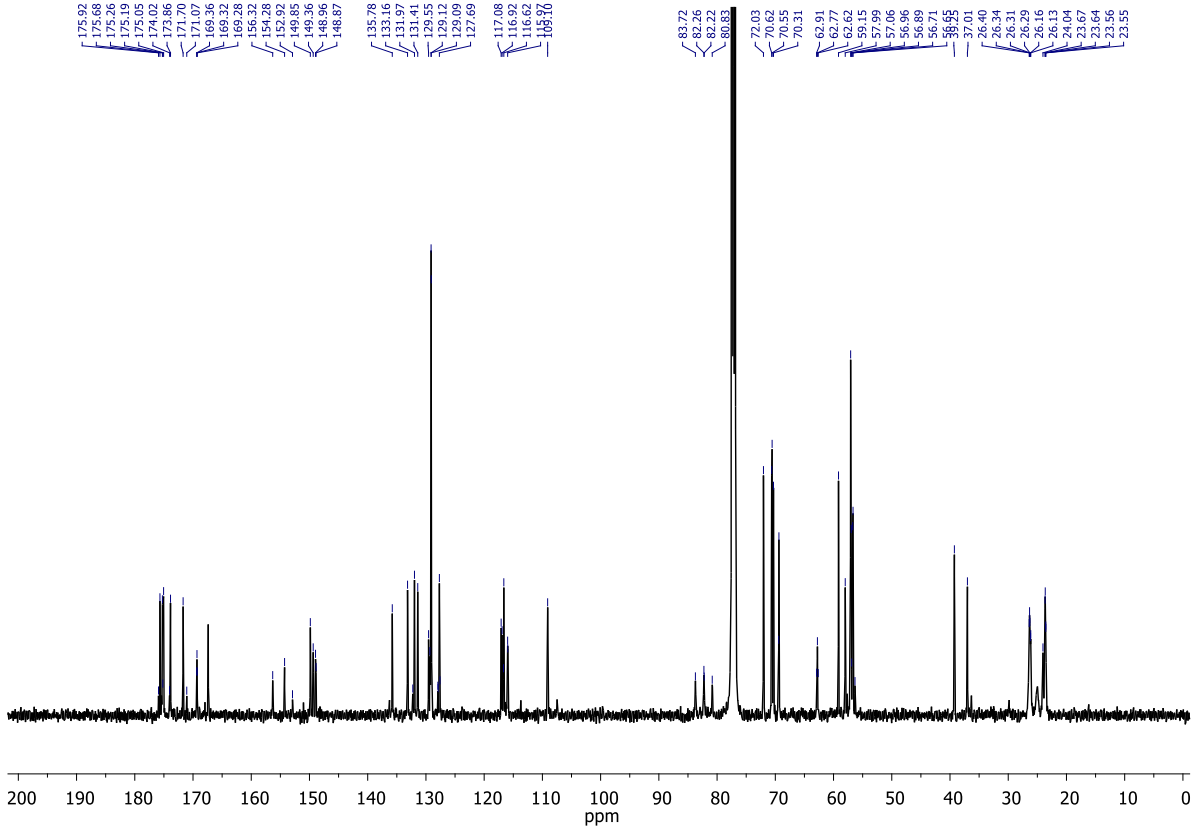
3g ($CDCl_3$, 126 MHz)



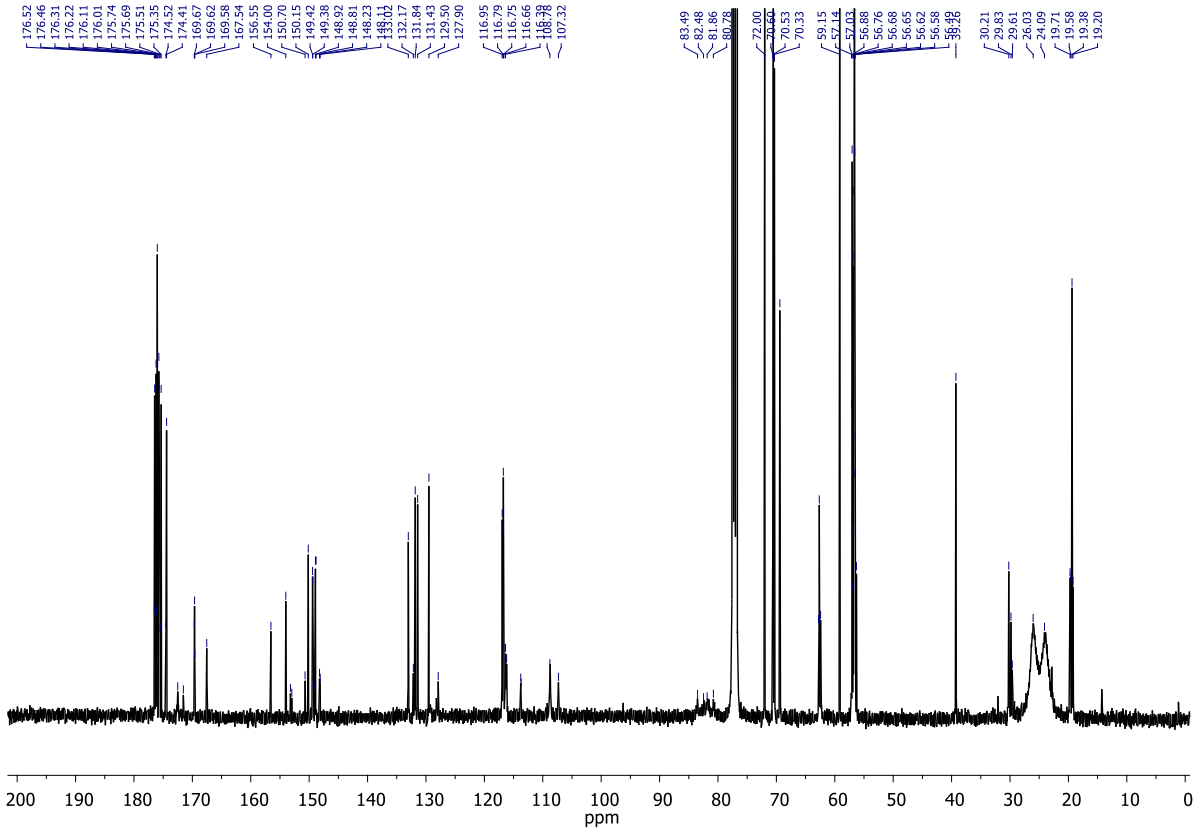
4 ($CDCl_3$, 126 MHz)



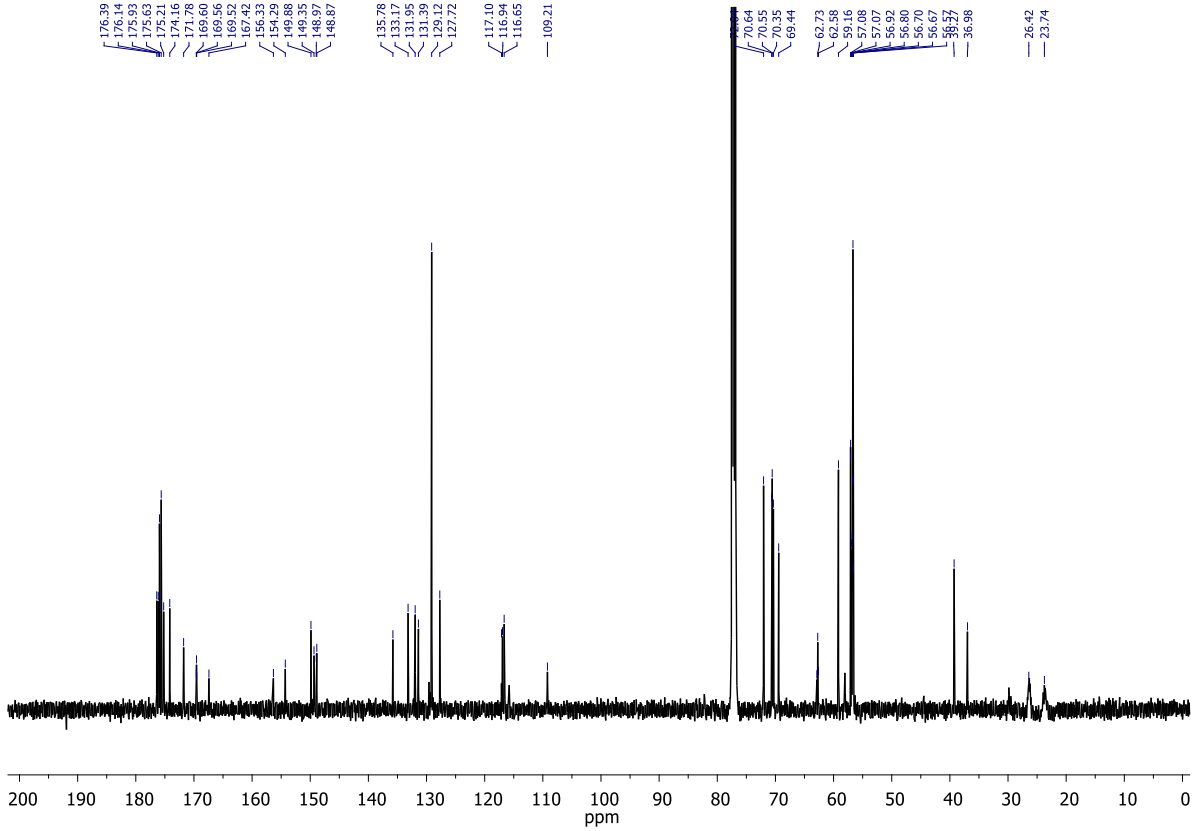
Phe-4 ($CDCl_3$, 126 MHz)



5 ($CDCl_3$, 101 MHz)

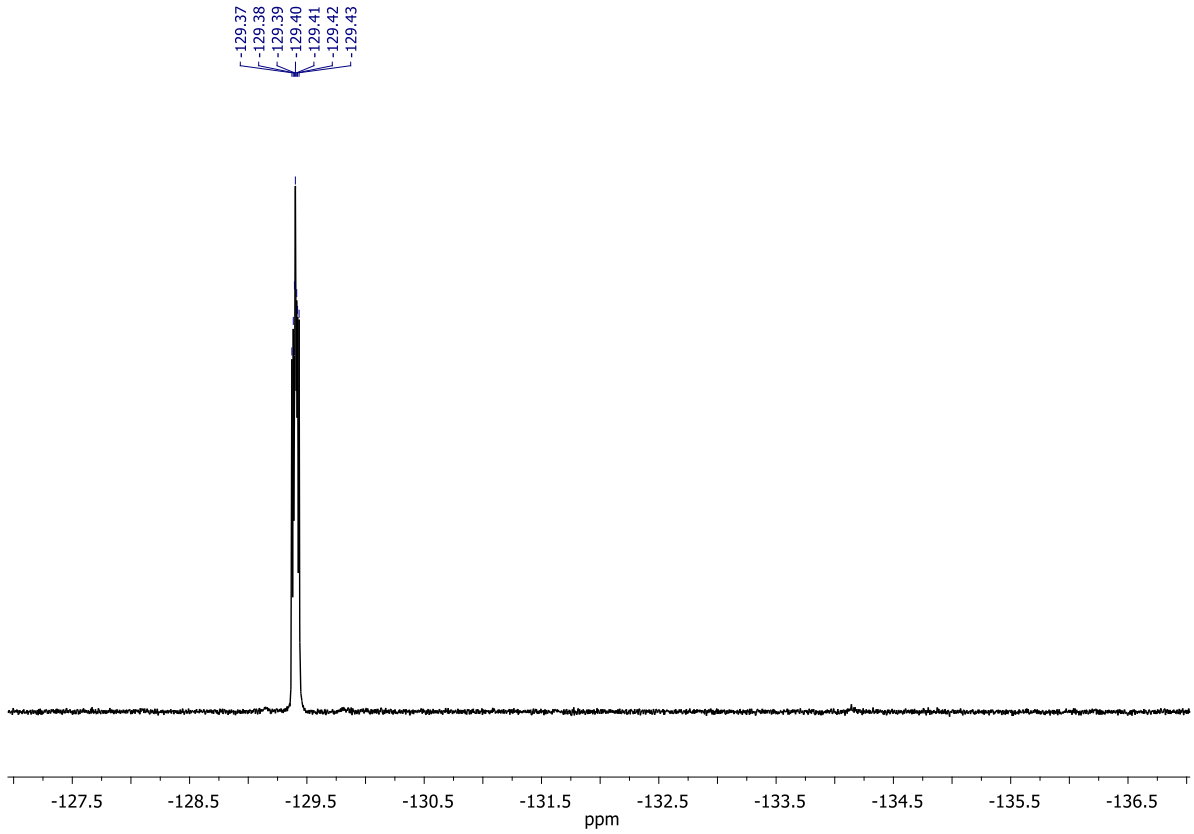


Phe-5 ($CDCl_3$, 126 MHz)

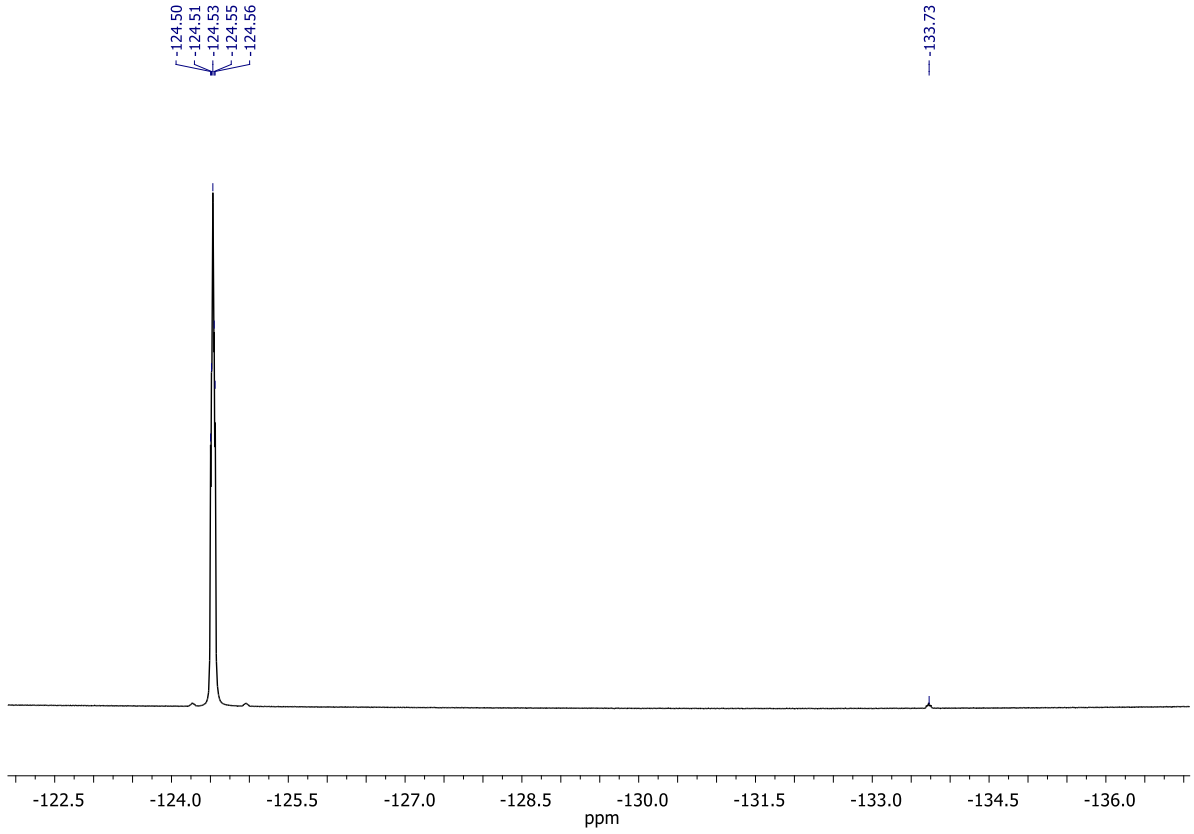


^{19}F NMR spectra in $CDCl_3$

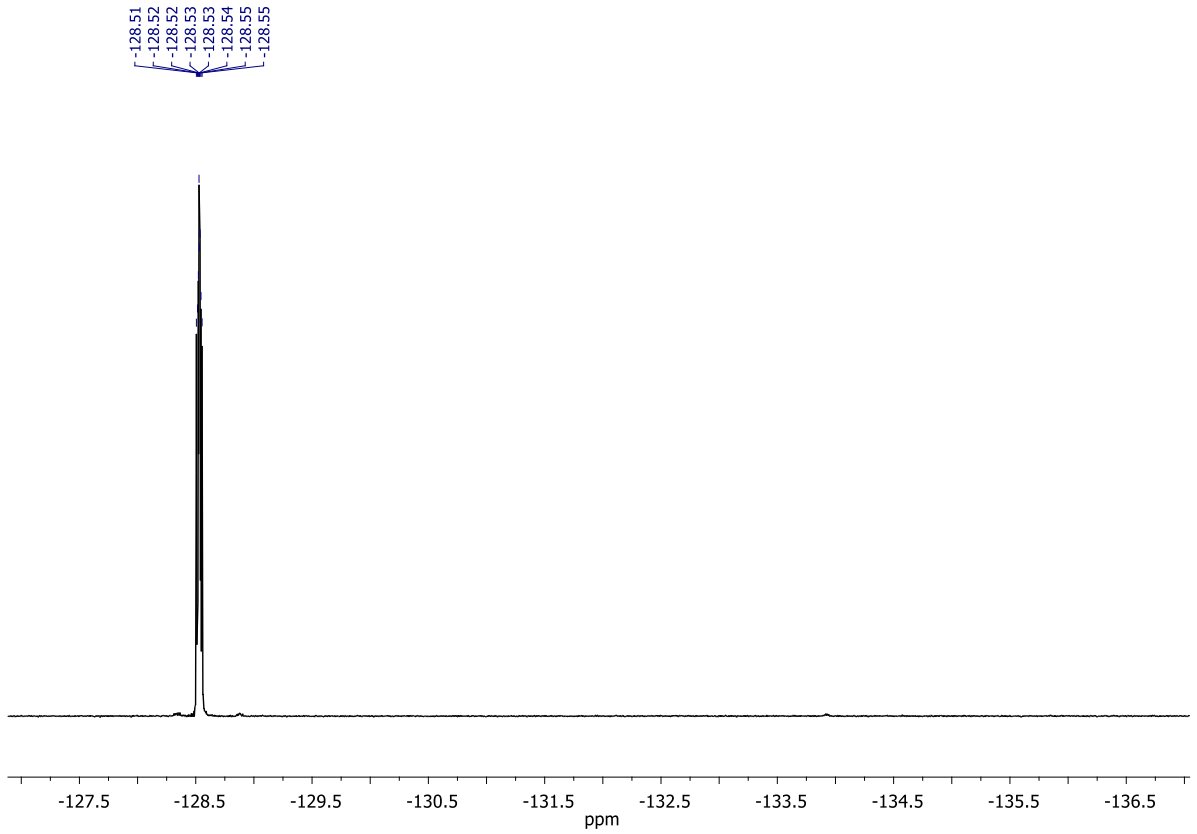
S11 (376 MHz)



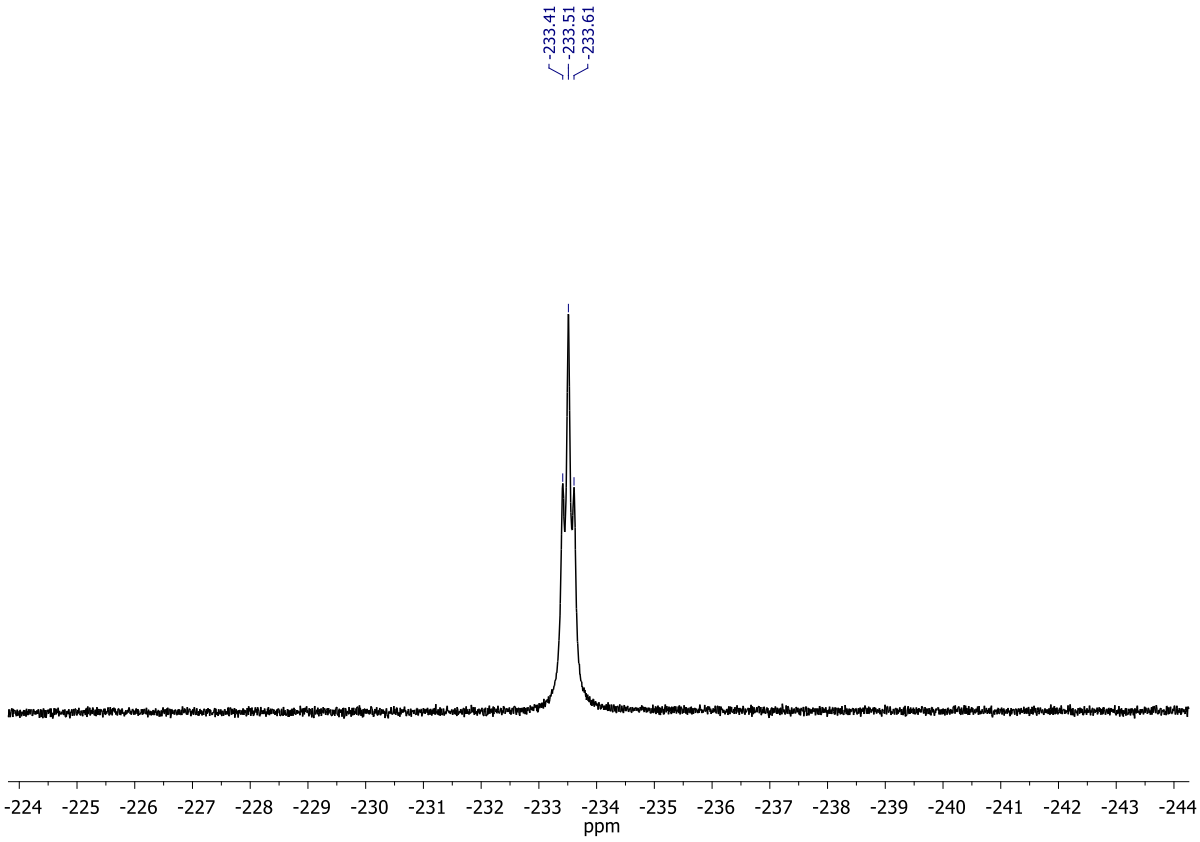
S12 (376 MHz)



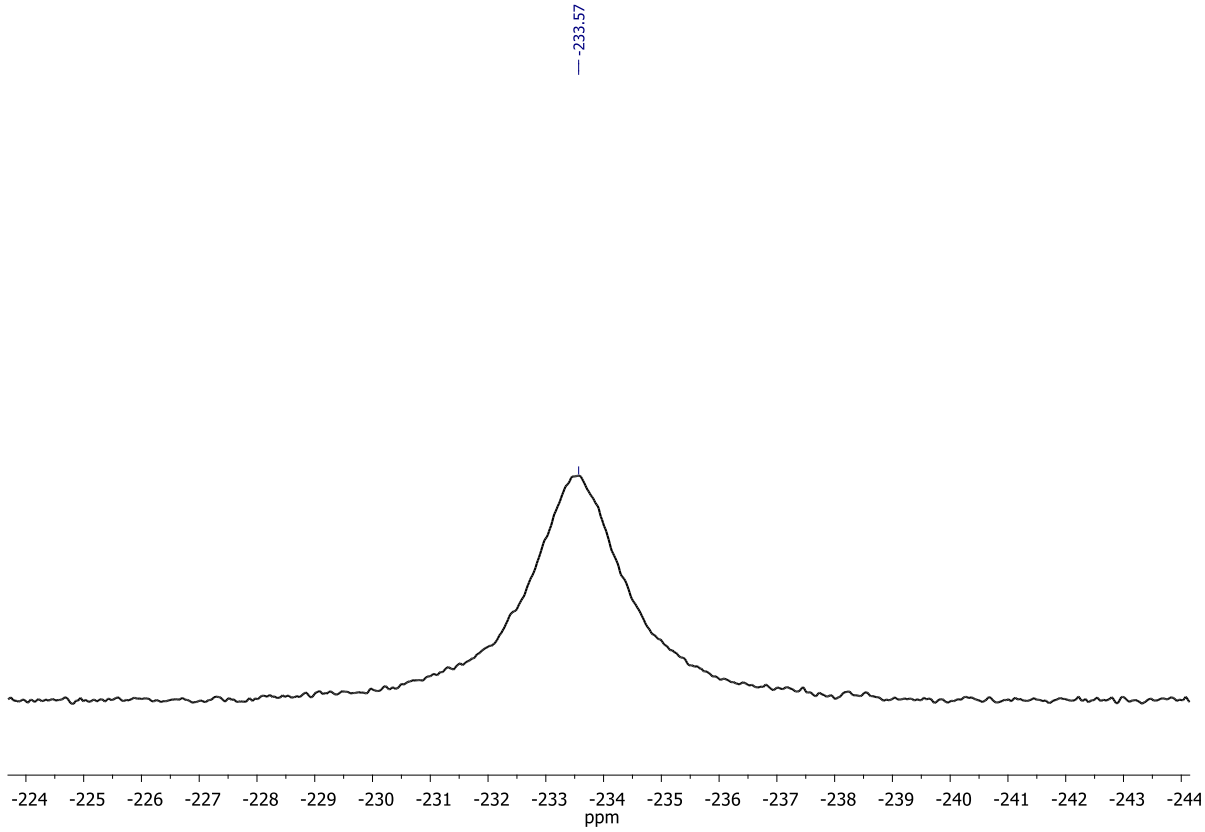
S13 (471 MHz)



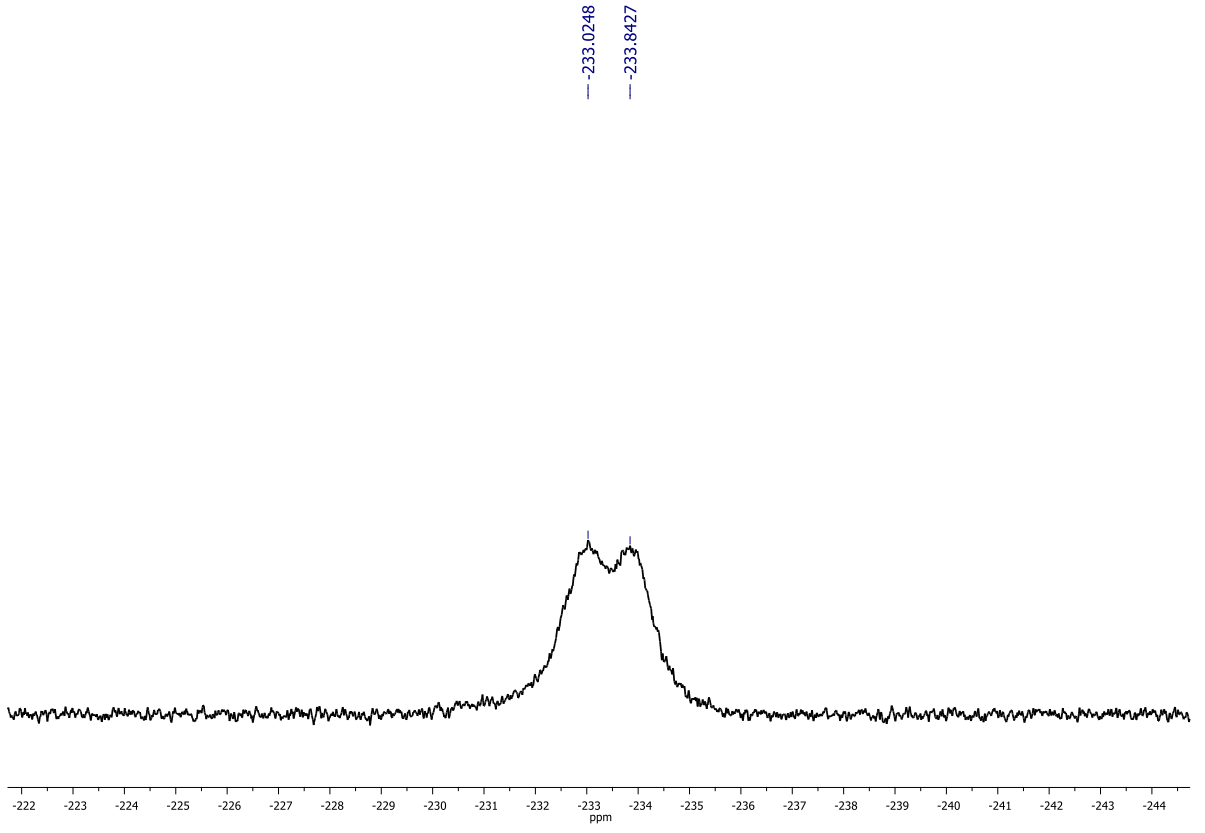
F3 (471 MHz)



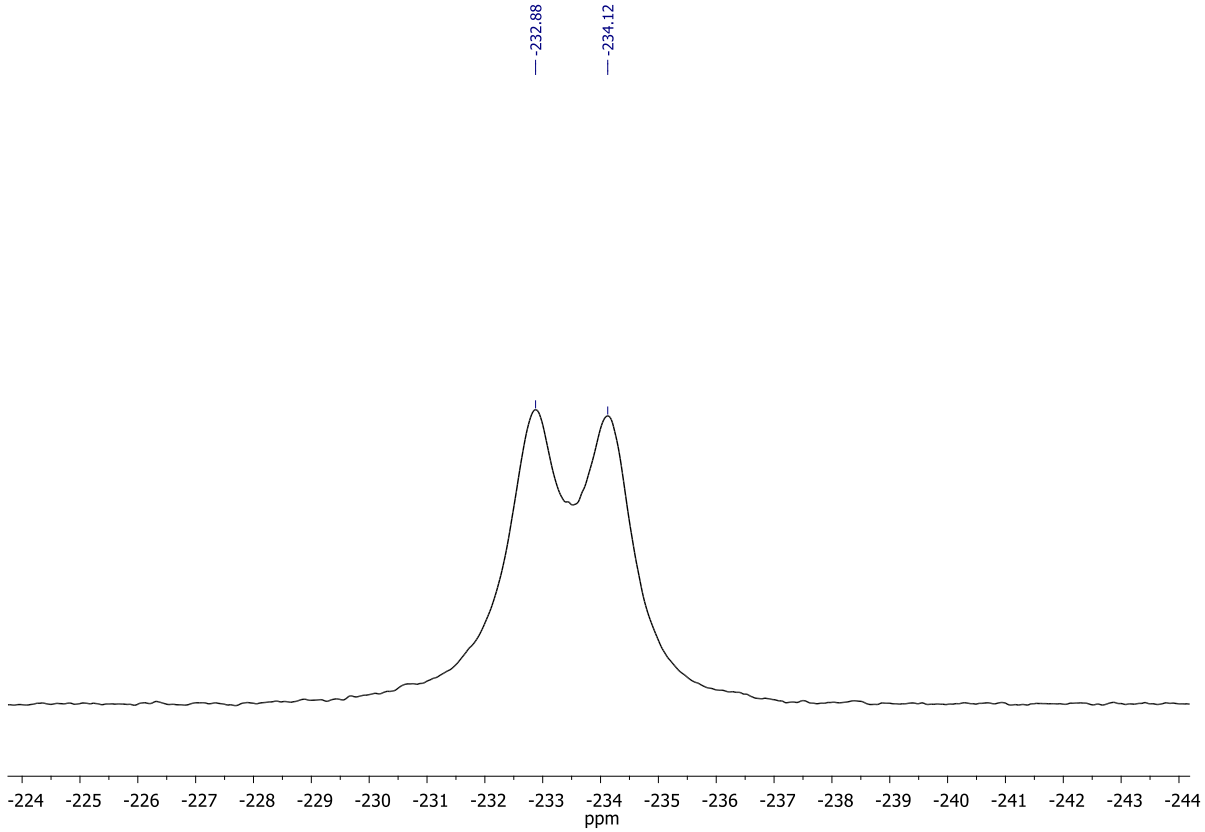
3a (471 MHz)



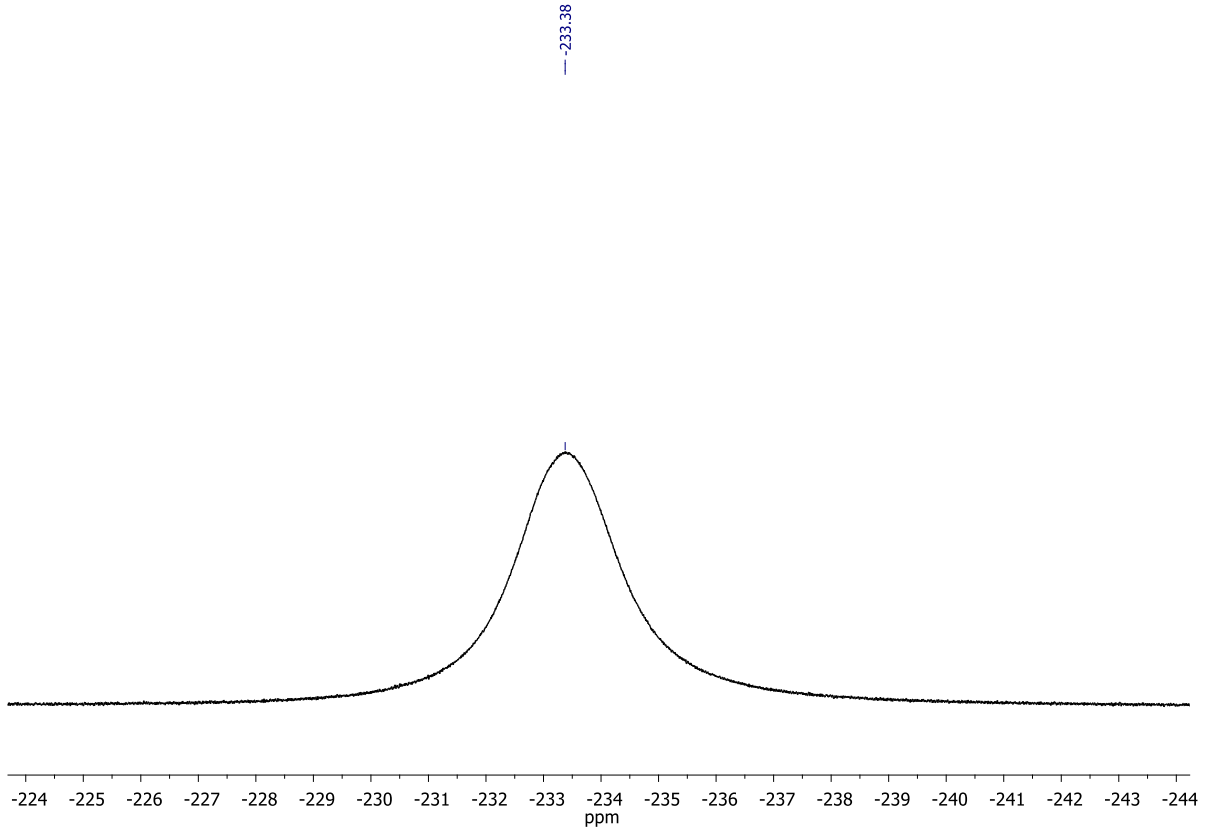
3b (471 MHz)



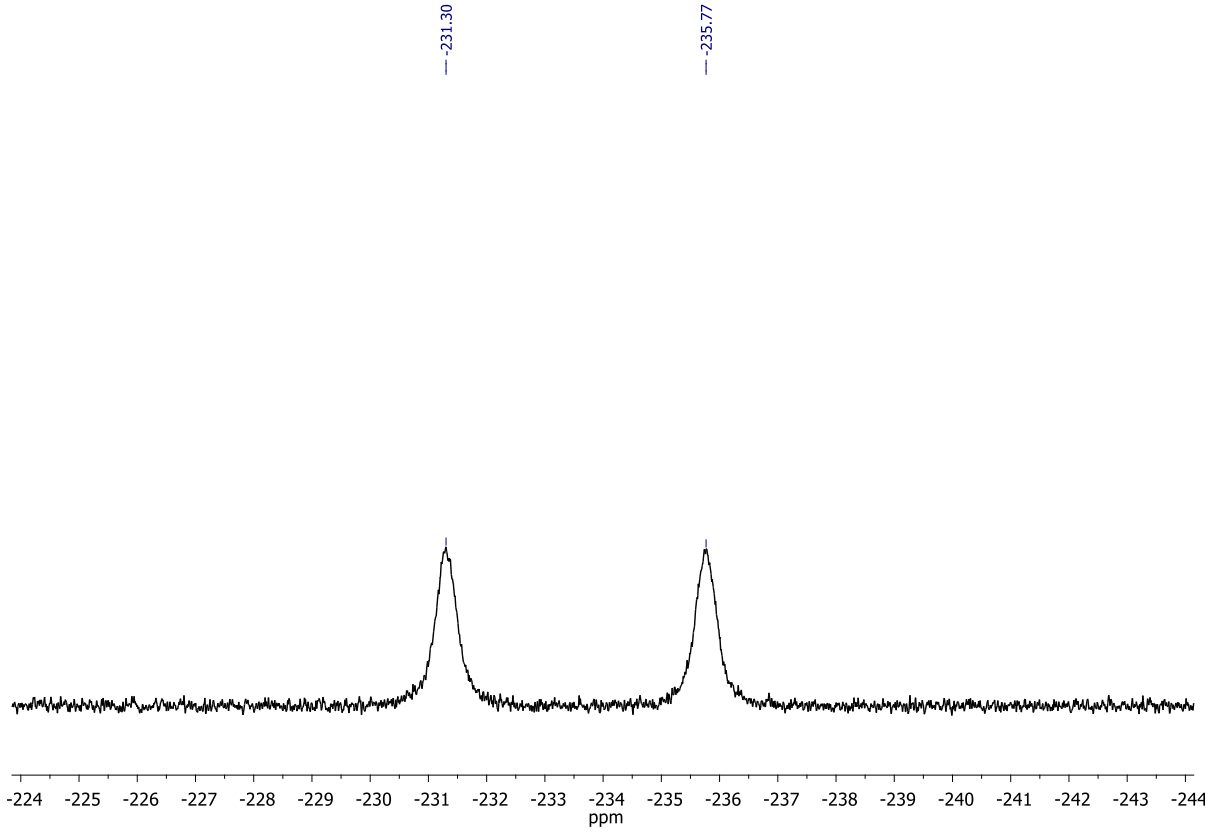
3c (471 MHz)



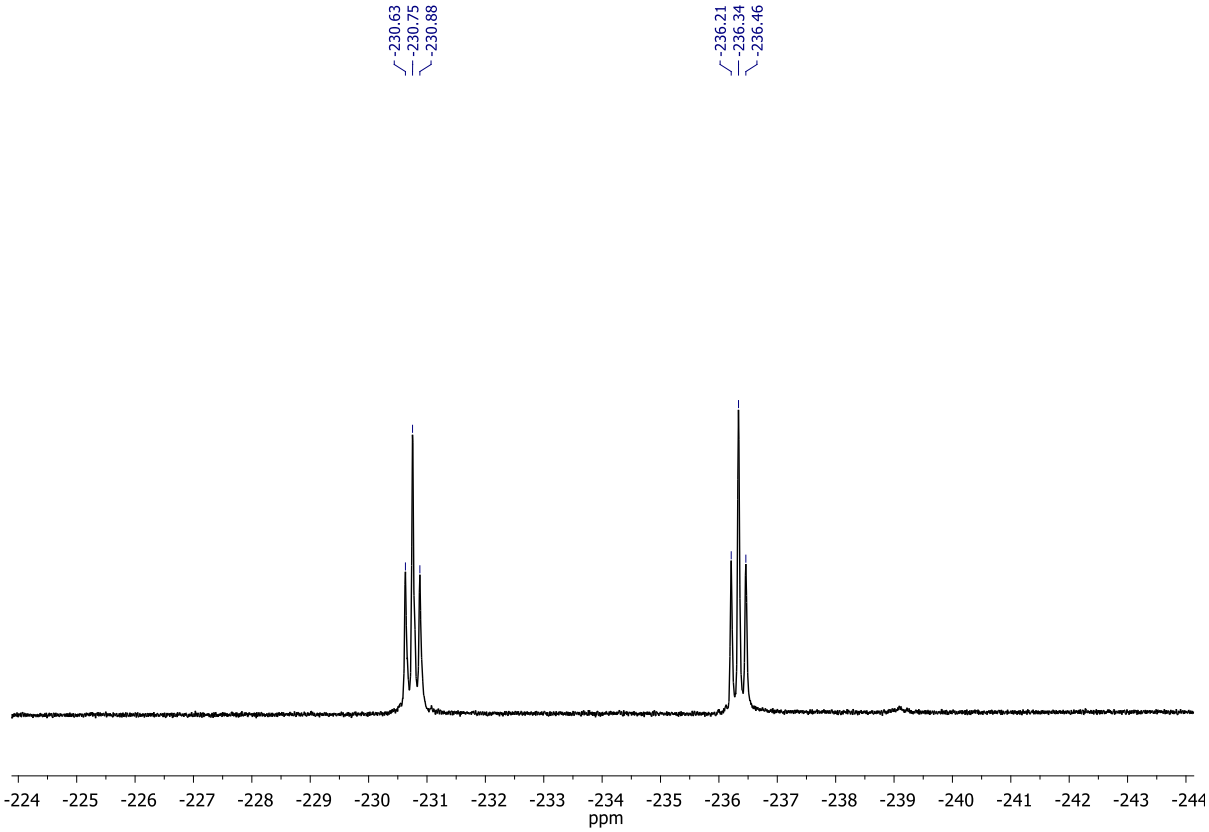
3d (471 MHz)



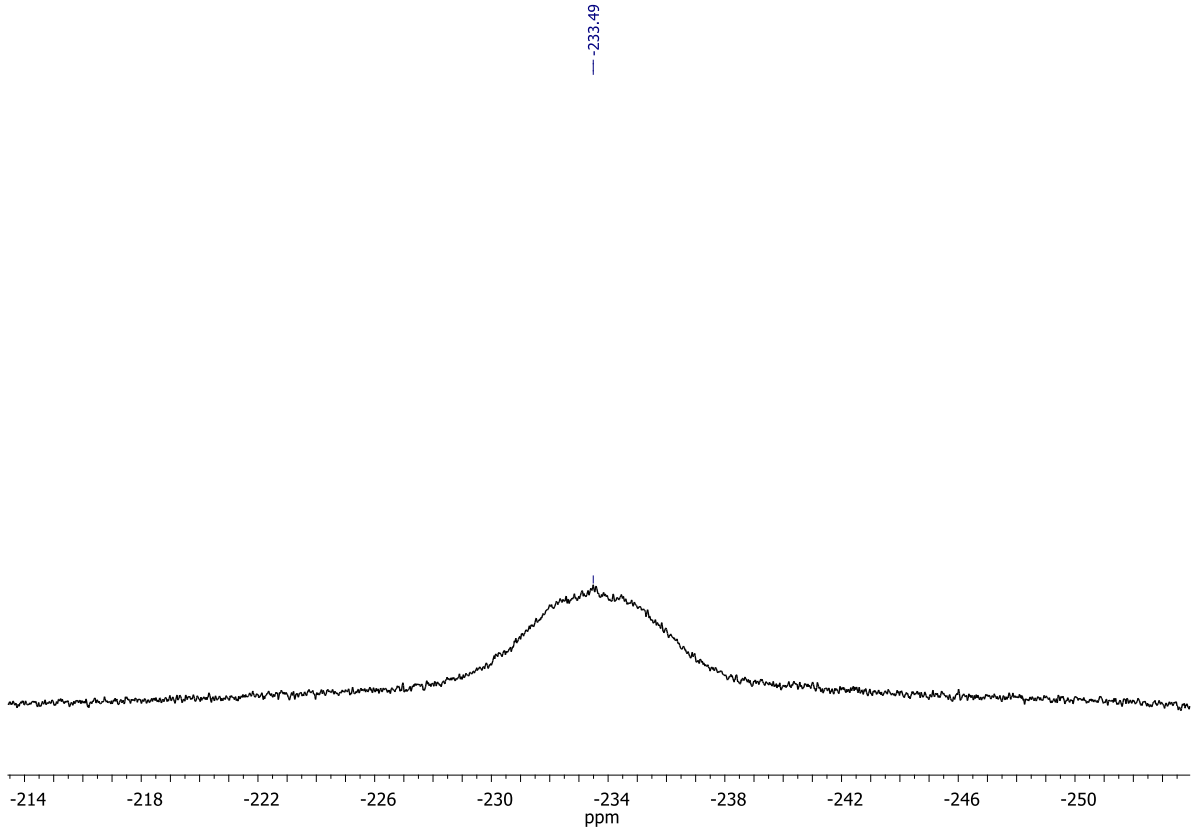
3e (376 MHz)



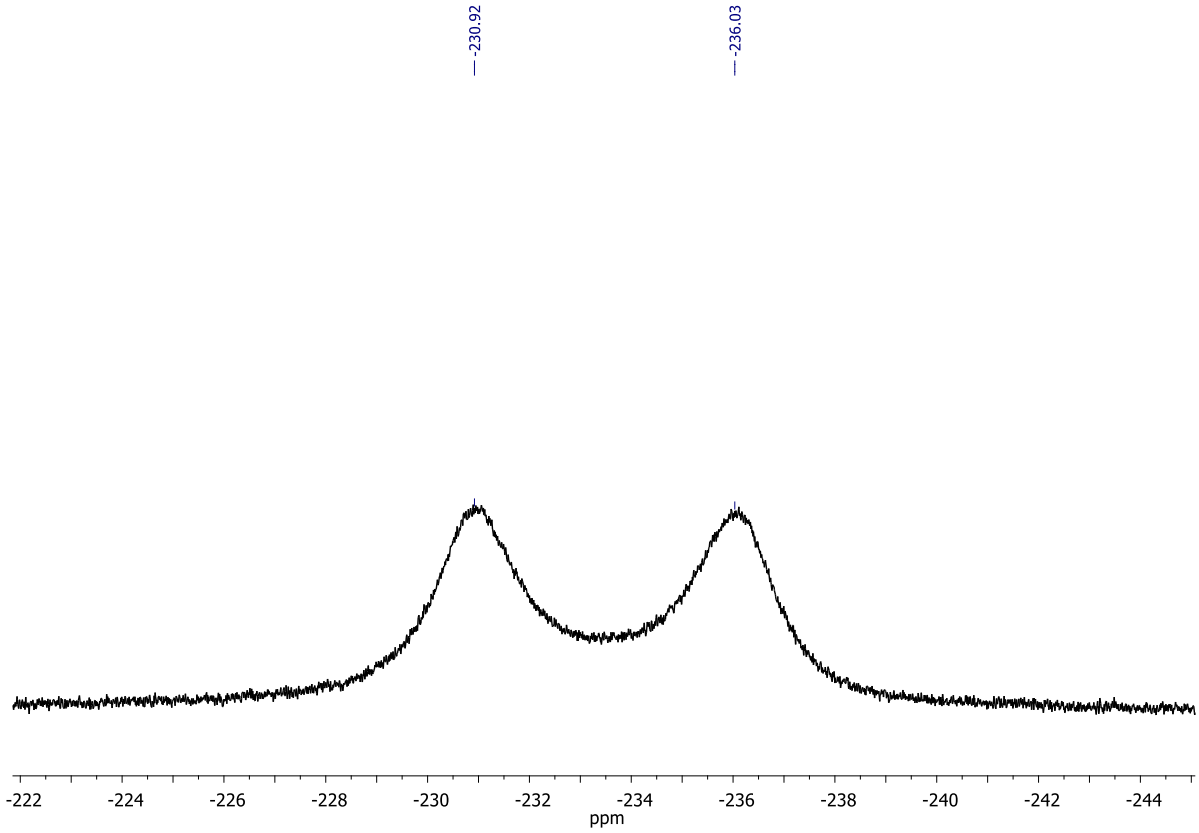
3f (376 MHz)



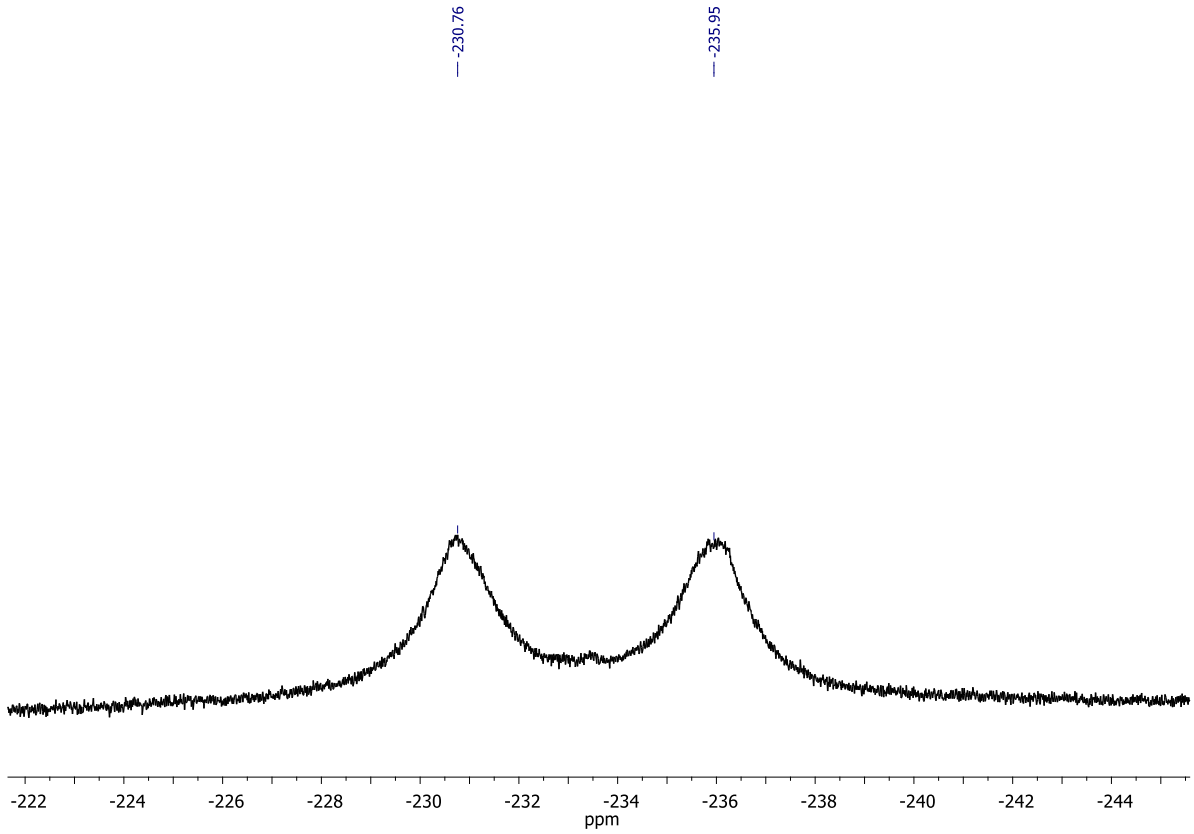
F4 (471 MHz)



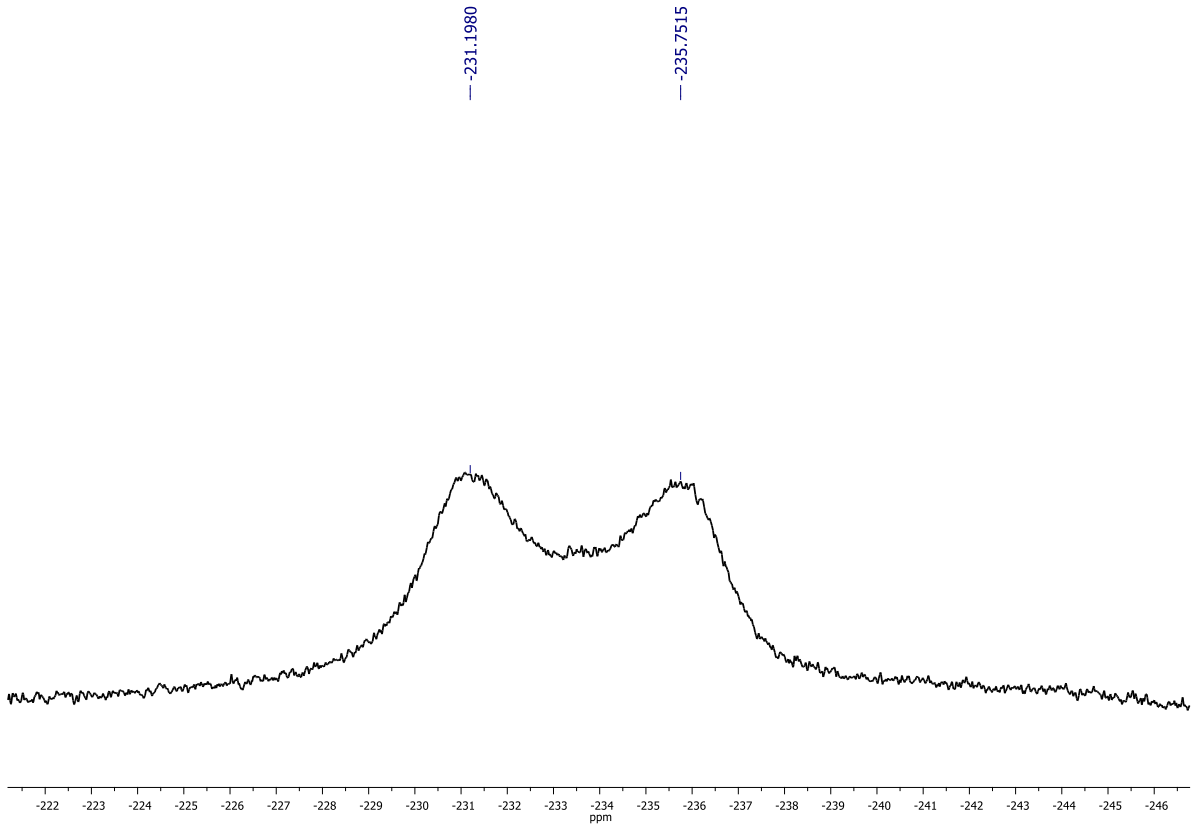
6a (471 MHz)



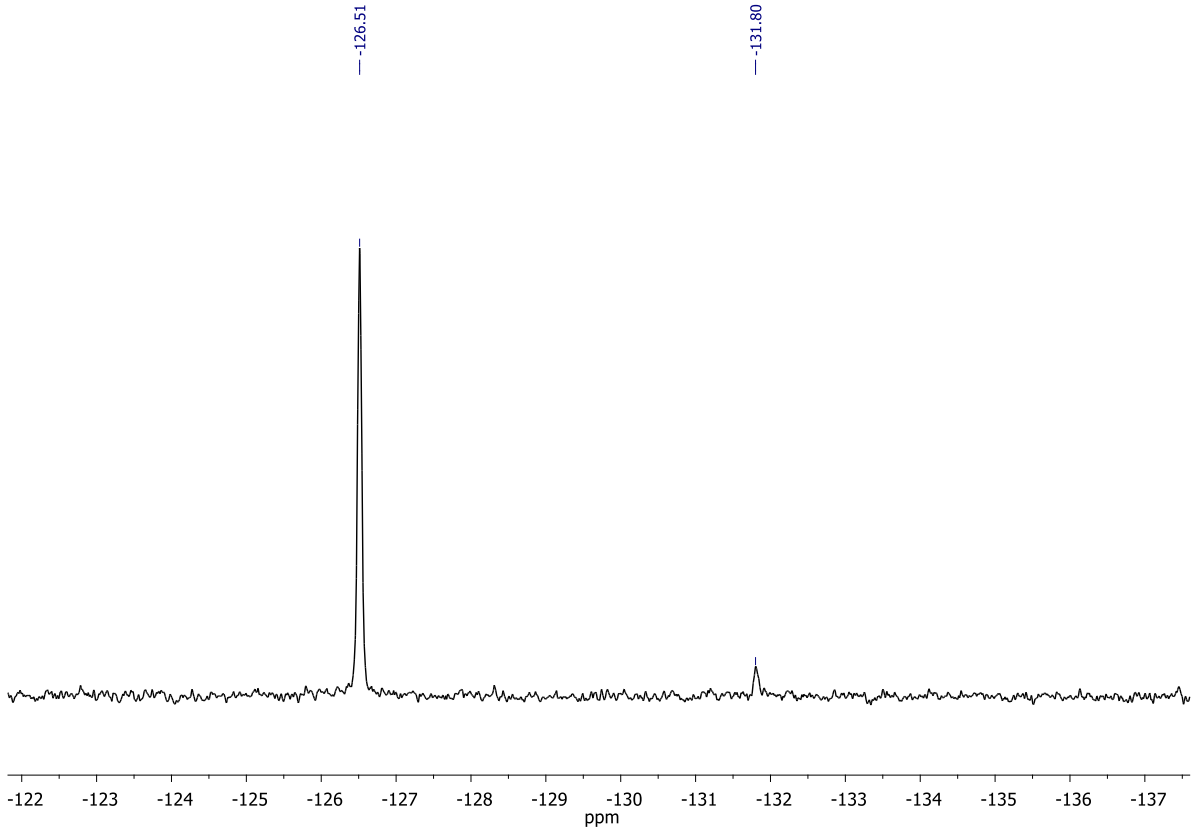
6c (471 MHz)



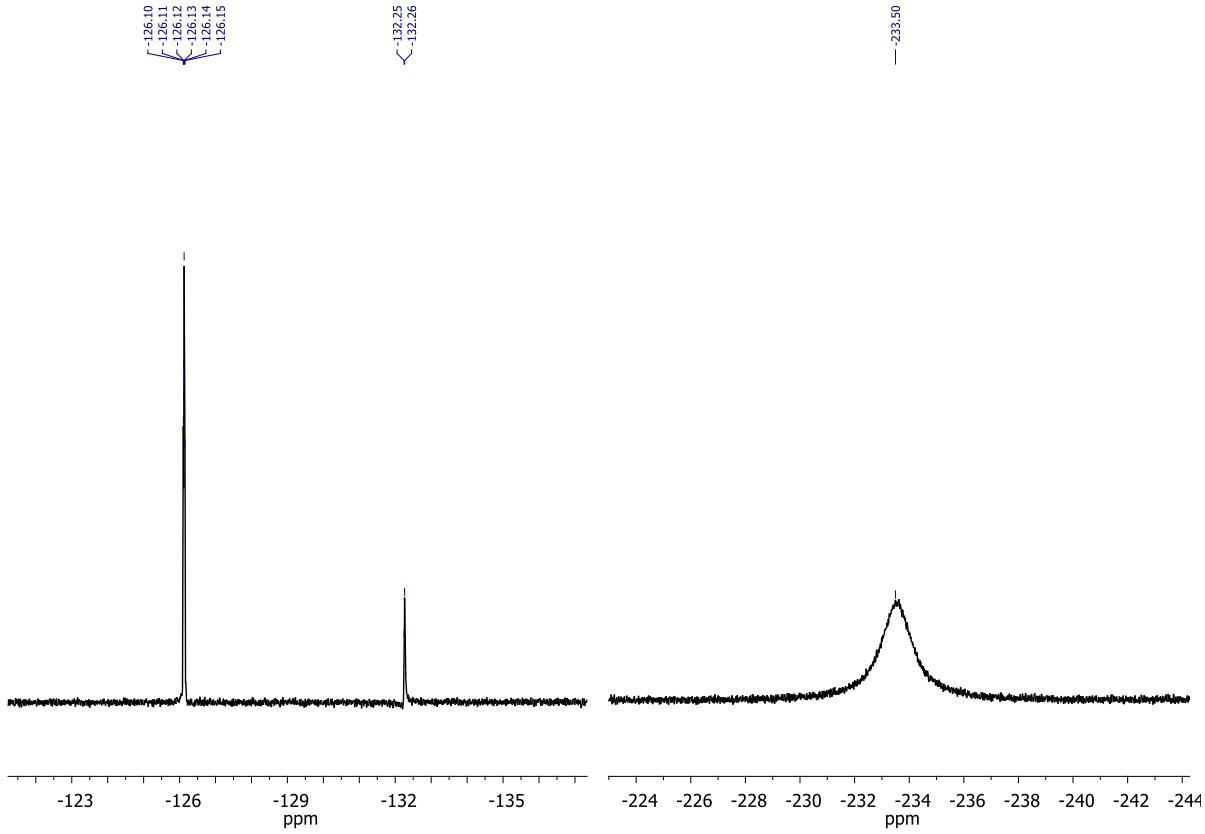
6d (376 MHz)



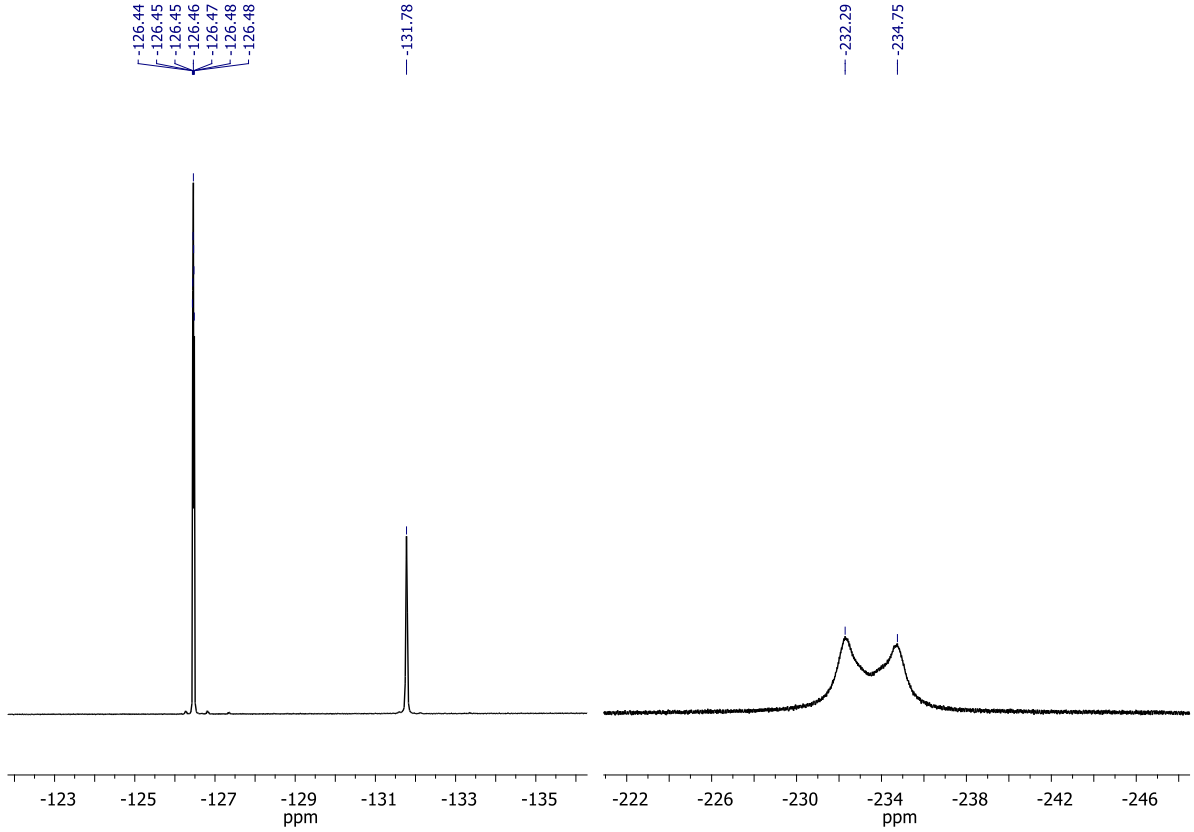
1d (376 MHz)



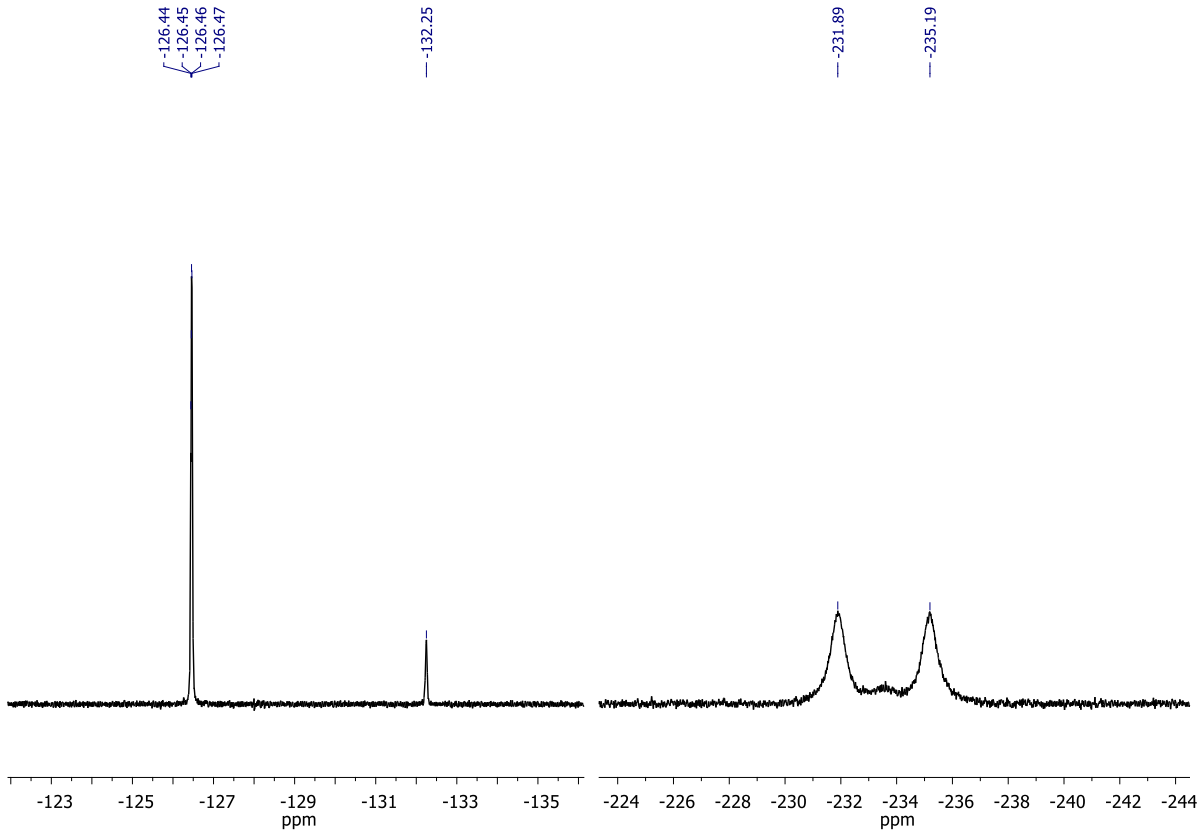
3g (471 MHz)



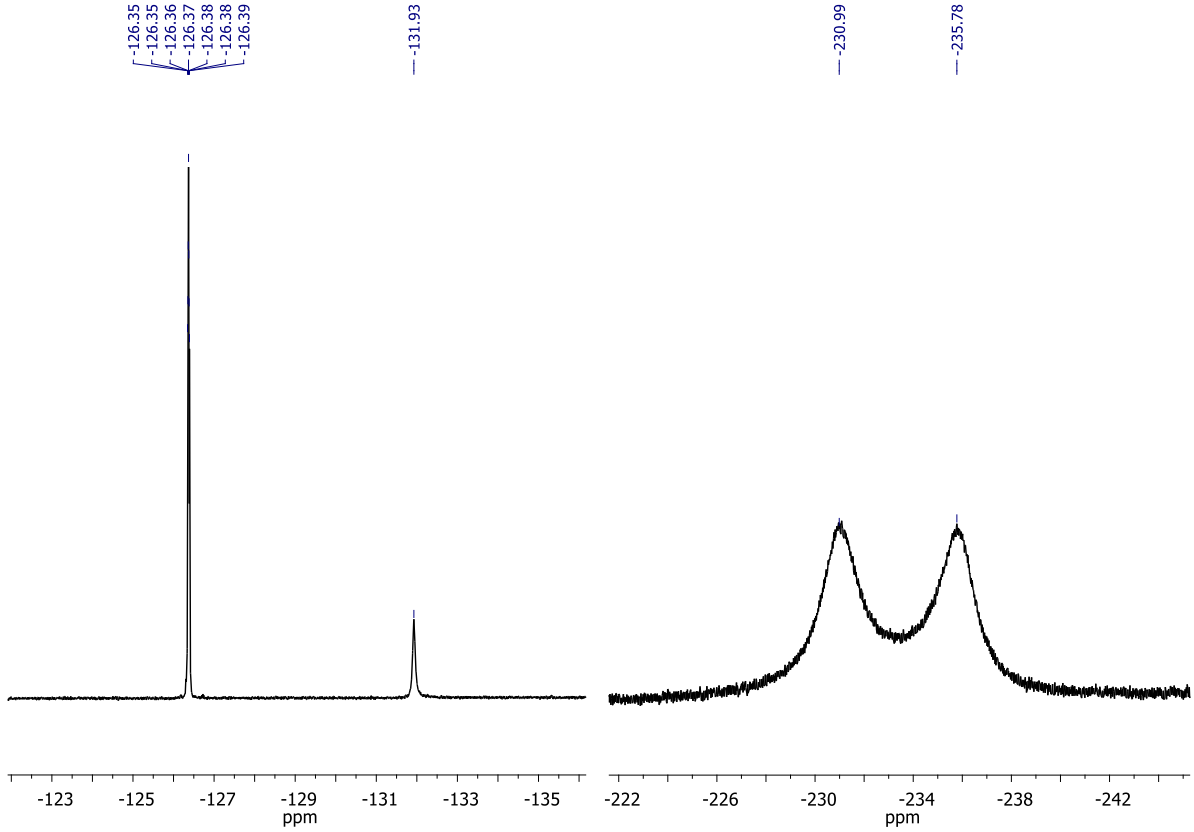
4 (471 MHz)



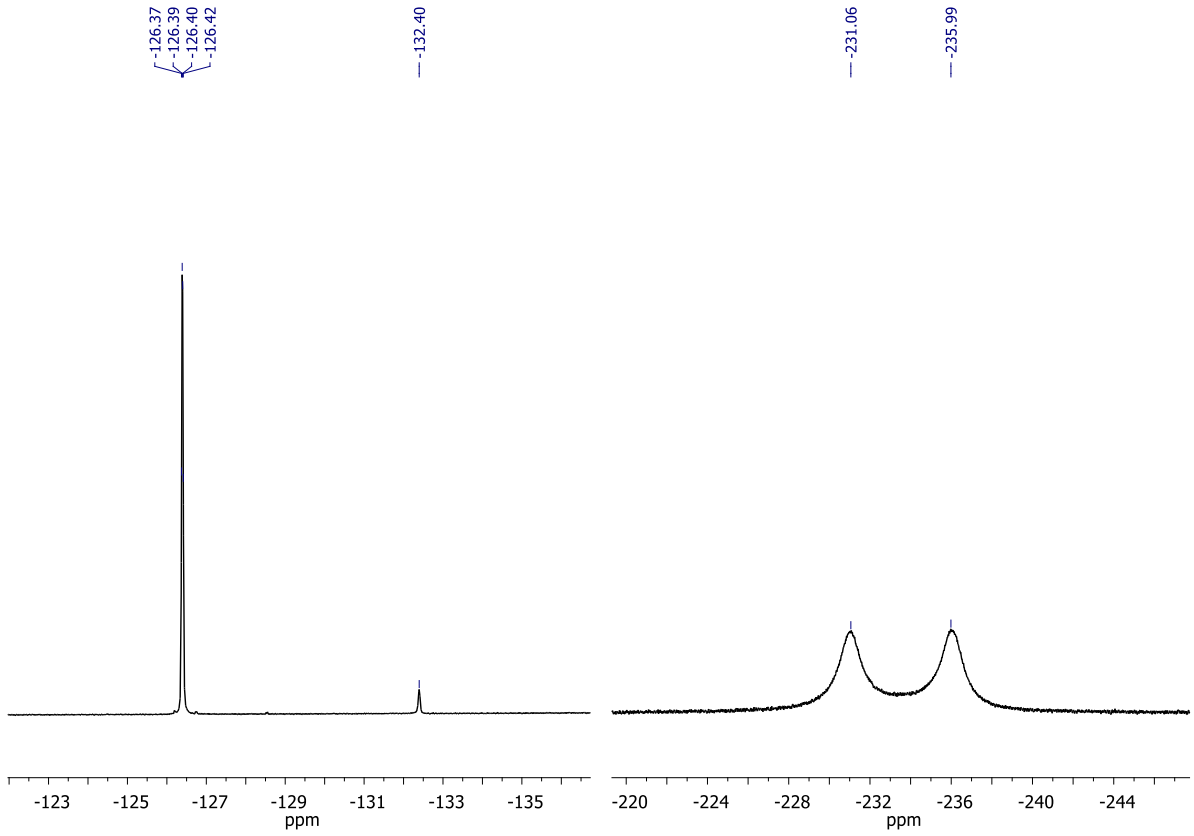
Phe-4 (471 MHz)



5 (471 MHz)

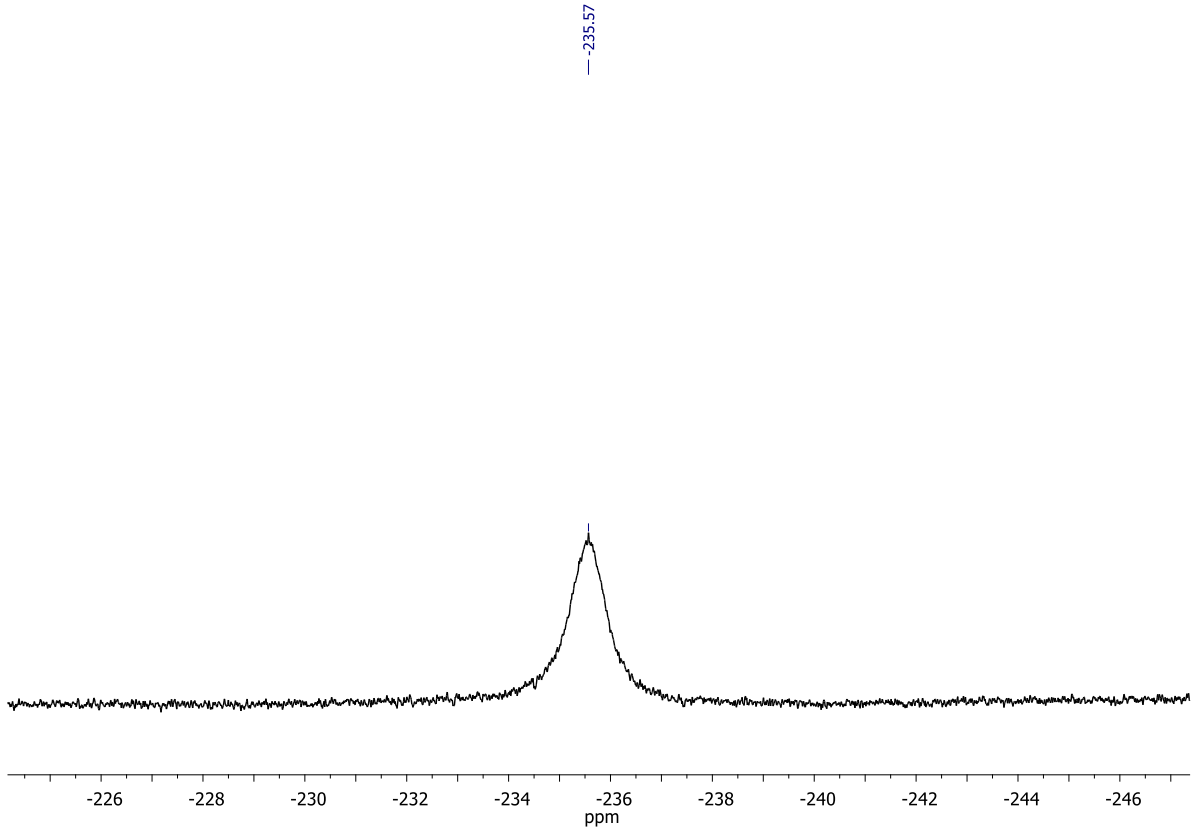


Phe-5 (471 MHz)

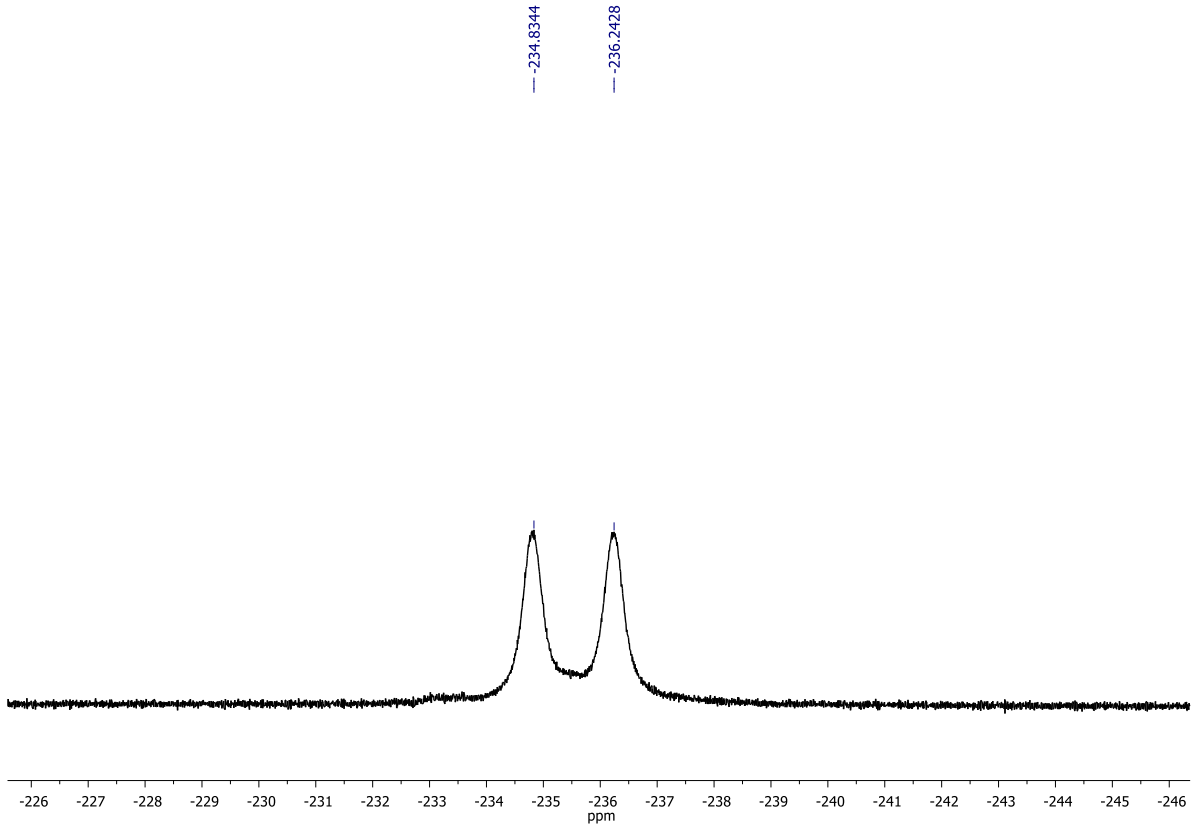


^{19}F NMR spectra in CD_3OD

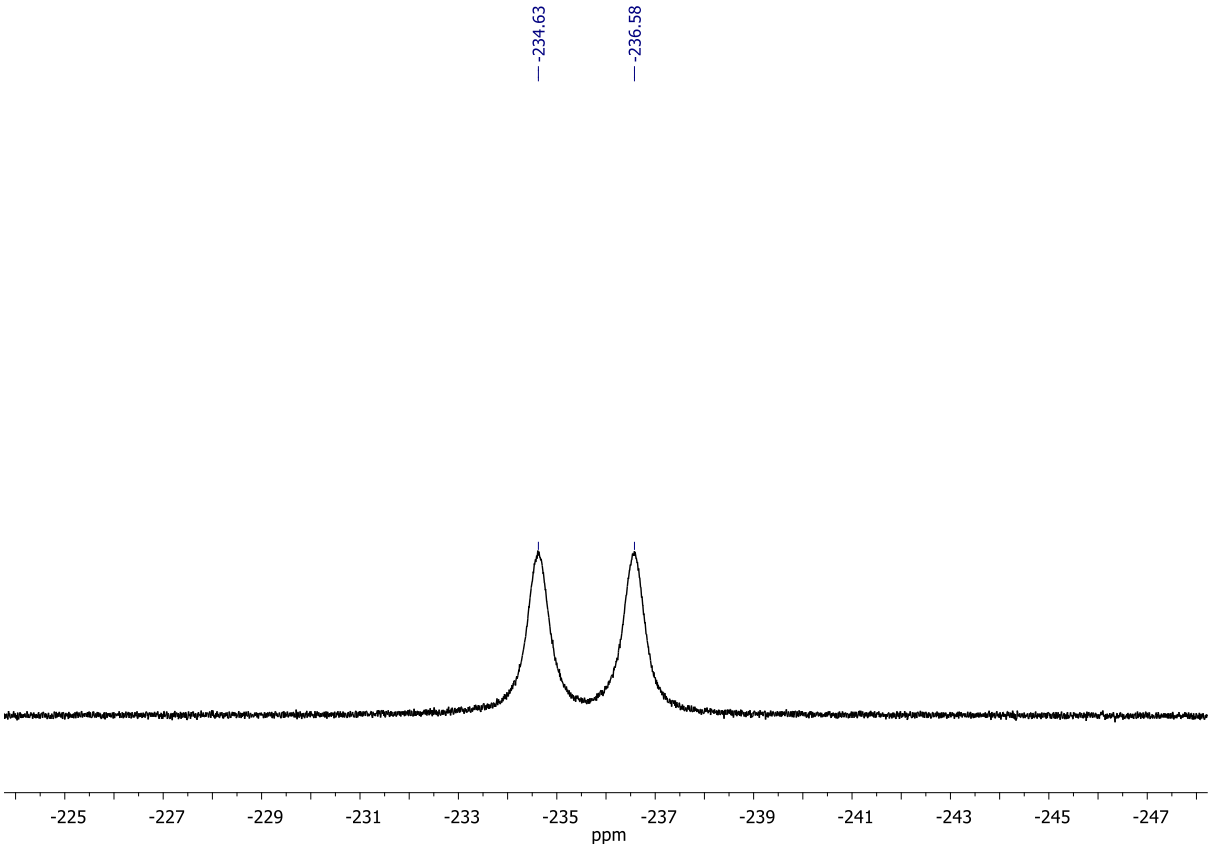
3a (376 MHz)



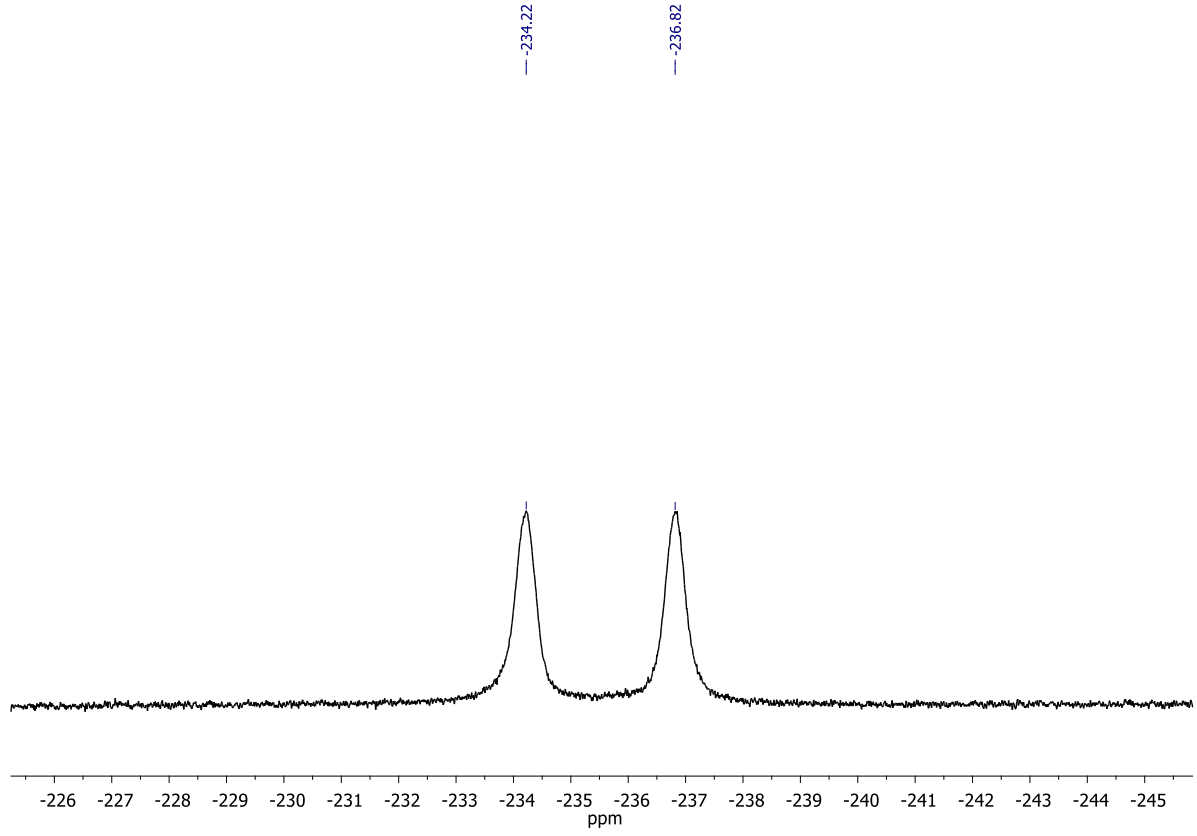
3b (471 MHz)



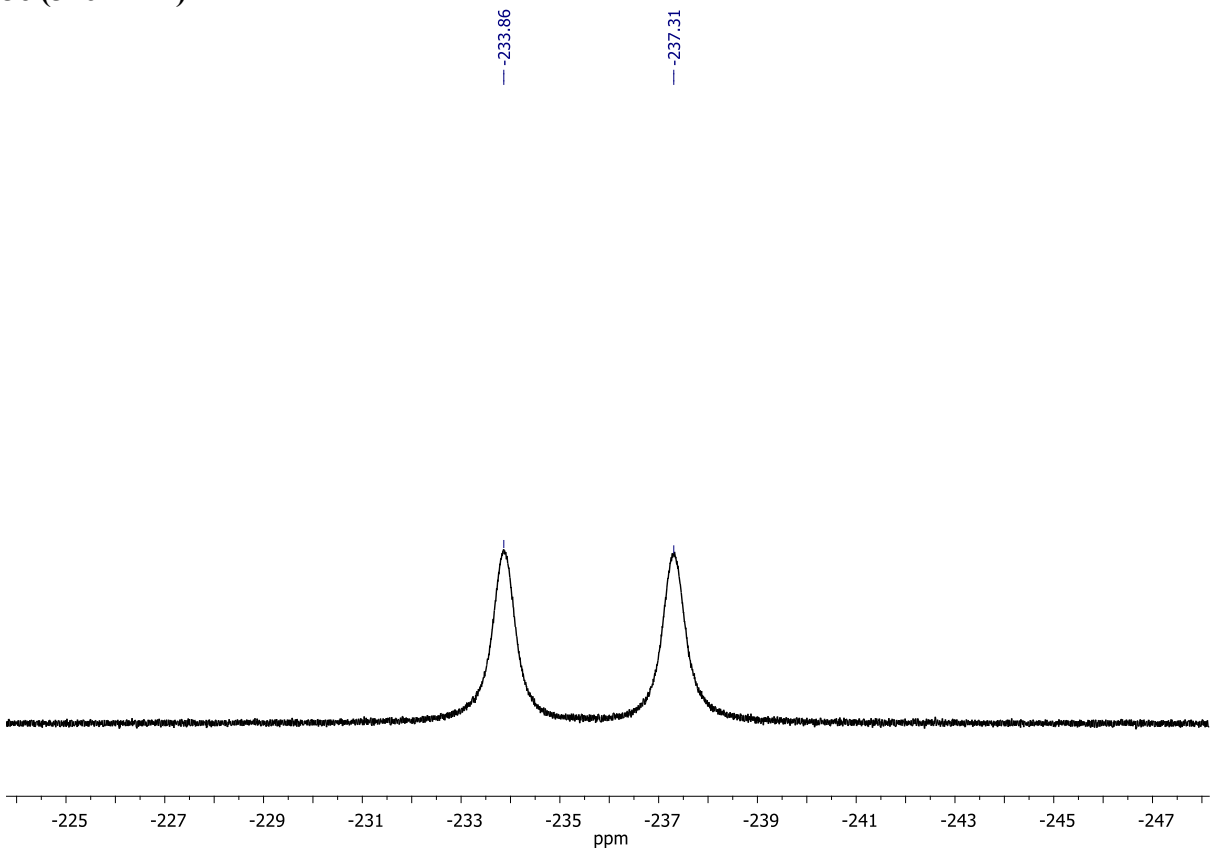
3c (376 MHz)



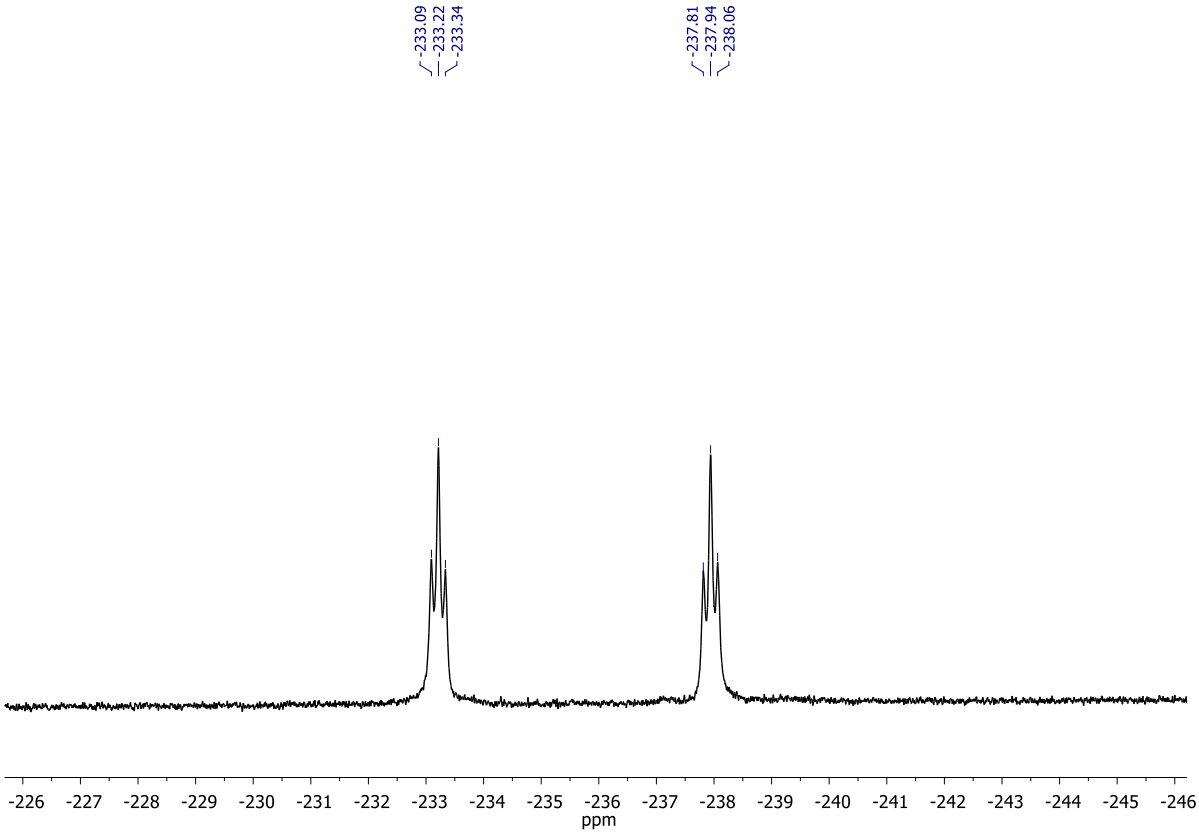
3d (376 MHz)



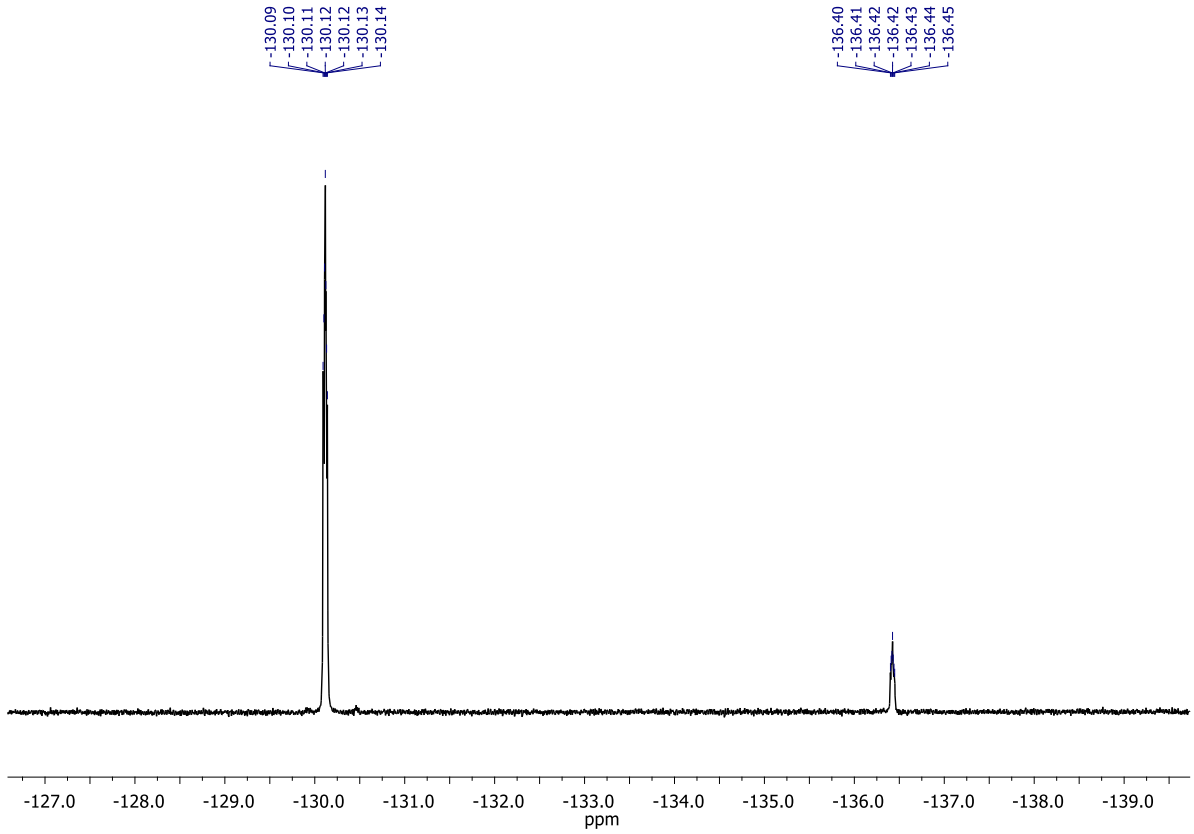
3e (376 MHz)



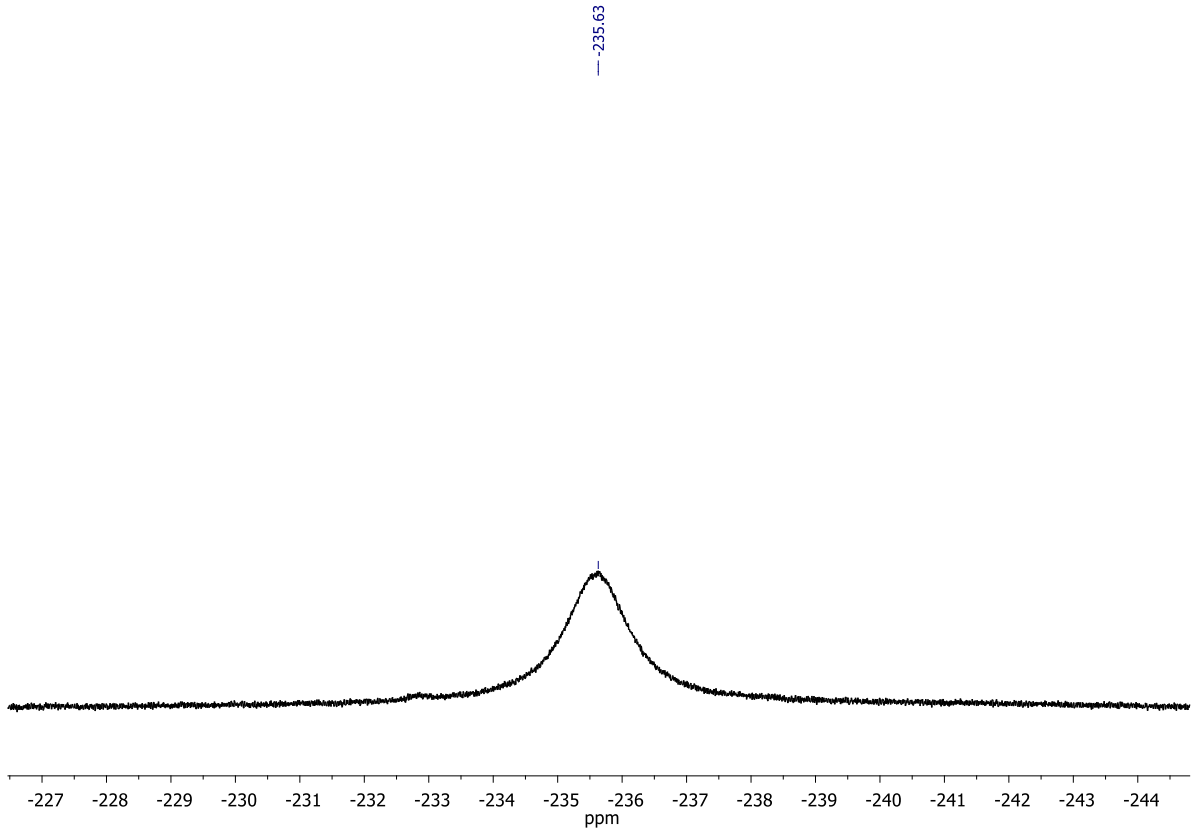
3f (376 MHz)



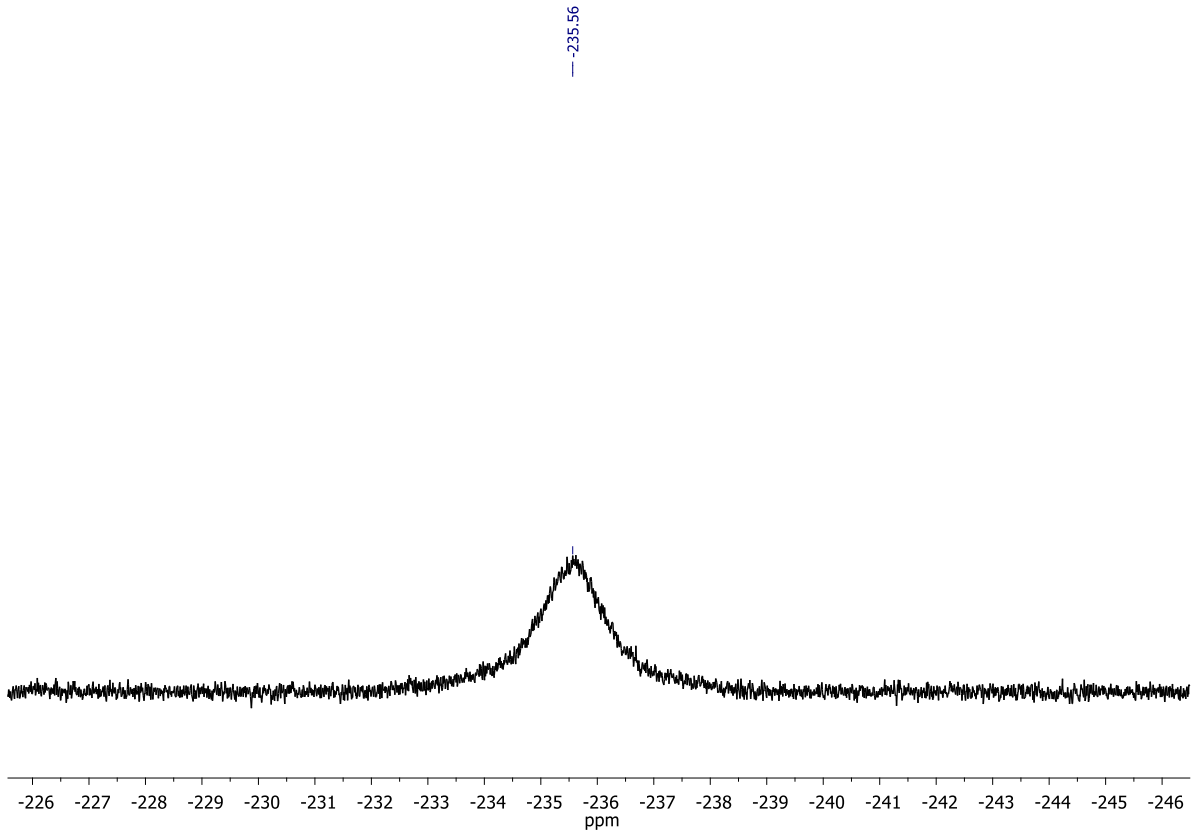
1h (471 MHz)



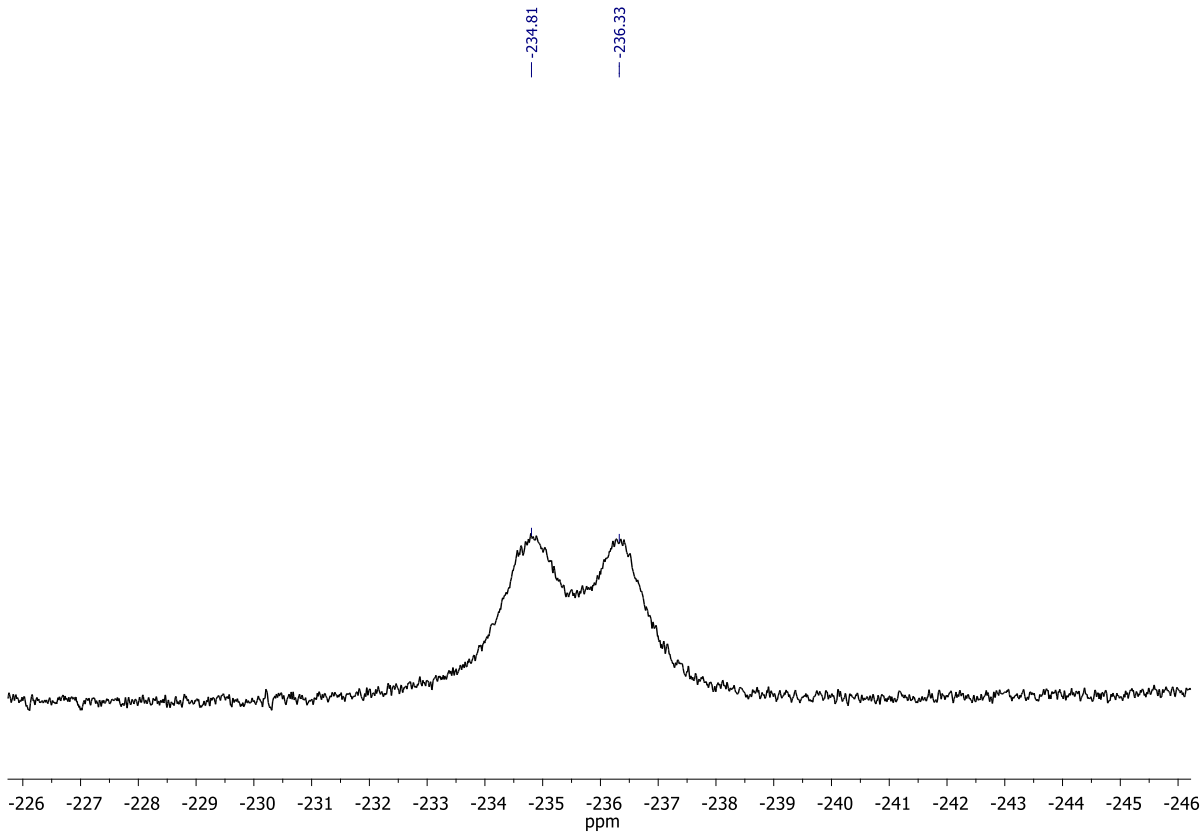
F4 (376 MHz)



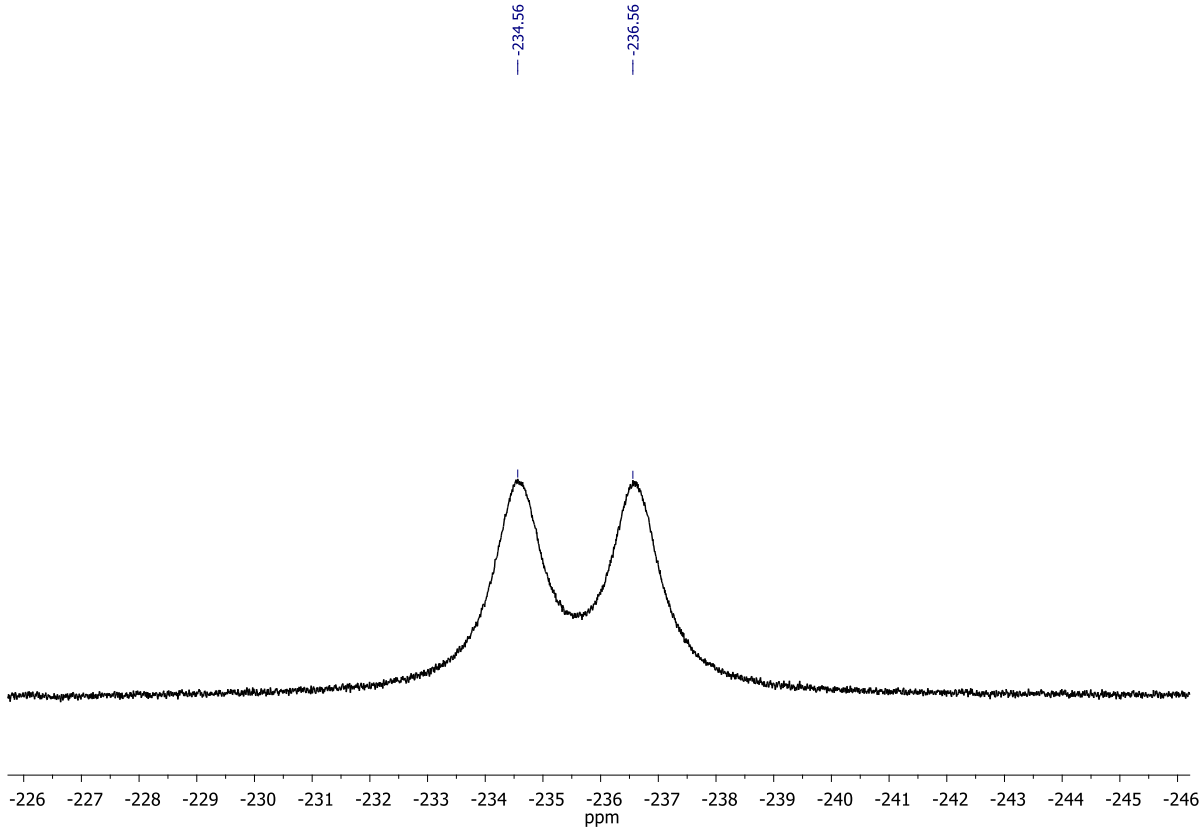
6a (376 MHz)



6c (376 MHz)



6d (471 MHz)


-234.56
-236.56
-226 -227 -228 -229 -230 -231 -232 -233 -234 -235 -236 -237 -238 -239 -240 -241 -242 -243 -244 -245 -246
ppm

Spectroscopic studies in solution

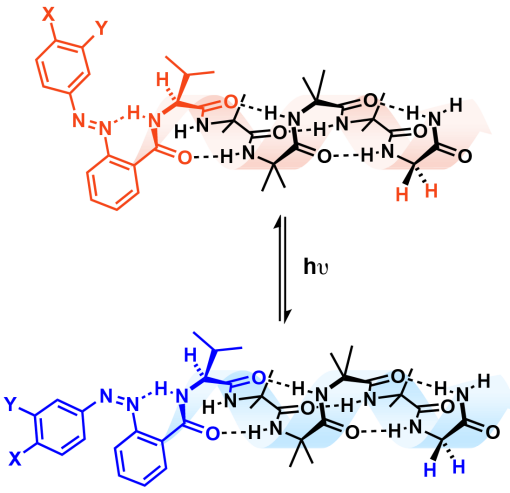
UV-visible absorption spectra were recorded using quartz cuvettes of 1 cm pathlength on an Agilent Cary 5000 UV-Vis-NIR spectrophotometer equipped with a Peltier-thermostat controlled cell holder at 25 ± 0.05 °C. Analytical irradiation experiments (figures S1, S2, S3 and Table S2) were carried out in spectrophotometric grade MeOH (concentration: 1×10^{-4} M) using a Thorlabs DC4100 (4 channel LED driver) equipped with mounted high-power LEDs (models M365L2, M405L2 and M455L3). $E \rightarrow Z$ isomerization was performed using 365 nm light (7.5 nm bandwidth, 360 mW output power, 700 mA current), while light of 405 nm (13 nm bandwidth, 760 mW output power, 1000 mA current) or 455 nm (18 nm bandwidth, 1020 mW output power, 1000 mA current) was used to trigger $Z \rightarrow E$ isomerization. Circular dichroism spectra (CD) were recorded on a Jasco J-815 spectrometer using a 1 mm cell length at 20 ^{o}C.

Pure *E* isomer spectra were obtained after warming the azobenzene-oligomer solutions at 40 °C under nitrogen for 2h in the dark.

Azobenzene-oligomer solutions in CD_3OD (concentration: 1×10^{-4} M) were irradiated at the appropriate wavelength in quartz tubes. *E*/*Z* isomer ratios and thermal $Z \rightarrow E$ isomerization parameters of **1c** and **1d** (fig. S6) were determined by NMR spectroscopy by integrating the peaks at δ ~4.2 and δ ~4.1 ppm (Val $C^{\alpha}H_E$ and Val $C^{\alpha}H_Z$ respectively, see fig. S2).

Quantitative spectra of *E* and *Z* isomers for model azobenzene oligomers **1a**, **1b**, **1c** and **1d** were determined combining UV/Vis and NMR data (see fig. S2).

Fig. S1. UV spectra of model azobenzene oligomers **1a-d** in MeOH solution. Pure *E* isomer (red spectra) and PSS mixture after 15 min at 365 nm (blue spectra).



	X	Y
1a	H	H
1b	H	NO_2
1c	H	OMe
1d	F	OMe

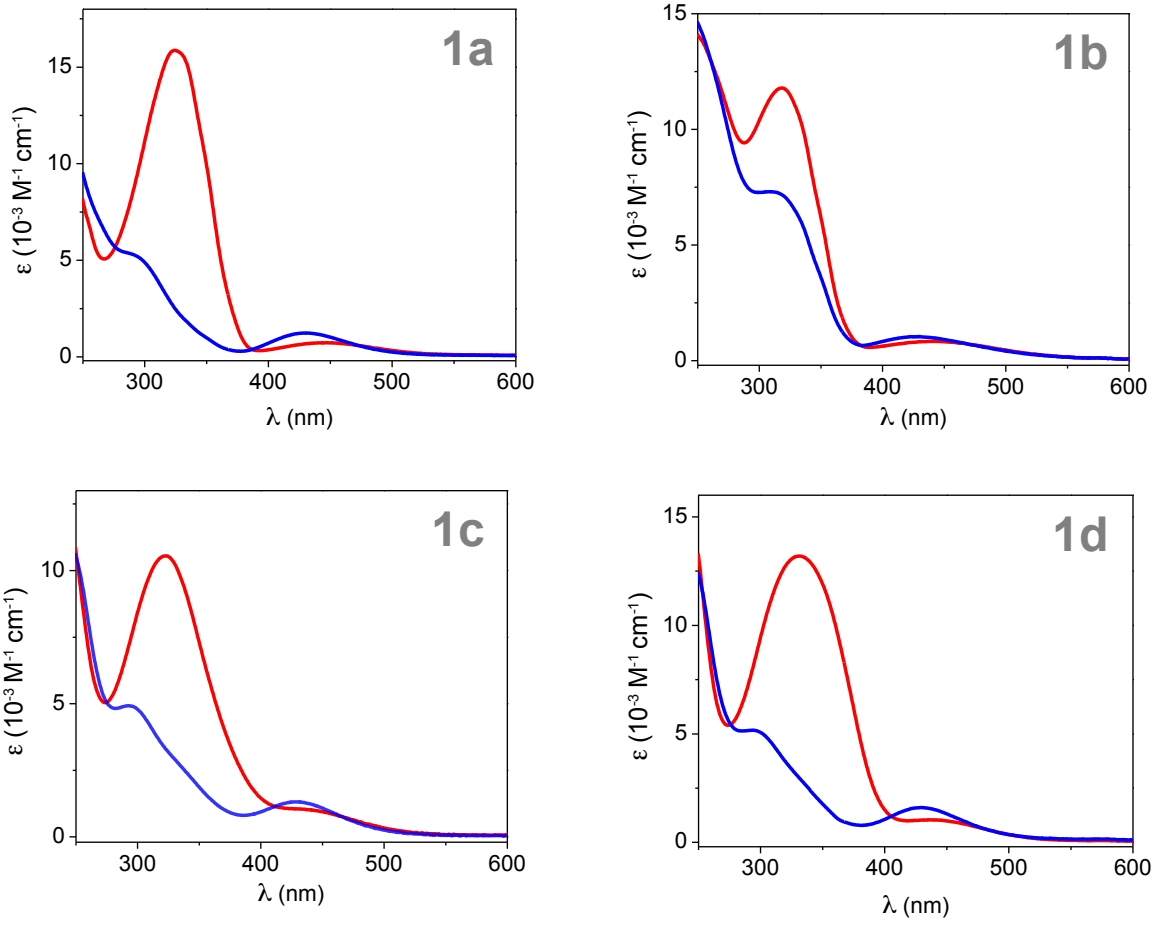
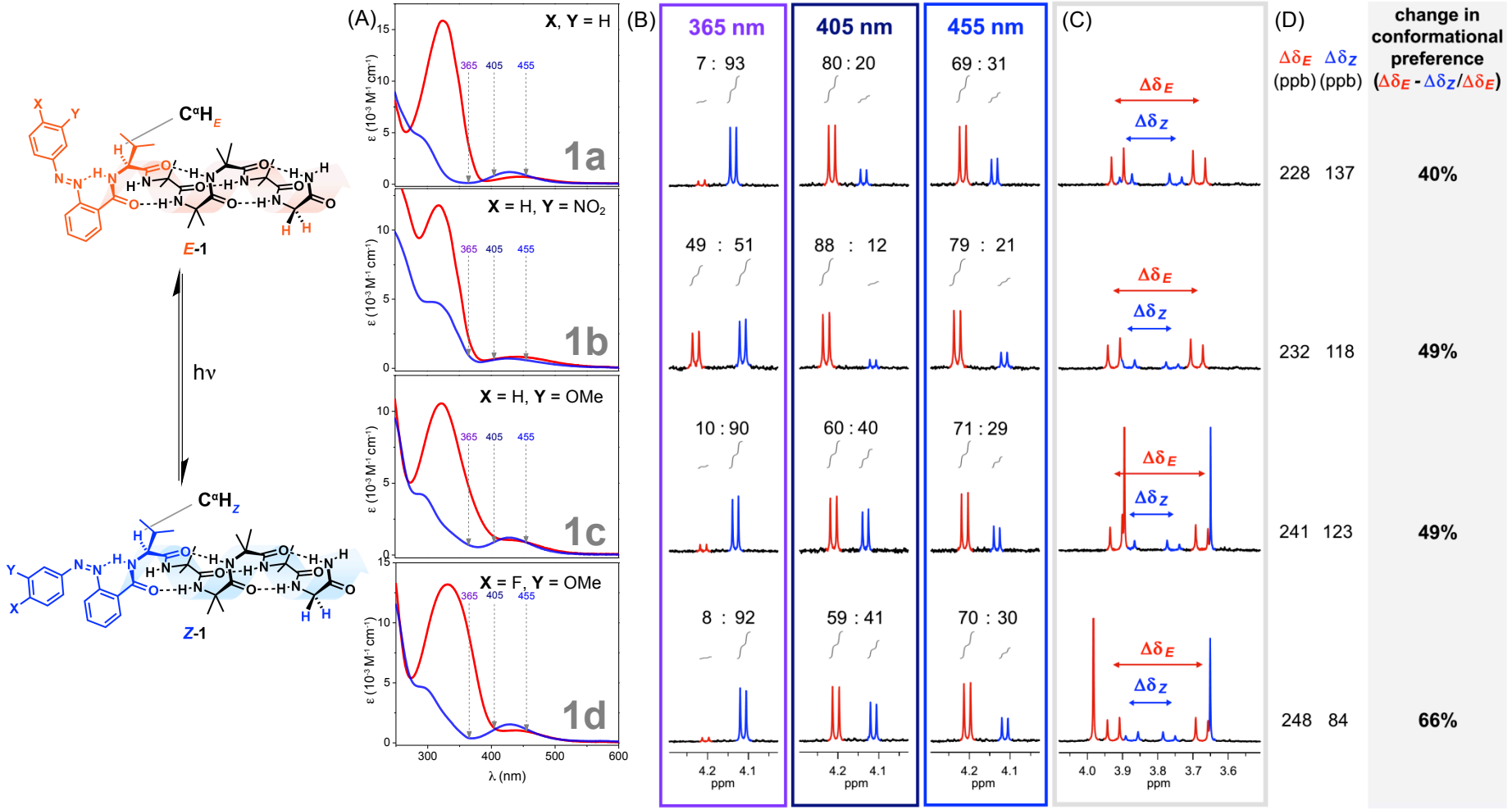
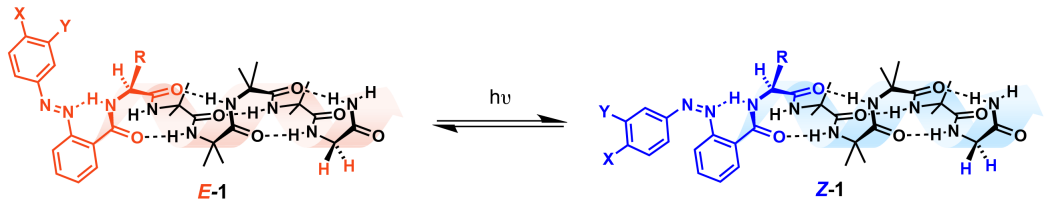


Fig. S2. Photochemical and conformational responsiveness of model azobenzene oligomers **1a-d**



(A) UV spectra of pure *E* and *Z* isomers (red and blue, respectively) of model oligomers **1a-d** in MeOH; (B) NMR spectra ($C^{\alpha}H$ area, CD_3OD) of *E*:*Z* mixtures at photostationary state (PSS) at 365, 405 and 455 nm. The relative integration is also reported; (C) $GlyNH_2$ area (455 nm PSS) showing the different anisochronicities (Δδ) of the reporter protons in each of the *E* or *Z* isomer (red and blue peaks, respectively); (D) Δδ values (ppb) for each *E* or *Z* isomer and change in population distribution, expressed as the relative % difference in Δδ between *E* and *Z* isomers: $(\Delta\delta_E - \Delta\delta_Z)/\Delta\delta_E$.

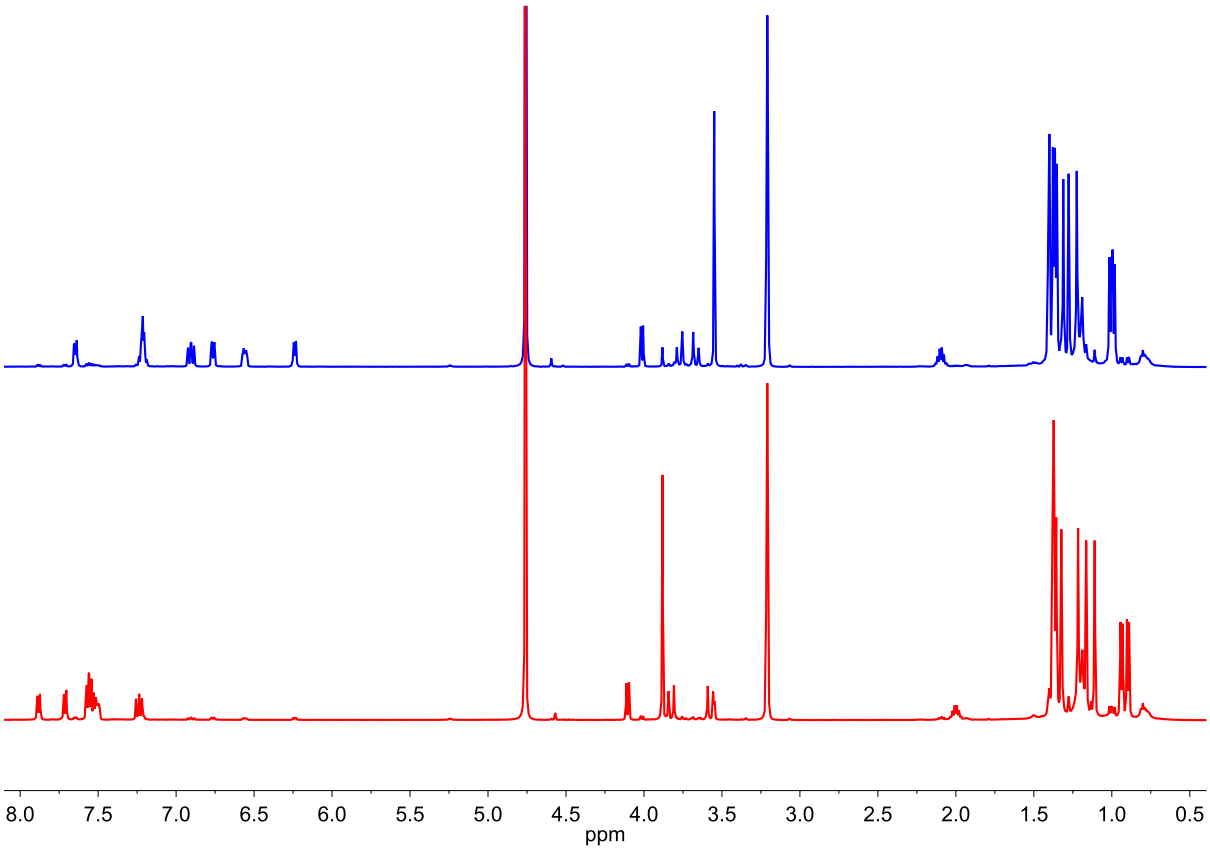
Table S1. Comparison of Δδ values in CD_3OD solution for model oligomers **1a-h**



Val-1 (R = *i*Pr)						Phe-1 (R = Bn)					
	X	Y	$\Delta\delta_E$ (ppb)	$\Delta\delta_Z$ (ppb)	change in (%) ($\Delta\delta_E$ - $\Delta\delta_E$ / $\Delta\delta_E$)·100		X	Y	$\Delta\delta_E$ (ppb)	$\Delta\delta_Z$ (ppb)	change in (%) ($\Delta\delta_E$ - $\Delta\delta_E$ / $\Delta\delta_E$)·100
1a	H	H	228	127	**44**	**1e**	H	H	248	199	**20**
1b	H	NO_2	232	118	**49**	**1f**	H	NO_2	246	208	**15**
1c	H	OMe	241	123	**49**	**1g**	H	OMe	259	188	**27**
1d	F	OMe	248	84	**66**	**1h**	F	OMe	259	188	**27**

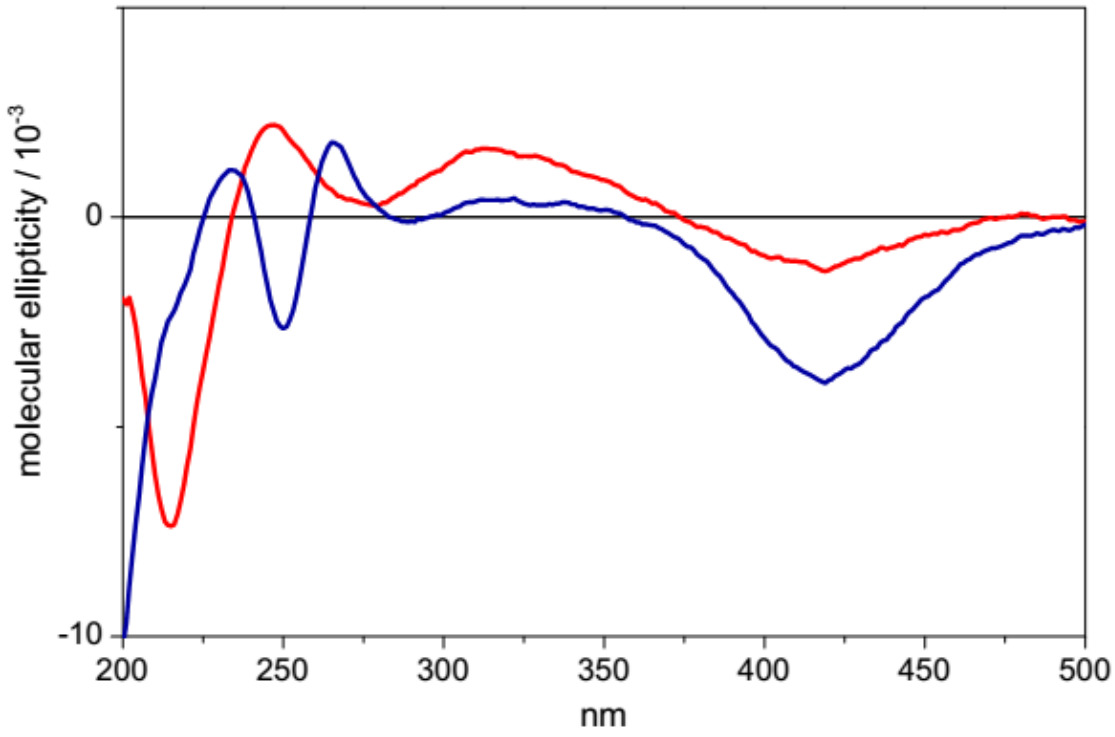
Δδ values (ppb) for each *E* or *Z* isomer of model oligomers **1a-d** (N-terminal residue: Valine) and **1e-h** (N-terminal residue: Phenylalanine). Their relative % change in population distribution (*cfr.* fig. 1 in main text and fig. S2) is also reported. This value is calculated by assuming that Δδ is proportional to helical excess (*12, 58*).

Fig. S3. Irradiation of **1d** in CD_3OD solution



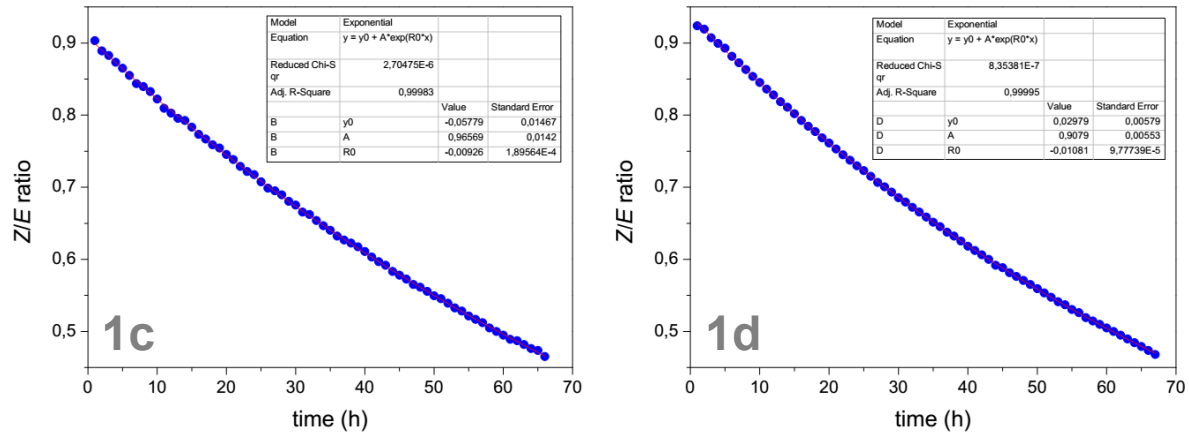
^1H NMR spectra (CD_3OD, 500 MHz) of oligomer **1d** before (red spectrum, mainly *E* isomer) and after 10' irradiation at 365 nm (blue spectrum, 92% *Z* isomer).

Fig. S4. CD spectra of oligomer **1c**



CD spectra of oligomer **1c** in (1M in CH_3OH) before (red spectrum, mainly *E* isomer) and after 10' irradiation at 365 nm (blue spectrum, mainly *Z* isomer). The absorption of the azobenzene chromophore obscures the diagnostic amide region (200-230 nm) indicative of secondary structure conformation, therefore only changes in the chiral environment around the azobenzene group can be reliably observed.

Fig. S5. Thermal $Z \rightarrow E$ relaxation parameters for **1c** and **1d**



1c

concentration: 10^{-2} M in CD_3OD

$k_{Z \rightarrow E} = 0.00926 \pm 0.00019$ h^{-1}

$t_{1/2} = \ln(2) / k = 0.693 / 0.00926$ $h^{-1} = 74.7 \pm 1.5$ h^{-1}

1d

concentration: 10^{-2} M in CD_3OD

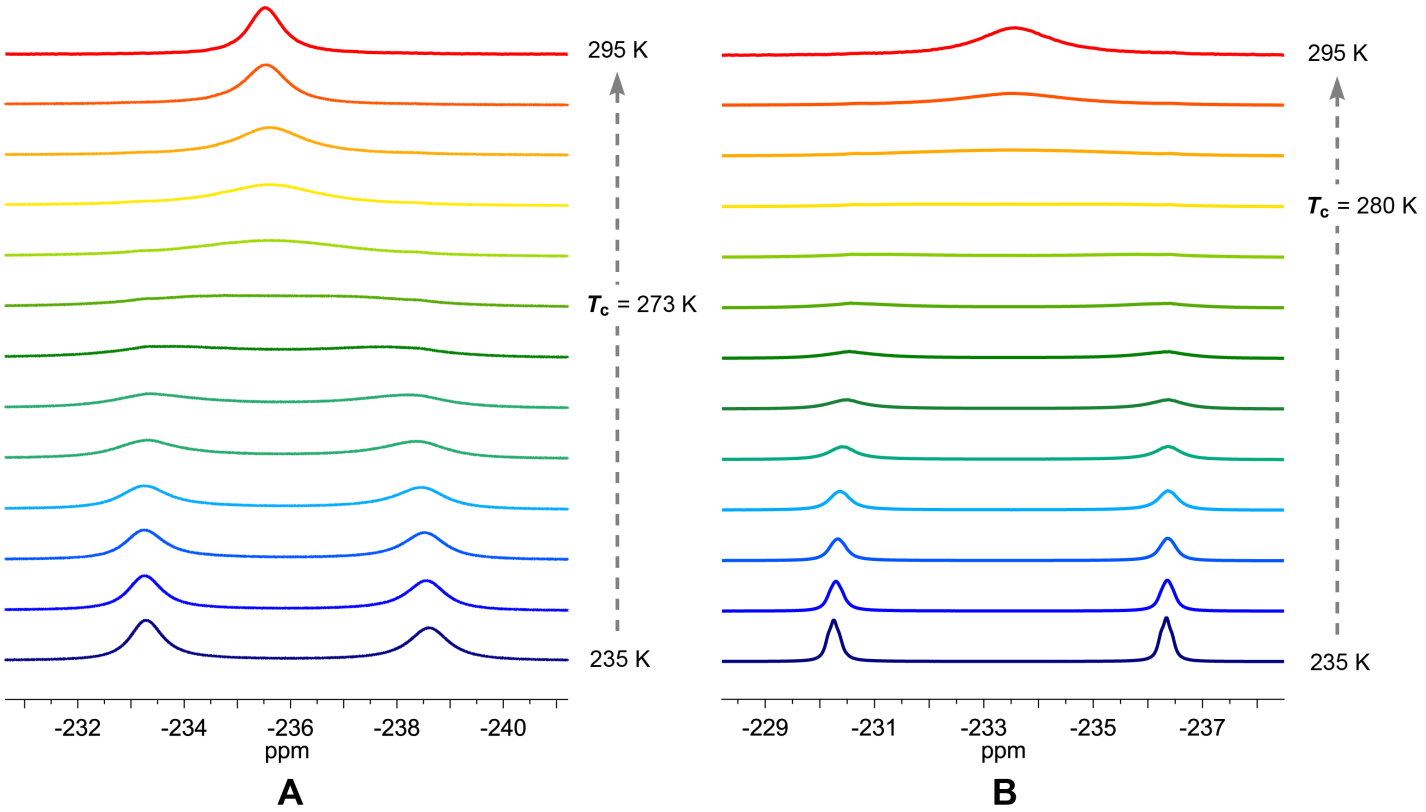
$k_{Z \rightarrow E} = 0.01081 \pm 0.000098$ h^{-1}

$t_{1/2} = \ln(2) / k = 0.693 / 0.01081$ $h^{-1} = 64.0 \pm 0.6$ h^{-1}

Table S2. Molar extinction coefficients (ε, $L \cdot mol^{-1} \cdot cm^{-1}$) for *E* ($\pi$–$\pi^*$ and n–π^* transitions) and *Z* (n–π^* transition) isomers of **1a-d**:

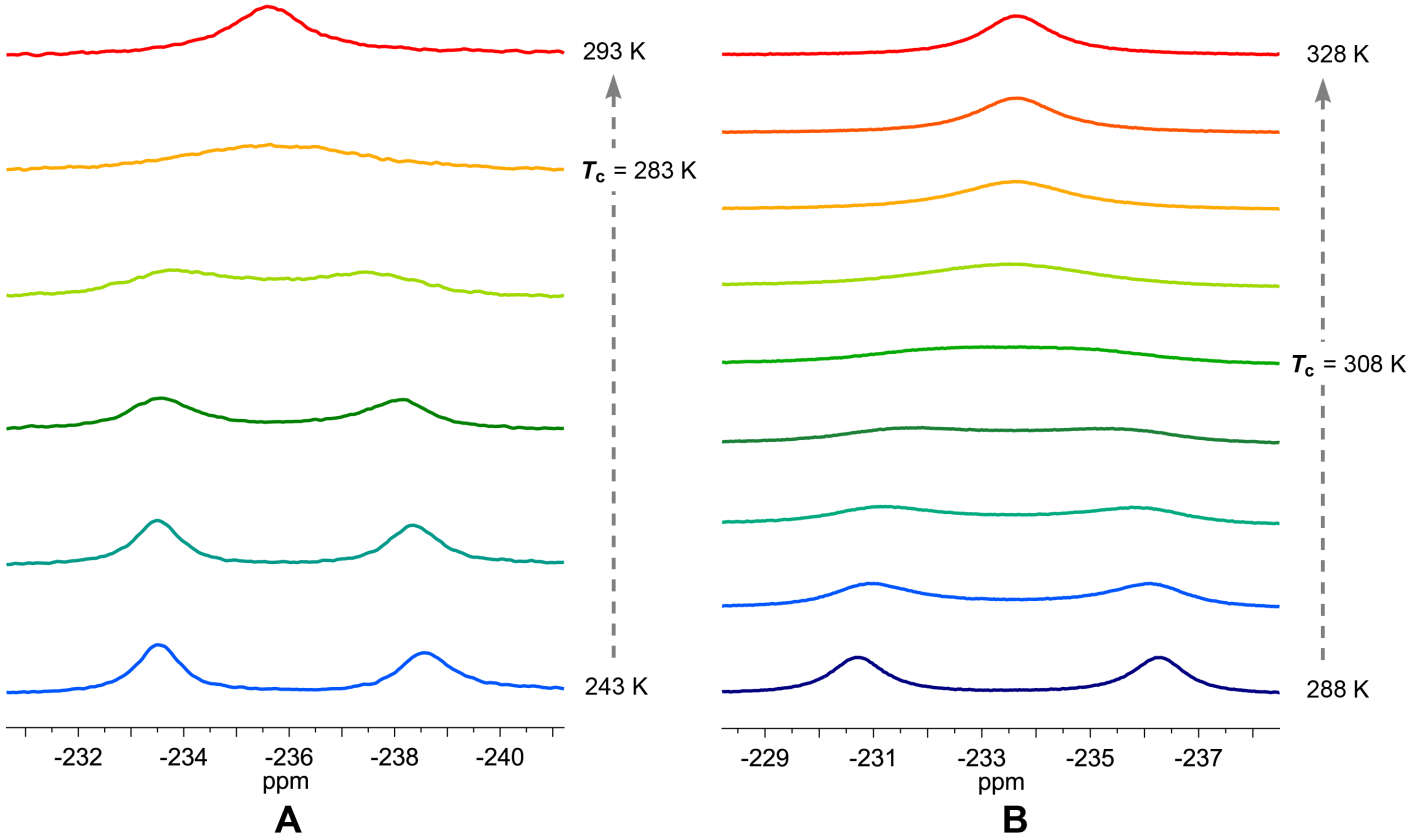
	1a (λ_{max}, nm)	**1b** (λ_{max}, nm)	**1c** (λ_{max}, nm)	**1d** (λ_{max}, nm)
E (π–π^*; n–π^*)	15860 (324); 730 (445)	11790 (317); 830 (443)	10550 (323); 1040 (436)	13200 (331); 1030 (439)
Z (n–π^*)	1230 (430)	700 (426)	1200 (429)	1610 (430)

Fig. S6. ^{19}F VT-NMR of foldamer **3a**



^{19}F VT NMR spectra (magnet strength: 476 MHz) of fluorinated oligomer **3a** in CD_3OH (A) and in $CDCl_3$ (B). At the coalescence temperature (T_c) of 273 K (0 °C) in CD_3OH and 280 K (+7 °C) in $CDCl_3$ the rate of screw-sense inversion approximates to $k = \frac{\pi\delta\upsilon}{\sqrt{2}} \sim 6000\ s^{-1}$, indicating that at 293 K screw sense interconversion occurs faster than this rate in both solvents.

Fig. S7. ^{19}F VT-NMR of foldamer **6a**



^{19}F VT NMR spectra (magnet strength: 476 MHz) of fluorinated oligomer **6a** in CD_3OH (A) and in $CDCl_3$ (B). At the coalescence temperature (T_c) of 283 K (+10 °C) in CD_3OH and 308 K (+35 °C) in $CDCl_3$ the rate of screw-sense inversion approximates to $k = \frac{\pi\delta\upsilon}{\sqrt{2}} \sim 6000\ s^{-1}$, indicating that at 293 K screw sense interconversion occurs faster than this rate in CD_3OH but more slowly that this rate in $CDCl_3$.

Spectroscopic studies in the membrane phase

General procedure (E): preparation of DOPC lipid bilayers embedded with fluorinated foldamers

Multilamellar liposomes doped with fluorinated foldamers were prepared by co-dissolving the oligomer and the lipids (1:40-1:9 oligomer/DOPC w/w ratio) in chloroform. The solvent was removed under reduced pressure and the resulting foldamer/lipid film was placed under high vacuum for >1 h, after which milliQ water was added (0.1 mL per 10 mg of DOPC used). After shaking the mixture with a vortex mixer until visually homogeneous (5 to 30 min), the suspension was freeze-dried overnight and rehydrated with Dulbecco's phosphate buffer solution (pH 7.2, 0.1 mL per 10 mg of DOPC). The suspension was again shaken until homogeneous and then centrifuged in a microfuge for 5 to 15 min at 13K rpm. The supernatant aqueous layer (Fig. S7A and S7B) was carefully removed with a micropipette and the viscous lipid phase (Fig. S7C) loaded into a MAS zirconia rotor (Fig. S7D) using a centrifuge or a micropipette. All the samples were freshly made and directly used for ss-NMR experiments. For time-dependent ss-NMR measurements, the lipid-foldamer mixtures were left in the capped MAS rotor in the dark.

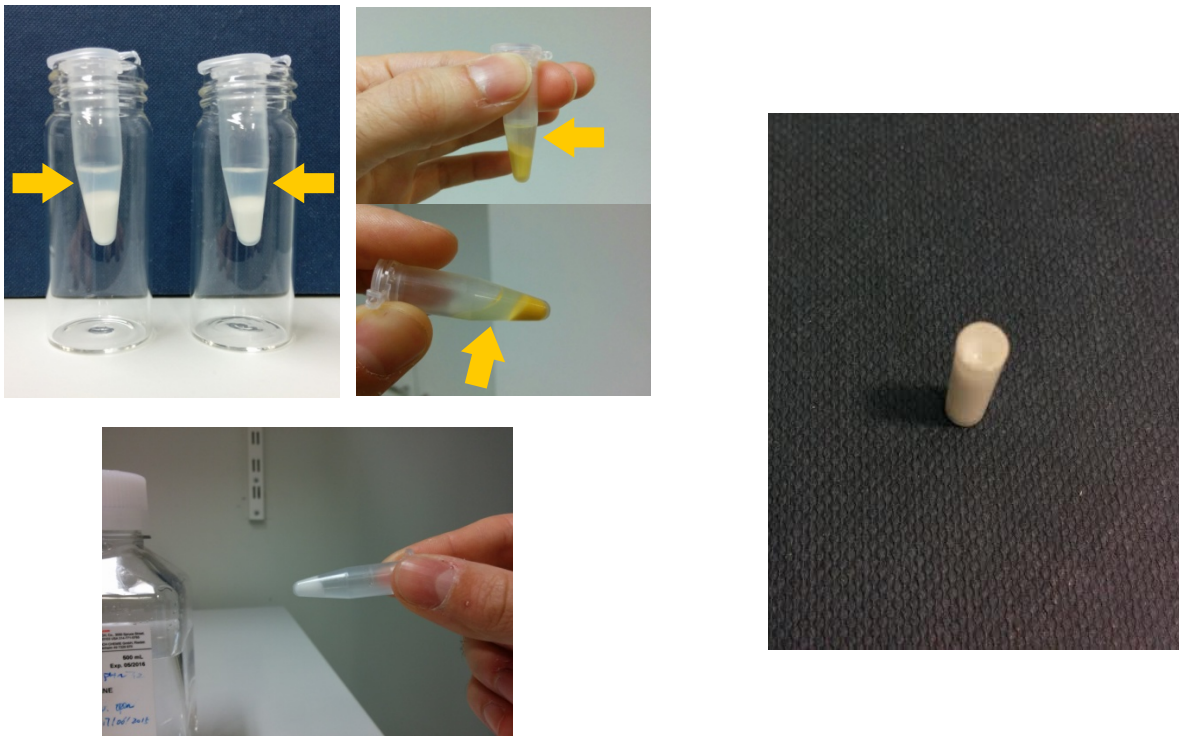
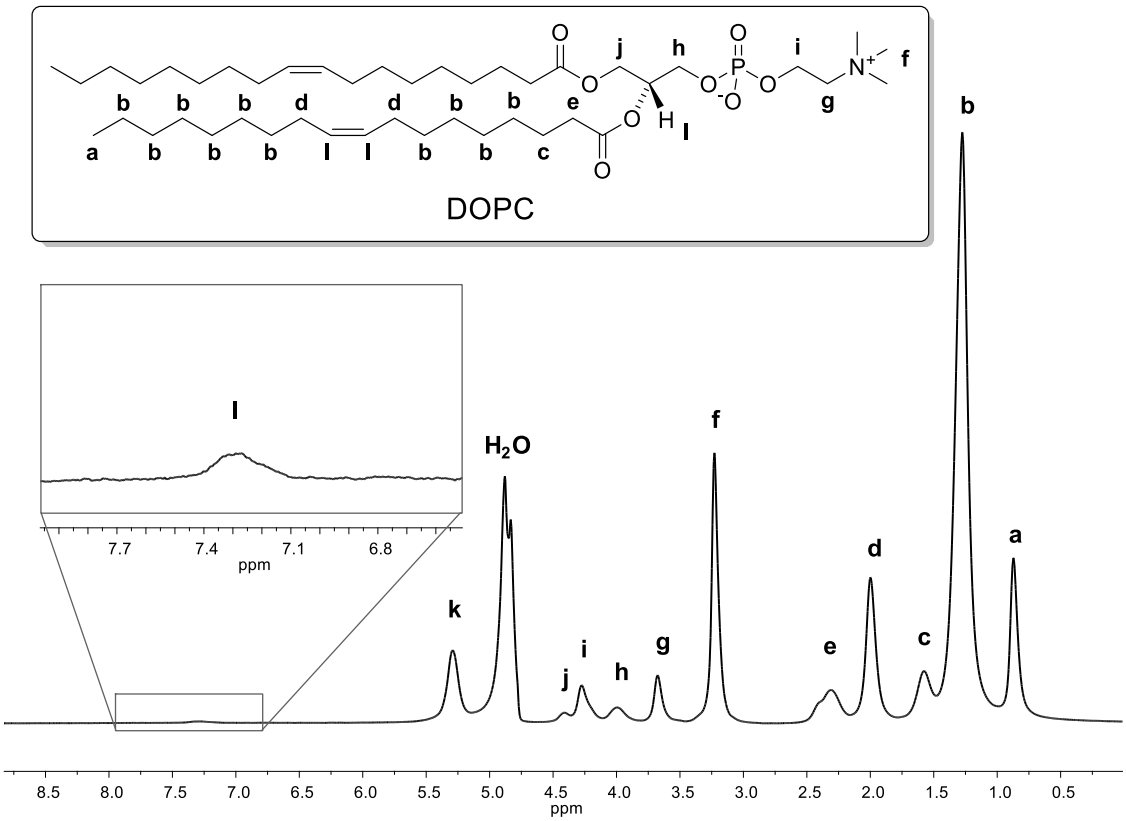


Fig. S8. (A-C) Preparation of multilamellar foldamer/phospholipid liposomes. The arrows (in A and B) show the top aqueous layer which is separated after centrifugation (C); (D) MAS zirconia rotor filled with freshly made foldamer/DOPC sample.

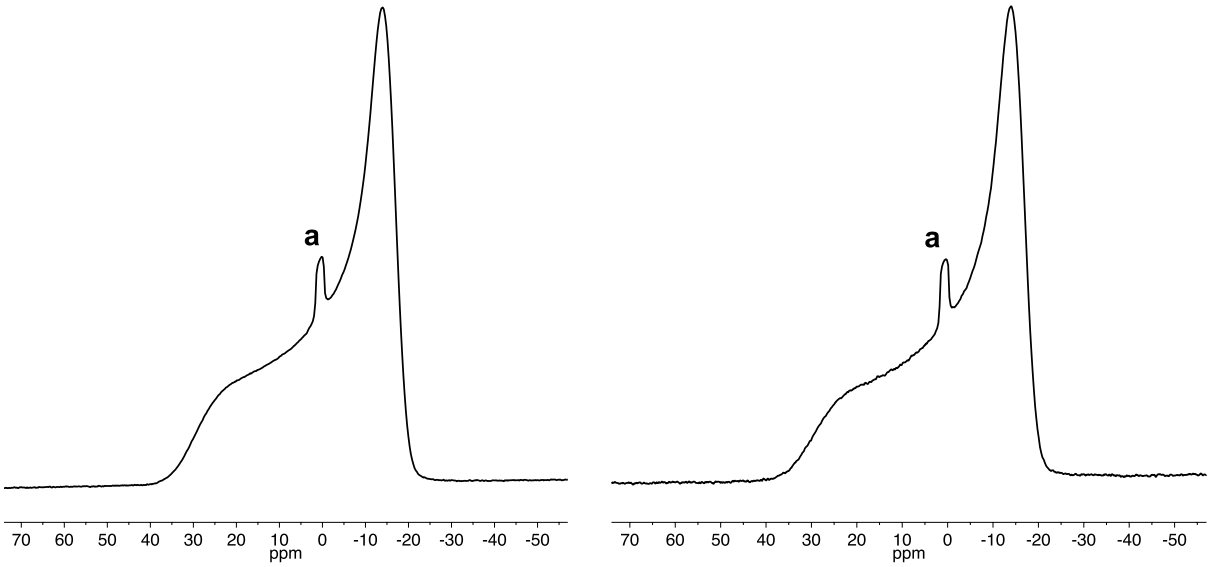
Fig. S9. ^{1}H ss-NMR of **6d** in DOPC



Water-suppressed ^{1}H MAS NMR spectrum of DOPC phospholipid bilayers containing 5% of foldamer **6d**. Assignments of the DOPC signals are made according to Yau *et. al* (*15*) and correspond to the labels on the DOPC molecule shown above the spectrum, with the CH_3 peak (**a**) referenced to δ 0.9 ppm. A 16-fold expansion of the low-field region around δ 7.3 ppm highlights the foldamer amides' peak. The lipid bilayer is in a fluid disordered phase characterised by rapid lateral and axial motion. This mobility, coupled with the MAS, results in well-resolved peaks that have been reported before (*39, 40, 59*). As for the lipid ones, the foldamer amides's peak at δ 7.3 ppm indicates that the foldamer is also undergoing rapid motions and is freely moving in the lipid bilayer.

The spectrum was acquired at 298 K on a Bruker Avance II 500 MHz spectrometer using a 4 mm MAS probe operating at frequencies of 500.1013 MHz (^{1}H) with a spinrate of 8 kHz. The ^{1}H experiment was carried out with a typical π/2 pulse length of 7 μs, a relaxation delay of 4s and processed with 2 Hz line broadening.

Fig. S10. ^{31}P NMR studies



^{31}P NMR spectra (500 MHz, 298 K, static conditions) of DOPC phospholipid bilayers (left) and of DOPC phospholipid bilayers containing 5% of foldamer **3e** (right). The samples were prepared according to the general procedure (E). Both spectra are consistent with those of a powder line shape and are indicative of a fluid lamellar phase (*41*). The small peak at 0 ppm (**a**) is assigned to the phosphate anion (phosphate buffer solution is used during sample preparation).

General procedure (F): irradiation of the DOPC bilayers

Freshly prepared multilamellar liposomes (see general procedure (E)) containing the fluorinated foldamers were transferred in a quartz cuvette (path length: 1 mm) using a Gilson micropipette and irradiated with the chosen wavelength using the same LED apparatus used for liquid-phase experiments for the appropriate amount of time (3-10 min, fig. S11). The illuminated phospholipid mixture was then directly loaded into the MAS rotor using a centrifuge (10 s at 1K rpm), with the whole transfer procedure taking typically less than 1 minute. When a second irradiation on the same sample was required, this procedure was repeated by spinning out the previously illuminated lipid-oligomer mixture from the MAS rotor back into a quartz cuvette, followed by irradiation and loading into the MAS rotor.

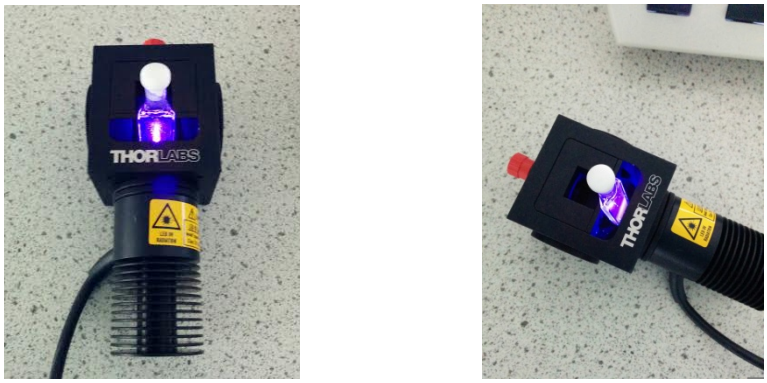


Fig. S11. LED irradiation of the phospholipid-oligomer samples in 1 mm quartz cuvettes using a Thorlabs DC4100 apparatus.

Control experiments

1) Concentration dependence assay

Following general procedure (E), three samples were prepared using **3d** (CbzPheAib$_4$FibTEG) and DOPC in different phospholipid/oligomer ratios (**A**, **B** or **C**) and the relative ^{19}F ss-NMR spectra were collected (fig. S12). The specifications of each sample are summarized in the following table:

sample	oligomer/DOPC (mg)	ratio (w/w)	number of scans (NS)	T (K)	^{19}F δ_F (ppm)	$\Delta\delta$
A	1.5 / 50	3%	1044	293	-232.23; -233.15	0.92
B	4.5 / 40	10%	963	293	-232.23; -233.12	0.89
C	6 / 35	15%	1175	293	-232.24; -233.14	0.90

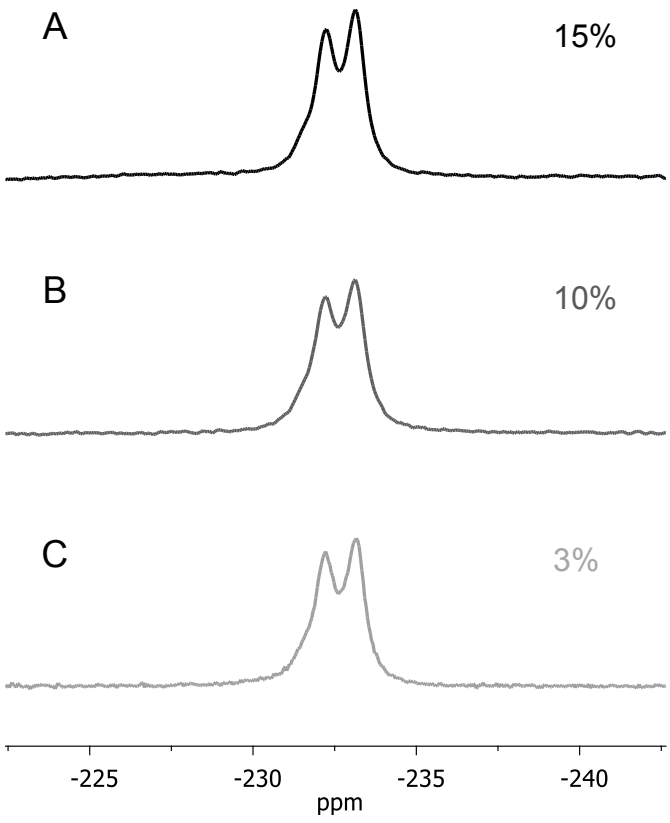


Fig. S12. ^{19}F ss-NMR spectra of **3d** at different oligomer/DOPC ratios (see above Table). Each spectrum was acquired at 10 KHz spinning rate and processed with 20 Hz line broadening.

2) Intermolecular communication of helicity assay

Following general procedure (E), **3d** (2 mg), Cbz(aMv)$_2$Aib$_4$OMe (2 mg, see Ref. (*57*)) and DOPC (40 mg) were used to prepare mixed oligomer/lipid sample (**A**, 5% + 5% w/w). The ^{19}F ss-NMR spectrum was recorded and compared (fig. S13) with that of **3d** in DOPC (**B**, 5% w/w), prepared using general procedure (E) starting from **3d** (2 mg) and DOPC (40 mg). The following table reports the spectral features of each sample:

sample	components (mg) in 40 mg DOPC	ratio (w/w)	number of scans (NS)	^{19}F δ_F (ppm)	$\Delta\delta$
A	**3d** (2) + Cbz(aMv)$_2$Aib$_4$OMe (2)	5% / 5%	1038	-232.27; -233.16	0.89
B	**3d** (2)	5%	962	-232.16; -233.05	0.89

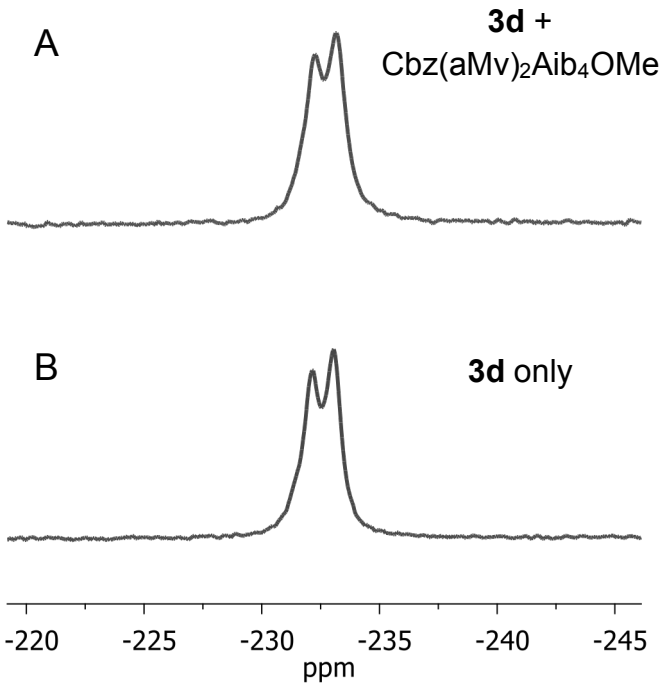


Fig. S13. ^{19}F ss-NMR spectra of sample (A) (**3d** + Cbz(aMv)$_2$Aib$_4$OMe 5% + 5% in DOPC) and (B) (**3d** 5% in DOPC). Each spectrum was acquired at 293 K (10 KHz spinning rate) and processed with 20 Hz line broadening.

3) Irradiation assay (no azobenzene chromophore present)

Following general procedure (E), **3d** and DOPC were used (13.5 and 120 mg respectively) to prepare a 10% oligomer/lipid sample. This mixture was split in three equal portions and each portion irradiated for 5 minutes as described in general procedure (F) using LED light at either 365 (**A**), 405 (**B**) or 455 nm (**C**). A ^{19}F ss-NMR spectrum was run immediately after each sample have been irradiated (fig. S14). The following table reports the experimental conditions for each experiment:

sample	wavelength (nm)	time (min)	output power (mW)	number of scans (NS)	^{19}F δ_F (ppm)	$\Delta\delta$
A	365	5	360	985	-232.24; -233.12	0.88
B	405	5	760	878	-232.23; -233.12	0.89
C	455	5	1020	775	-232.24; -233.13	0.89

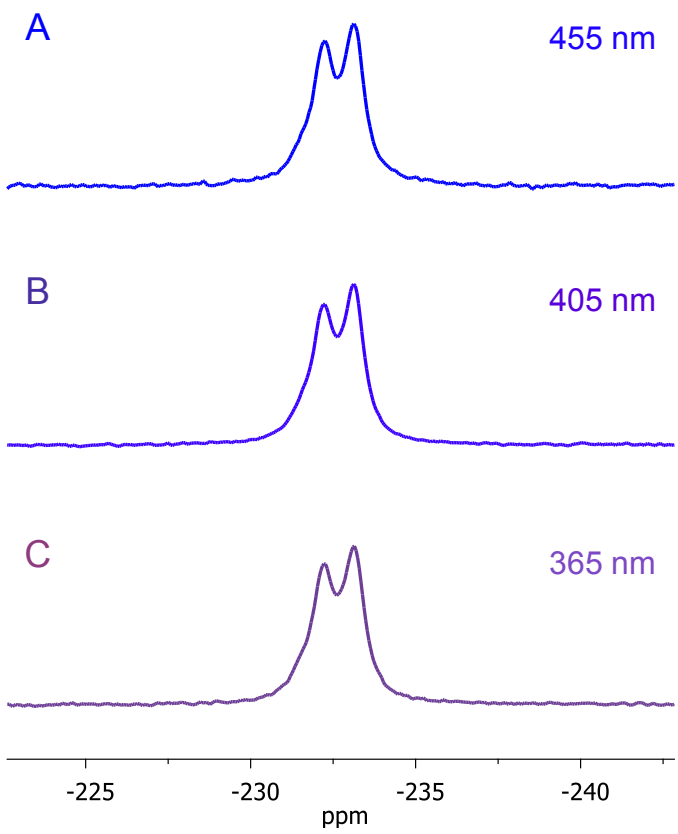
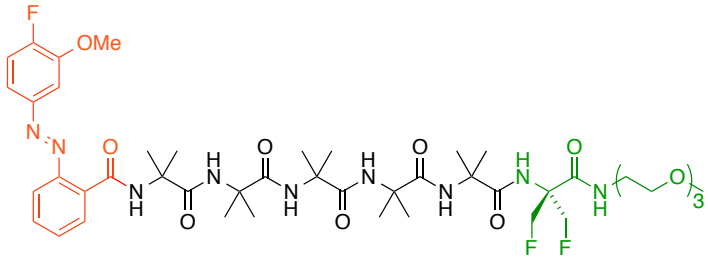


Fig. S14. ^{19}F ss-NMR spectra of **3d** (10% in DOPC) after exposure to different wavelengths (see above Table). Each spectrum was acquired at 293 K (10 KHz spinning rate) and processed with 20 Hz line broadening.

4) Irradiation assay (no chiral stereocontroller present)

Following general procedure (E), achiral oligomer **3g** and DOPC were used (2 and 40 mg respectively) to prepare a 5% foldamer/lipid sample. This mixture was split in three equal portions and each portion irradiated for 5 minutes as described in general procedure (F) using LED light at either 365 (**A**), 405 (**B**) or 455 nm (**C**). A ^{19}F ss-NMR spectrum was run immediately after each sample have been irradiated (fig. S15). No change upon azobenzene photoswitching is observed in the broad singlet at δ –234 ppm, confirming that the achiral, but helical environment in which the FibTEG reporter is located is in fast exchange.

The following table reports the experimental conditions for each experiment:



3g

sample	wavelength (nm)	time (min)	output power (mW)	number of scans (NS)	*E/Z* integral ratio
A	365	5	360	502	68/32
B	405	5	760	756	63/37
C	455	5	1020	325	16/84

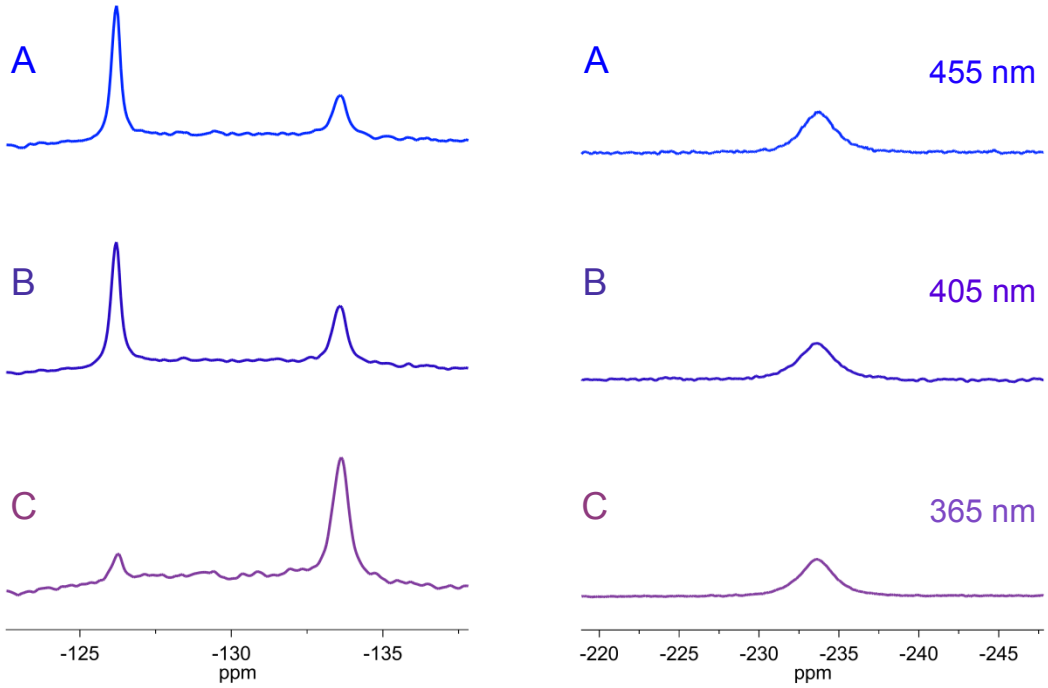
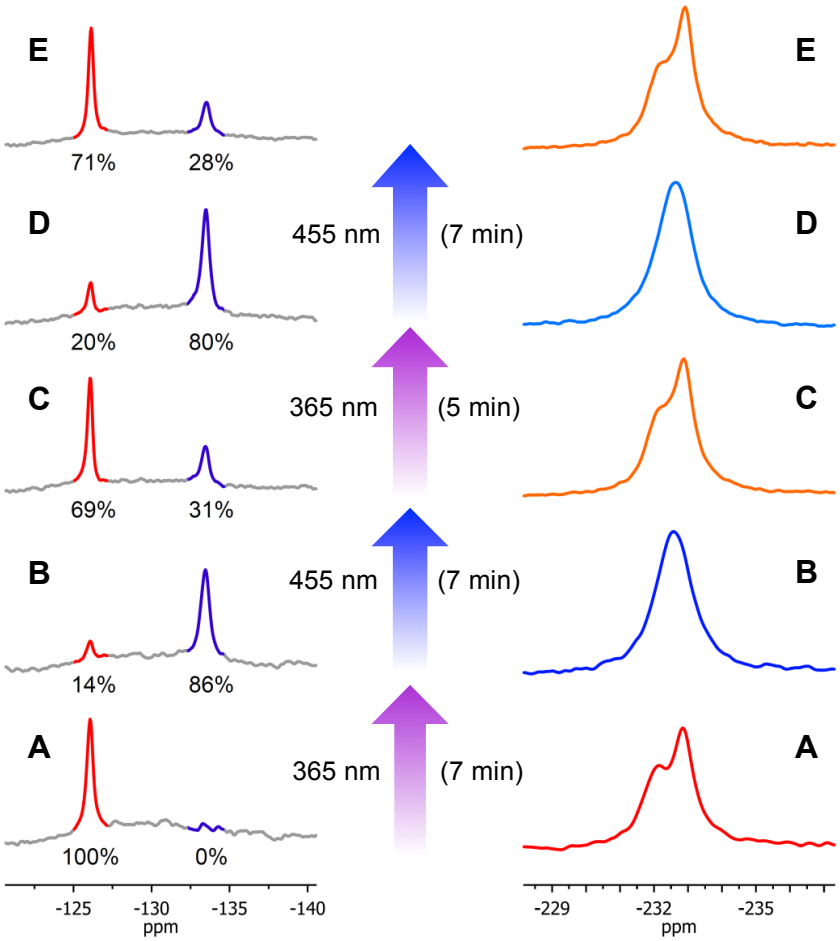


Fig. S15. ^{19}F ss-NMR spectra of **3g** (5% in DOPC) after exposure to different irradiation wavelengths. Each spectrum was acquired at 293 K (10 KHz spinning rate) and processed with 20 Hz line broadening.

Additional photoswitching experiments

Fig. S16. Reversible photoswitching of **4** in DOPC



^{19}F ss-NMR spectra showing the reversible behavior of photoswitchable foldamer **4** (1% in DOPC) during different illumination cycles (**A**-**E**). Each spectrum has been processed using 20 Hz line broadening. Irradiation times and *E*/*Z* ratios based on the integration of the azobenzene ^{19}F signals (δ –125 to –135 ppm) are reported and summarized in the graph below:

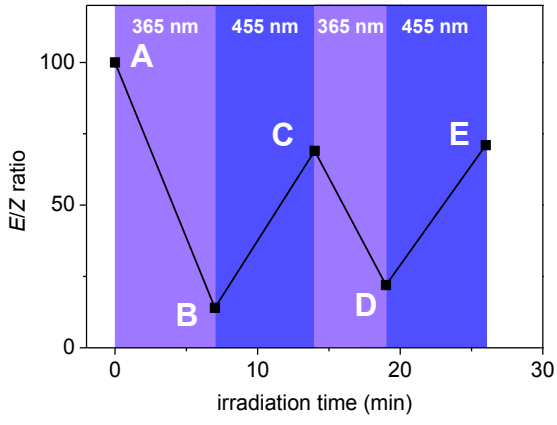
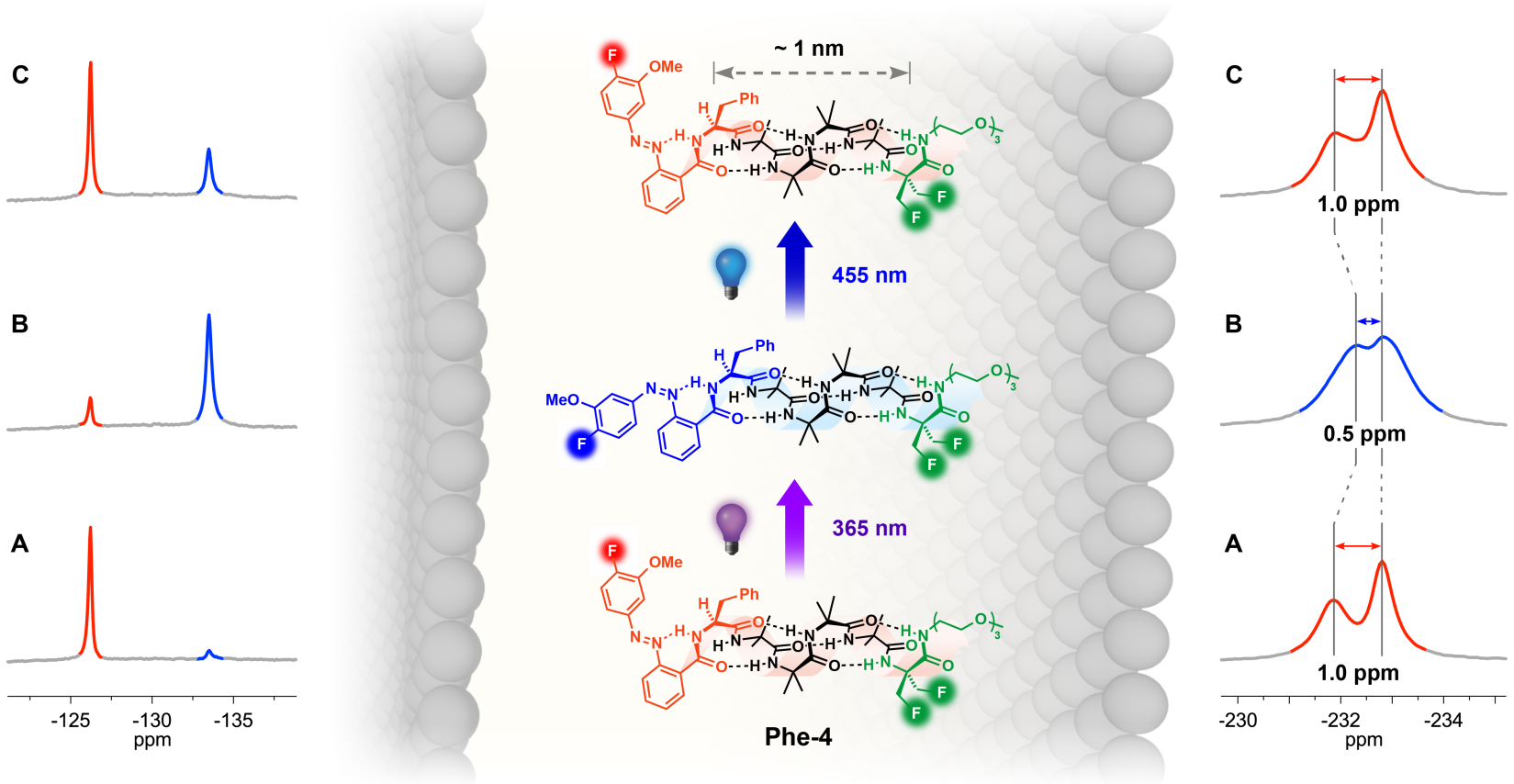
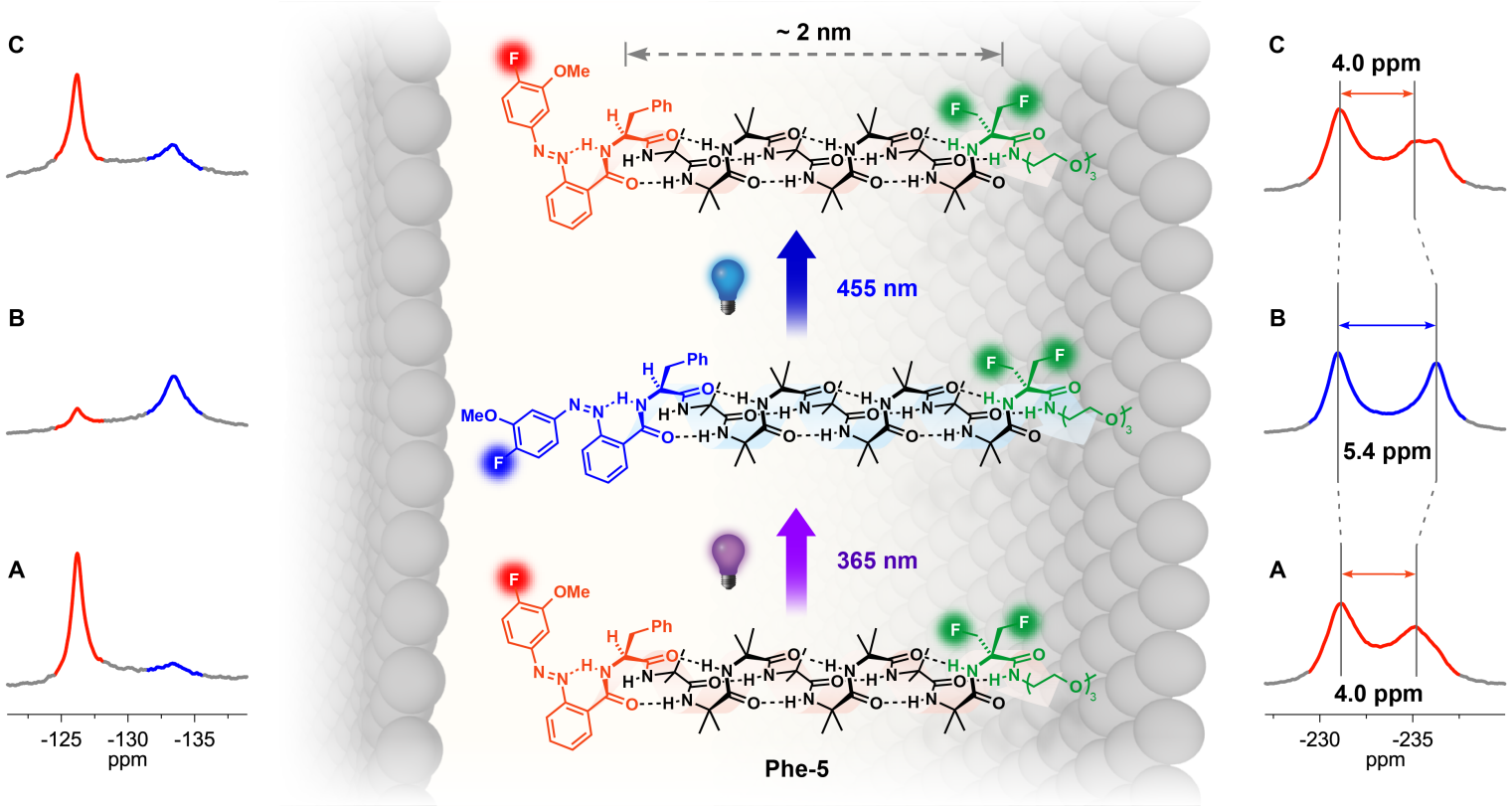


Fig. S17. Photoswitching of **Phe-4** in DOPC



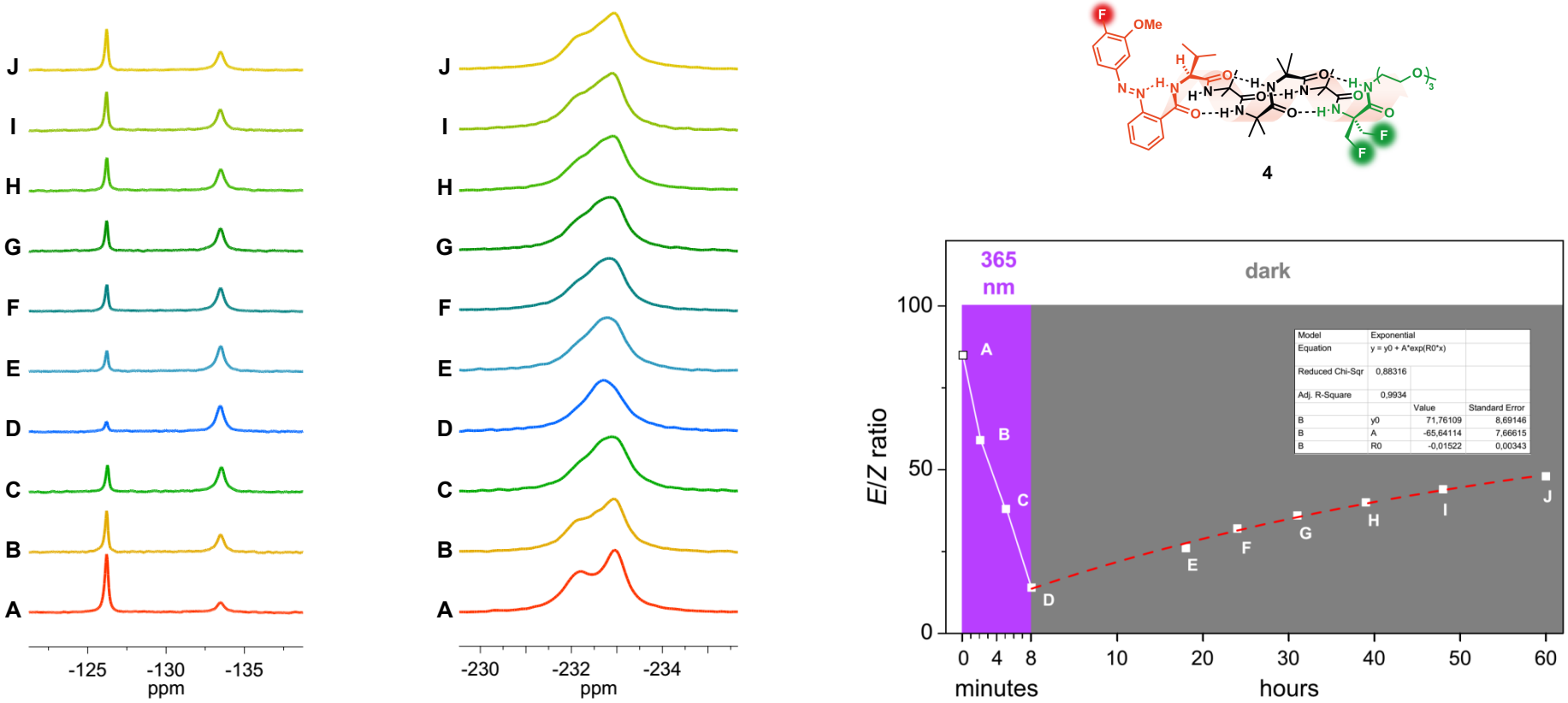
Conformational switching of rhodopsin mimic **Phe-4** by irradiation in a DOPC phospholipid bilayer (10% w/w), showing portions of the ^{19}F ss-NMR spectra corresponding to the N-terminal fluoroarene substituent (δ –125 to –135 ppm, left) and the C terminal FibTEG reporter (δ –230 to –235 ppm, right; the different Δδ separations observed at each irradiation stage are reported). (**A**) *E*-rich sample (96:4 *E*/*Z* azobenzene ratio); (**B**) same sample after 5 min irradiation at 365 nm (13:87 *E*/*Z* ratio) and (**C**) after subsequent 5 min irradiation at 455 nm (67:33 *E*/*Z* ratio).

Fig. S18. Photoswitching of **Phe-5** in DOPC



Conformational switching of rhodopsin mimic **Phe-5** by irradiation in a DOPC phospholipid bilayer (5% w/w), showing portions of the ^{19}F ss-NMR spectra corresponding to the N-terminal fluoroarene substituent (δ –125 to –135 ppm, left) and the C terminal FibTEG reporter (δ –230 to –235 ppm, right; the different Δδ separations observed at each irradiation stage are reported). (**A**) *E*-rich sample (95:5 *E*/*Z* azobenzene ratio); (**B**) same sample after 5 min irradiation at 365 nm (16:84 *E*/*Z* ratio) and (**C**) after subsequent 5 min irradiation at 455 nm (69:31 *E*/*Z* ratio).

Fig. S19. Photoswitching and $Z \rightarrow E$ thermal relaxation of **4** in DOPC

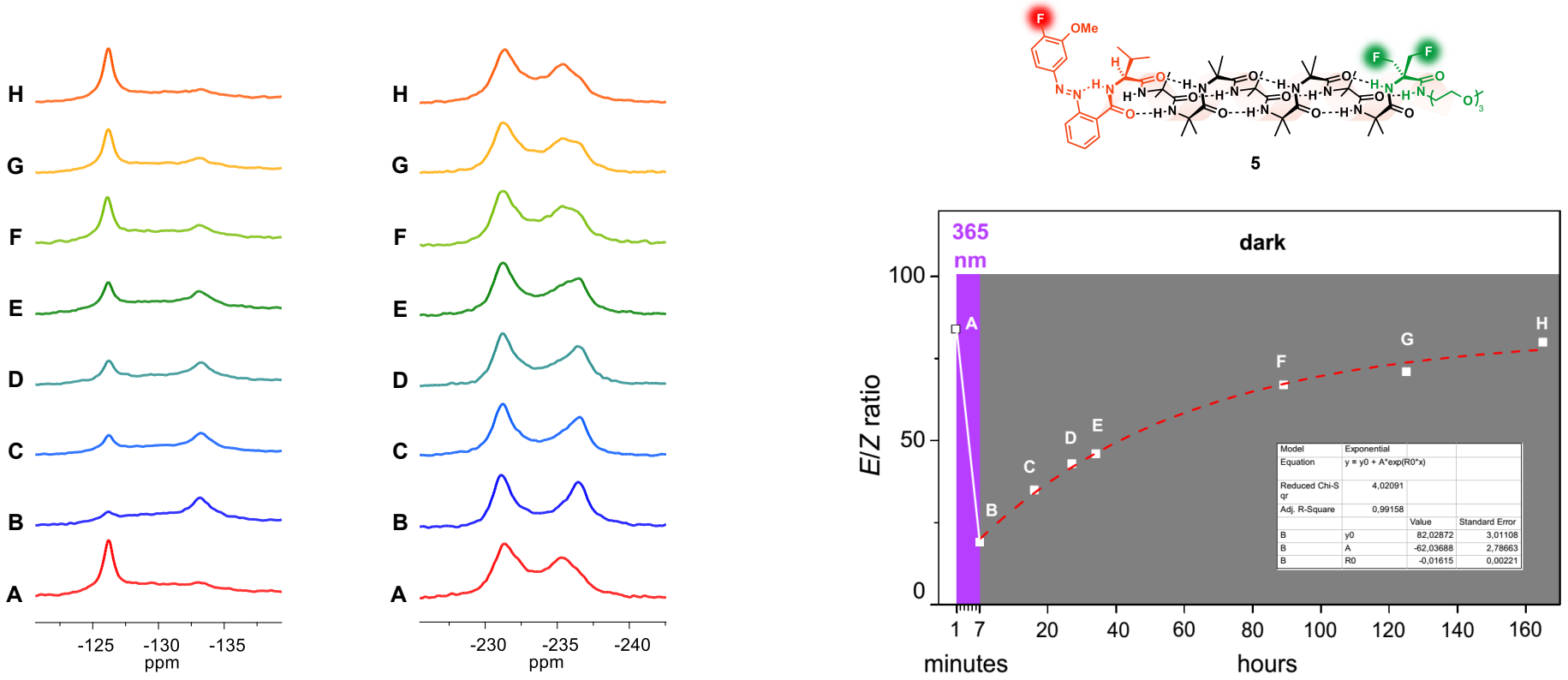


^{9}F ss-NMR spectra showing the irradiation (**A**-**D**) and $Z \rightarrow E$ thermal relaxation (**D**-**J**) of foldamer **4** (10% in DOPC). The graph on the right reports the variation of the integral ratio of the azobenzene ^{19}F peaks (δ –126 to –133 ppm) upon 365 nm irradiation and during back-switching in the dark. Fitting of the thermal relaxation data gives the following parameters:

$k_{Z \rightarrow E} = 0.01522 \pm 0.00343$ h^{-1}

$t_{1/2} = \ln(2) / k = 45.5 \pm 10.2$ h^{-1} [*cfr.* thermal relaxation in CD_3OD solution of compound **1d** (fig. **S5**): $t_{1/2} = 64.0$ h]

Fig. S20. Photoswitching and $Z \rightarrow E$ thermal relaxation of **5** in DOPC

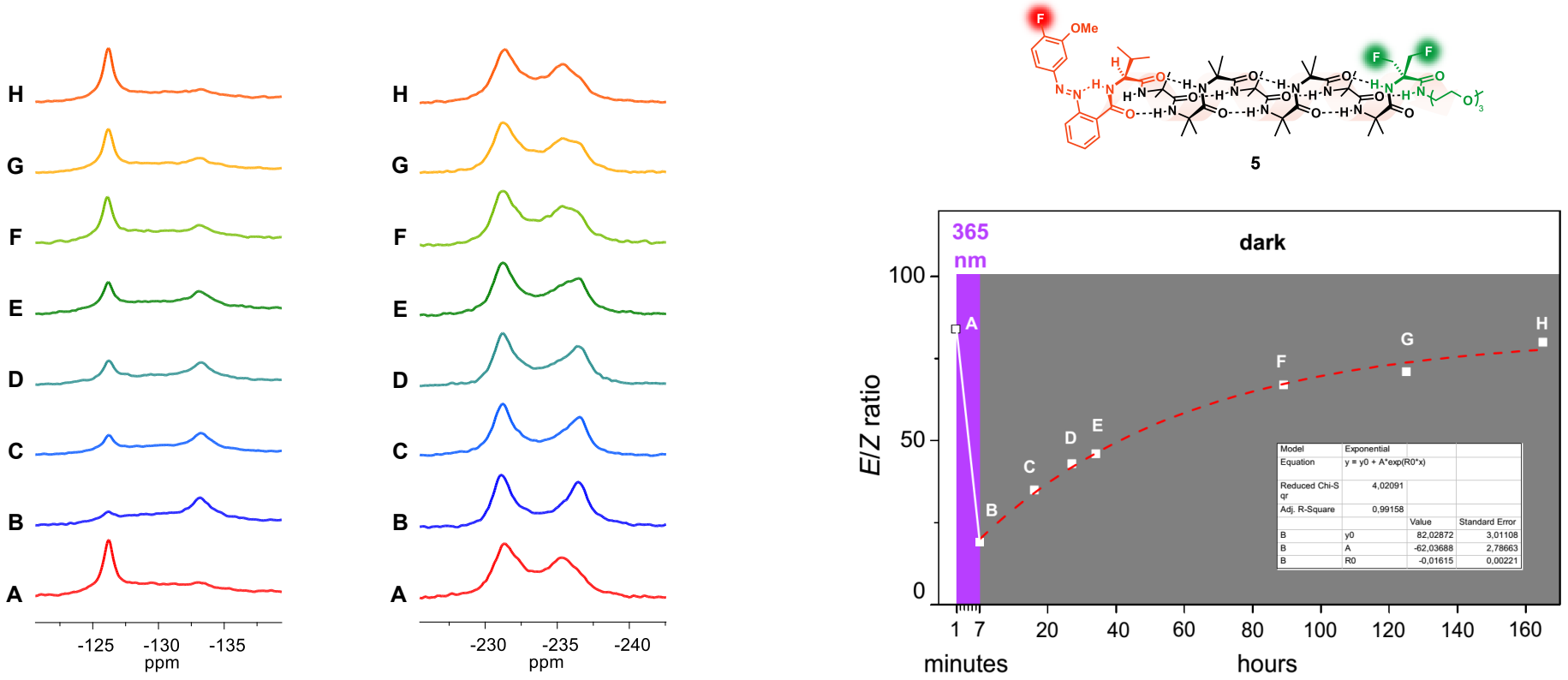


^{19}F ss-NMR spectra showing the irradiation (**A**-**B**) and $Z \rightarrow E$ thermal relaxation (**B**-**H**) of foldamer **5** (10% in DOPC). The graph on the right reports the variation of the integral ratio of the azobenzene ^{19}F peaks (δ –126 to –133 ppm) upon 365 nm irradiation and during back-switching in the dark. Fitting of the thermal relaxation data gives the following parameters:

$k_{Z \rightarrow E} = 0.01615 \pm 0.00221$ h^{-1}

$t_{1/2} = \ln(2) / k = 42.8 \pm 5.9$ h^{-1}

Fig. S20. Photoswitching and $Z \rightarrow E$ thermal relaxation of **5** in DOPC



^{19}F ss-NMR spectra showing the irradiation (**A**-**B**) and $Z \rightarrow E$ thermal relaxation (**B**-**H**) of foldamer **5** (10% in DOPC). The graph on the right reports the variation of the integral ratio of the azobenzene ^{19}F peaks (δ –126 to –133 ppm) upon 365 nm irradiation and during back-switching in the dark. Fitting of the thermal relaxation data gives the following parameters:

$k_{Z \rightarrow E} = 0.01615 \pm 0.00221$ h^{-1}

$t_{1/2} = \ln(2) / k = 42.8 \pm 5.9$ h^{-1}

X-ray data: compound 2

Full X-ray data deposited with the CCDC: Deposition number 1415763

Table S3. Crystal data and structure refinement for compound **2**.

Identification code	s4224ma	
Empirical formula	C39 H56 N10 O9	
Formula weight	808.94	
Temperature	100(2) K	
Wavelength	1.54178 Å	
Crystal system	Orthorhombic	
Space group	P2(1)2(1)2(1)	
Unit cell dimensions	a = 9.2058(2) Å	α= 90°.
	b = 14.2974(3) Å	β= 90°.
	c = 32.2718(7) Å	γ = 90°.
Volume	4247.58(16) $Å^3$	
Z	4	
Density (calculated)	1.265 Mg/m^3	
Absorption coefficient	0.754 mm^{-1}	
F(000)	1728	
Crystal size	0.29 x 0.12 x 0.08 mm^3	
Theta range for data collection	2.74 to 72.09°.	
Index ranges	-10<=h<=11, -12<=k<=16, -36<=l<=38	
Reflections collected	18026	
Independent reflections	7847 [R(int) = 0.0292]	
Completeness to theta = 67.00°	97.8 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.9421 and 0.84334	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	7847 / 0 / 535	
Goodness-of-fit on F^2	1.017	
Final R indices [I>2sigma(I)]	R1 = 0.0309, wR2 = 0.0753	
R indices (all data)	R1 = 0.0329, wR2 = 0.0762	
Absolute structure parameter	0.02(11)	
Largest diff. peak and hole	0.190 and -0.191 $e.Å^{-3}$	

Table S4. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$ x 10^3) for compound **2**. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
C(1)	8845(3)	12798(2)	9281(1)	58(1)
C(2)	8845(2)	13671(1)	8652(1)	24(1)
C(3)	7564(2)	13267(1)	8515(1)	23(1)
C(4)	6945(2)	13595(1)	8146(1)	21(1)
C(5)	7596(2)	14310(1)	7918(1)	25(1)
C(6)	8876(2)	14707(1)	8064(1)	29(1)
C(7)	9499(2)	14396(1)	8427(1)	27(1)
C(8)	3665(2)	12308(1)	8015(1)	19(1)
C(9)	3202(2)	11366(1)	8021(1)	18(1)
C(10)	1773(2)	11168(1)	7907(1)	23(1)
C(11)	809(2)	11873(1)	7796(1)	27(1)
C(12)	1270(2)	12798(1)	7798(1)	27(1)
C(13)	2680(2)	13012(1)	7908(1)	23(1)
C(14)	4115(2)	10527(1)	8131(1)	17(1)
C(15)	6379(2)	9904(1)	8424(1)	16(1)
C(16)	7662(2)	10350(1)	8653(1)	22(1)
C(17)	6893(2)	9312(1)	8060(1)	20(1)
C(18)	5523(2)	9296(1)	8737(1)	15(1)
C(19)	3799(2)	9263(1)	9309(1)	16(1)
C(20)	2844(2)	9971(1)	9536(1)	25(1)
C(21)	2861(2)	8467(1)	9141(1)	16(1)
C(22)	1229(2)	7924(1)	8584(1)	19(1)
C(23)	767(2)	8303(1)	8160(1)	26(1)
C(24)	-107(2)	7736(1)	8851(1)	27(1)
C(25)	2101(2)	7012(1)	8517(1)	19(1)
C(26)	4379(2)	6340(1)	8241(1)	21(1)
C(27)	5781(2)	6742(1)	8056(1)	24(1)
C(28)	3685(2)	5657(1)	7935(1)	27(1)
C(29)	4762(2)	5843(1)	8653(1)	16(1)
C(30)	5896(2)	6088(1)	9340(1)	18(1)
C(31)	6193(2)	6953(1)	9611(1)	23(1)
C(32)	7299(2)	5562(1)	9242(1)	25(1)

C(33)	4849(2)	5446(1)	9580(1)	14(1)
C(34)	2318(2)	5120(1)	9772(1)	18(1)
C(35)	843(2)	5495(1)	9628(1)	25(1)
C(36)	2465(2)	5202(1)	10242(1)	23(1)
C(37)	2389(2)	4081(1)	9642(1)	18(1)
C(38)	3116(2)	2958(1)	9115(1)	27(1)
C(39)	4419(2)	2418(1)	9274(1)	27(1)
N(1)	5579(2)	13284(1)	7986(1)	22(1)
N(2)	5102(2)	12540(1)	8147(1)	19(1)
N(3)	5449(1)	10673(1)	8278(1)	17(1)
N(4)	4604(1)	9748(1)	8986(1)	16(1)
N(5)	2180(1)	8630(1)	8777(1)	17(1)
N(6)	3401(2)	7126(1)	8328(1)	18(1)
N(7)	5216(1)	6419(1)	8955(1)	16(1)
N(8)	3437(1)	5664(1)	9557(1)	15(1)
N(9)	2969(1)	3901(1)	9269(1)	18(1)
N(10)	5158(2)	2753(1)	9591(1)	27(1)
O(1)	9548(1)	13437(1)	9008(1)	34(1)
O(2)	3601(1)	9731(1)	8093(1)	20(1)
O(3)	5724(1)	8442(1)	8756(1)	18(1)
O(4)	2693(1)	7748(1)	9344(1)	20(1)
O(5)	1612(1)	6247(1)	8613(1)	26(1)
O(6)	4696(1)	4988(1)	8691(1)	21(1)
O(7)	5308(1)	4780(1)	9783(1)	18(1)
O(8)	1884(1)	3469(1)	9866(1)	27(1)
O(9)	4723(2)	1664(1)	9104(1)	42(1)

Table S5. Bond lengths [Å] and angles [°] for compound **2**.

C(1)-O(1)	1.424(2)
C(1)-H(1A)	0.9800
C(1)-H(1B)	0.9800
C(1)-H(1C)	0.9800
C(2)-O(1)	1.361(2)
C(2)-C(3)	1.385(2)
C(2)-C(7)	1.401(2)
C(3)-C(4)	1.400(2)
C(3)-H(3)	0.9500
C(4)-C(5)	1.396(2)
C(4)-N(1)	1.431(2)
C(5)-C(6)	1.390(3)
C(5)-H(5)	0.9500
C(6)-C(7)	1.380(3)
C(6)-H(6)	0.9500
C(7)-H(7)	0.9500
C(8)-C(13)	1.398(2)
C(8)-C(9)	1.412(2)
C(8)-N(2)	1.429(2)
C(9)-C(10)	1.395(2)
C(9)-C(14)	1.508(2)
C(10)-C(11)	1.390(2)
C(10)-H(10)	0.9500
C(11)-C(12)	1.388(3)
C(11)-H(11)	0.9500
C(12)-C(13)	1.380(3)
C(12)-H(12)	0.9500
C(13)-H(13)	0.9500
C(14)-O(2)	1.2386(19)
C(14)-N(3)	1.333(2)
C(15)-N(3)	1.4704(19)
C(15)-C(17)	1.523(2)
C(15)-C(16)	1.533(2)
C(15)-C(18)	1.548(2)
C(16)-H(16A)	0.9800
C(16)-H(16B)	0.9800

C(16)-H(16C)	0.9800
C(17)-H(17A)	0.9800
C(17)-H(17B)	0.9800
C(17)-H(17C)	0.9800
C(18)-O(3)	1.2362(19)
C(18)-N(4)	1.334(2)
C(19)-N(4)	1.4561(19)
C(19)-C(20)	1.526(2)
C(19)-C(21)	1.529(2)
C(19)-H(19)	1.0000
C(20)-H(20A)	0.9800
C(20)-H(20B)	0.9800
C(20)-H(20C)	0.9800
C(21)-O(4)	1.2292(19)
C(21)-N(5)	1.350(2)
C(22)-N(5)	1.4743(19)
C(22)-C(24)	1.526(2)
C(22)-C(23)	1.532(2)
C(22)-C(25)	1.547(2)
C(23)-H(23A)	0.9800
C(23)-H(23B)	0.9800
C(23)-H(23C)	0.9800
C(24)-H(24A)	0.9800
C(24)-H(24B)	0.9800
C(24)-H(24C)	0.9800
C(25)-O(5)	1.222(2)
C(25)-N(6)	1.353(2)
C(26)-N(6)	1.467(2)
C(26)-C(28)	1.530(2)
C(26)-C(27)	1.534(2)
C(26)-C(29)	1.547(2)
C(27)-H(27A)	0.9800
C(27)-H(27B)	0.9800
C(27)-H(27C)	0.9800
C(28)-H(28A)	0.9800
C(28)-H(28B)	0.9800
C(28)-H(28C)	0.9800
C(29)-O(6)	1.2305(19)

C(29)-N(7)	1.343(2)
C(30)-N(7)	1.469(2)
C(30)-C(32)	1.527(2)
C(30)-C(31)	1.539(2)
C(30)-C(33)	1.540(2)
C(31)-H(31A)	0.9800
C(31)-H(31B)	0.9800
C(31)-H(31C)	0.9800
C(32)-H(32A)	0.9800
C(32)-H(32B)	0.9800
C(32)-H(32C)	0.9800
C(33)-O(7)	1.2311(18)
C(33)-N(8)	1.339(2)
C(34)-N(8)	1.4659(19)
C(34)-C(36)	1.528(2)
C(34)-C(35)	1.532(2)
C(34)-C(37)	1.545(2)
C(35)-H(35A)	0.9800
C(35)-H(35B)	0.9800
C(35)-H(35C)	0.9800
C(36)-H(36A)	0.9800
C(36)-H(36B)	0.9800
C(36)-H(36C)	0.9800
C(37)-O(8)	1.2276(19)
C(37)-N(9)	1.340(2)
C(38)-N(9)	1.444(2)
C(38)-C(39)	1.516(3)
C(38)-H(38A)	0.9900
C(38)-H(38B)	0.9900
C(39)-O(9)	1.240(2)
C(39)-N(10)	1.319(2)
N(1)-N(2)	1.2627(19)
N(3)-H(3A)	0.8800
N(4)-H(4)	0.8800
N(5)-H(5A)	0.8800
N(6)-H(6A)	0.8800
N(7)-H(7A)	0.8800
N(8)-H(8)	0.8800

N(9)-H(9)	0.8800
N(10)-H(10A)	0.8800
N(10)-H(10B)	0.8800

O(1)-C(1)-H(1A)	109.5
O(1)-C(1)-H(1B)	109.5
H(1A)-C(1)-H(1B)	109.5
O(1)-C(1)-H(1C)	109.5
H(1A)-C(1)-H(1C)	109.5
H(1B)-C(1)-H(1C)	109.5
O(1)-C(2)-C(3)	124.84(16)
O(1)-C(2)-C(7)	114.49(15)
C(3)-C(2)-C(7)	120.63(16)
C(2)-C(3)-C(4)	118.55(16)
C(2)-C(3)-H(3)	120.7
C(4)-C(3)-H(3)	120.7
C(5)-C(4)-C(3)	121.32(16)
C(5)-C(4)-N(1)	114.41(15)
C(3)-C(4)-N(1)	124.16(15)
C(6)-C(5)-C(4)	118.88(16)
C(6)-C(5)-H(5)	120.6
C(4)-C(5)-H(5)	120.6
C(7)-C(6)-C(5)	120.66(16)
C(7)-C(6)-H(6)	119.7
C(5)-C(6)-H(6)	119.7
C(6)-C(7)-C(2)	119.94(16)
C(6)-C(7)-H(7)	120.0
C(2)-C(7)-H(7)	120.0
C(13)-C(8)-C(9)	119.56(15)
C(13)-C(8)-N(2)	120.46(14)
C(9)-C(8)-N(2)	119.82(14)
C(10)-C(9)-C(8)	118.36(15)
C(10)-C(9)-C(14)	115.25(14)
C(8)-C(9)-C(14)	126.38(14)
C(11)-C(10)-C(9)	121.54(16)
C(11)-C(10)-H(10)	119.2
C(9)-C(10)-H(10)	119.2
C(12)-C(11)-C(10)	119.55(16)

C(12)-C(11)-H(11)	120.2
C(10)-C(11)-H(11)	120.2
C(13)-C(12)-C(11)	120.03(16)
C(13)-C(12)-H(12)	120.0
C(11)-C(12)-H(12)	120.0
C(12)-C(13)-C(8)	120.94(16)
C(12)-C(13)-H(13)	119.5
C(8)-C(13)-H(13)	119.5
O(2)-C(14)-N(3)	122.07(14)
O(2)-C(14)-C(9)	119.65(14)
N(3)-C(14)-C(9)	118.26(14)
N(3)-C(15)-C(17)	110.45(12)
N(3)-C(15)-C(16)	107.00(12)
C(17)-C(15)-C(16)	111.35(13)
N(3)-C(15)-C(18)	109.43(12)
C(17)-C(15)-C(18)	110.39(12)
C(16)-C(15)-C(18)	108.12(12)
C(15)-C(16)-H(16A)	109.5
C(15)-C(16)-H(16B)	109.5
H(16A)-C(16)-H(16B)	109.5
C(15)-C(16)-H(16C)	109.5
H(16A)-C(16)-H(16C)	109.5
H(16B)-C(16)-H(16C)	109.5
C(15)-C(17)-H(17A)	109.5
C(15)-C(17)-H(17B)	109.5
H(17A)-C(17)-H(17B)	109.5
C(15)-C(17)-H(17C)	109.5
H(17A)-C(17)-H(17C)	109.5
H(17B)-C(17)-H(17C)	109.5
O(3)-C(18)-N(4)	122.79(14)
O(3)-C(18)-C(15)	120.84(13)
N(4)-C(18)-C(15)	116.35(13)
N(4)-C(19)-C(20)	108.70(12)
N(4)-C(19)-C(21)	112.74(12)
C(20)-C(19)-C(21)	109.81(13)
N(4)-C(19)-H(19)	108.5
C(20)-C(19)-H(19)	108.5
C(21)-C(19)-H(19)	108.5

C(19)-C(20)-H(20A)	109.5
C(19)-C(20)-H(20B)	109.5
H(20A)-C(20)-H(20B)	109.5
C(19)-C(20)-H(20C)	109.5
H(20A)-C(20)-H(20C)	109.5
H(20B)-C(20)-H(20C)	109.5
O(4)-C(21)-N(5)	123.33(14)
O(4)-C(21)-C(19)	120.25(14)
N(5)-C(21)-C(19)	116.30(13)
N(5)-C(22)-C(24)	111.08(14)
N(5)-C(22)-C(23)	107.52(12)
C(24)-C(22)-C(23)	110.13(14)
N(5)-C(22)-C(25)	109.13(12)
C(24)-C(22)-C(25)	110.41(13)
C(23)-C(22)-C(25)	108.49(14)
C(22)-C(23)-H(23A)	109.5
C(22)-C(23)-H(23B)	109.5
H(23A)-C(23)-H(23B)	109.5
C(22)-C(23)-H(23C)	109.5
H(23A)-C(23)-H(23C)	109.5
H(23B)-C(23)-H(23C)	109.5
C(22)-C(24)-H(24A)	109.5
C(22)-C(24)-H(24B)	109.5
H(24A)-C(24)-H(24B)	109.5
C(22)-C(24)-H(24C)	109.5
H(24A)-C(24)-H(24C)	109.5
H(24B)-C(24)-H(24C)	109.5
O(5)-C(25)-N(6)	123.24(15)
O(5)-C(25)-C(22)	121.84(15)
N(6)-C(25)-C(22)	114.85(13)
N(6)-C(26)-C(28)	110.92(14)
N(6)-C(26)-C(27)	107.71(13)
C(28)-C(26)-C(27)	109.83(13)
N(6)-C(26)-C(29)	109.10(12)
C(28)-C(26)-C(29)	110.88(13)
C(27)-C(26)-C(29)	108.31(13)
C(26)-C(27)-H(27A)	109.5
C(26)-C(27)-H(27B)	109.5

H(27A)-C(27)-H(27B)	109.5
C(26)-C(27)-H(27C)	109.5
H(27A)-C(27)-H(27C)	109.5
H(27B)-C(27)-H(27C)	109.5
C(26)-C(28)-H(28A)	109.5
C(26)-C(28)-H(28B)	109.5
H(28A)-C(28)-H(28B)	109.5
C(26)-C(28)-H(28C)	109.5
H(28A)-C(28)-H(28C)	109.5
H(28B)-C(28)-H(28C)	109.5
O(6)-C(29)-N(7)	123.50(14)
O(6)-C(29)-C(26)	122.04(14)
N(7)-C(29)-C(26)	114.42(13)
N(7)-C(30)-C(32)	110.18(13)
N(7)-C(30)-C(31)	107.28(13)
C(32)-C(30)-C(31)	111.24(13)
N(7)-C(30)-C(33)	110.49(12)
C(32)-C(30)-C(33)	109.86(13)
C(31)-C(30)-C(33)	107.75(13)
C(30)-C(31)-H(31A)	109.5
C(30)-C(31)-H(31B)	109.5
H(31A)-C(31)-H(31B)	109.5
C(30)-C(31)-H(31C)	109.5
H(31A)-C(31)-H(31C)	109.5
H(31B)-C(31)-H(31C)	109.5
C(30)-C(32)-H(32A)	109.5
C(30)-C(32)-H(32B)	109.5
H(32A)-C(32)-H(32B)	109.5
C(30)-C(32)-H(32C)	109.5
H(32A)-C(32)-H(32C)	109.5
H(32B)-C(32)-H(32C)	109.5
O(7)-C(33)-N(8)	122.90(14)
O(7)-C(33)-C(30)	120.96(13)
N(8)-C(33)-C(30)	116.14(13)
N(8)-C(34)-C(36)	111.56(13)
N(8)-C(34)-C(35)	107.07(12)
C(36)-C(34)-C(35)	110.66(13)
N(8)-C(34)-C(37)	110.61(12)

C(36)-C(34)-C(37)	109.87(13)
C(35)-C(34)-C(37)	106.94(13)
C(34)-C(35)-H(35A)	109.5
C(34)-C(35)-H(35B)	109.5
H(35A)-C(35)-H(35B)	109.5
C(34)-C(35)-H(35C)	109.5
H(35A)-C(35)-H(35C)	109.5
H(35B)-C(35)-H(35C)	109.5
C(34)-C(36)-H(36A)	109.5
C(34)-C(36)-H(36B)	109.5
H(36A)-C(36)-H(36B)	109.5
C(34)-C(36)-H(36C)	109.5
H(36A)-C(36)-H(36C)	109.5
H(36B)-C(36)-H(36C)	109.5
O(8)-C(37)-N(9)	122.90(15)
O(8)-C(37)-C(34)	120.60(14)
N(9)-C(37)-C(34)	116.44(13)
N(9)-C(38)-C(39)	115.65(14)
N(9)-C(38)-H(38A)	108.4
C(39)-C(38)-H(38A)	108.4
N(9)-C(38)-H(38B)	108.4
C(39)-C(38)-H(38B)	108.4
H(38A)-C(38)-H(38B)	107.4
O(9)-C(39)-N(10)	122.81(18)
O(9)-C(39)-C(38)	118.12(17)
N(10)-C(39)-C(38)	119.05(15)
N(2)-N(1)-C(4)	114.73(13)
N(1)-N(2)-C(8)	113.25(13)
C(14)-N(3)-C(15)	122.23(13)
C(14)-N(3)-H(3A)	118.9
C(15)-N(3)-H(3A)	118.9
C(18)-N(4)-C(19)	121.67(13)
C(18)-N(4)-H(4)	119.2
C(19)-N(4)-H(4)	119.2
C(21)-N(5)-C(22)	121.71(12)
C(21)-N(5)-H(5A)	119.1
C(22)-N(5)-H(5A)	119.1
C(25)-N(6)-C(26)	122.44(13)

C(25)-N(6)-H(6A)	118.8
C(26)-N(6)-H(6A)	118.8
C(29)-N(7)-C(30)	123.33(13)
C(29)-N(7)-H(7A)	118.3
C(30)-N(7)-H(7A)	118.3
C(33)-N(8)-C(34)	122.13(13)
C(33)-N(8)-H(8)	118.9
C(34)-N(8)-H(8)	118.9
C(37)-N(9)-C(38)	121.73(14)
C(37)-N(9)-H(9)	119.1
C(38)-N(9)-H(9)	119.1
C(39)-N(10)-H(10A)	120.0
C(39)-N(10)-H(10B)	120.0
H(10A)-N(10)-H(10B)	120.0
C(2)-O(1)-C(1)	117.65(15)

Symmetry transformations used to generate equivalent atoms:

Table S6. Anisotropic displacement parameters ($Å^2$ x 10^3) for compound **2**. The anisotropic displacement factor exponent takes the form: $-2\pi^2$ [h^2 $a^{*2}U^{11}$ + ... + 2 h k a* b* U^{12}].

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
C(1)	51(1)	83(2)	40(1)	30(1)	-25(1)	-37(1)
C(2)	24(1)	24(1)	24(1)	-4(1)	1(1)	0(1)
C(3)	28(1)	19(1)	23(1)	1(1)	3(1)	-3(1)
C(4)	26(1)	14(1)	24(1)	-1(1)	2(1)	1(1)
C(5)	28(1)	19(1)	27(1)	4(1)	4(1)	4(1)
C(6)	29(1)	20(1)	38(1)	2(1)	7(1)	-3(1)
C(7)	22(1)	22(1)	36(1)	-7(1)	4(1)	-3(1)
C(8)	25(1)	18(1)	12(1)	1(1)	-1(1)	2(1)
C(9)	23(1)	19(1)	12(1)	1(1)	1(1)	2(1)
C(10)	25(1)	24(1)	20(1)	1(1)	1(1)	-1(1)
C(11)	21(1)	34(1)	26(1)	-2(1)	-3(1)	3(1)
C(12)	30(1)	29(1)	22(1)	-1(1)	-4(1)	12(1)
C(13)	30(1)	20(1)	18(1)	0(1)	-2(1)	4(1)
C(14)	23(1)	17(1)	12(1)	2(1)	2(1)	-1(1)
C(15)	17(1)	14(1)	18(1)	2(1)	0(1)	1(1)
C(16)	22(1)	18(1)	25(1)	2(1)	-1(1)	-3(1)
C(17)	25(1)	18(1)	18(1)	3(1)	3(1)	1(1)
C(18)	16(1)	15(1)	14(1)	0(1)	-4(1)	-1(1)
C(19)	21(1)	15(1)	13(1)	0(1)	1(1)	1(1)
C(20)	30(1)	22(1)	22(1)	-3(1)	6(1)	3(1)
C(21)	14(1)	17(1)	17(1)	0(1)	5(1)	2(1)
C(22)	18(1)	18(1)	23(1)	4(1)	-4(1)	-4(1)
C(23)	26(1)	23(1)	30(1)	7(1)	-11(1)	-2(1)
C(24)	19(1)	24(1)	38(1)	8(1)	0(1)	-1(1)
C(25)	23(1)	19(1)	16(1)	1(1)	-6(1)	-4(1)
C(26)	29(1)	16(1)	17(1)	-1(1)	4(1)	-1(1)
C(27)	34(1)	19(1)	19(1)	0(1)	9(1)	-1(1)
C(28)	44(1)	18(1)	18(1)	-3(1)	-2(1)	-1(1)
C(29)	17(1)	15(1)	18(1)	0(1)	4(1)	0(1)
C(30)	17(1)	17(1)	19(1)	2(1)	-2(1)	-2(1)
C(31)	30(1)	15(1)	25(1)	3(1)	-9(1)	-5(1)
C(32)	17(1)	27(1)	31(1)	8(1)	2(1)	0(1)
C(33)	19(1)	12(1)	12(1)	-3(1)	-1(1)	-2(1)

C(34)	17(1)	20(1)	17(1)	3(1)	4(1)	1(1)
C(35)	19(1)	31(1)	25(1)	5(1)	3(1)	5(1)
C(36)	25(1)	27(1)	18(1)	0(1)	4(1)	2(1)
C(37)	15(1)	21(1)	18(1)	3(1)	-3(1)	-4(1)
C(38)	43(1)	17(1)	22(1)	-4(1)	-2(1)	-7(1)
C(39)	42(1)	16(1)	22(1)	1(1)	10(1)	-2(1)
N(1)	28(1)	16(1)	21(1)	2(1)	2(1)	1(1)
N(2)	24(1)	15(1)	18(1)	0(1)	0(1)	1(1)
N(3)	21(1)	10(1)	19(1)	2(1)	-1(1)	-1(1)
N(4)	21(1)	10(1)	15(1)	0(1)	0(1)	0(1)
N(5)	20(1)	13(1)	18(1)	3(1)	-1(1)	-2(1)
N(6)	26(1)	12(1)	17(1)	2(1)	-1(1)	-2(1)
N(7)	21(1)	10(1)	18(1)	1(1)	0(1)	0(1)
N(8)	18(1)	13(1)	15(1)	2(1)	1(1)	1(1)
N(9)	23(1)	14(1)	18(1)	0(1)	-2(1)	-4(1)
N(10)	34(1)	18(1)	29(1)	1(1)	1(1)	9(1)
O(1)	29(1)	42(1)	30(1)	4(1)	-6(1)	-12(1)
O(2)	24(1)	16(1)	19(1)	0(1)	-4(1)	-2(1)
O(3)	23(1)	11(1)	21(1)	1(1)	3(1)	2(1)
O(4)	22(1)	17(1)	21(1)	4(1)	0(1)	0(1)
O(5)	30(1)	16(1)	31(1)	2(1)	1(1)	-6(1)
O(6)	28(1)	13(1)	20(1)	-1(1)	5(1)	0(1)
O(7)	19(1)	15(1)	20(1)	3(1)	-4(1)	0(1)
O(8)	32(1)	24(1)	26(1)	6(1)	4(1)	-9(1)
O(9)	72(1)	16(1)	39(1)	-6(1)	14(1)	3(1)

Table S7. Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$ x 10^3) for compound **2**.

	x	y	z	U(eq)
H(1A)	8732	12192	9143	87
H(1B)	7886	13043	9356	87
H(1C)	9432	12719	9532	87
H(3)	7115	12778	8668	28
H(5)	7171	14522	7666	30
H(6)	9326	15196	7912	35
H(7)	10371	14674	8526	32
H(10)	1451	10537	7905	28
H(11)	-159	11723	7718	32
H(12)	615	13283	7724	32
H(13)	2986	13646	7911	27
H(16A)	8223	10737	8460	33
H(16B)	8287	9858	8767	33
H(16C)	7297	10741	8880	33
H(17A)	6050	9084	7904	31
H(17B)	7453	8778	8164	31
H(17C)	7507	9692	7878	31
H(19)	4509	8996	9512	20
H(20A)	3456	10461	9656	37
H(20B)	2305	9654	9756	37
H(20C)	2159	10252	9339	37
H(23A)	221	8886	8197	39
H(23B)	153	7841	8020	39
H(23C)	1633	8425	7991	39
H(24A)	197	7469	9117	40
H(24B)	-749	7295	8708	40
H(24C)	-627	8324	8900	40
H(27A)	5556	7069	7797	36
H(27B)	6464	6232	8000	36
H(27C)	6218	7181	8253	36
H(28A)	2769	5423	8050	40
H(28B)	4346	5131	7887	40

H(28C)	3494	5979	7672	40
H(31A)	6863	7373	9466	35
H(31B)	6628	6755	9874	35
H(31C)	5278	7280	9665	35
H(32A)	7083	5030	9061	38
H(32B)	7735	5336	9501	38
H(32C)	7980	5984	9102	38
H(35A)	739	6148	9714	37
H(35B)	64	5120	9752	37
H(35C)	782	5456	9325	37
H(36A)	3416	4963	10328	35
H(36B)	1697	4835	10376	35
H(36C)	2375	5859	10323	35
H(38A)	3173	2983	8809	33
H(38B)	2226	2606	9188	33
H(3A)	5786	11249	8287	20
H(4)	4482	10354	8954	19
H(5A)	2307	9171	8653	20
H(6A)	3671	7693	8255	22
H(7A)	5100	7025	8921	20
H(8)	3172	6150	9407	18
H(9)	3268	4370	9115	22
H(10A)	5901	2439	9691	32
H(10B)	4907	3291	9703	32

Table S8. Torsion angles [°] for compound **2**.

O(1)-C(2)-C(3)-C(4)	178.46(16)
C(7)-C(2)-C(3)-C(4)	0.5(2)
C(2)-C(3)-C(4)-C(5)	0.3(2)
C(2)-C(3)-C(4)-N(1)	-175.64(15)
C(3)-C(4)-C(5)-C(6)	-0.7(2)
N(1)-C(4)-C(5)-C(6)	175.56(15)
C(4)-C(5)-C(6)-C(7)	0.4(3)
C(5)-C(6)-C(7)-C(2)	0.3(3)
O(1)-C(2)-C(7)-C(6)	-178.97(16)
C(3)-C(2)-C(7)-C(6)	-0.8(3)
C(13)-C(8)-C(9)-C(10)	1.8(2)
N(2)-C(8)-C(9)-C(10)	177.23(14)
C(13)-C(8)-C(9)-C(14)	-179.52(15)
N(2)-C(8)-C(9)-C(14)	-4.1(2)
C(8)-C(9)-C(10)-C(11)	-0.9(2)
C(14)-C(9)-C(10)-C(11)	-179.77(15)
C(9)-C(10)-C(11)-C(12)	-0.2(3)
C(10)-C(11)-C(12)-C(13)	0.5(3)
C(11)-C(12)-C(13)-C(8)	0.4(3)
C(9)-C(8)-C(13)-C(12)	-1.5(2)
N(2)-C(8)-C(13)-C(12)	-176.98(14)
C(10)-C(9)-C(14)-O(2)	4.3(2)
C(8)-C(9)-C(14)-O(2)	-174.46(15)
C(10)-C(9)-C(14)-N(3)	-174.19(14)
C(8)-C(9)-C(14)-N(3)	7.1(2)
N(3)-C(15)-C(18)-O(3)	145.98(14)
C(17)-C(15)-C(18)-O(3)	24.22(19)
C(16)-C(15)-C(18)-O(3)	-97.81(16)
N(3)-C(15)-C(18)-N(4)	-35.81(17)
C(17)-C(15)-C(18)-N(4)	-157.57(13)
C(16)-C(15)-C(18)-N(4)	80.40(16)
N(4)-C(19)-C(21)-O(4)	144.66(14)
C(20)-C(19)-C(21)-O(4)	-93.97(16)
N(4)-C(19)-C(21)-N(5)	-39.30(18)
C(20)-C(19)-C(21)-N(5)	82.07(16)
N(5)-C(22)-C(25)-O(5)	133.32(15)

C(24)-C(22)-C(25)-O(5)	11.0(2)
C(23)-C(22)-C(25)-O(5)	-109.81(17)
N(5)-C(22)-C(25)-N(6)	-49.60(17)
C(24)-C(22)-C(25)-N(6)	-171.96(13)
C(23)-C(22)-C(25)-N(6)	67.27(17)
N(6)-C(26)-C(29)-O(6)	132.23(15)
C(28)-C(26)-C(29)-O(6)	9.8(2)
C(27)-C(26)-C(29)-O(6)	-110.80(17)
N(6)-C(26)-C(29)-N(7)	-50.02(18)
C(28)-C(26)-C(29)-N(7)	-172.46(14)
C(27)-C(26)-C(29)-N(7)	66.96(17)
N(7)-C(30)-C(33)-O(7)	146.01(14)
C(32)-C(30)-C(33)-O(7)	24.25(19)
C(31)-C(30)-C(33)-O(7)	-97.08(16)
N(7)-C(30)-C(33)-N(8)	-34.83(18)
C(32)-C(30)-C(33)-N(8)	-156.59(14)
C(31)-C(30)-C(33)-N(8)	82.08(16)
N(8)-C(34)-C(37)-O(8)	157.61(14)
C(36)-C(34)-C(37)-O(8)	34.0(2)
C(35)-C(34)-C(37)-O(8)	-86.14(17)
N(8)-C(34)-C(37)-N(9)	-25.02(18)
C(36)-C(34)-C(37)-N(9)	-148.62(14)
C(35)-C(34)-C(37)-N(9)	91.23(16)
N(9)-C(38)-C(39)-O(9)	-169.02(15)
N(9)-C(38)-C(39)-N(10)	12.6(2)
C(5)-C(4)-N(1)-N(2)	168.68(14)
C(3)-C(4)-N(1)-N(2)	-15.1(2)
C(4)-N(1)-N(2)-C(8)	173.18(13)
C(13)-C(8)-N(2)-N(1)	-30.5(2)
C(9)-C(8)-N(2)-N(1)	154.04(14)
O(2)-C(14)-N(3)-C(15)	-3.2(2)
C(9)-C(14)-N(3)-C(15)	175.26(13)
C(17)-C(15)-N(3)-C(14)	70.85(17)
C(16)-C(15)-N(3)-C(14)	-167.79(13)
C(18)-C(15)-N(3)-C(14)	-50.88(18)
O(3)-C(18)-N(4)-C(19)	1.8(2)
C(15)-C(18)-N(4)-C(19)	-176.38(13)
C(20)-C(19)-N(4)-C(18)	-179.65(13)

C(21)-C(19)-N(4)-C(18)	-57.65(18)
O(4)-C(21)-N(5)-C(22)	-3.3(2)
C(19)-C(21)-N(5)-C(22)	-179.21(13)
C(24)-C(22)-N(5)-C(21)	64.91(18)
C(23)-C(22)-N(5)-C(21)	-174.53(14)
C(25)-C(22)-N(5)-C(21)	-57.04(18)
O(5)-C(25)-N(6)-C(26)	-3.3(2)
C(22)-C(25)-N(6)-C(26)	179.70(13)
C(28)-C(26)-N(6)-C(25)	63.81(18)
C(27)-C(26)-N(6)-C(25)	-175.97(13)
C(29)-C(26)-N(6)-C(25)	-58.61(18)
O(6)-C(29)-N(7)-C(30)	9.9(2)
C(26)-C(29)-N(7)-C(30)	-167.83(13)
C(32)-C(30)-N(7)-C(29)	61.24(18)
C(31)-C(30)-N(7)-C(29)	-177.54(14)
C(33)-C(30)-N(7)-C(29)	-60.34(18)
O(7)-C(33)-N(8)-C(34)	-0.3(2)
C(30)-C(33)-N(8)-C(34)	-179.49(13)
C(36)-C(34)-N(8)-C(33)	66.14(18)
C(35)-C(34)-N(8)-C(33)	-172.65(14)
C(37)-C(34)-N(8)-C(33)	-56.48(18)
O(8)-C(37)-N(9)-C(38)	-3.6(2)
C(34)-C(37)-N(9)-C(38)	179.09(15)
C(39)-C(38)-N(9)-C(37)	-81.1(2)
C(3)-C(2)-O(1)-C(1)	-6.6(3)
C(7)-C(2)-O(1)-C(1)	171.5(2)

Symmetry transformations used to generate equivalent atoms:

Table S9. Hydrogen bonds for compound **2** [Å and °].

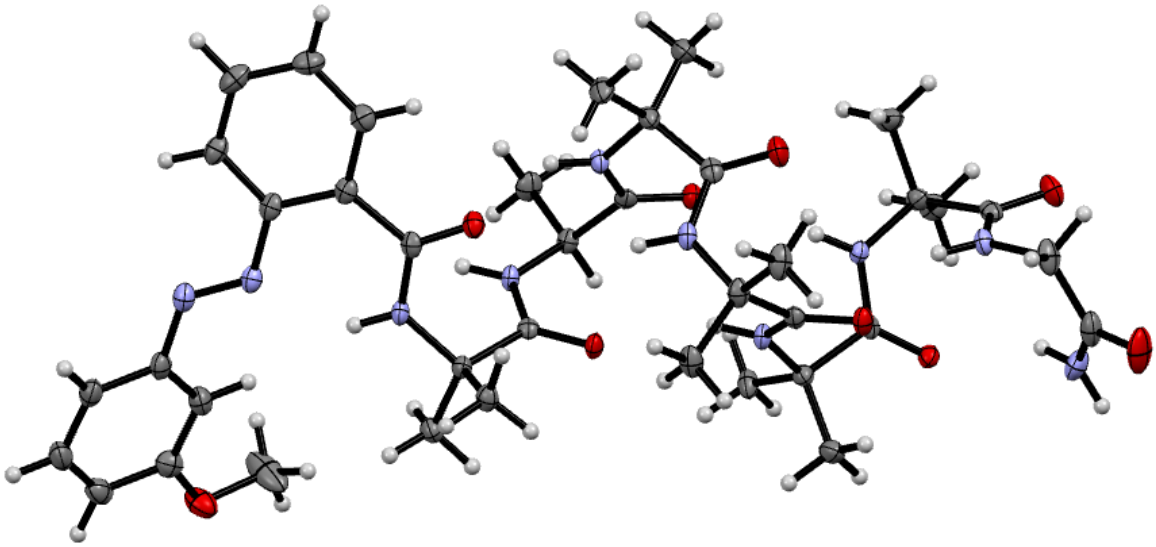
D-H...A	d(D-H)	d(H...A)	d(D...A)	<(DHA)
N(3)-H(3A)...N(2)	0.88	2.00	2.7218(18)	138.1
N(4)-H(4)...O(9)#1	0.88	1.95	2.7693(18)	154.6
N(5)-H(5A)...O(2)	0.88	2.31	3.0115(17)	137.1
N(7)-H(7A)...O(3)	0.88	2.17	2.9998(17)	156.5
N(8)-H(8)...O(4)	0.88	2.33	3.1328(16)	150.8
N(9)-H(9)...O(6)	0.88	2.09	2.9026(17)	152.7
N(10)-H(10A)...O(8)#2	0.88	2.13	2.9409(18)	152.4
N(10)-H(10B)...O(7)	0.88	2.18	2.9663(18)	149.2

Symmetry transformations used to generate equivalent atoms:

#1 x,y+1,z #2 x+1/2,-y+1/2,-z+2

ORTEP image for crystal structure of 2

Fig. S20. Thermal ellipsoids at 50% probability.



2-(3-methoxyphenyl)-azobenzoyl-AibAlaAib$_4$GlyNH$_2$ (**2**)

References

1. J. Broichhagen, D. Trauner, The *in vivo* chemistry of photoswitched tethered ligands. *Curr. Op. Chem. Biol.* **21**, 121−127 (2014).
2. R. Göstl, A. Senf, S. Hecht, Remote-controlling chemical reactions by light: towards chemistry with high spatio-temporal resolution. *Chem. Soc. Rev.* **43**, 1982−1996 (2014).
3. B. L. Feringa, W. E. Browne, Eds., *Molecular Switches* (Wiley-VCH, Weinheim, 2011) [second edition].
4. W. J. De Grip, K. J. Rothschild, in *Molecular Mechanisms of Visual Transduction*, D. G. Stavenga, W. J. De Grip, E. N. Pugh Jr., Eds. (Elsevier, Amsterdam, 2000), pp. 1−54.
5. R. Nygaard *et al.*, The dynamic process of β_2-adrenergic receptor activation. *Cell* **152**, 532−542 (2013).
6. K. Henzler-Wildman, D. Kern, Dynamic personalities of proteins. *Nature* **450**, 964−972 (2007).
7. F. Hu, W. Luo, M. Hong, Mechanisms of proton conduction and gating by influenza M2 proton channels from solid-state NMR, *Science* **330**, 505−508 (2010).
8. S. H. Gellman, Foldamers: a manifesto. *Acc. Chem. Res.* **31**, 173−180 (1998).
9. C. Toniolo, E. Benedetti, The polypeptide 3_{10}-helix. *Trends Biochem. Sci.* **16**, 350−353 (1991).
10. C. Toniolo, H. Brückner, Eds., *Peptaibiotics* (Wiley-VCH, Weinheim, 2009).
11. H. M. D. Bandara, S. C. Burdette, Photoisomerization in different classes of azobenzene. *Chem. Soc. Rev.* **41**, 1809−1825 (2012).
12. M. De Poli *et al.*, Engineering the structure of an N-terminal β-turn to maximize screw-sense preference in achiral helical peptide chains. *J. Org. Chem.* **79**, 4659−4675 (2014).
13. G. Shanmugan, P. L. Polavarapu, Structure of Aβ(25–35) peptide in different environments. *Biophys. J.* **87**, 622−630 (2004).
14. S. J. Pike, V. Diemer, J. Raftery, S. J. Webb, J. Clayden, Designing foldamer–foldamer interactions in solution: the roles of helix length and terminus functionality in promoting the self-association of aminoisobutyric acid oligomers. *Chem. Eur. J.* **20**, 15981−15990 (2014).
15. Electron-donating groups *para* to the azo linkage were avoided as they are known to promote fast thermal relaxation to the E isomer. See (*16*).

16. N. Nishimura *et al.*, Thermal *cis*-to-*trans* isomerization of substituted azobenzenes. II. Substituents and solvent effects. *Bull. Chem. Soc. Jpn.* **49**, 1381−1387 (1976).
17. B. A. F. Le Bailly, L. Byrne, V. Diemer, M. Foroozandeh, G. A. Morris, J. Clayden, Flaws in foldamers: conformational uniformity and signal decay in achiral helical peptide oligomers. *Chem. Sci.*, **6**, 2313−2322 (2015).
18. F. Gerson, E. Heilbronner, A. van Veen, B. M. Wepster, Elektronenstruktur und physikalisch-chemische eigenschaften von azo-verbindungen. Teil VIII: die konjugaten säuren des trans- und des cis-azobenzols. *Helv. Chim. Acta* **43**, 1889−1898 (1960).
19. M. J. Duer, *Introduction to Solid-State NMR Spectroscopy* (Blackwell, Oxford, 2004).
20. D. Huster, Solid-state NMR spectroscopy to study protein–lipid interactions. *Biochim. et Biophys. Acta (BBA) - Molecular and Cell Biology of Lipids* **1841**, 1146−1160 (2014).
21. E. Strandberg, A. S. Ulrich, NMR methods for studying membrane-active antimicrobial peptides. *Concepts Magn. Reson.* **A 23**, 89−120 (2004).
22. M. Hong, Y. Zhang, F. Hu, Membrane protein structure and dynamics from NMR spectroscopy. *Annu. Rev. Phys. Chem.* **63**, 1−24 (2012).
23. E. D. Watt, C. M. Rienstra, Recent advances in solid-state nuclear magnetic resonance techniques to quantify biomolecular dynamics. *Anal. Chem.* **86**, 58−64 (2014).
24. L. A. Baker, M. Baldus, Characterization of membrane protein function by solid-state NMR spectroscopy, *Curr. Op. Struct. Biol.* **27**, 48−55 (2014).
25. C. Aisenbrey, N. Pendem, G. Guichard, B. Bechinger, Solid state NMR studies of oligourea foldamers: interaction of ^{15}N-labelled amphiphilic helices with oriented lipid membranes. *Org. Biomol. Chem.* **10**, 1440−1447 (2012).
26. A. V. Struts, U. Chawla, S. M. Perera, M. F. Brown, Investigation of rhodopsin dynamics in its signaling state by solid-state deuterium NMR spectroscopy. *Methods Mol. Biol.* **1271**, 133−158 (2015).
27. T. Nagao *et al.*, Structure and orientation of antibiotic peptide alamethicin in phospholipid bilayers as revealed by chemical shift oscillation analysis of solid state nuclear magnetic resonance and molecular dynamics simulation. *Biochim Biophys Acta* **1848**, 2789−2798 (2015).
28. T. Polenova, R. Gupta, A. Goldbourt, Magic angle spinning NMR spectroscopy: a versatile technique for structural and dynamic analysis of solid-phase systems. *Anal. Chem.* **87**, 5458−5469 (2015).

29. A. Ramamoorthy, J. Xu, 2D $^{1}H/^{1}H$ RFDR and NOESY NMR experiments on a membrane-bound antimicrobial peptide under magic angle spinning. *J. Phys. Chem. B* **117**, 6693−7000 (2013).
30. K. Koch, S. Afonin, M. Ieronimo, M. Berditsch, A. S. Ulrich, in *Topics in current Chemistry*, J. C. C. Chan, Ed., (Springer, Berlin, 2012), vol. 306, pp. 89−118.
31. Y. Su, W. F. DeGrado, M. Hong, Orientation, dynamics, and lipid interaction of an antimicrobial arylamide investigated by ^{19}F and ^{31}P solid-state NMR spectroscopy. *J. Am. Chem. Soc.* **132**, 9197−9205 (2010).
32. J. K. Williams *et al.*, Drug-induced conformational and dynamical changes of the S31N mutant of the influenza M2 proton channel investigated by solid-state NMR. *J. Am. Chem. Soc.* **135**, 9885−9897 (2013).
33. N. Joh, T. Wang, M. Bhate, R. Acharya, Y. Wu, M. Grabe, M. Hong, G. Grigoryan, W.F. DeGrado, De novo design of a transmembrane Zn(II) transporting four-helix bundle, *Science* **346**, 1520−1524 (2014).
34. S. J. Pike *et al.*, Diastereotopic fluorine substituents as ^{19}F NMR probes of screw-sense preference in helical foldamers. *Org. Biomol. Chem.* **11**, 3168−3176 (2013).
35. P. Wadhwani, E. Strandberg, in *Fluorine in Medicinal Chemistry and Chemical Biology*, I. Ojima, Ed., (Wiley, Chichester, 2009) pp. 463−494.
36. S. Mazeres, V. Schram, J.-F. Tocanne, A. Lopez, 7-nitrobenz-2-oxa-1,3-diazole-4-yl-labeled phospholipids in lipid membranes: differences in fluorescence behavior. *Biophys. J.* **71**, 327−335 (1996).
37. F. Szoka, D. Papahadjopoulos, Comparative properties and methods of preparation of lipid vesicles (liposomes). *Ann. Rev. Biophys. Bioeng.* **9**, 467−508 (1980).
38. D. E. Warschawski *et al.*, Choosing membrane mimetics for NMR structural studies of transmembrane proteins. *Biochim. Biophys. Acta, Biomembr.* **1808**, 1957−1974 (2011).
39. J. H. Davis, M. Auger, R. S. Hodges, High resolution ^{1}H nuclear magnetic resonance of a transmembrane peptide. *Biophys. J.* **69**, 1917−1932 (1995).
40. M. Bouchard, J. H. Davis, M. Auger, High-speed magic angle spinning solid-state ^{1}H nuclear magnetic resonance study of the conformation of gramicidin A in lipid bilayers. *Biophys. J.* **69**, 1933−1938 (1995).
41. A. V. Filippov, A. M. Khakimov, B. V. Munavirov, ^{31}P NMR Studies of phospholipids, *Ann. Rep. NMR Spectr.* **85**, 27-92 (2015).

42. N. Kučerka, J. F. Nagle, J. N. Sachs, S. E. Feller, J. Pencer, A. Jackson, J. Katsaras, Lipid bilayer structure determined by the simultaneous analysis of neutron and x-ray scattering data, *Biophys J.* **95**, 2356–2367 (2008).
43. R. A. Brown, T. Marcelli, M. De Poli, J. Solà, J. Clayden, Induction of unexpected left-handed helicity by an N-terminal L-amino acid in an otherwise achiral peptide chain. *Angew. Chem. Int. Ed.* **51**, 1395−1399 (2012).
44. H.-W. Choe *et al.*, Crystal structure of metarhodopsin II. *Nature* **471**, 651−655 (2011)
45. R. Gessmann, H. Brückner, K. Petratos, Three complete turns of a 310-helix at atomic resolution: the crystal structure of Z-$(Aib)_{11}$-OtBu. *J. Pept. Sci.* **9**, 753−762 (2003).
46. R.-P. Hummel, C. Toniolo, G. Jung, Conformational transitions between enantiomeric 310 helices, *Angew. Chemie Int. Ed.* **26**, 1150−1152 (1987).
47. B. A. F. Le Bailly, L. Byrne, J. Clayden, Refoldable foldamers: global conformational switching by deletion or insertion of a single hydrogen bond. *Angew. Chemie Int. Ed.* **55**, 2132-2136 (2016).
48. G. M. Badger, R. J. Drewer, G. E. Lewis, Photochemical reactions of azo compounds. III. Photochemical cyclodehydrogenations of substituted azobenzenes. *Austr. J. Chem.* **17**, 1036−1049 (1964).
49. T. W. M. Spence, G. Tennant, The chemistry of nitro-compounds. Part II. The scope and mechanism of the base-catalysed transformations of some N,N-disubstituted o-nitrobenzamides. *J. Chem. Soc. Perkin Trans.* **1**, 97−102 (1972).
50. S. Keiper, J. S. Vyle, Reversible photocontrol of deoxyribozyme-catalyzed RNA cleavage under multiple-turnover conditions. *Angew. Chem. Int. Ed.* **45**, 3306−3309 (2006).
51. A. J. Harvey, A. D. Abell, Azobenzene-containing, peptidyl α-ketoesters as photobiological switches of α-chymotrypsin. *Tetrahedron* **56**, 9763 (2000).
52. F. Tibiletti *et al.*, One-pot synthesis of meridianins and meridianin analogues via indolization of nitrosoarenes. *Tetrahedron* **66**, 1280−1288 (2010).
53. A. Defoin, Simple preparation of nitroso benzenes and nitro benzenes by oxidation of anilines with H_2O_2 catalysed with molybdenum salts. *Synthesis* **5**, 706−710 (2004).
54. R. Jurok *et al.*, Planar chiral flavinium salts: synthesis and evaluation of the effect of substituents on the catalytic efficiency in enantioselective sulfoxidation reactions. *Eur. J. Org. Chem.* **2013**, 7724−7738 (2013).

55. K. Dan, N. Bose, S. Ghosh, Vesicular assembly and thermo-responsive vesicle-to-micelle transition from an amphiphilic random copolymer. *Chem. Comm.* **47**, 12491−12493 (2011).

56. J. Clayden, A. Castellanos, J. Solà, G. A. Morris, Quantifying end-to-end conformational communication of chirality through an achiral peptide chain. *Angew. Chem. Int. Ed.* **48**, 5962 (2009).

57. L. Byrne *et al.*, Foldamer-mediated remote stereocontrol: >1,60 asymmetric induction. *Angew. Chem. Int. Ed.* **53**, 151 (2014).

58. J. Solà, G. A. Morris, J. Clayden, Measuring screw-sense preference in a helical oligomer by comparison of ^{13}C NMR signal separation at slow and fast exchange. *J. Am. Chem. Soc.* **133**, 3712 (2011).

59. W. M. Yau, W. C. Wimley, K. Gawrisch, S. H. White, The preference of tryptophan for membrane interfaces. *Biochemistry* **37**, 14713 (1998).