Supramolecular chemistry of helical foldamers at the solid-liquid interface: self-assembled monolayers and anion recognition

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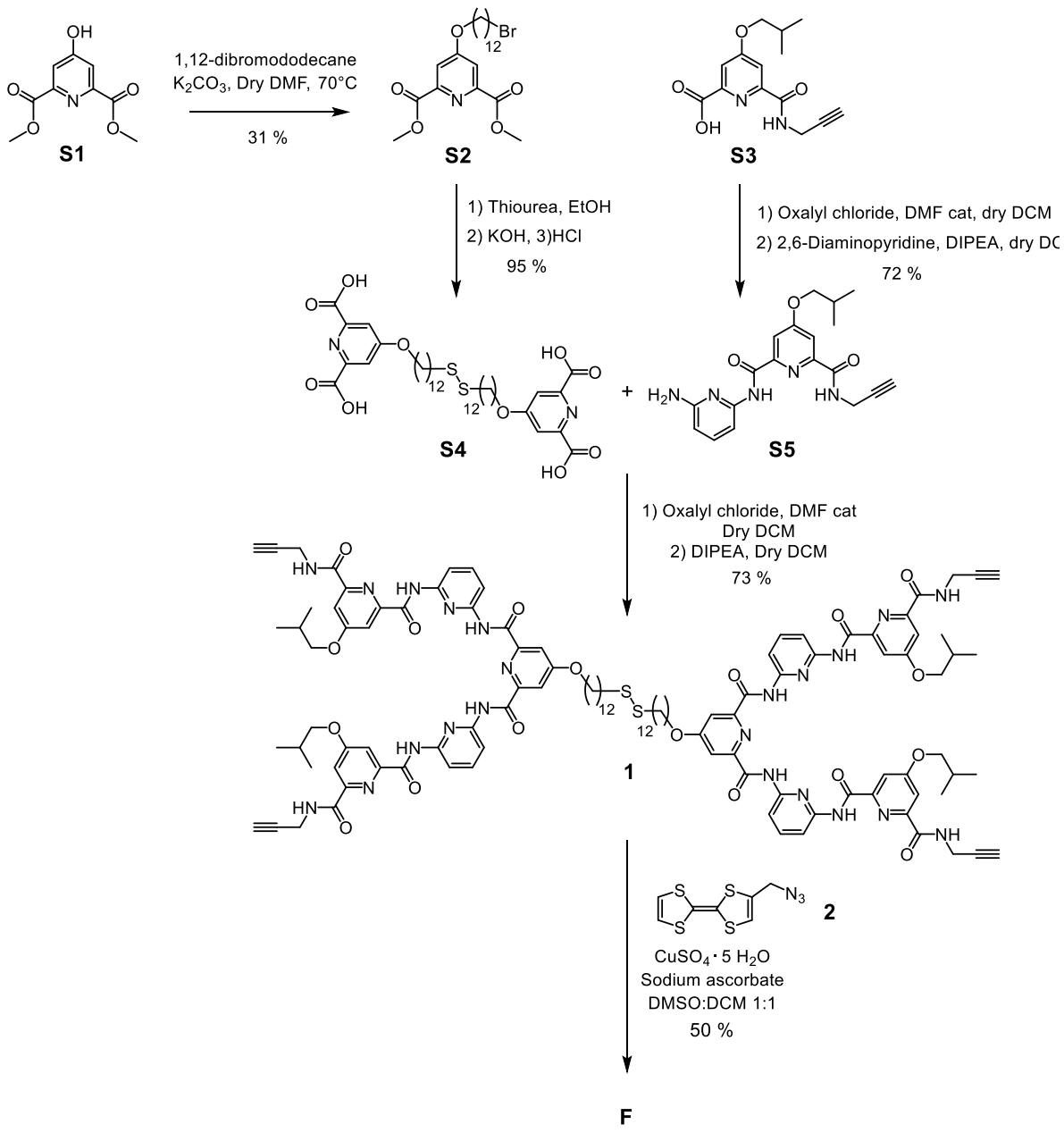
Supporting information



Scheme S1. Synthesis of target compound **F**.

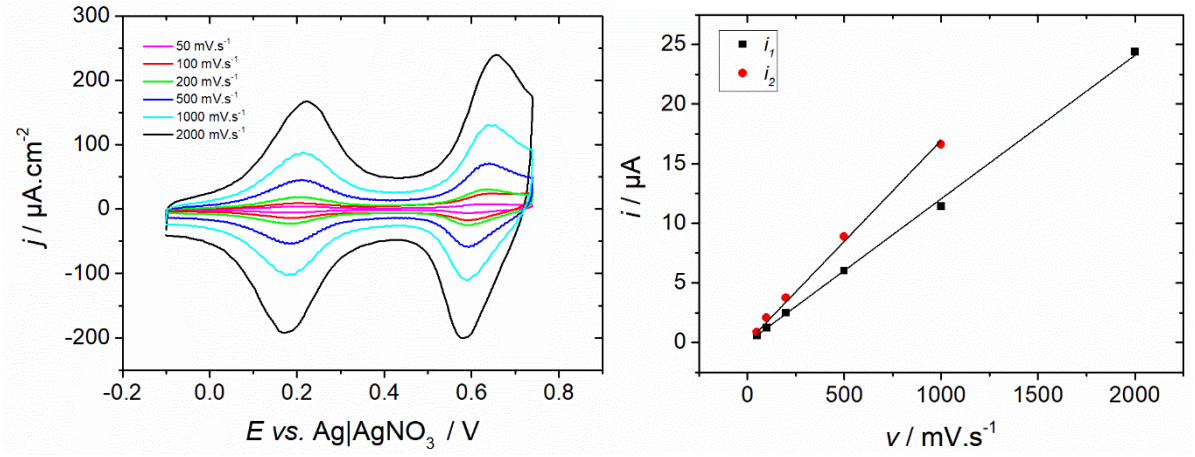


Figure S1. *Left.* Cyclic voltammograms of a **F**-based self-assembled monolayer at various scan rates (nBu$_4$NPF$_6$ 0.1 M, CH_2Cl_2). *Right.* Corresponding linear relationships between the intensities of the oxidation peaks and the scan rate.

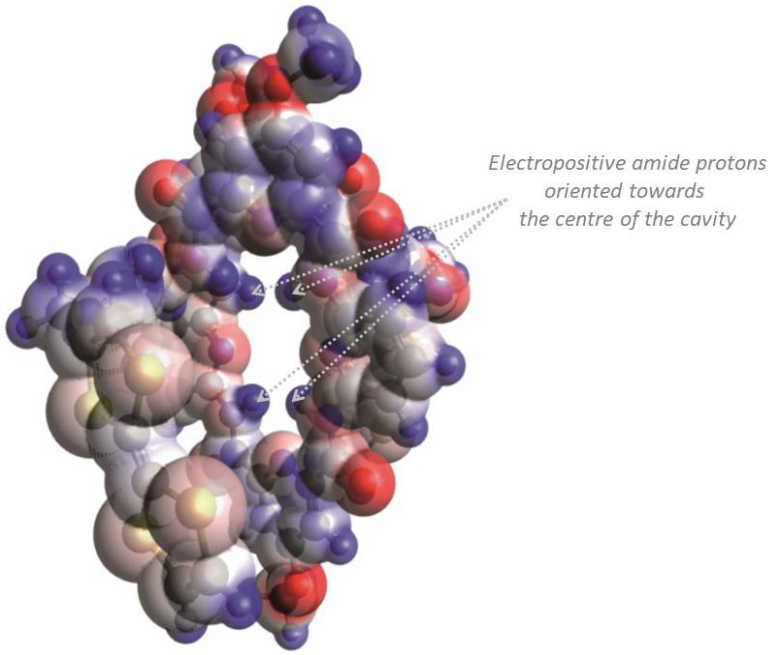


Figure S2. Electrostatic potential map of a foldamer **F** analogue (alkoxy chains were replaced by methoxy groups – calculations led with Avogadro (https://avogadro.cc/)).

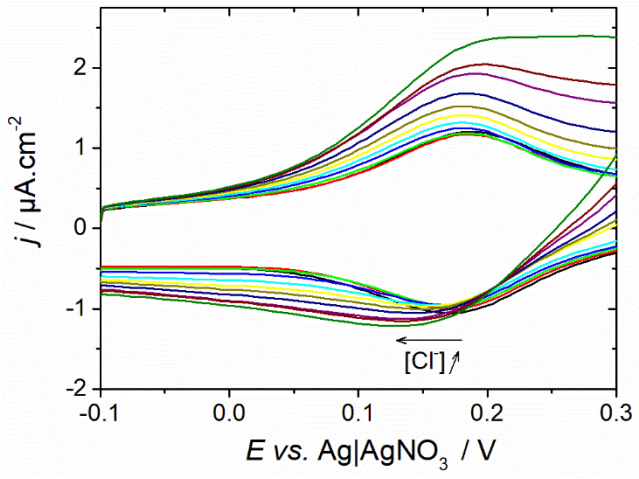


Figure S3. Cyclic voltammograms of a **F**-based self-assembled monolayer upon successive additions of tetrabutylammonium chloride (nBu$_4$NPF$_6$ 0.1 M, CH_2Cl_2, v = 100 mV.s^{-1}). The corresponding ΔE values are plotted in Figure 3b.

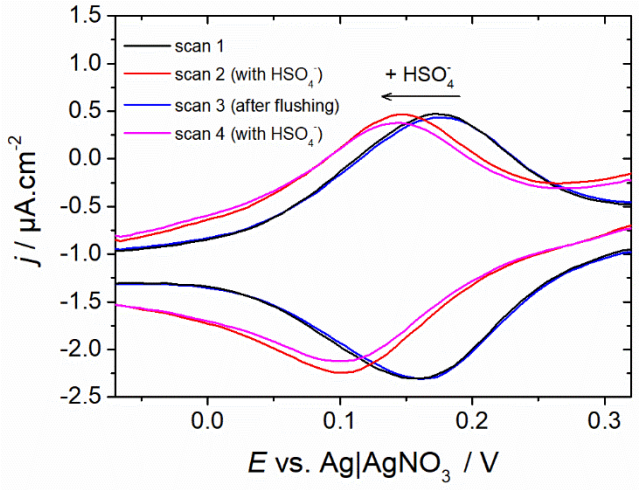


Figure S4. Successive cyclic voltammograms of a **F**-based self-assembled monolayer in the presence (200 µM) and the absence of HSO_4^- anion (nBu$_4$NPF$_6$ 0.1 M, CH_2Cl_2, v = 100 mV.s^{-1}).

Adapted Frumkin model to describe the evolution of the oxidation potential as a function of anion concentration

The equilibrium between immobilized foldamers and the anionic guest (A^-) is defined by equation (S1). The variations of potential were fitted to the concentrations of anions according to Equation S2.

$$\text{Fold} + A^- \rightleftharpoons [\text{Fold} \cdot A]^- \quad \text{(S1)}$$

$$\frac{\Delta E}{\Delta E_{sat} - \Delta E} exp\left(g \frac{\Delta E}{\Delta E_{sat}}\right) = \beta . C \quad \text{(S2)}$$

The parameters are described in equation (2), where C is the anion concentration, $\Delta E = E - E_i$ is the variation of electrochemical potential upon anion binding and ΔE_{sat} the value at saturation.

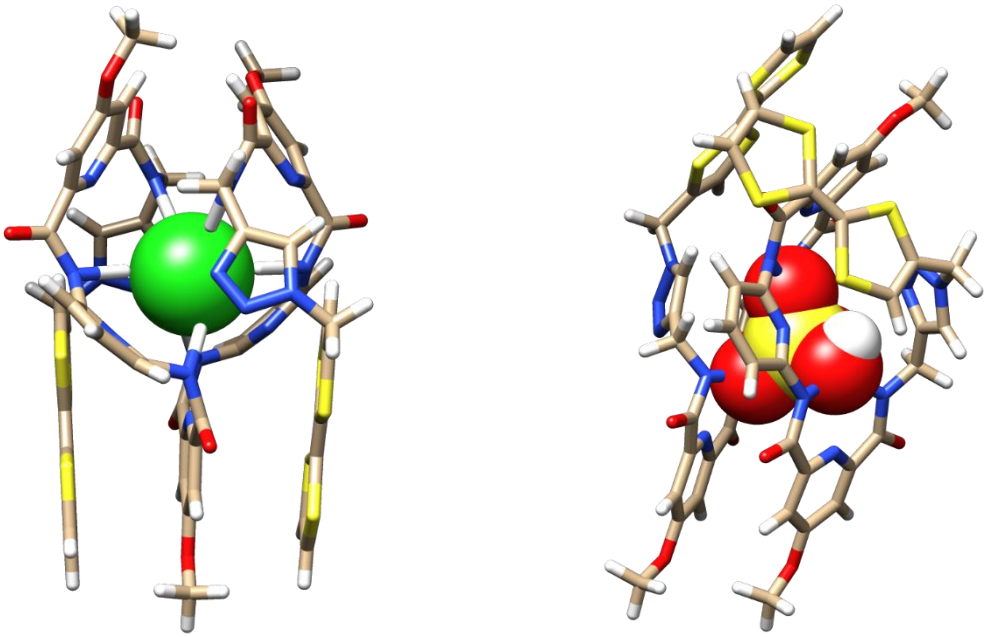


Figure S5. Possible binding modes between the grafted foldamer and chloride and hydrogen sulfate anions (geometrical optimizations led through Molecular Mechanics (MM+) calculations)

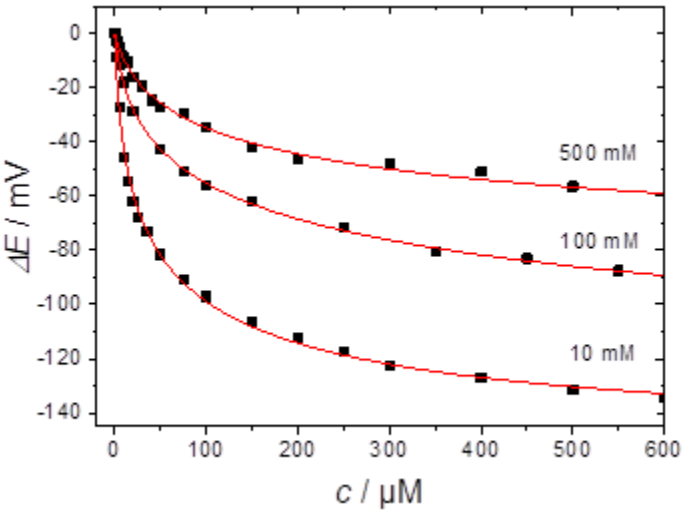


Figure S6. Variations of the electrochemical potential shift $\Delta E = E - E_i$ of **F**-based self-assembled monolayers upon addition of tetrabutylammonium hydrogen sulfate ($C(n\text{Bu}_4\text{NPF}_6)$ = 0.01, 0.1 or 0.5 M in dichloromethane, v = 100 mV.s^{-1}).

Experimental details

Synthesis

The starting materials were purchased and used without further purification. Compound **S3** and azidomethyltetrathiafulvalene **2** were prepared according to the literature (*Chem. Commun.* 2019, **55**, 5743-5746).

All solvents and reagents were dried according to standard procedures (sodium/benzophenone for tetrahydrofuran and diethyl ether, CaH_2 for dichloromethane, acetonitrile, triethylamine and *N,N*-diisopropylethylamine, P_2O_5 for chloroform).

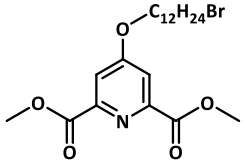
Thin-layer chromatography (TLC) was performed on aluminium plates coated with MerckSilica gel 60 F254. Developed plates were air-dried and scrutinized under a UV lamp. Silica gel SIGMA Aldrich Chemistry (SiO_2, pore size 60 Å, 40-63 µm technical grades) was used for preparative silica gel chromatography.

Coupling constants (J) are denoted in Hz and chemical shifts (δ) in parts per million (ppm). Multiplicities are described as follows: s = singlet, d = doublet, t = triplet, m = multiplet, br = broad. The mass spectra were recorded on a Jeol JMS 700 (high resolution mass spectra (HRMS) or a Bruker Biflex III spectrometer (MALDI-TOF).

Recycling size-exclusion chromatography (SEC)

SEC Purifications were led on a LC-9160NEXT equipment from the Japan Analytical Industry Company. Crude were dissolved in chloroform (HPLC grade stabilized with ethanol), filtered through a 0.45 µm PTFE filter and injected. The separation was performed through a set of two JAIGEL-2H and 2.5H columns (10 $mL.min^{-1}$) and the detection was possible through UV-vis 4Ch NEXT and RI-700 II detectors.

Dimethyl 4-((12-bromododecyl)oxy)pyridine-2,6-dicarboxylate ***S2***



Chemical Formula: $C_{21}H_{32}BrNO_5$
Molecular Weight: 458.39

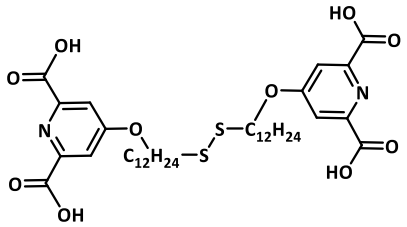
Dimethyl 4-hydroxypyridine-2,6-dicarboxylate (3 g, 14.2 mmol), potassium carbonate (3.93 g, 28.5 mmol) and 1,12-dibromododecane (13.98 g, 42.6 mmol) were dissolved in dry DMF (30 mL). The reaction was stirred under argon atmosphere at 70°C overnight. The solvent was removed under reduced pressure and dichloromethane was added. The resulting suspension was filtered and the filtrate was concentrated *in vacuo*. The desired compound was purified by silica gel chromatography (Petroleum ether/EtOAc Ac 8/2) to afford **S2** as a white solid (2 g, 31 %).

^{1}H NMR (300 MHz, $CDCl_3$): δ 7.77 (s, 2H), 4.11 (t, *J* = 6.5 Hz, 2H), 3.98 (s, 6H), 3.38 (t, *J* = 6.9 Hz, 2H), 1.89 – 1.75 (m, 4H), 1.51 – 1.20 (m, 18H).

^{13}C NMR (75 MHz, $CDCl_3$): δ 167.2, 165.3, 149.8, 114.6, 69.2, 53.3, 53.3, 34.1, 32.9, 29.6, 29.5, 29.3, 28.8, 28.8, 28.2, 25.9.

HRMS (Cl^+) calcd. for $C_{21}H_{32}BrNO_5$ $[M+H]^+$, 458.1464; found, 458.1542.

*Compound **S4*** (procedure adapted from Martín, Echegoyen and coll. *J. Org. Chem.,* 2003, **68**, 8379–8385)



Chemical Formula: $C_{38}H_{56}N_2O_{10}S_2$
Molecular Weight: 764.99

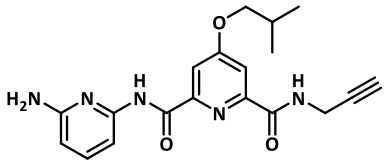
A mixture of compound **S2** (100 mg, 0.2 mmol) and thiourea (83 mg, 1.1 mmol) in dry ethanol (20 mL) was stirred and refluxed under an argon atmosphere for 24 h. After the solution was cooled down, the solvent was removed under vacuum. An aqueous solution of potassium hydroxide (4 mL, 1 M) was added to the residue, and the resulting suspension was stirred for 2 h. The mixture was acidified with hydrochloric acid. The precipitate was filtered, washed with water, acetone and dichloromethane to afford **S4** as a white solid (80 mg, 95 %).

^{1}H NMR (500 MHz, DMSO-d_6, 100°C): δ 7.66 (s, 4H), 4.25 (t, *J* = 6.5 Hz, 4H), 1.83 – 1.73 (m, 4H), 1.60 – 1.51 (m, 4H), 1.50 – 1.40 (m, 4H), 1.41 – 1.23 (m, 32H).

^{13}C NMR: this spectrum could not recorded because of solubility issues, including in DMSO-d_6 at 373 K.

HRMS (FAB$^+$) calcd. for $C_{38}H_{56}N_2O_{10}S_2$ $[M+H]^+$, 765.3376; found, 765.3463.

*Compound **S5***



Chemical Formula: $C_{19}H_{21}N_5O_3$
Molecular Weight: 367.41

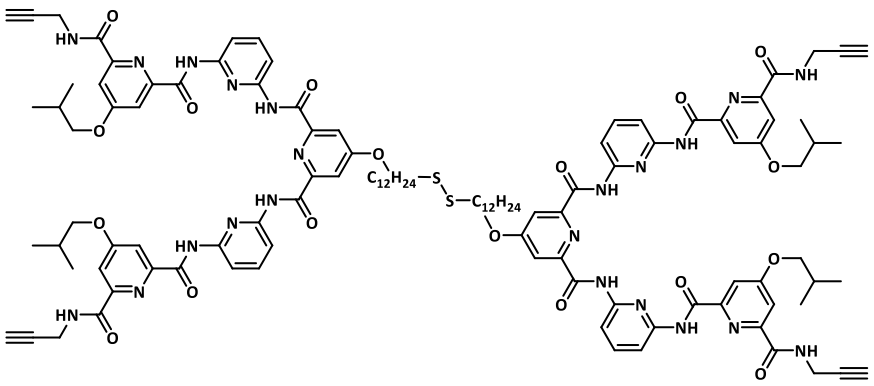
Under inert atmosphere, carboxylic acid **S3** (150 mg, 0.5 mmol) was solubilized in dry dichloromethane (2 mL). Oxalyl chloride (105 mg, 0.8 mmol, 1.6 eq.) and a drop of dry dimethylformamide were added. After the gas release stopped, the medium was stirred at room temperature for one hour. Dichloromethane and oxalyl chloride were evaporated *in vacuo* and the resulting solid was dissolved in dry dichloromethane (6 mL). This solution was added dropwise to a mixture of 2,6-diaminopyridine (296 mg, 2.7 mmol, 5.4 eq.) and DIPEA (351 mg, 2.7 mmol, 5.4 eq.) in dry dichloromethane (12 mL). The mixture was subsequently stirred for 16 hours at room temperature under argon atmosphere. The solvent was removed under reduced pressure and compound **S5** was isolated by silica gel chromatography (eluent: CH_2Cl_2/EtOAc 80/20) as a light yellow solid (150 mg, 72 %).

^{1}H NMR (300 MHz, $CDCl_3$): δ 10.01 (s, 1H), 7.94 – 7.85 (m, 2H), 7.77 (d, *J* = 7.9 Hz, 1H), 7.55 (t, *J* = 7.9 Hz, 1H), 6.33 (d, *J* = 8.0 Hz, 1H), 4.40 (s, 2H), 4.34 (dd, *J* = 5.8, 2.5 Hz, 2H), 3.92 (d, *J* = 6.5 Hz, 2H), 2.30 (t, *J* = 2.6 Hz, 1H), 2.25 – 2.06 (m, 1H), 1.05 (d, *J* = 6.7 Hz, 6H).

^{13}C NMR (75 MHz, CDCl3): δ 168.3, 163.4, 161.6, 157.4, 150.5, 150.5, 149.4, 140.5, 112.0, 111.9, 105.1, 103.9, 79.7, 75.4, 71.7, 53.6, 29.4, 28.1, 19.2.

HRMS (EI$^+$) calcd. for $C_{19}H_{21}N_5O_3$ $[M]^+$, 367.1644; found, 367.1637.

*Foldamer **1***



Chemical Formula: $C_{114}H_{132}N_{22}O_{18}S_2$
Molecular Weight: 2162.57

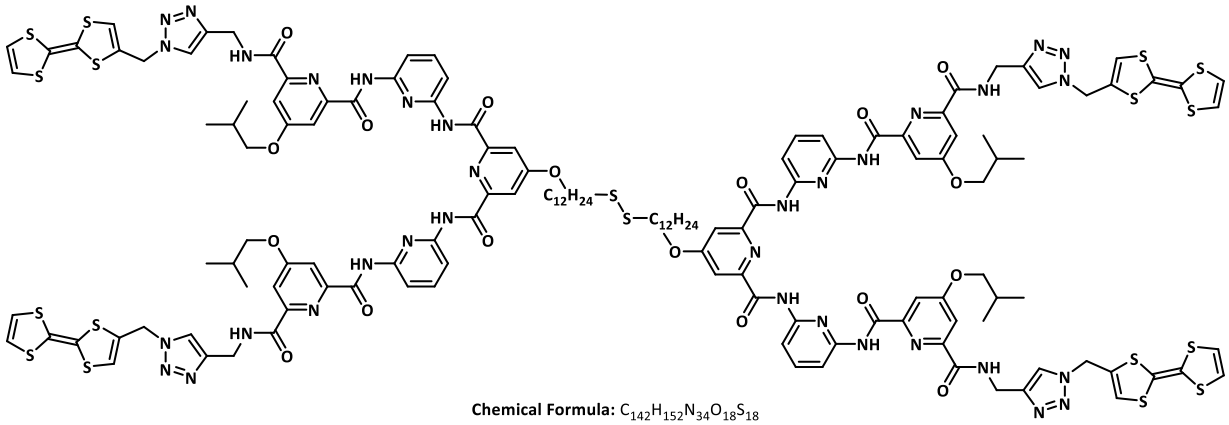
Tetracarboxylic acid **S4** (50 mg, 0.07 mmol) was suspended in dry dichloromethane (2 mL) under inert conditions. Oxalyl chloride (42 mg, 0.3 mmol, 4.3 eq.) and a drop of dry dimethylformamide were added. After the gas release stopped, the mixture was stirred for an additional hour at room temperature. The medium was concentrated *in vacuo* affording a yellow oil, which was dissolved in dry dichloromethane (1 mL) and added dropwise to a solution of amine **S5** (116 mg, 0.3 mmol, 4.3 eq.) and DIPEA (41 mg, 0.3 mmol, 4.3 eq.) in dry dichloromethane (0.5 mL). The mixture was stirred for 16 hours at room temperature under argon atmosphere. The solvent was evaporated under reduced pressure and tetraalkyne **1** was isolated by recycling size-exclusion chromatography (eluent: chloroform) as a light-yellow solid (100 mg, 73 %).

^{1}H NMR (300 MHz, $CDCl_3$): δ 10.62 (s, 4H), 10.41 (s, 4H), 10.01 (t, *J* = 5.8 Hz, 4H), 8.29 – 8.15 (m, 8H), 8.03 – 7.94 (m, 8H), 7.81 – 7.68 (m, 8H), 4.39 – 4.19 (m, 4H), 4.10 – 3.85 (m, 12H), 3.58 – 3.42 (m, 2H), 3.07 – 2.92 (m, 2H), 2.16 (hept, *J* = 6.6 Hz, 4H), 1.66 (p, *J* = 7.1 Hz, 4H), 1.45 – 0.70 (m, 68H).

^{13}C NMR (76 MHz, $CDCl_3$): δ 168.2, 168.1, 165.7, 163.6, 162.8, 153.2, 151.6, 150.8, 150.4, 148.5, 140.8, 112.5, 112.4, 112.2, 111.8, 110.5, 79.8, 75.5, 70.6, 69.0, 39.3, 29.7, 29.7, 29.6, 29.5, 29.5, 29.4, 29.2, 29.2, 29.1, 29.0, 28.7, 28.2, 25.4, 19.2.

MS (MALDI) calcd. for $C_{114}H_{132}N_{22}O_{18}S_2$ $[M]^+$, 2160.9531; found, 2160.9513.

*Foldamer **F***



Chemical Formula: $C_{142}H_{152}N_{34}O_{18}S_{18}$
Molecular Weight: 3200.08

Compound **1** (42 mg, 0.02 mmol) and azidomethyltetrathiafulvalene **2** (40 mg, 0.16 mmol, 8 eq.) were dissolved in a mixture of dimethylsulfoxide and dichloromethane (1/1 (*v/v*)). The solution was purged through argon bubbling for five minutes. Copper sulfate pentahydrate (0.5 mg, 2 µmol, 0.1 eq.) and sodium ascorbate (0.8 mg, 4 µmol, 0.2 eq.) were added and the medium was stirred for 16 hours at room temperature. Dichloromethane (20 mL) was added and the organic phase was washed three times with water. The organic layer was dried over magnesium sulfate, filtered, and concentrated *in vacuo*. Foldamer **F** was isolated by silica gel chromatography (eluent CH_2Cl_2/MeOH/Et_3N 98:1:1) as a yellow solid (35 mg, 56 %).

^{1}H NMR (300 MHz, DMSO-d_6): δ 11.20 (s, 4H), 11.12 (s, 4H), 9.93 (t, *J* = 6.2 Hz, 4H), 8.15 – 7.98 (m, 12H), 7.91 – 7.80 (m, 8H), 7.70 (d, *J* = 2.5 Hz, 4H), 7.37 (d, *J* = 2.5 Hz, 4H), 6.79 (s, 4H), 6.68 – 6.54 (m, 8H), 5.30 (s, 8H), 4.34 – 4.19 (m, 8H), 3.99 (d, *J* = 6.5 Hz, 8H), 2.18 – 2.03 (m, 4H), 1.83 – 1.70 (m, 4H), 1.65 – 1.53 (m, 4H), 1.51 – 1.15 (m, 40H), 1.04 (d, *J* = 6.6 Hz, 24H).

^{13}C NMR (125MHz, DMSO-d_6): δ 167.7, 166.8, 162.8, 162.2, 161.7, 150.4, 150.1, 150.0, 149.6, 145.4, 140.9, 130.1, 122.9, 120.6, 119.9, 119.9, 111.8, 111.6, 111.3, 110.6, 107.3, 74.4, 69.0, 62.6, 52.0, 47.8, 45.5, 38.0, 38.0, 34.3, 29.0, 28.9, 28.7, 28.6, 28.5, 28.2, 27.7, 27.5, 25.3, 18.8, 8.5, 7.2.

MS (MALDI) calcd. for $C_{142}H_{152}N_{34}O_{18}S_{18}$ $[M]^+$, 3196.6997; found, 3196.7054.

Preparation and characterization of self-assembled monolayers

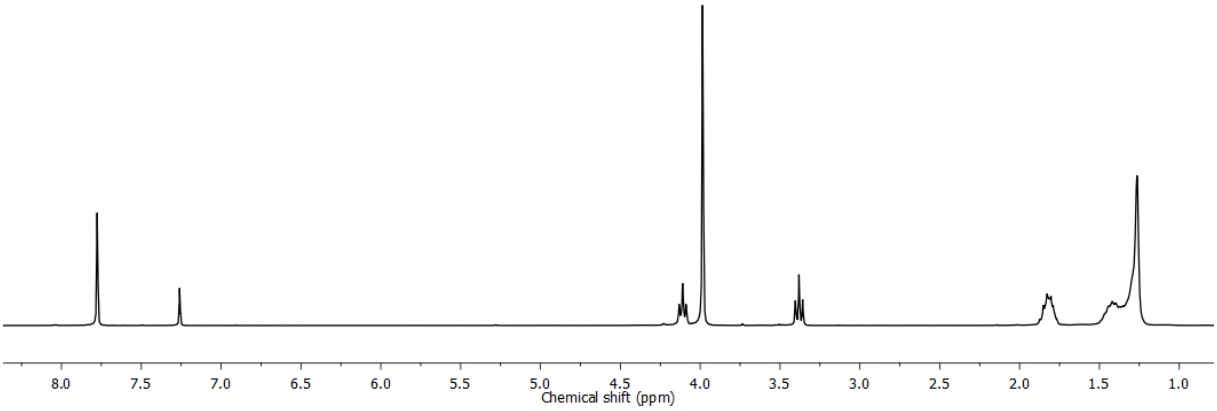
Gold PVD electrode were prepared as reported elsewhere.[S1] SAMs were prepared on fresh Au substrates (0.2 cm^2) by immersion in a solution of **F** (5 µM, CH_2Cl_2) for 15 hours. After immobilization, the electrodes were thoroughly rinsed using dichloromethane. Electrochemical experiments were carried out with a Biologic SP-150 potentiostat. Cyclic voltammograms were recorded in a glovebox in a three-electrode cell equipped with a platinum-plate counter electrode and a $Ag/AgNO_3$ (0.01 M CH_3CN) reference electrode. These measurements were performed in methylene chloride with tetrabutylammonium hexafluorophosphate ($n$$Bu_4NPF_6$) as supporting electrolyte.

[S1] O. Alévêque, P.-Y. Blanchard, T. Breton, M. Dias, C. Gautier, E. Levillain, *Electrochem. Commun.* 2012, **16**, 6–9.

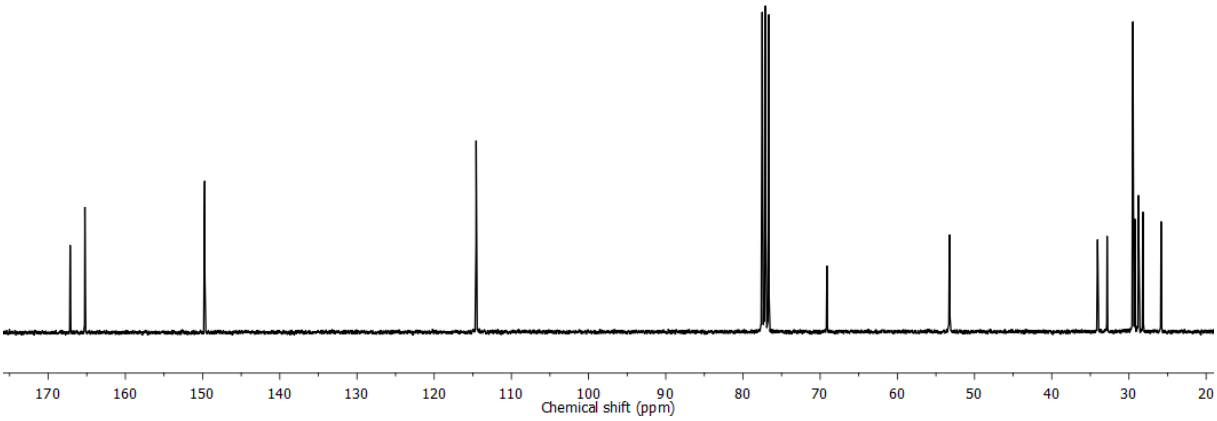
Collection of spectra

Dimethyl 4-((12-bromododecyloxy)pyridine-2,6-dicarboxylate ***S2***

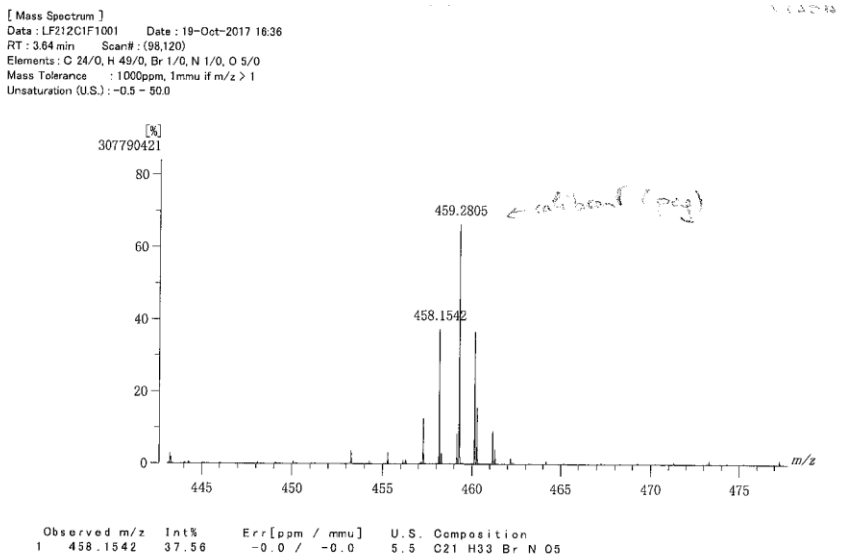
^{1}H NMR ($CDCl_3$)



^{13}C NMR ($CDCl_3$)

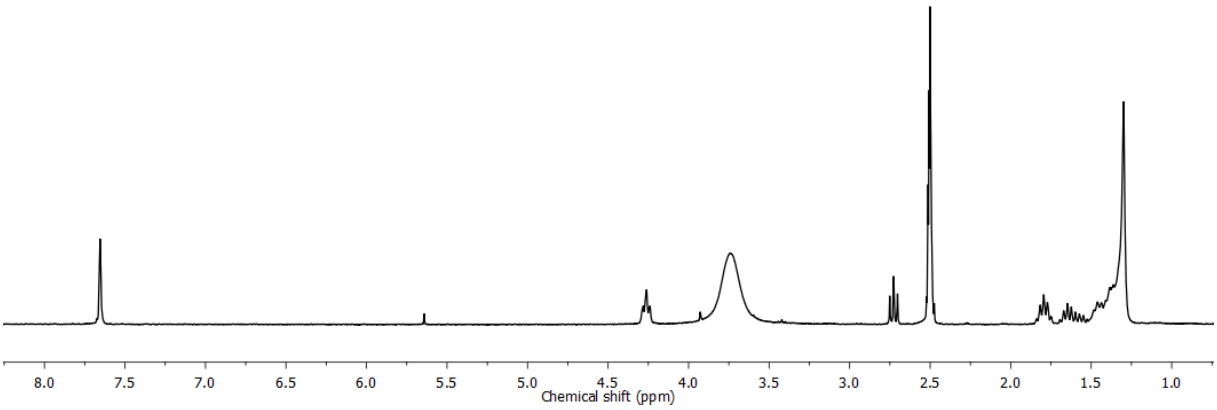


HRMS



*Compound **S4***

^{1}H NMR (DMSO-d_6, 100°C)



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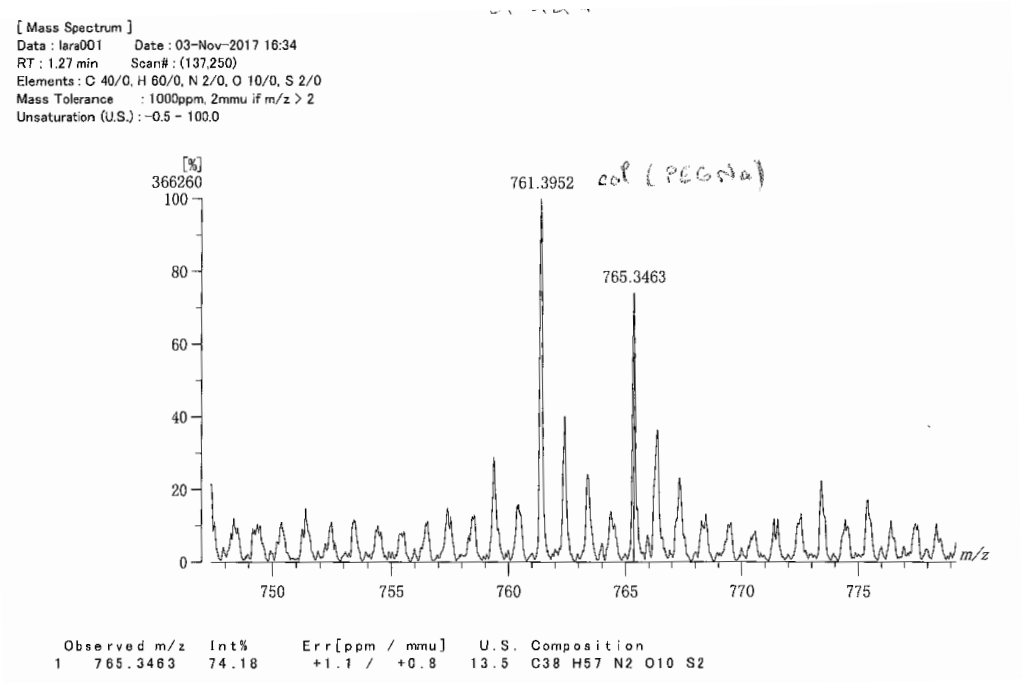
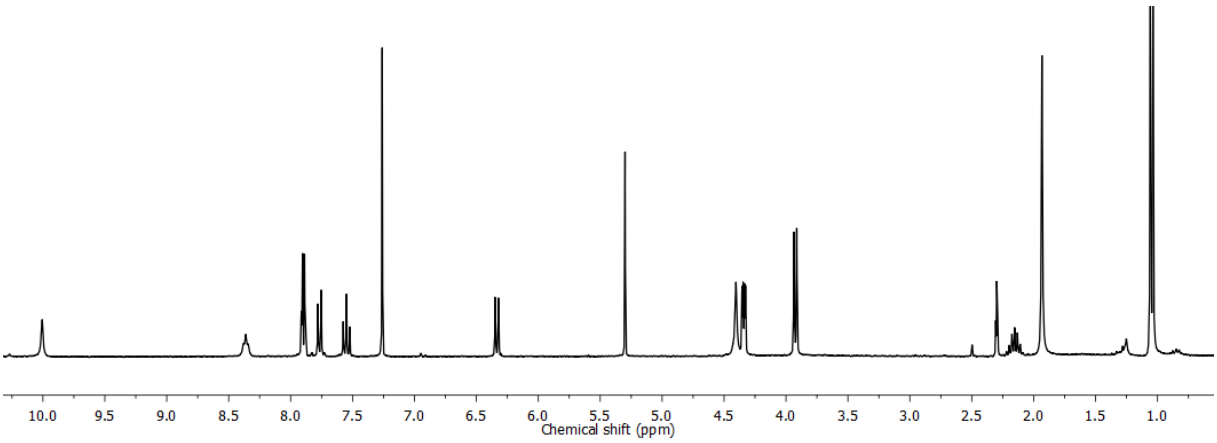
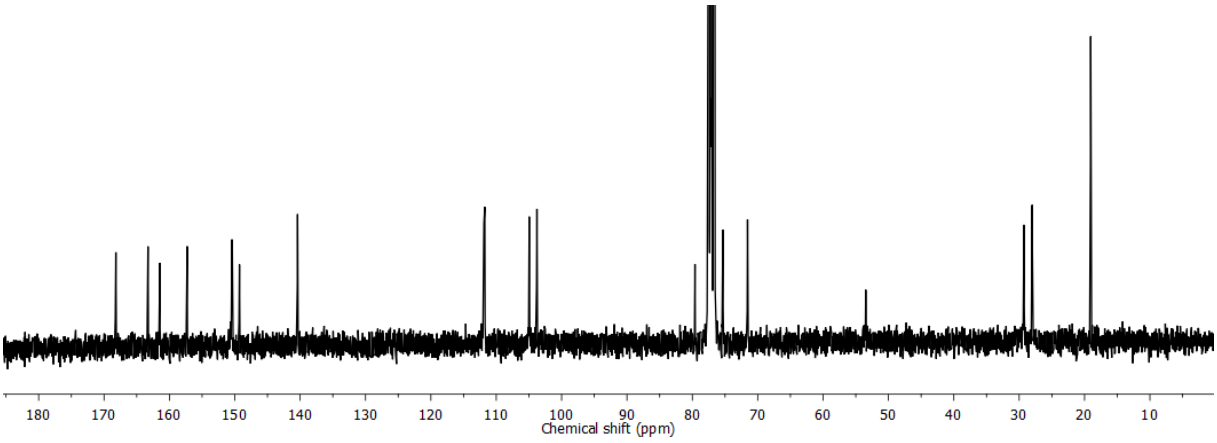


*Compound **S5***

^{1}H NMR ($CDCl_3$)



^{13}C NMR ($CDCl_3$)



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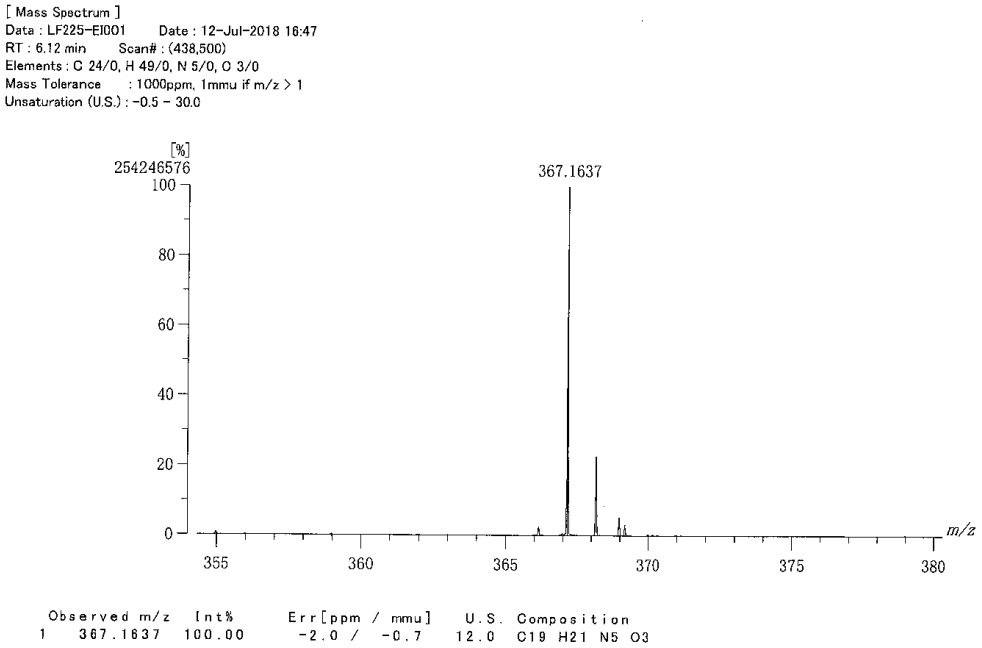
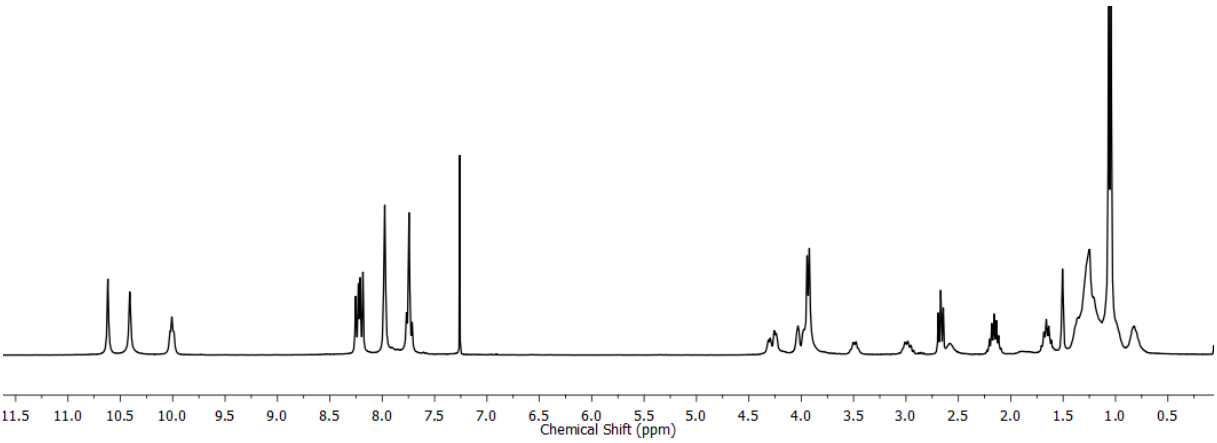
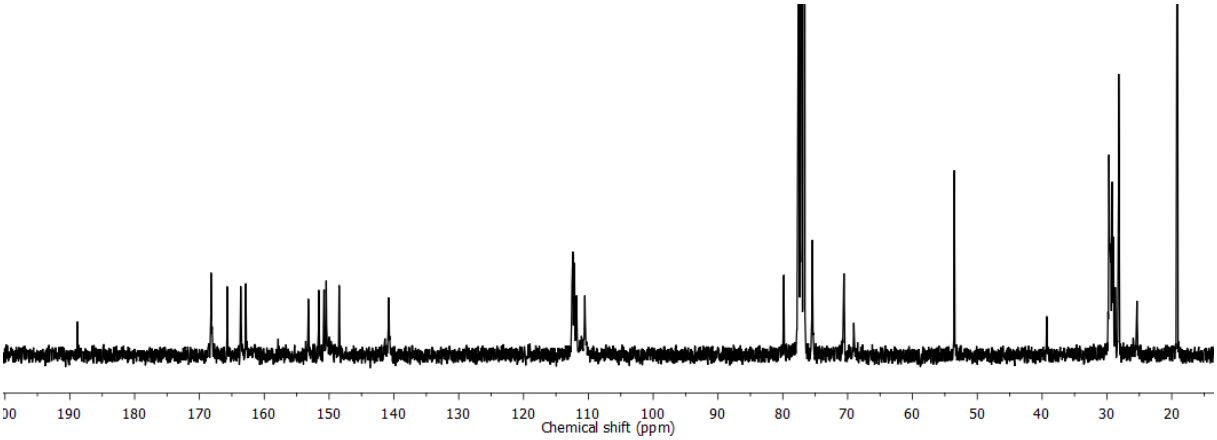


*Foldamer **1***

^{1}H NMR ($CDCl_3$)



^{13}C NMR ($CDCl_3$)



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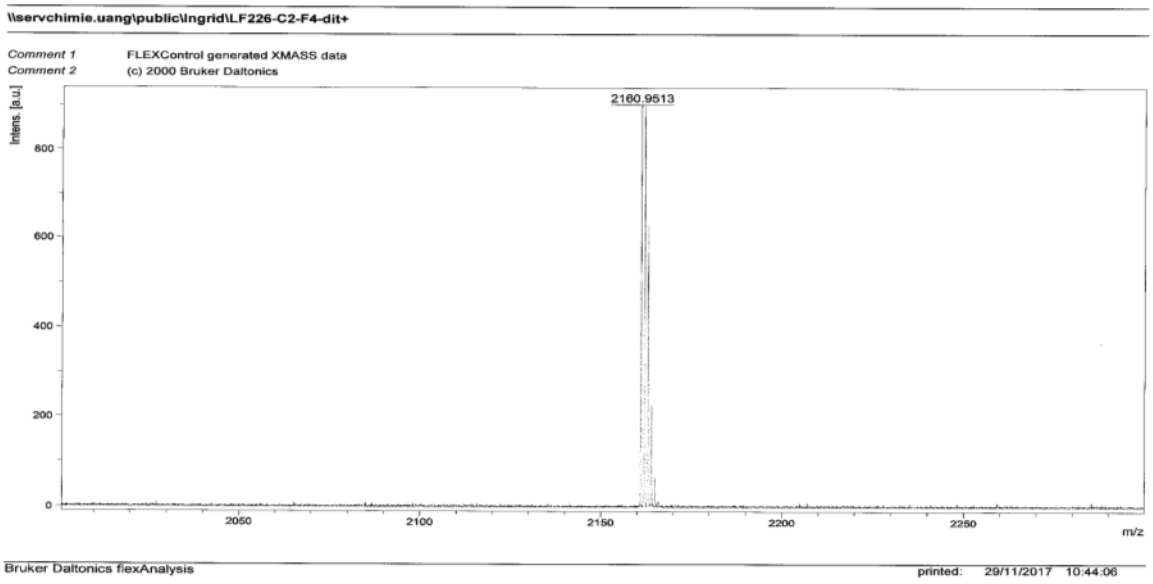
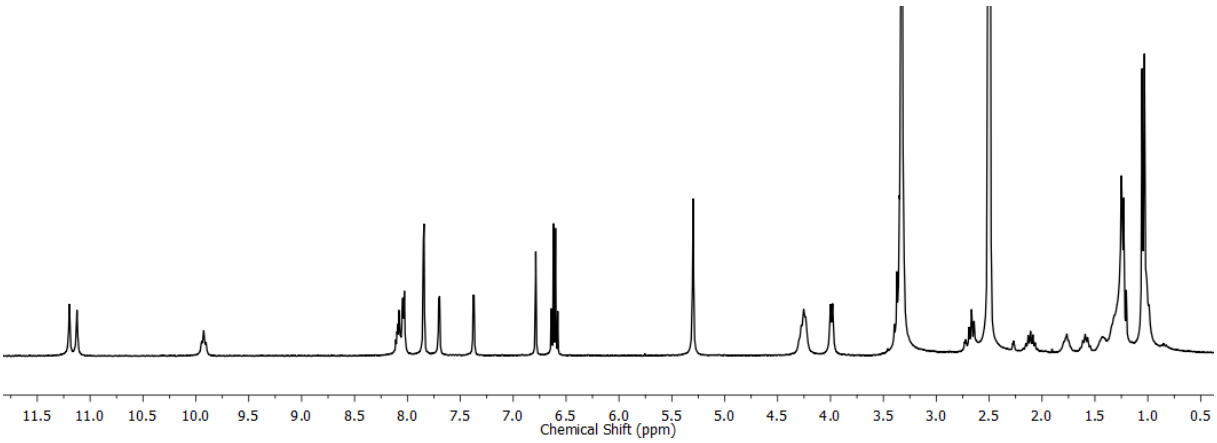
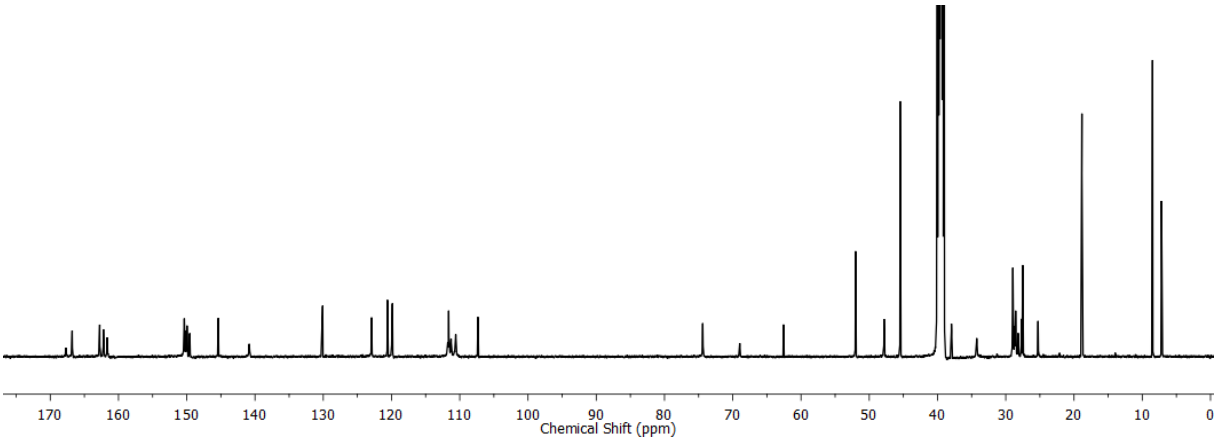


*Foldamer **F***

^{1}H NMR (DMSO-d_6)



^{13}C NMR (DMSO-d_6)



HRMS