Conformational Properties and Folding Analysis of a Series of Seven Oligoamide Foldamers

Supplementary Information

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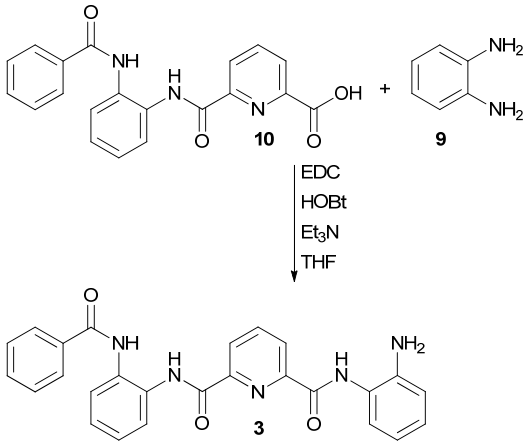
1 Synthesis and NMR spectra of foldamer 3

The starting materials were commercially available and used as such unless otherwise noted. The glassware was dried at 120°C prior to use. Dichloromethane was dried by distilling it over $CaCl_2$ and stored over Linde type 3 Å sieves under nitrogen atmosphere. Tetrahydrofurane (THF) was dried with MBraun solvent purification system. Triethylamine (Et_3N) was stored on molecular sieves (3 Å) and under nitrogen atmosphere.

NMR spectra were measured with Bruker Avance DRX 500 spectrometer and the chemical shifts were calibrated to the residual proton and carbon resonance of the deuterated solvent. The melting point was measured in an open capillary using a Stuart SMP30 melting point apparatus and is uncorrected. An ESI-TOF mass spectrum was measured with a LCT Micromass spectrometer. Elemental analysis was done with a Vario EL III instrument.

Synthesis of N^2-(2-aminophenyl)-N^6-(2-benzamidophenyl)-pyridine-2,6-dicarboxamide 3.[1]



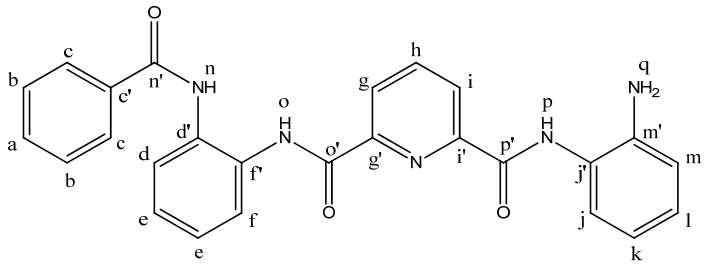
Scheme 1. The reaction scheme for the synthesis of compound **3**.

The synthesis was carried out under an argon atmosphere. *O*-phenylenediamine **9** (1.20 g; 11.13 mmol), 6-((2-benzamidophenyl)carbamoyl)picolinic acid **10** (1.00 g; 2.76 mmol) and hydroxybenzotriazole hydrate (HOBT) (0.43 g; 2.82 mmol) were dissolved in THF (120 ml). The solution was cooled to 0°C, and Et_3N (0.4 ml; 2.87 mmol) and 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide (EDC) (0.5 ml; 2.82 mmol) were added to the solution. The cooled solution was stirred for an hour, allowed to warm to RT and stirred overnight. The solution was concentrated as oil and ethyl acetate (EtOAc) was added. This resulted in the product **3** precipitating as a white solid, yield 0.85 g (68%). mp. 243-245 °C; ^{1}H NMR (ESI†)

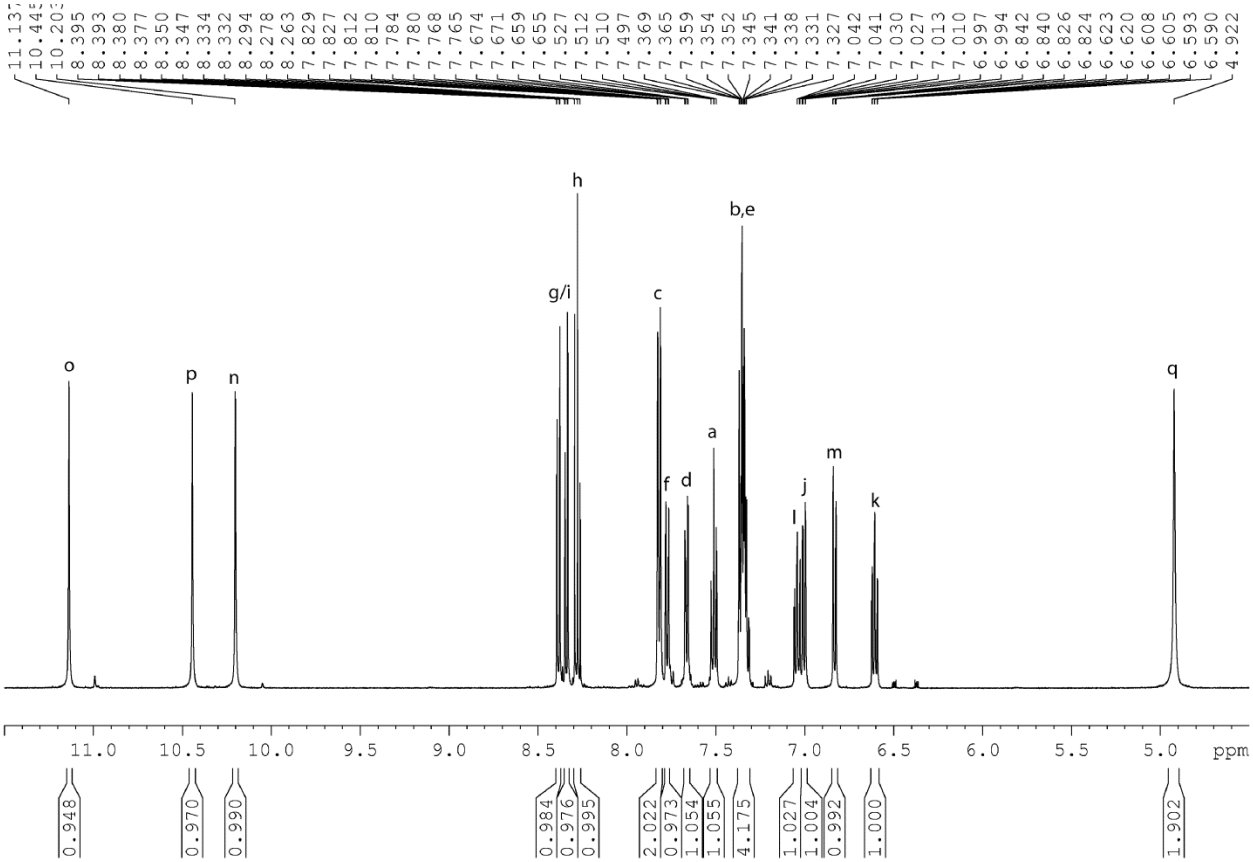
(500 MHz, DMSO-d_6, 30 °C): δ = 4.92 (s, 2H; q), 6.61 (td, $^3J_{HH}$ = 1.4 Hz, $^3J_{HH}$ = 7.6 Hz 1H; k), 6.83 (dd, $^3J_{HH}$ = 1.4 Hz, $^3J_{HH}$ = 8.0 Hz, 1H; m), 7.00 (dd, $^3J_{HH}$ = 1.4 Hz, $^3J_{HH}$ = 7.9 Hz, 1H; j), 7.03-7.06 (m, 1H; l), 7.31-7.37 (m, 4H; b,e), 7.49-7.53 (m, 1H; a), 7.66-7.67 (m, 1H; d), 7.76-7.78 (m, 1H; f), 781-7.83 (m, 2H; c), 8.28 (t, $^3J_{HH}$ = 7.7 Hz, 1H; h), 8.33-8.35 (m, 1H; g/i), 8.38-8.40 (m, 1H; g/i), 10.20 (s, 1H; n), 10.44 (s, 1H; p), 11.14 (s, 1H; o), ^{13}C NMR (ESI†) (126 MHz, DMSO-d_6, 30 °C): δ = 116.05 (m/k), 116.19 (m/k), 122.15 (j'), 124.80 (g/i), 125.12 (g/i), 125.70 d/e/f), 125.81 (d/e/f), 125.94 (d/e/f), 127.17 (j,l), 127.59 (c), 128.34 (b), 130.63 (d'), 131.41 (f'), 131.74 (a), 133.85 (c'), 139.95 (h), 143.83 (m'), 148.36 (g'/i'), 148.79 (g'/i'), 161.66 (o',p'), 166.01 (n'); MS (ESI-TOF) *m/z*: 474.09 [M + Na^+]; Elemental analysis calcd (%) for $C_{26}H_{21}N_5O_3$: C 69.2, H 4.7, N 15.5; found C 68.8, H 4.7, N 15.3.

NMR spectra for the foldamer 3

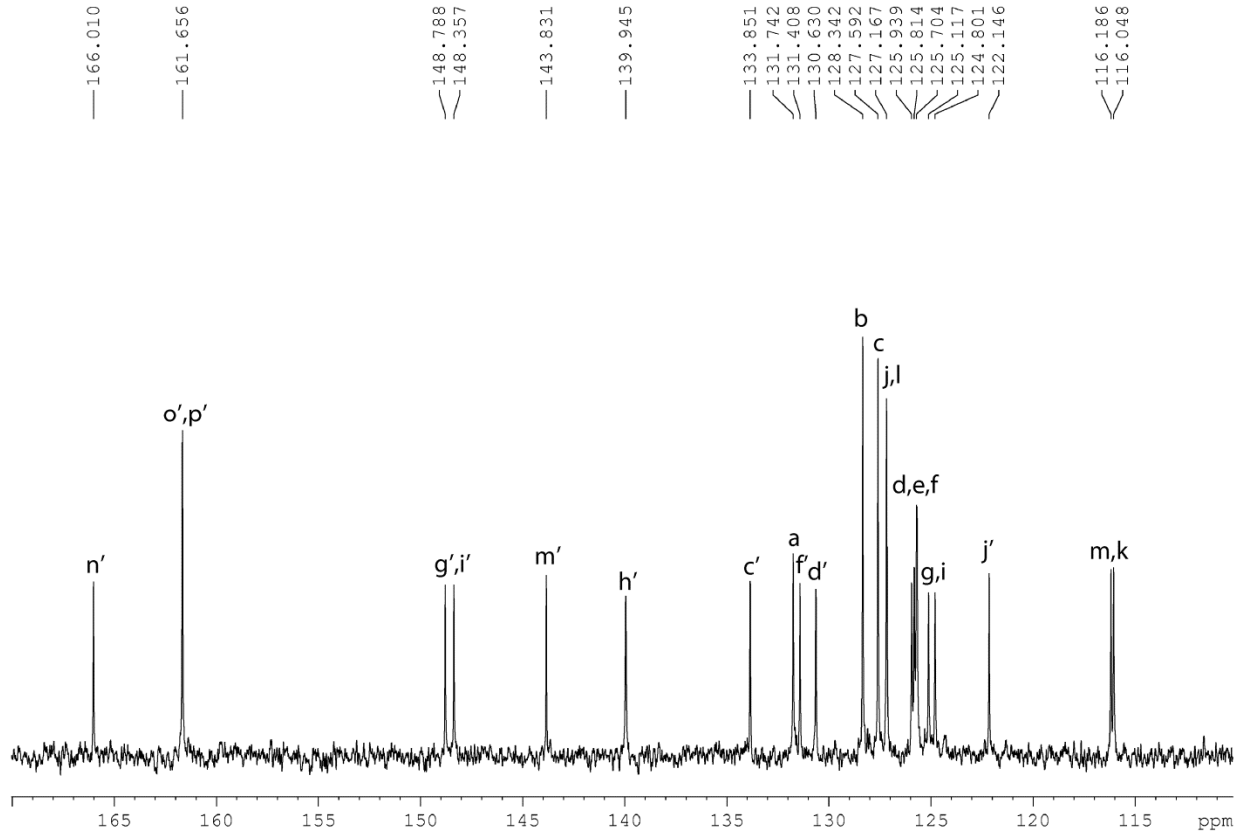
^{1}H, ^{13}C, COSY, HMBC and HMQC spectra were measured for the foldamer **3** from DMSO-d_6. The spectra have been scaled for clarity to display only the aromatic, amine and amide peaks.



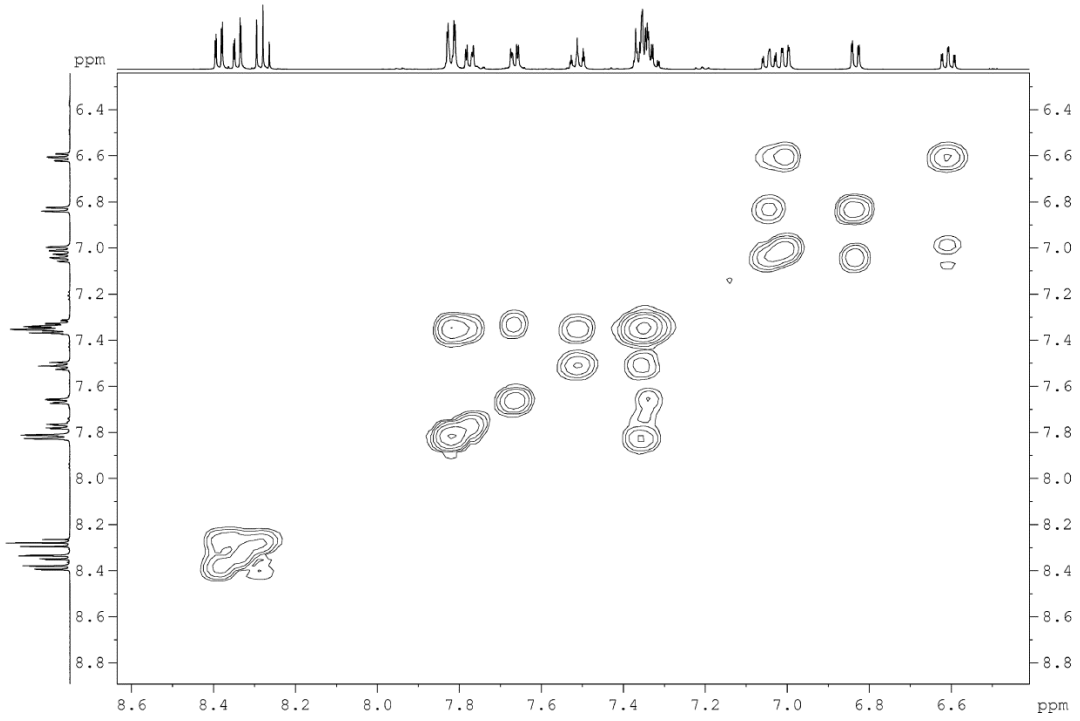
^{1}H NMR spectrum



^{13}C NMR spectrum



COSY



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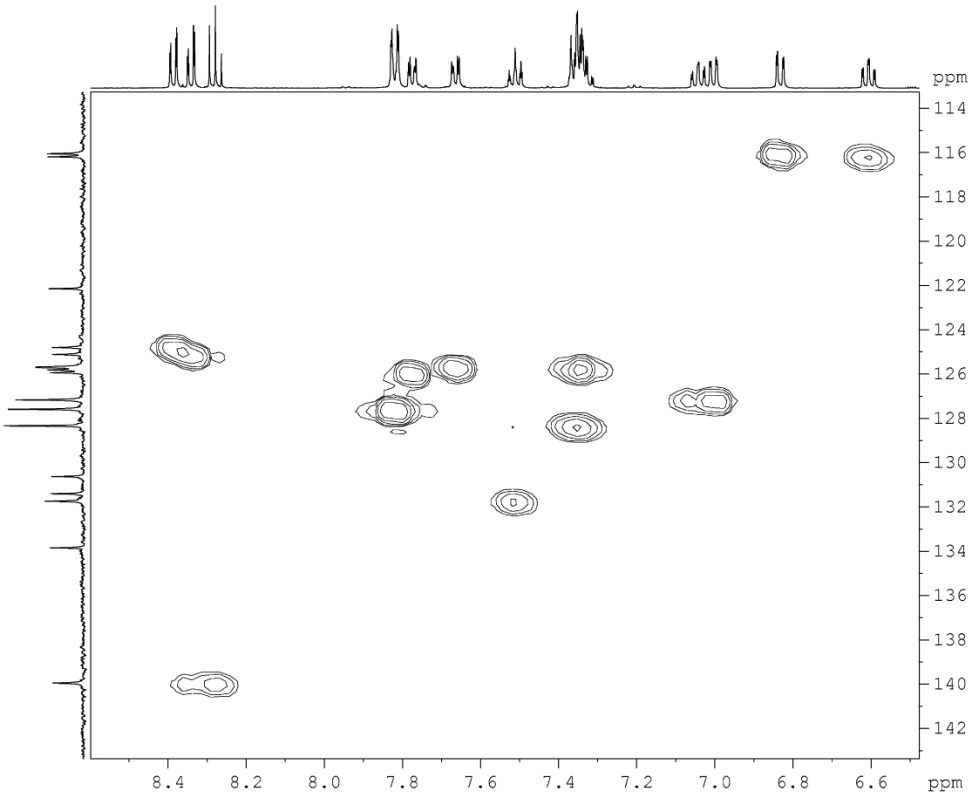
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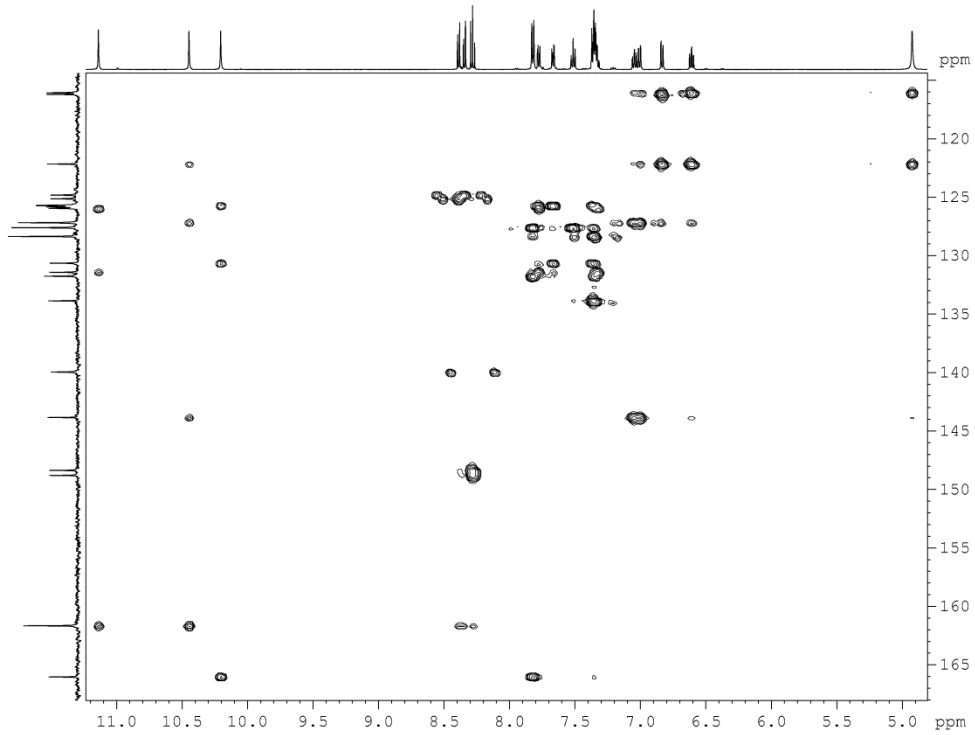
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2 Powder X-ray diffraction and TGA-DTA data for foldamers 1 and 2

TG-DTA measurement was performed with a Perkin Elmer STA600 simultaneous thermal analyzer. Powder X-ray diffraction samples were pressed to a zero background silicon plate and the data was collected with a PANalytical X'Pert PRO MPD diffractometer in reflection mode with CuKα1 radiation (λ = 1.5406 Å). A 2θ angle range of 3-35° and step time of 170 s were used with a step resolution of 0.016°. The figures were drawn with X'Pert Highscrore Plus.[2]

2.1 Foldamer 1

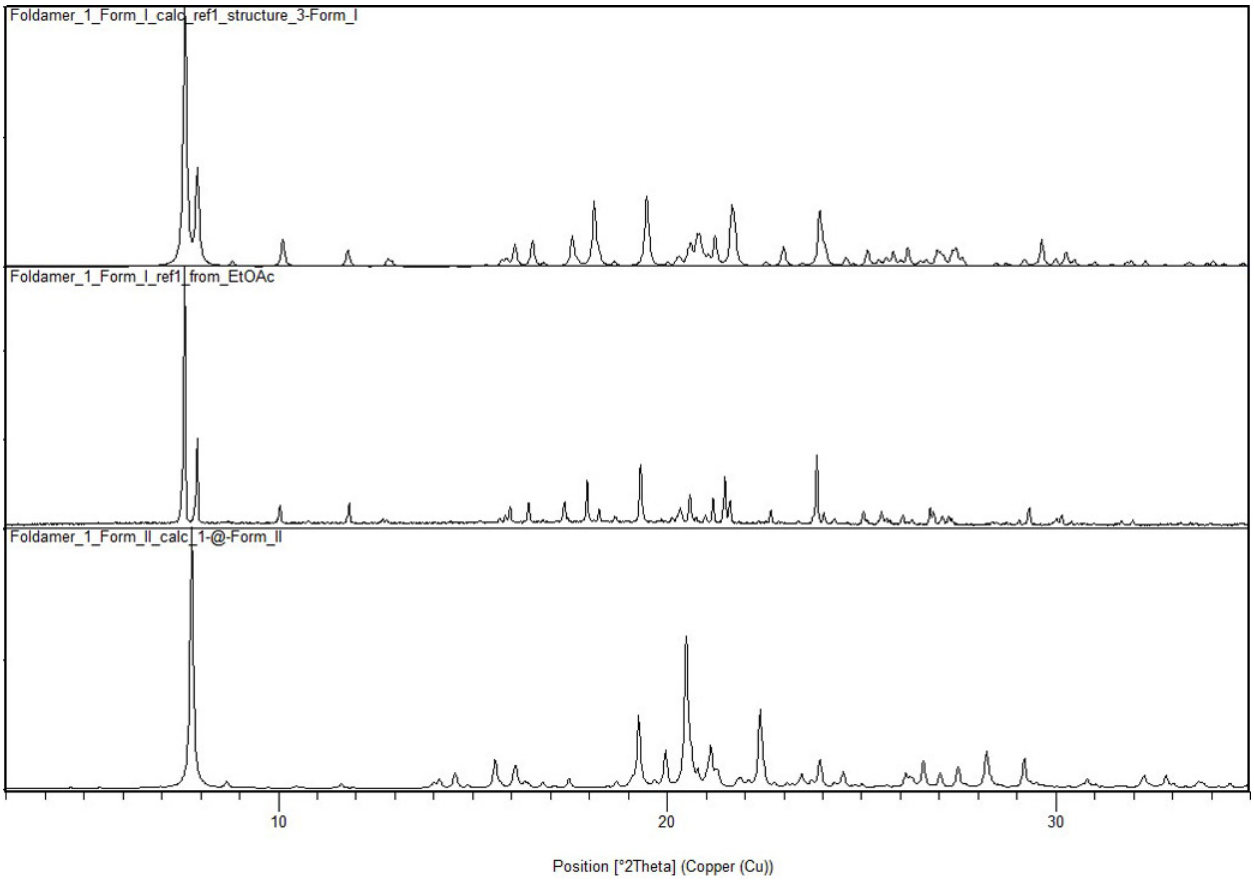

Figure 1. Examples of foldamer **1** PXRD patterns. The calculated patterns were produced with Mercury.[3]

2.2 Foldamer 2

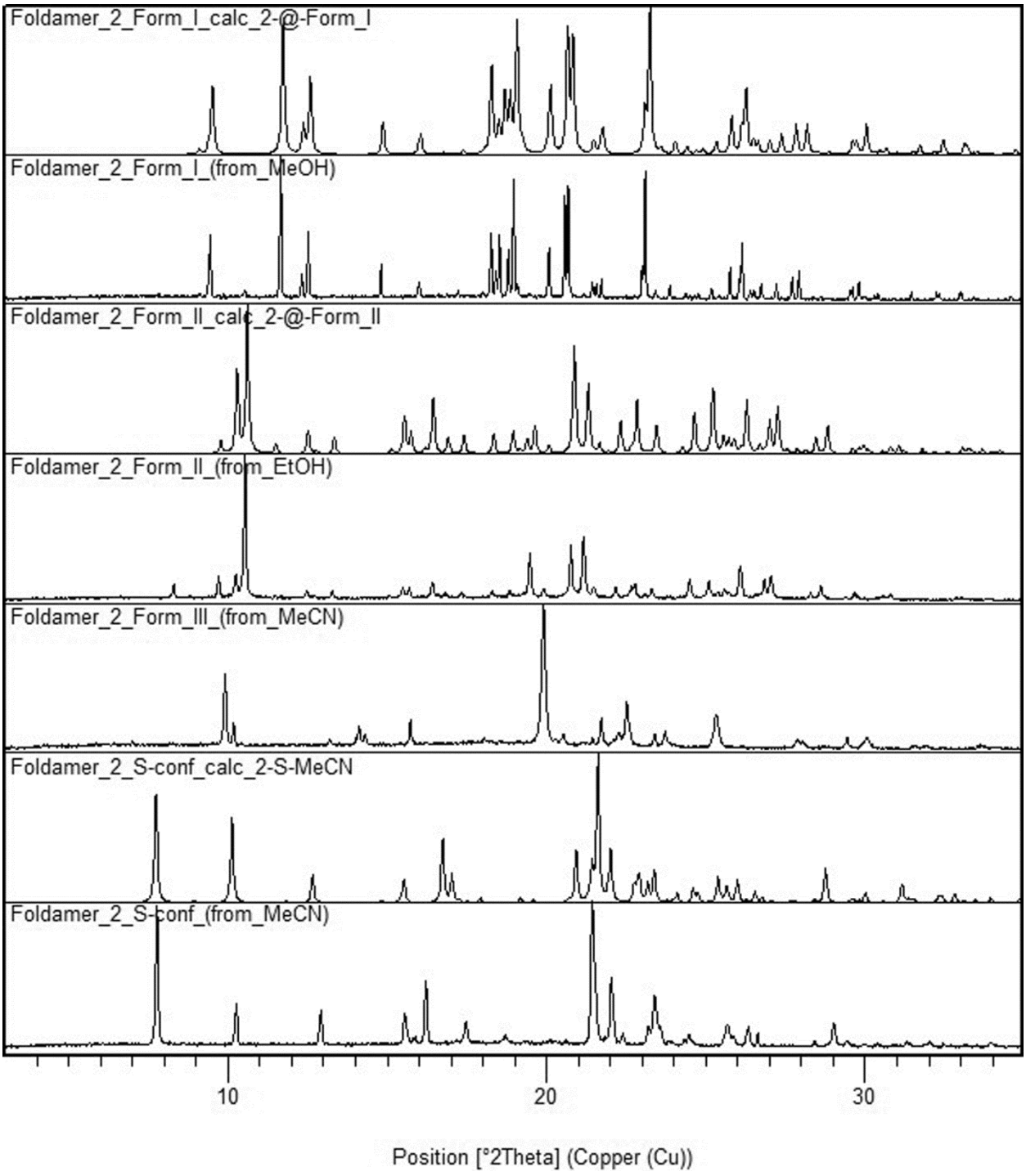

Figure 2. Examples of foldamer **2** PXRD patterns. The calculated patterns were produced with Mercury.[3]

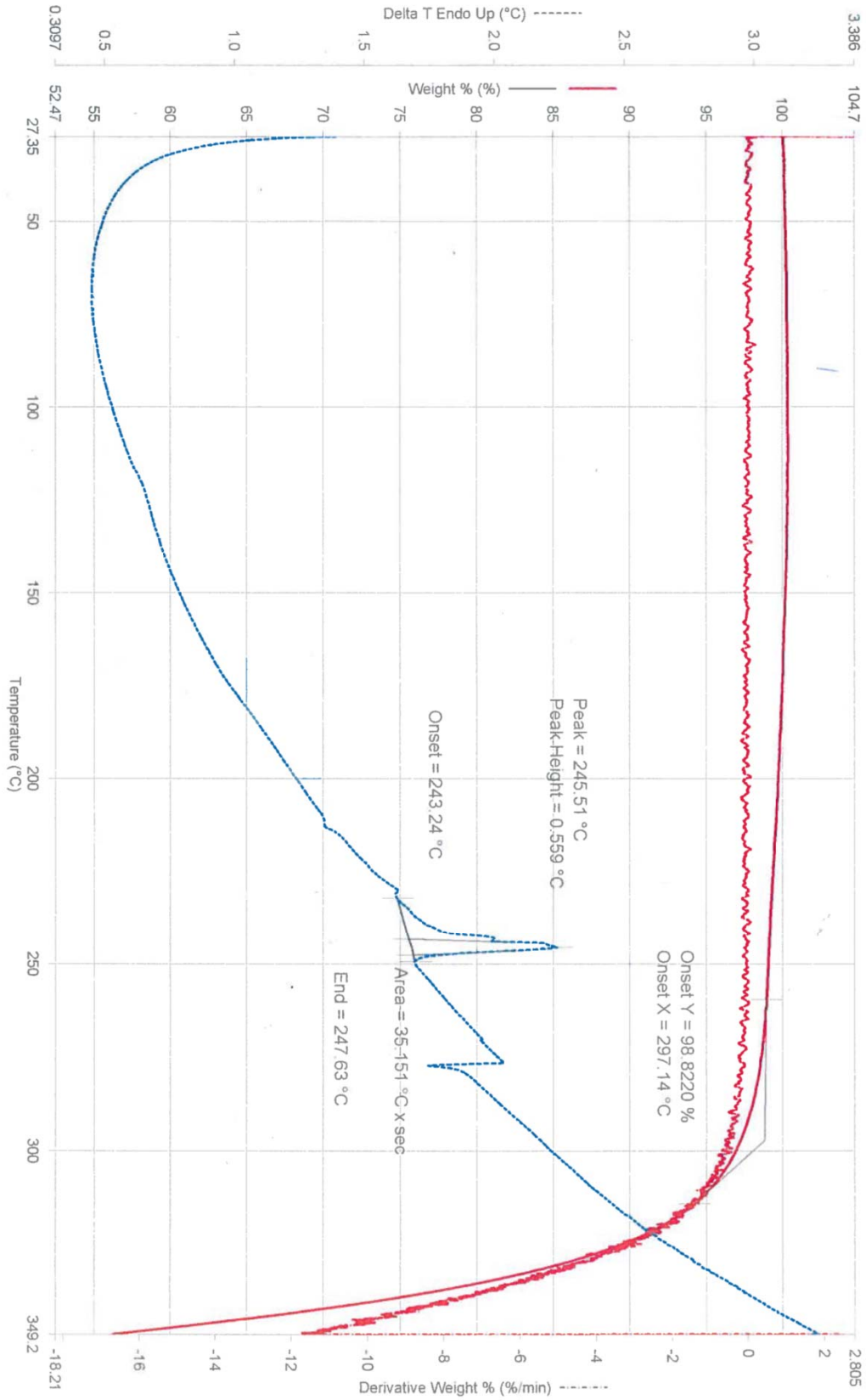

Figure 3. Foldamer **2** Form III TGA-DTA graph.

3 Additional crystallography material

3.1 Details on the crystallization experiments

Foldamer 1: **1@**-Form I was obtained from ethyl acetate and acetonitrile solutions. The MeCN solvate of **1**, however, was obtained by seed crystallization from acetonitrile. The DMA solvate was obtained by evaporation crystallization from DMA. The DMSO-d_6 solvate (**1@**-DMSO-H_2O), acetone-d_6 solvate (**1@**-Ac) and the polymorphic form II (**1@**-Form II) were obtained from the NMR samples that were transferred to test tubes for crystallization after the NMR measurements which were originally made to study the complexation behaviour of the pyridine foldamer with TBA-F trihydrate (DMSO-d_6 and Form II) or TBA-Cl (Acetone-d_6). The sample producing the structure **1@**-DMSO-H_2O had a 1:4 **1** to TBA-F ratio, **1**@-Form II had a 5:1 **1**:TBA-F ratio and **1@**-Ac had a 3:1 **1**:TBA-Cl ratio.

Foldamers 2-7, general procedure: Crystallization studies for compounds **2-7** were made in a series of different solvents (acetone, acetonitrile (MeCN), chloroform, 1,2-dichloroethane (DCE), dichloromethane (DCM), dimethylacetamide (DMA), dimethylformamide (DMF), dimethyl sulfoxide (DMSO), 1,4-dioxane, ethanol (EtOH), ethyl acetate (EtOAc), methanol (MeOH), tetrahydrofuran (THF) and toluene) by dissolving the amounts of 5-50 mg of compounds to 0.1-6 ml of solvent. In some cases, a small drop of DMA, DMF or DMSO (20-60 µl) was added to the solutions to increase the solubility. Foldamer **2** was additionally crystallized in *n*-propanol and by seed crystallization from DCM. Heating and stirring were used to help the dissolving process. After the compounds had dissolved the solutions were allowed to evaporate at room temperature until the crystals formed.

*Foldamer **2***: **2**@-Form I was obtained from acetone, but also the crystallization experiments from MeOH-DMA and EtOH-DMA solutions and from THF, DMSO and n-propanol produced the same crystal form based on the unit cell measurements. Crystallization from ethanol produced both unsolvated forms, **2**@-Form I and **2**@-Form II. Crystallization experiments from DMF produced both crystals of **2**@-Form I and **2**@-S-DMF solvate, and the crystallization experiments from DMA produced the crystals of **2**@-Form I, **2**@-Form II and **2**@-DMA solvate. Crystallization from DCM produced the crystals of 2@-Form II and two different DCM solvates the foldamer adopting an S conformation. Polymorphic form II was also obtained from acetone.

Foldamer **3**: The only observed crystal form for foldamer **3**, **3**@-Form I, was obtained from crystallization experiments from acetonitrile, DMF, ethyl acetate, acetone and methanol.

Foldamer **4**: Four diffusion crystallizations were also made, which all produced previously published 4$\mathbf{S}_1$-Form I structure. In diffusion crystallizations 2-5 mg of compound was dissolved in 1 ml of solvent and layered with 1 ml of antisolvent (solvent:antisolvent: EtOAc:hexane, MeOH:hexane, MeOH:water and MeCN:water). The same crystal form was also obtained by evaporation crystallizations from methanol, acetonitrile, DCE, DMF and $CDCl_3$.

Foldamer **5**: Crystal form **5**@$_2$-Form I was obtained from ethyl acetate, acetone and DMSO solutions as well as MeOH-DMA and acetonitrile-DMA solutions.

Foldamer **6**: In addition to acetone, also the crystallization experiments from ethyl acetate, acetonitrile, DMA, DMF and DMSO produced the crystals of **6**S_2-Form I.

Foldamer **7**: Form **7**@$_2$-Form I was also obtained from methanol solution.

Foldamer 8: Crystallizations of foldamer **8** were attempted only in DMF, DMSO and DMA due to the low solubility of foldamer **8** yielding only precipitates with low crystallinity. The PXRD pattern measured from the DMF crystallization of foldamer **8** show that the sample is mostly amorphous but has also a crystalline component (Figure 4).

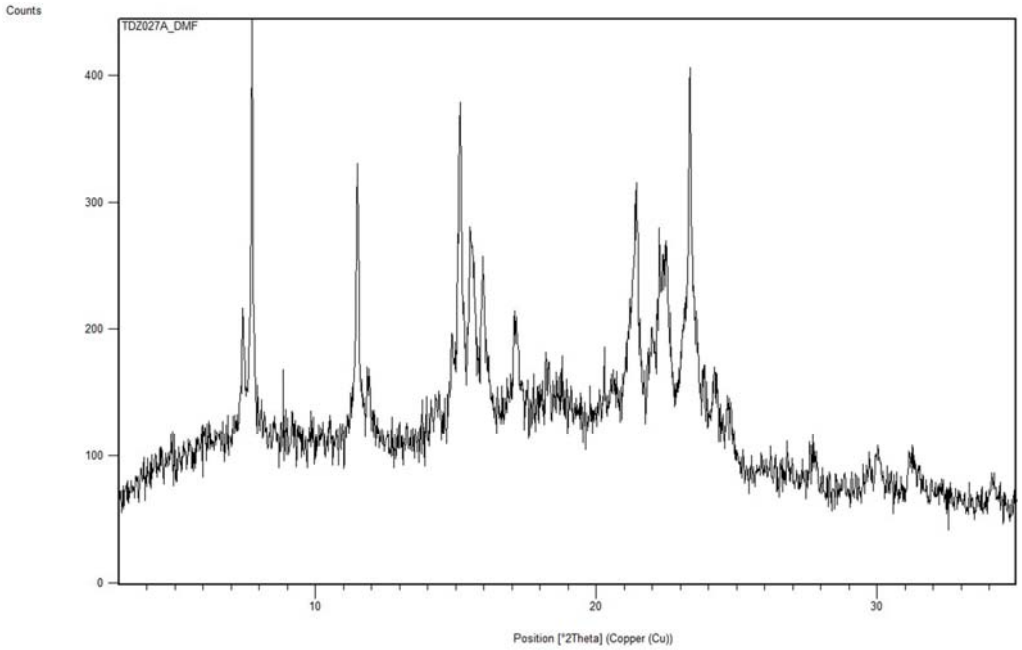

Figure 4. PXRD measured of foldamer **8** DMF crystallization.

3.2 Slurry experiments

Slurry of foldamer **1** was made by stirring 50 mg of the compound in 4 ml of MeCN for two weeks at room temperature. After two weeks the mixture was allowed to dry in open vessels. Slurries of the foldamer **2** were made by stirring 30-50 mg of the compound in 2 ml of solvent (acetone, MeCN, DCM, 1,4-dioxane, EtOH, EtOAc or THF) for two weeks at room temperature. After two weeks the mixtures were allowed to dry in open vessels. Analytical grade solvents and Millipore water were used for the slurries.

3.3 Crystal data and collection parameters for isomorphous solvates

Table 1. Crystal data and collection parameters for isomorphous solvates of **1-@**-DMA (**1-@**-MeCN and **1@**-Ac) and **7S**$_1$-DMA (**7S**$_1$-THF)

	1@-MeCN	**1@**-Ac	**7S**$_1$-THF
Formula	$C_{33}H_{25}N_5O_4$• C_2H_3N	$C_{33}H_{25}N_5O_4$• C_3D_6O	$C_{35}H_{25}N_6O_4$• C_4H_8O
Crystallization solvent	MeCN	Acetone-d_6	THF
M/gmol^{-1}	596.63	619.69	652.70
Crystal system	Monoclinic	Monoclinic	Monoclinic
Space group	$P2_1/c$	$P2_1/c$	$P2_1/n$
a/Å	13.934(3)	13.8945(3)	12.2684(4)
b/Å	19.1670(19)	19.3946(4)	20.2242(7)
c/Å	11.1543(14)	11.2987(2)	13.8112(5)
α/º	90	90	90
β/º	94.855(18)	92.960(2)	98.246(2)
γ/º	90	90	90
V/Å^3	2968.4(8)	3040.69(10)	3391.4(2)
Z	4	4	4
ρ_{calc}/g cm^{-3}	1.335	1.354	1.278
Meas. reflns	13229	10310	10320
Indep. reflns	5828	6088	5819
T/K	123	123	173
Radiation	Cu-Kα	Cu-Kα	Cu-Kα
λ/Å	1.5418	1.5418	1.54178
Monochromation	Mirror	Mirror	Graphite
Absorption correction	multi-scan	Analytical	multi-scan
Abs. Corr. program	CrysalisPro[4]	CrysalisPro[4]	Denzo-SMN 1997[5]
Refinement programs	SHELX-2013[6], ShelXle[7]	SHELX-2013[8], ShelXle[9]	SHELX-97[8]
R_{int}	0.0826	0.0425	0.0653
R_1 [I> 2σ(I)]	0.0591	0.0581	0.0830
wR_2 [I> 2σ(I)]	0.1500	0.1478	0.2100
GooF	0.952	1.077	1.031

3.4 Crystal data and collection parameters for previously published structures

Table 2. Crystal data and collection parameters for structures discussed in the paper, but originally published in a previous paper.[10]

	2@-Form I	**2S**-MeCN	**2@-S**-DMF	**4S**$_1$-Form I	**5@**$_2$-Form I	**5S**$_1$-Form II
Formula	$C_{26}H_{20}N_4O_3$	$C_{26}H_{20}N_4O_3$• C_2H_3N	2x $C_{26}H_{20}N_4O_3$• 2xC_3H_7NO	$C_{28}H_{23}N_5O_4$	$C_{30}H_{27}N_5O_4$	$C_{30}H_{27}N_5O_4$
Crystallization solvent	Acetone	MeCN	DMF	Acetone	EtOAc	Toluene
M/gmol^{-1}	436.46	477.51	1019.0	493.51	521.57	521.57
Crystal system	Orthorhombic	Triclinic	Triclinic	Triclinic	Monoclinic	Monoclinic
Space group	$P2_12_12_1$	P-1	P-1	P-1	$P2_1/c$	$P2_1/n$
a/Å	10.5611(3)	8.8168(1)*	9.1113(4)	8.8855(7)	10.9496(6)	8.6808(4)
b/Å	10.7433(4)	12.1010(1)	13.2244(6)	11.9875(10)	25.1634(12)	27.9305(12)
c/Å	19.3836(6)	12.2384(1)	21.6506(11)	12.8210(11)	9.6787(4)	11.8298(6)
α/º	90	70.3574(1)	89.589(3)	73.667(3)	90	90
β/º	90	81.4003(1)	85.854(2)	72.430(3)	103.832(3)	110.663(3)
γ/º	90	88.0499(1)	84.031(2)	75.241(2)	90	90
V/Å^3	2199.3(2)	1215.74(5)	2587.8(2)	1227.7(2)	2589.4(2)	2683.7(2)
Z	4	2	4	2	4	4
ρ_{calc}/g cm^{-3}	1.318	1.304	1.308	1.335	1.338	1.291
Meas. reflns	11801	5652	13074	5502	7545	7773
Indep. reflns	3762	3936	8822	3964	4398	4458
R_{int}	0.0293	0.0703	0.0649	0.1054	0.0749	0.0768
R_1 [I> 2σ(I)]	0.0427	0.0544	0.0539	0.0586	0.0572	0.0642
wR_2 [I> 2σ(I)]	0.0968	0.1315	0.1288	0.1222	0.1277	0.1473
GooF	1.064	1.020	1.018	1.058	1.026	1.074

	6S$_2$-Form I	**7@**$_2$-Form I	**7S**$_1$-EtOAc
Formula	$C_{31}H_{29}N_5O_4$	$C_{34}H_{24}N_6O_4$	$C_{34}H_{24}N_6O_4$• $C_4H_8O_2$
Crystallization solvent	Acetone	MeCN	EtOAc
M/gmol^{-1}	535.59	580.59	668.70
Crystal system	Triclinic	Monoclinic	Monoclinic
Space group	P-1	$P2_1/c$	$P2_1/c$
a/Å	9.6020(2)	12.7434(9)	12.6680(5)
b/Å	10.6657(2)	19.5084(13)	20.0990(8)
c/Å	13.7389(3)	11.4050(8)	16.7620(6)
α/º	89.617(3)	90	90
β/º	83.538(3)	98.925(4)	128.179(2)
γ/º	76.401(3)	90	90
V/Å^3	1358.8(1)	2801.0(3)	3354.9(2)
Z	2	4	4
ρ_{calc}/g cm^{-3}	1.309	1.377	1.324
Meas. reflns	6417	7686	9999
Indep. reflns	4610	4576	5487
R_{int}	0.0539	0.1610	0.0854
R_1 [I> 2σ(I)]	0.0489	0.0720	0.0636
wR_2 [I> 2σ(I)]	0.1165	0.1348	0.1304
GooF	1.032	1.105	1.046

3.5 Notes on the crystallographic data

1@-Form II was crystallized from DMSO-d_6 with TBA-F trihydrate (**1**:TBA-F 5:1) by slow evaporation as colorless block crystals. Seven (I_{obs}-I_{calc})/SigmaW outliers are likely caused by non-merohedral twinning. The twinned component is very small and has only little effect on the overall quality of the structure.

1@-DMA was crystallized from DMA by slow evaporation as colorless plate crystals. DMA molecule is disordered over two partially overlapped positions (85:15). Four EADP and EXYZ restraints were used to build the model.

1@-DMSO-H_2O was crystallized from DMSO-d_6 in the presence of TBA-F trihydrate (**1**:TBA-F 1:4) by slow evaporation as colorless needle crystals. Four (I_{obs}-I_{calc})/SigmaW outliers are likely caused by faults in the crystal. The O-H bond lengths of the water molecule were restrained to 0.82 Å using DFIX.

1@-MeCN was crystallized from MeCN seed crystallization as colorless plate crystals. Seed crystals were obtained from MeCN slurry (see page 6 for details of the slurry experiments).

1@-Ac was crystallized from acetone-d_6 in the presence of TBA-Cl (**1**:TBA-Cl 3:1) by slow evaporation as colorless needle crystals. Two (I_{obs}-I_{calc})/SigmaW outliers are likely caused by faults in the crystal. Low solvent U_{eq} of carbonyl C100 compared to neighbors is due to the larger U_{eq} of the adjacent methyl groups. Reflection 1 0 0 was omitted (OMIT) because it was blocked by the beamstop of the instrument.

2@-Form II was crystallized from DMA by slow evaporation as colorless plate crystals.

2@-DMA was crystallized from 1,4-dioxane-DMA solution as colorless block crystals. The DMA molecule is disordered over two partially overlapped positions (site occupancies 67:33). Three EADP and EXYZ restraints were used to build the chemically reasonable model.

2S-DCM-1 was crystallized from DCM with the help of seed crystals obtained from DCM slurry (see page 6 for details of the slurry experiments). The structure crystallized as colorless block crystals. The DCM molecule is disordered over two positions (site occupancies 50:50 for the chlorine atoms). Large solvent U_{eq}(max)/U_{eq}(min) ratio is caused by the solvent disorder. High U_{eq} of C23 is caused by the disordered solvent molecule nearby. Short intramolecular hydrogen-hydrogen distance of 1.98 Å between aromatic H1 and amide H1N is caused by the intramolecular hydrogen bonding between H1N and O2 and intermolecular hydrogen bonding between O1 and H2N and O1 and H3N.

2S-DCM-2 was crystallized from DCM by very slow evaporation crystallization (closed container) as colorless block crystals. DCM molecule is disordered over an inversion center (site occupancies 50:50).

3@-Form I was crystallized from MeCN by slow evaporation as colorless block crystals. Four (I_{obs}-I_{calc})/SigmaW outliers are likely caused by non-merohedral twinning. The twinned component is very small and has only little effect on the overall quality of the structure. No hydrogen bond is formed by the hydrogen bond donor H5NB due to crystal packing.

4S$_1$-Form II was crystallized from EtOAc by slow evaporation as colorless plate crystals.

4S$_1$-DMSO was crystallized from DMSO by slow evaporation as colorless plate crystals. Both DMSO molecules are disordered with site occupancies 80:20 and 92:8. Four EADP and three EXYZ restraints were used to build the models. The bond lengths between nitrogen and hydrogen atoms were restrained to 0.84 Å using DFIX.

4S$_1$-Diox was crystallized from 1,4-dioxane by slow evaporation as colorless plate crystals. Reflections 1 0 0, 1 -1 1, -1 0 1, -1 1 0, -1 -1 1 and 0 -1 2 were omitted (OMIT) because they were blocked by the beamstop of the instrument.

6S$_2$-Diox was crystallized from 1,4-dioxane by slow evaporation as colorless block crystals.

7S$_1$-CHCl$_3$ was crystallized from $CHCl_3$ by slow evaporation as colorless block crystals. $CHCl_3$ molecule is disordered over two positions (74:26). EADP restraint was used on the C atom of $CHCl_3$ to model the disordered positions of C10A and C10B. DFIX was used to restrain distances between disordered carbon C10B and chlorides CL2B and CL3B to 1.79 Å. The bond lengths between nitrogen and hydrogen are restrained to 0.84 Å using DFIX. An unlikely bond between disordered chlorides Cl2B and Cl3B was removed with FREE. The high anion/solvent ADP max/min ration of atom Cl2B is due to the disorder of the chloroform molecule.

7S$_1$-THF was crystallized from THF by slow evaporation as colorless block crystals. High electron density is located near the severely disordered THF molecule. No reasonable model for the disorder could be built and THF was refined isotropically. The structure contains a solvent accessible void (42 Å^3) near the disordered THF molecule.

7S$_1$-DMA was crystallized from DMA by slow evaporation as colorless block crystals. Short intramolecular hydrogen-hydrogen distance between H10F and H10G is due to non-optimal calculated atom positions.

3.6 Packing coefficient analysis

The structures discussed in the paper (Table 1) have an average packing coefficient of 0.717±0.015. The average packing coefficient of @-conformation structures was 0.723±0.013 and the packing coefficient for S-conformation structures was 0.709±0.015. The difference between the average @- and S-conformation packing coefficients is 0.014. The average packing coefficients of the structures are separated by roughly one standard deviation which, while not statistically relevant, indicates a trend where the @-conformation structures tend to pack more efficiently.

3.7 Additional Foldamer Figures

3.7.1 Foldamer **1**

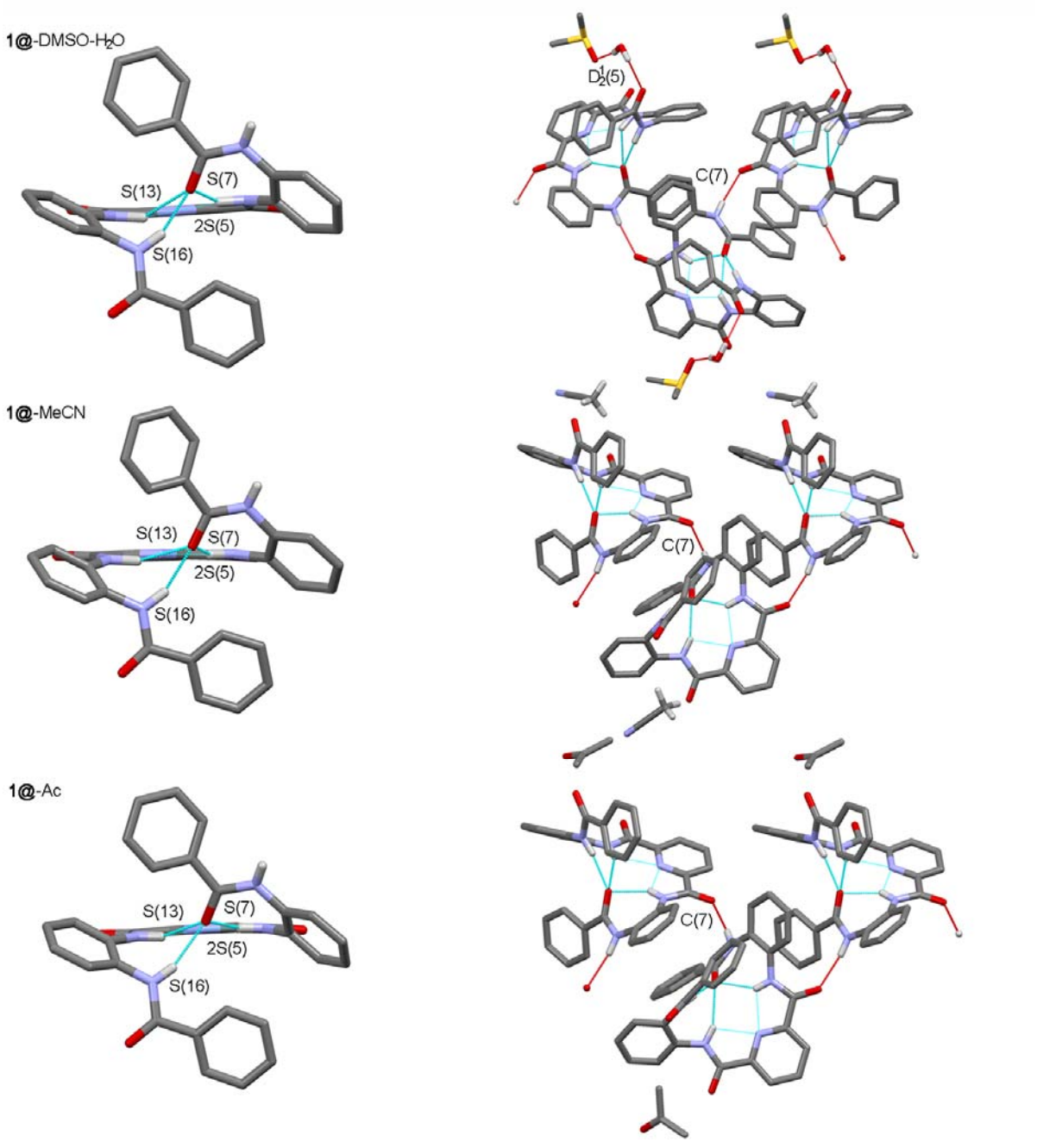

Figure 5. The conformations and crystal packing of foldamer **1**. The conformation presented for the structure **1@**-Form II is the molecule that is not in a perfect **@**-conformation. Two other molecules in the asymmetric unit adopting an @-conformation are not shown. Non-hydrogen bonding hydrogens and DMA disorder have been removed for clarity.

3.7.2 Foldamer **2**

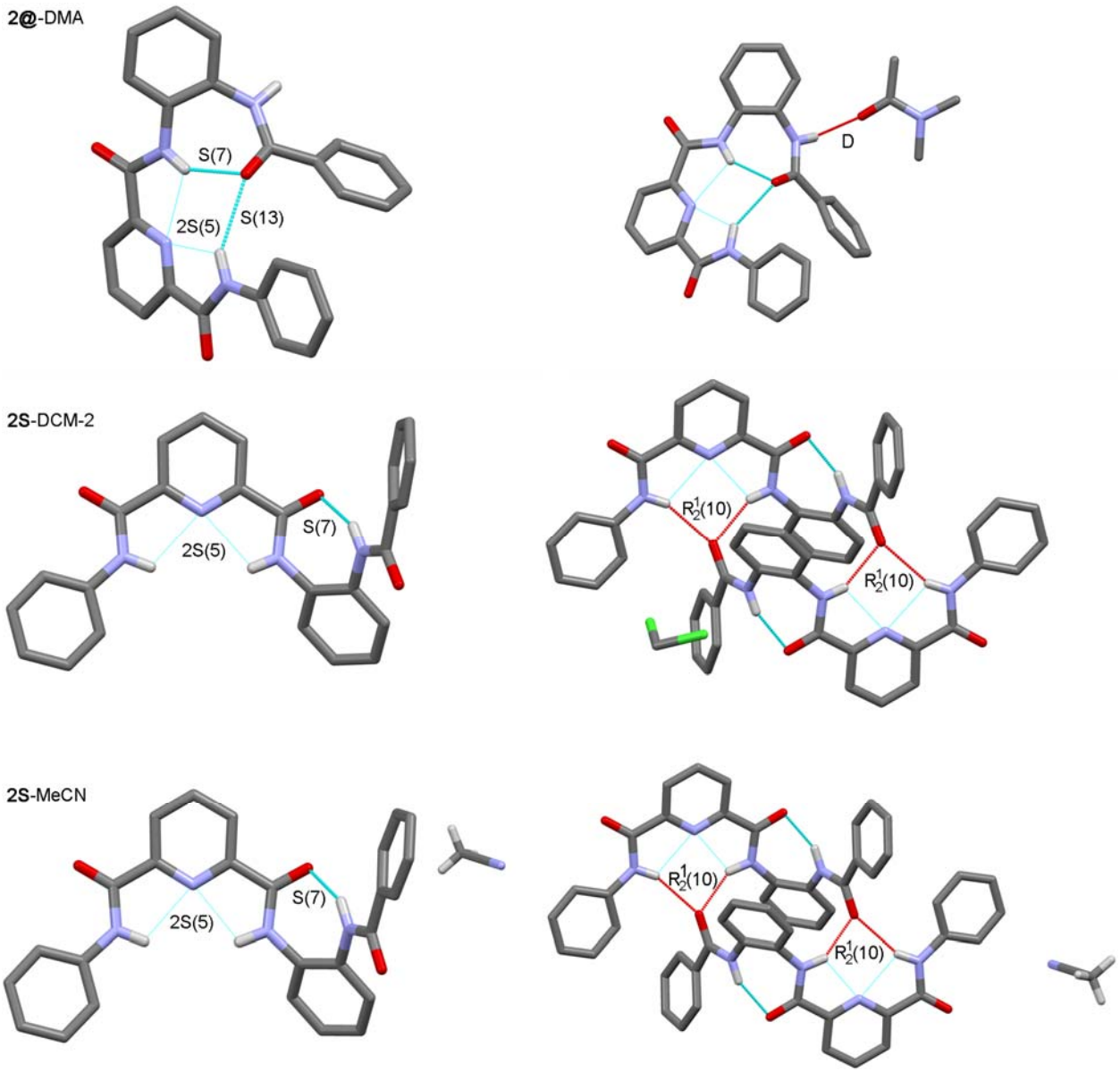

Figure 6. The conformations and crystal packing of foldamer **2**. Non-hydrogen bonding hydrogens and DMA disorder have been removed for clarity.

3.7.3 Foldamer **3**

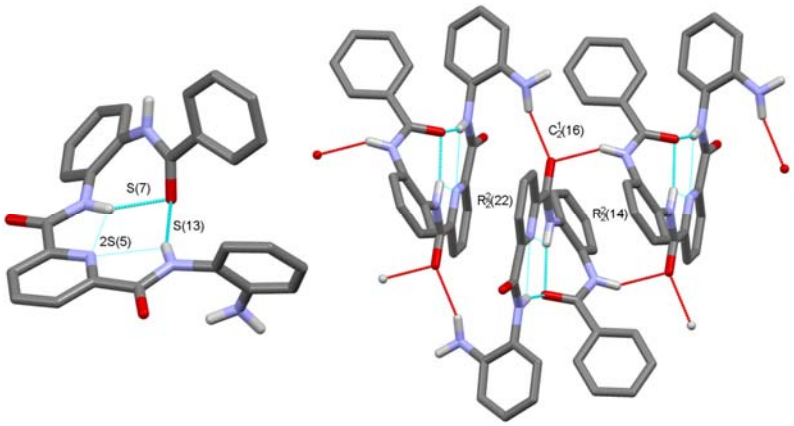

Figure 7. The conformation and crystal packing of foldamer **3**. Non-hydrogen bonding hydrogens have been removed for clarity.

3.7.4 Foldamer **4**

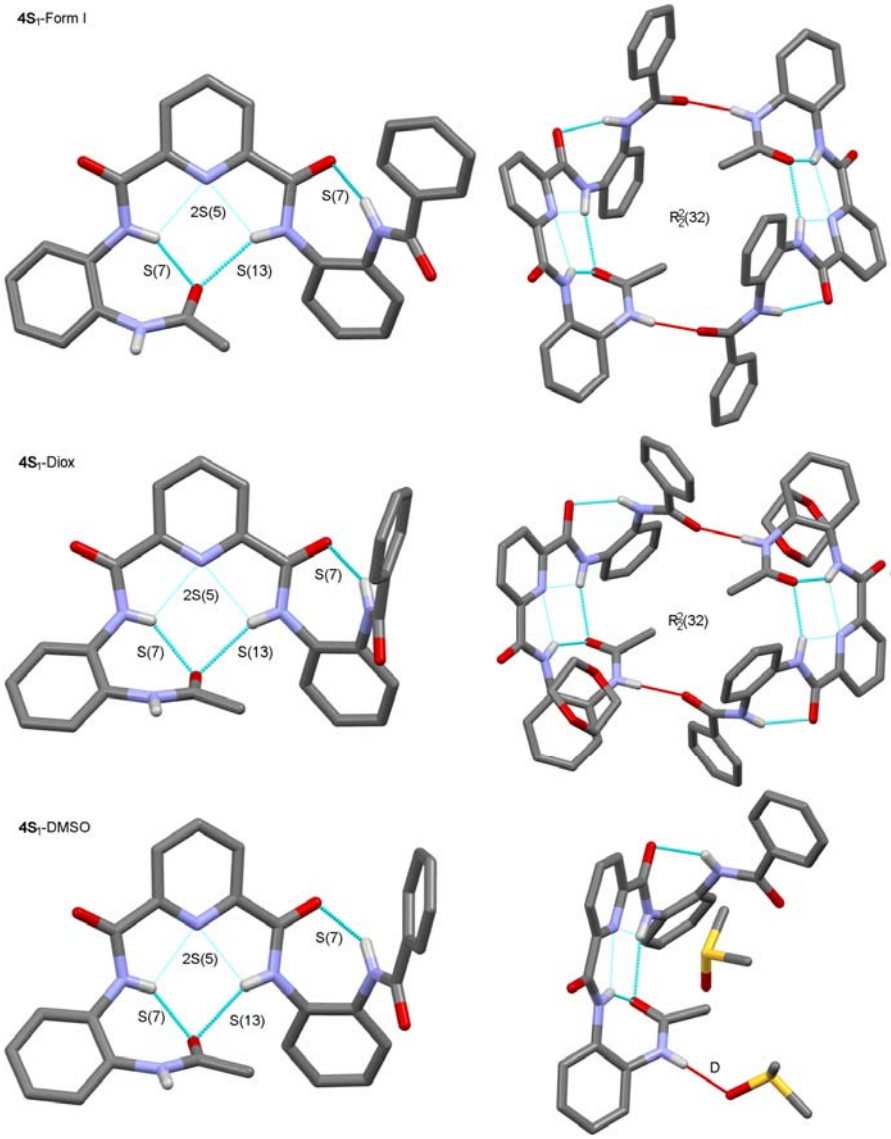

Figure 8. The conformation and crystal packing of foldamer **4**. Non-hydrogen bonding hydrogens and DMSO disorder have been removed for clarity.

3.7.5 Foldamer **5**

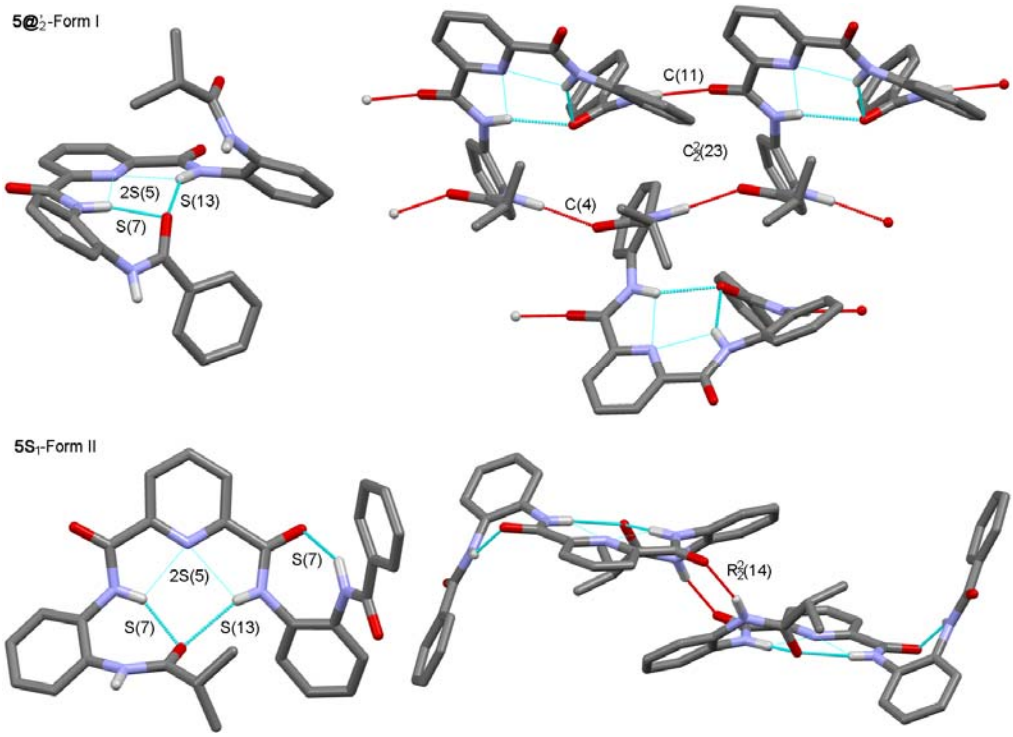

Figure 9. The conformation and crystal packing of foldamer **5**. Non-hydrogen bonding hydrogens have been removed for clarity.

3.7.6 Foldamer **6**

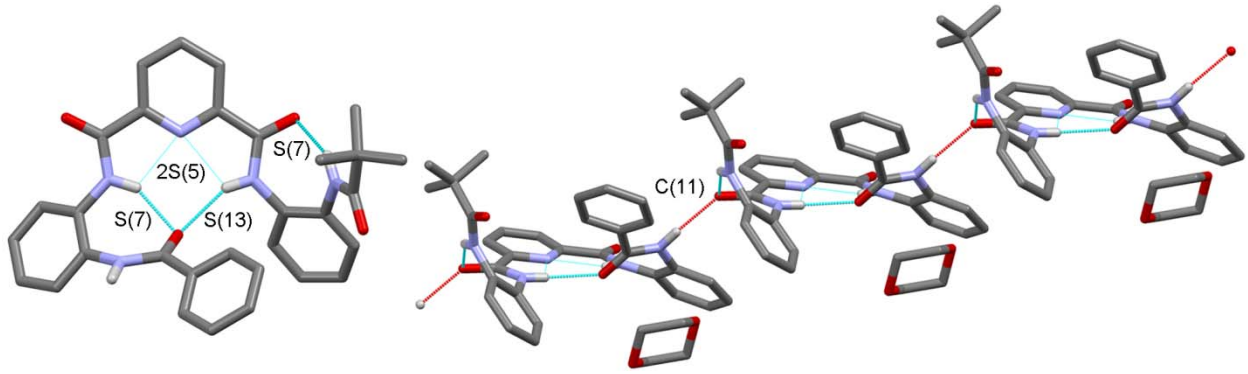

Figure 10. The conformation and crystal packing of foldamer **6**. Non-hydrogen bonding hydrogens have been removed for clarity.

3.7.7 Foldamer **7**

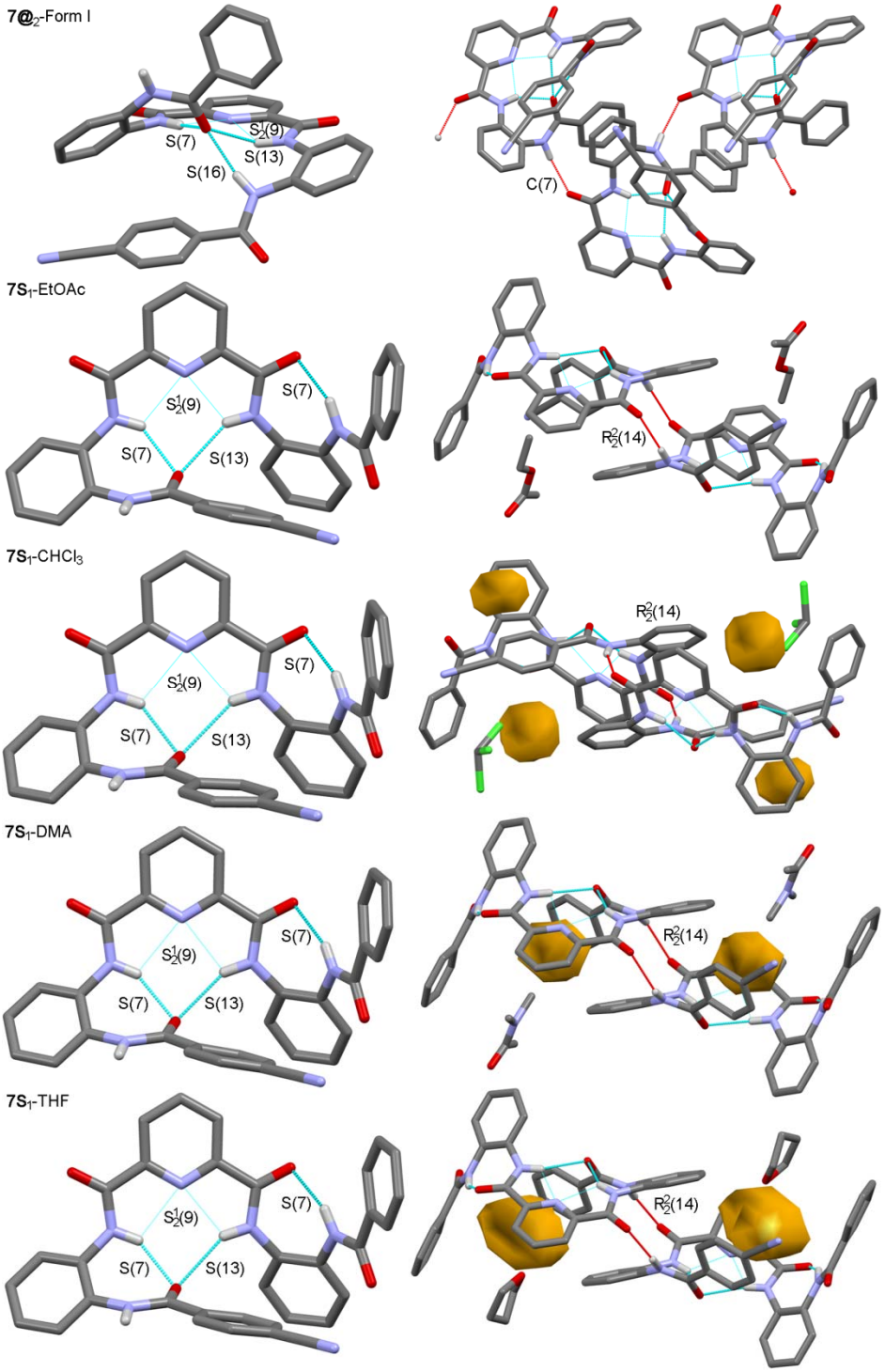

Figure 11. The conformation and crystal packing of foldamer **7**. Non-hydrogen bonding hydrogens and $CHCl_3$ disorder have been removed for clarity. Voids that were visualized with Mercury[3] are presented with yellow.

3.8 Hydrogen bonding parameters

Table 3. Hydrogen bonding parameters for the crystal structures.

1@-Form II

Intramolecular			Intermolecular		
Bond	**d(D…A)**	**<(DHA)**	**Bond**	**d(D…A)**	**<(DHA)**
N101-H11N…O104	2.9090(17)	153.9(18)	N104-H14N…O302	2.8365(16)	162.4(17)
N102-H12N…O104	3.0990(17)	143.8(17)	N201-H21N…O301	2.9793(17)	144.9(17)
N102-H12N…N105	2.6417(18)	114.5(16)	N204-H24N…O101	2.8488(17)	151.4(16)
N103-H13N…O104	2.7975(17)	142.1(18)	N304-H34N…O202	2.9302(16)	169.3(17)
N103-H13N…N105	2.6579(17)	113.7(16)			
N202-H22N…O201	2.8375(17)	136.2(16)			
N203-H23N…N205	2.6870(17)	112.8(16)			
N301-H31N…O304	2.9717(16)	154.8(18)			
N302-H32N…O304	2.1983(16)	150.6(16)			
N302-H32N…N305	2.6595(17)	111.0(14)			
N303-H33N…O304	2.7888(16)	143.5(17)			
N303-H33N…N305	2.6700(17)	111.0(15)			

1@-DMA

Intramolecular			Intermolecular		
Bond	**d(D…A)**	**<(DHA)**	**Bond**	**d(D…A)**	**<(DHA)**
N1-H1N…O4	2.8676(14)	154.3(15)	N4-H4N…O3	2.9849(14)	164.4(15)
N2-H2N…O4	3.1551(14)	140.5(15)			
N2-H2N…N5	2.6424(15)	114.9(15)			
N3-H3N…O4	2.6935(13)	140.7(15)			
N3-H3N…N5	2.6429(14)	112.3(13)			

1@-DMSO-H_2O

Intramolecular			Intermolecular		
Bond	**d(D…A)**	**<(DHA)**	**Bond**	**d(D…A)**	**<(DHA)**
N1-H1N…O4	2.813(4)	154(4)	N4-H4N…O3	2.977(4)	171(4)
N2-H2N…O4	3.173(4)	142(4)	O200-H1O…O100	2.872(5)	169(6)
N3-H3N…O4	2.684(3)	136(4)	O200-H2O…O1	2.903(4)	173(6)
N3-H3N…N5	2.644(4)	114(3)			

1@-MeCN

Intramolecular			Intermolecular		
Bond	**d(D…A)**	**<(DHA)**	**Bond**	**d(D…A)**	**<(DHA)**
N2-H2…O1	2.693(3)	139(4)	N1-H1…O2	2.913(3)	163(5)
N3-H3…O1	3.073(3)	152(4)			
N4-H4…O1	2.878(3)	158(4)			
N2-H2…N5	2.635(3)	112(4)			

1@-Ac

Intramolecular			Intermolecular		
Bond	**d(D…A)**	**<(DHA)**	**Bond**	**d(D…A)**	**<(DHA)**
N2-H2N…O1	2.694(2)	142(3)	N1-H1N…O2	2.929(2)	170(3)
N2-H2N…N5	2.635(3)	116(3)			
N3-H3N…O1	3.045(2)	153(3)			
N4-H4N…O1	2.869(3)	161(3)			

2@-Form II

Intramolecular			Intermolecular		
Bond	**d(D…A)**	**<(DHA)**	**Bond**	**d(D…A)**	**<(DHA)**
N2-H2N...O1	2.682(3)	145(2)	N1-H1N…O2	2.989(3)	163(2)
N2-H2N...N4	2.643(3)	107(2)			
N3-H3N…O1	3.207(3)	153(2)			
N3-H3N…N4	2.684(3)	114(2)			

2@-DMA

Intramolecular			Intermolecular		
Bond	**d(D…A)**	**<(DHA)**	**Bond**	**d(D…A)**	**<(DHA)**
N2-H2N…O1	2.732(3)	146(2)	N1-H1N…O100	2.939(3)	160(2)
N2-H2N…N4	2.667(3)	110(2)			
N3-H3N…O1	3.263(3)	149(2)			
N3-H3N…N4	2.694(3)	112(2)			

2S-DCM-1

Intramolecular			Intermolecular		
Bond	**d(D…A)**	**<(DHA)**	**Bond**	**d(D…A)**	**<(DHA)**
N1-H1N…O2	2.730(3)	151(3)	N2-H2N…O1	2.869(3)	150(3)
N2-H2N…N4	2.695(3)	107(3)	N3-H3N…O1	3.200(3)	155(3)
N3-H3N…N4	2.725(3)	113(3)			

2S-DCM-2

Intramolecular			Intermolecular		
Bond	**d(D…A)**	**<(DHA)**	**Bond**	**d(D…A)**	**<(DHA)**
N1-H1N…O2	2.704(2)	147(3)	N2-H2N…O1	2.857(2)	154(3)
N2-H2N…N4	2.685(2)	109(2)	N3-H3N…O1	3.083(2)	157(3)
N3-H3N…N4	2.726(3)	111(2)			

3@-Form I

Intramolecular			Intermolecular		
Bond	**d(D…A)**	**<(DHA)**	**Bond**	**d(D…A)**	**<(DHA)**
N2-H2N…O1	2.7279(15)	148.4(16)	N1-H1N…O2	2.8667(17)	150.8(16)
N3-H3N…O1	3.1757(17)	164.4(16)	N5-H5NA…O2	3.0881(17)	164.2(17)

$4S_1$-Form II

Intramolecular			Intermolecular		
Bond	**d(D…A)**	**<(DHA)**	**Bond**	**d(D…A)**	**<(DHA)**
N1-H1N…O2	2.686(3)	142(3)	N4-H4N…O1	2.844(3)	167(3)
N2-H2N…O4	3.013(3)	153(2)			
N2-H2N…N5	2.671(3)	110(2)			
N3-H3N…O4	2.739(3)	144(3)			
N3-H3N…N5	2.648(3)	114(2)			

$4S_1$-Diox

Intramolecular			Intermolecular		
Bond	**d(D…A)**	**<(DHA)**	**Bond**	**d(D…A)**	**<(DHA)**
N1-H1N…O2	2.699(2)	146(2)	N4-H4N…O1	2.875(2)	177(2)
N2-H2N…O4	3.014(2)	157(2)			
N2-H2N…N5	2.663(2)	107.6(18)			
N3-H3N…O4	2.720(2)	143(2)			
N3-H3N…N5	2.642(2)	116(2)			

$4S_1$-DMSO

Intramolecular			Intermolecular		
Bond	**d(D…A)**	**<(DHA)**	**Bond**	**d(D…A)**	**<(DHA)**
N1-H1N…O2	2.702(2)	144(2)	N4-H4N…O11A	2.826(2)	174(2)
N2-H2N…O4	2.986(2)	157(2)			
N2-H2N…N5	2.674(2)	109.7(18)			
N3-H3N…O4	2.724(2)	148(2)			
N3-H3N…N5	2.635(2)	111.2(18)			

$6S_2$-Diox

Intramolecular			Intermolecular		
Bond	**d(D…A)**	**<(DHA)**	**Bond**	**d(D…A)**	**<(DHA)**
N2-H2N…O1	2.726(2)	148(2)	N1-H1N…O3	2.906(2)	159.5(19)
N2-H2N…N5	2.641(2)	111.6(18)			
N3-H3N…O1	2.911(2)	152(2)			
N3-H3N…N5	2.662(2)	112.3(18)			
N4-H4N…O3	2.765(2)	144(2)			

$7S_1$-$CHCl_3$

Intramolecular			Intermolecular		
Bond	**d(D…A)**	**<(DHA)**	**Bond**	**d(D…A)**	**<(DHA)**
N1-H1N…O2	2.719(2)	151(2)	N4-H4N…O3	2.827(2)	160(2)
N2-H2N…O4	3.0117(2)	149(2)			
N2-H2N…N5	2.643(4)	112.9(19)			
N3-H3N…O4	2.7488(19)	145(2)			
N3-H3N…N5	2.653(2)	110.4(17)			

$7S_1$-THF

Intramolecular			Intermolecular		
Bond	**d(D…A)**	**<(DHA)**	**Bond**	**d(D…A)**	**<(DHA)**
N1-H1N…O2	2.744(4)	148(4)	N4-H4N…O3	2.837(4)	153(4)
N2-H2N…O4	3.127(4)	150(4)			
N2-H2N…N5	2.649(4)	112(3)			
N3-H3N…O4	2.750(4)	148(4)			
N3-H3N…N5	2.662(4)	107(3)			

$7S_1$-DMA

Intramolecular			Intermolecular		
Bond	**d(D…A)**	**<(DHA)**	**Bond**	**d(D…A)**	**<(DHA)**
N1-H1N…O2	2.765(4)	149(4)	N4-H4N…O3	2.869(5)	146(5)
N2-H2N…O4	3.085(4)	150(3)			
N2-H2N…N5	2.648(4)	106(3)			
N3-H3N…O4	2.736(4)	151(4)			
N3-H3N…N5	2.667(4)	106(3)			

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