Supporting information

Formation and Trapping of The Thermodynamically Unfavoured *inverted*-hemicucurbit[6]uril

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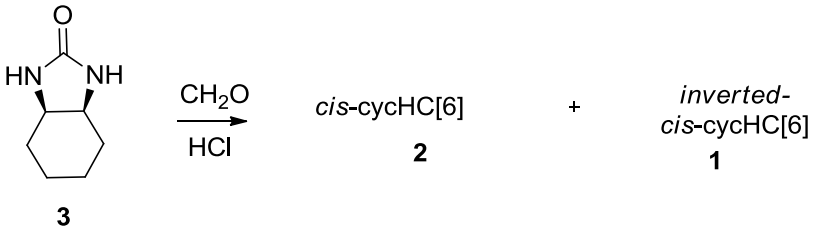
Contents

General information

Unless otherwise stated, all reagents were purchased from commercial suppliers and used as received. Solvents used for flash chromatography were reagent grade, which were dried and distilled prior to use according to standard procedures. (*R,S*)-*N,N'*-cyclohexa-1,2-diylurea **3** was synthesized starting from either *cis*-1,2-diaminocylohexane or mixture of *cis*- and *trans*-1,2-diaminocylohexane according to literature procedure[1]. Reactions under microwave were performed in CEM Discover® microwave reactor. Flash chromatography was run over Thomar CC Silica Gel 60 (0.04-0.063 mm) stationary phase. Infrared spectra were obtained on a Bruker Tensor 27 FT-IR spectrometer and are reported in wavenumbers. HPLC based reaction rate monitoring was performed on an Agilent 1200 Series HPLC system with a Kinetex C18 column (2.1x100 mm, 2.6 µm) and UV-detection at 210 nm. Identification of reaction products and traces was performed by RP-HPLC-HRMS on an Agilent 6540 UHD Accurate-Mass Q-TOF LC/MS spectrometer with a Zorbax Eclipse Plus C18 column (2.1x150 mm, 1.8 µm) and AJ-ESI ionization. 1D ^{1}H and ^{13}C-NMR spectra were acquired on a Bruker AvanceIII 400 MHz spectrometer or a Bruker Avance III 800 MHz. Chemical shifts were referenced to the chloroform residual solvent signal in ^{13}C 77,160 ppm and ^{1}H 7,260 ppm. Samples were vortexed on vortex mixer Scientific Industries, Inc Vortex-Genie 2. Sonication was performed on ultrasonic bath Bandelin Sonorex Digitec DT 52 H.

Synthesis of cycHCs

General synthetic procedure for **1** and **2** from (*R,S*)-*N,N'*-cyclohexa-1,2-diylurea:



Suspension of (*R,S*)-*N,N'*-cyclohexa-1,2-diylurea **3** (prepared according to procedure in ref. 1) and paraformaldehyde was heated in aqueous HCl acid on oil bath. All reaction mixtures were heterogeneous, ratio of formed macrocycles **2** and **1** was determined from crude reaction mixture by HPLC-UV analysis (See SI section "Quantitative analysis of cycHCs"). Reaction mixture was filtered, washed with water and dried in open air. Crude product was dissolved from the filter with CH_2Cl_2, solvent evaporated and crude product was purified and macrocycles **1** and **2** were separated by flash chromatography on silica gel, gradient elution with 1-5% of *i*-PrOH in CH_2Cl_2.

Table S1. Reaction conditions and products of reactions that were performed according to general procedure, unless stated otherwise.

reaction conditions						products				
N^{o}	**3**	paraformaldehyde	4M HCl	reaction time	temp.	Ratio of **1**:**2**	**1**	**2**	mixture of **1** and **2**	total
1	318 mg, 2.27 mmol	71 mg, 2.4 mmol	9 mL	17h	70^{o}C	1:1.2	76 mg, 22%	137 mg, 40%	23 mg, 7%	69%
2	100 mg, 0.71 mmol	22 mg, 0.74 mmol	2.9 mL	18h	70^{o}C	1:1.2	28 mg, 26%	54 mg, 51%		77%
3	100 mg, 0.71 mmol	24 mg , 0.8 mmol	2.9 mL	4h	70^{o}C	1.4:1	26 mg, 24%	37 mg, 34%	10 mg, 9%	67%
4	1000 mg, 7.13 mmol	218 mg, 7.27 mmol	29 mL	4h	70^{o}C	1:1.4				598 mg, 55%
5	200 mg, 1.43 mmol	43 mg, 1.43 mmol	5.7 mL	4h	70^{o}C	1.4:1	71 mg, 33%	68mg, 31%	28 mg, 13%	77%
6	50 mg, 0.36 mmol	11 mg, 0.36 mmol	1.4 mL	3h 45min	110^{o}C	1.1:1				40 mg, 78%
7	40 mg, 0.29mmol	9 mg, 0.29mmol	1 mL	1h 45 min	MW 80^{o}C	1.2:1				32 mg, 74%
8	200 mg, 1.43 mmol	43 mg, 1.43 mmol	5.7 mL; 8M	4h	70^{o}C	1:3.3	34 mg, 16%	131 mg, 60%	18 mg, 8%	84%

[a]Standard deviation for measured ratios of **1** to **2** by Quantitative HPLC-UV analysis from the crude mixture is 1-11%

[b]No. 5 and No. 8 were performed in parallel in identical conditions, except for the molarity of aq. HCl solution, 4M and 8M.

Characterization of *cis*-cycHC[6] **2**

NMR data was in agreement with literature data[2]

White solid

IR (KBr): ν, (cm^{-1}): 2933, 2854, 1708, 1437, 1377, 1361, 1268, 1245, 1211, 1182, 1145, 1121, 994, 964, 773, 702, 620, 565.

mp. 261 °C (dec).

Characterization of *i-cis*-cycHC[6] **1**

NMR identification is in following section.

White solid

HRMS: $C_{48}H_{72}N_{12}O_6$ calc.*m/z*: 913.5771 $[M+H]^+$, 935.5590 $[M+Na]^+$, exp.*m/z*: 913.5779 $[M+H]^+$, 935.5599 $[M+Na]^+$.

IR (KBr): ν, (cm^{-1}): 2934, 2858, 1706, 1437, 1361, 1270, 1243, 1210, 1183, 1145, 1120, 960, 774, 701, 621, 566.

mp. 290°C (dec).

HPLC analysis of cycHCs

HPLC analysis of cycHCs was performed according to the previously developed method.[3]

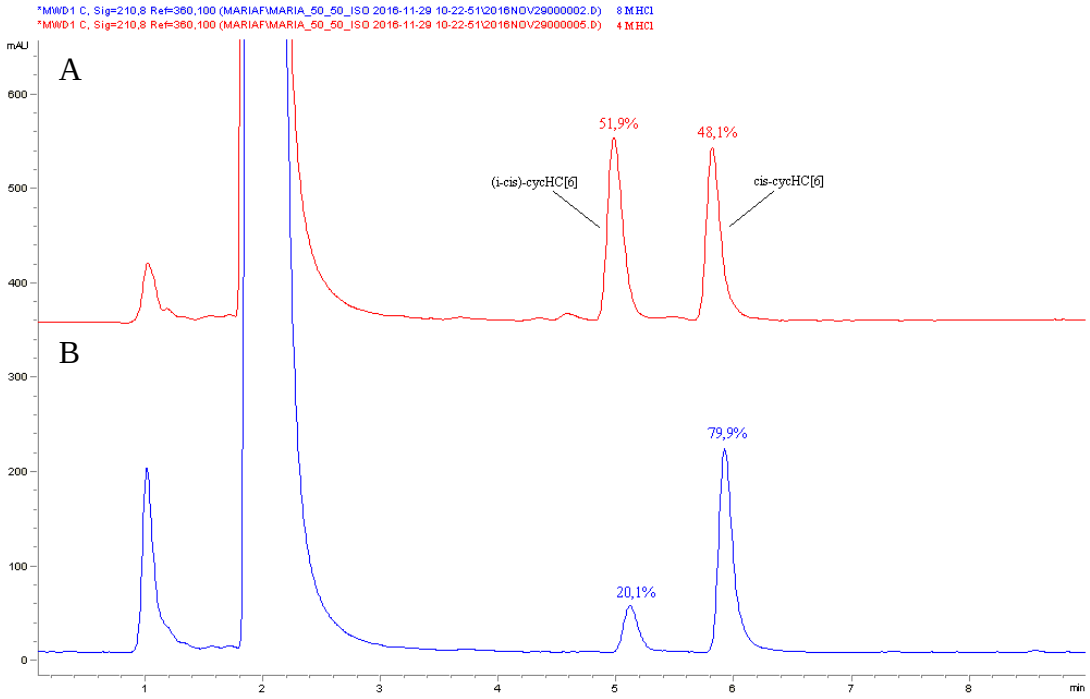


Figure S1. HPLC-UV chromatogram of crude reaction mixture performed in A) 4 M and B) 8 M HCl (see Table S1 row 5 and 8, and sample preparation details in next section).

The formation of *cis*-cycHC[8] starting from *cis*-cycHC[6] **2** was also investigated. cycHC **2** was subjected to following reaction conditions: mixture of formic acid and acetonitrile, mixture of acetic acid, acetonitrile and $NaPF_6$ and mixture of trifluoroacetic acid and acetonitrile, all at room temperature and analogously to our previous study for formation of (*R*,*R*)-cycHC[8][4]. MS analysis of crude reaction mixtures confirmed formation of other homologues form *cis*-cycHC[6] (See Figure S2), but these compounds were formed in very low yield and therefore their isolation was not attempted.

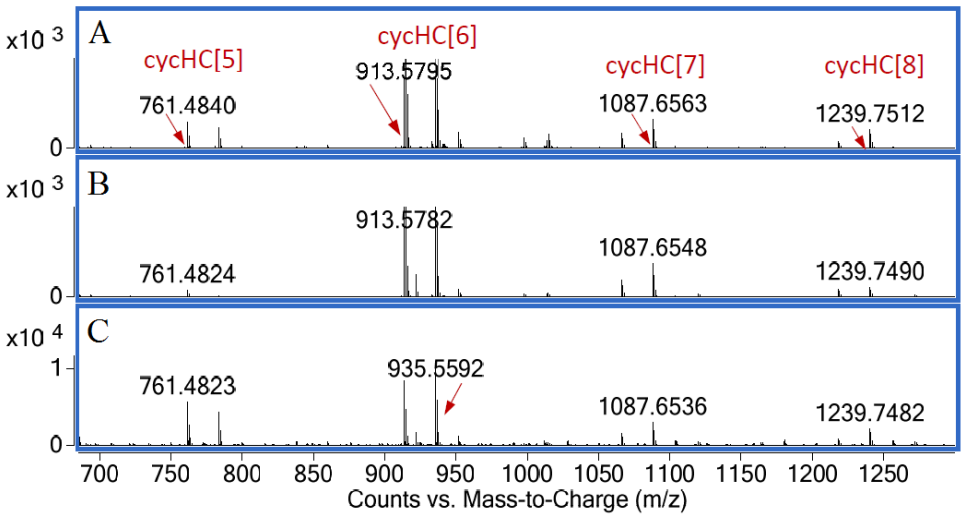


Figure S2. Mass-spectra of the trans-macrocyclisation reaction of *cis*-cycHC[6] **2** performed in A) mixture of formic acid and acetonitrile for 48 h, B) in mixture of $NaPF_6$ acetic acid and acetonitrile for 48 h and C) mixture of trifluoroacetic acid and acetonitrile for 1 h. The calculated m/z value for the $[cycHC[5] + H]^+$ is 761.4821; for the $[cycHC[6] + H]^+$ and $[cycHC[6] + Na]^+$ are 913.5771 and 935.5590, respectively; for the $[cycHC[7] + Na]^+$ is 1087.6540; for the $[cycHC[8] + Na]^+$ is 1239.7489.[5]

Quantitative analysis of cycHCs

Table S2. Characteristic parameters for calibration of *i-cis*-cycHC[6] **1**.

	Equation	**R**	**LoD (µg/mL)**	**LoQ (µg/mL)**
i-cis-cycHC[6] **1**	$y=(10.1\pm0.2)x+(5\pm7)$	0.9951	0.057±0.002	0.188±0.008
cis-cycHC[6] **2**	$y=(10.6\pm0.1)x+(1\pm5)$	0.9980	0.111±0.004	0.37±0.02

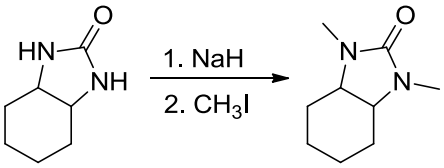
For chromatographic analysis of crude reaction mixtures three parallels were taken (20 µl) as a suspension and diluted in $CHCl_3/CH_3OH$ (1:4) mixture to reach fully dissolved sample. The concentrations were found using the equation $y=ax+b$ equation from the calibration curve (Table S2).

Synthetic procedure of inter-conversion of cycHCs

1. Heterogeneous mixture of *cis*-cycHC[6] **2** (10 mg, 0.01 mmol) in 4M aq. HCl (0.26 mL) was stirred for 3 h at 100 °C. Molar ratio of *i-cis*-cycHC[6] **1** to *cis*-cycHC[6] **2** in crude mixture was 1:19.3, respectively, determined by UV-HPLC (See "Quantitative analysis of cycHCs").

2. Heterogeneous mixture of *i-cis*-cycHC[6] **1** (10 mg, 0.01 mmol) in 4M aq. HCl (0.26 mL) was stirred for 3 h at 100 °C. Molar ratio of *i-cis*-cycHC[6] **1** to *cis*-cycHC[6] **2** in crude mixture was 1:1.3, respectively, determined by UV-HPLC (See "Quantitative analysis of cycHCs").

Synthesis of *N,N'*-dimethylcyclohexa-1,2-diylureas



Synthesis was performed according to literature[6] as follows:

(*R,S*)-*N,N'*-dimethylcyclohexa-1,2-diylurea **7**

Under argon atmosphere dioxane (7.2 mL) was added to (*R,S*)-*N,N'*-cyclohexa-1,2-diylurea **3** (102 mg, 0.728 mmol) and NaH (377 mg, 9.85 mmol, 60% in oil). Reaction mixture was heated 3 h at 55-60 ^{o}C and cooled to room temperature. Then methyl iodide (270 µl, 4.34 mmol) was added and reaction was stirred at room temperature for 3 h. Reaction mixture was filtered, washed with CH_2Cl_2. Crude product was purified by flash chromatography on silica gel, gradient elution with 0-3% of *i*-PrOH in CH_2Cl_2. 74 mg of (*R,S*)-*N,N'*-dimethylcyclohexa-1,2-diylurea **7** as yellow oil was isolated in 60% yield.

HRMS: $C_9H_{16}N_2O$ calc. *m/z*: 169.1335 $[M+H]^+$, 191.1155 $[M+Na]^+$, exp.*m/z*: 169.1333 $[M+H]^+$, 191.1154 $[M+Na]^+$.

IR (neat): ν, (cm^{-1}): 2933, 2859, 1699, 1445, 1394, 1288, 1255, 1068, 1020, 993, 772, 695.

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 3.30 – 3.27 (m, 2H), 2.71 (s, 6H), 1.78 – 1.66 (m, 2H), 1.63 – 1.53 (m, 2H), 1.53 – 1.41 (m, 2H), 1.37 – 1.25 (m, 2H).

^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) 162.57, 55.34, 28.60, 25.38, 20.70.

(*R*,R**)-*N,N'*-dimethyl-cyclohexa-1,2-diylurea **8**

Under argon atmosphere dioxane (7.2 mL) was added to racemic (*R**,*R**)-*N,N'*-cyclohexa-1,2-diylurea **3** (102 mg, 0.728 mmol) and NaH (360 mg, 9.39 mmol, 60% in oil). Reaction mixture was heated 3 h at 55-60 ^{o}C and cooled to room temperature. Then methyl iodide (280 µl, 4.5 mmol) was added and reaction was stirred at room temperature for 3.5h. Reaction mixture filtered, washed with CH_2Cl_2. Crude product purified by flash chromatography on silica gel, gradient elution with 0-3% of *i*-PrOH in CH_2Cl_2. 90 mg of racemic (*R**,*R**)-*N,N'*-dimethyl-cyclohexa-1,2-diylurea **8** as yellow oil was isolated in 74% yield.

HRMS: $C_9H_{16}N_2O$ calc.*m/z*: 169.1335 $[M+H]^+$, 191.1155 $[M+Na]^+$, exp. *m/z*: 169.1332 $[M+H]^+$, 191.1151 $[M+Na]^+$.

IR (neat): ν, (cm^{-1}): 2937, 2866, 1710, 1433, 1374, 1258, 1132, 1073, 1025, 921, 841, 772.

^{1}H-NMR(400 MHz, $CDCl_3$) δ (ppm) 2.65 (s, 6H), 2.58 – 2.44 (m, 2H), 2.01 – 1.93 (m, 2H), 1.90 – 1.75 (m, 2H), 1,41 – 1,18 (m, 4H).

^{13}C-NMR (101 MHz, $CDCl_3$) δ (ppm) 164.76, 63.90, 29.64, 28.18, 24.32.

Solubility measurements

To ensure that equilibrium between *cis*- and *i-cis*-cycHC[6] is not influenced by difference in solubility in aqueous media we measured their solubility in pure water, 4M aq. HCl and 8M aq. HCl.

Sample preparation

To 3 mg of macrocycle **1** or **2** (*i-cis*- or *cis*-cycHC[6]) 10 mL of solvent (pure water, 4M aq. HCl or 8M aq. HCl) were added. Resulted heterogeneous mixture was vortexed for 1 min and sonicated for 10 min at room temperature. Solid part was filtered and aqueous phase was evaporated in vacuum at 50°C. Solid residue obtained after aqueous solvent evaporation was transferred to vial with chloroform and organic solvent was evaporated. HPLC samples were prepared by addition of 100 µl of chloroform and 400 µl of methanol with Hamilton syringes to ensure exact volume. Amount of dissolved macrocycles in investigated solvents were found using calibration equations from Table S2.

In case of samples prepared in 4M and 8M aq. HCl partial decomposition of macrocycles to oligomers were observed in HPLC chromatogram (see Figure S3), which is consistent with proposed mechanism for cycHCs[4].

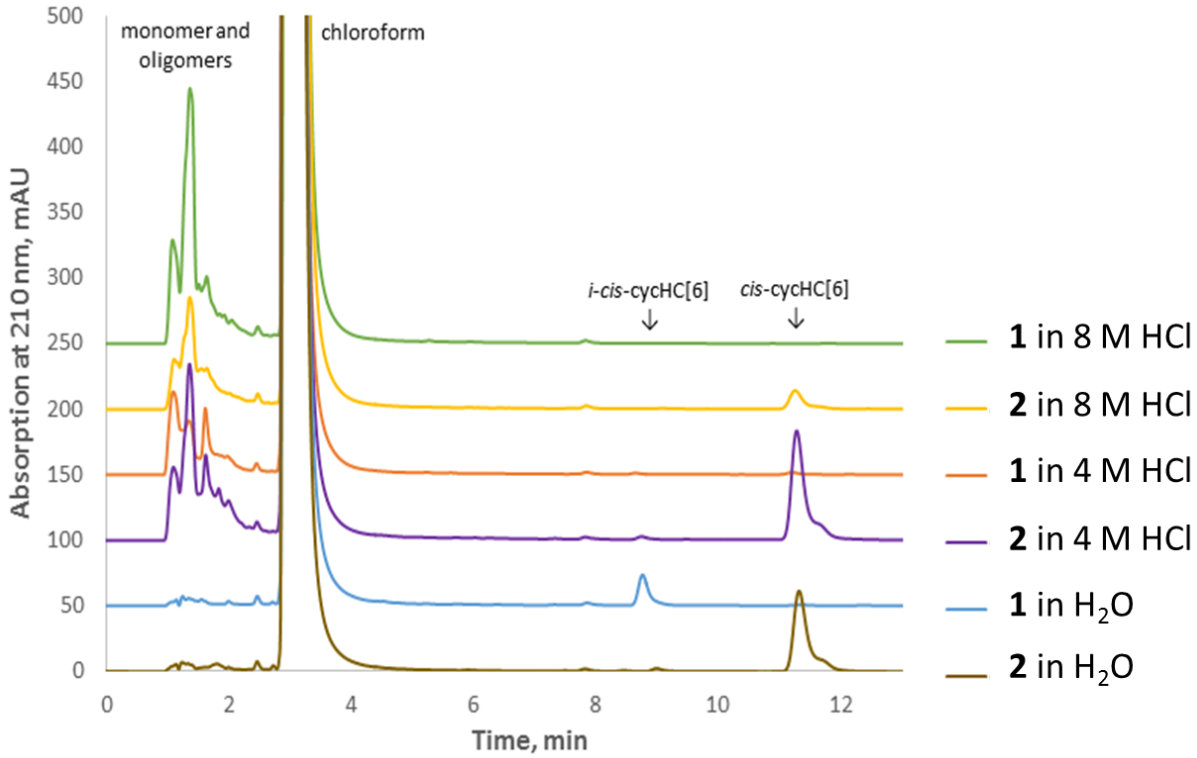


Figure S3. RP-HPLC chromatogram of **1** (*i-cis*-cycHC[6]) and **2** (*cis*-cycHC[6]) in pure water, 4M and 8M aq. HCl solution.

Table S3. Concentration of **1** and **2** obtained from solubility measurement.

Solvent	***cis*-cycHC[6] 2 µg/ml (µM)**	***i-cis*-cycHC[6] 1 µg/ml (µM)**
Water	4.30 (4.71)	1.41 (1.54)
4 M aq. HCl	5.35 (5.96)	0.04 (0.04)
8 M aq. HCl	0.97 (1.06)	below LoD

In acidic solutions of **1** and **2** due to formation of dynamic covalent library of linear and cyclic oligomers the exact solubility of macrocycles cannot be determined, nevertheless obtained results reflect that solubility of **1** and **2** is in micromolar range in aqueous media.

NMR analysis

NMR identification of *inverted-cis*-cycHC[6] **1**

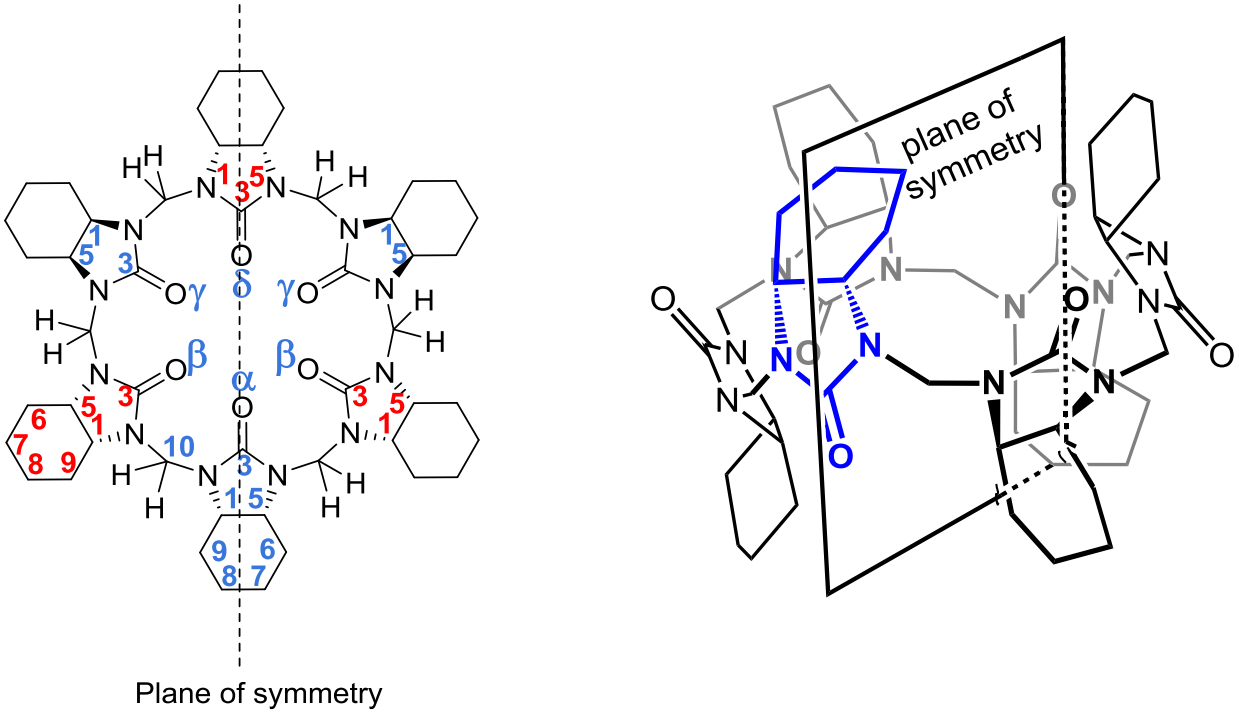


Figure S4. Structure of the *i-cis*-cycHC[6] **1** for NMR assignment.

Inverted-cis-cycHC[6] **1** has one plane of symmetry, which simplifies the analysis of its NMR spectra. As two halves of the molecule are equivalent, we will consider only 4 monomers (α, β, γ, δ), where α denotes the inverted monomer. It is also important that monomers are in a zig-zag orientation and therefore numeration of the carbon atoms of the subsequent monomers alternates in each direction.

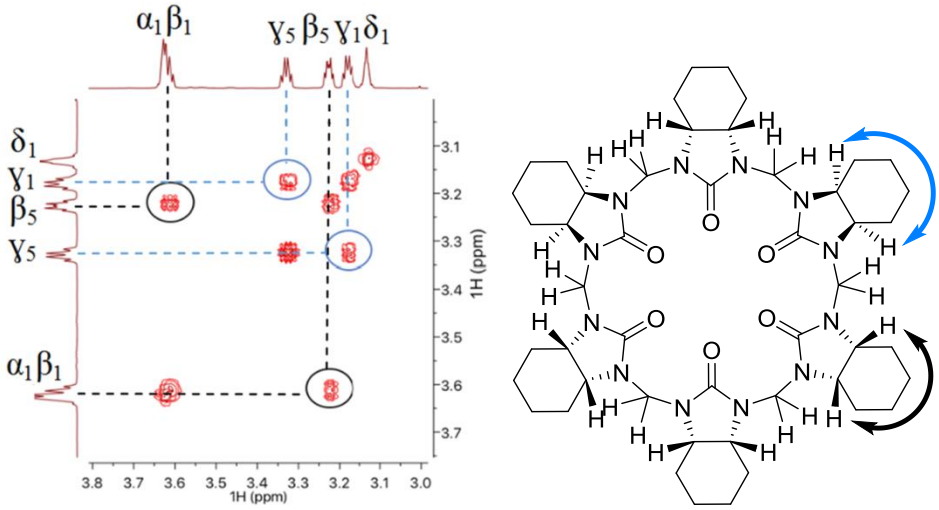


Figure S5. Part of a COSY spectrum, indicating neighbouring hydrogens, marked by arrows on the structure. The respective crosspeaks are indicated by circles in the figure.

The COSY spectrum in Fig. S5 indicates that β_1 and β_5 as well as γ_1 and γ_5 hydrogen atoms show a correlation cross peak and are therefore hydrogen atoms of the same monomer. These pairs of hydrogen atoms are marked with arrows and the respective cross peaks are circled in Fig. S5. The α_1 and δ_1 hydrogen atoms originate from symmetrical monomers and give only a single peak in the ^{1}H NMR spectrum and therefore no cross peaks in the COSY spectrum.

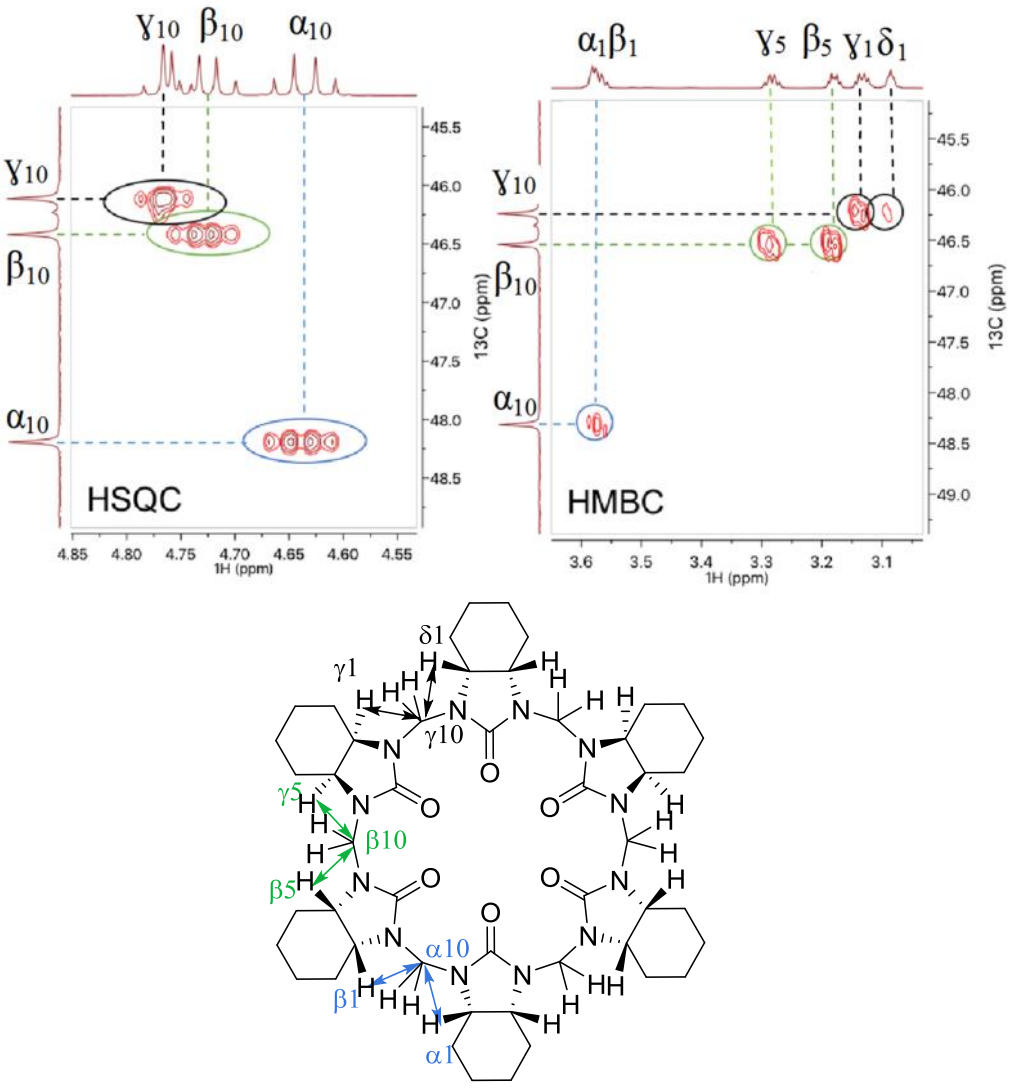


Figure S6. Parts of a HSQC and a HMBC spectra. The correlations in the spectrum are marked by arrows on the molecular structure.

The HSQC signals in Fig. S6 indicate correlations between α_{10}, β_{10} and γ_{10} bridge carbon atoms and the respective hydrogen atoms. Moreover, the HMBC spectrum in Fig. S6 shows that α_1 and β_1 hydrogen atoms both give a correlation with α_{10} bridge carbon atom and therefore must be next to the same bridge moiety in the macrocycle. From the earlier analysis of the COSY spectrum we know that the α_1 hydrogen atoms belong to a symmetrical monomer. We have denoted α_1 and β_1 hydrogens and their correlation with α_{10} carbon atoms with blue arrows in Fig. S6. The same logic applies to δ_1 and γ_1 hydrogen atoms with these hydrogen atoms giving a correlation with γ_{10} bridge carbon atom, which is marked with black arrows; here δ_1 hydrogen atoms are from the symmetrical monomer. Furthermore, β_5 and γ_5 hydrogen atoms give a correlation in the HMBC spectrum with β_{10} bridge carbon atoms, which can be marked with green arrows in Fig. S6.

The NOESY spectrum in Fig. S7 indicates cross peaks between δ_1 and $\gamma_1$hydrogen atoms as well as between δ_1 and β_5 hydrogen atoms, showing that all these hydrogen atoms point towards the cavity of the macrocycle. There is a cross peak between γ_5 and β_5 hydrogen atoms, demonstrating the same logic. These correlations map well with the positions of the hydrogen atoms in the crystal structure, also demonstrated in Fig. S7. No cross peaks are observed for α_1 hydrogen atoms, which confirms that these hydrogen atoms point away from the cavity of the macrocycle.

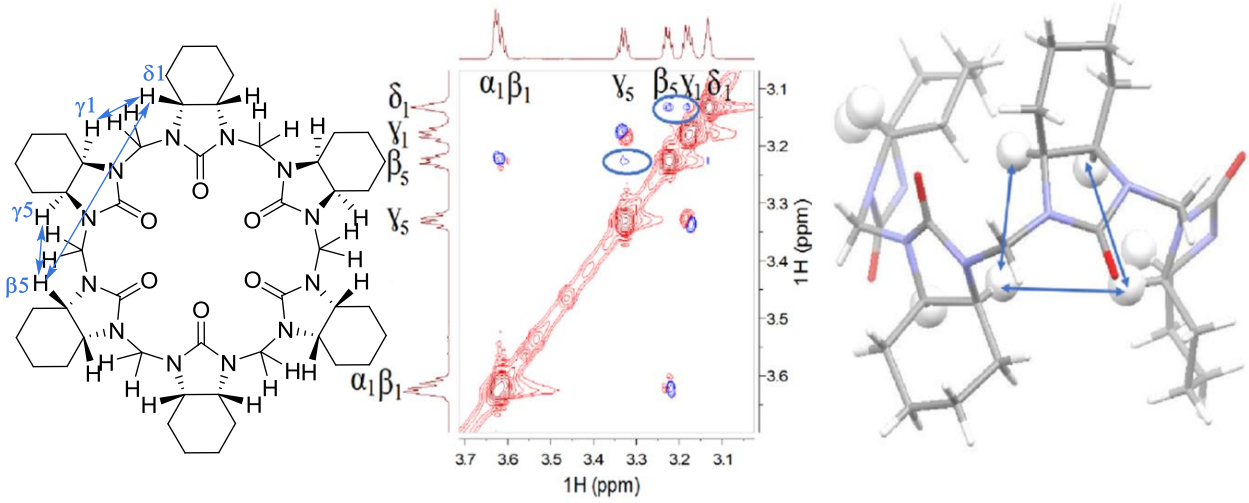


Figure S7. Part of a NOESY spectrum indicating hydrogen atoms, which are in close proximity with each other. The crystal structure shows the same hydrogens in the solid state and demonstrates their close proximity. We have omitted two monomer units in the crystal structure for clarity. The arrows indicate NOE correlations.

Table S4. Summary of cross peaks from the 2D NMR experiments.

COSY	HMBC	NOESY
γ_1-γ_5	α_1-α_{10}	γ_1-δ_1
β_1-β_5	β_1-α_{10}	β_5-δ_1
	β_5-β_{10}	γ_5-β_5
	γ_5-β_{10}	
	γ_1-γ_{10}	
	δ_1-γ_{10}	

The rest of the hydrogen and carbon atoms were assigned in analyzing the COSY and the HSQC spectra and their chemical shifts and coupling constants are brought further.

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm)

4.75 and 4.77 (d. J=14.5 Hz, 4H, γ_{10} and 2H, δ_{10}), 4.72 and 4.74 (d. J=14.5 Hz, 4H, β_{10}), 4.65-4.62 and (dd, J=14.5 Hz, 2H, α_{10}), 3.59-3.58 (m, 2H, α_1 and α_5), 3.56 (dt. J=7.5; 5.5 Hz, 2H, β_1), 3.28 (dt. J=7.2; 5.3 Hz, 2H, γ_5), 3.19 (dt., J=7.5; 4.6 Hz, 2H, β_5), 3.13 (dt., J=7.2; 5.0 Hz, 2H, γ_1), 3.08 (t. J=3.8 Hz, 2H, δ_1 and δ_5), 2.15-2.11 and 1.63-1.59 (m, 4H, β_6), 2.08-2.04 and 1.61-1.56 (m, 4H, β_9), 1.91-1.87 and 1.66-1.62 (m, 4H, γ_9), 1.87-1.83 and 1.63-1.58 (m, 4H, γ_6), 1.87-1.78 (m, 4H, δ_6 and δ_9), 1.85-1.74 (m, 4H, α_6 and α_9), 1.52-1.49 and 1.28-1.25 (m, 4H, γ_7), 1.57-1.51 and 1.24-1.19 (m, 4H, δ_7 and δ_8), 1.62-1.58 and 1.31-1.27 (m, 4H, β_8), 1.45-1.41 and 1.37-1.32 (m, 4H, γ_8), 1.43-1.38 (m, 4H, β_7), 1.35-1.30 and 1.20-1.13 (m, 4H, α_7 and α_8).

^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm)

162.02 (α_3), 161.18 (γ_3), 160.39 (β_3), 160.80 (δ_3), 55.10 (α_1 and α_5), 52.61 (β_1), 51.85 (δ_1 and δ_5), 51.79 (β_5), 51.59 (γ_1), 51.29 (γ_5), 48.32 (α_{10}), 46.54 (β_{10}), 46.24 (γ_{10} and δ_{10}), 26.46 (α_6 and α_9), 25.79 (β_9), 25.57 (γ_6), 24.88 (γ_9), 24.81 (δ_6 and δ_9), 24.49 (β_6), 21.29 (α_7 and α_8), 20.97 (β_8), 20.79 (γ_7), 20.71 (δ_7 and δ_8), 20.26 (γ_8), 20.06 (β_7).

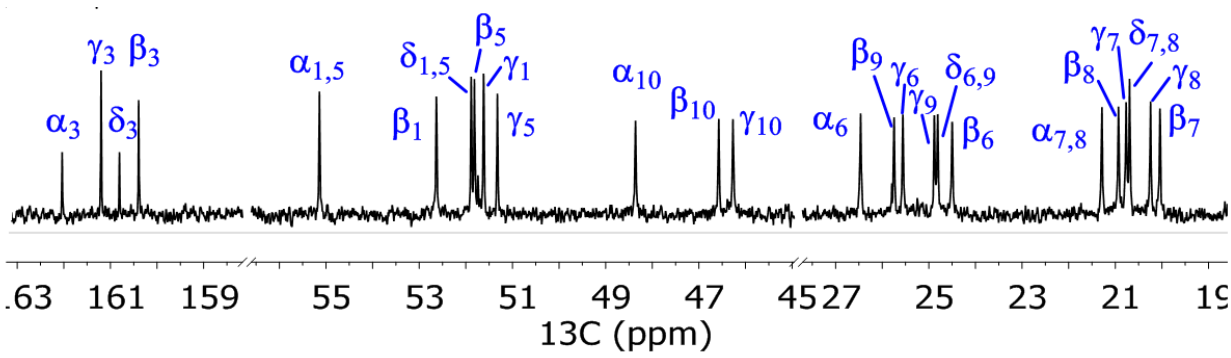
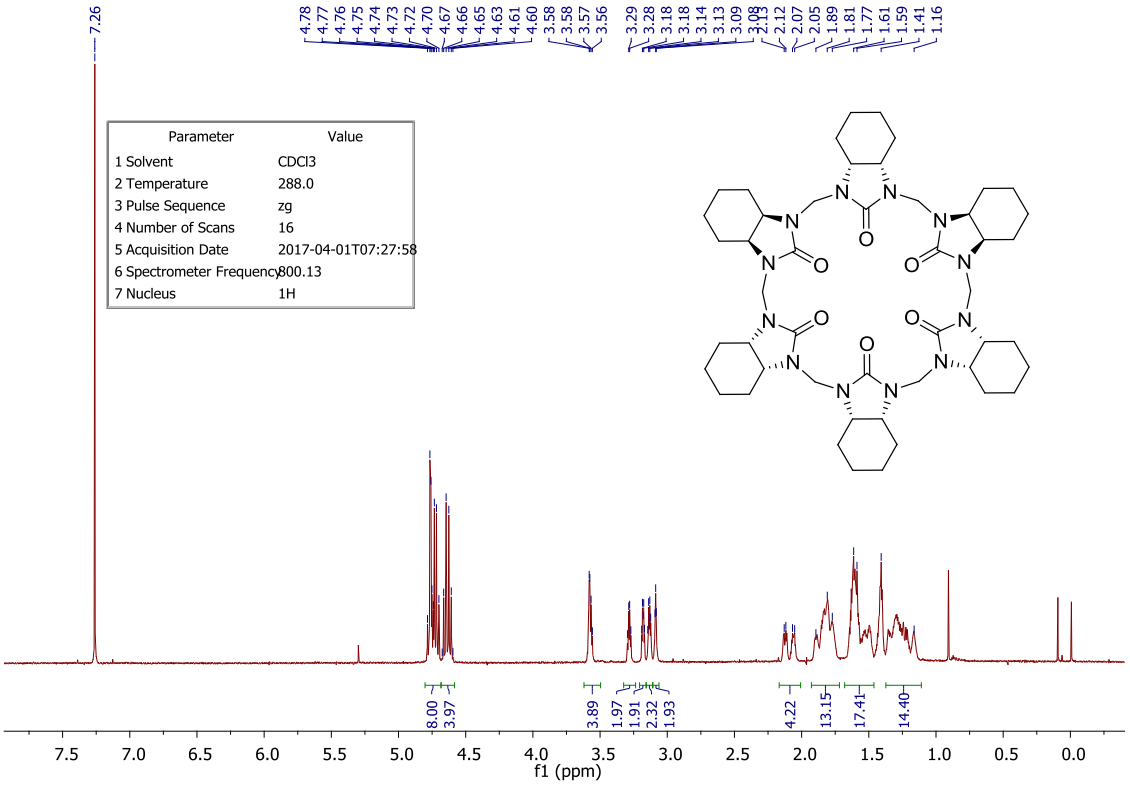
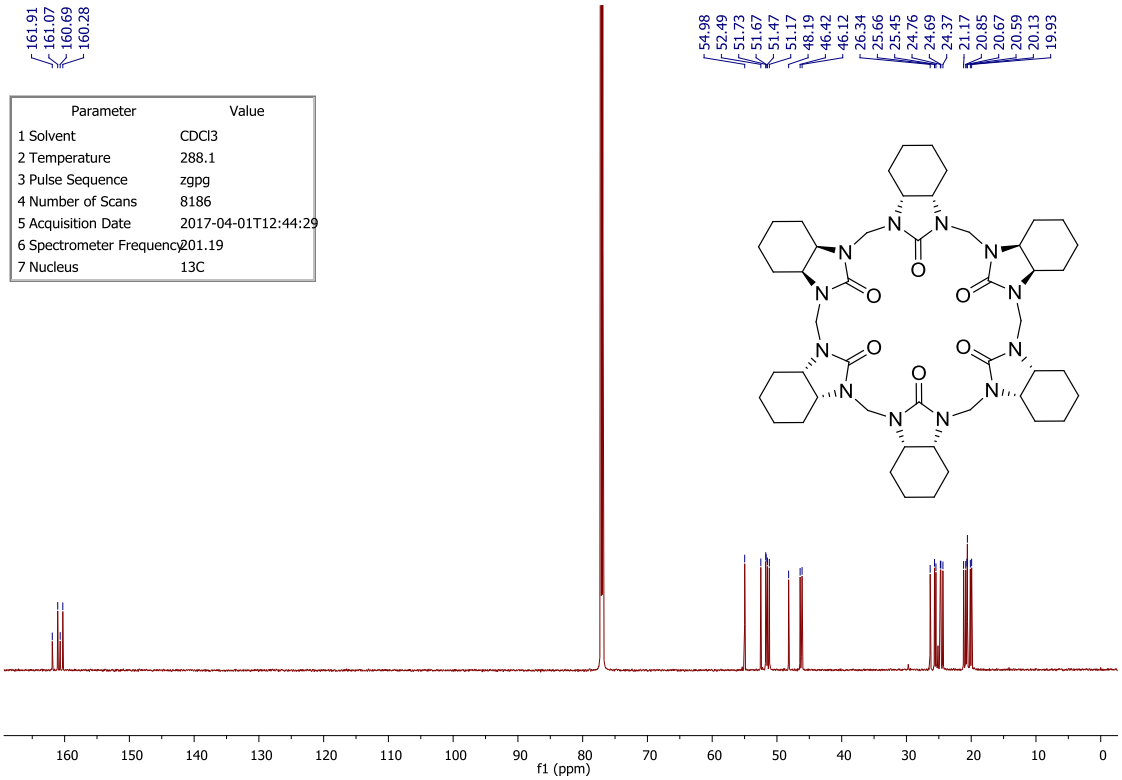


Figure S8. ^{13}C-NMR spectra of *i-cis*-cycHC[6] **1** with atom numbers.

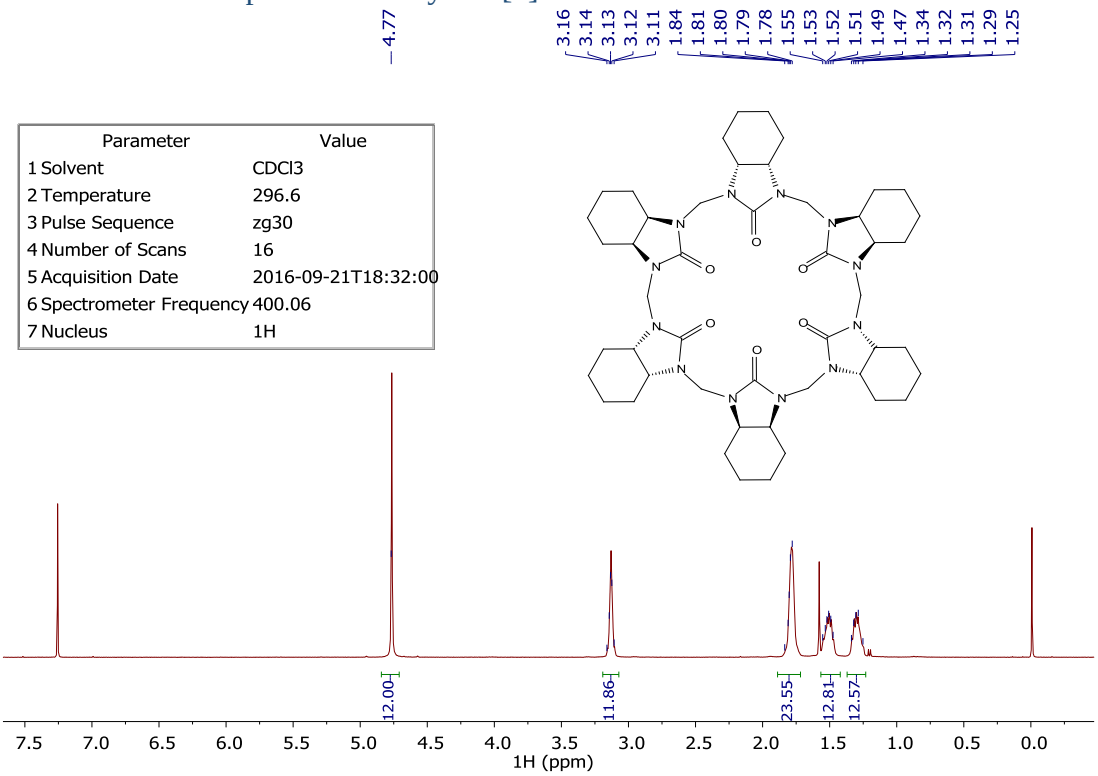
^{1}H and ^{13}C-NMR spectra of compounds **1, 2, 7, 8**.

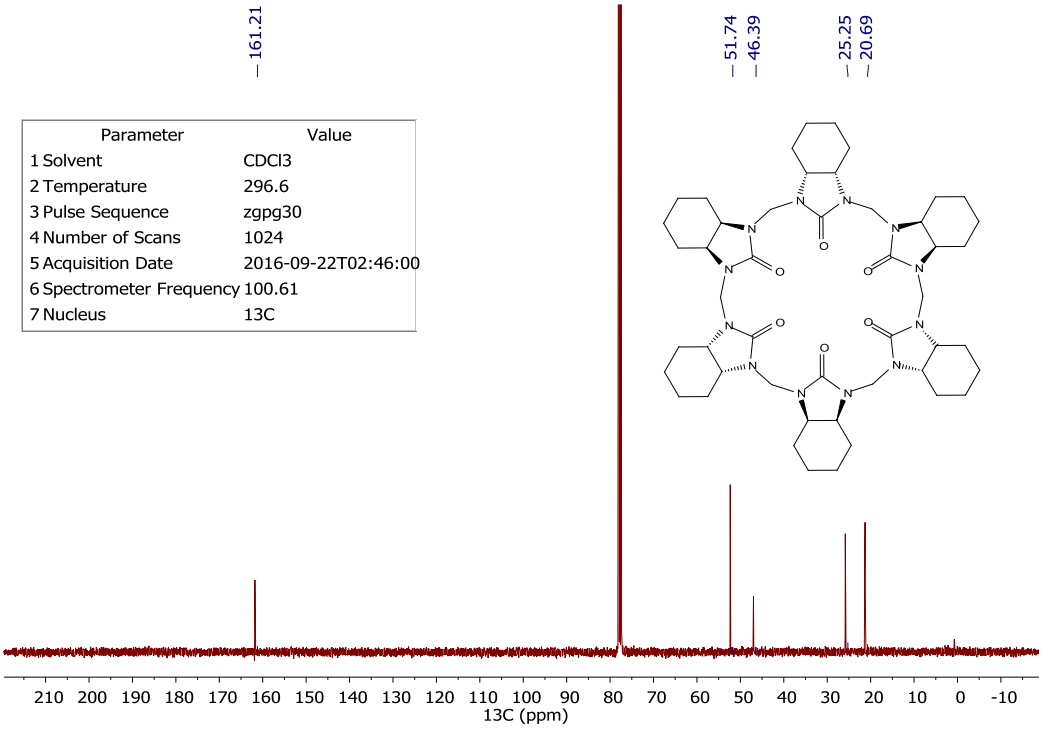
^{1}H and ^{13}C-NMR spectra of *i-cis*-cycHC[6] **1**



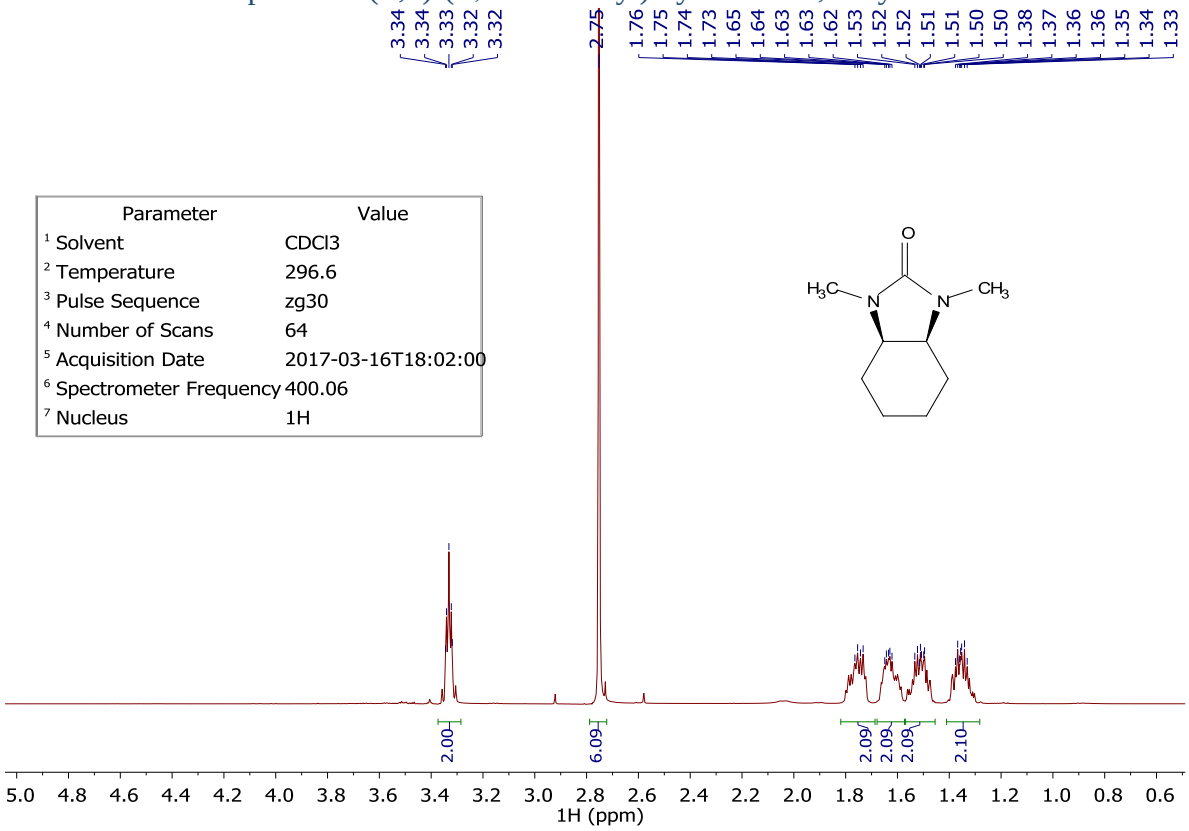


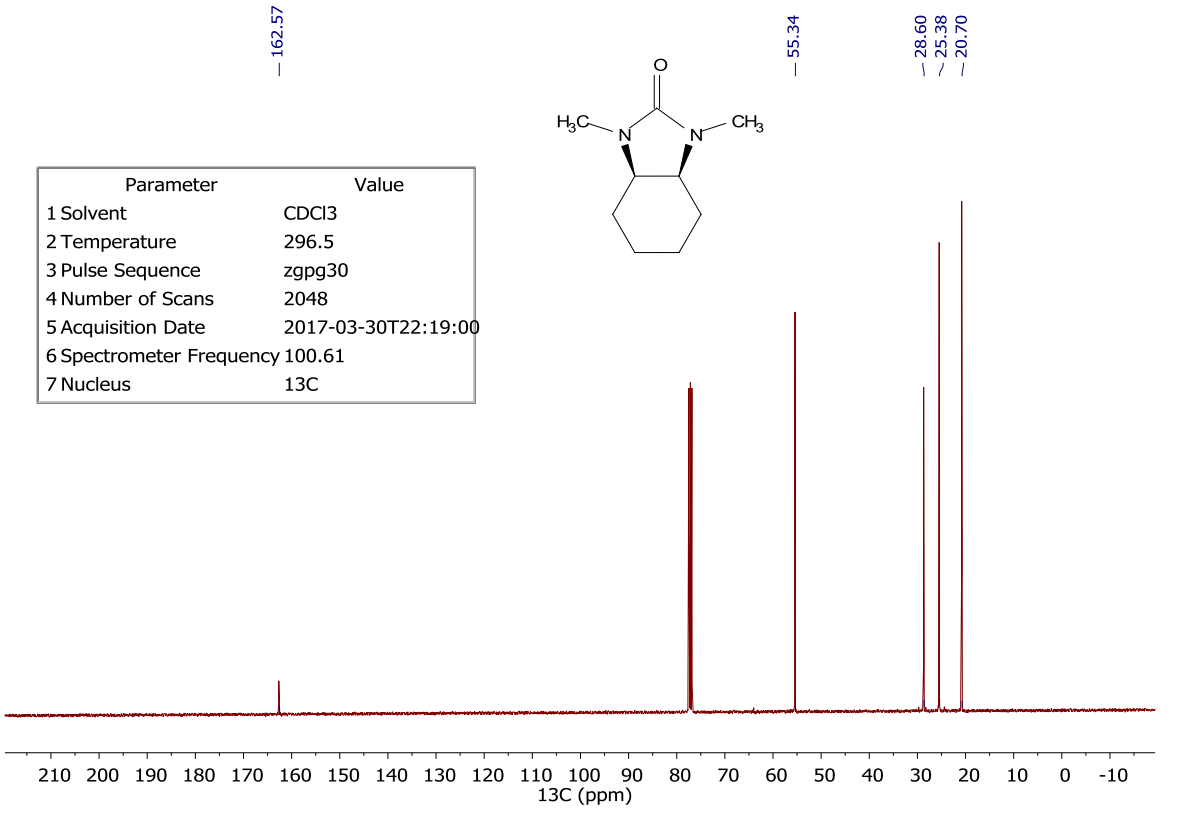
^{1}H and ^{13}C-NMR spectra of *cis*-cycHC[6] **2**



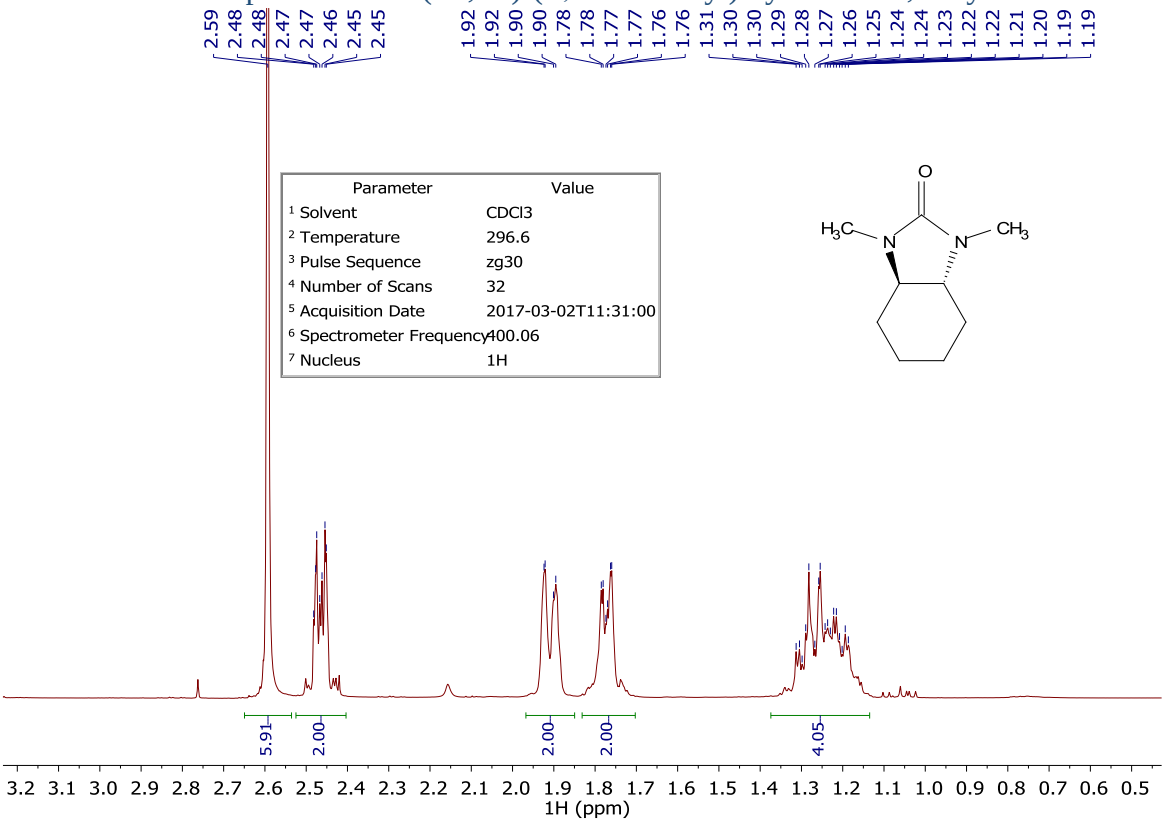


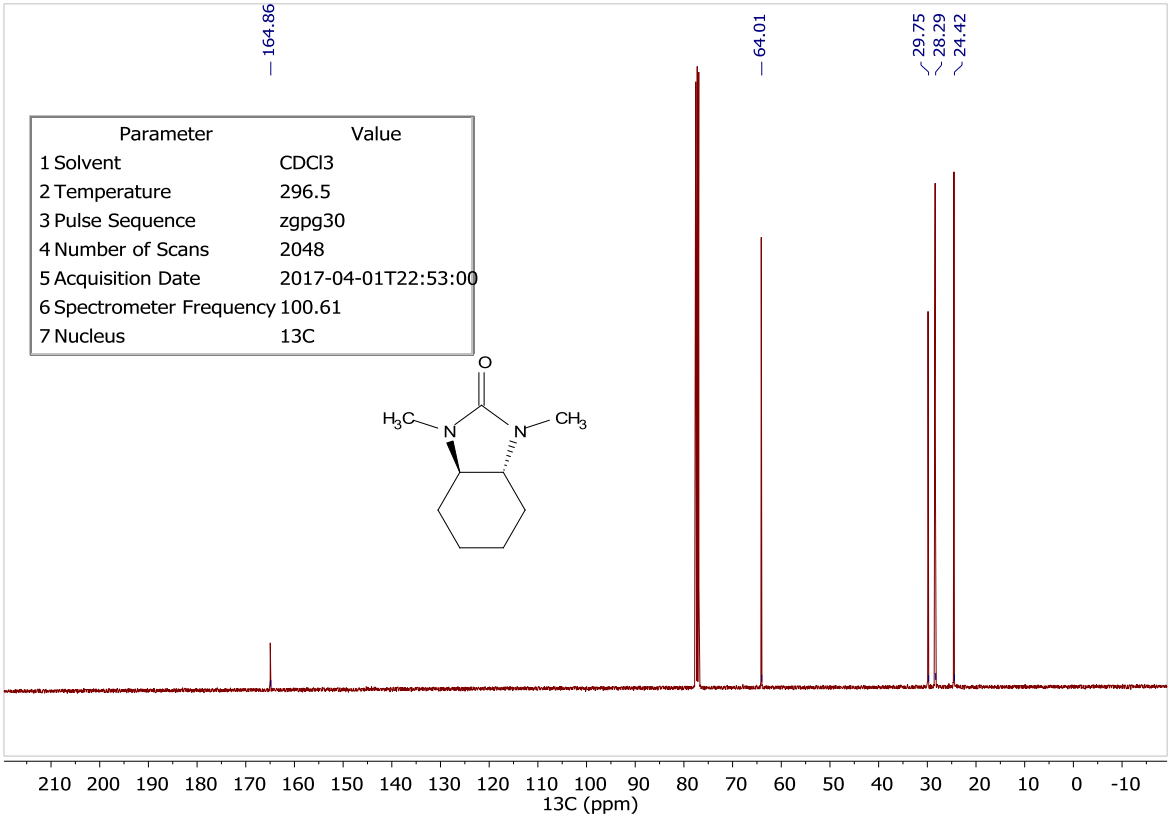
^{1}H and ^{13}C-NMR spectra of (*R,S*)-(*N,N'*-dimethyl)-cyclohexa-1,2-diylurea **7**





^{1}H and ^{13}C-NMR spectra of rac. (*R**,*R**)-(*N,N'*-dimethyl)-cyclohexa-1,2-diylurea **8**





Crystallographic analysis of *inverted-cis*-cycHC[6] **1**

Single crystal X-ray diffraction data was collected at 123K on Rigaku Compact HomeLab diffractometer, equipped with a Saturn 944 HG CCD detector and Oxford Cryostream cooling system using monochromatic Cu-*Kα* radiation (1.54178Å) from a MicroMax^{TM}-003 sealed tube microfocus X-ray source. The strategy of data collection was calculated using Rigaku*CollectionStrategy*[7]. CrysAlisPro[8] was used for data reduction and empirical absorption correctionusing spherical harmonics implemented in *SCALE3ABSPACK* scaling algorithm[9]. The structure was solved using *SHELXT*[10] and refined by full-matrix least-squares method against $F^2$with *SHELXL-2014*[10] through *OLEX2*[11] program package. All non-hydrogen and non-deuterium atoms were refined with anisotropic atomic displacement parameters. Hydrogen atoms attached to carbon atoms were treated as riding atoms, using isotropic displacement parameters U_{iso}(H) = 1.2U_{iso}(C) for CH and CH_2. The figures were drawn using the program Mercury CSD 3.9[12] and POV-Ray 3.7[13].

Crystal data

$C_{54}H_{72}Cl_{18}D_6N_{12}O_6$, M =1635.42 g/mol, triclinic, P-1 (no. 2), a = 12.5904(4) Å, b = 12.8566(4) Å, c = 13.5535(5) Å, α = 62.870(3)°, β = 73.384(3)°, γ = 75.940(3)°, V = 1854.63(12) Å^3, Z = 1, Cu-*Kα* radiation (λ = 1.54184Å) at T = 123.0 K, μ(Cu-*Kα*) = 6.531 mm^{-1}, 18638 reflections measured (7.392° ≤ 2Θ ≤ 134.554°) of which 6432 unique(5532 with $I>2\sigma(I)$), R_{int} = 0.0368, $R_1[F^2>2\sigma(F^2)]$ = 0.0862, wR_2(all data) = 0.2309, S = 1.06. The crystallographic data is deposited with the Cambridge Crystallographic Data Centre (CCDC 1569570) and can be obtained free of charge from The Cambridge Crystallographic Data Centre *via* www.ccdc.cam.ac.uk/data_request/cif.

The compound crystallizes in a centrosymmetric space group *P*-1, with half of the macrocycle and three solvent molecules in the asymmetric unit. An inversion center is located at the centre of the cavity of *i-cis*-cycHC[6] **1**. The position of the inverted monomer in the hexamericcycHC[6] appears to be disordered between four locations (Figure 9 A). Two independent disorder components were found for two neighboring monomers in the asymmetric unit. The relative occupancies of these were refined freely with the sum of site occupation factors restrained to be a constant at 0.500, resulting in sof 0.330(2) and 0.170(2) for the two sites respectively. The remaining two disorder components are generated by symmetry around the inversion center.

The packing of the macrocycles seems not to be affected by the position of the inverted monomer, as the crystal structure is largely isostructural to the *cis*-cycHC[6] previously reported in the literature (CCDC 716122). This is most likely due to the fact that the orientation of the hydrogen bond accepting carbonyl group in the inverted monomer is not drastically changed compared to the other monomers, so the hydrogen bonding to the solvent is not altered by the presence of the inverted monomer (Figure 9 B).

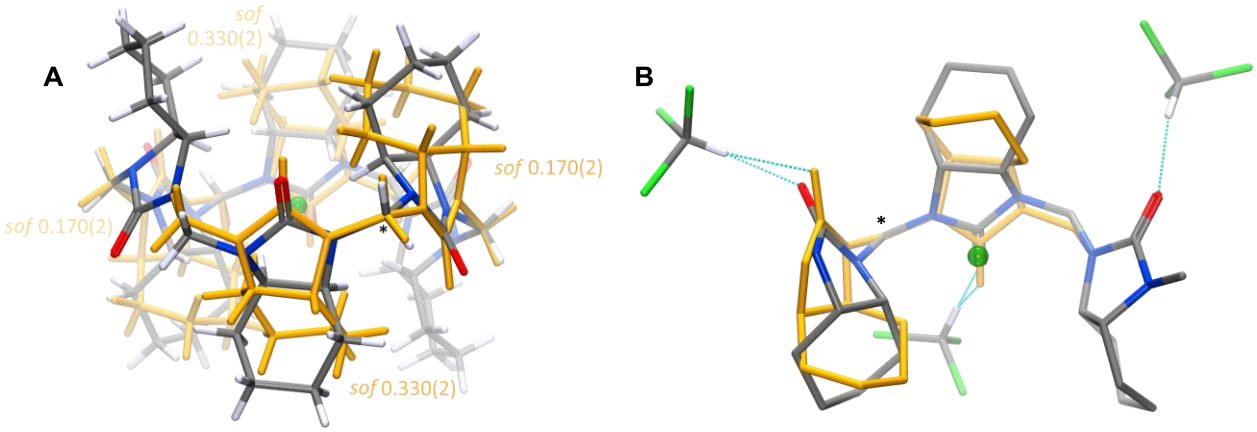


Figure S9. A) *i-cis*-cycHC[6] **1** in the crystal structure, showing in orange the four positional disorder components of the inverted monomer around the hexameric macrocycle with respective site occupancies and B) the asymmetric unit of the crystal structure showing the interactions to the surrounding chloroform molecules. The inversion centre located at the center of the cavity is depicted in green. The carbon atom marked with an asterisk is modeled with full occupancy.

The chloroform molecules in the structure, which make up channels along the unit cell *c*-axis have high degree of freedom and are thus more disordered. These were modeled in three disorder components each. The occupancies of the disorder components were allowed to refine freely, and resulted in *sof* 0.471(3)/0.276(3)/0.253(3) and *sof* 0.485(3)/0.363(3)/0.152(3). The relatively large anisotropic displacement ellipsoids of these solvent molecules and the remaining electron density (max 0.47) in close vicinity indicate further disorder, but modeling more than three disorder components per site was not attempted. The third chloroform molecule in the asymmetric unit was modeled in two disorder components, with the relative occupancy of the two components refined freely, giving *sof* 0.788(9)/0.212(9).

Computational studies

General information

The effect of chloride ion on different stages of the formation of cyclohexanohemicucurbit[6]urils was studied computationally. The input coordinates of *cis*-cycHC[6] **2** and *i-cis*-cycHC[6] **1** were generated from the X-ray crystal structures of the molecules. All geometries were fully optimized, and stationary points characterized with vibrational analysis. In the case of the system HCl@**1** B (described below), a residual imaginary vibration of 3.03 cm^{-1} remained; all other systems were characterized as true minima. Vibrational zero-point energies were added to electronic energies and the resulting differences evaluated. All the calculations were performed with the density functional theory, using the functional BP86, the basis set def2-TZVP[14,15,16,17] and the program package Turbomole 6.3. [18]

Methylated *R,S,S,R*- and *R,S,R,S*-ordered dimers

From the optimized isomeric cyclic structures both *R,S,S,R*- and *R,S,R,S*-ordered dimers were isolated and their methylated geometries (**9** and **10**) optimized (Figure S10). Next, the effect of the presence of chloride ion close to named dimers was modelled (Figure S11), adding the chloride ion „inside“ of the dimer, where it would mimic the chloride ion's position being in the cavity of the cycles. From the optimized Cl^-*@R,S,S,R*-ordered dimer and Cl^-*@R,S,R,S*-ordered dimer complexes the chloride ions were then removed and single-point calculations (SPC) for both dimers were performed.

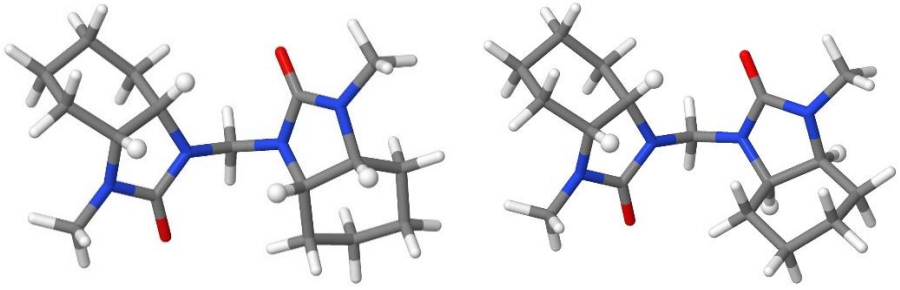


Figure S10. DFT models of dimers **9** (C-shaped and *R,S,S,R*-ordered) and **10** (S-shaped and *R,S,R,S*-ordered).

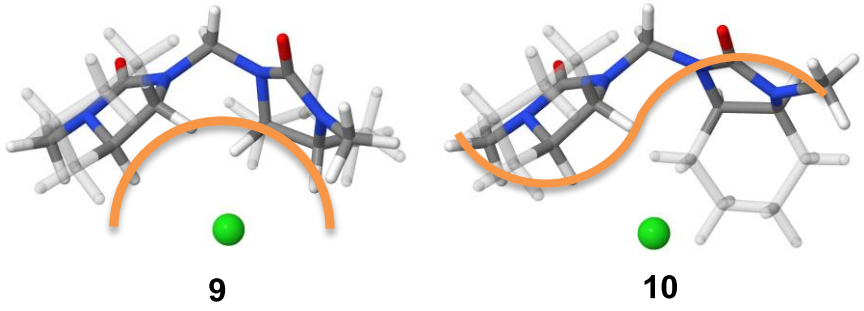
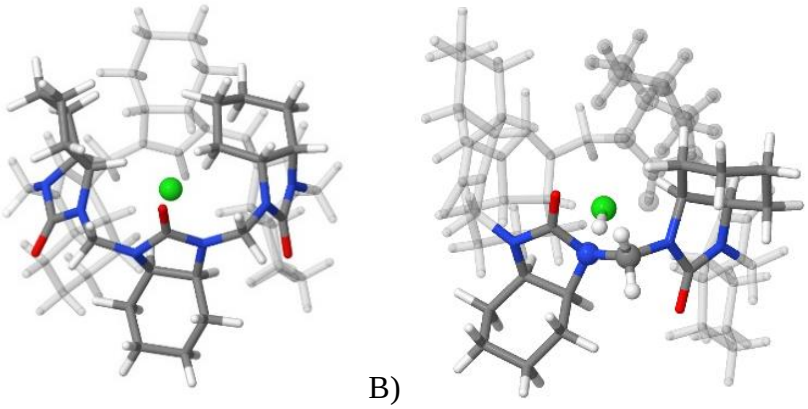


Figure S11. DFT models of dimers **9** (C-shaped and *R,S,S,R*-ordered) and **10** (S-shaped and *R,S,R,S*-ordered) complexes with chloride anion.

Macrocycles without and with chloride ion

Geometries of diastereomeric cycHC[6] macrocycles **1** and **2** were optimized with an included chloride ion and without it. Without the chloride, compound **1** has 17 kJ/mol higher energy than **2**. Upon encapsulation of the chloride anion, the energy difference is increased to 30 kJ/mol (Figure S12).



A) B)

Figure S12. DFT models A) Cl^-@**1** complex and B) lowest energy geometry HCl@**1** formed during geometry optimisation of iminium chloride intermediate.

Iminium intermediates

Modelling of the formation of **1** and **2** from six-membered iminium intermediates unexpectedly showed, that all the studied hexameric iminium chloride geometries formed HCl@cycHC[6] inclusion complexes upon energy minimization. Therefore, we can state that the final macrocyclisation step proceeds without a transition state. Even more significantly, the resulting inclusion complexes of the diastereomeric macrocycles with hydrochloric acid were energetically very similar. The lowest-energy geometry of the HCl inclusion complex of **1**, which is depicted in Figure S12 B, was even 1.5 kJ/mol lower than that of **2**.

Initial geometries for seven different iminium intermediates were obtained from optimized geometries of corresponding closed cycles (Figure S12a) via moving atoms apart at the appropriate C-N bond (shown on Figure S12b). The bond was broken by changing a bond angle at the opposite side of the macrocycle and adding a proton to the nitrogen atom of the broken bond. Then the chloride ion was positioned in the middle of the cavity of all different iminium intermediates (Figure S12b) and the reactions between the intermediates and the chloride ion were modelled. In the structure of *cis*-cycHC[6] **2** all C-N bonds in methylene bridges are equivalent, therefore only a single iminium structure with encapsulated Cl^- anion was built. The inverted isomer has six non-equivalent C-N bonds, therefore six iminium chloride complexes were constructed. All the studied oligomeric iminium chloride geometries formed HCl@cycHC[6] inclusion complexes upon energy minimization. All the HCl@*i-cis*-cycHC[6] complexes formed from the "pairs" of the iminium intermediates of *i-cis*-cycHC[6] **1** (A1 and A2, B1 and B2, C1 and C2) had the same final structures with almost equivalent energies. Therefore as a result of seven different cyclisation reactions only four different HCl@cycHC[6] complexes were formed: one HCl@*cis*-cycHC[6] and three HCl@*i-cis*-cycHC[6] (Figure S12c). The final structures and energies are given for the complexes with the lowest energies, as the

energy difference between the same complexes formed from different input geometries (for example complex A formed from either A1 or A2) was below 1 kJ·mol^{-1}.

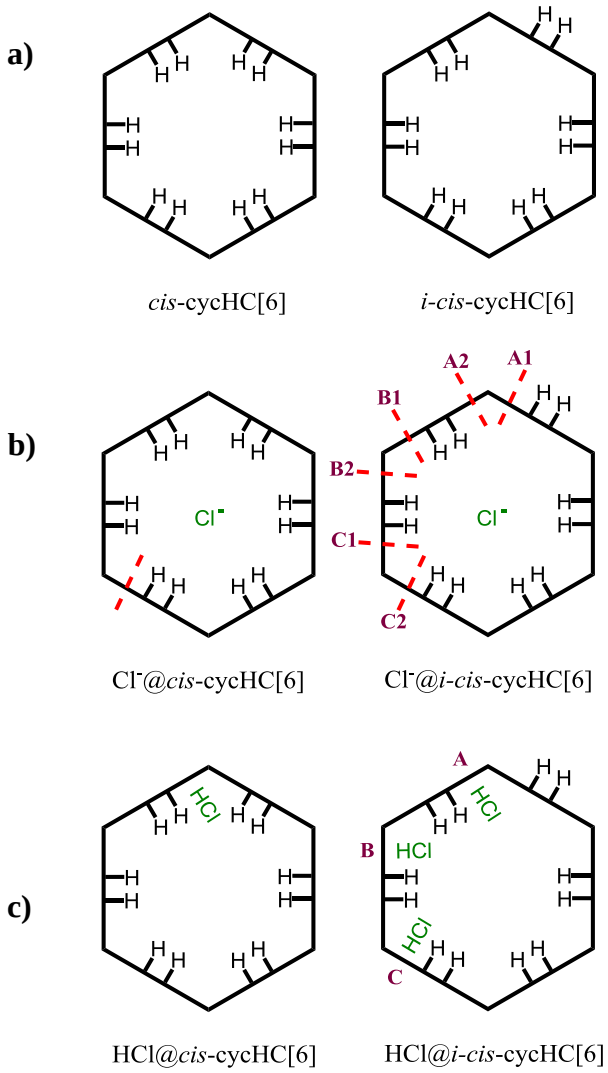


Figure S13. a) A schematic representation of *cis*-cycHC[6] **2** and *i-cis*-cycHC[6] **1** with inverted monomer depicted with outward-projecting hydrogens. b) A schematic representation of the formation of seven iminium intermediates, where the dotted red line indicates the location of the broken C-N bond. After the breakage of the bond a proton was added to the nitrogen atom of the broken bond and chloride ion into the cavity of the intermediate. c) HCl@*cis*-cycHC[6] and three HCl@*i-cis*-cycHC[6] complexes showing the position of HCl in formed complexes. All the pairs of the intermediates (A1 and A2, B1 and B2, C1 and C2), when supplemented with a chloride ion, led to formation of the same HCl@*i-cis*-cycHC[6] complex, A, B, or C, respectively.

Energies of studied compounds

Table S5. Main results of computations.

Molecule	DFT energy, a.u.	ZPE, a.u.	E(DFT)+ZPE, a.u.	Relative energy, kJ·mol^{-1}
cis-cycHC[6] **2**	-2982.3279797	1.1758775	-2981.1521022	0
i-cis-cycHC[6] **1**	-2982.3213605	1.1759102	-2981.1454503	17.5
Cl^- *@cis-cycHC[6]* Cl^- @**2**	-3442.7169059	1.1761083	-3441.5407976	0
Cl^- *@i-cis-cycHC[6]* Cl^- @**1**	-3442.7051891	1.1757239	-3441.5294652	29.8

Molecule	DFT energy, a.u.	ZPE, a.u.	E(DFT)+ZPE, a.u.	Relative energy, kJ·mol^{-1}
R,S,S,R-ordered dimer **9**	-1034.6326172	0.4373198	-1034.1952974	0
R,S,R,S-ordered dimer **10**	-1034.6313471	0.4371914	-1034.1941557	3.0
Cl^- *@R,S,S,R* -ordered dimer Cl^- @**9**	-1494.9933009	0.4371933	-1494.5561076	0
Cl^- *@R,S,R,S* -ordered dimer Cl^- @**10**	-1494.9879286	0.4370796	-1494.5508490	13.8
SPC of *R,S,S,R* -ordered dimer **9** with the removed Cl^-	-1034.6245332			0
SPC of *R,S,R,S* -ordered dimer **10** with the removed Cl^-	-1034.6268491			-6.1

Molecule	DFT energy, a.u.	ZPE, a.u.	E(DFT)+ZPE, a.u.	Relative energy, kJ·mol^{-1}
HCl@*cis*-cycHC[6] HCl@**2**	-3443.1936880	1.1848601	-3442.0088279	0
HCl@*i-cis*-cycHC[6] HCl@**1** A	-3443.1933374	1.1845829	-3442.0087545	0.2
HCl@*i-cis*-cycHC[6] HCl@**1** B	-3443.1929023	1.1849358	-3442.0079665	2.3
HCl@*i-cis*-cycHC[6] HCl@**1** C	-3443.1938778	1.1844665	-3442.0094113	-1.5

Optimized geometries of key compounds

cis-cycHC[6] **2** coordinates in angstroms

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O	7.1171526	9.3811765	10.0852672
N	9.1614080	8.2634392	9.8830616
N	7.3262618	7.2980074	9.0276245
C	7.7949623	8.4237963	9.7087597
C	9.5676491	6.8981064	9.5075311
H	10.5589474	6.9123589	9.0339609
C	8.4724263	6.5591874	8.4671333
H	8.7517509	7.0264169	7.5016906
C	8.2463719	5.0645664	8.2277029
H	9.0772133	4.7164341	7.5901220
H	7.3348412	4.9266426	7.6268873
C	8.2255950	4.2230511	9.5074629
H	8.1341226	3.1581988	9.2446483
H	7.3402845	4.4761628	10.1144669
C	9.4934184	4.4739950	10.3306121
H	9.5027067	3.8485269	11.2358113
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H	5.3607392	7.8938045	9.0351925
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C	5.8204810	9.4672927	6.8685939
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H	3.3650192	10.2709522	4.7416129
H	3.6670189	12.0085394	4.6295539
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H	5.5691196	10.7157334	3.5842575
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H	5.2745664	6.8958702	3.4025425
H	5.2848014	8.6001577	2.8429200
O	7.1608642	9.6607702	1.6803448
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N	8.9001039	8.0868923	1.6606469
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C	7.9411283	6.5062396	3.0748346
H	8.0038356	6.1325721	4.1062550
C	9.3184239	7.0314684	2.6013239
H	9.8236352	7.5107818	3.4633819
C	10.2554459	5.9656057	2.0282014
H	10.6695387	5.4113354	2.8881679
H	11.1177785	6.4571401	1.5524390
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H	9.2406937	5.4840330	0.1671609
H	10.2904297	4.2002435	0.7785498
C	8.3552115	4.3373026	1.7746991
H	8.6849420	3.7870642	2.6737723
H	7.8745867	3.5971982	1.1168852
C	7.3379356	5.4176968	2.1608447
H	6.9688198	5.8989411	1.2400633
H	6.4681809	4.9716746	2.6656168
C	9.8548034	8.9613741	1.0049049
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N	13.7051220	10.0521128	4.7270037
C	13.9504440	10.7448082	5.9029139
C	13.6669501	8.4840436	6.4368141
H	12.5694438	8.4274772	6.5816993
C	13.9520006	8.6131667	4.9203747
H	13.2305454	8.0212547	4.3402282
C	15.3905437	8.2222597	4.5182977
H	15.4487062	8.1603379	3.4213399
H	16.0738021	9.0268178	4.8365069
C	15.8483414	6.9075963	5.1613566
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H	15.2245353	6.0707067	4.8002758
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C	14.3028802	7.2670488	7.1130500
H	13.6874375	6.3932481	6.8369108
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H	9.1899327	9.7292543	11.3338481

i-cis-cycHC[6] **1** coordinates in angstroms

138

O	7.0502881	9.3145272	10.0812254
N	9.1057153	8.2175910	9.9037289
N	7.2906631	7.2420525	9.0109295
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C	9.5128802	6.8355214	9.5973789
H	10.5172557	6.8235062	9.1528384
C	8.4480837	6.4529707	8.5404228
H	8.7662627	6.8535105	7.5595161
C	8.2168313	4.9468389	8.3865628
H	9.0662454	4.5597574	7.7973763
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C	8.1486841	4.1772685	9.7082101
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C	9.4937878	5.9525423	10.8653204
H	10.3938368	6.1669764	11.4603216
H	8.6229489	6.2390510	11.4783466
C	6.0267242	7.2873195	8.3049307
H	5.6803299	6.2544757	8.1612642
H	5.3200741	7.8232712	8.9513275
O	7.0527113	9.3468289	1.5687385
N	7.2278707	7.4410463	2.9107024
N	8.9171637	7.9221783	1.5151307
C	7.6613627	8.3478663	1.9568227
C	8.1076523	6.2583138	2.9292365
H	8.2094780	5.8843588	3.9565142
C	9.4304049	6.8911106	2.4368731
H	9.9131580	7.3988607	3.2951410
C	10.4348815	5.9050795	1.8365514
H	10.9010635	5.3729668	2.6836770
H	11.2512638	6.4648496	1.3556918
C	9.8098407	4.8731295	0.8937501
H	9.4285175	5.3691631	-0.0146813
H	10.5822353	4.1619232	0.5639901
C	8.6600227	4.1413533	1.5932403
H	9.0460744	3.6082047	2.4799184
H	8.2241124	3.3745888	0.9344944
C	7.5723846	5.1387675	2.0098257
H	7.1529722	5.6010382	1.1010666
H	6.7467924	4.6207443	2.5207252
C	9.7983605	8.8804755	0.8713194
H	9.1735250	9.4730009	0.1906888
H	10.5582975	8.3370875	0.2955421
O	12.6038236	8.7506301	1.5944342
N	10.5048794	9.7627964	1.7866674
N	12.2746173	10.7913183	2.7037742
C	11.8734363	9.6632978	1.9836812
C	10.0244525	11.0946020	2.1907077
H	9.0287004	11.0180139	2.6488616
C	11.0843089	11.4606606	3.2585405
H	10.8109430	10.9581307	4.2076844
C	11.2350508	12.9582703	3.5365127
H	10.3806724	13.2513173	4.1702777
H	12.1314990	13.1252748	4.1528445
C	11.2333596	13.8308907	2.2776237
H	11.2698416	14.8921936	2.5668689
H	12.1382304	13.6348629	1.6785501
C	9.9909227	13.5401604	1.4292562
H	9.9643902	14.1872755	0.5396387
H	9.0822295	13.7731513	2.0122090
C	9.9769027	12.0700597	0.9946744
H	9.0839822	11.8504883	0.3908276
H	10.8556705	11.8829094	0.3559389
C	13.5454548	10.7662315	3.4044637
H	13.8742303	11.7951642	3.5971531
H	14.2603072	10.2714420	2.7330121
O	13.8087790	11.9917129	6.0184230
N	13.9610935	9.8128114	6.8721589
N	13.5141143	10.0876962	4.6909378
C	13.7650558	10.7688887	5.8739233
C	13.4997173	8.5004031	6.3841096
H	12.4038096	8.4355993	6.5362992
C	13.7734691	8.6485552	4.8672694
H	13.0520709	8.0566996	4.2867056
C	15.2114712	8.2718964	4.4504133
H	15.2614500	8.2229134	3.3524870
H	15.8918135	9.0772360	4.7731599
C	15.6823266	6.9530003	5.0751657
H	16.7128201	6.7402195	4.7526612
H	15.0618210	6.1162508	4.7081500
C	15.5930753	7.0264513	6.6029291
H	16.2484047	7.8348542	6.9685106
H	15.9571287	6.0943297	7.0611033
C	14.1473598	7.2790988	7.0409602
H	13.5350766	6.4054788	6.7573486
H	14.0537661	7.3623204	8.1343581
C	13.8564586	10.2091350	8.2643574
H	14.3696681	11.1755518	8.3532113
H	14.3658479	9.4632913	8.8876032
O	12.5102479	8.3855757	10.0688931
N	12.4957860	10.3255326	8.7643043
N	10.7871858	9.9734417	10.1759063
C	11.9919294	9.4437104	9.7079275
C	11.7261810	11.5810059	8.7755918
H	11.6365107	11.9825443	7.7567175
C	10.3569998	11.0617461	9.2790151
H	9.8160804	10.6161577	8.4208212
C	9.4573680	12.1246138	9.9141971
H	9.0241471	12.7104740	9.0857521
H	8.6027012	11.6329597	10.4028701
C	10.1900676	13.0789072	10.8611916
H	10.5424273	12.5337007	11.7528875
H	9.4909453	13.8504127	11.2184356
C	11.3875126	13.7179577	10.1503218
H	11.0341167	14.2981004	9.2796066
H	11.9010962	14.4321908	10.8118085
C	12.3751081	12.6362497	9.6979580
H	12.7696196	12.1248948	10.5916476
H	13.2328697	13.0855706	9.1757314
C	9.8353245	9.0839447	10.8175503
H	10.4043204	8.4745782	11.5312767
H	9.0940335	9.6860415	11.3580594
O	6.5245188	5.9881477	5.8063211
N	5.6891185	7.9019508	4.7748321
N	6.0476149	7.9546471	6.9950391
C	6.1326202	7.1567359	5.8496947
C	5.4472656	9.2934649	5.1734311
H	4.5462653	9.6788699	4.6702477
C	5.1594876	9.1027091	6.6848037
H	4.1104328	8.7568739	6.7884887
C	5.3261264	10.3638939	7.5359430
H	5.3754151	10.0894045	8.5997210
H	4.4037040	10.9548654	7.4013678
C	6.5296096	11.2353696	7.1634958
H	7.4613986	10.7208481	7.4493105
H	6.4934468	12.1643466	7.7513501
C	6.5522873	11.5322982	5.6621032

H	7.4045224	12.1794204	5.4044340
H	5.6420541	12.0892673	5.3752177
C	6.6402078	10.2206988	4.8756628
H	6.6875669	10.3950925	3.7906402
H	7.5677477	9.6968033	5.1592713
C	5.8633013	7.4407476	3.4075582
H	5.4677303	6.4168057	3.3531022
H	5.2717412	8.0966211	2.7552293

Cl^- @*cis*-cycHC[6] Cl^-@**2** coordinates in angstroms

139

O	7.0179267	9.1894826	10.3128981
N	9.1140409	8.2405896	9.9022702
N	7.3115113	7.2624369	8.9997626
C	7.7397577	8.3320444	9.7928382
C	9.6164326	7.0027907	9.2939127
H	10.5441047	7.2019221	8.7377348
C	8.4804049	6.6943740	8.2905651
H	8.6723745	7.3001384	7.3839983
C	8.3528768	5.2240376	7.8885976
H	9.1417825	5.0344949	7.1410423
H	7.3994432	5.0723270	7.3588616
C	8.5246444	4.2329664	9.0439321
H	8.4905600	3.2018656	8.6569653
H	7.6877708	4.3328326	9.7564612
C	9.8451425	4.4954384	9.7770214
H	10.0007120	3.7600467	10.5826704
H	10.6871526	4.3718291	9.0731632
C	9.8522124	5.9123414	10.3626377
H	10.8003429	6.1203706	10.8810519
H	9.0468527	5.9836708	11.1140358
C	6.0100022	7.3409142	8.3568538
H	5.6242374	6.3294799	8.1728911
H	5.3523696	7.8637641	9.0664670
O	5.4751825	6.1597804	5.7491275
N	5.6748290	8.3338030	4.8802349
N	6.0126695	8.0110165	7.0712341
C	5.7034064	7.3655447	5.8888627
C	6.3373487	9.5617429	5.3731279
H	7.4313694	9.4532277	5.2422783
C	6.0425823	9.4672393	6.8892400
H	6.8808322	9.9043530	7.4508912
C	4.7093669	10.1107414	7.3303606
H	4.6936899	10.1788987	8.4284061
H	3.8859025	9.4393634	7.0331083
C	4.4715796	11.4833872	6.6911874
H	3.5036701	11.8867429	7.0293188
H	5.2437680	12.1978466	7.0280011
C	4.5140574	11.3696146	5.1634725
H	3.7232042	10.6765318	4.8290508
H	4.3021939	12.3430047	4.6922971
C	5.8858994	10.8632962	4.7065202
H	6.6441677	11.6242486	4.9587867
H	5.9337603	10.7479052	3.6125100
C	5.7884221	7.9146871	3.4936580
H	5.2617086	6.9518243	3.4256272
H	5.2986601	8.6495141	2.8405877
O	7.0885414	9.5339421	1.4543339
N	7.1490358	7.7904856	3.0096668
N	8.9366883	8.1022220	1.6954056
C	7.6598223	8.5840700	2.0002710
C	8.0340043	6.6534816	3.2911083
H	8.0951094	6.4774990	4.3745779
C	9.3859460	7.2117622	2.7897443
H	9.8046425	7.8352404	3.6033114
C	10.4166815	6.1532009	2.3924460
H	10.8544804	5.7754738	3.3321916
H	11.2457792	6.6357617	1.8516909
C	9.8408764	4.9691449	1.6084114
H	9.4899391	5.3052725	0.6176319
H	10.6315389	4.2232094	1.4285313
C	8.6680361	4.3453184	2.3736839
H	9.0213228	3.9830579	3.3554896
H	8.2726272	3.4662909	1.8398371
C	7.5514524	5.3786280	2.5641725
H	7.1719625	5.6697642	1.5698251
H	6.7068411	4.9480473	3.1228456
C	9.8720030	8.9741362	1.0051017
H	9.2699549	9.5691042	0.3032999
H	10.6011291	8.3719101	0.4468300
O	12.7470340	8.8980911	1.4688912
N	10.6454421	9.8366772	1.8767070
N	12.4385934	10.8075923	2.8034548
C	12.0194825	9.7464677	1.9949628
C	10.1381656	11.0686886	2.4924998
H	9.2034323	10.8658184	3.0352011
C	11.2649818	11.3669031	3.5099595
H	11.0662142	10.7538430	4.4104823
C	11.3892268	12.8338158	3.9268506
H	10.5932652	13.0178506	4.6683914
H	12.3378455	12.9798808	4.4667556
C	11.2291518	13.8358525	2.7793239
H	11.2602735	14.8630686	3.1766147
H	12.0728372	13.7423111	2.0740733
C	9.9157494	13.5812011	2.0309969
H	9.7684310	14.3241660	1.2307798
H	9.0668418	13.6989062	2.7276044
C	9.9140093	12.1699095	1.4322213
H	8.9712230	11.9669347	0.9022815
H	10.7270152	12.1049054	0.6885982
C	13.7443445	10.7416230	3.4381545
H	14.1224513	11.7566196	3.6188207
H	14.4014299	10.2244910	2.7237287
O	14.2859051	11.9316117	6.0384219
N	14.1224183	9.7562571	6.9123907
N	13.7576760	10.0726215	4.7240079
C	14.0718372	10.7224784	5.9022923
C	13.4661170	8.5210031	6.4265273
H	12.3729614	8.6227126	6.5683910
C	13.7413471	8.6162437	4.9072707
H	12.8975912	8.1729008	4.3587583
C	15.0732234	7.9821493	4.4492025
H	15.0753583	7.9121786	3.3511219
H	15.8958562	8.6595466	4.7349012
C	15.3288180	6.6119839	5.0872178
H	16.2951578	6.2150602	4.7371910
H	14.5573356	5.8918328	4.7611791
C	15.3049490	6.7271903	6.6153285
H	16.0949388	7.4264466	6.9389035
H	15.5300335	5.7557648	7.0844930
C	13.9351893	7.2240418	7.0889926
H	13.1788696	6.4579788	6.8468980
H	13.8996006	7.3400693	8.1833497
C	13.9937432	10.1799627	8.2967678
H	14.5125542	11.1468893	8.3670764
H	14.4827591	9.4504343	8.9561602
O	12.6818465	8.5535963	10.3245216
N	12.6274807	10.2960485	8.7674539
N	10.8278287	9.9729522	10.0612345
C	12.1104476	9.4986225	9.7710870
C	11.7403277	11.4300832	8.4813094
H	11.6920590	11.6123015	7.3982822
C	10.3848471	10.8641930	8.9664037
H	9.9738969	10.2440484	8.1461686
C	9.3467235	11.9177679	9.3597986
H	8.9164975	12.3005812	8.4185470
H	8.5142104	11.4292812	9.8899992

C	9.9107832	13.0989518	10.1564088
H	10.2537795	12.7579596	11.1482509
H	9.1155390	13.8405904	10.3336581
C	11.0880481	13.7316781	9.4056138
H	10.7422344	14.0987513	8.4228997
H	11.4755005	14.6089175	9.9481851
C	12.2100402	12.7035931	9.2193274
H	12.5818472	12.4085594	10.2153557
H	13.0579260	13.1402044	8.6704735
C	9.8936210	9.1090713	10.7620629
H	10.4982885	8.5190339	11.4658519
H	9.1683149	9.7171536	11.3191024
Cl	9.9216839	8.9517056	5.8930069

Cl^-@*i-cis*-cycHC[6] Cl^-@**1** coordinates in angstroms

139

O	6.8877417	9.1856458	10.1965831
N	9.0182770	8.3091087	9.8032566
N	7.2528132	7.2647454	8.8958089
C	7.6415305	8.3522497	9.6810568
C	9.5555409	7.0522243	9.2689111
H	10.4900323	7.2405427	8.7215510
C	8.4501779	6.6651194	8.2586495
H	8.6584200	7.2146228	7.3211777
C	8.3688648	5.1664916	7.9554802
H	9.1886896	4.9519903	7.2487694
H	7.4442089	4.9622924	7.3979482
C	8.5273714	4.2530351	9.1737510
H	8.5169143	3.1995892	8.8498041
H	7.6726037	4.3819151	9.8604039
C	9.8254049	4.5817170	9.9173354
H	9.9745170	3.9046308	10.7740507
H	10.6849979	4.4271441	9.2415149
C	9.7944907	6.0329623	10.4063313
H	10.7302877	6.2951016	10.9223892
H	8.9757136	6.1345219	11.1400720
C	5.9506212	7.2524795	8.2544308
H	5.6421991	6.2055088	8.1217031
H	5.2588170	7.7568106	8.9427805
O	6.9811935	9.2796537	1.4080686
N	7.1517307	7.5245564	2.9440133
N	8.9394484	8.0099646	1.6844486
C	7.6196091	8.3756018	1.9572596
C	8.1154001	6.4415988	3.1992496
H	8.1517895	6.2120267	4.2715888
C	9.4306298	7.1216135	2.7607231
H	9.7827900	7.7465092	3.6048923
C	10.5503304	6.1592723	2.3567368
H	10.9818319	5.7721635	3.2955563
H	11.3591802	6.7233116	1.8662890
C	10.0903669	4.9733255	1.5031403
H	9.7488134	5.3270388	0.5151722
H	10.9399199	4.2960282	1.3202132
C	8.9434838	4.2321628	2.1981914
H	9.2910875	3.8508452	3.1746177
H	8.6292070	3.3530423	1.6124458
C	7.7501454	5.1736432	2.3966719
H	7.3792456	5.4819884	1.4041740
H	6.9250018	4.6551447	2.9081327
C	9.8236790	8.9389054	1.0013334
H	9.1813339	9.5313293	0.3337667
H	10.5602496	8.3816752	0.4064607
O	12.6993757	8.8975805	1.4452802
N	10.5880283	9.8027453	1.8791033
N	12.3761389	10.7846618	2.8067776
C	11.9646392	9.7300803	1.9876933
C	10.0688401	11.0209674	2.5117660
H	9.1422571	10.7993158	3.0613707
C	11.1990909	11.3250974	3.5237977
H	11.0137703	10.7023353	4.4207519
C	11.3086965	12.7898889	3.9510885
H	10.5171035	12.9575587	4.7011791
H	12.2598190	12.9428842	4.4846834
C	11.1269795	13.7998813	2.8138681
H	11.1483525	14.8240867	3.2195571
H	11.9659376	13.7231796	2.1007248
C	9.8106161	13.5353190	2.0741385
H	9.6474153	14.2830894	1.2814822
H	8.9661776	13.6362415	2.7786878
C	9.8222837	12.1292337	1.4631062
H	8.8786151	11.9209368	0.9362262
H	10.6304470	12.0812365	0.7128538
C	13.6819006	10.7166270	3.4440905
H	14.0532603	11.7314896	3.6389225
H	14.3432873	10.2132765	2.7238469
O	14.1974708	11.8786473	6.0618335
N	14.0363167	9.6936224	6.9087414
N	13.6970738	10.0306067	4.7206840
C	13.9917306	10.6695279	5.9102192
C	13.4059809	8.4536844	6.4029626
H	12.3070761	8.5260993	6.5279543
C	13.6977089	8.5718760	4.8870982
H	12.8661037	8.1241779	4.3236103
C	15.0432982	7.9621115	4.4348484
H	15.0566809	7.9027866	3.3361175
H	15.8525981	8.6497810	4.7339339
C	15.3161447	6.5902467	5.0621438
H	16.2918467	6.2126156	4.7166877
H	14.5594763	5.8603773	4.7230246
C	15.2769635	6.6906282	6.5909713
H	16.0514990	7.4009220	6.9278903
H	15.5154190	5.7189590	7.0530702
C	13.8938635	7.1582522	7.0554688
H	13.1543349	6.3807807	6.7982179
H	13.8439159	7.2609960	8.1506078
C	13.9246495	10.0963087	8.2994204
H	14.4876020	11.0362615	8.3900609
H	14.3797531	9.3314070	8.9427550
O	12.5226500	8.4888114	10.2856999
N	12.5669487	10.2721375	8.7765542
N	10.7487866	10.0149149	10.0620862
C	12.0048665	9.4782142	9.7576264
C	11.7530566	11.4678149	8.5308733
H	11.7170580	11.6896313	7.4551783
C	10.3650741	10.9734380	9.0026496
H	9.9124412	10.4083593	8.1651445
C	9.4057990	12.0789911	9.4478509
H	8.9986880	12.5331872	8.5292860
H	8.5420278	11.6277162	9.9600455
C	10.0528948	13.1812768	10.2922943
H	10.3843945	12.7725430	11.2622703
H	9.3087369	13.9628944	10.5141744
C	11.2593418	13.7711687	9.5537695
H	10.9267857	14.2019660	8.5925795
H	11.7081671	14.5974513	10.1282824
C	12.3099925	12.6823230	9.3090352
H	12.6769221	12.3266463	10.2868345
H	13.1757205	13.0861347	8.7628045
C	9.7568428	9.1716501	10.7068808
H	10.3025060	8.5751231	11.4524968
H	9.0108042	9.7972313	11.2146826
O	6.1432013	5.9068563	5.7294225
N	5.4958824	7.9072873	4.7239883
N	5.8714580	7.8966301	6.9412292
C	5.8760701	7.1106787	5.7926976
C	5.3502146	9.3080617	5.1459457
H	4.4520253	9.7423680	4.6739087

C	5.0822865	9.1165905	6.6639948
H	4.0092508	8.8557553	6.7872645
C	5.3623562	10.3473903	7.5292588
H	5.4350656	10.0484490	8.5862340
H	4.4710209	10.9952358	7.4431437
C	6.5989240	11.1507196	7.1189523
H	7.5129901	10.5724663	7.3270318
H	6.6459398	12.0653342	7.7297515
C	6.5689108	11.4810724	5.6254753
H	7.4467287	12.0841303	5.3480425
H	5.6757210	12.0899109	5.3863568
C	6.5750871	10.1776664	4.8214547
H	6.5893593	10.3722725	3.7382263
H	7.4983599	9.6267513	5.0722233
C	5.7623896	7.4859793	3.3565292
H	5.3808784	6.4582452	3.2613691
H	5.2087578	8.1472863	2.6765669
Cl	9.9278360	8.9896380	5.9322487

R,*S*,*S*,*R*-ordered dimer **9** coordinates in angstroms

51

O	6.8134701	9.2006249	10.3957707
N	8.9578590	8.3780153	9.9521579
N	7.1891892	7.2370723	9.1717690
C	7.5678688	8.3673725	9.8970173
C	9.4994400	7.1087829	9.4426910
H	10.4325961	7.2839061	8.8883742
C	8.3632893	6.6976960	8.4741472
H	8.4938903	7.2573538	7.5223975
C	8.3070032	5.2041036	8.1400488
H	9.1021871	5.0077106	7.4010709
H	7.3585570	4.9814090	7.6258256
C	8.5149146	4.2843819	9.3466503
H	8.5334484	3.2359738	9.0115537
H	7.6668730	4.3802241	10.0449962
C	9.8135875	4.6473609	10.0737667
H	9.9877272	3.9677966	10.9216740
H	10.6704140	4.5182305	9.3894259
C	9.7536050	6.0936923	10.5774685
H	10.6860945	6.3660544	11.0931905
H	8.9355457	6.1777628	11.3125426
C	5.8727241	7.1954866	8.5682940
H	5.4613126	6.1765406	8.5878966
H	5.2185815	7.8556793	9.1504752
H	5.8900929	7.5478278	7.5194471
H	13.6779616	11.0883263	7.4240590
C	13.6102533	10.8400513	8.4938325
H	14.1894238	11.5854288	9.0656337
H	14.0554469	9.8520973	8.6636237
O	12.4140168	8.8387278	10.2050414
N	12.2249366	10.7735299	8.9077861
N	10.5234769	10.2285575	10.2648938
C	11.7962690	9.8358291	9.8330504
C	11.3246775	11.9311026	8.9022630
H	11.2177026	12.3254620	7.8784266
C	10.0027110	11.2601232	9.3520462
H	9.5516807	10.7589267	8.4728388
C	8.9612547	12.2086303	9.9489321
H	8.4928323	12.7422019	9.1038788
H	8.1537859	11.6183776	10.4083239
C	9.5417647	13.2391362	10.9213992
H	9.9177157	12.7367288	11.8284501
H	8.7459820	13.9254164	11.2478764
C	10.6866181	14.0119854	10.2588819
H	10.3042332	14.5505810	9.3733314
H	11.0876130	14.7788669	10.9393691
C	11.8095499	13.0515595	9.8491843
H	12.2206288	12.5824889	10.7579666
H	12.6361516	13.5996897	9.3714761
C	9.6605442	9.2421799	10.8864603
H	10.3024495	8.6467450	11.5496675
H	8.8907995	9.7527805	11.4793288

R,*S*,*R*,*S*-ordered dimer **10** coordinates in angstroms

51

H	6.1986863	7.8385812	9.0639094
C	5.6807138	7.2823977	8.2697917
H	6.1066382	6.2739619	8.2027173
H	4.6110318	7.1973716	8.5396185
O	6.8557727	9.2671270	1.3898358
N	7.2064416	7.5020624	2.8809251
N	8.7921738	7.9435687	1.3562011
C	7.5396686	8.3416786	1.8253501
C	8.1616587	6.3870272	2.9729575
H	8.3459055	6.1300717	4.0254493
C	9.4117249	7.0480860	2.3423836
H	9.9073969	7.6711000	3.1179771
C	10.4508449	6.0712822	1.7854046
H	11.0104673	5.6679958	2.6465184
H	11.1869415	6.6263152	1.1827789
C	9.8512937	4.9041778	0.9947104
H	9.3835730	5.2761401	0.0679091
H	10.6535410	4.2142627	0.6913254
C	8.7987016	4.1781656	1.8387440
H	9.2706719	3.7733388	2.7511291
H	8.3875378	3.3159902	1.2920720
C	7.6636017	5.1384487	2.2125741
H	7.1625258	5.4681675	1.2873692
H	6.9095584	4.6262488	2.8280434
C	9.5884050	8.8810558	0.5899454
H	8.9024969	9.6068912	0.1363692
H	10.1448703	8.3687022	-0.2070700
H	10.3091327	9.4248305	1.2292761
O	6.3048977	5.9382561	5.8078217
N	5.6639675	7.9188031	4.7493449
N	5.8608049	7.9214427	6.9820147
C	5.9807652	7.1249077	5.8413529
C	5.5424972	9.3251053	5.1496232
H	4.7314604	9.8104499	4.5843928
C	5.1252614	9.1446447	6.6317182
H	4.0373777	8.9192196	6.6639552
C	5.3851130	10.3551066	7.5328114
H	5.2640744	10.0572784	8.5865040
H	4.5815001	11.0840447	7.3330902
C	6.7377235	11.0349821	7.2987983
H	7.5562454	10.3643362	7.6092785
H	6.8089967	11.9358174	7.9271123
C	6.9063370	11.3862837	5.8171404
H	7.8603421	11.9080583	5.6469238
H	6.1096726	12.0868034	5.5097242
C	6.8560447	10.1150133	4.9620902
H	6.9798300	10.3456600	3.8940665
H	7.6955045	9.4626002	5.2499696
C	5.8475432	7.4486788	3.3923891
H	5.4874828	6.4104583	3.3657974
H	5.2335955	8.0700092	2.7262062

Cl^- @*R*,*S*,*S*,*R*-ordered dimer Cl^- @**9** coordinates in angstroms

52

O	6.8378894	9.1036898	10.9644674

N	8.9744751	8.3652733	10.3633116
N	7.2054182	7.4133037	9.3731479
C	7.5964171	8.3807473	10.3091552
C	9.5359471	7.2917895	9.5317016
H	10.4074373	7.6459656	8.9547826
C	8.3768213	7.0843607	8.5336052
H	8.4936230	7.8510589	7.7404806
C	8.3594362	5.7158230	7.8522920
H	9.1257727	5.7701613	7.0608273
H	7.3949750	5.5708395	7.3376433
C	8.6734304	4.5377678	8.7817083
H	8.7219859	3.6057720	8.1942473
H	7.8630953	4.4072514	9.5205464
C	9.9942776	4.7833192	9.5210619
H	10.2511688	3.9210264	10.1580116
H	10.8103837	4.8925339	8.7860725
C	9.8926953	6.0516014	10.3752749
H	10.8350785	6.2492777	10.9082926
H	9.1075183	5.9032094	11.1373043
C	5.8951281	7.5376497	8.7726636
H	5.4778087	6.5483938	8.5316090
H	5.2393775	8.0385961	9.4963422
H	5.9224210	8.1391058	7.8428833
H	13.5983137	9.1259721	7.7843024
C	13.8536456	9.5001740	8.7907825
H	14.6430892	10.2676344	8.7161552
H	14.2237756	8.6719255	9.4080156
O	12.4840791	8.4754788	11.1582241
N	12.6654943	10.0220127	9.4252036
N	10.7627473	9.9903850	10.6169264
C	12.0312293	9.3890735	10.4609390
C	11.8474856	11.0858831	8.8430982
H	11.8391565	10.9779001	7.7455176
C	10.4396868	10.7165672	9.3680937
H	10.0261208	10.0010918	8.6332187
C	9.4618423	11.8837271	9.5270621
H	9.0493718	12.0925477	8.5248103
H	8.6061985	11.5611356	10.1408920
C	10.0889770	13.1705022	10.0726498
H	10.4154856	13.0207526	11.1164176
H	9.3358841	13.9756116	10.0878475
C	11.2976726	13.5701091	9.2192970
H	10.9729567	13.7253725	8.1745402
H	11.7216808	14.5280508	9.5628480
C	12.3674429	12.4740939	9.2843596
H	12.7197701	12.3924161	10.3264279
H	13.2443122	12.7456016	8.6737717
C	9.7378706	9.1977901	11.2756709
H	10.2690206	8.5941704	12.0280656
H	9.0007320	9.8408049	11.7760748
Cl	10.9371012	8.6145480	6.5111989

Cl^- @*R,S,R,S*-ordered dimer Cl^- @**10** coordinates in angstroms

52

H	5.8616005	7.3427735	8.8200418
C	5.2023793	7.0371434	7.9946814
H	5.3240126	5.9606969	7.8213092
H	4.1515757	7.2332956	8.2908111
O	6.4095245	8.9355326	0.7418276
N	6.9091484	7.6350677	2.6216713
N	8.5140125	7.9523775	1.0941030
C	7.1874378	8.2496867	1.4153950
C	8.0214791	6.7770926	3.0551516
H	8.2146202	6.8761570	4.1362348
C	9.1912584	7.4573913	2.3125815
H	9.5171480	8.3135847	2.9369508
C	10.4141297	6.5662816	2.1009657
H	10.9318982	6.5608792	3.0753561
H	11.1019155	7.0456138	1.3839364
C	10.0911072	5.1286158	1.6807039
H	9.6579874	5.1121172	0.6644539
H	11.0214727	4.5382044	1.6406421
C	9.0944832	4.5009406	2.6623784
H	9.5326233	4.4963007	3.6747488
H	8.8894177	3.4512305	2.3942211
C	7.7876659	5.3025012	2.6707009
H	7.3395531	5.2625600	1.6615959
H	7.0603382	4.8651597	3.3715572
C	9.2112221	8.8242837	0.1747266
H	8.4664997	9.2719701	-0.4959504
H	9.9427796	8.2599709	-0.4226580
H	9.7479145	9.6363071	0.7029852
O	5.4045921	5.8055228	5.4247917
N	5.4487856	7.9760162	4.5490793
N	5.5534298	7.7147356	6.7703509
C	5.4722164	7.0281943	5.5614277
C	5.6864415	9.3293565	5.0816362
H	5.0039164	10.0404099	4.5852546
C	5.2294367	9.1260860	6.5543725
H	4.1211612	9.2370061	6.5961537
C	5.8381903	10.0987167	7.5705530
H	5.6450585	9.7195714	8.5880250
H	5.2736308	11.0452200	7.4907076
C	7.3251888	10.3865835	7.3483023
H	7.9326525	9.4768022	7.4855403
H	7.6703215	11.1252158	8.0903980
C	7.5476769	10.8915789	5.9214928
H	8.6125749	11.1171511	5.7643708
H	6.9781429	11.8274031	5.7566514
C	7.1452565	9.8003020	4.9250157
H	7.2951682	10.1433174	3.8911153
H	7.8463144	8.9609836	5.0884063
C	5.5660818	7.5823431	3.1608200
H	5.1565953	6.5598133	3.1151168
H	4.9643364	8.2467314	2.5232105
Cl	10.1502570	8.0121877	5.6346938

HCl@*cis*-cycHC[6] HCl@**2** final coordinates in angstroms

140

O	6.9017626	9.5102083	9.6357106
N	8.6566560	7.9772267	9.5644394
N	6.6526655	7.3220460	8.8153516
C	7.3456895	8.3939171	9.3599851
C	8.8213986	6.5498754	9.2487794
H	9.7656129	6.3866843	8.7092289
C	7.6242461	6.3326788	8.2894563
H	7.9335693	6.6654497	7.2831671
C	7.1257116	4.8894301	8.2022637
H	7.8380319	4.3519726	7.5531158
H	6.1698767	4.8701329	7.6589161
C	7.0473054	4.1629176	9.5480995
H	6.7486960	3.1163640	9.3841470
H	6.2691524	4.6177706	10.1840980
C	8.3978037	4.2346153	10.2693546
H	8.3650723	3.6845268	11.2218793
H	9.1727779	3.7470279	9.6520725
C	8.7737080	5.6970415	10.5351824
H	9.7449922	5.7659238	11.0495633
H	8.0203244	6.1351436	11.2106848
C	5.3909810	7.5820831	8.1292604
H	4.8561587	6.6307269	8.0165316
H	4.8118697	8.2544178	8.7750255
O	5.1986129	6.2144290	5.5781368
N	5.3767882	8.3351431	4.5853806

N	5.5317875	8.1689035	6.8138746
C	5.3556725	7.4345904	5.6517436
C	5.9197081	9.6268041	5.0522238
H	7.0244636	9.5677619	5.0306399
C	5.4707020	9.6114611	6.5321198
H	6.1965413	10.1510308	7.1555182
C	4.0503119	10.1696631	6.7650275
H	3.8861253	10.2959949	7.8461826
H	3.3199894	9.4227164	6.4125593
C	3.8010632	11.4858059	6.0199399
H	2.7753333	11.8334352	6.2166651
H	4.4764107	12.2728994	6.4007600
C	4.0345289	11.2928519	4.5183377
H	3.3321729	10.5333977	4.1352690
H	3.8247542	12.2222955	3.9670428
C	5.4785050	10.8566801	4.2548632
H	6.1536284	11.6803964	4.5448633
H	5.6655778	10.6825412	3.1840816
C	5.6174606	7.8422442	3.2399423
H	5.1327195	6.8577732	3.1838304
H	5.1562128	8.5218041	2.5115890
O	7.0483616	9.4949404	1.3354800
N	7.0196299	7.7405730	2.8795412
N	8.8690208	8.0472802	1.6500743
C	7.5825999	8.5352797	1.8963329
C	7.8727894	6.5769865	3.1633163
H	7.8734986	6.3576945	4.2403865
C	9.2559919	7.1308538	2.7410529
H	9.6548455	7.7303128	3.5814153
C	10.2949388	6.0690545	2.3702287
H	10.6806109	5.6592721	3.3193141
H	11.1546214	6.5551426	1.8831926
C	9.7449599	4.9166860	1.5237507
H	9.4552509	5.2839144	0.5249450
H	10.5342105	4.1654211	1.3671531
C	8.5246597	4.2904950	2.2068578
H	8.8183952	3.8908649	3.1937328
H	8.1449332	3.4364452	1.6253351
C	7.4145832	5.3354142	2.3682634
H	7.0935671	5.6635172	1.3654573
H	6.5348012	4.8995152	2.8643618
C	9.8322660	8.9096103	0.9933659
H	9.2679937	9.4856349	0.2464311
H	10.5971098	8.3055237	0.4884201
O	12.6978471	8.9650812	1.5038707
N	10.5473738	9.7971757	1.8958012
N	12.2921905	10.9005566	2.7678908
C	11.9260338	9.7894146	1.9975523
C	9.9929189	11.0438846	2.4427895
H	9.0482185	10.8430564	2.9681738
C	11.0964468	11.4165532	3.4631725
H	10.9334948	10.8159553	4.3795182
C	11.1431708	12.8969359	3.8481771
H	10.3169531	13.0645163	4.5601989
H	12.0667836	13.0980559	4.4129692
C	10.9747253	13.8588189	2.6682859
H	10.9487725	14.8952404	3.0386962
H	11.8437068	13.7859361	1.9929934
C	9.6980334	13.5267751	1.8884368
H	9.5515730	14.2352064	1.0589615
H	8.8212556	13.6366473	2.5507325
C	9.7677542	12.0978949	1.3378358
H	8.8504682	11.8420578	0.7876891
H	10.6058231	12.0372185	0.6231178
C	13.6141249	10.9435598	3.3572301
H	13.8628051	11.9787146	3.6228638
H	14.3126971	10.5839340	2.5896037
O	13.9303687	11.9068673	6.1029056
N	14.2515570	9.6601788	6.7022323
N	13.7698052	10.1498039	4.5683221
C	13.9756793	10.7098536	5.8070317
C	13.8461690	8.3812506	6.0705168
H	12.7574059	8.2462532	6.2126150
C	14.0918839	8.7136425	4.5794567
H	13.3852038	8.1633424	3.9443415
C	15.5361844	8.4572882	4.1003029
H	15.5643610	8.5349905	3.0030917
H	16.1865192	9.2532006	4.5003863
C	16.0782555	7.1008705	4.5647420
H	17.1109891	6.9730846	4.2063223
H	15.4884558	6.2823345	4.1160564
C	16.0165640	7.0010911	6.0923444
H	16.6407754	7.7958327	6.5348459
H	16.4333684	6.0429611	6.4384636
C	14.5698783	7.1327244	6.5773245
H	13.9916728	6.2662682	6.2138805
H	14.4977272	7.0856628	7.6746264
C	14.0740867	9.9101685	8.1107819
H	14.5946583	10.8424188	8.3592779
H	14.5083274	9.0802306	8.6813753
O	12.2221603	7.8449834	9.1044929
N	12.6698778	10.0592288	8.5256255
N	10.4977131	9.4588751	8.9105231
C	11.9057031	9.0009693	8.8822154
C	11.9945373	11.3496909	8.7367739
H	12.2727627	12.0379237	7.9266990
C	10.5063178	10.9525020	8.5972940
H	10.2531114	10.9706591	7.5264995
C	9.5036554	11.8388643	9.3398294
H	9.3233070	12.7002085	8.6749617
H	8.5348678	11.3207268	9.4201059
C	9.9784888	12.3796109	10.6946213
H	10.0109460	11.5765607	11.4521505
H	9.2472642	13.1151926	11.0608011
C	11.3712427	13.0060414	10.5752448
H	11.3425573	13.8509010	9.8652547
H	11.6962860	13.4203494	11.5408336
C	12.3765963	11.9506946	10.1029495
H	12.4140424	11.1388350	10.8504861
H	13.3924519	12.3698874	10.0428377
C	9.6671778	8.8495981	10.0366628
H	10.0789895	9.0035616	7.8409858
H	10.3756025	8.3083511	10.6760960
H	9.1937891	9.6699081	10.5858100
Cl	9.7038224	8.6670282	6.2830815

HCl@*i*-*cis*-cycHC[6] HCl@**1** A final coordinates in angstroms

140

O	6.9794180	9.2474500	10.0769196
N	9.0762022	8.2217370	9.9579095
N	7.2966615	7.1171870	9.1512293
C	7.7066191	8.3040975	9.7613892
C	9.5434445	6.8459434	9.7227713
H	10.5405087	6.8551933	9.2617897
C	8.4863131	6.3577881	8.7028472
H	8.7722248	6.7178472	7.6995567
C	8.3206038	4.8377095	8.6370678
H	9.1740935	4.4557508	8.0509145
H	7.4315933	4.5987075	8.0370144
C	8.3084126	4.1391634	9.9994015
H	8.2562839	3.0493791	9.8529946
H	7.4067156	4.4250285	10.5678345
C	9.5547901	4.5215448	10.8033077
H	9.5754710	3.9974440	11.7707656
H	10.4597386	4.2032041	10.2556516
C	9.5850281	6.0357161	11.0373657
H	10.4825506	6.3241437	11.6048386

H	8.7102214	6.3144077	11.6481999
C	6.0295848	7.0807213	8.4558450
H	5.7695942	6.0261659	8.2850175
H	5.2804925	7.5345134	9.1161921
O	7.2494955	9.4798852	1.8791239
N	7.5585547	7.5394803	3.1734772
N	9.0667724	8.0459645	1.5623081
C	7.8953210	8.4734358	2.1514372
C	8.3352506	6.2920456	2.9103177
H	8.5474781	5.7952329	3.8666011
C	9.6249365	6.8922600	2.2989321
H	10.2625130	7.2738918	3.1155387
C	10.4571093	5.9183313	1.4618345
H	10.9842080	5.2624663	2.1753240
H	11.2489880	6.4773077	0.9419689
C	9.6325574	5.0501833	0.5086361
H	9.1774463	5.6731323	-0.2796863
H	10.2920893	4.3309418	-0.0001164
C	8.5306432	4.3217572	1.2829156
H	8.9870171	3.6617782	2.0413918
H	7.9442509	3.6716727	0.6162325
C	7.5928792	5.3293050	1.9597212
H	7.0859462	5.9165081	1.1750567
H	6.8107041	4.7975803	2.5206832
C	9.9079088	9.0095722	0.8572723
H	9.2379558	9.6243407	0.2430650
H	10.5987592	8.4564672	0.2090169
O	12.7053826	8.6908786	1.5312407
N	10.6922020	9.8585721	1.7265866
N	12.5303765	10.7504681	2.6460138
C	12.0498031	9.6566922	1.9260124
C	10.3007121	11.2138219	2.1478807
H	9.3076923	11.1958317	2.6174239
C	11.3894352	11.4997836	3.2101043
H	11.0855383	11.0095329	4.1541822
C	11.6437673	12.9821083	3.4929226
H	10.8151171	13.3277468	4.1346237
H	12.5525759	13.0836557	4.1046854
C	11.6907479	13.8616529	2.2399393
H	11.8012881	14.9160471	2.5355730
H	12.5749139	13.6098849	1.6306186
C	10.4239873	13.6620587	1.4013755
H	10.4321671	14.3154212	0.5158077
H	9.5384575	13.9506358	1.9950652
C	10.3094632	12.1988105	0.9584271
H	9.4014759	12.0439906	0.3561363
H	11.1705211	11.9580968	0.3136519
C	13.7962930	10.6349957	3.3513147
H	14.2067410	11.6387319	3.5199503
H	14.4677370	10.0686329	2.6922316
O	14.0271728	11.9119180	5.9426888
N	14.0268196	9.7512698	6.8565489
N	13.7084744	9.9899687	4.6495440
C	13.9297422	10.6888949	5.8268021
C	13.5292248	8.4486332	6.3761225
H	12.4267032	8.4354942	6.4771840
C	13.8769641	8.5445214	4.8702743
H	13.1463929	7.9795446	4.2745544
C	15.3087254	8.0812027	4.5249384
H	15.4034771	7.9997499	3.4317717
H	16.0161461	8.8593763	4.8557308
C	15.6838255	6.7584683	5.2034976
H	16.7134366	6.4831871	4.9292038
H	15.0342988	5.9444079	4.8351709
C	15.5382268	6.8829245	6.7235017
H	16.2175465	7.6700785	7.0916843
H	15.8378092	5.9489754	7.2231181
C	14.0905253	7.2186185	7.0938512
H	13.4473166	6.3668499	6.8129771
H	13.9618793	7.3416076	8.1801592
C	13.8554451	10.1866427	8.2307723
H	14.3564602	11.1609902	8.3100952
H	14.3398947	9.4682044	8.9044249
O	12.5137941	8.5121423	10.1775077
N	12.4714248	10.2932726	8.6622735
N	10.7258292	10.0251373	10.0462971
C	11.9670061	9.4990994	9.6820015
C	11.6490380	11.5035636	8.5024580
H	11.5777570	11.7807052	7.4412557
C	10.2838867	10.9819292	9.0148806
H	9.7963991	10.4160289	8.1970303
C	9.3169103	12.0681650	9.4918529
H	8.8909688	12.5329408	8.5862819
H	8.4670137	11.5967473	10.0086397
C	9.9706288	13.1609446	10.3429938
H	10.3112024	12.7411345	11.3042863
H	9.2253689	13.9347458	10.5821341
C	11.1670350	13.7677450	9.6025679
H	10.8235257	14.2255755	8.6580146
H	11.6237748	14.5771395	10.1923006
C	12.2166213	12.6877329	9.3148410
H	12.5957078	12.3014236	10.2754656
H	13.0744869	13.1114514	8.7721816
C	9.7900966	9.1874685	10.7761220
H	10.3728138	8.6672281	11.5476157
H	9.0352409	9.8245915	11.2542071
O	6.8923965	6.0295209	5.9301419
N	5.8497346	7.8522072	4.9368706
N	5.9838061	7.8029750	7.1751575
C	6.3066033	7.1118167	6.0101550
C	5.2336727	9.1130502	5.3742171
H	4.2954165	9.2827292	4.8205030
C	4.8965059	8.7606983	6.8503761
H	3.9414852	8.1962862	6.8491283
C	4.7220251	9.9663372	7.7799335
H	4.8042721	9.6395561	8.8265267
H	3.6855886	10.3200359	7.6399679
C	5.6811465	11.1317291	7.5227486
H	6.6967037	10.8465591	7.8373889
H	5.3853726	11.9820859	8.1559266
C	5.6891535	11.5224977	6.0429828
H	6.3549591	12.3815712	5.8697601
H	4.6790924	11.8429475	5.7294678
C	6.1576976	10.3304283	5.2039879
H	6.2242738	10.5795634	4.1344039
H	7.1706475	10.0512809	5.5321195
Cl	9.5007843	8.6133991	5.4453077
H	8.5874039	8.1977588	4.5451432
C	6.1350006	7.4668430	3.5782395
H	5.5714658	8.1354896	2.9148148
H	5.8013667	6.4314958	3.4296106

HCl@*i*-*cis*-cycHC[6] HCl@**1** B final coordinates in angstroms

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O	7.0959949	8.9546217	10.4103644
N	9.2379023	8.1406058	9.9489221
N	7.4652529	6.9798968	9.2015439
C	7.8497460	8.1206036	9.9053010
C	9.7747878	6.8399875	9.5158225
H	10.7115804	6.9781891	8.9581753
C	8.6495515	6.3702679	8.5605332
H	8.7994082	6.8519458	7.5762708
C	8.5917919	4.8549632	8.3450880
H	9.4064998	4.6101280	7.6423008
H	7.6644246	4.6054806	7.8112741
C	8.7772373	4.0248414	9.6171214
H	8.7876991	2.9546897	9.3585598

H	7.9237471	4.1765314	10.2993732
C	10.0720137	4.4256976	10.3289900
H	10.2342073	3.8123995	11.2286229
H	10.9329071	4.2384881	9.6632282
C	10.0196813	5.9057524	10.7207520
H	10.9510846	6.2100923	11.2209085
H	9.1993809	6.0474047	11.4445781
C	6.1328768	6.8919956	8.6357704
H	5.8952176	5.8293579	8.4877783
H	5.4453543	7.3213618	9.3757195
O	6.9013693	9.2097189	2.1947601
N	6.8084475	7.1070982	3.2210503
N	8.6037349	7.6169364	1.9878299
C	7.3753790	8.1002586	2.4478693
C	7.5345231	5.8360788	3.0406573
H	7.5526882	5.2874614	3.9908351
C	8.9479460	6.3613282	2.6881582
H	9.4638401	6.6090373	3.6325504
C	9.8269317	5.3809302	1.9063252
H	10.2064100	4.6486409	2.6392441
H	10.7190120	5.9061334	1.5311774
C	9.0999346	4.6253962	0.7904768
H	8.8078423	5.3200724	-0.0148510
H	9.7830603	3.8894445	0.3394898
C	7.8483158	3.9374832	1.3451792
H	8.1400191	3.2116365	2.1240649
H	7.3361365	3.3631930	0.5583338
C	6.8892652	4.9816460	1.9274026
H	6.5642453	5.6513715	1.1137564
H	5.9834015	4.4979689	2.3244971
C	9.5624056	8.5281070	1.4311216
H	9.0309262	9.1729264	0.7218443
H	10.3374543	7.9576308	0.9047398
O	12.3565396	8.3583242	2.0113149
N	10.2794400	9.3953892	2.4106973
N	12.1922182	10.5109338	2.9016865
C	11.7090413	9.3270010	2.3911363
C	9.9098274	10.8365458	2.5614667
H	8.9617284	10.9100685	3.1110877
C	11.0883850	11.3385804	3.4320167
H	10.9075829	11.0461446	4.4807156
C	11.3225327	12.8497732	3.3914838
H	10.5396275	13.3055912	4.0213449
H	12.2727028	13.0800603	3.8965013
C	11.2427757	13.4573577	1.9900622
H	11.3494057	14.5504977	2.0553284
H	12.0790355	13.0966738	1.3669432
C	9.9145609	13.0793819	1.3293824
H	9.8276187	13.5342348	0.3311894
H	9.0772077	13.4786391	1.9282393
C	9.7886160	11.5560884	1.2039060
H	8.8256123	11.2922015	0.7432915
H	10.5845692	11.1943937	0.5310446
C	13.5455758	10.5580324	3.4514071
H	13.8664364	11.6059532	3.4981457
H	14.1879452	10.0064325	2.7526516
O	13.7425559	12.0236550	5.9407126
N	14.1080598	9.9467380	6.9735171
N	13.6618715	9.9992208	4.7782587
C	13.8259142	10.7946200	5.9026642
C	13.7797531	8.5574662	6.5919345
H	12.6963191	8.4007736	6.7500426
C	14.0402346	8.6062759	5.0669172
H	13.3675121	7.9113154	4.5457518
C	15.5062821	8.3282392	4.6690691
H	15.5637676	8.1953128	3.5776829
H	16.1096038	9.2164268	4.9196917
C	16.0987896	7.1149861	5.3952988
H	17.1440376	6.9718137	5.0815091
H	15.5571027	6.1968802	5.1064812
C	16.0052813	7.3105073	6.9120758
H	16.5816360	8.2056421	7.2010812
H	16.4575370	6.4593936	7.4435201
C	14.5428519	7.4621147	7.3401078
H	14.0150819	6.5147689	7.1345110
H	14.4409100	7.6245106	8.4236243
C	13.9229625	10.4342145	8.3300541
H	14.3272883	11.4547938	8.3543319
H	14.4941129	9.7964462	9.0163419
O	12.7080699	8.5701273	10.1860193
N	12.5451461	10.4397672	8.7923509
N	10.8326306	9.9800260	10.1669211
C	12.0979359	9.5526058	9.7603720
C	11.6570961	11.6120548	8.7219208
H	11.5587882	11.9533050	7.6820987
C	10.3288069	10.9866981	9.2148737
H	9.8559770	10.4587631	8.3639918
C	9.3177778	11.9836880	9.7860614
H	8.8487099	12.4892797	8.9251416
H	8.5046165	11.4335145	10.2839267
C	9.9317324	13.0449015	10.7037115
H	10.3144131	12.5760198	11.6257667
H	9.1525643	13.7583116	11.0121974
C	11.0776868	13.7665441	9.9878005
H	10.6904703	14.2698050	9.0841913
H	11.5039328	14.5564196	10.6252040
C	12.1757992	12.7667616	9.6068437
H	12.5936935	12.3361963	10.5316310
H	13.0000748	13.2740519	9.0836272
C	9.9496361	9.0437319	10.8397991
H	10.5771263	8.4756879	11.5396241
H	9.1866599	9.5994774	11.3995788
O	6.4142758	5.6957446	6.0537566
N	5.3900063	7.5949442	5.1779150
N	5.9352388	7.5870477	7.3586477
C	5.9657370	6.8379923	6.1790501
C	5.0694876	8.9448225	5.6636900
H	4.0956154	9.2675897	5.2613229
C	4.9317318	8.6654470	7.1829393
H	3.9281564	8.2242869	7.3570461
C	5.0623841	9.8996125	8.0784098
H	5.2283067	9.5866946	9.1196675
H	4.0831100	10.4082307	8.0508667
C	6.1470898	10.8924966	7.6506410
H	7.1414162	10.4536304	7.8300793
H	6.0808487	11.7890249	8.2849971
C	6.0119452	11.2507787	6.1690355
H	6.7798373	11.9814466	5.8722219
H	5.0351565	11.7353936	5.9868009
C	6.1475824	9.9854638	5.3168798
H	6.0982596	10.2061863	4.2413565
H	7.1372791	9.5366674	5.4995304
C	5.4716029	7.2025459	3.7778880
H	4.9912198	6.2198190	3.6682690
H	4.9066156	7.9455860	3.1994985
Cl	9.9179562	8.5918850	5.3808491
H	10.0316018	8.8628628	4.0471877

HCl@*i*-*cis*-cycHC[6] HCl@**1** C final coordinates in angstroms

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O	7.0683256	9.2301890	10.1858225
N	9.1236483	8.1535560	9.9090986
N	7.3053315	7.2498783	8.9518339
C	7.7567853	8.3155958	9.7275988
C	9.5357999	6.8058316	9.4843093
H	10.5323159	6.8389645	9.0233479
C	8.4603469	6.5010179	8.4126482

H	8.7702772	6.9767984	7.4636463
C	8.2310697	5.0097868	8.1484189
H	9.0737280	4.6724506	7.5202636
H	7.3365069	4.8916179	7.5225066
C	8.1844987	4.1405573	9.4075185
H	8.0823828	3.0832101	9.1185568
H	7.2958785	4.3897104	10.0120990
C	9.4456773	4.3565439	10.2484955
H	9.4422547	3.7113900	11.1402702
H	10.3355281	4.0721071	9.6592413
C	9.5425782	5.8238899	10.6778064
H	10.4512917	5.9951285	11.2738292
H	8.6809933	6.0565794	11.3256016
C	6.0259254	7.3286478	8.2739782
H	5.6601575	6.3049871	8.1137147
H	5.3443599	7.8601344	8.9510564
O	7.0123256	9.3921003	1.5105699
N	7.0597213	7.4917733	2.8732016
N	8.7769958	7.8457681	1.4750079
C	7.5517186	8.3585139	1.9120329
C	7.8646659	6.2571240	2.9108962
H	7.9413468	5.8919440	3.9428461
C	9.2256925	6.7986476	2.4166104
H	9.7345981	7.2876317	3.2682125
C	10.1637431	5.7396851	1.8335496
H	10.5915895	5.1926819	2.6912556
H	11.0186827	6.2367126	1.3513045
C	9.4771827	4.7363867	0.9027198
H	9.1301898	5.2430350	-0.0138106
H	10.2028802	3.9718299	0.5855456
C	8.2802937	4.0897190	1.6077153
H	8.6290015	3.5459845	2.5034469
H	7.7982835	3.3429534	0.9580833
C	7.2586776	5.1612352	2.0066810
H	6.8703463	5.6355715	1.0900233
H	6.4010292	4.7051319	2.5239141
C	9.7123022	8.7325481	0.8107964
H	9.1450492	9.2926115	0.0569544
H	10.4770252	8.1222227	0.3136020
O	12.3813554	8.4727204	1.9604338
N	10.3946924	9.6791642	1.6827811
N	12.0885142	10.6459476	2.7780018
C	11.6893475	9.4808375	2.1180003
C	10.0099826	11.0938131	1.8294643
H	8.9515197	11.1673344	2.1140500
C	10.9190968	11.5191092	3.0110823
H	10.4259804	11.2085260	3.9494942
C	11.2122201	13.0193263	3.0963227
H	10.3138654	13.4900074	3.5303946
H	12.0153920	13.1947111	3.8286034
C	11.5119467	13.6851820	1.7504598
H	11.6323538	14.7695273	1.8959959
H	12.4671383	13.3125258	1.3444088
C	10.3877800	13.3914037	0.7519346
H	10.5755478	13.8950151	-0.2086164
H	9.4359652	13.7967437	1.1371106
C	10.2665857	11.8801299	0.5249565
H	9.4614758	11.6573060	-0.1911321
H	11.2059207	11.5159891	0.0765269
C	13.2898988	10.6472054	3.5620783
H	13.5811463	11.6837979	3.7709808
H	14.0691869	10.1553187	2.9685617
O	13.4210854	11.9788873	6.0859025
N	13.9301242	9.9074560	7.0347207
N	13.2073239	9.9629509	4.8855689
C	13.5274018	10.7586361	6.0317482
C	13.7317608	8.4981572	6.6318618
H	12.7024987	8.2015204	6.8958074
C	13.8399895	8.6239250	5.0913230
H	13.2294552	7.8576783	4.5945749
C	15.2863839	8.5717569	4.5633300
H	15.2649351	8.4684602	3.4689380
H	15.7904518	9.5262878	4.7918402
C	16.1010148	7.4313986	5.1861845
H	17.1219766	7.4485035	4.7762017
H	15.6664938	6.4574143	4.9007516
C	16.1207467	7.5568716	6.7119135
H	16.5981076	8.5103704	6.9955169
H	16.7270346	6.7562312	7.1614729
C	14.6950967	7.4911018	7.2627297
H	14.2791900	6.4898961	7.0573780
H	14.6630736	7.5985122	8.3570576
C	13.8559903	10.3539600	8.4247943
H	14.3111583	11.3518984	8.4642139
H	14.4414922	9.6586349	9.0386083
O	12.5754750	8.3734000	10.1000403
N	12.5144220	10.4103109	8.9596245
N	10.7974972	9.8949676	10.3040762
C	12.0222828	9.4378981	9.8188987
C	11.7007269	11.6348181	9.0428479
H	11.6112204	12.1005460	8.0520048
C	10.3437423	11.0340810	9.4812599
H	9.8368872	10.6339972	8.5828037
C	9.3992150	12.0170660	10.1757025
H	8.9611127	12.6474628	9.3832522
H	8.5527499	11.4633151	10.6089920
C	10.0826477	12.9232111	11.2028918
H	10.4404152	12.3268081	12.0591702
H	9.3519919	13.6425897	11.6031499
C	11.2674794	13.6532974	10.5621834
H	10.9073865	14.2820314	9.7288038
H	11.7455306	14.3347262	11.2825698
C	12.2980334	12.6399434	10.0519215
H	12.6924615	12.0767575	10.9139390
H	13.1520936	13.1541412	9.5848437
C	9.8604545	8.9451958	10.8802179
H	10.4453070	8.2841951	11.5328920
H	9.1235785	9.4947744	11.4799578
O	6.3044002	6.0390721	5.7412937
N	5.5838301	8.0281222	4.7688743
N	6.0263134	8.0155160	6.9753696
C	6.0076294	7.2340309	5.8161613
C	5.4391468	9.4246590	5.1980903
H	4.5353284	9.8636549	4.7452529
C	5.2087458	9.2269780	6.7198789
H	4.1442352	8.9519574	6.8679653
C	5.4986725	10.4579752	7.5813020
H	5.5816885	10.1593924	8.6370021
H	4.6094363	11.1080147	7.5052413
C	6.7321135	11.2612256	7.1588063
H	7.6466454	10.6854052	7.3761970
H	6.7848226	12.1783190	7.7644838
C	6.6908101	11.5895905	5.6644834
H	7.5661257	12.1903055	5.3739993
H	5.8006480	12.2046860	5.4394343
C	6.6622523	10.2918942	4.8514342
H	6.6610428	10.4872979	3.7688851
H	7.5765938	9.7188591	5.0699144
C	5.7056299	7.5873310	3.3876395
H	5.2283263	6.5999341	3.3146562
H	5.1618504	8.3029822	2.7570639
H	11.5876979	9.5397397	5.2541451
Cl	10.3621109	9.0821241	5.6578472

Complexation

General information

^{19}F NMR was recorded on Bruker Avance III 400 MHz spectrometer using a Bruker BBO probe equipped with a z-gradient coil.

Determination of the stoichiometry of the complexes

The stoichiometry of the complexes of trifluoroacetic acid (TFA) with ureas **1**, **2**, **6** and **7** were determined by Job's method using ^{19}F- and ^{1}H-NMR spectroscopy. The experiments were conducted for binary systems of the host [H] urea and a guest [G] TFA, where the total concentration of [H]+[G] was held constant (5 mM or 1.7 mM), and the relative proportions of [H] and [G] were varied from [H]/[G] = 1 to [H]/[G] = 0. The ^{19}F- and ^{1}H-NMR data for the Job plots was measured in deuterated chloroform at room temperature using a Bruker Avance III 400 MHz spectrometer. The Job plots were drawn by following the chemical shift of the TFA fluorine signal or *i-cis*-cycHC[6] **1** proton signals ($\delta_1$at 3.1ppm and α_{10} at 4.6 ppm) while varying the [H]/[G] ratio. The maximum shift change was seen at $\alpha = 0.5$ of the Job plot curve for mono-urea **7**, indicating a 1:1 molecular association. Following ^{19}F signal of TFA in 5mM solutions, the concentration maximum shift change was seen at $\alpha = 0.7$of the Job plot curve for all cycHCs **1**, **2**, **6**. Following the ^{1}H signals of *i-cis*-cycHC[6] **1** during Job's analysis in 5mM concentration, maximum shift change was seen at $\alpha = 0.3$. ^{19}F and ^{1}H measurements were in agreement indicating 1:2 stoichiometry of complexes, where two TFA molecules form complex with one cycHC[6]. In 1.7 mM solutions maximum shift change moved toward $\alpha = 0.5$, but did not reached it, reflecting higher proportion of 1:1 complex in presence of 1:2 complex (Figure S14).

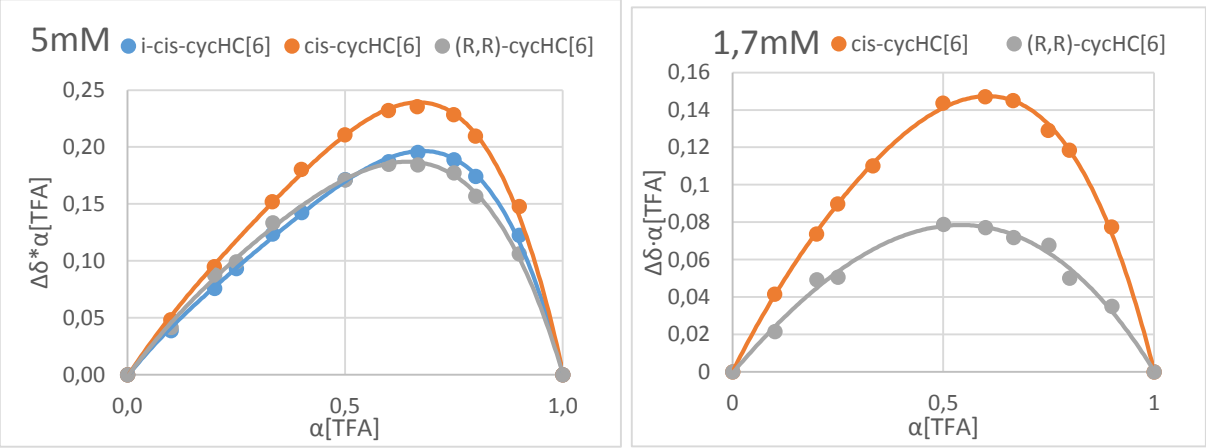


Figure S14. Job plots for 5 mM and 1.7 mM solutions of *i-cis*-cycHC[6] **1**, *cis*-cycHC[6] **2** and (*R*,*R*)-cycHC[6] **6** with TFA.

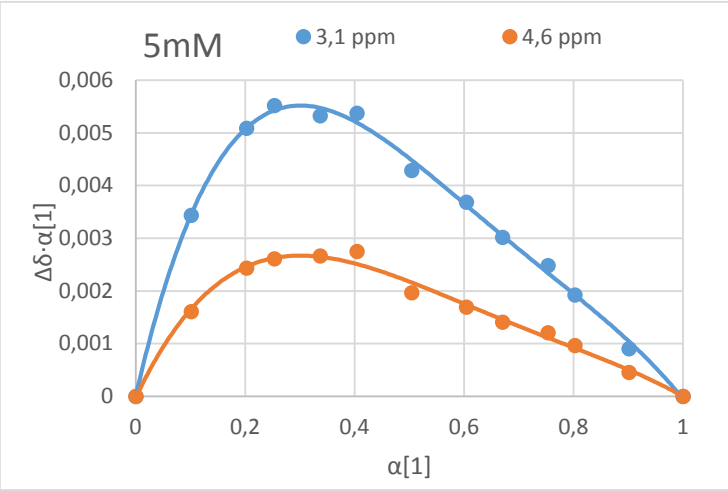


Figure S15. Job plot for 5 mM solutions of **1** with TFA, following protons of **1** protons at 3,1 ppm (δ_1) and 4,6 ppm (α_{10}) by ^{1}H-NMR (see S3-S7 for assignment)

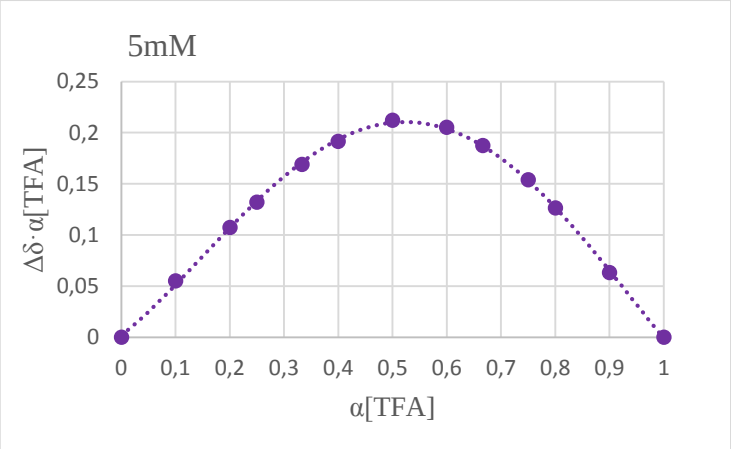


Figure S16. Job plot for 5 mM solutions of monourea **7** with TFA, following TFA by ^{19}F-NMR.

Determination of the association constants

General remarks

^{19}F-NMR titration experiments were conducted in deuterated chloroform at 297 K. The concentration of TFA solution in the beginning of titration was in between 0.97 to 1.75 mM and urea derivatives **1**, **2**, **6**, **7** and **8** stock solution in between 70 to 33 mM. Urea was added by syringe in small portions and the spectra recorded after each addition, resulting in a set of spectra (15-18 per titration). The ^{19}F-NMR spectra were recorded on a Bruker Avance II 400MHz spectrometer using regular 5 mm NMR tubes. The progressive changes of the chemical shifts of TFA were followed. In order to avoid interactions with chemical shift reference compound, ^{19}F TFA chemical

Binding of TFA to cycHC[6]s can be expressed as follows:

$$\mathrm{TFA} + \mathrm{cycHC[6]} \xrightarrow{K11} \mathrm{TFA \cdot cycHC[6]}$$

$$\mathrm{TFA \cdot cycHC[6]} + \mathrm{TFA} \xrightarrow{K12} 2\mathrm{TFA \cdot cycHC[6]}$$

Binding of TFA to monoureas **7** and **8** can be expressed as follows:

$$\mathrm{TFA} + \mathrm{urea\ derivative} \xrightarrow{K11} \mathrm{TFA \cdot urea\ derivative}$$

Association constants K_{11} and K_{12} were calculated using free online tool BindFit from http://supramolecular.org/ (accessed March 22, 2018).

Table S6. Association constants *K* of urea derivatives **1**, **2**, **6**, **7**, **8** with TFA, determined by ^{19}F-NMR titration in $CDCl_3$.

No	Urea derivative	K_{11} (M^{-1})	error (%)	K_{12} (M^{-1})	error (%)	K_{tot}	error (%)
1	**1**	$8.8 \cdot 10^2$	8.3	$7.6 \cdot 10^2$	11	$6.7 \cdot 10^5$	14
2	**2**	$7.3 \cdot 10^2$	9.8	$16 \cdot 10^2$	9.4	$1.2 \cdot 10^6$	14
3	**6**	$2.8 \cdot 10^2$	3.7	$6.3 \cdot 10^2$	2.9	$1.8 \cdot 10^5$	4.7
4	**7**	$43 \cdot 10^2$	11				
5	**8**	$21 \cdot 10^2$	8.1				

Table S7. Titration data of TFA with urea derivatives.

TFA / M	(*R*,*R*)-cycHC[6] **6** / M	δ (^{19}F) of TFA
0.00175	0.00000	-75.444
0.00173	0.00064	-75.579
0.00172	0.00127	-75.660
0.00171	0.00171	-75.696
0.00170	0.00216	-75.723
0.00168	0.00276	-75.750
0.00167	0.00335	-75.768
0.00165	0.00393	-75.782
0.00163	0.00485	-75.799
0.00159	0.00639	-75.816
0.00154	0.00836	-75.829
0.00149	0.01047	-75.835
0.00140	0.01406	-75.839
0.00127	0.01917	-75.839
0.00117	0.02343	-75.839

TFA / M	*cis*-cycHC[6] **2** / M	δ (^{19}F) of TFA
0.00097	0.00000	-75.347

0.00096	0.00022	-75.476
0.00096	0.00043	-75.563
0.00095	0.00064	-75.624
0.00094	0.00096	-75.683
0.00093	0.00126	-75.722
0.00092	0.00166	-75.756
0.00091	0.00210	-75.781
0.00089	0.00258	-75.801
0.00087	0.00326	-75.820
0.00085	0.00416	-75.836
0.00082	0.00509	-75.848
0.00077	0.00675	-75.861
0.00070	0.00911	-75.872
0.00064	0.01108	-75.877
0.00058	0.01305	-75.877
0.00054	0.01469	-75.880

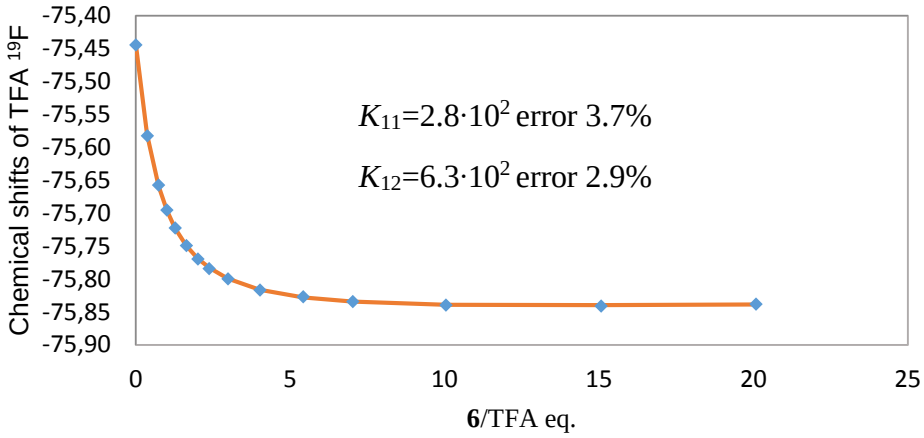
TFA / M	*i-cis*-cycHC[6] **1** / M	δ (^{19}F) of TFA
0.00174	0.00000	-75.501
0.00172	0.00069	-75.670
0.00170	0.00137	-75.751
0.00168	0.00204	-75.797
0.00166	0.00301	-75.828
0.00164	0.00396	-75.848
0.00161	0.00488	-75.861
0.00158	0.00636	-75.872
0.00153	0.00833	-75.882
0.00148	0.01043	-75.887
0.00139	0.01400	-75.896
0.00126	0.01909	-75.901
0.00116	0.02333	-75.904
0.00105	0.02758	-75.905
0.00096	0.03111	-75.905

TFA / M	Monourea **7** / M	δ (^{19}F) of TFA
0.00097	0.00000	-75.358
0.00096	0.00030	-75.538
0.00096	0.00059	-75.674
0.00095	0.00088	-75.769
0.00094	0.00131	-75.854
0.00093	0.00173	-75.903

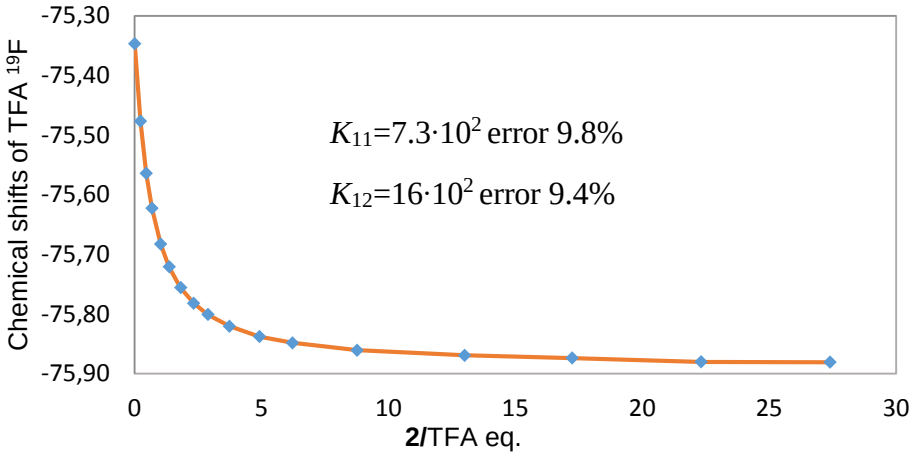
0.00092	0.00228	-75.941
0.00091	0.00288	-75.945
0.00089	0.00352	-75.982
0.00087	0.00446	-75.998
0.00085	0.00570	-76.01
0.00082	0.00697	-76.011
0.00077	0.00923	-76.027
0.00070	0.01246	-76.033
0.00064	0.01516	-76.036
0.00058	0.01786	-76.038
0.00054	0.02011	-76.038
0.00050	0.02201	-76.038

TFA / M	Monourea **8** / M	δ (^{19}F) of TFA
0.00097	0.00000	-75.410
0.00096	0.00031	-75.542
0.00096	0.00061	-75.647
0.00095	0.00092	-75.725
0.00094	0.00136	-75.804
0.00093	0.00180	-75.854
0.00092	0.00237	-75.859
0.00091	0.00299	-75.925
0.00089	0.00366	-75.946
0.00087	0.00463	-75.965
0.00085	0.00592	-75.981
0.00082	0.00724	-75.992
0.00077	0.00959	-76.004
0.00070	0.01294	-76.012
0.00064	0.01574	-76.017
0.00058	0.01854	-76.019
0.00054	0.02088	-76.021
0.00050	0.02286	-76.021

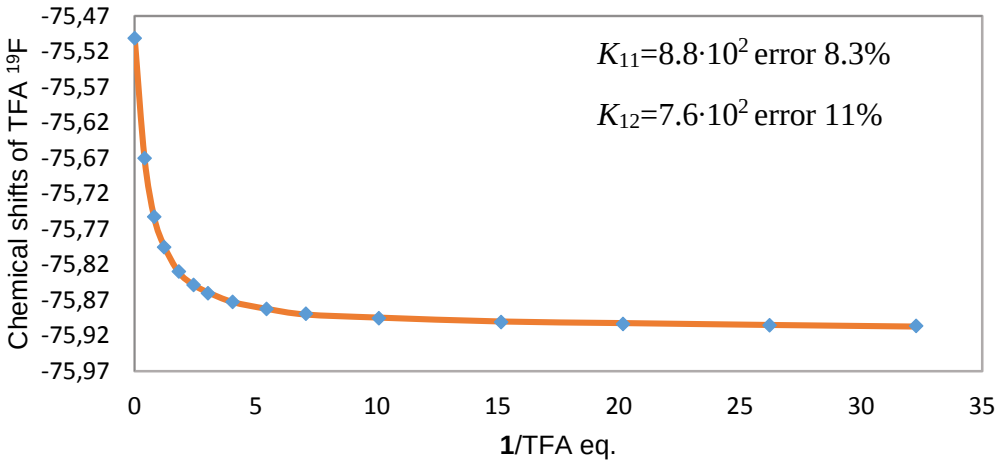
(*R*,*R*)-cycHC[6] **6**+TFA



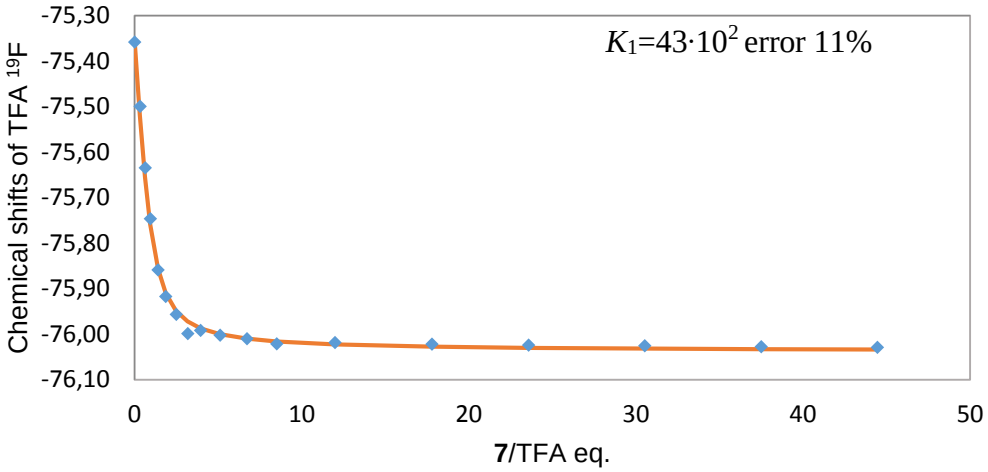
cis-cycHC[6] **2**+TFA



i-cis-cycHC[6] **1** +TFA



7+TFA



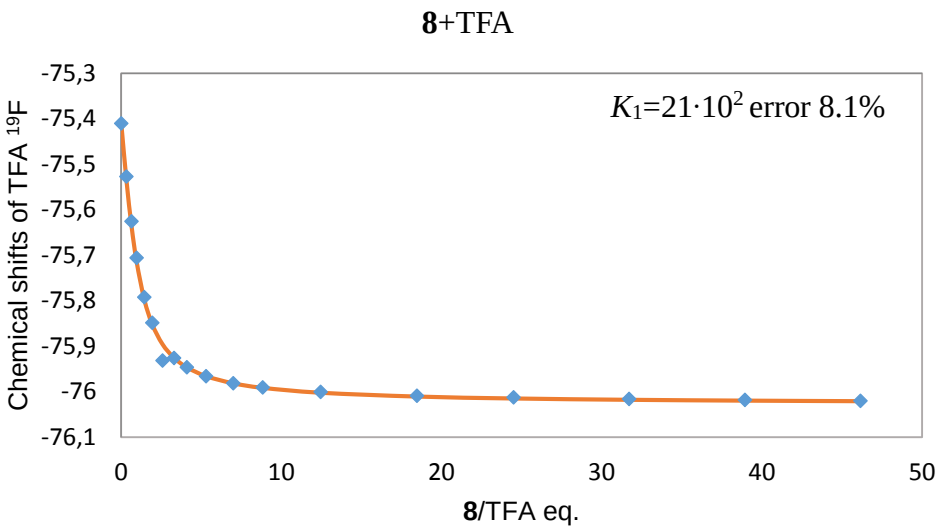


Figure S17. Titration data and fitting curves of TFA with urea derivatives **1**, **2**, **6**, **7**, **8**.

[1]H-NMR titration of (*R*,*R*)-cycHC[6] **6** with TFA

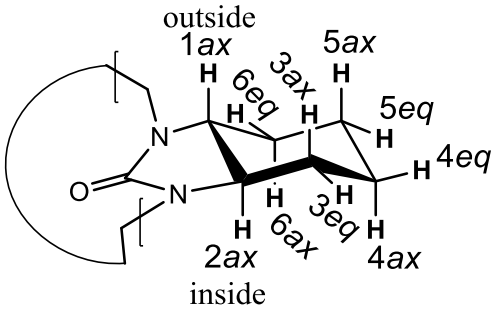


Figure S18. [1]H-NMR of titration of (*R*,*R*)-cycHC[6] **6** with TFA. Identification of [1]H-NMR signals is reported previously[19]. Proton 1*ax* at 2.77 ppm shifts upon addition of 16 eq. of TFA to 2.86 ppm. Therefore external binding is proposed as proton 1*ax*. which is positioned outside of the cavity. chemical shift value changes and 2*ax* at 2.40 ppm. which is positioned inside the cavity. does not change upon addition of TFA.

[1]H-NMR titration data was used only for identification of complexation site and was not used for calculation of association constant because acidity of the media affects chemical shift values and during titration large change in strong acid (TFA) concentration occurs. Also one can follow shift of H_2O in the spectra and formed H_3O^+ ion will also influence binding of TFA to urea.

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