

Supplemental information

Mechanochemically driven covalent self-assembly of a chiral mono-biotinylated hemicucurbit[8]uril

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Supplemental Experimental Procedures

Table of contents

| | |
|--|-----|
| General Information..... | S2 |
| 1. Theoretical Number of Linear and Cyclic Oligomers | S3 |
| 2. Screening and Optimization of Reaction Conditions | S4 |
| 2.1 Synthesis in Solution..... | S5 |
| 2.2 Synthesis in Solid State | S6 |
| 2.3 Analysis of Oligomers and Side-Products | S17 |
| 3. Preparative Synthesis, Purification, and Characterization of mixHC[8] | S28 |
| 3.1 NMR spectra | S31 |
| 3.2 IR spectra..... | S46 |
| 4. Single Crystal X-ray Diffraction Analysis..... | S48 |
| 5. The Computational Study | S55 |
| 5.1 Methods..... | S55 |
| 5.2 Results | S55 |
| 5.3 Comparing the Calculated Structure to the Crystal Structure | S57 |
| 5.4 The Cartesian Coordinates of the Found Conformers..... | S60 |
| 6. Anion Binding Studies..... | S68 |
| 6.1 Isothermal Calorimetric Titration..... | S68 |
| 6.2 Immobilization of mixHC[8] on APS | S83 |
| 6.3 Removal of Perchlorate from Methanol Solutions..... | S84 |
| References..... | S88 |

General Information

Unless otherwise stated, all reagents were purchased from commercial suppliers and used without further purification. (*R,R*)- and (*S,S*)-*N,N'*-cyclohexa-1,2-diylurea (CU) monomers, and (*R,R*)-cycHC[8] were synthesised in our laboratory following the procedures described in literature.¹⁻³

Mechanochemical experiments were carried out in FTS-1000 ball mill, at a frequency of 30 Hz in 14 mL ZrO₂-coated grinding jars charged with two 10 mm ZrO₂ milling balls. For aging reaction mixtures at elevated temperatures VWR Incu-line Digital Incubator was used.

¹H, ¹³C and 2D NMR spectra were acquired using a Triple Resonance Probe (TXI) on a Bruker AVANCE III 800 MHz spectrometer at 298.15 K. The samples were dissolved in CDCl₃ and the chemical shifts were referenced to CDCl₃ residual peak. Optical rotation was measured with an Anton Paar MCP 500 polarimeter. IR spectra were recorded on a Bruker Tensor 27 FT spectrometer. HRMS data was collected on Agilent 6540 Accurate-Mass Q-TOF mass spectrometer. Thermodynamic measurements by ITC were performed on MicroCal PEAQ-ITC calorimeter using a 200 μ L calorimetric cell and a 40 μ L syringe.

Silica gel 40-63 μ m was used for column chromatography, silica gel 60 F₂₅₄ plates were used for TLC. Visualization of TLC plates was performed using phosphomolybdic acid (PMA) stain. To perform automatic column chromatography Biotage Isolera Prime machine was used. HPLC-UV-MS analysis was performed on Agilent 1200 Series System equipped with multiple wavelength detector (MWD) and single quadrupole mass detector (MSD), using Phenomenex Kinetex XB-C18 column (150 mm \times 4.6 mm, 2.6 μ m). Ion chromatographic analysis was carried out on Metrohm Ltd 761 Compact IC with chemical suppression of eluent conductivity.

1. Theoretical Number of Linear and Cyclic Oligomers

All combinations

Number of all possible oligomers was calculated assuming that up to 10-membered oligomers are formed. Three different monomers were considered, CU and D-biotin (B) in its two orientations (See Figure 1 in main text for clarity). Oligomers could form either in linear or cyclic forms, latter would be HC[*n*]s. By considering all non-superimposable combinations with the length from 2 to 10, we found that up to 5293 different cyclic and 44646 linear oligomers can form, leading to total 49939 possible combinations.

Combinations were found by a Python script using SymPy iterables module (bracelets combinations) and Python Itertools module for finding the possible linear oligomers. Corresponding script is attached as a Data S1 (alloligos.py) and requires SymPy module in addition to the standard Python installation.

HC[8] combinations

To predict theoretical distribution of cyclic 8-membered oligomers (HC[8]s), we considered CU and biotin in its two orientations (See Figure 1 in main text for clarity). It was assumed that the formation of a specific HC[8] is directly proportional to the product of the initial concentrations of the constituent monomers. For biotin, the concentration of the both orientations were considered to be equal to each other and the half of the total biotin concentration. Based on these assumptions, we found the list of all possible cyclic oligomers and their relative concentration in the mixture of all 8-membered HC[*n*]s. Combinations and concentrations were found by a Python script attached as Data S1 (necgen.py) using SymPy iterables module.

Table S1. Theoretical distribution of 8-membered macrocycles (HC[8]s) resulting from various molar ratios of starting monomers B and CU.

| Monomer* ratio B:CU | HC[8]s distribution | | |
|------------------------|---------------------|----------|-------------|
| | mixHC[8] | cycHC[8] | other HC[8] |
| 1:5 | 0.15 | 0.73 | 0.12 |
| 1:7 | 0.12 | 0.82 | 0.06 |
| 1:15 | 0.062 | 0.925 | 0.014 |

*biotin unit can be incorporated into macrocycles in 2 different orientations with equal probabilities

2. Screening and Optimization of Reaction Conditions

General procedure for screening reaction conditions

D-biotin (46 mg, 0.19 mmol, 1 eq.), (*R,R*)- or (*S,S*)-*N,N'*-cyclohexa-1,2-diylurea (183 mg, 1.30 mmol, 7 eq.), paraformaldehyde (45 mg, 1.50 mmol, 8 eq.) and triphenylmethane (10 mg, internal standard for HPLC yield estimation) were placed into a 14 mL ZrO₂-coated jar charged with two 10 mm ZrO₂ balls (3.5 g). The template consisting of aqueous acid or acid and corresponding salt (0.56 mmol, 3 eq.) was added to the mixture, which was then set to mill at 30 Hz for 60 minutes. After milling the jar was sealed with parafilm and the reaction mixture was aged at 60 °C for 24 hours. The resulting crude mixture was further washed on a glass filter with distilled water until neutral pH, which was determined by test strips. The quenched mixture was dried in open air at room temperature.

General conditions for HPLC analysis

System A (estimation of HPLC yield). Eluents A (water / 0.1% formic acid) and B (acetonitrile / 0.1% formic acid) were used in a gradient mode from A:B 50:50 (v/v) to A:B 10:90 (v/v) with the flow rate of 0.75 mL/min. The column temperature was set at 30 °C, injection volume at 2 μ L and detection wavelength at 210 nm. The peaks of the macrocycles were identified by ESI-MS.

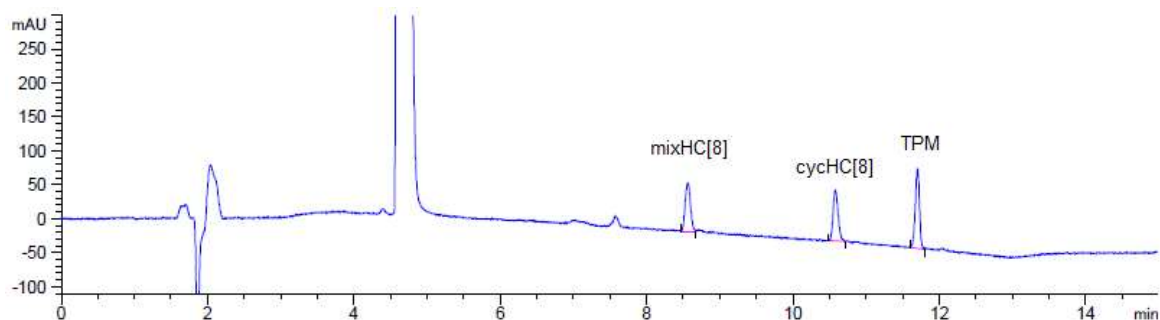


Figure S1. Typical HPLC-UV chromatogram at 210 nm used for yield determination.

HPLC yields were calculated based on calibration graphs for isolated macrocycles and internal standard (triphenylmethane) introduced into reaction mixture before milling. The sampling was performed in triplicate, ~1 mg of crude mixture after aging was dissolved in chloroform: isopropanol 1:1 (v/v) and filtered through 0.2 μ m PTFE syringe filter.

System B (MS analysis of oligomers). Eluents A (water / 0.1% formic acid) and B (acetonitrile / 0.1% formic acid) were used in a gradient mode from A:B 90:10 (v/v) to A:B 0:100 (v/v), followed by the isocratic stage at A:B 0:100 (v/v). The flow rate was set at 0.5 mL/min, column temperature at 30 °C and injection volume at 2 or 5 μ L. The general oligomeric profile was studied by ESI-HRMS in scan mode with positive polarity. The quantitative analysis was carried out using selected ion monitoring (SIM).

2.1 Synthesis in Solution

HPF₆ as template

D-biotin (10 mg, 0.041 mmol, 1 eq.), (*R,R*)-*N,N'*-cyclohexa-1,2-diyliurea (40 mg, 0.29 mmol, 7 eq.), paraformaldehyde (10 mg, 0.33 mmol, 8 eq.) were placed in a vial, followed by addition of 55% aq. HPF₆ (20 μ L) and ACN (0.6 mL). The heterogeneous mixture was stirred for 2 hours at room temperature. The heterogeneous solution mixture was analysed by HPLC-UV-MS. Complex mixture formed and only trace amounts of products were detected (0.03 ± 0.01 % of mixHC[8] and 0.24 ± 0.07 % of cycHC[8]).

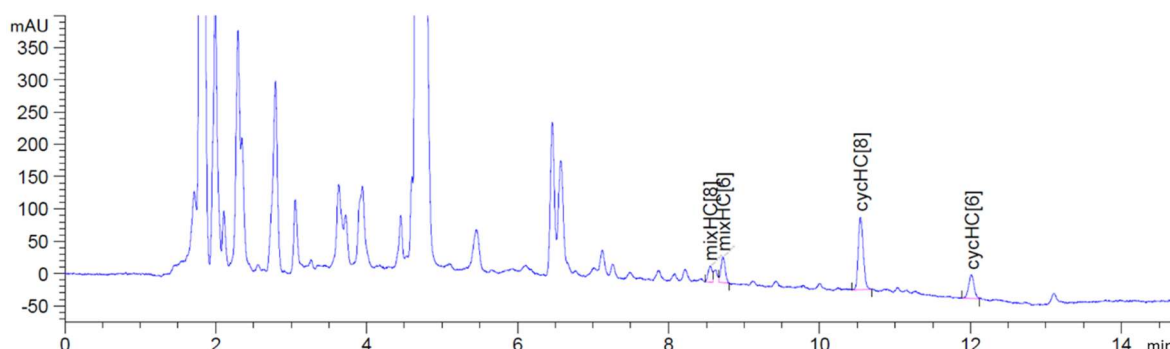
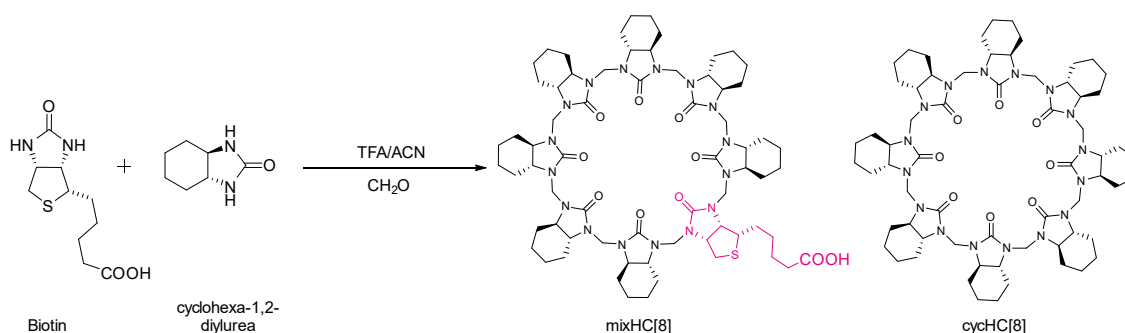


Figure S2. HPLC chromatogram (210 nm) of crude mixture with HPF₆ used as template.

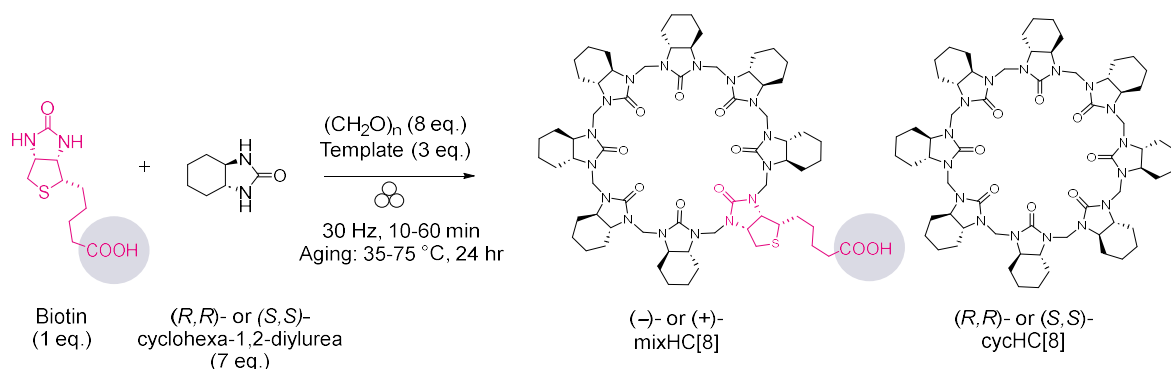
TFA as template

The reaction was performed following the standard procedure for cycHC[8] synthesis with TFA in acetonitrile², using 1:7 ratio of biotin to cyclohexa-1,2-diylurea monomer.



D-biotin (73 mg, 0.30 mmol, 1 eq.), (*R,R*)-*N,N'*-cyclohexa-1,2-diylurea (293 mg, 2.09 mmol, 7 eq.), paraformaldehyde (72 mg, 2.40 mmol, 8 eq.) were placed in a round bottom flask, followed by addition of TFA (4.5 mL) and ACN (4.5 mL). The heterogeneous mixture was stirred for 2 hours at room temperature. Reaction progress was monitored by TLC. To the resulting clear solution water (13 mL) was added, and the mixture was stirred on ice bath for 30 min. Then the solid mixture was filtered out, washed with 3×10 mL of water and dried in open air. HPLC-UV-MS analysis of the dried solid confirmed the formation of mixHC[8] and cycHC[8] in $(9.48 \pm 0.04)\%$ and $(38 \pm 1)\%$ yields, respectively.

2.2 Synthesis in Solid State



Screening of conditions using RSM

Reaction conditions: D-biotin (26–65 mg, 0.11–0.27 mmol, 1 eq.), (R,R) - N,N' -cyclohexa-1,2-diylurea (187–225 mg, 1.33–1.60 mmol, 5–15 eq.), paraformaldehyde (48–52 mg, 1.6–1.7 mmol, 8 eq.) and 70% aq. HClO_4 (8.6–75 μl , 0.10–0.87 mmol, 0.5–4 eq.) were milled for 10–60 minutes and aged at 35–75 $^{\circ}\text{C}$ for 24 hours. The HPLC yields were determined in triplicate, standard deviation between measurements did not exceed 2%.

Table S2. Simultaneous screening of monomer ratio, acid amount, milling time and aging temperature using HClO_4 as the catalyst and template.

| Entry | Monomer molar ratio (B:CU) | HClO_4 , eq. | Milling time, min | Aging T, $^{\circ}\text{C}$ | HPLC yield, % | |
|-------|----------------------------|-----------------------|-------------------|-----------------------------|---------------|----------|
| | | | | | mixHC[8] | cycHC[8] |
| 1 | 1.0 : 5.0 | 4.0 | 60.0 | 35 | 9 | 16 |
| 2 | 1.0 : 15.0 | 0.5 | 50.0 | 75 | 4 | 12 |
| 3 | 1.0 : 11.0 | 1.9 | 36.0 | 35 | 10 | 18 |
| 4 | 1.0 : 7.6 | 3.1 | 60.0 | 75 | 7 | 17 |
| 5 | 1.0 : 5.0 | 4.0 | 10.0 | 75 | 2 | 2 |
| 6 | 1.0 : 15.0 | 3.0 | 12.8 | 75 | 15 | 50 |
| 7 | 1.0 : 8.0 | 0.5 | 12.3 | 75 | 5 | 9 |
| 8 | 1.0 : 11.1 | 4.0 | 34.0 | 59 | 9 | 33 |
| 9 | 1.0 : 15.0 | 0.5 | 12.5 | 47 | 2 | 6 |
| 10 | 1.0 : 5.0 | 1.9 | 36.8 | 59 | 16 | 24 |
| 11 | 1.0 : 6.6 | 0.5 | 60.0 | 75 | 5 | 6 |
| 12 | 1.0 : 11.4 | 1.8 | 48.3 | 59 | 20 | 44 |
| 13 | 1.0 : 5.0 | 0.5 | 10.0 | 35 | 2 | 4 |
| 14 | 1.0 : 15.0 | 3.0 | 60.0 | 45 | 20 | 72 |
| 15 | 1.0 : 5.0 | 1.9 | 36.8 | 59 | 17 | 28 |
| 16 | 1.0 : 7.9 | 0.5 | 60.0 | 45 | 2 | 3 |
| 17 | 1.0 : 11.0 | 1.9 | 36.0 | 35 | 8 | 17 |
| 18 | 1.0 : 8.5 | 2.7 | 10.0 | 49 | 17 | 44 |
| 19 | 1.0 : 15.0 | 4.0 | 10.0 | 35 | 9 | 51 |
| 20 | 1.0 : 5.0 | 4.0 | 25.7 | 35 | 11 | 17 |
| 21 | 1.0 : 11.1 | 4.0 | 37.0 | 59 | 7 | 36 |
| 22 | 1.0 : 8.5 | 2.7 | 10.0 | 49 | 14 | 39 |
| 23 | 1.0 : 7.0 | 3.0 | 60.0 | 60 | 19 | 40 |

The experiments were planned in Design-Expert 13 using Optimal (Custom) Design for 4 numeric factors and polynomial model with quadratic process order. The total 23 runs included 15 required model points, 3 lack-of-fit points, 4 replicate points and 1 additional model point. The collected data were processed using polynomial analysis.

Table S3. Optimal (Custom) Design: the choice of variable factors.

| Factor | Name | Units | Minimum value | Maximum value |
|--------|----------------------|-------|---------------|---------------|
| A | Monomer ratio (CU:B) | eq | 5 | 15 |
| B | Acid amount | eq | 0.5 | 4 |
| C | Milling time | min | 10 | 60 |
| D | Aging temperature | °C | 35 | 75 |

The factors **A–D** were chosen based on our previous experience in the solid-state synthesis of cycHC[*n*].⁵ **A** determines the tolerance and selectivity of the self-assembly process with respect to the content of the non-*C*₂-symmetric biotin. Additionally, the ratio of monomers might affect the number of biotin units incorporated into the macrocyclic scaffold. Compared to the stoichiometric 7:1 monomer ratio, the excess of biotin would be beneficial in case it reacts slower than CU. The excess of CU was meant to suppress the formation of polybiotinylated side-products. **B** characterizes the number of template anions and protons mediating the cyclization and condensation reactions, as well as the quantity of water acting as a liquid grinding additive. The maximal loading was chosen to confine the system within liquid-assisted grinding conditions. The minimal amount of acid modelled the conditions close to neat grinding. **C** reflects the duration of the polycondensation and monomer crossover reaction, as well as the amount of mechanical force transferred. In general, ball-milling accelerates chemical reactions, and our previous study on cycHC[*n*] showed that 30–60 min milling provided quantitative yields after aging. We wondered if the milling time can be decreased, bearing in mind that it must be sufficient to ensure proper mixing of the reagents and transfer of mechanical energy. **D** impacts the self-assembly step in the conversion of the oligomers into macrocycles via dynamic exchange between reactive acyliminium intermediates and templating. Our previous study on solid-state synthesis of cycHC[*n*] demonstrated that elevated temperatures accelerate the aging; the preliminary experiments in the current work resulted in poor yields at 80 °C, pointing to optimal range for the studied molecular system.

Table S4. Fit summary.

| Response | Sequential p-value | Lack of Fit p-value | Adjusted R ² | Predicted R ² |
|---------------------|--------------------|---------------------|-------------------------|--------------------------|
| mixHC[8] HPLC yield | 0.0002 | 0.0281 | 0.8215 | 0.0802 |
| cycHC[8] HPLC yield | < 0.0001 | 0.0690 | 0.9487 | 0.6575 |

The analysis of variance (ANOVA) for mixHC[8] quadratic model identified acid amount as significant factor, and to some extent temperature. For cycHC[8], monomer ratio and acid amount were found significant, and to a lesser extent milling time and temperature.

Table S5. Analysis of variance for mixHC[8] quadratic model.

| Source | Sum of Squares | df | Mean Square | F-value | p-value ^b | |
|----------------------------------|----------------|----|-------------|-------------------|----------------------|-------------|
| Model | 774.32 | 14 | 55.31 | 8.23 ^a | 0.0027 | significant |
| A (monomer ratio) | 0.3676 | 1 | 0.3676 | 0.0547 | 0.8209 | |
| B (acid) | 64.97 | 1 | 64.97 | 9.67 | 0.0144 | |
| C (milling time) | 1.76 | 1 | 1.79 | 0.2667 | 0.6195 | |
| D (T) | 1.26 | 1 | 1.26 | 0.1880 | 0.6761 | |
| AB (monomer ratio, acid) | 20.04 | 1 | 20.04 | 2.98 | 0.1224 | |
| AC (monomer ratio, milling time) | 5.70 | 1 | 5.70 | 0.8493 | 0.3837 | |
| AD (monomer ratio, T) | 9.86 | 1 | 9.86 | 1.47 | 0.2602 | |
| BC (acid, milling time) | 1.54 | 1 | 1.54 | 0.2297 | 0.6446 | |
| BD (acid, T) | 101.87 | 1 | 101.87 | 15.17 | 0.0046 | |
| CD (milling time, T) | 1.42 | 1 | 1.42 | 0.2111 | 0.6581 | |
| A ² (monomer ratio) | 24.26 | 1 | 24.26 | 3.61 | 0.0939 | |
| B ² (acid) | 378.87 | 1 | 378.87 | 56.40 | < 0.0001 | |
| C ² (milling time) | 4.32 | 1 | 4.32 | 0.6432 | 0.4457 | |
| D ² (T) | 103.23 | 1 | 103.23 | 15.37 | 0.0044 | |
| Residual | 53.74 | 8 | 6.72 | | | |
| Lack of Fit | 48.35 | 4 | 12.09 | 8.98 ^c | 0.0281 | significant |
| Pure Error | 5.39 | 4 | 1.35 | | | |
| Cor Total | 828.05 | 22 | | | | |

[a] The **Model F-value** of 8.23 implies the model is significant. [b] **P-values** less than 0.0500 indicate model terms are significant. In this case B, BD, B², D² are significant model terms (highlighted in blue). [c] The **Lack of Fit F-value** of 8.98 implies the Lack of Fit is significant, which can be attributed to smaller variance between mixHC[8] yields in replicate points compared to cycHC[8].⁴

Table S6. Analysis of variance for cycHC[8] quadratic model.

| Source | Sum of Squares | df | Mean Square | F-value | p-value ^b | |
|----------------------------------|----------------|----|-------------|--------------------|----------------------|-------------|
| Model | 7639.89 | 14 | 545.71 | 30.06 ^a | < 0.0001 | significant |
| A (monomer ratio) | 1549.10 | 1 | 1549.10 | 85.34 | < 0.0001 | |
| B (acid) | 2037.44 | 1 | 2037.44 | 112.24 | < 0.0001 | |
| C (milling time) | 7.88 | 1 | 7.88 | 0.4339 | 0.5286 | |
| D (T) | 7.14 | 1 | 7.14 | 0.3932 | 0.5481 | |
| AB (monomer ratio, acid) | 866.62 | 1 | 866.62 | 47.74 | 0.0001 | |
| AC (monomer ratio, milling time) | 185.00 | 1 | 185.00 | 10.19 | 0.0128 | |
| AD (monomer ratio, T) | 87.12 | 1 | 87.12 | 4.80 | 0.0599 | |
| BC (acid, milling time) | 9.67 | 1 | 9.67 | 0.5330 | 0.4862 | |
| BD (acid, T) | 536.39 | 1 | 536.39 | 29.55 | 0.0006 | |
| CD (milling time, T) | 4.03 | 1 | 4.03 | 0.2220 | 0.6501 | |
| A ² (monomer ratio) | 95.75 | 1 | 95.75 | 5.28 | 0.0507 | |
| B ² (acid) | 1241.57 | 1 | 1241.57 | 68.40 | < 0.0001 | |
| C ² (milling time) | 284.19 | 1 | 284.19 | 15.66 | 0.0042 | |
| D ² (T) | 776.69 | 1 | 776.69 | 42.79 | 0.0002 | |

| | | | | | | |
|-------------|---------|----|-------|-------------------|--------|-----------------|
| Residual | 145.22 | 8 | 18.15 | | | |
| Lack of Fit | 121.91 | 4 | 30.48 | 5.23 ^c | 0.0690 | not significant |
| Pure Error | 23.31 | 4 | 5.83 | | | |
| Cor Total | 7785.10 | 22 | | | | |

[a] The **Model F-value** of 30.06 implies the model is significant. [b] **P-values** less than 0.0500 indicate model terms are significant. In this case A, B, AB, AC, BD, B², C², D² are significant model terms (highlighted in yellow). [c] The **Lack of Fit F-value** of 5.23 implies there is a 6.90% chance that a Lack of Fit F-value this large could occur due to noise.

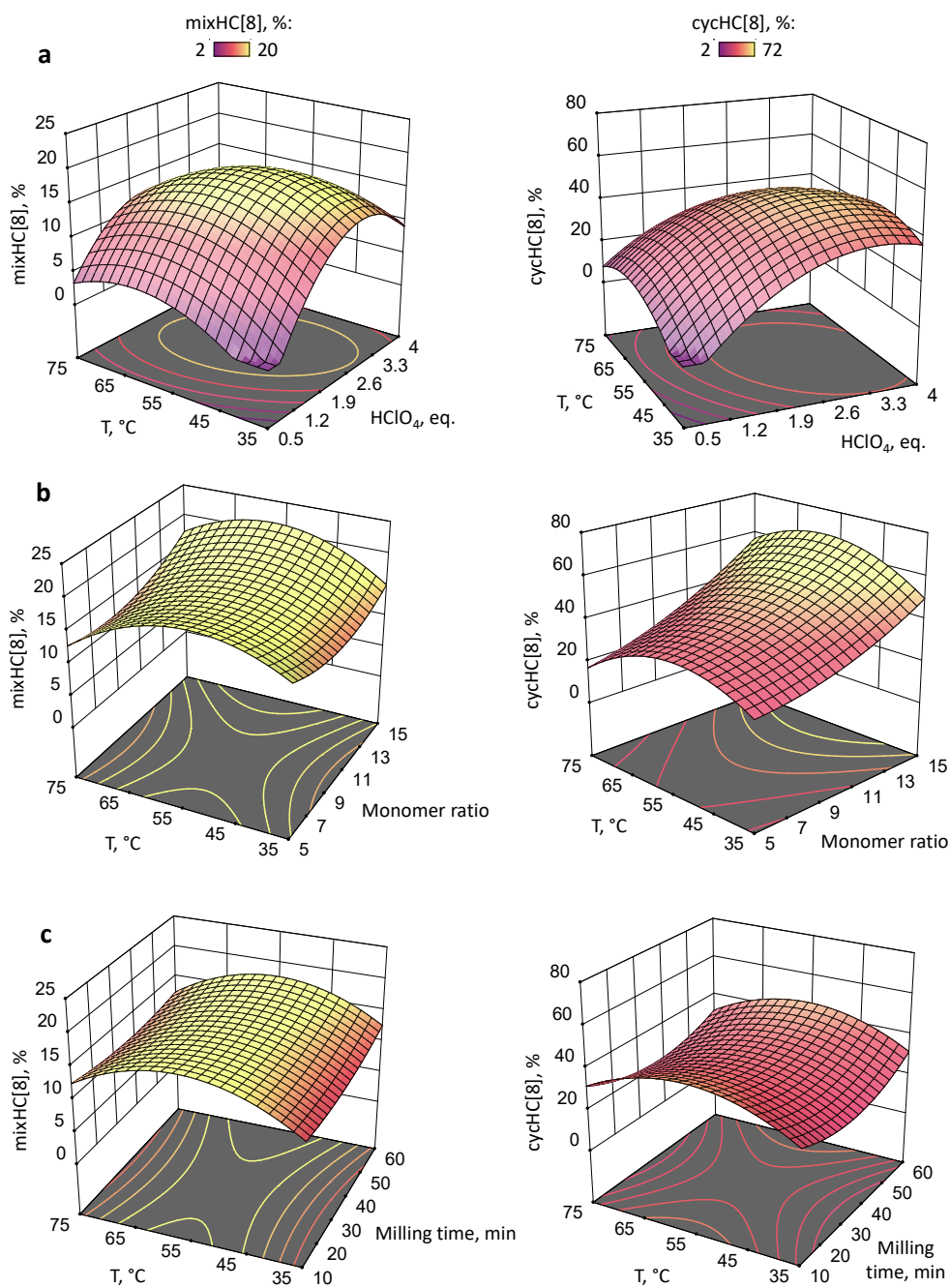


Figure S3. 3D response surfaces describing the trends upon varying the aging temperature and acid amount (a), temperature and monomer ratio (b), temperature and milling time (c).

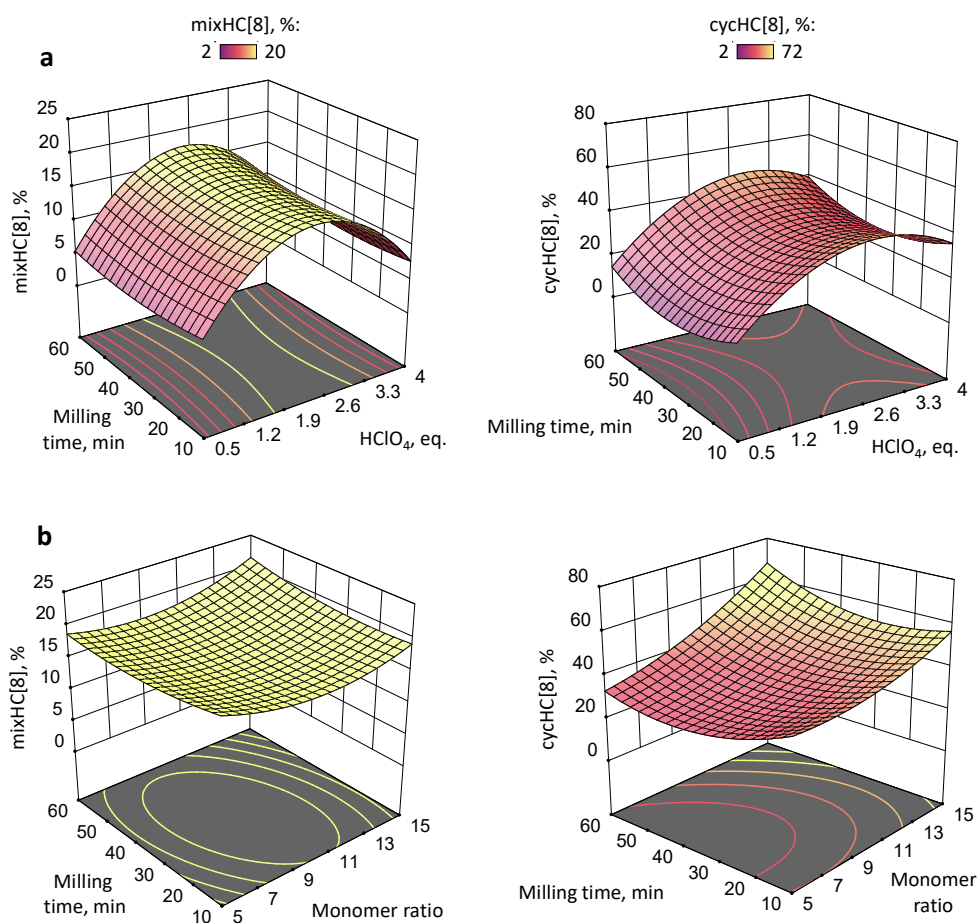


Figure S4. 3D response surfaces describing the trends upon varying the milling time and acid amount (a), milling time and monomer ratio (b).

Screening different templates

Reaction conditions: D-biotin (38–52 mg, 0.15–0.21 mmol, 1 eq.), (*R,R*)-*N,N'*-cyclohexa-1,2-diylurea (151–208 mg, 1.08–1.48 mmol, 7 eq.), paraformaldehyde (38–52 mg, 1.3–1.7 mmol, 8 eq.) and template (3 eq.) were milled for 60 minutes and aged at 60 °C for 24 hours.

Individual HPLC yields were determined from triplicate measurements, the deviation between parallel measurements did not exceed 1.1%; Average HPLC yields expressed as the mean value \pm standard deviation between reactions reproduced *n* times. See results in Table S7.

Table S7. Comparison of various acids and salt additives. (see experimental details in previous page)

| Entry | Acid (eq.) | Salt (eq.) | Template anion | LAG (η, μl/mg) | mixHC[8] HPLC yield, % | | cycHC[8] HPLC yield, % | |
|-------|---|---|-------------------------------|----------------|------------------------|----------|------------------------|---------|
| | | | | | Individual | Average | Individual | Average |
| 1 | 70% aq HClO ₄ (3) | — | ClO ₄ [−] | 0.18 | 17.7 | 19±2 | 38.2 | 40±3 |
| | | | | | 19.2 | | 41.1 | |
| | | | | | 19.9 | | 40.0 | |
| | | | | | 19.7 | | 39.8 | |
| | | | | | 18.1 | | 40.1 | |
| | | | | | 16.6 | | 35.8 | |
| | | | | | 20.6 | | 41.8 | |
| | | | | | 23.3 | | 44.3 | |
| 2 | 55% aq. HPF ₆ (2.4) | — | PF ₆ [−] | 0.26 | 27.5 | 27.6±0.1 | 36.0 | 34±2 |
| | 55% aq. HPF ₆ (3) | | | 0.33 | 27.7 | | 32.8 | |
| 3 | 50% aq. H ₂ SO ₄ (3) | KPF ₆ (3) | PF ₆ [−] | 0.21 | 14.7 | 15.0±0.3 | 19.5 | 22±4 |
| | | KPF ₆ (1.5) | | 0.24 | 15.2 | | 24.5 | |
| 4 | 55% aq. HPF ₆ (2) | KPF ₆ (1) | PF ₆ [−] | 0.20 | 40.5 | 37±2 | 38.1 | 38±2 |
| | | | | | 36.5 | | 41.0 | |
| | | | | | 36.3 | | 36.4 | |
| | | | | | 34.9 | | 36.3 | |
| 5 | 55% aq. HPF ₆ (2) | AgPF ₆ (1) | PF ₆ [−] | 0.19 | 27.3 | 29±2 | 47.9 | 42±8 |
| | | | | | 29.8 | | 36.4 | |
| 6 | 55% aq. HPF ₆ (2) | [Cu(CH ₃ CN) ₄]PF ₆ (1) | PF ₆ [−] | 0.18 | 31.3 | 31.1±0.4 | 43.2 | 44±2 |
| | | | | | 30.8 | | 45.4 | |

Optimization of KPF₆/HPF₆ amount

Reaction conditions: D-biotin (44.3–45.8 mg, 0.181–0.188 mmol, 1 equiv.), (*R,R*)-*N,N'*-cyclohexa-1,2-diylurea (178.4–188.7 mg, 1.273–1.346 mmol, 7 equiv.), paraformaldehyde (43.8–52.1 mg, 1.46–1.54 mmol, 8 equiv.), KPF₆ (2.0–104.5 mg, 0.011–0.568 mmol, 0–3 eq.), 55% aq. HPF₆ (3–234 μ l, 0.019–1.455 mmol, 0.1–8 equiv.) and water (0–233 mg, LAG additive η =0.2–0.85 μ l/mg) were milled for 60 min and aged at 60 °C for 24 h. The HPLC yields were determined in triplicate, standard deviation did not exceed 2%.

Table S8. Screening of KPF₆/HPF₆ added as the template.

| Entry | KPF ₆ , eq. | HPF ₆ , eq. | mixHC[8] yield, % | cycHC[8] yield, % |
|-------|------------------------|------------------------|-------------------|-------------------|
| 1 | 2.1 | 4.5 | 22 | 49 |
| 2 | 3.0 | 4.0 | 25 | 43 |
| 3 | 0 | 3.8 | 29 | 30 |
| 4 | 0.1 | 6.1 | 10 | 32 |
| 5 | 0 | 2.0 | 27 | 33 |
| 6 | 1.7 | 2.7 | 29 | 43 |
| 7 | 0.3 | 2.6 | 25 | 33 |
| 8 | 0 | 8.0 | 11 | 34 |
| 9 | 2.6 | 8.0 | 20 | 37 |
| 10 | 3.0 | 5.6 | 25 | 39 |
| 11 | 0 | 2.0 | 28 | 36 |
| 12 | 0.8 | 7.9 | 6 | 32 |
| 13 | 1.8 | 6.8 | 11 | 46 |
| 14 | 0 | 1.0 | 25 | 47 |
| 15 | 1.2 | 4.9 | 21 | 50 |
| 16 | 0.0 | 3.8 | 29 | 38 |
| 17 | 0 | 5.0 | 30 | 35 |
| 18 | 2.0 | 0.1 | 4 | 10 |
| 19 | 1.0 | 2.0 | 37 | 41 |
| 20 | 1.0 | 2.0 | 36 | 46 |

The experiments were planned in Design-Expert 13 using Optimal (Custom) Design for 2 numeric factors and polynomial model with quadratic process order. The total 20 runs included 8 required model points, 3 lack-of-fit points, 3 replicate points and 6 additional model points. The collected data were processed using polynomial analysis.

Table S9. Optimal (Custom) Design: the choice of variable factors.

| Factor | Name | Units | Minimum value | Maximum value |
|--------|--------------------------|-------|---------------|---------------|
| A | Salt (KPF ₆) | eq | 0 | 3.0 |
| B | Acid (HPF ₆) | eq | 0.1 | 8.0 |

Table S10. Fit summary.

| Response | Sequential p-value | Lack of Fit p-value | Adjusted R ² | Predicted R ² |
|---------------------|-----------------------|------------------------|----------------------------|--------------------------|
| mixHC[8] HPLC yield | 0.0128 | 0.0020 | 0.7834 | 0.1043 |
| cycHC[8] HPLC yield | 0.0116 | 0.4193 | 0.7242 | -1.7409 |

The software suggested cubic model for processing the collected data. The analysis of variance (ANOVA) for mixHC[8] and cycHC[8] cubic models identified components attributed to both salt and acid amount as significant. The amount of acid, however, was more crucial for mixHC[8] formation.

Table S11. Analysis of variance for mixHC[8] cubic model.

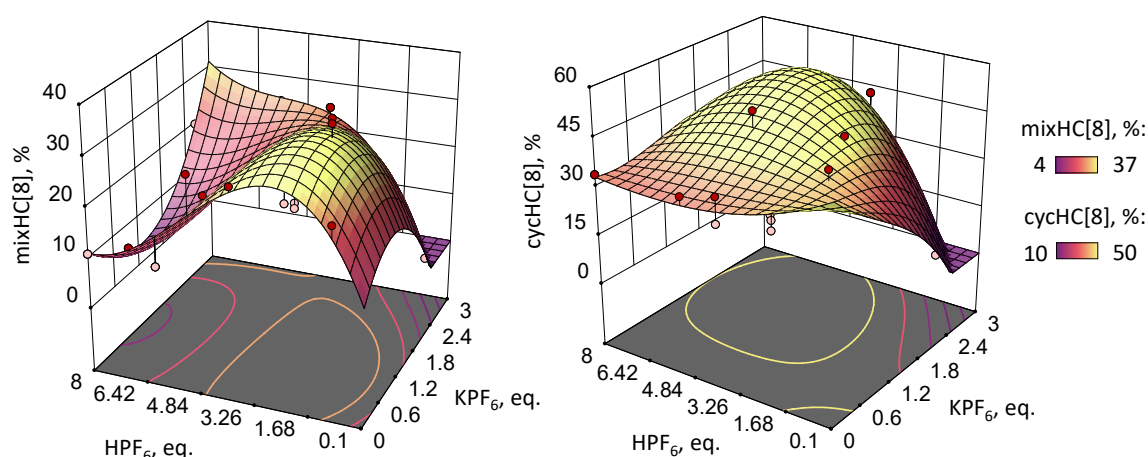
| Source | Sum of Squares | df | Mean Square | F-value | p-value ^b | |
|-------------------------------|----------------|----|-------------|--------------------|----------------------|-------------|
| Model | 1501.76 | 9 | 166.86 | 8.63 ^a | 0.0012 | significant |
| A (salt) | 9.24 | 1 | 9.24 | 0.4780 | 0.5050 | |
| B (acid) | 318.28 | 1 | 318.28 | 16.47 | 0.0023 | |
| AB (salt, acid) | 134.79 | 1 | 134.79 | 6.98 | 0.0247 | |
| A ² (salt) | 3.40 | 1 | 3.40 | 0.1758 | 0.6838 | |
| B ² (acid) | 551.59 | 1 | 551.59 | 28.54 | 0.0003 | |
| A ² B (salt, acid) | 140.23 | 1 | 140.23 | 7.26 | 0.0226 | |
| AB ² (salt, acid) | 2.03 | 1 | 2.03 | 0.1049 | 0.7527 | |
| A ³ (salt) | 3.57 | 1 | 3.57 | 0.1846 | 0.6766 | |
| B ³ (acid) | 124.72 | 1 | 124.72 | 6.45 | 0.0293 | |
| Residual | 193.24 | 10 | 19.32 | | | |
| Lack of Fit | 192.24 | 7 | 27.46 | 82.39 ^c | 0.0020 | significant |
| Pure Error | 1.0000 | 3 | 0.3333 | | | |
| Cor Total | 1695.00 | 19 | | | | |

[a] The **Model F-value** of 8.63 implies the model is significant. [b] **P-values** less than 0.0500 indicate model terms are significant. In this case B, AB, B², A²B, B³ are significant model terms (highlighted in yellow). [c] The **Lack of Fit F-value** of 82.39 implies the Lack of Fit is significant, which can be related to a smaller variance of mixHC[8] yields compared to cycHC[8].

Table S12. Analysis of variance for cycHC[8] cubic model.

| Source | Sum of Squares | df | Mean Square | F-value | p-value ^b | |
|-------------------------------|----------------|----|-------------|-------------------|----------------------|-----------------|
| Model | 1249.10 | 9 | 138.79 | 6.54 ^a | 0.0035 | significant |
| A (salt) | 89.81 | 1 | 89.81 | 4.23 | 0.0666 | |
| B (acid) | 57.07 | 1 | 57.07 | 2.69 | 0.1320 | |
| AB (salt, acid) | 222.44 | 1 | 222.44 | 10.49 | 0.0089 | |
| A ² (salt) | 242.30 | 1 | 242.30 | 11.42 | 0.0070 | |
| B ² (acid) | 521.37 | 1 | 521.37 | 24.58 | 0.0006 | |
| A ² B (salt, acid) | 3.53 | 1 | 3.53 | 0.1667 | 0.6917 | |
| AB ² (salt, acid) | 405.68 | 1 | 405.68 | 19.13 | 0.0014 | |
| A ³ (salt) | 54.10 | 1 | 54.10 | 2.55 | 0.1413 | |
| B ³ (acid) | 0.7610 | 1 | 0.7610 | 0.0359 | 0.8536 | |
| Residual | 212.10 | 10 | 21.21 | | | |
| Lack of Fit | 163.10 | 7 | 23.30 | 1.43 ^c | 0.4193 | not significant |
| Pure Error | 49.00 | 3 | 16.33 | | | |
| Cor Total | 1461.20 | 19 | | | | |

[a] The **Model F-value** of 6.54 implies the model is significant. [b] **P-values** less than 0.0500 indicate model terms are significant. In this case AB, A², B², AB² are significant model terms (highlighted in yellow). [c] The **Lack of Fit F-value** of 1.43 implies the Lack of Fit is not significant relative to the pure error.

**Figure S5.** 3D response surfaces describing the trends upon varying the amounts of KPF₆ and HPF₆ used as the template.

Screening monomer ratios

Ratio 1:5: D-biotin (60 mg, 0.25 mmol, 1 eq.), (*R,R*)-*N,N'*-cyclohexa-1,2-diylurea (172 mg, 1.23 mmol, 5 eq.), paraformaldehyde (44 mg, 1.5 mmol, 6 eq.), KPF₆ (34 mg, 0.19 mmol, 1 eq.) and 55% aq. HPF₆ (59 μ l, 0.37 mmol, 2 eq.) as LAG additive (η =0.19 μ l/mg);

Ratio 1:7: D-biotin (45–46 mg, 0.19 mmol, 1 eq.), (*R,R*)-*N,N'*-cyclohexa-1,2-diylurea (182–184 mg, 1.30–1.31 mmol, 7 eq.), paraformaldehyde (44–45 mg, 1.5 mmol, 8 eq.), KPF₆ (35 mg, 0.19 mmol, 1 eq.) and 55% aq. HPF₆ (60 μ l, 0.37 mmol, 2 eq.) as LAG additive (η =0.20 μ l/mg);

Ratio 1:15: D-biotin (23 mg, 0.094 mmol, 1 eq.), (*R,R*)-*N,N'*-cyclohexa-1,2-diylurea (198 mg, 1.41 mmol, 15 eq.), paraformaldehyde (45 mg, 1.19 mmol, 16 eq.), KPF₆ (35 mg, 0.19 mmol, 1 eq.) and 55% aq. HPF₆ (61 µl, 0.34 mmol, 2 eq.) as LAG additive ($\eta=0.20$ µl/mg) were milled at 30 Hz for 60 minutes and aged at 60 °C for 24 hours.

Table S13. Effect of ratios of starting monomers

| Entry | Monomer molar ratio | HPLC yield, % | |
|----------------|---------------------|---------------|----------|
| | | mixHC[8] | cycHC[8] |
| 1 ^a | 1:5 | 34 | 30 |
| 2 ^b | 1:7 | 37±2 | 38±2 |
| 3 ^c | 1:15 | 27 | 62 |

The HPLC yields are provided as the ^bmean value ± standard deviation for the reaction reproduced ^b 4 times (see Table S3) or ^{a, c} once. The deviation between triplicate measurements did not exceed 0.7%.

Screening milling duration

Reaction conditions: D-biotin (45–46 mg, 0.19 mmol, 1 eq.), (*R,R*)-*N,N'*-cyclohexa-1,2-diylurea (182–184 mg, 1.30–1.31 mmol, 7 eq.), paraformaldehyde (44–46 mg, 1.5–1.5 mmol, 8 eq.) and KPF₆ (34–35 mg, 0.19 mmol, 1 eq.) and 55% aq. HPF₆ (60 µl, 0.37 mmol, 2 eq.; $\eta=0.20$ µl/mg) were milled for 5–90 minutes and aged at 60 °C for 24 hours.

Table S14. Screening milling time.

| Entry | Milling time, min | mixHC[8] HPLC yield, % | | cycHC[8] HPLC yield, % | |
|-------|-------------------|-------------------------|----------------------|-------------------------|----------------------|
| | | Individual ^a | Average ^b | Individual ^a | Average ^b |
| 1 | 5 | 15.1 | 15.5±0.4 | 55.4 | 55±3 |
| | | 15.6 | | 51.8 | |
| | | 15.8 | | 57.6 | |
| 2 | 10 | 24.1 | 23.9±0.2 | 36.7 | 39±3 |
| | | 23.9 | | 38.1 | |
| | | 23.7 | | 41.6 | |
| 3 | 20 | 37.4 | 37±1 | 39.2 | 39±1 |
| | | 37.3 | | 39.6 | |
| | | 36.1 | | 38.0 | |
| 4 | 30 | 28.2 | 33±4 | 29.2 | 32±3 |
| | | 29.6 | | 30.4 | |
| | | 36.3 | | 34.1 | |
| | | 36.2 | | 35.5 | |
| 5 | 45 | 23.3 | 26±4 | 25.2 | 29±4 |
| | | 23.8 | | 26.1 | |
| | | 32.8 | | 33.9 | |
| | | 25.9 | | 28.9 | |
| 6 | 60 | 40.5 | 37±2 | 38.1 | 38±2 |
| | | 36.5 | | 41.0 | |
| | | 36.3 | | 36.4 | |
| | | 34.9 | | 36.3 | |
| 7 | 90 | 34.5 | 34±1 | 32.5 | 32±1 |
| | | 33.1 | | 31.0 | |

^a HPLC yields from triplicate measurements, the deviation between parallel measurements did not exceed 3.1%; ^b HPLC yields expressed as the mean value ± standard deviation between reactions reproduced *n* times.

60 min is the optimal milling time, which ensures efficient shuffling of the intermediates. Increasing milling time to 90 min did not improve the yields. Shorter milling times required long aging time, see Table S15.

Screening aging duration

Reaction conditions: D-biotin (45–46 mg, 0.19 mmol, 1 eq.), (*R,R*)-*N,N'*-cyclohexa-1,2-diylurea (183– mg, 1.31 mmol, 7 eq.), paraformaldehyde (45 mg, 1.5 mmol, 8 eq.), KPF₆ (34–35 mg, 0.19 mmol, 1 eq.) and 55% aq. HPF₆ (60 µl, 0.37 mmol, 2 eq., $\eta=0.20$ µl/mg) were milled for 60 minutes and aged at 60 °C for 0, 3, 6, 12 or 24 hours.

Table S15. Screening aging time.

| Entry | Aging time, h | mixHC[8] HPLC yield, % | | cycHC[8] HPLC yield, % | |
|-------|----------------|-------------------------|----------------------|-------------------------|----------------------|
| | | Individual ^a | Average ^b | Individual ^a | Average ^b |
| 1 | 0 | 14.8 | 13±3 | 20.7 | 18±4 |
| | | 11.4 | | 14.7 | |
| 2 | 3 | 38.6 | 38±1 | 33.3 | 34±2 |
| | | 37.7 | | 35.6 | |
| 3 | 6 | 36.9 | 38±1 | 35.4 | 35.3±0.1 |
| | | 38.0 | | 35.2 | |
| 4 | 12 | 31.6 | 31.2±0.5 | 33.9 | 33±2 |
| | | 30.9 | | 31.6 | |
| 5 | 24 | 40.5 | 37±2 | 38.1 | 38±2 |
| | | 36.5 | | 41.0 | |
| | | 36.3 | | 36.4 | |
| | | 34.9 | | 36.3 | |
| 6 | 3 ^c | 30.4 | 30.1±0.3 | 31.8 | 31.7±0.2 |
| | | 29.9 | | 31.6 | |

^a HPLC yields from triplicate measurements, the deviation between parallel measurements did not exceed 1.5%;

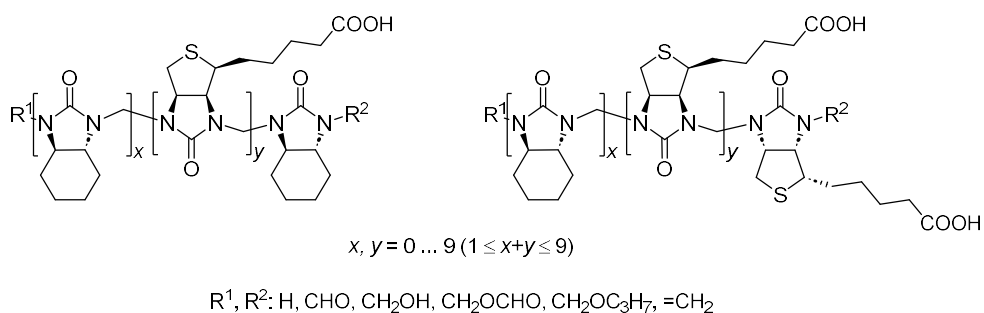
^b HPLC yields expressed as the mean value ± standard deviation between reactions reproduced n times.

^c Reaction mixture was milled for 20 min and it resulted in lower yields compared to 60 min milling.

Optimal aging time is 3 hours for 60 min milled reactions.

2.3 Analysis of Oligomers and Side-Products

2.3.1. General oligomeric and macrocyclic profile



The iminium intermediates can react with isopropanol used in sample preparation (1:1 chloroform : isopropanol solvent mixture), which results in $-CH_2OC_3H_7$ terminal groups.

General oligomeric and macrocyclic profile of crude reaction mixtures was studied on Agilent 6540 Accurate-Mass Q-TOF mass-spectrometer, using the HPLC setup from system B. The mass spectra were acquired in positive polarity, mass range m/z 50 – 3200 and fragmentor voltage 175 V. The AJS-ESI source parameters were set as follows: gas temperature 200 °C, drying gas flow 6 L/min, nebulizer pressure 30 psi, sheath gas temperature 200 °C, sheath gas flow 8 L/min, capillary voltage 3500 V, nozzle voltage 1000 V, skimmer voltage 65 V, octopole peak-peak voltage 750 V. Prior to analysis the instrument was tuned in m/z 50–3200 mass range.

The collected data was processed with the aid of MatchMass Tool.⁶

Composition of the crude mixtures after different milling duration (HPLC-HRMS)

| | | | |
|----------|----------------|----------|-----------------------------|
| A | 5 min milling | G | 5 min milling + 24 h aging |
| B | 10 min milling | H | 10 min milling + 24 h aging |
| C | 20 min milling | I | 20 min milling + 24 h aging |
| D | 30 min milling | J | 30 min milling + 24 h aging |
| E | 45 min milling | K | 45 min milling + 24 h aging |
| F | 60 min milling | L | 60 min milling + 24 h aging |

Reaction conditions: D-biotin (45–46 mg, 0.19 mmol, 1 eq.), (*R,R*)-*N,N'*-cyclohexa-1,2-diylurea (183 mg, 1.31 mmol, 7 eq.), paraformaldehyde (45 mg, 1.50 mmol, 8 eq.) and KPF_6 (34–35 mg, 0.19 mmol, 1 eq.) and 55% aq. HPF_6 (60 μ l, 0.37 mmol, 2 eq.) were milled for 5–60 minutes and aged 60 °C for 24 hours. The samples for analysis were collected after milling and after aging.

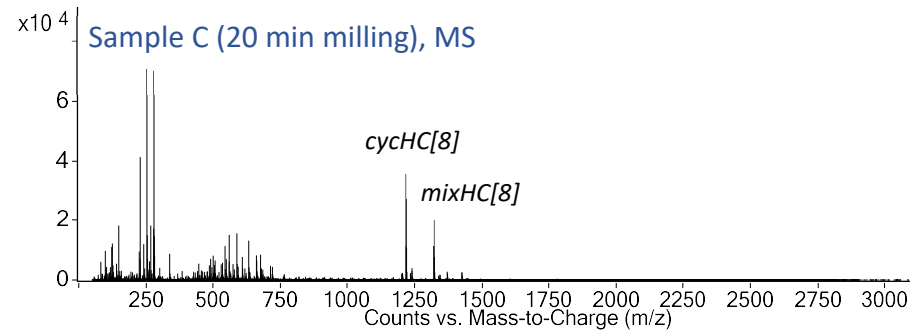
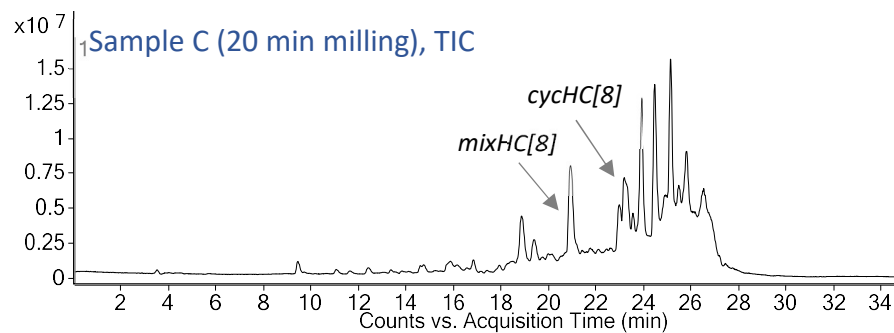
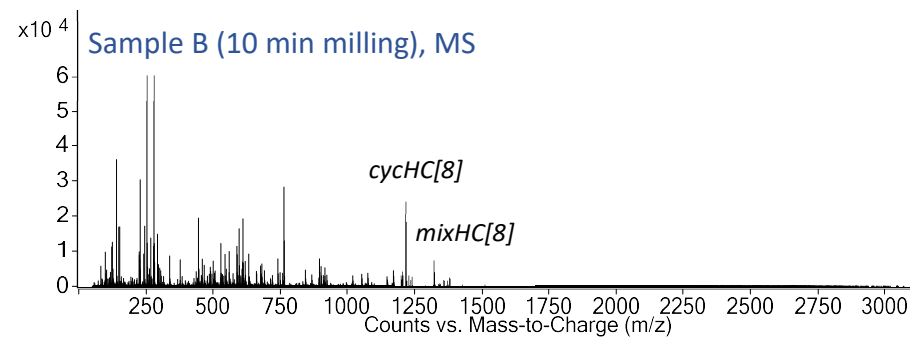
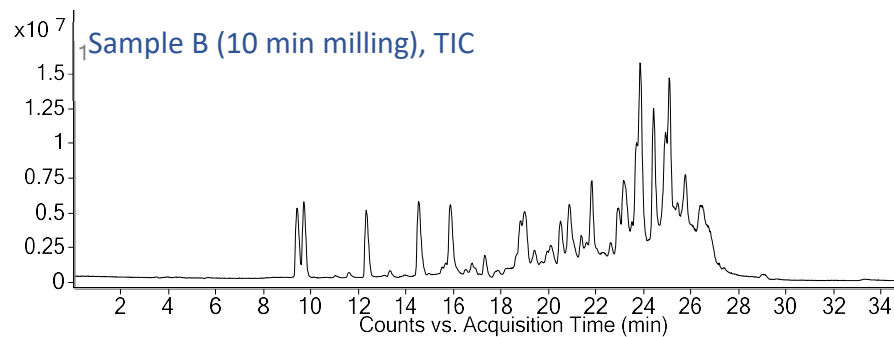
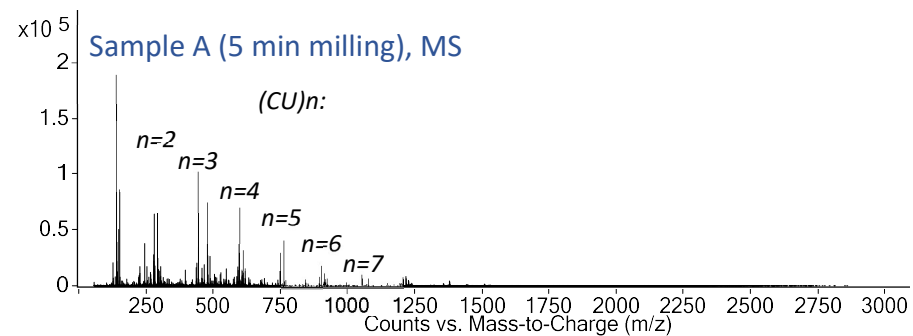
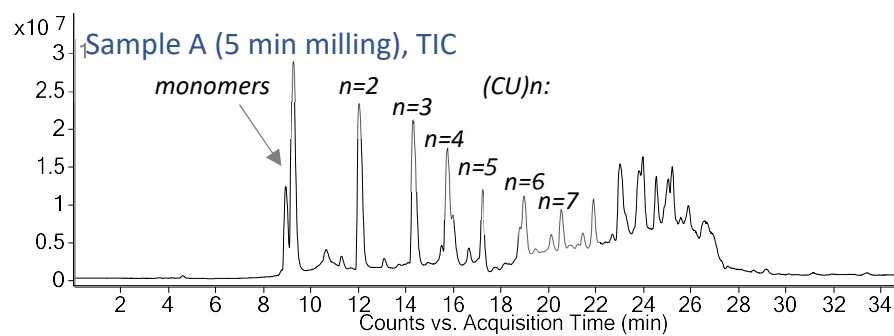


Figure S6. Total ion chromatograms and mass spectra of samples A–C.

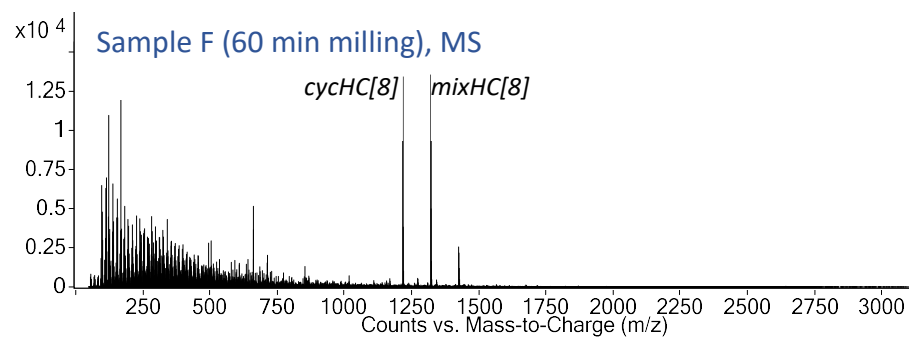
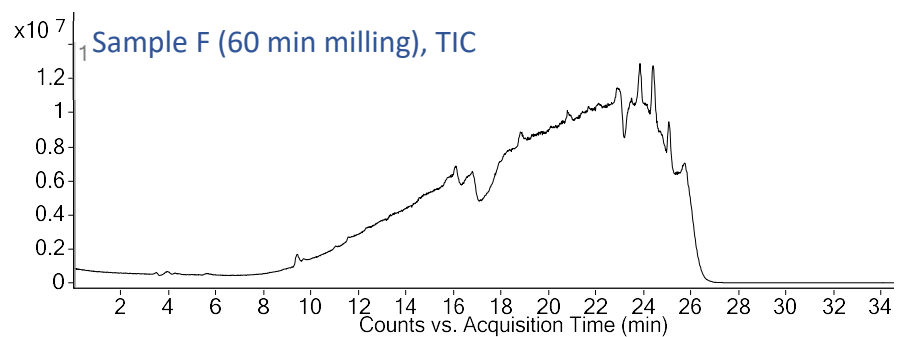
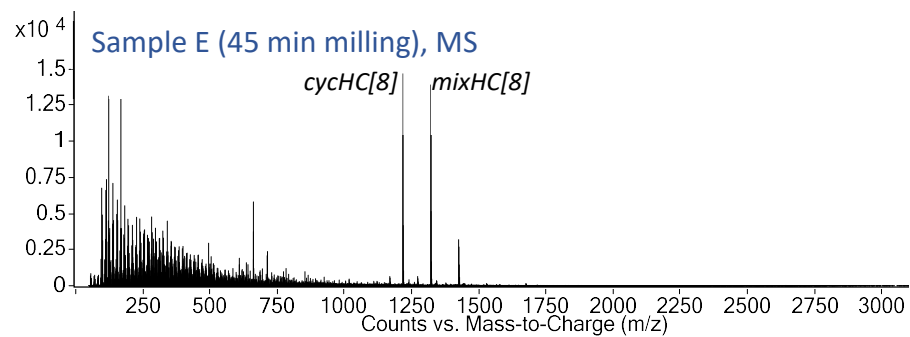
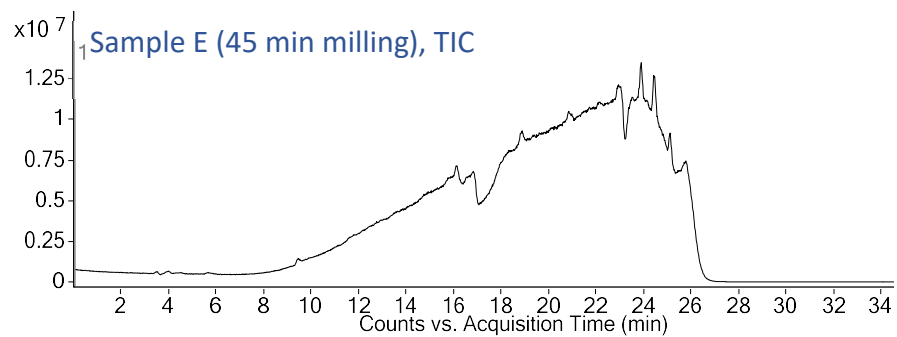
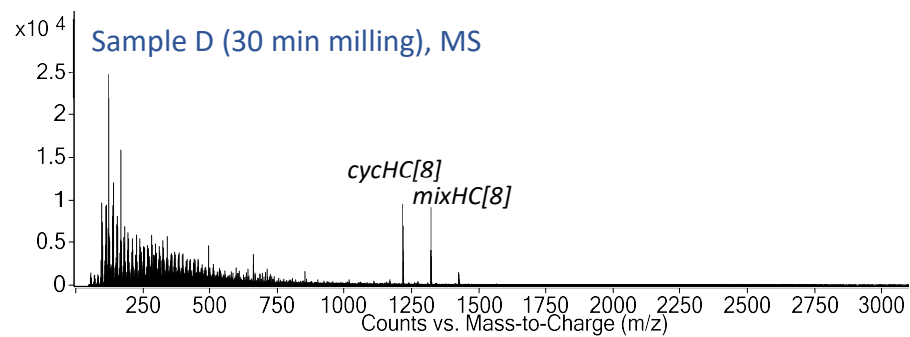
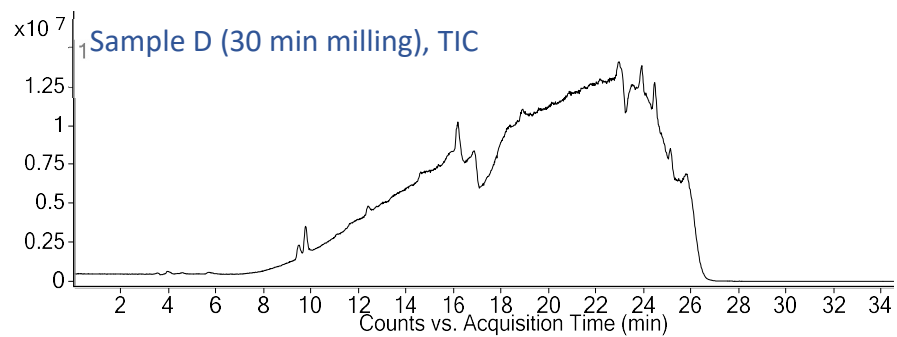


Figure S7. Total ion chromatograms and mass spectra of samples D–F.

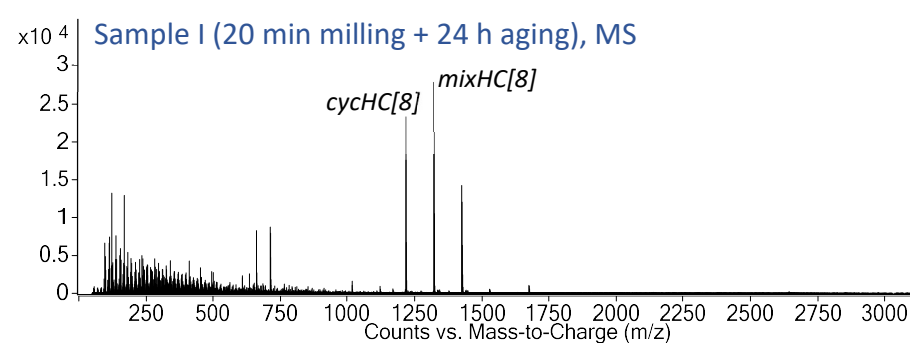
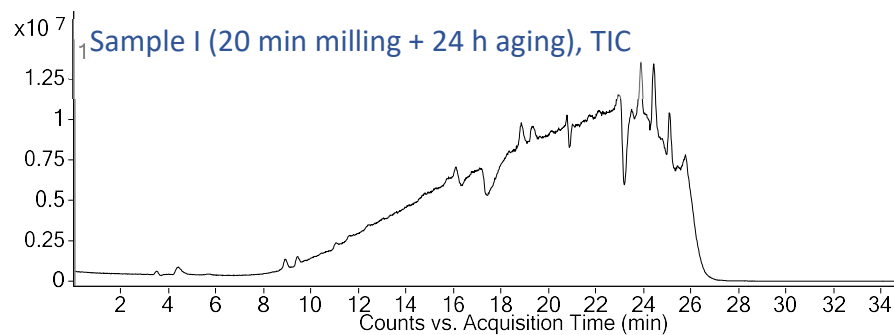
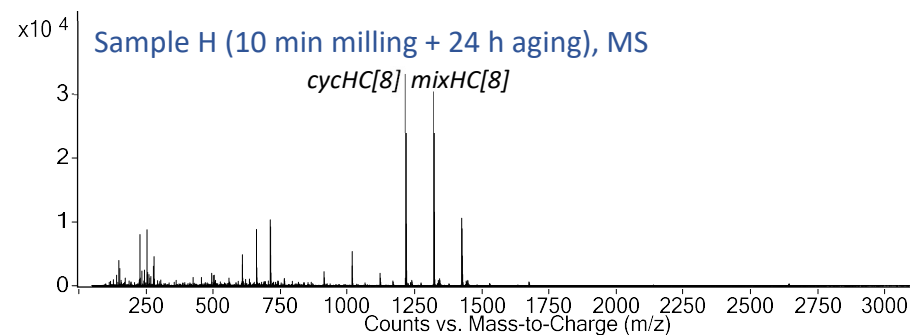
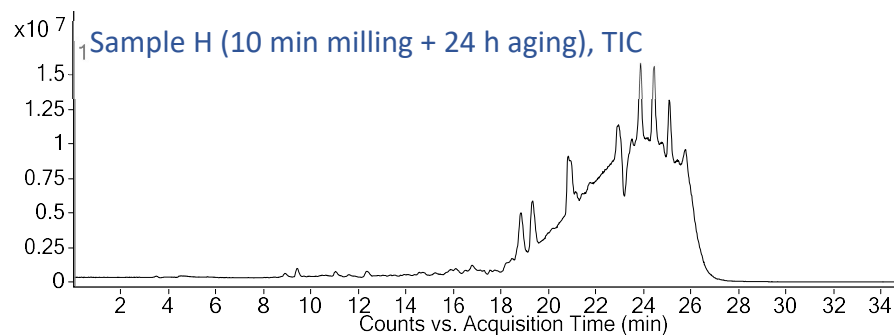
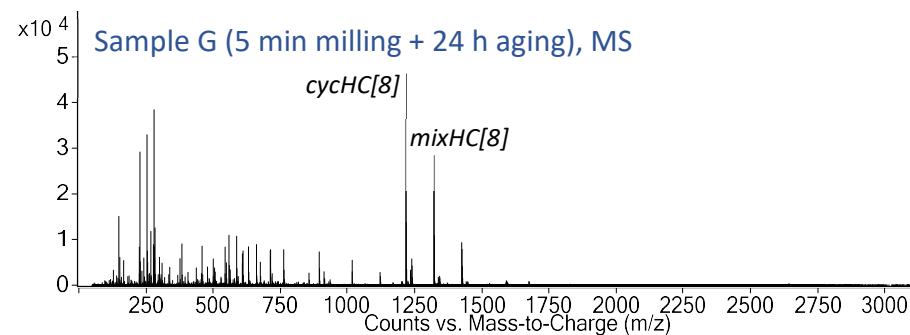
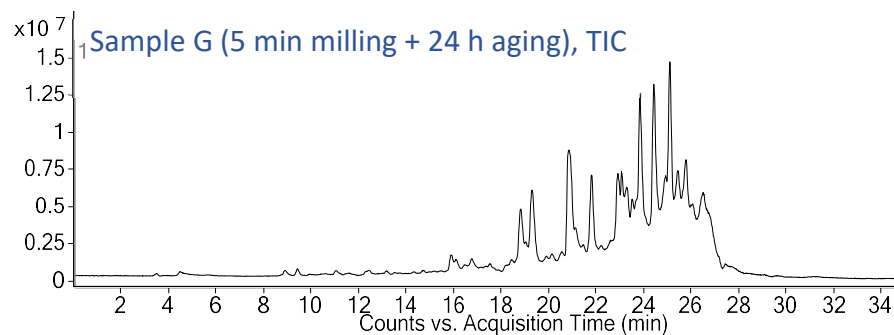


Figure S8. Total ion chromatograms and mass spectra of samples G–I.

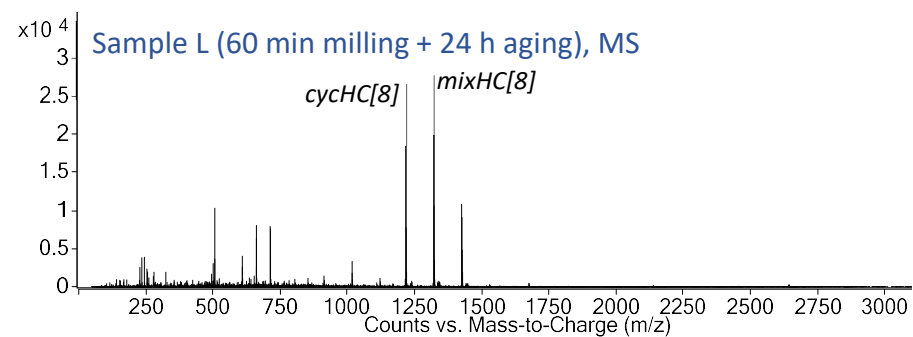
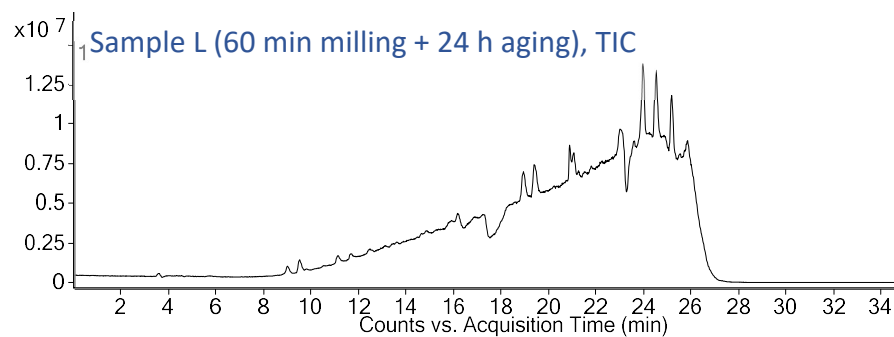
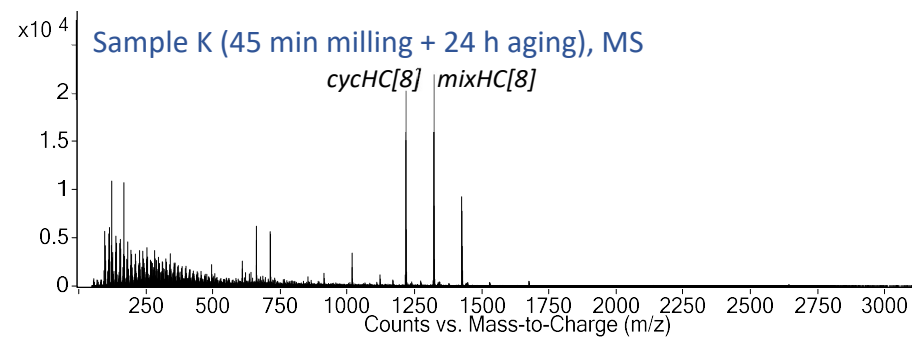
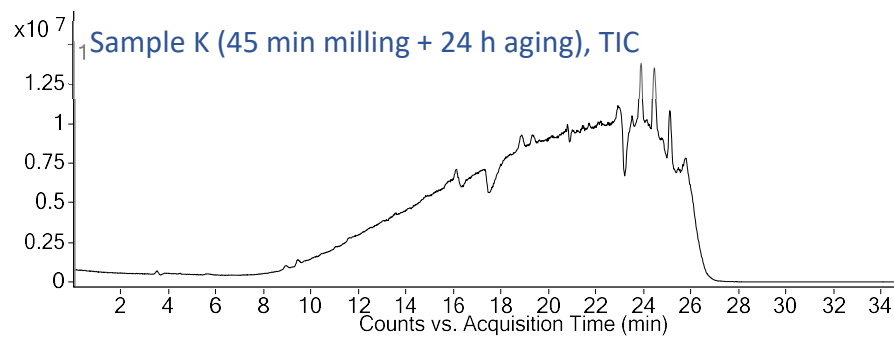
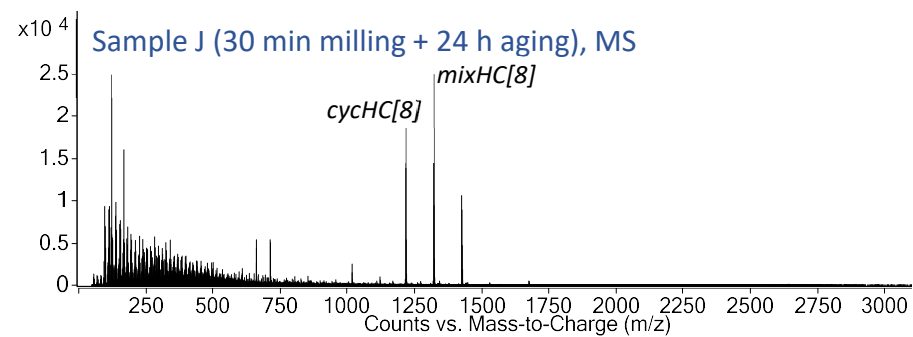
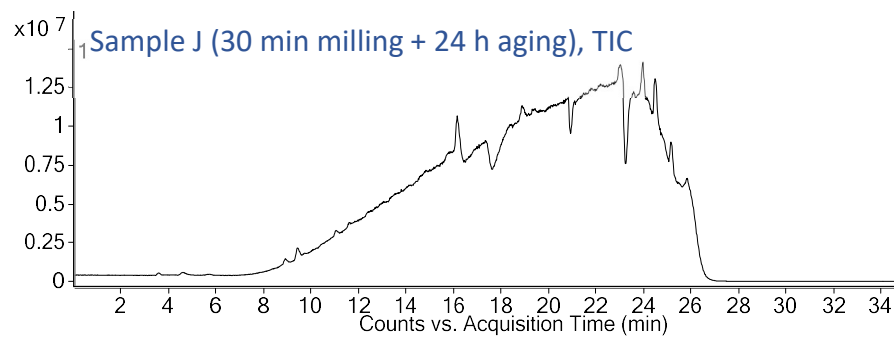


Figure S9. Total ion chromatograms and mass spectra of samples J–L.

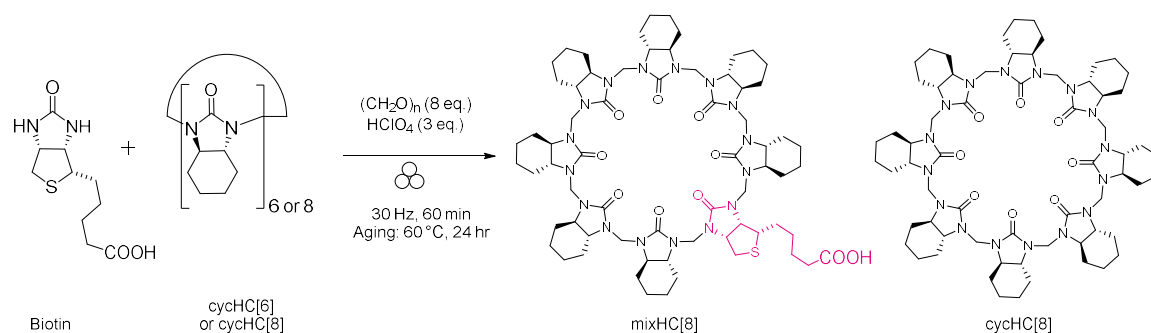


Figure S10. Relative abundance of the observed monomers, oligomers and macrocycles⁶, visualized as a heat map⁷. See details in separate file with Table S29 .

Table S16. Relative abundance (%) of detected species used in the heat map in the main text.

| Oligomers | <i>n</i> | A | B | C | D | E | F | G | H | I | J | K | L |
|---------------------|----------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|
| Monomers | 1 | 25.92 | 15.51 | 12.27 | 18.48 | 4.51 | 7.77 | 2.01 | 3.27 | 3.19 | 3.84 | 1.89 | 4.54 |
| Homomeric oligomers | 2-3 | 37.69 | 33.24 | 17.96 | 29.16 | 21.54 | 23.67 | 18.24 | 4.65 | 16.69 | 18.66 | 12.70 | 5.63 |
| | 4-5 | 23.65 | 26.32 | 8.72 | 4.89 | 2.48 | 3.38 | 9.05 | 4.54 | 1.34 | 2.55 | 2.59 | 0.62 |
| | 6-8 | 7.30 | 10.76 | 10.40 | 4.99 | 5.96 | 5.35 | 0.28 | 0.03 | - | 4.97 | 5.87 | 0.08 |
| | 9-10 | 0.92 | 0.18 | 0.30 | 0.05 | 0.00 | 0.03 | 0.14 | - | - | - | - | - |
| Mixed oligomers | 2-3 | 2.03 | 1.74 | 2.64 | 1.84 | 1.81 | 3.34 | 0.92 | 1.67 | 2.56 | 1.88 | 1.68 | 1.97 |
| | 4-5 | 0.80 | 1.75 | 2.62 | 6.76 | 3.49 | 6.42 | 1.11 | 1.94 | 3.42 | 5.45 | 2.62 | 3.33 |
| | 6-8 | 0.26 | 1.28 | 4.67 | 8.08 | 11.95 | 10.47 | 8.73 | 13.50 | 15.83 | 13.47 | 14.31 | 16.63 |
| | 9-10 | 0.02 | 0.03 | 0.00 | 0.20 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.04 | 0.00 | 0.05 |
| mixHC[8] | 8 | 0.02 | 1.11 | 8.95 | 10.79 | 20.40 | 17.74 | 16.89 | 24.77 | 22.68 | 20.64 | 22.38 | 26.51 |
| cycHC[8] | 8 | 1.31 | 7.32 | 30.06 | 11.07 | 21.21 | 17.73 | 29.04 | 27.10 | 19.05 | 15.74 | 20.61 | 25.89 |
| other HC[8] | 8 | - | 0.14 | 1.42 | 1.97 | 4.94 | 3.32 | 5.93 | 9.96 | 12.24 | 8.80 | 9.67 | 10.44 |
| other HC | 6-7 | 0.08 | 0.62 | - | 1.72 | 1.70 | 0.77 | 7.66 | 8.56 | 3.00 | 3.96 | 5.67 | 4.31 |

2.3.2 Crossover of monomer units between cycHC[*n*] and biotin



General synthesis procedure for screening reaction with cycHC[6] as starting material: D-biotin (56 mg, 0.23 mmol, 1 eq.) and (*R,R*)-cyclohexanohemicucurbit[6]uril (249 mg, 0.270 mmol, 1.2 eq.) and 70% aq. HClO₄ (60 μl, 0.69 mmol, 3 eq.) were milled for 60 minutes and aged at 60 °C for 24 hours.

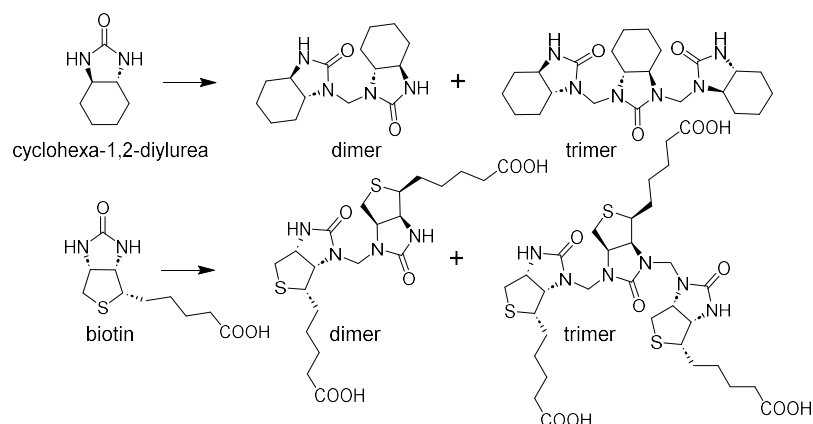
General synthesis procedure for screening reaction with cycHC[8] as starting material: D-biotin (55 mg, 0.23 mmol, 1 eq.) and (*R,R*)-cyclohexanohemicucurbit[8]uril (240 mg, 0.196 mmol, 0.9 eq.) and 70% aq. HClO₄ (58 μl, 0.68 mmol, 3 eq.) were milled for 60 minutes and aged at 60 °C for 24 hours.

Table S17. MixHC[8] synthesis using cycHC[*n*] macrocycles as starting material

| Entry | Biotin:cycHC[<i>n</i>] molar ratio ^a | HClO ₄ , eq. | HPLC yield, % | |
|-------|--|-------------------------|---------------|----------|
| | | | mixHC[8] | cycHC[8] |
| 1 | 1:1.2 (cycHC[6]) | 3 | 10 | 47 |
| 2 | 1:0.9 (cycHC[8]) | 3 | 9 | 51 |

^a Ratio of starting materials was chosen to satisfy 1:7 ratio of monomers in mixHC[8], each reaction was performed once. The deviation between triplicate HPLC measurements did not exceed 1%.

2.3.3 Quantitative analysis of dimers and trimers



The quantitative determination of uniformly composed $\text{CU}[n]$ and $\text{B}[n]$ ($n = 2$ or 3) in crude reaction mixtures was performed for the samples A–L (see 1.3.1) and additional sample T0 for 0 min reaction time. The sampling was performed in triplicate, as outlined in page S3. If necessary, the solutions were diluted to ensure the peak areas were within the linear range of the method.

Quantification of the oligomers was performed using the HPLC setup from system B, following the target m/z values corresponding to the chosen oligomeric species $[\text{M}+\text{H}]^+$ and $[\text{M}+\text{Na}]^+$. The chromatograms were acquired in positive polarity with the following ESI source parameters: drying gas temperature 300 °C, drying gas flow 5 L/min, nebulizer pressure 60 psig, vaporizer temperature 150 °C, capillary voltage 2000 V, charging voltage 2000 V, fragmentor voltage 140 V.

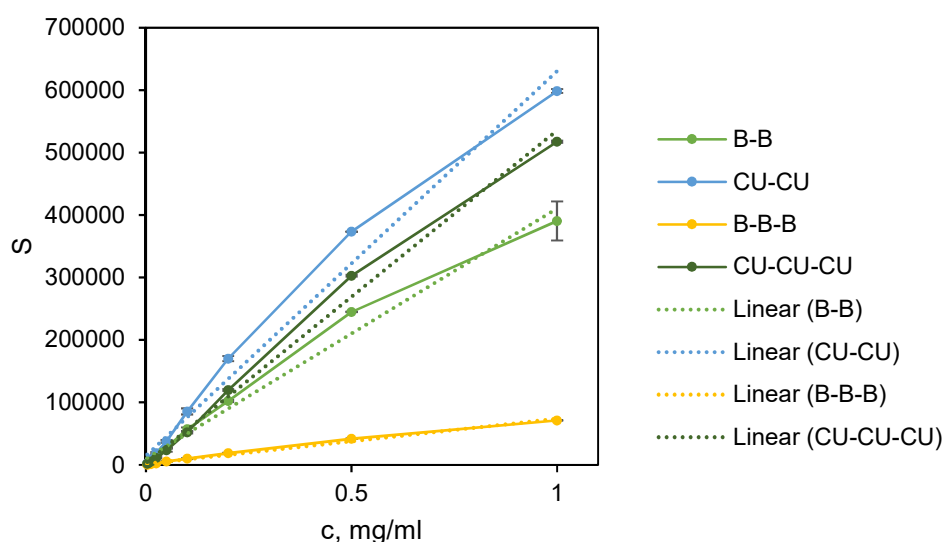


Figure S11. Full studied range for determination of the method linearity. The error bars express deviation between two parallel measurements. Note: the concentration units are not related to the real concentrations of the oligomers, as the latter have not been isolated.

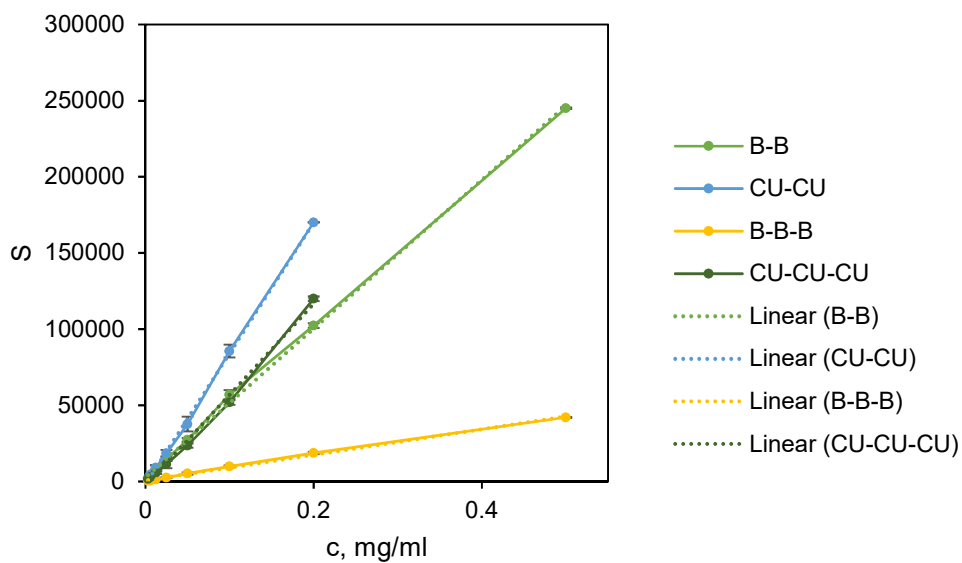


Figure S12. Established linear range of the method. The error bars express deviation between two parallel measurements. Note: the concentration units are not related to the real concentrations of the oligomers, as the latter have not been isolated.

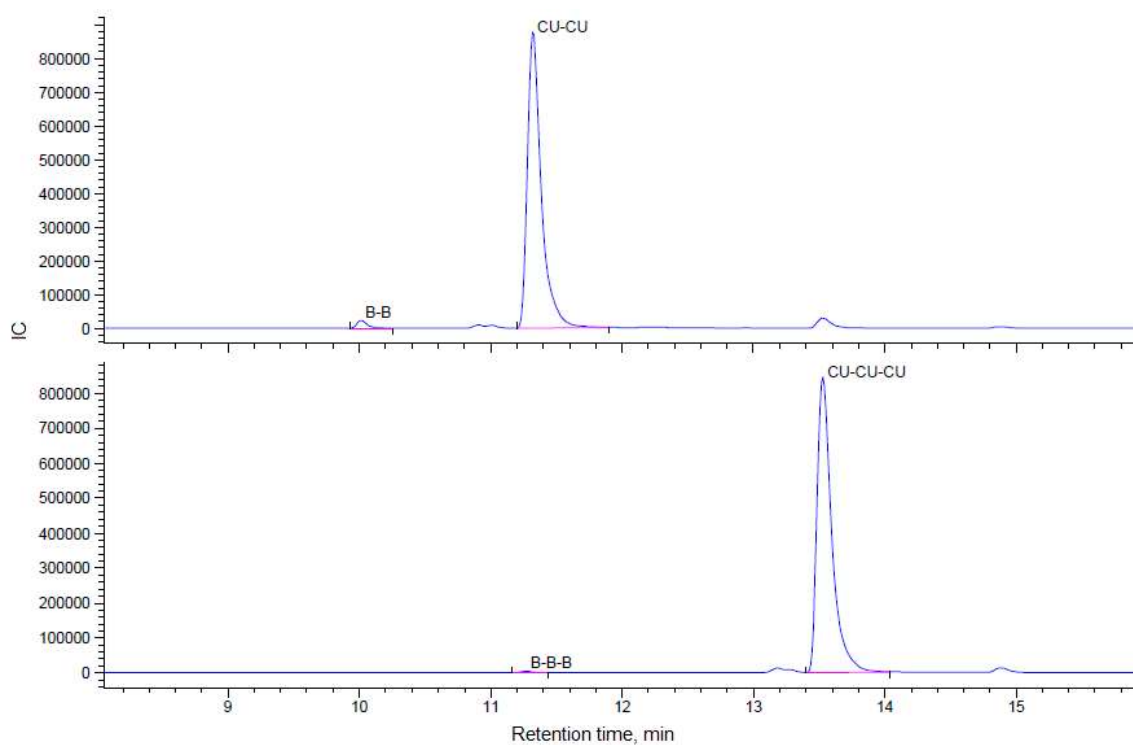


Figure S13. SIM chromatograms of dimers and trimers in sample A.

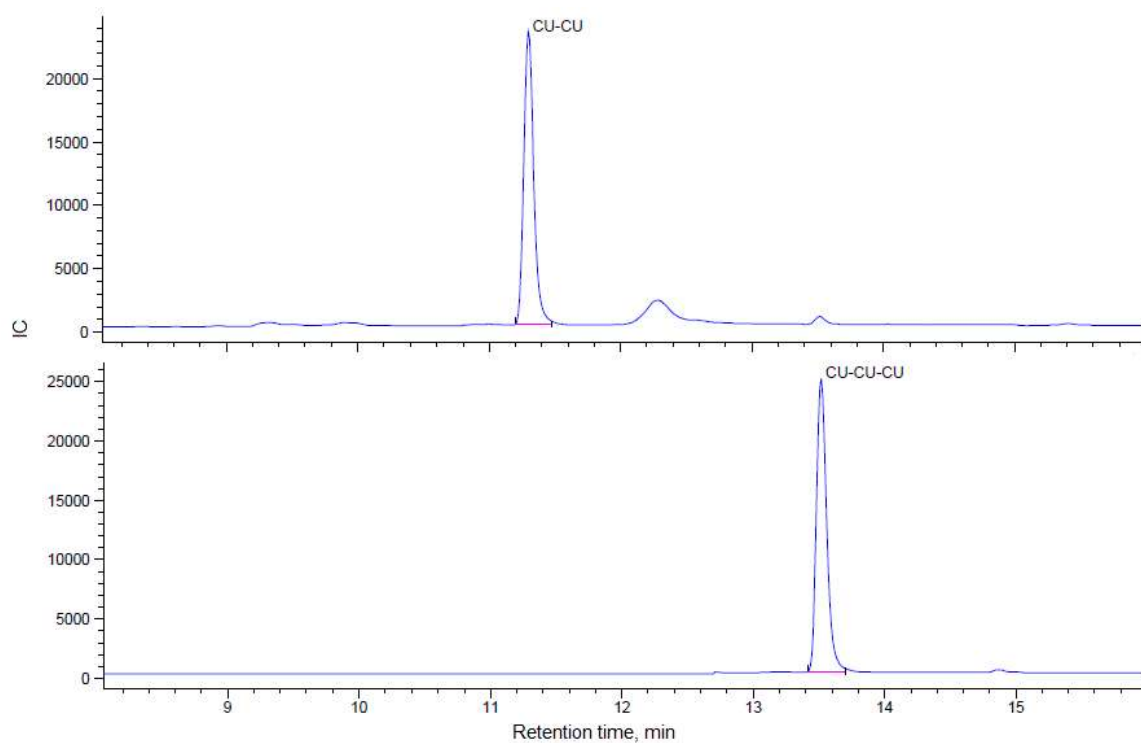


Figure S14. SIM chromatograms of dimers and trimers in sample A diluted 200 times.

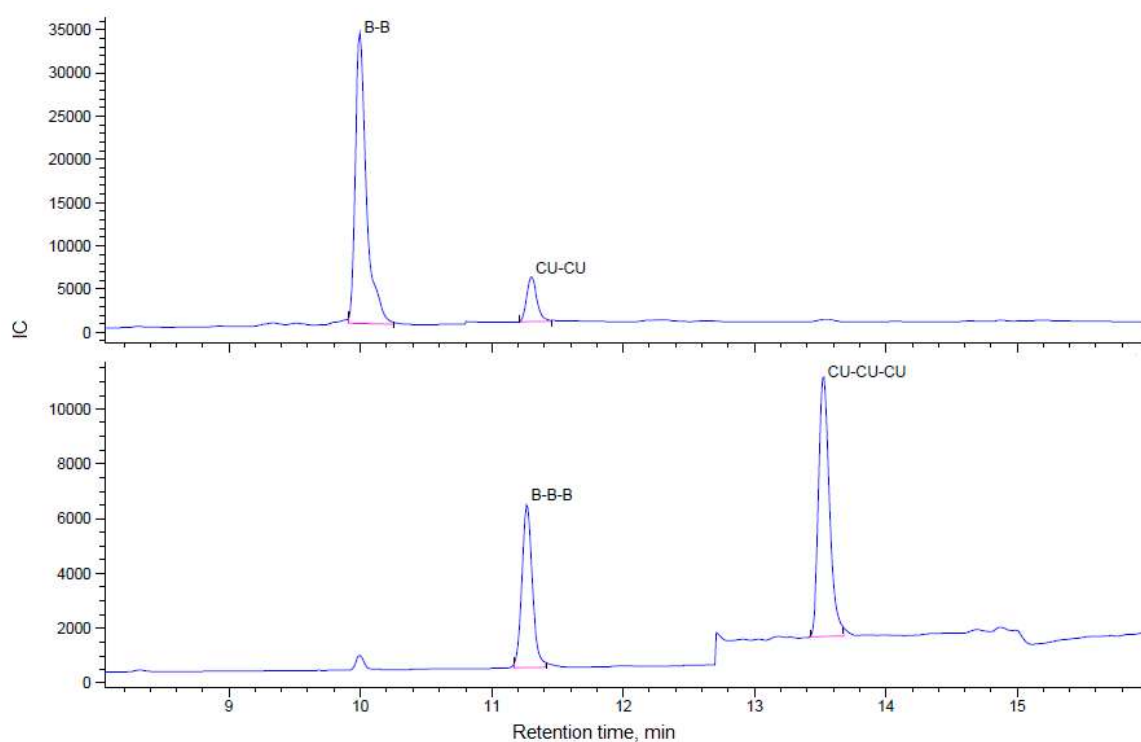


Figure S15. SIM chromatograms of dimers and trimers in sample L.

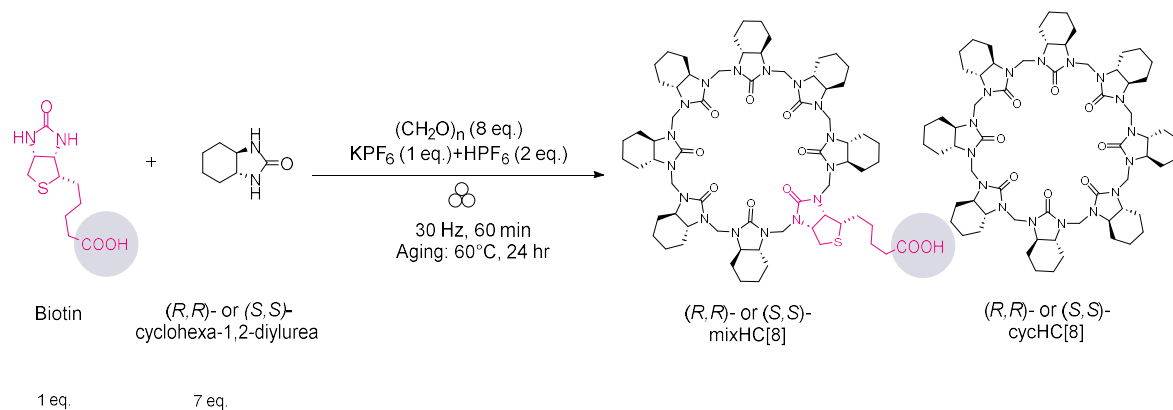
Table S18. Distribution of short homomeric oligomers after milling and aging.

| Sample | Milling time, min | Aging time, h | Peak area, IC's | | | | HPLC yield, % | |
|--------|-------------------|---------------|-----------------|-------------------------------|------------|-------------------------------|---------------|------------|
| | | | B-B | CU-CU | B-B-B | CU-CU-CU | mixHC[8] | cycHC[8] |
| T0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| A | 5 | 0 | 118000±14000 | 30400000±8400000 ^a | 25100±3100 | 29700000±4300000 ^a | 1.9±0.3 | 4±2 |
| B | 10 | 0 | 46500±9200 | 1100000±310000 ^b | 13200±2200 | 1620000±460000 ^b | 3.4±0.2 | 11±1 |
| C | 20 | 0 | 130300±5200 | 38000±1900 | 22300±1200 | 73000±2900 | 7.7±0.3 | 18.13±0.01 |
| D | 30 | 0 | 84100±4900 | 115000±50000 | 10490±490 | 160000±56000 | 6.6±0.2 | 10±1 |
| E | 45 | 0 | 50100±6700 | 11165±940 | 5770±180 | 26100±2400 | 11.0±0.3 | 17±1 |
| F | 60 | 0 | 96600±2200 | 33000±3000 | 10200±120 | 75500±5800 | 11.4±0.3 | 15±1 |
| G | 5 | 60 | 57200±8200 | 32800±1300 | 7570±340 | 2470±560 | 15.8±0.3 | 57.6±0.1 |
| H | 10 | 60 | 94000±12000 | 31500±6200 | 19900±1800 | 28600±2100 | 24±1 | 41.6±0.3 |
| I | 20 | 60 | 175500±3600 | 25130±710 | 32100±1100 | 38990±960 | 36±1 | 38±1 |
| J | 30 | 60 | 185900±6500 | 33400±1800 | 31390±930 | 60500±370 | 36±1 | 36±1 |
| K | 45 | 60 | 74100±1100 | 17430±540 | 9850±240 | 35300±470 | 26±1 | 29±1 |
| L | 60 | 60 | 206000±5800 | 28300±910 | 34200±1500 | 52800±2200 | 34.9±0.2 | 36±1 |

The peak areas are reported as the mean value ± standard deviation of triplicates. [a] The sample was diluted 200 times. [b] The sample was diluted 50 times. For the diluted samples, the peak area was divided by corresponding dilution factor

3. Preparative Synthesis, Purification, and Characterization of mixHC[8]

Best reaction conditions from the screening was selected for the synthesis of mixHC[8] in gram-scale.



General synthesis procedure: D-Biotin (45 mg, 0.19 mmol, 1 eq.), (R,R) -or (S,S) - N,N' -cyclohexa-1,2-diylurea (183 mg, 1.30 mmol, 7 eq.) and paraformaldehyde (45 mg, 1.49 mmol, 8 eq.) were placed into a 14 mL ZrO_2 -coated jar charged with two 10 mm ZrO_2 balls (3.5 g). After addition of 55% aq. HPF_6 (60 μL , 0.37 mmol, 2 eq.) and KPF_6 (34 mg, 0.19 mmol, 1 eq.) the mixture was milled at 30 Hz for 60 minutes. The jar was then sealed with parafilm and reaction mixture was aged at 60 °C for 24 hours. The crude mixture was further washed on a glass filter with distilled water until neutral pH, which was determined by test strips. The quenched mixture was dried in open air at room temperature. The procedure was repeated 8 times with both diastereoisomers, resulting in 2.6 g of crude product with each diastereoisomer for further purification.

Purification procedure: To convert mixHC[8] into potassium salt 350 mL of 5% KOH/MeOH solution was added to the dry quenched reaction mixture, followed by stirring for 45 min and resulting in white heterogeneous mixture. MeOH and water were evaporated via azeotropic removal with toluene (50 mL \times 3) until light yellow dry mixture was obtained. Solid-liquid toluene extraction was performed three times with 70 mL of toluene and allowed to remove cycHC[8]. The remaining mixture in the flask and on the filter was dissolved in 350 mL of distilled water, providing white milky suspension. The aqueous mixture was then acidified with conc. HCl till pH 2–3. The precipitated solid was then filtered and left to dry. The dried solid was purified by flash column chromatography (gradient 0–50% $i\text{PrOH}$ (1% acetic acid)/ CH_2Cl_2). This procedure afforded pure mixHC[8] and cycHC[8] with oligomers which were not separated in pure form.

225 mg of (+)-mixHC[8] (isolated yield 11%, NMR purity 90%), and 320 mg (–)-mixHC[8] (isolated yield 16%, NMR purity 88%) was obtained. NMR purity was assessed using internal standard.⁸

Both diastereoisomers were characterized with HRMS, 1D and 2D (COSY, TOCSY, HSQC, TOCSY-HSQC, HMBC, NOESY) NMR, IR and optical rotation.

(-)-((S,S,R)(R,R)₇)-mixHC[8]:

¹H NMR (800 MHz, CDCl₃) δ 4.93 (d, *J* = 14.5 Hz, 1H, CH[h8(1)]), 4.83 (d, *J* = 14.4 Hz, 1H, CH[h8(2)]), 4.83–4.80 (m, 1H, CH[a11(1)]), 4.83–4.76 (m, 6H, CH₂[b8, d8, f8]), 4.67–4.64 (m, 1H, CH[a11(2)]), 4.67–4.58 (m, 6H, CH₂[c8, e8, g8]), 4.25 (dt, *J* = 9.9, 6.2 Hz, 1H, CH(a2)), 3.86 (dd, *J* = 9.9, 6.0 Hz, 1H, CH(a3)), 3.46 (ddd, *J* = 12.6, 6.1, 2.5 Hz, 1H, CH(a4)), 3.09 (dd, *J* = 12.8, 5.6 Hz, 1H, CH[a5(1)]), 2.94–2.89 (m, 1H, CH[a5(2)]), 2.90–2.79 (m, 7H), 2.70–2.61 (m, 7H), 2.59 (tt, *J* = 11.2, 3.2 Hz, 2H), 2.51 (tt, *J* = 11.1, 2.6 Hz, 2H), 2.49 – 2.45 (m, 2H), 2.41 – 2.35 (m, 2H), 2.37 (t, *J* = 7.2 Hz, 2H, CH₂(a9)), 2.35–2.28 (m, 3H), 2.28–2.24 (m, 1H), 2.18–2.14 (m, 1H), 1.94–1.64 (m, 12H), 1.82–1.63 (m, 6H, CH₂(a8)+4H), 1.49–1.39 (m, 7H, CH₂(a7)+5H), 1.38–1.30 (m, 6H, CH₂(a6)+4H), 1.29–1.23 (m, 8H), 1.21–1.07 (m, 10H).

¹³C NMR (201 MHz, CDCl₃) δ 177.33(a10), 162.62, 162.60(h1), 162.07(b1), 162.01, 161.89, 161.80, 161.79, 157.99(a1), 65.31, 65.06, 64.93, 64.68, 64.62, 64.50, 62.07(a3), 59.82, 59.79, 59.74(4C), 59.67, 58.99(h2), 58.54(a2), 56.59, 56.00, 55.48, 52.52(a4), 51.96(a11), 48.34(h8), 46.80, 46.79, 46.59, 33.93(a9), 33.81(a5), 28.90(2C), 28.89(2C), 28.82, 28.57, 28.44, 28.18(a8), 27.72, 27.66(2C), 27.64, 27.62, 27.51, 27.49(a6), 27.35, 25.45, 24.72, 24.58, 24.54, 24.48(a7+C), 24.44, 24.43, 24.39(2C), 24.26(2C), 24.23, 24.15(3C).

HRMS (AJS-ESI) calcd. for C₆₇H₉₉N₁₆O₁₀S⁻ [M-H]⁻ 1319.7456, found *m/z* 1319.7469.

IR (KBr pellet): ν = 3484, 2936, 2858, 1710, 1436, 1358, 1332, 1309, 1231, 1133, 1057, 1013, 986, 918, 830, 772, 627, 531, 515 cm⁻¹.

Optical rotation [α]_D²⁰ = -76.0 (*c* 0.132, CHCl₃)

Melting point 238-242 °C

(+)-((S,S,R)(S,S)₇)-mixHC[8]:

¹H NMR (800 MHz, CDCl₃) δ 4.83–4.74 (m, 8H, CH₂[c8, e8, g8, a11]), 4.75 (d, *J* = 7.0 Hz, 1H, CH[h8(1)]), 4.69 (d, *J* = 14.4 Hz, 1H, CH[h8(2)]), 4.60 (dd, *J* = 10.0, 3.7 Hz, 6H, CH₂[b8, d8, f8]), 4.10 (dd, *J* = 9.7, 5.8 Hz, 1H, CH(a3)), 3.88 (dt, *J* = 10.5, 6.0 Hz, 1H, CH(a2)), 3.36 (ddd, *J* = 12.6, 5.9, 2.9 Hz, 1H, CH(a4)), 3.11 (dd, *J* = 13.0, 5.2 Hz, 1H, CH[a5(1)]), 3.04 (dd, *J* = 13.0, 6.6 Hz, 1H, CH[a5(2)]), 2.89 – 2.77 (m, 8H), 2.66 – 2.55 (m, 10H), 2.47 (qd, *J* = 10.9, 3.0 Hz, 2H), 2.46 – 2.42 (m, 2H), 2.40–2.24 (m, 10H), 2.15 (d, *J* = 11.4 Hz, 1H), 1.91–1.75 (m, 12H), 1.72–1.71 (m, 1H, CH[a6(1)]), 1.75–1.63 (m, 7H), 1.49 (q, *J* = 6.6 Hz, 1H), 1.46–1.35 (m, 7H), 1.33 (d, *J* = 4.2 Hz, 1H, CH[a6(2)]), 1.32–1.28 (m, 4H), 1.27–1.04 (m, 14H).

¹³C NMR (201 MHz, CDCl₃) δ 177.10(a10), 163.11(h1), 162.37(b1), 162.17, 161.95, 161.84, 161.74, 161.71, 158.19(a1), 65.20, 65.20, 65.08, 65.06, 64.97, 64.93, 64.87, 64.55, 64.49, 61.54(a3), 59.87, 59.75, 59.73, 59.71, 59.59(a2), 59.23, 56.55, 56.38, 55.32, 53.88(h8),

53.35(a4), 46.82, 46.78, 46.68(a11), 46.63, 34.42(a5), 33.97, 28.98, 28.92, 28.92, 28.89, 28.86, 28.64, 28.63, 28.48, 28.21, 27.74, 27.69, 27.66, 27.63, 27.59, 27.58, 27.47, 27.38, 24.59, 24.57, 24.54, 24.49, 24.47, 24.46, 24.41, 24.41, 24.24, 24.22, 24.17, 24.16, 24.06, 24.05.

HRMS (AJS-ESI) calcd. for $C_{67}H_{99}N_{16}O_{10}S^-$ $[M-H]^-$ 1319.7456, found m/z 1319.7436.

IR (KBr pellet): $\nu = 3502, 2936, 2859, 1710, 1437, 1357, 1332, 1309, 1259, 1132, 1057, 1013, 986, 918, 831, 773, 627, 531, 515\text{ cm}^{-1}$.

Optical rotation $[\alpha]_D^{20} = +31.6$ (c 0.121, $CHCl_3$)

Melting point 245-250 °C

3.1 NMR spectra

(-)-mixHC[8] (left) and (+)-mixHC[8] (right):

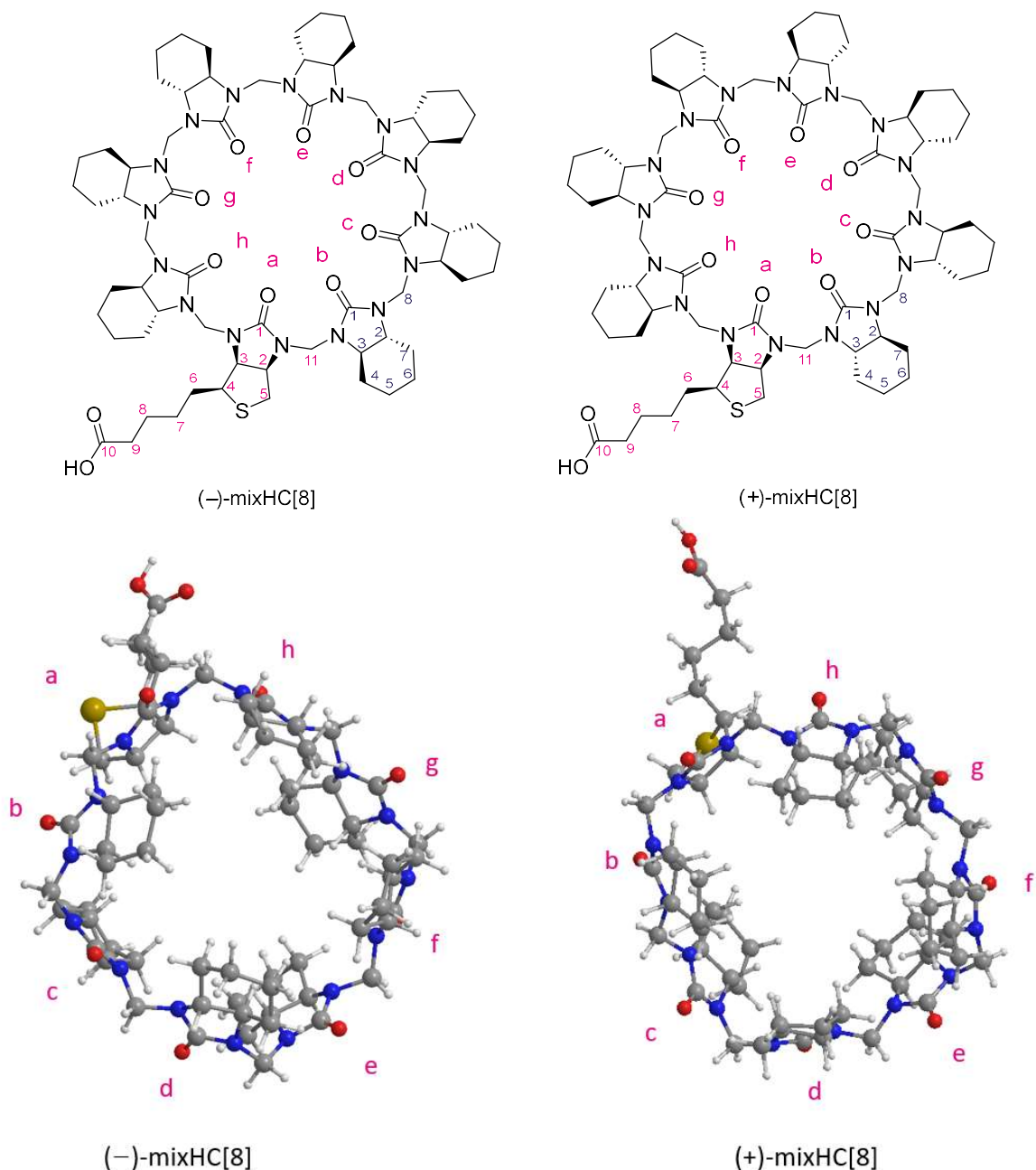


Figure S16. Structures of mixHC[8] diastereoisomers for NMR assignment. 3D structures were obtained from DFT calculations.

MixHC[8] macrocycle is not symmetrical, therefore the NMR analysis is complex. Determining the bridge protons of the diastereoisomers were analogous to cycHC[8]. From 3D structure viewed from above it is seen that there are 90 degree angles and the protons which are on that angle are coupled by each other (geminal coupling) and those protons have bigger chemical shift.

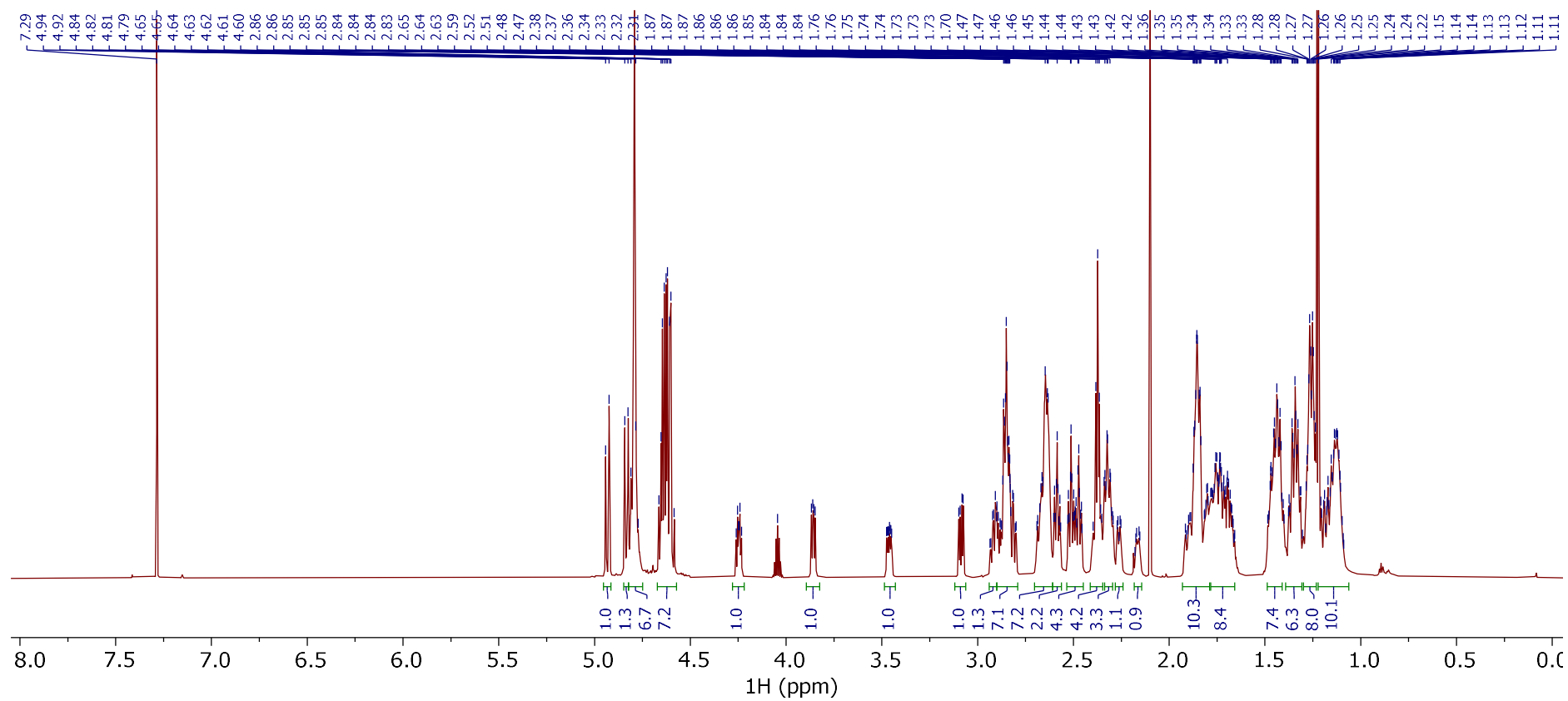


Figure S17. The full ^1H NMR spectra from (-)-mixHC[8]

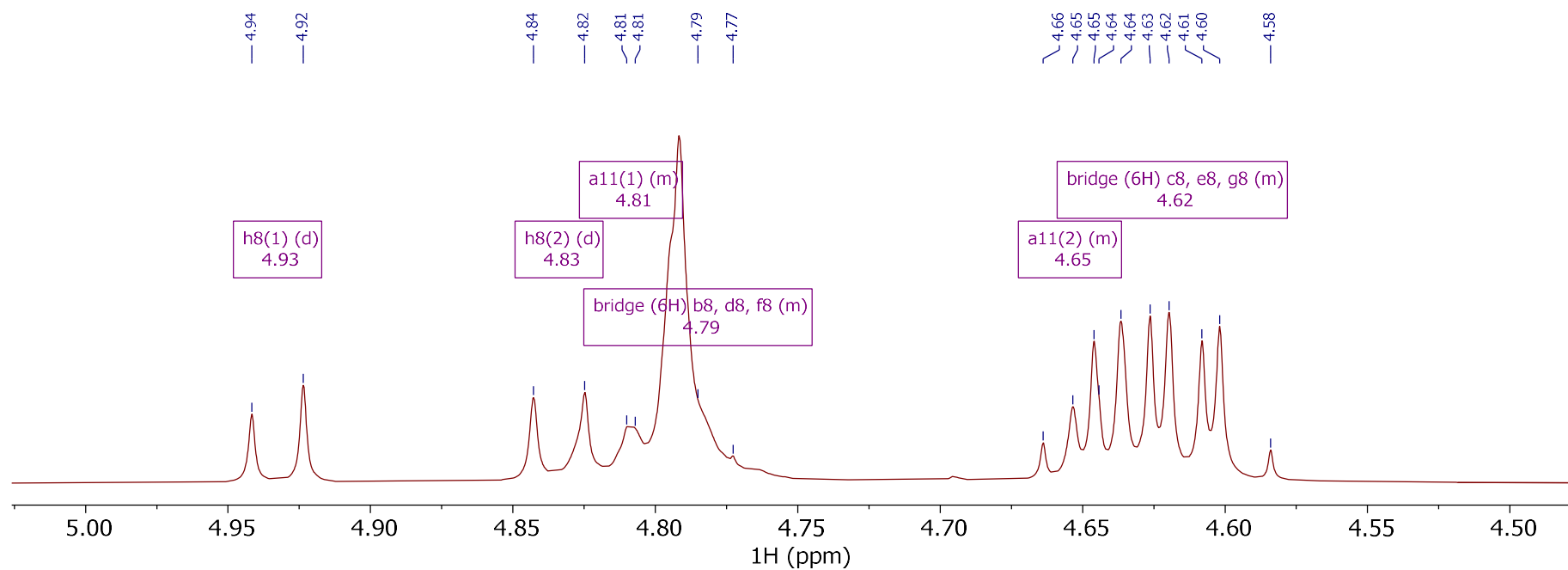


Figure S18. Fragment of ^1H NMR spectra showing bridge protons of $(-)\text{-mixHC[8]}$ in range of 4.58-4.94 ppm.

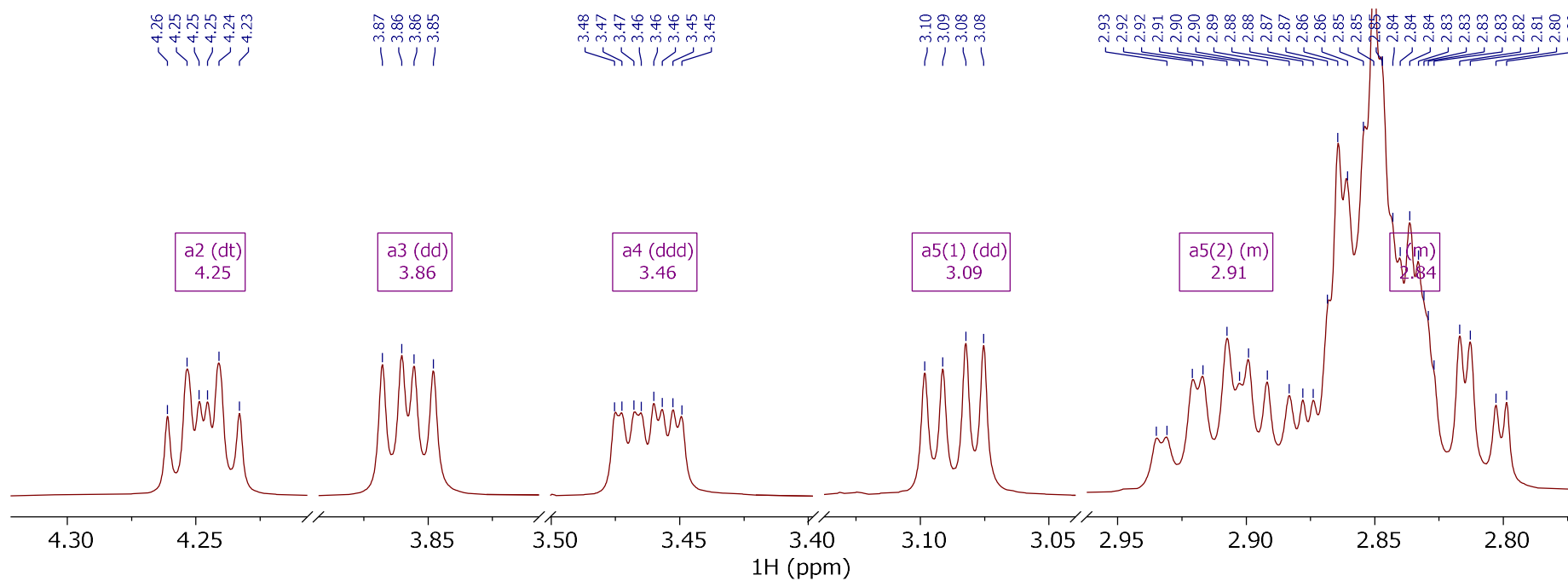


Figure S19. Fragment of ^1H NMR spectra showing biotin monomer's thiolane motif protons of (-)-mixHC[8] in range of 2.87-4.26 ppm.

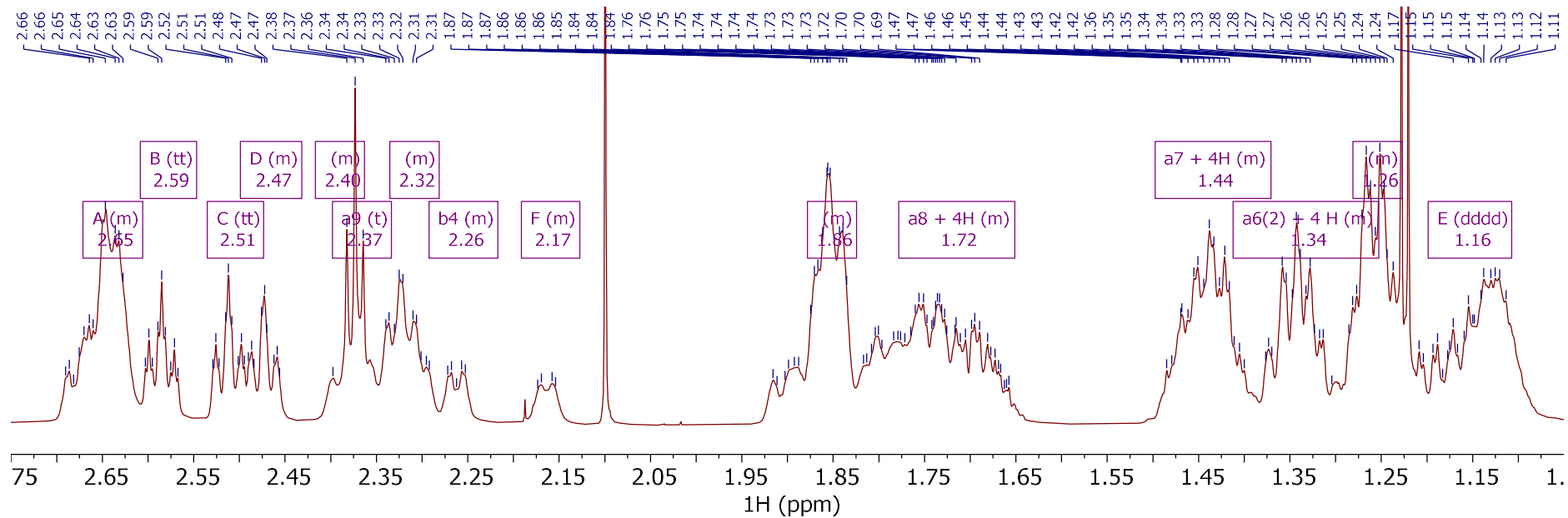


Figure S20. Fragment of the ^1H NMR spectra of $(-)\text{-mixHC[8]}$ including cyclohexane unit and biotin aliphatic chain protons in range of 1.11-2.66 ppm.

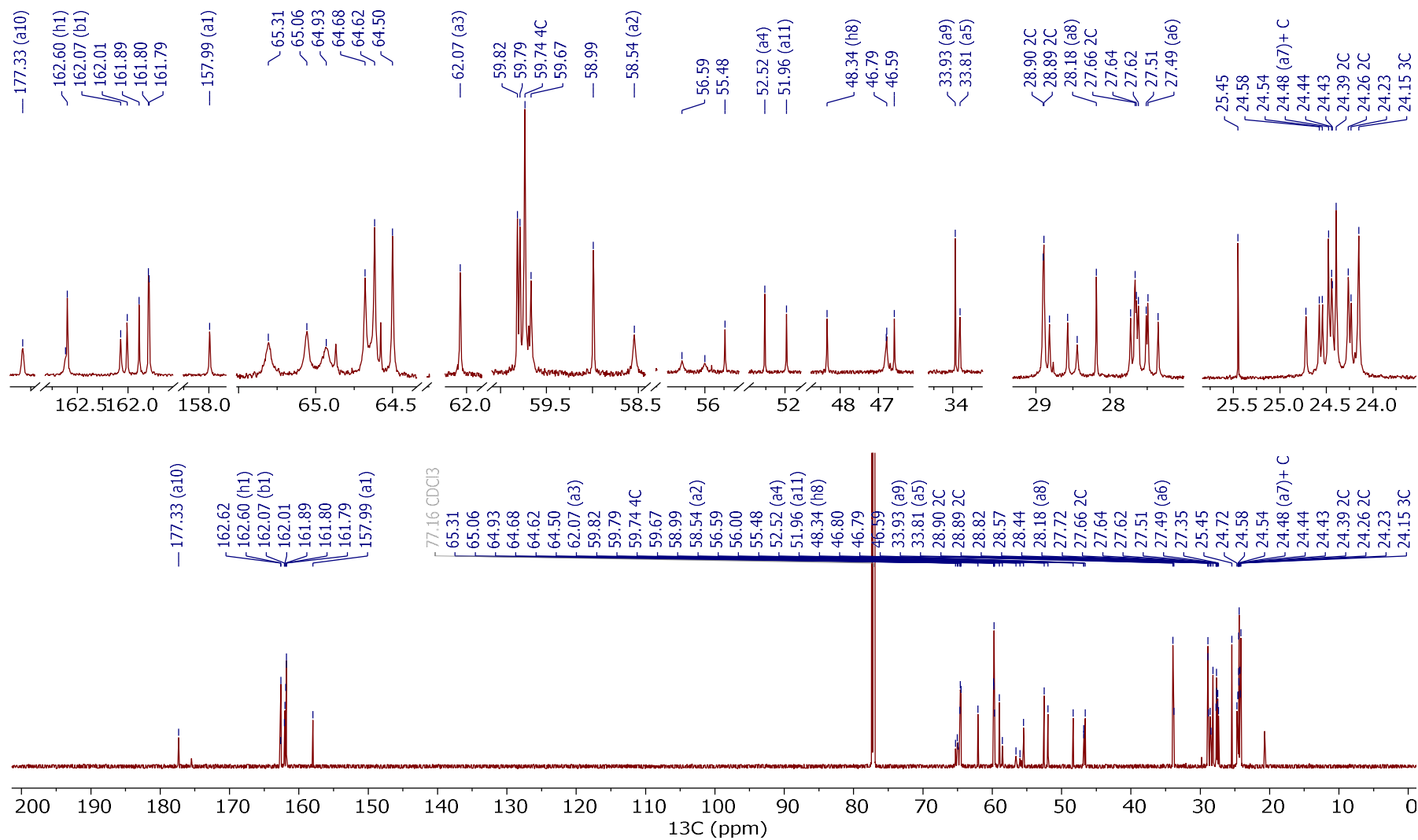


Figure S21. The ^{13}C NMR spectra from (-)-mixHC[8], the full spectra is at the bottom and zoomed in regions are at the top.

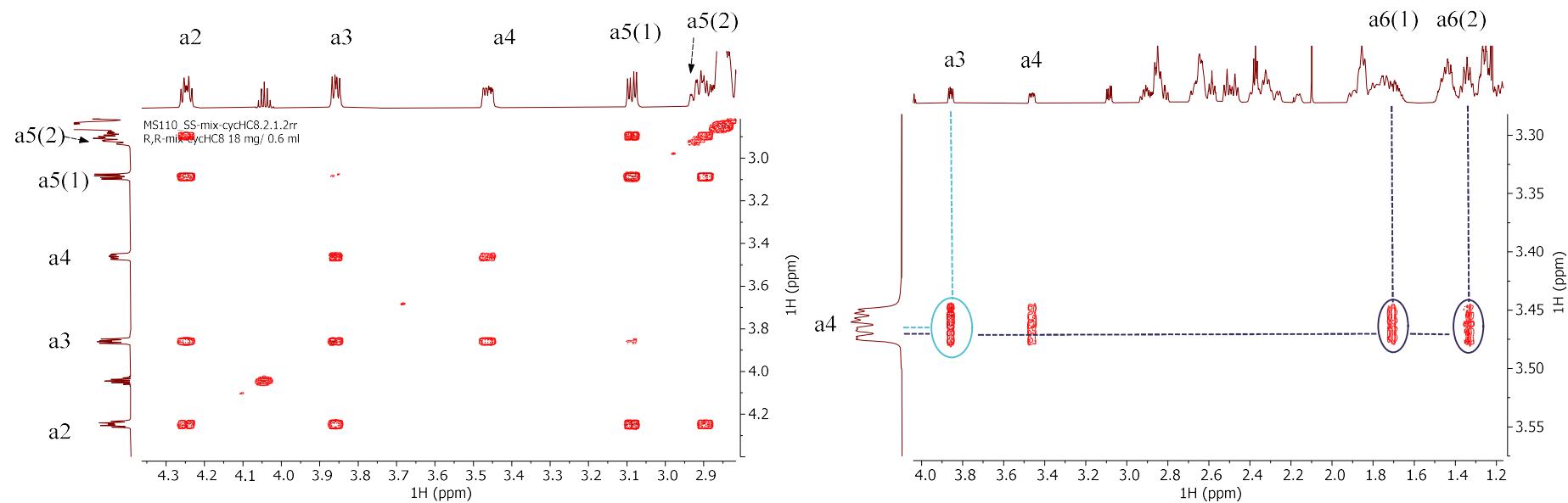


Figure S22. On the left: part of COSY spectrum, indicating neighbouring hydrogens in biotin monomer thiolane structure in (–)-mixHC[8]. On the right: part of COSY spectrum, showing the correlation between a proton in biotin thiolane motif (a4) with protons in biotin side chain (a6) in (–)-mixHC[8].

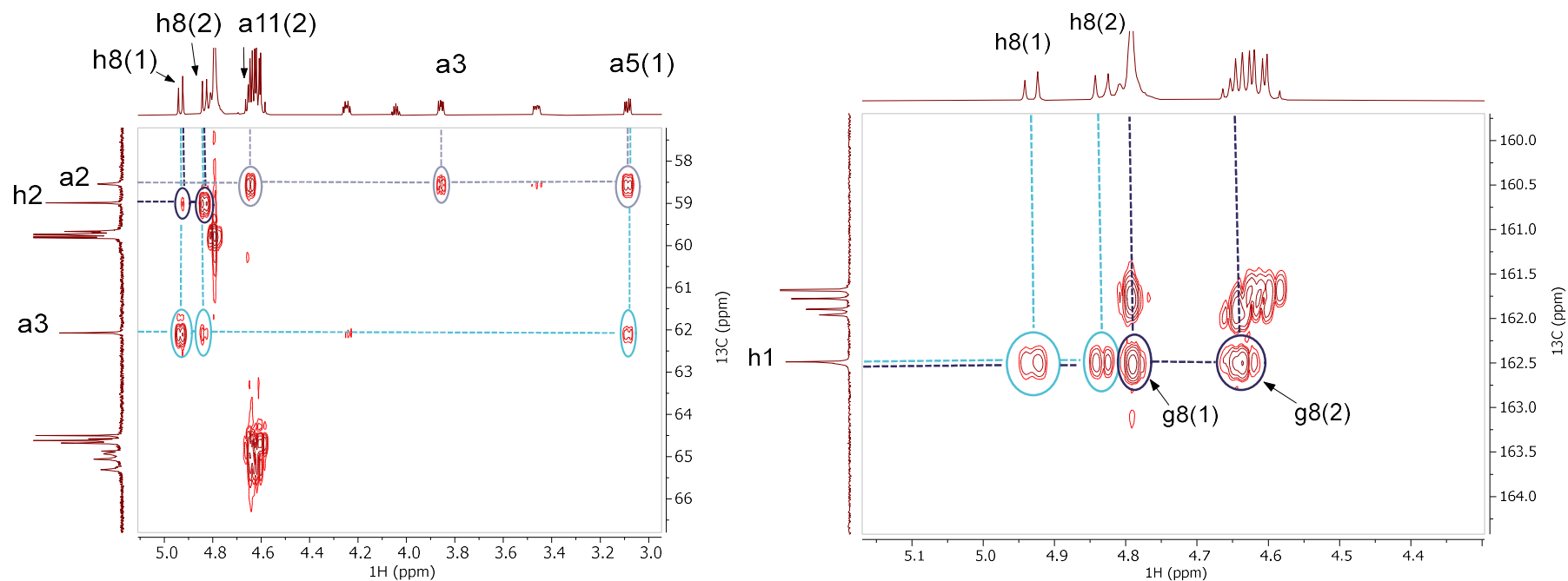


Figure S23. On the left: part of HMBC spectra, indicating the correlations between h8 bridge protons to a3 and h2 carbon, and a2 carbon correlation to a11(2) bridge proton, a3 proton and a5(1) proton in biotin monomer in (–)-mixHC[8], also it is seen a3 carbon correlation to a5(1) proton. On the right: part of HMBC spectra showing the correlation between h1 carbonyl carbon to h8 bridge protons and the correlation with g8 bridge protons in (–)-mixHC[8].

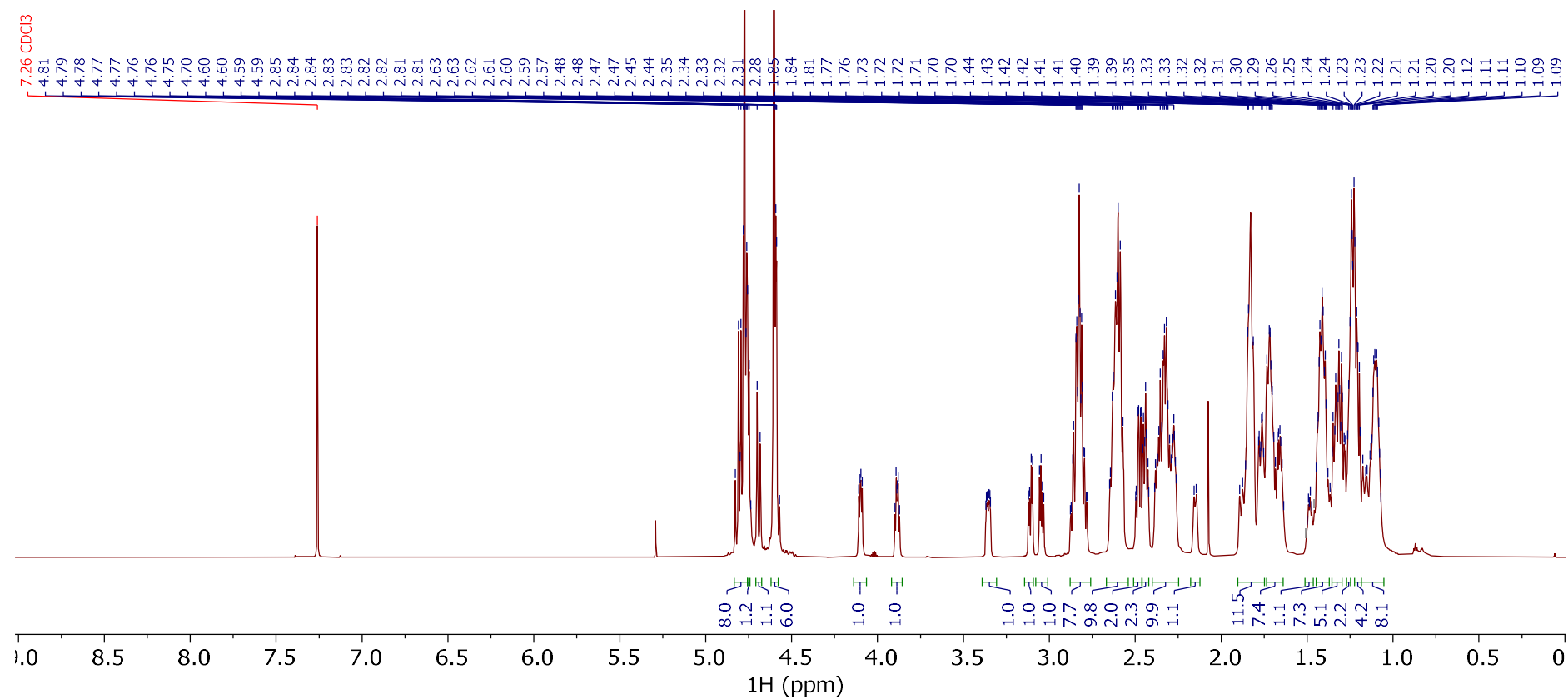


Figure S24. The full ^1H NMR spectra from (+)-mixHC[8].

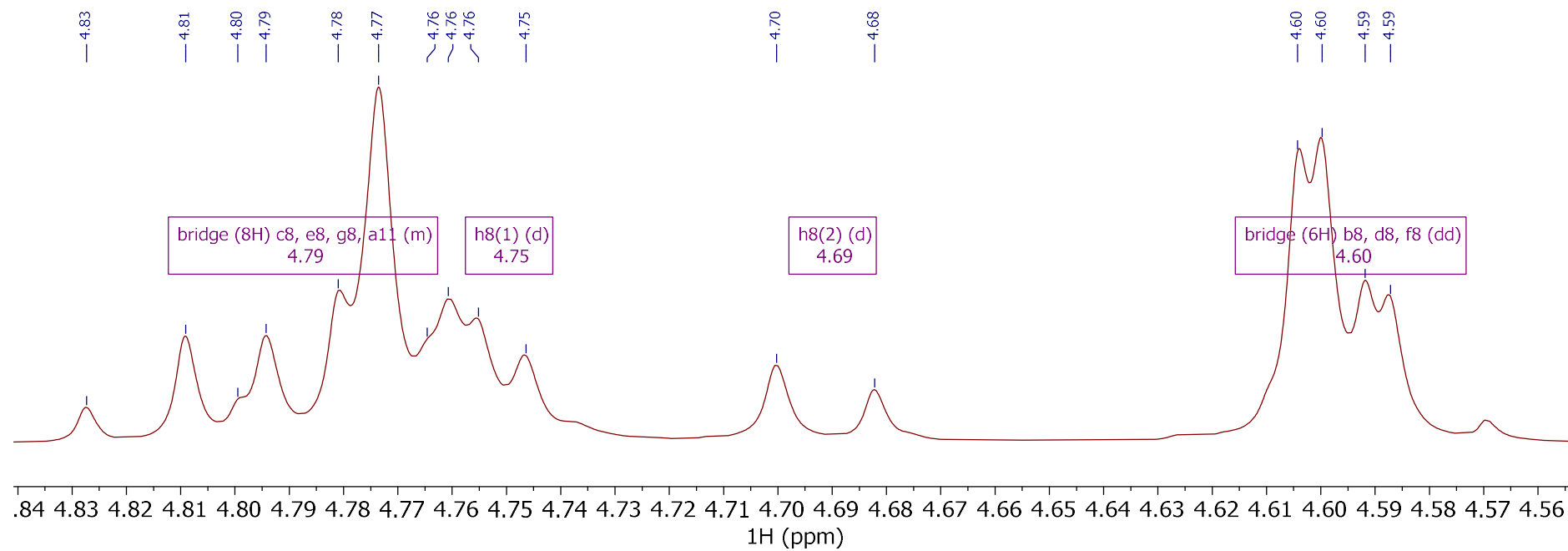


Figure S25. Fragment of ^1H NMR spectra showing bridge protons of (+)-mixHC[8] in range of 4.59-4.83 ppm.

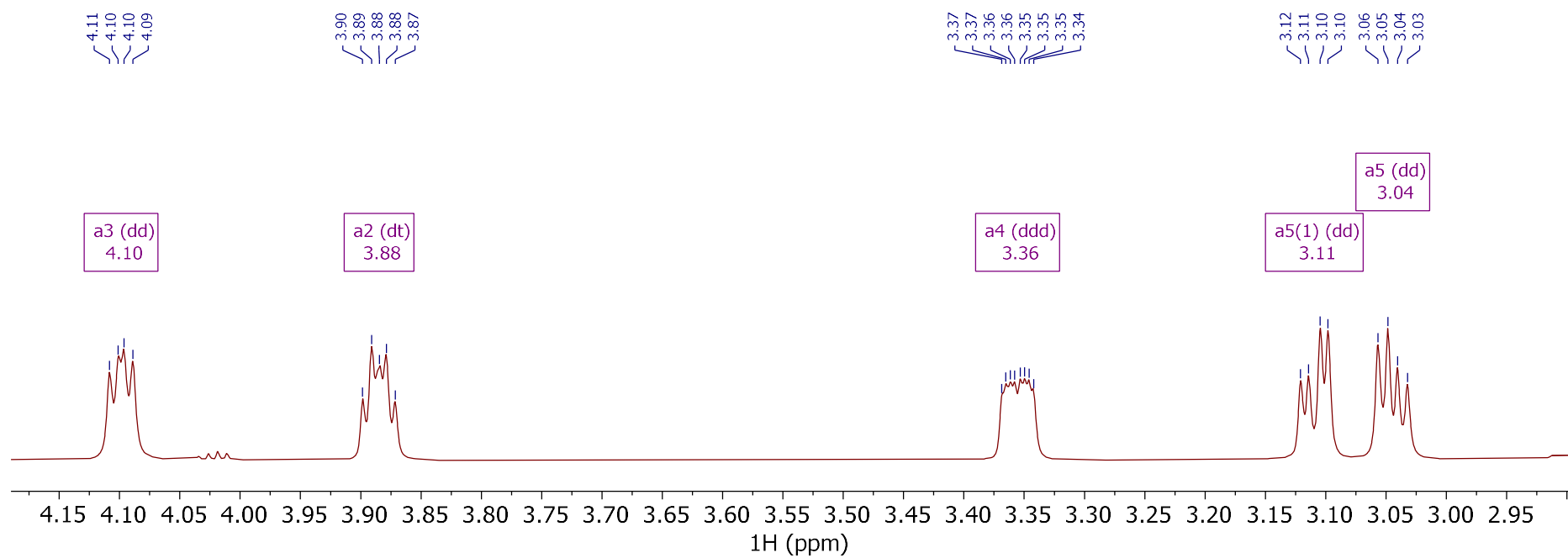


Figure S26. Fragment of ^1H NMR spectra showing biotin monomer's thiolane motif protons of (+)-mixHC[8] in range of 3.03-4.11 ppm.

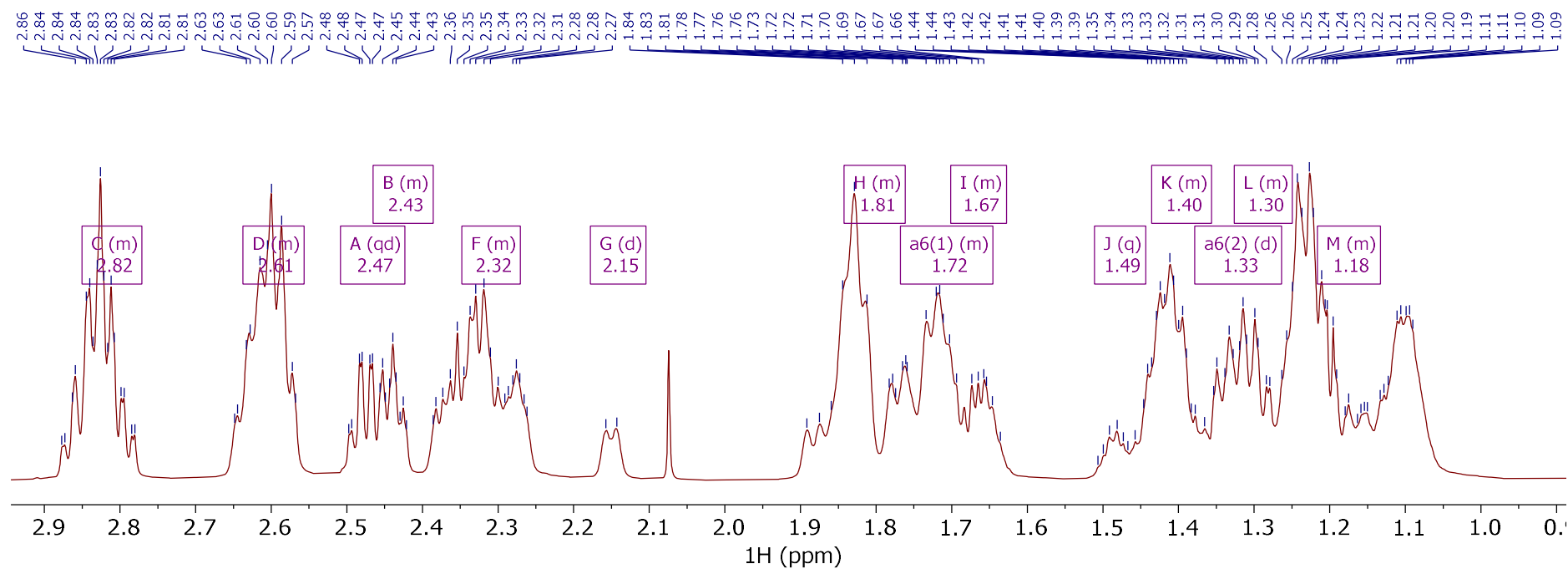


Figure S27. Fragment of ^1H NMR spectra of (+)-mixHC[8] including cyclohexane unit and biotin aliphatic chain protons in range of 1.09-2.86 ppm.

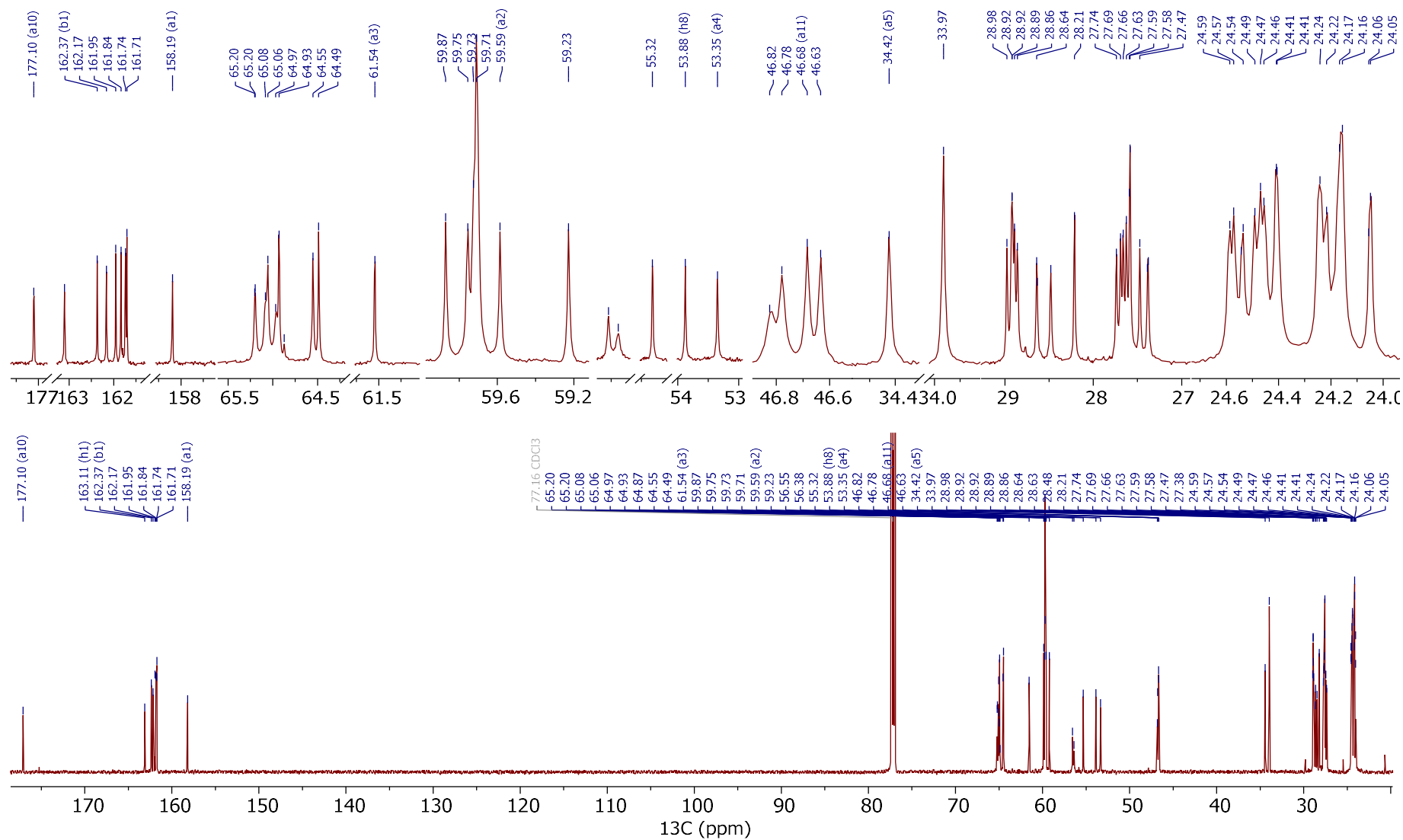


Figure S28. The ^{13}C NMR spectra from (+)-mixHC[8], the full spectra is at the bottom and zoomed in regions are at the top.

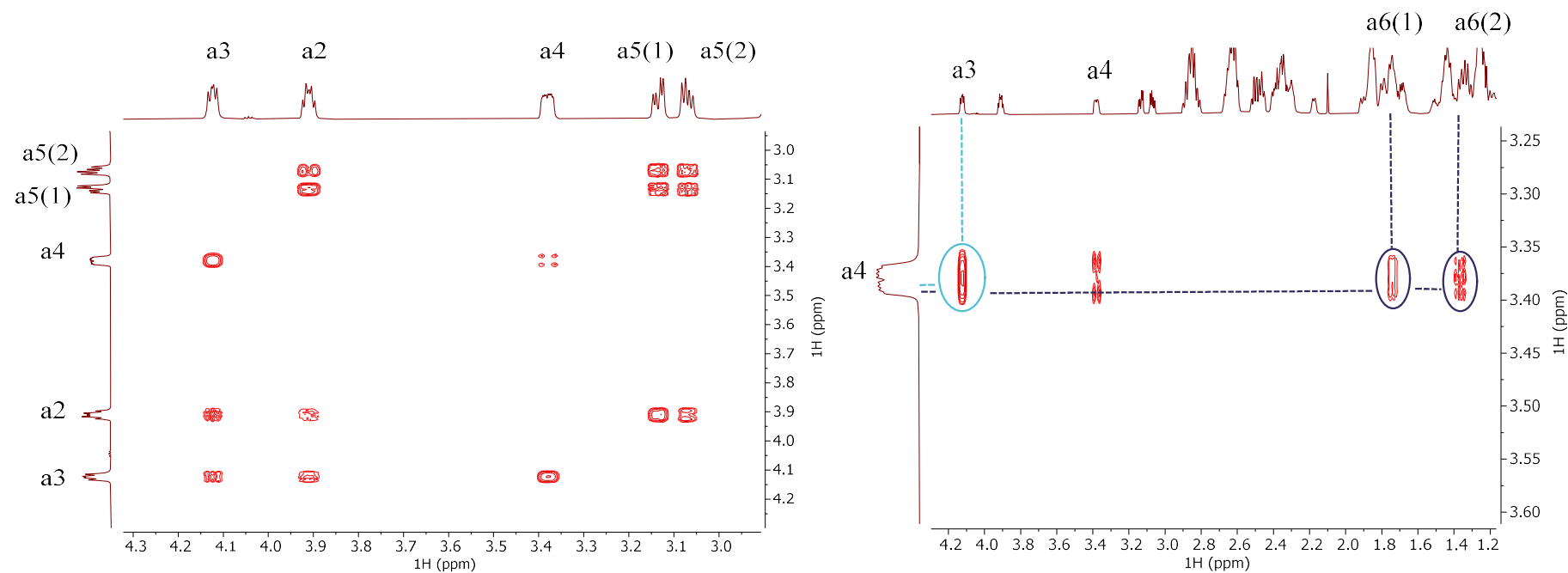


Figure S29. On the left: part of COSY spectrum, indicating neighbouring hydrogens in biotin monomer thiolane structure in (+)-mixHC[8]. On the right: part of COSY spectrum, showing the correlation between a proton in biotin thiolane motif (a4) with protons in biotin side chain (a6) in (+)-mixHC[8].

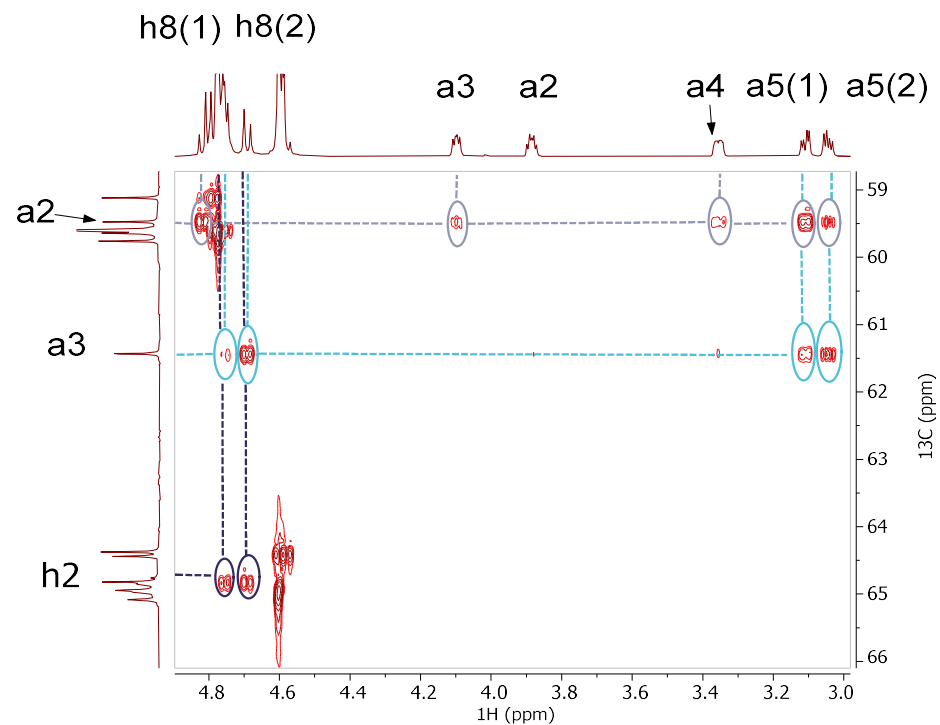


Figure S30. Part of HMBC spectra, indicating the correlations between a3 carbon to h8 bridge protons, a2 , a4 and to both a5 protons in biotin monomer in (+)-mixHC[8]; here it is also shown the correlation between h8 bridge protons and h2 carbon and finally a2 carbon correlation to a3 , a4 and to both a5 protons.

3.2 IR spectra

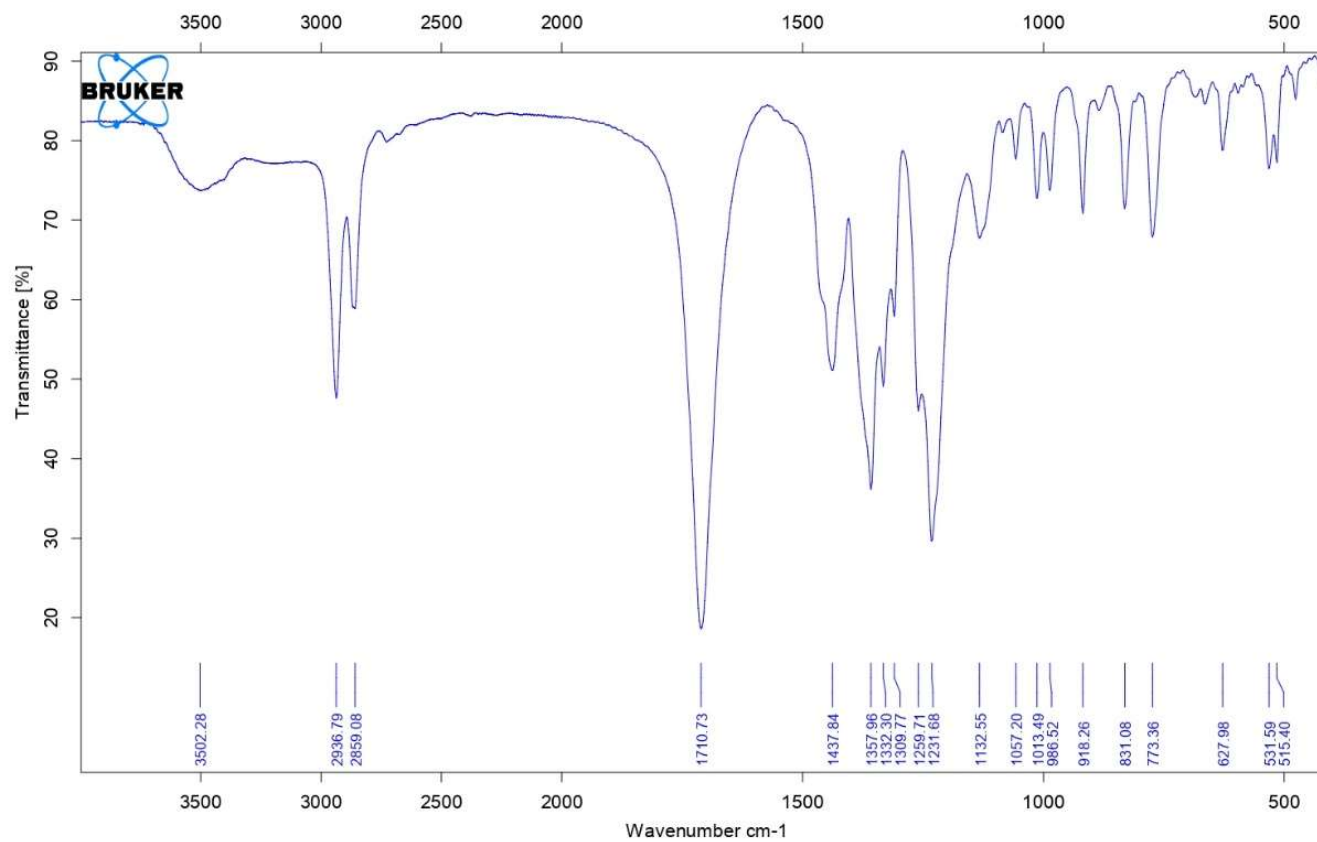


Figure S31. IR spectrum of (+)-mixHC[8].

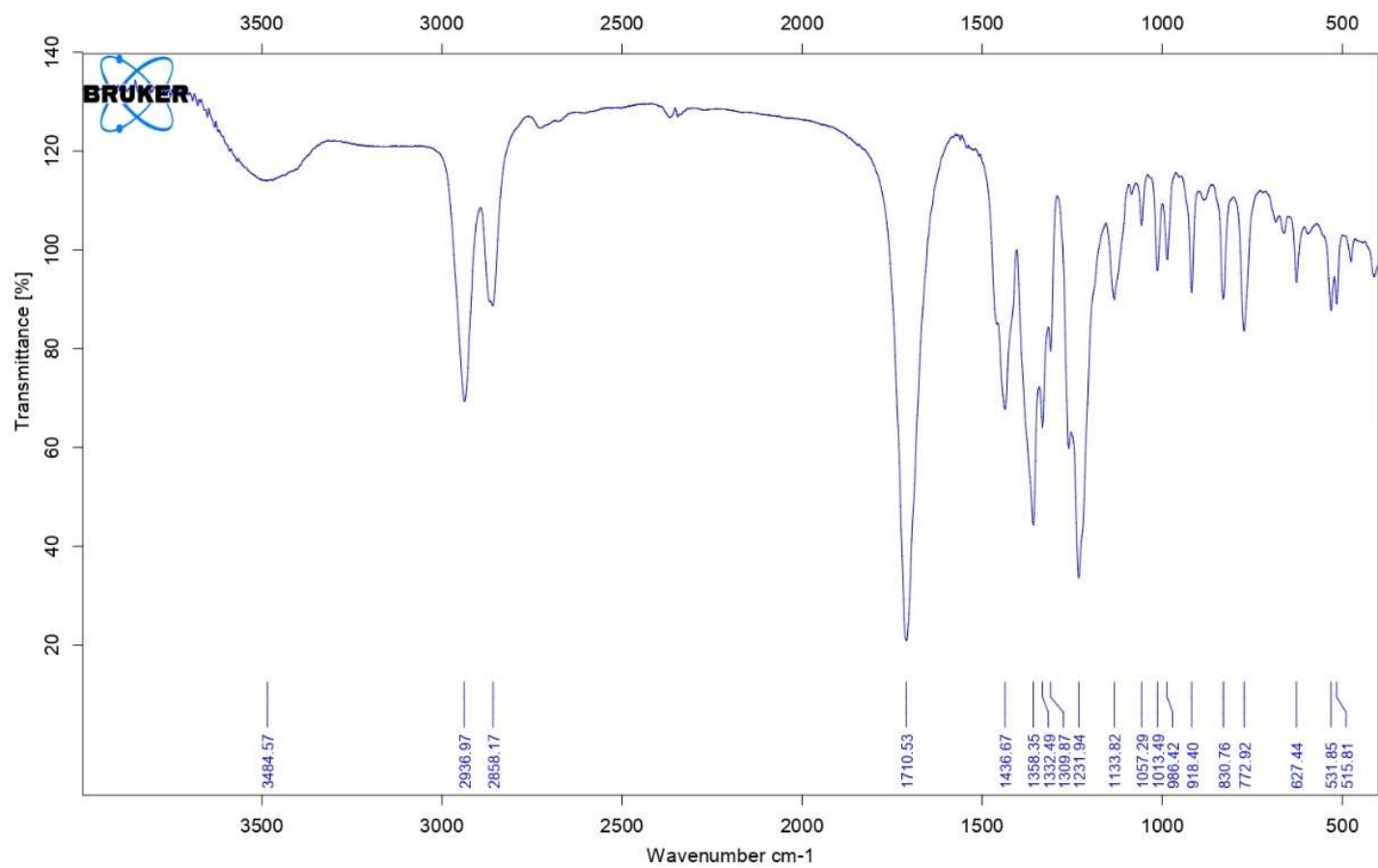


Figure S32. IR spectrum of (-)-mixHC[8].

4. Single Crystal X-ray Diffraction Analysis

General remarks

Single crystal X-ray diffraction data was collected at 120 K using a Rigaku XtaLAB Synergy-R diffractometer with a HyPix-Arc 100 detector using mirror-monochromated Cu-K α ($\lambda = 1.54184$ Å) radiation. The data was solved by intrinsic phasing (SHELXT)⁹ and refined by full-matrix least squares on F^2 using Olex2¹⁰, utilising the SHELXL module⁹. Anisotropic displacement parameters were assigned to non-H atoms and isotropic displacement parameters for all H atoms were constrained to multiples of the equivalent displacement parameters of their parent atoms with $U_{\text{iso}}(\text{H}) = 1.2 U_{\text{eq}}(\text{methylene, methine})$ or $U_{\text{iso}}(\text{H}) = 1.5 U_{\text{eq}}(\text{methyl, hydroxy})$ of their respective parent atoms. The crystallographic data is deposited with the Cambridge Crystallographic Data Centre (CCDC 2251913) and can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

Crystallographic details for TBA(PF₆⁻@(-)-((S,S,R)(R,R)7)-mixHC[8]) as a 1:1 co-crystal with TBA(PF₆⁻@cycHC[8])

[C₁₆H₃₆N][C₆₇H₁₀₀N₁₆O₁₀S][PF₆] \cdot [C₁₆H₃₆N][C₆₄H₉₆N₁₆O₈][PF₆]: Single crystals of the complex were obtained from a methanol solution of (-)-((S,S,R)(R,R)7)-mixHC[8] with twofold excess of TBAPF₆ by slow evaporation of the solvent. The resulting crystals were found to be of an inclusion complex of the PF₆⁻ in a 1:1 co-crystal of (-)-((S,S,R)(R,R)7)-mixHC[8] and cycHC[8].

C₁₆₃H₂₆₈F₁₂N₃₄O₁₈P₂S, $M = 3314.10 \text{ g mol}^{-1}$, colorless plates, $0.06 \times 0.09 \times 0.14$, orthorhombic, $P2_12_12_1$, $a = 20.2233(2) \text{ Å}$, $b = 20.5002(2) \text{ Å}$, $c = 20.7796(2) \text{ Å}$, $V = 8614.84(15) \text{ Å}^3$, $Z = 2$, Cu-K α radiation ($\lambda = 1.54184 \text{ Å}$), $T = 120.0(1) \text{ K}$, $\mu(\text{Cu-K}\alpha) = 1.04 \text{ mm}^{-1}$, 17604 reflections measured ($6.032^\circ \leq 2\theta \leq 148.476^\circ$), $R_{\text{int}} = 0.098$, 1273 parameters, 394 restraints, $S = 1.00$, $0.58 < d\rho < -0.29 \text{ e Å}^{-3}$, $R_1[F^2 > 2\sigma(F^2)] = 0.083$, $wR_2(\text{all data}) = 0.238$, Flack = 0.015(10).

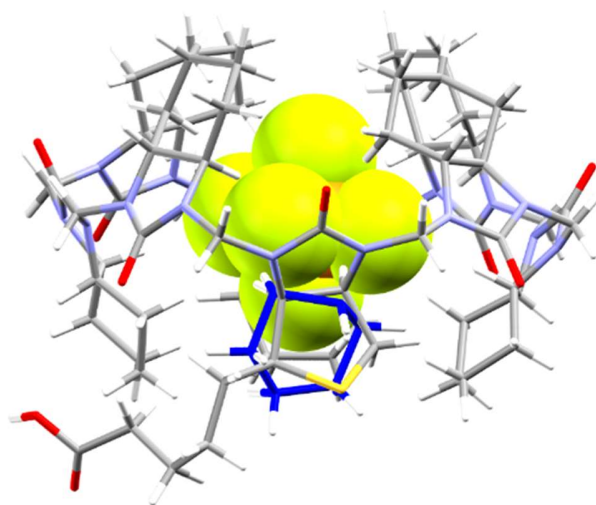


Figure S33. Crystal structure of a co-crystal with the cycHC[8] and (–)-((*S,S,R*)(*R,R*)₇)-mixHC[8] with the 50:50 disorder of the cyclohexyl and biotin 5-membered ring (cyclohexyl unit is coloured blue for clarity)

Additionally, the TBA salt of ClO₄[–], as well as Ag⁺, K⁺, and Na⁺ salts of PF₆[–] were screened; however, only the TBA salt of PF₆[–] yielded single crystals. Crystallizations were also set up with (+)-((*S,S,R*)(*S,S*)₇)-mixHC[8], yet, crystals did not form under any of the conditions used.

Single-crystal XRD analysis unambiguously revealed that we obtained a crystal structure of a 1:1 co-crystal of (–)-((*S,S,R*)(*R,R*)₇)-mixHC[8] and cycHC[8], modelled with overlapping hosts of the co-crystal with 50:50 disorder of the biotin 5-membered ring and one of the cyclohexyl groups (and shared TBA/PF₆ positions). The identity of the co-crystal was established through examination of the electron density with respect to the biotin sulfur atom, which was only observed in the exo conformation. The occupancies of the disordered biotin 5-membered ring and a cyclohexyl group were refined as a group using a single free variable (with total occupancy of 100%), then manually rounded to the nearest integer for ease of reporting. No other significant residual electron density in a feasible position to be the sulfur atom of further disordered biotin groups (in either exo or endo conformations) was identified in the final model. Although the crystallisations were set using 88% (by NMR) pure (–)-((*S,S,R*)(*R,R*)₇)-mixHC[8], cycHC[8] happened to be present as a minor additive. The composition of the SC-XRD model was confirmed by HPLC analysis (Figure S57), which showed that a dissolved crystal contains 96.7% of (–)-((*S,S,R*)(*R,R*)₇)-mixHC[8] and 2% of cycHC[8]. The latter was sufficient for spontaneous co-crystallisation to occur.

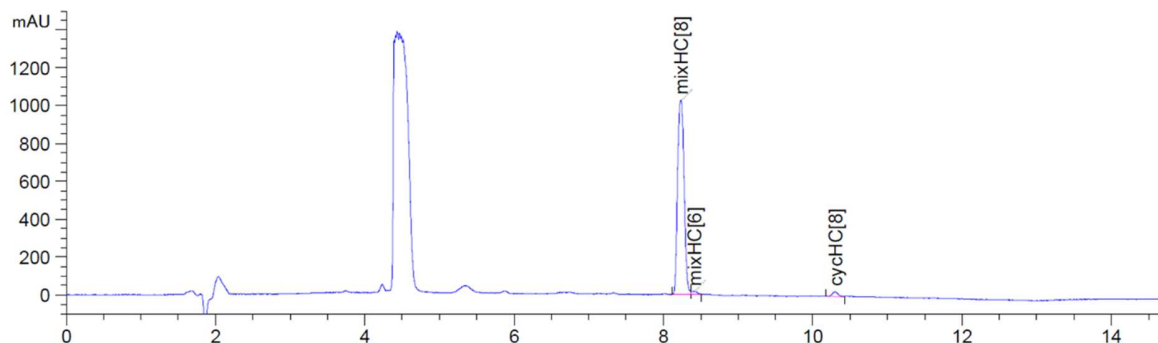


Figure S34. HPLC-UV chromatogram (210 nm) of the sample used for crystallization.

Measured crystal structure was compared to DFT calculated one by overlaying two structures using Mercury program (Figure S58). Molecular overlay verifies the thiolane envelope to be pointing outwards from the cavity with only minor differences in spatial arrangement.

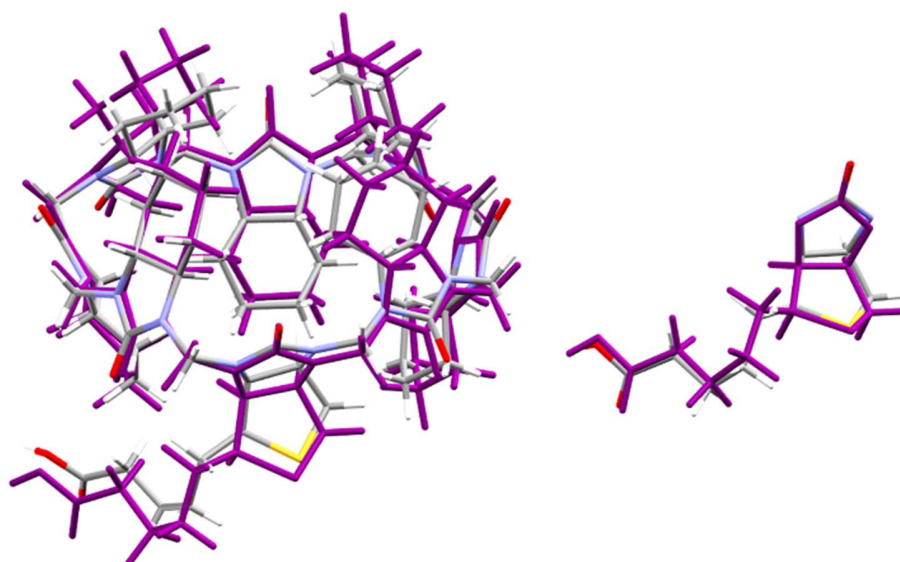


Figure S35. Overlay of SC-XRD and DFT calculation of inclusion complex (left) and closer overlay of biotin thiolane unit (right) (cyclohexyl unit, TBA and PF_6^- are omitted for clarity, DFT calculated structure is presented in purple).

Besides overlaying the structures of the obtained crystal structure and DFT calculated one, measured crystal structure was overlaid with crystal structure of regular cycHC[8] with PF_6^- to visualize the differences or similarities between those two inclusion complexes (Figure S59). Solvent molecules and cation were omitted from molecular overlay for clarity. PF_6^- was taken as center to overlay the structures. As seen, two structures are almost identical in their spatial arrangement.

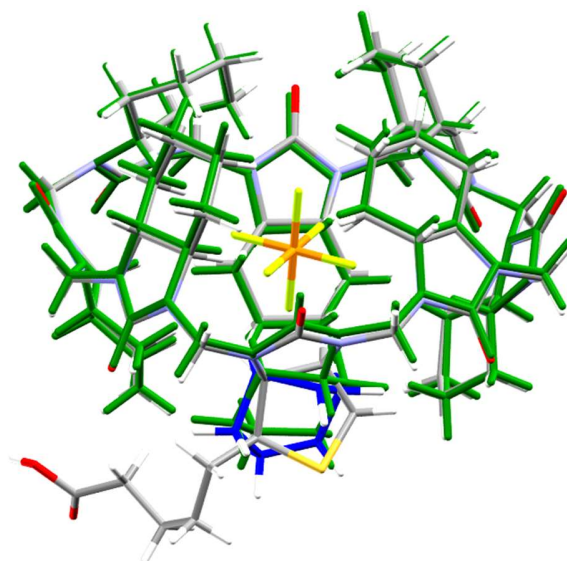


Figure S36. Overlay of SC-XRD of regular cycHC[8] with PF_6^- and $(-)-((S,S,R)(R,R)_7)\text{-mixHC[8]}$ with PF_6^- inclusion complexes (regular cycHC[8] is presented in green).

Analysis of Hirshfeld surfaces and host-guest interactions

Hirshfeld surface analysis was performed to analyze close contacts or intermolecular interactions between moieties present in crystal structure¹¹. This tool generates a surface around a molecule, where its electron density exceeds that from all the neighboring molecules, helping define the space that the molecule is occupying in the crystal. In this work analysis was used to investigate Hirshfeld surface of PF_6^- anion which occupies the cavity of macrocycle. The program CrystalExplorer¹² was used to generate the Hirshfeld surfaces and to highlight the close contacts between the anion and the neighboring host molecule ($\text{C-H}\cdots\text{anion}$). The surfaces were mapped with d_{norm} where a red spot signifies areas with $d(\text{D-H}\cdots\text{A}) \leq \sum r(\text{vdW})[\text{H}, \text{A}]$.

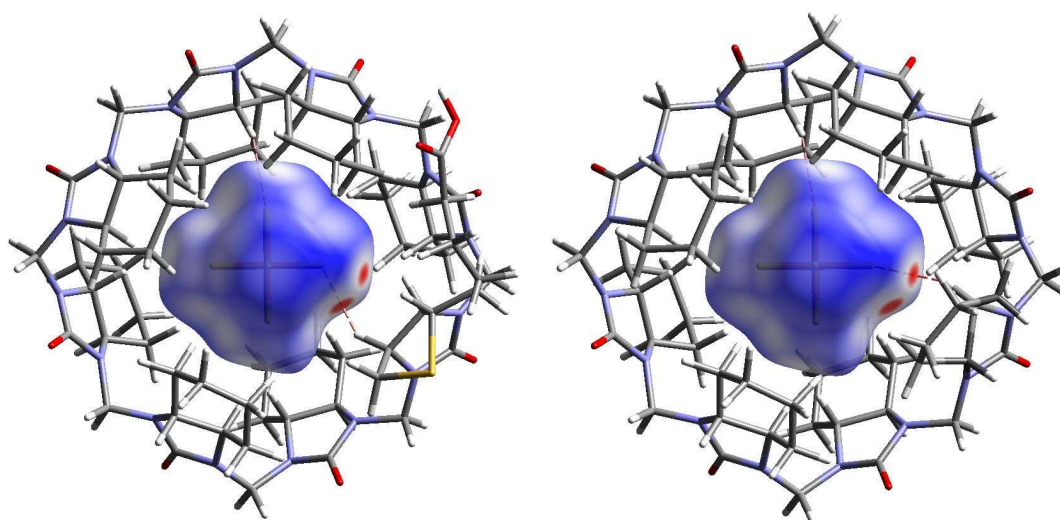


Figure S37. Hirshfeld surface for the encapsulated PF_6^- anion, mapped with d_{norm} over the range -0.1 to 1.0 . Close contacts where $d(\text{DH}\cdots\text{F})$ is shorter than $\sum r(\text{vdW})[\text{H}, \text{A}]$ are displayed with a dashed line. Hirshfeld surface for PF_6^- anion with biotin 5-membered ring as monomeric unit (left) and Hirshfeld surface for PF_6^- anion with cyclohexyl ring as monomeric unit (right)

Shortest distances between the host molecule and the encapsulated anion were investigated using Mercury, the result of which is shown in Tables S21–22. Distances shorter than the sum of van der Waals radii of hydrogen and the acceptor atom $\sum r(\text{vdW})[\text{H}, \text{A}]$ are marked in black, as they indicate influential host-guest interactions.

Hexafluorophosphate (PF₆⁻) – close contacts within PF₆⁻@(-)-((*S,S,R*)(*R,R*)7)-*mixHC*[8], with monomeric unit D being biotin 5-membered ring

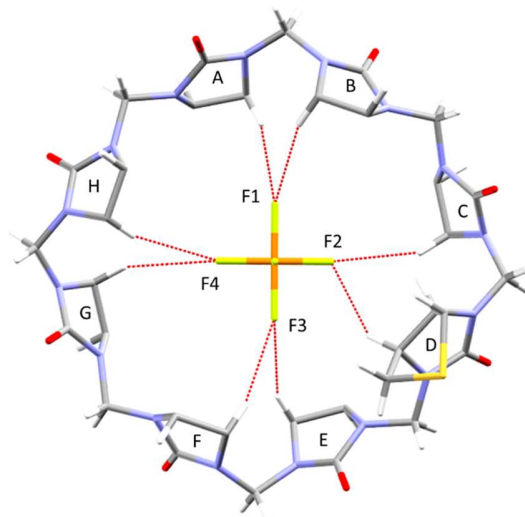


Figure S38. Close contacts within PF₆⁻@(-)-((*S,S,R*)(*R,R*)7)-*mixHC*[8]. (CH₂)₄ groups are omitted for clarity, atoms involved in equalent monomeric units are denoted with suffixes A-H. Monomeric unit D is biotin 5-membered ring.

Table S19. Shortest $d(\text{D-H}\cdots\text{A})$ distances from the crystal structure of ***TBA*(PF₆⁻@(-)-((*S,S,R*)(*R,R*)7)-*mixHC*[8]))**, between the encapsulated PF₆⁻ and the host.

| D–H \cdots A | $d(\text{H}\cdots\text{A})$, Å | $\text{D}(\text{H}\cdots\text{A}) - \sum r(\text{vdW})[\text{H}, \text{A}]$, Å |
|---------------------|---------------------------------|---|
| C2A–H2A...F1 | 2.53 | -0.03 |
| C2B–H2B...F1 | 2.61 | 0.05 |
| C2C–H2C...F2 | 2.81 | 0.25 |
| C2D–H2D...F2 | 2.45 | -0.11 |
| C2E–H2E...F3 | 2.63 | 0.07 |
| C2F–H2F...F3 | 2.64 | 0.08 |
| C2G–H2G...F3 | 2.92 | 0.36 |
| C2H–H2H...F3 | 2.67 | 0.11 |

Hexafluorophosphate (PF_6^-) – close contacts within $\text{PF}_6^-@(-)-((S,S,R)(R,R)7)\text{-mixHC}[8]$, with monomeric unit D being cyclohexyl ring

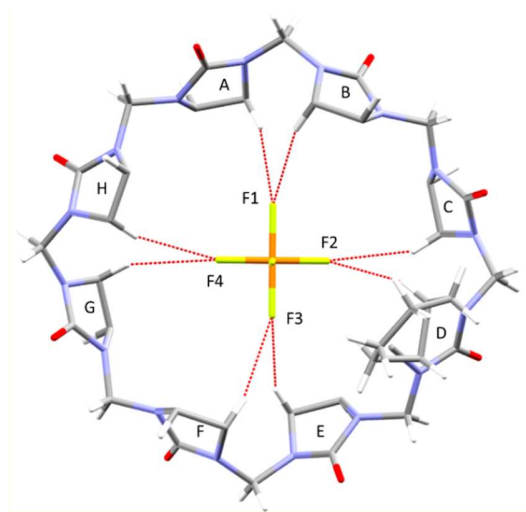


Figure S39. Close contacts within $\text{PF}_6^-@(-)-((S,S,R)(R,R)7)\text{-mixHC}[8]$. $(\text{CH}_2)_4$ groups are omitted for clarity, atoms involved in equalent monomeric units are denoted with suffixes A-H. Monomeric unit D is cyclohexyl ring.

Table S20. Shortest $d(\text{D-H}\cdots\text{A})$ distances from the crystal structure of $\text{TBA}(\text{PF}_6^-@(-)-((S,S,R)(R,R)7)\text{-mixHC}[8])$, between the encapsulated PF_6^- and the host.

| $\text{D-H}\cdots\text{A}$ | $d(\text{H}\cdots\text{A}), \text{\AA}$ | $\text{D}(\text{H}\cdots\text{A}) - \sum r(\text{vdW})[\text{H}, \text{A}], \text{\AA}$ |
|----------------------------|---|---|
| C2A–H2A...F1 | 2.53 | -0.03 |
| C2B–H2B...F1 | 2.61 | 0.05 |
| C2C–H2C...F2 | 2.81 | 0.25 |
| C2D–H2D...F2 | 2.50 | -0.06 |
| C2E–H2E...F3 | 2.63 | 0.07 |
| C2F–H2F...F3 | 2.64 | 0.08 |
| C2G–H2G...F3 | 2.92 | 0.36 |
| C2H–H2H...F3 | 2.67 | 0.11 |

5. The Computational Study

5.1 Methods

The geometries for (+)-((*S,S,R*)(*S,S*)₇)-mixHC[8] and (–)-((*S,S,R*)(*R,R*)₇)-mixHC[8] were drawn using Chem3D 18.2. The Density Functional Theory (DFT) method used to optimize the geometries was the B3LYP exchange-correlation functional^{13–17} with a 6-31G** basis set^{18–20}. The energy values of the local minima were refined by single point calculations with the inclusion of the Grimme's D3 empirical dispersion correction²¹. Atomic configuration was allowed to relax until the remaining atomic forces reached below 5×10^{-2} eVÅ^{–1}. Calculations were performed with the Gaussian16 program package.²²

5.2 Results

Two conformers were found for both (+)-((*S,S,R*)(*S,S*)₇)-mixHC[8] and (–)-((*S,S,R*)(*R,R*)₇)-mixHC[8] by studying the potential energy surface of the thiolane ring (Figure S64). The conformers had either the sulfur atom in biotin oriented towards the inside or the outside the macrocycle. The relative energy values for the conformers are listed in Table 1. For (+)-((*S,S,R*)(*S,S*)₇)-mixHC[8], the experimentally determined crystal structure was in close agreement with the DFT calculated structure, where the sulfur atom is oriented towards outside the macrocycle. Currently no crystal structure for (–)-((*S,S,R*)(*R,R*)₇)-mixHC[8] have been reported. It should be noted that the differences in the energy of the two conformations (the differences in the sulfur atom orientation) are negligible and the geometry seen in the crystal structure is probably favored due to crystal packing forces, solvent effects, and the guest molecule during crystallization. See optimized geometries as XYZ format files in Data S2.

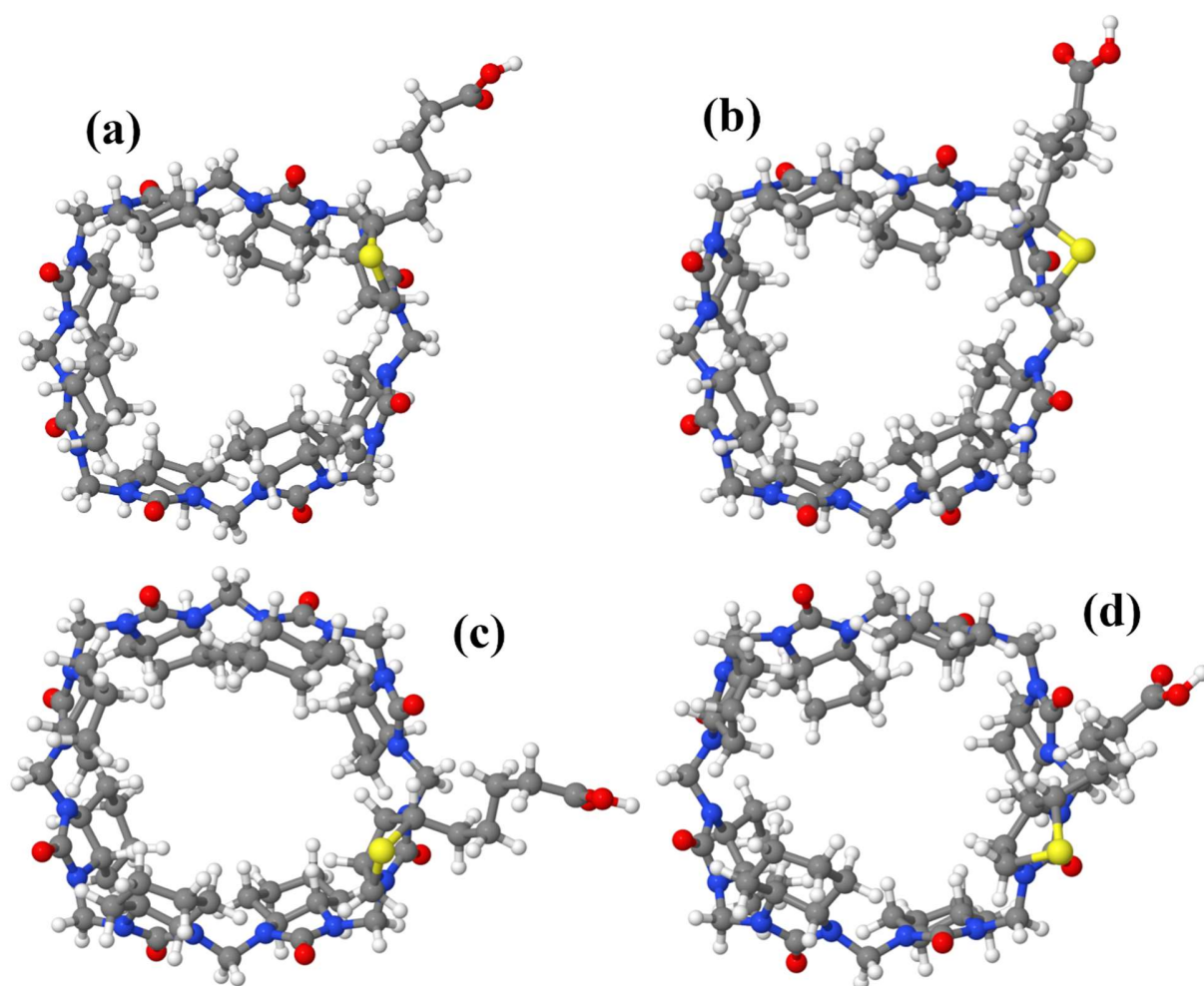


Figure S40. The found conformers: (a) the (–)-mixHC[8] conformer with the sulfur atom oriented towards the centre of the macrocycle, (b) the (–)-mixHC[8] conformer with the sulfur atom oriented towards outside of the macrocycle, (c) the (+)-mixHC[8] conformer with the sulfur atom oriented towards the centre of the macrocycle, (d) the (+)-mixHC[8] conformer with the sulfur atom oriented towards outside of the macrocycle.

Table S21. The relative energies values for the mixHC[8] conformers.

| | Sulfur atom oriented towards inside of the macrocycle, ΔE (kJ/mol) | Sulfur atom oriented towards outside of the macrocycle, ΔE (kJ/mol) |
|---|--|---|
| (+)-((S,S,R)(S,S) ₇)- mixHC[8] | 0.67 | 0.26 |
| (-)-((S,S,R)(R,R) ₇)- mixHC[8] | 0.00 | 0.28 |

Table S22. The relative energies values for the PF₆⁻@mixHC[8] conformers.

| | Sulfur atom oriented towards inside of the macrocycle, ΔE (kJ/mol) | Sulfur atom oriented towards outside of the macrocycle, ΔE (kJ/mol) |
|---|--|---|
| PF ₆ ⁻ @(+)-((S,S,R)(S,S) ₇)- mixHC[8] | 11.70 | 3.50 |
| PF ₆ ⁻ @(-)-((S,S,R)(R,R) ₇)- mixHC[8] | 2.10 | 0.00 |

4.3 Comparing the Calculated Structure to the Crystal Structure

Previously published results for cyclohexanohemicucurbiturils have shown that the position of the cyclohexyl rings is quite variable and depends on the guest molecule.²³ Furthermore, the structure of the cyclohexyl rings is influenced by the packing forces during crystallization. Thus, in the following study we are comparing structure features such as distances between atoms and angles between bonds, which do not vary due to the aforementioned reasons. The bond lengths (Table 2), which are of interest are the bonds between the carbonyl carbon atom and the nitrogen atom of the monomer, and the bonds between the nitrogen atom of the monomer and the carbon atom of the bridge (–CH₂–). These two bond types also form the angles which will be measured. The angles, however, are not equal as the angles, which are aligned with the fluorine atoms of the PF₆⁻ are more obtuse than the angles, which do not align with the fluorine atoms.

Table S23. The bond lengths of interest. The numbers with the green background show the average bond length.

| O=C–N | | N–CH ₂ | |
|-------------------|----------------------|-------------------|----------------------|
| Crystal Structure | Calculated Structure | Crystal Structure | Calculated Structure |
| 1.339 | 1.384 | 1.455 | 1.453 |
| 1.361 | 1.375 | 1.469 | 1.442 |
| 1.347 | 1.398 | 1.460 | 1.457 |
| 1.36 | 1.387 | 1.409 | 1.453 |
| 1.370 | 1.391 | 1.421 | 1.452 |
| 1.356 | 1.394 | 1.451 | 1.453 |
| 1.384 | 1.394 | 1.405 | 1.451 |
| 1.335 | 1.391 | 1.454 | 1.454 |
| 1.357 | 1.391 | 1.466 | 1.453 |
| 1.386 | 1.393 | 1.442 | 1.452 |
| 1.360 | 1.394 | 1.433 | 1.452 |
| 1.378 | 1.390 | 1.460 | 1.453 |
| 1.361 | 1.390 | 1.423 | 1.454 |
| 1.370 | 1.395 | 1.435 | 1.452 |
| 1.381 | 1.394 | 1.458 | 1.452 |
| 1.387 | 1.389 | 1.431 | 1.451 |
| 1.365 | 1.391 | 1.442 | 1.452 |

The standard deviation values for the O=C–N and the C–CH₂ bond lengths in the crystal structure is 0.020 and 0.016 Å, respectively. The standard deviation values for the same bonds in the calculated structure are 0.003 and 0.005 Å, respectively. The absolute differences between the average bond length for the O=C–N and the C–CH₂ bonds in the crystal and calculated structures were 0.010 and 0.026 Å, respectively.

Table S24. The angles between angles of interest. The numbers with the green background show the average angle value.

| O=C–N–CH ₂ (More Obtuse) | | O=C–N–CH ₂ | |
|-------------------------------------|----------------------|-----------------------|----------------------|
| Crystal Structure | Calculated Structure | Crystal Structure | Calculated Structure |
| 115.84 | 116.20 | 111.41 | 114.20 |
| 115.19 | 116.70 | 111.05 | 113.80 |
| 115.67 | 116.60 | 112.20 | 113.80 |
| 115.20 | 116.60 | 112.27 | 113.90 |
| 115.48 | 116.53 | 111.73 | 113.93 |

The absolute differences between the crystal and calculated structures for the more and less obtuse angles were 1.05° and 2.19°, respectively. The difference in the less obtuse angle is small, but noticeable and is most likely caused by the guest, PF₆[−], which forces the structure to contract; thus, reducing the aforementioned “less obtuse” angles.

The overall (meaningful) structural features between the calculated and the crystal structure of the mixHC[8] remain analogous and the differences are likely due to the guest structure and packing forces of the crystal structure. These results indicate that the structure of the mixHC[8] does not vary much in different media nor with different guests (with the exception of the aforementioned cyclohexyl rings, which are known to be flexible). Furthermore, the methods used can be considered suitable for predicting structures for cyclohexanohemicucurbiturils in the future.

Optimized geometry of (-)-((*S,S,R*)(*R,R*)₇)-mixHC[8] sulfur atom oriented towards inside:

| | | | | | | | | | | | |
|------------------------|----------|----------|----------|---|----------|----------|----------|---|----------|----------|----------|
| 194 | | | | C | 1.04520 | -4.74195 | -1.08629 | H | 0.55164 | -3.84612 | 3.39652 |
| E(au) = -4640.58481258 | | | | C | -3.06021 | -5.23019 | 2.92310 | H | 3.90654 | -0.20621 | 4.42376 |
| C | -2.20282 | 3.41552 | -2.94085 | C | -4.06930 | 3.09696 | 2.06072 | H | 4.02015 | -1.89646 | 4.93870 |
| H | 3.08164 | 1.81681 | -0.54419 | C | -0.45129 | -4.96982 | -1.31071 | H | 1.58850 | -5.61780 | -1.48669 |
| C | -4.53445 | -4.00508 | 1.31412 | C | 1.28863 | 3.67195 | 4.66550 | H | -2.09491 | -5.72038 | 3.07553 |
| C | 5.81785 | 0.00681 | -1.31042 | C | 1.52188 | -3.51424 | -1.85167 | H | -3.85126 | -5.97109 | 3.09599 |
| C | -5.12963 | 3.22174 | 0.97419 | C | -1.32763 | 3.58863 | -4.20428 | H | -3.54161 | 4.04512 | 2.20774 |
| C | 3.19806 | -1.64348 | 2.95714 | C | -4.63309 | -2.74007 | 2.15703 | H | -3.32426 | 2.34627 | 1.76788 |
| C | -5.83544 | 1.88199 | 0.75392 | C | -4.40956 | -0.00428 | -4.74355 | H | -0.97656 | -0.41475 | -1.13410 |
| C | 0.87859 | 4.83324 | 2.03296 | C | 0.13802 | 3.96810 | -3.89474 | H | 1.05914 | 2.85279 | 5.35601 |
| C | 4.32807 | 3.77487 | 1.09256 | C | -0.01267 | 4.41861 | 4.29582 | H | 1.95105 | 4.35629 | 5.21268 |
| C | -2.02804 | 4.67778 | -2.10634 | C | 1.14414 | -2.35295 | 4.88246 | H | 2.58687 | -3.32846 | -1.67799 |
| C | -2.05480 | -6.48528 | 0.04248 | C | 1.25264 | -3.78856 | -3.34982 | H | 0.97245 | -2.62748 | -1.51097 |
| C | 4.17624 | 1.77505 | -0.48415 | C | 2.05764 | 3.12402 | 3.44051 | H | -1.35036 | 2.67005 | -4.80109 |
| C | -3.89589 | -5.00435 | -0.67561 | C | 1.99310 | -1.06990 | 5.03146 | H | -1.77517 | 4.37171 | -4.83118 |
| C | 2.49767 | -3.00309 | 2.92623 | C | -0.70629 | -5.38070 | -2.75630 | H | -5.59241 | -2.23589 | 2.00238 |
| C | 2.39802 | -4.74364 | 1.06780 | C | -4.80278 | 2.67256 | 3.35464 | H | -3.84082 | -2.03842 | 1.86567 |
| C | -0.56283 | 4.86001 | -1.70429 | C | -6.67553 | 1.52641 | 1.97510 | H | -4.48352 | 0.30054 | -5.79317 |
| C | 5.39953 | -0.96769 | 1.81102 | C | -4.47098 | -3.17334 | 3.63272 | H | -3.59459 | 0.59054 | -4.30866 |
| C | 2.23967 | 4.28763 | 2.74551 | C | -0.20085 | -4.22116 | -3.64783 | H | 0.66755 | 4.17775 | -4.83041 |
| C | 4.95403 | 1.46656 | 1.71811 | C | -3.21179 | -4.03149 | 3.89013 | H | 0.64413 | 3.10318 | -3.44440 |
| N | 1.26954 | 5.61179 | 0.85539 | C | -5.70382 | 1.42966 | 3.17553 | H | -0.44456 | 4.87040 | 5.19542 |
| C | 2.39581 | 5.03875 | 0.28702 | H | -3.25254 | 3.26780 | -3.21480 | H | -0.75225 | 3.69154 | 3.93308 |
| N | 4.97704 | 0.22702 | 1.10668 | H | -1.88518 | 2.53976 | -2.36063 | H | 1.57407 | -3.14123 | 5.51509 |
| N | -0.75351 | -5.88735 | -0.20748 | H | -5.31346 | -4.70484 | 1.66912 | H | 0.13442 | -2.17053 | 5.26678 |
| C | 3.97521 | -2.86101 | 1.14510 | C | 7.22028 | 0.41546 | -0.82831 | H | 1.93691 | -4.57949 | -3.68568 |
| O | -7.31517 | -1.28396 | 0.27106 | H | -5.88236 | 3.95228 | 1.32405 | H | 1.50030 | -2.89962 | -3.94011 |
| N | -4.75040 | 3.57180 | -0.39531 | H | 2.54755 | -0.90810 | 2.45093 | H | 3.02253 | 2.70477 | 3.74232 |
| N | 4.35097 | -1.92229 | 2.10160 | H | -5.06411 | 1.10072 | 0.63632 | H | 1.48859 | 2.32627 | 2.95058 |
| N | -5.73424 | -2.07873 | -1.25075 | H | 0.25315 | 3.98367 | 1.70684 | H | 1.46072 | -0.23240 | 4.55970 |
| N | -5.82215 | 3.30894 | -2.45202 | H | 4.81272 | 3.96644 | 2.05387 | H | 2.08757 | -0.81401 | 6.09239 |
| O | -0.70259 | 5.83854 | -0.62256 | H | 4.75094 | 4.43081 | 0.32789 | H | -1.77109 | -5.55767 | -2.93090 |
| O | 4.62653 | 2.40351 | 0.75342 | H | -2.31858 | 5.53832 | -2.73701 | H | -0.16445 | -6.30830 | -2.98136 |
| N | -2.30899 | 6.18144 | 1.03871 | H | -1.92013 | -7.16897 | 0.88165 | H | -4.07394 | 2.48588 | 4.15127 |
| O | -3.93597 | -5.38598 | -1.84274 | H | -2.36508 | -7.04374 | -0.84160 | H | -5.41932 | 3.51521 | 3.69574 |
| N | -4.61160 | -3.93297 | -0.14579 | C | 4.78261 | 2.37279 | -1.76938 | H | -7.19358 | 0.57464 | 1.82924 |
| O | 2.88544 | 5.31819 | -0.80358 | H | 3.03770 | -3.68309 | 3.61050 | H | -7.43038 | 2.30417 | 2.14803 |
| N | -6.70803 | -0.08330 | -1.64027 | H | 2.32491 | -5.43485 | 1.91381 | H | -4.45170 | -2.28936 | 4.27997 |
| O | 0.03391 | -6.07426 | 1.98512 | H | 3.19430 | -5.07035 | 0.39119 | H | -5.36093 | -3.74684 | 3.92535 |
| N | 2.90394 | 4.08709 | 1.18109 | H | -0.20003 | 3.90759 | -1.27886 | H | -0.86747 | -3.35995 | -3.50260 |
| N | -6.47001 | 2.12141 | -0.54599 | H | 5.84770 | -0.62895 | 2.74635 | H | -0.29015 | -4.50202 | -4.70293 |
| N | -3.14155 | -5.56949 | 0.34778 | H | 6.14325 | -1.50774 | 1.22150 | H | -3.21873 | -4.39146 | 4.92479 |
| N | 2.76591 | -3.42338 | 1.54849 | H | 2.76986 | 5.09295 | 3.01503 | H | -2.32042 | -3.96949 | 3.79262 |
| N | 1.12312 | -4.78189 | 0.37525 | H | 3.84483 | -0.39291 | -0.55608 | H | -5.06847 | 0.54473 | 3.03295 |
| N | -2.69883 | 4.81037 | -0.81122 | H | -6.18778 | -2.13482 | -3.29374 | H | -6.27138 | 1.25335 | 4.09580 |
| O | 5.19453 | 1.69582 | 2.90064 | H | -5.86079 | 1.44022 | -3.98983 | H | 5.79877 | -1.05529 | -1.56706 |
| O | 4.60069 | -3.14430 | 0.12688 | H | -6.58601 | -0.09571 | -4.50404 | H | 4.07463 | 2.99937 | -2.31284 |
| C | 4.65681 | 0.29730 | -0.31419 | H | 1.33217 | 5.31765 | -2.66079 | S | 5.26774 | 0.93738 | -2.81439 |
| C | -5.40991 | -1.71319 | -2.63071 | H | -0.07572 | 6.09369 | -3.40924 | H | 5.66228 | 2.97780 | -1.53529 |
| C | -5.72004 | 0.35611 | -4.00346 | H | -0.05799 | 7.21018 | 0.74888 | H | 7.42512 | -0.09741 | 0.11952 |
| C | 0.28320 | 5.17199 | -2.93345 | H | 1.03438 | 6.98185 | -0.64328 | H | 7.23011 | 1.48585 | -0.59389 |
| C | 0.39466 | 6.47569 | 0.08118 | H | -8.15949 | 0.90592 | -0.58776 | C | 8.36414 | 0.10501 | -1.80627 |
| C | 0.11962 | -5.62959 | 0.84298 | H | -7.69710 | 1.68283 | -2.12555 | H | 9.28318 | 0.53730 | -1.39635 |
| C | -6.65655 | -1.15833 | -0.75870 | H | -3.89778 | -3.15306 | -2.33387 | H | 8.17115 | 0.60907 | -2.76164 |
| C | -7.32452 | 1.17004 | -1.23792 | H | -3.25449 | -1.62496 | -2.62038 | C | 8.59689 | -1.39285 | -2.05234 |
| C | -4.05415 | -2.06960 | -3.22675 | H | -2.38922 | -3.90492 | 1.38532 | C | 9.79409 | -1.67559 | -2.96512 |
| C | -1.93929 | 5.66553 | -0.01325 | H | -6.66571 | -3.55126 | -0.15114 | H | 7.71034 | -1.84588 | -2.50985 |
| C | -3.17204 | -4.67399 | 1.50796 | H | -5.95525 | -4.10740 | -1.69799 | H | 8.55585 | -1.90215 | -1.09479 |
| C | -5.80704 | -3.46475 | -0.82445 | H | -4.39422 | 5.58023 | 0.06746 | H | 9.81364 | -2.73016 | -3.26959 |
| C | -4.14776 | 4.85326 | -0.71305 | H | -4.57145 | 5.17896 | -1.66876 | C | 11.13249 | -1.39029 | -2.31690 |
| C | -5.69561 | 3.02686 | -1.26312 | H | -4.69252 | 0.24943 | -2.13170 | H | 9.73669 | -1.10163 | -3.89761 |
| C | -5.59456 | -0.19496 | -2.58765 | H | -0.79266 | 5.91008 | 2.90458 | O | 12.14528 | -1.46052 | -3.21681 |
| C | 0.17568 | 5.50277 | 3.20838 | H | 0.78914 | 6.33013 | 3.58781 | O | 11.32487 | -1.14788 | -1.14496 |
| C | -4.03599 | -1.50190 | -4.66527 | H | -3.04870 | -1.65798 | -5.11408 | H | 12.96095 | -1.29035 | -2.71578 |
| C | 1.06536 | -2.87989 | 3.43017 | H | -4.74374 | -2.07985 | -5.27492 | | | | |
| C | 3.39842 | -1.17556 | 4.39278 | H | 0.50576 | -2.18484 | 2.79127 | | | | |

Optimized geometry of $(-)-(S,S,R)(R,R)_7$ -mixHC[8] sulfur atom oriented towards outside

| | | | | | | | | | | | |
|------------------------|----------|----------|----------|---|----------|----------|----------|---|----------|----------|----------|
| 194 | | | | C | -1.33593 | 3.45327 | -4.32370 | H | 1.47156 | -2.57449 | -1.26299 |
| E(au) = -4640.58470461 | | | | C | -4.39682 | -3.00118 | 2.07761 | H | -1.20971 | 2.52386 | -4.89017 |
| C | -2.29005 | 3.21506 | -3.12979 | C | -3.90290 | -0.55711 | -4.89213 | H | -1.81114 | 4.16713 | -5.00999 |
| H | 2.82925 | 1.87498 | -0.32071 | C | 0.04915 | 3.99964 | -3.90960 | H | -5.38800 | -2.60838 | 1.82897 |
| C | -4.10927 | -4.28904 | 1.31654 | C | -0.87718 | 4.42020 | 4.15992 | H | -3.65971 | -2.23581 | 1.80250 |
| C | 5.90012 | 0.75348 | -1.02981 | C | 1.22987 | -1.90367 | 5.16388 | H | -3.91500 | -0.30639 | -5.95848 |
| C | -5.49706 | 2.80933 | 0.56826 | C | 1.98487 | -3.83157 | -2.98483 | H | -3.20035 | 0.14379 | -4.42058 |
| C | 3.30048 | -1.10424 | 3.28968 | C | 1.35327 | 3.31080 | 3.46254 | H | 0.62912 | 4.24542 | -4.80578 |
| C | -6.02279 | 1.38777 | 0.35807 | C | 1.95755 | -0.54525 | 5.28231 | H | 0.60679 | 3.20659 | -3.39235 |
| C | 0.16265 | 4.95921 | 1.98858 | C | 0.12935 | -5.54721 | -2.40475 | H | -1.41759 | 4.81426 | 5.02742 |
| C | 3.73714 | 4.14754 | 1.33335 | C | -5.32791 | 2.40163 | 2.99306 | H | -1.52324 | 3.64676 | 3.72209 |
| C | -2.32258 | 4.50838 | -2.32599 | C | -6.92490 | 0.98674 | 1.51953 | H | 1.69549 | -2.61989 | 5.85426 |
| C | -1.31860 | -6.57608 | 0.37041 | C | -4.30283 | -3.34167 | 3.58326 | H | 0.19111 | -1.79294 | 5.49445 |
| C | 3.90081 | 2.07985 | -0.18899 | C | 0.59892 | -4.41232 | -3.34606 | H | 2.75654 | -4.57937 | -3.21231 |
| C | -3.22672 | -5.31502 | -0.56327 | C | -2.98680 | -4.05033 | 3.97567 | H | 2.19894 | -2.96811 | -3.62456 |
| C | 2.72592 | -2.52248 | 3.30506 | C | -6.06190 | 1.05501 | 2.80221 | H | 2.32247 | 2.96722 | 3.83900 |
| C | 2.88074 | -4.36848 | 1.55857 | H | -3.29106 | 2.94498 | -3.48152 | H | 0.89567 | 2.47682 | 2.91428 |
| C | -0.92444 | 4.85853 | -1.81201 | H | -1.92901 | 2.39411 | -2.49703 | H | 1.37624 | 0.21907 | 4.74829 |
| C | 5.52482 | -0.31491 | 2.23020 | H | -4.83995 | -5.04713 | 1.65412 | H | 1.98222 | -0.23302 | 6.33202 |
| C | 1.51878 | 4.50716 | 2.53529 | C | 7.16421 | -0.00886 | -0.62736 | H | -0.90122 | -5.82982 | -2.63612 |
| C | 4.71872 | 1.99766 | 2.02562 | H | -6.35663 | 3.45985 | 0.81433 | H | 0.76258 | -6.43592 | -2.52223 |
| N | 0.59258 | 5.79566 | 0.86440 | H | 2.60652 | -0.45794 | 2.72277 | H | -4.65816 | 2.33545 | 3.85778 |
| C | 1.80641 | 5.32235 | 0.38731 | H | -5.16021 | 0.69855 | 0.34795 | H | -6.06458 | 3.17934 | 3.23596 |
| N | 5.11370 | 0.81852 | 1.41853 | H | -0.36516 | 4.07353 | 1.59296 | H | -7.31593 | -0.02461 | 1.37940 |
| N | -0.06059 | -5.87736 | 0.16584 | H | 4.13591 | 4.38082 | 2.32485 | H | -7.77581 | 1.67672 | 1.58661 |
| C | 4.27618 | -2.34752 | 1.59179 | H | 4.19045 | 4.81498 | 0.59642 | H | -4.42062 | -2.42950 | 4.17890 |
| O | -7.08905 | -1.94672 | -0.08178 | H | -2.64932 | 5.31673 | -3.00594 | H | -5.15017 | -3.98945 | 3.84577 |
| N | -5.03716 | 3.14489 | -0.78021 | H | -1.18492 | -7.19153 | 1.26098 | H | -0.14692 | -3.60625 | -3.31162 |
| N | 4.50934 | -1.31667 | 2.49292 | H | -1.51349 | -7.21444 | -0.49229 | H | 0.61139 | -4.77304 | -4.38036 |
| N | -5.29983 | -2.62001 | -1.42080 | C | 4.42937 | 2.82666 | -1.42159 | H | -3.03462 | -4.35650 | 5.02642 |
| O | -5.87916 | 2.67128 | -2.90500 | H | 3.29035 | -3.11217 | 4.05079 | H | -2.15840 | -3.33213 | 3.90330 |
| N | -1.25718 | 5.83957 | -0.77551 | H | 2.80723 | -5.00646 | 2.44524 | H | -5.31993 | 0.24575 | 2.76075 |
| N | 4.11512 | 2.78126 | 1.07052 | H | 3.74793 | -4.66582 | 0.96019 | H | -6.68729 | 0.85153 | 3.67832 |
| O | -3.02425 | 6.03717 | 0.74060 | H | -0.49929 | 3.96067 | -1.32924 | H | 5.48449 | 0.29877 | -1.93769 |
| O | -3.14041 | -5.75539 | -1.70706 | H | 5.85889 | 0.10819 | 3.17840 | H | 3.96798 | 2.40972 | -2.32384 |
| N | -4.08157 | -4.29645 | -0.14704 | H | 6.35168 | -0.83695 | 1.75354 | S | 6.23097 | 2.52701 | -1.45701 |
| O | 2.36511 | 5.66767 | -0.65072 | H | 1.93937 | 5.33724 | 3.13196 | H | 4.20165 | 3.89379 | -1.39563 |
| H | -6.44751 | -0.76626 | -1.99433 | H | 4.11971 | -0.12978 | -0.17052 | H | 6.86985 | -1.04225 | -0.40443 |
| O | 0.57703 | -5.84036 | 2.41392 | H | -5.56079 | -2.81306 | -3.48882 | H | 7.55739 | 0.42831 | 0.29704 |
| N | 2.30033 | 4.38682 | 1.30125 | H | -5.56600 | 0.74301 | -4.33992 | C | 8.28672 | -0.01960 | -1.67950 |
| N | -6.55875 | 1.49612 | -1.00234 | H | -6.06858 | -0.88592 | -4.83305 | H | 9.14294 | -0.54839 | -1.24745 |
| N | -2.50159 | -5.74936 | 0.54131 | H | 0.98477 | 5.49747 | -2.62613 | H | 8.61802 | 1.00898 | -1.87656 |
| N | 3.09785 | -2.99165 | 1.96794 | H | -0.43034 | 6.09966 | -3.50934 | C | 7.91266 | -0.69477 | -3.00597 |
| N | 1.66659 | -4.56829 | 0.78793 | H | -0.86440 | 7.26563 | 0.63650 | C | 9.06944 | -0.73952 | -4.00912 |
| N | -3.11009 | 4.59648 | -1.09476 | H | 0.36033 | 7.14442 | -0.65529 | H | 7.08165 | -0.15860 | -3.47823 |
| O | 4.87451 | 2.28875 | 3.21005 | H | -8.09078 | 0.09233 | -1.12530 | H | 7.57022 | -1.71770 | -2.81144 |
| O | 4.98133 | -2.64304 | 0.62977 | H | -7.57845 | 0.85086 | -2.65651 | H | 8.71675 | -1.05488 | -4.99982 |
| C | 4.73099 | 0.76057 | 0.00730 | H | -3.18879 | -3.56276 | -3.18587 | C | 10.17679 | -1.69701 | -3.62217 |
| C | -4.89572 | -2.27855 | -2.78561 | H | -2.77201 | -1.94794 | -2.59875 | H | 9.51224 | 0.25247 | -4.15824 |
| C | -5.30610 | -0.31755 | -4.28519 | H | -1.99590 | -3.96623 | 1.53071 | O | 11.25602 | -1.56076 | -4.43335 |
| C | -0.01641 | 5.23334 | -2.97764 | H | -6.15805 | -4.13673 | -0.32253 | O | 10.14069 | -2.51217 | -2.72611 |
| C | -0.28882 | 6.57871 | 0.01452 | H | -5.27405 | -4.67826 | -1.78273 | H | 11.90259 | -2.22113 | -4.13145 |
| C | 0.70770 | -5.46920 | 1.25008 | H | -4.94863 | 5.19675 | -0.38754 | | | | |
| C | -6.35834 | -1.79040 | -1.05711 | H | -4.93405 | 4.71230 | -2.11143 | | | | |
| C | -7.23428 | 0.42336 | -1.71393 | H | -4.44478 | -0.22737 | -2.33074 | | | | |
| C | -3.46145 | -2.50422 | -3.24682 | H | -1.65528 | 5.88138 | 2.73582 | | | | |
| C | -2.51565 | 5.54441 | -0.26329 | H | -0.17351 | 6.40547 | 3.55731 | | | | |
| C | -2.70607 | -4.80424 | 1.64317 | H | -2.34218 | -2.06038 | -5.06165 | | | | |
| C | -5.26229 | -3.98743 | -0.93371 | H | -3.95994 | -2.67731 | -5.34257 | | | | |
| C | -4.55764 | 4.47443 | -1.11122 | H | 0.67884 | -1.89386 | 3.04113 | | | | |
| C | -5.83042 | 2.45603 | -1.69642 | H | 0.84059 | -3.51336 | 3.73288 | | | | |
| C | -5.24828 | -0.79045 | -2.83718 | H | 3.81363 | 0.45720 | 4.71017 | | | | |
| C | -0.68602 | 5.54293 | 3.11232 | H | 4.05059 | -1.19129 | 5.31320 | | | | |
| C | -3.37673 | -1.99828 | -4.70593 | H | 2.33671 | -5.48738 | -0.96962 | | | | |
| C | 1.26598 | -2.50453 | 3.73897 | H | -1.64978 | -5.65329 | 3.33837 | | | | |
| C | 3.39418 | -0.55368 | 4.70741 | H | -3.36933 | -6.08313 | 3.25267 | | | | |
| C | 1.69297 | -4.63835 | -0.67422 | H | -4.13092 | 3.86380 | 1.88858 | | | | |
| C | -2.64525 | -5.27409 | 3.09213 | H | -3.68419 | 2.18511 | 1.55743 | | | | |
| C | -4.53263 | 2.85520 | 1.74647 | H | -0.37450 | -4.10162 | -0.91258 | | | | |
| C | 0.24189 | -5.01520 | -0.98068 | H | 0.22259 | 2.91780 | 5.28187 | | | | |
| C | 0.44375 | 3.76804 | 4.62710 | H | 1.00181 | 4.48872 | 5.23988 | | | | |
| C | 2.11874 | -3.42941 | -1.49735 | H | 3.14848 | -3.13769 | -1.26588 | | | | |

| | | | | | | | | | | | |
|------------------------|-----------|----------|----------|---|---------|----------|----------|---|----------|----------|----------|
| 194 | | | | C | 5.13666 | -3.18749 | 0.84787 | C | -8.48642 | 0.73558 | -2.27270 |
| E(au) = -4640.58455699 | | | | C | 2.67621 | -5.49773 | -0.06735 | H | -3.71852 | 3.88282 | -1.73415 |
| C | -4.05879 | -2.28508 | -0.39943 | H | 5.13612 | -3.39107 | 4.27019 | C | -2.12129 | 3.44536 | -3.15782 |
| C | -2.69975 | 3.01168 | 2.76101 | H | 3.84395 | -2.79301 | 3.24475 | N | 0.19324 | 5.15052 | 0.00436 |
| H | -0.74711 | -5.70476 | 2.80576 | H | 5.20187 | -5.86583 | -0.15989 | N | 2.60912 | 5.00034 | 0.24389 |
| H | 5.47903 | -5.30644 | -1.83130 | H | 5.21019 | -0.89002 | 3.96557 | C | -2.75017 | 4.29689 | -2.02902 |
| H | 6.40320 | 1.10701 | -3.44052 | H | 6.69076 | -1.68115 | 3.45684 | H | -2.91049 | 5.32945 | -2.36495 |
| H | 5.72810 | 4.85806 | 2.59302 | C | 5.34039 | -3.91987 | 2.16921 | N | -4.43424 | -2.82436 | 0.90541 |
| H | -2.96810 | -2.28956 | -0.51400 | C | 5.62791 | -1.56125 | 3.20680 | N | -4.95700 | -0.66247 | 1.06705 |
| C | -5.72420 | -0.60915 | -1.37570 | H | 6.12930 | 0.00933 | 1.76600 | O | -4.98783 | 2.93366 | 0.10118 |
| C | -9.67189 | 0.94844 | -3.21904 | C | 4.96941 | -5.09073 | -0.89132 | H | 0.44521 | 2.98684 | -1.85798 |
| H | -5.71456 | 0.35024 | 2.66850 | H | 4.48911 | -0.62493 | 1.58353 | H | -2.75449 | 3.49158 | -0.45043 |
| H | 0.72886 | -3.05653 | 2.44163 | C | 5.52626 | -0.90333 | 1.81068 | H | -2.12072 | 2.39424 | -2.83858 |
| H | 1.30731 | -5.84870 | -2.43077 | H | 2.80761 | -3.28822 | -1.74845 | H | -0.70600 | 4.83560 | -0.43255 |
| C | 2.79572 | -4.34150 | -2.07965 | H | 4.72742 | -4.82419 | 2.21389 | C | -0.67918 | 3.86151 | -3.52562 |
| H | 6.39245 | -4.21446 | 2.27386 | H | 4.08011 | -2.87027 | 0.79784 | H | 1.23442 | 4.38426 | -2.60156 |
| H | 7.63378 | -0.32950 | -0.50911 | H | 7.04154 | -2.22491 | 1.09009 | H | -0.26652 | 3.15146 | -4.25089 |
| H | 3.32182 | 0.28519 | -5.23901 | C | 6.01434 | -1.93496 | 0.80147 | C | 0.26412 | 3.97274 | -2.30485 |
| C | 4.43404 | 3.90454 | 1.15005 | C | 5.86716 | -2.83208 | -1.32922 | O | 7.17050 | 1.89708 | 0.23213 |
| H | -9.60598 | 0.30221 | -4.10244 | C | 4.93195 | -2.93839 | 3.29370 | O | -2.45340 | -5.36307 | -0.62596 |
| C | -7.13639 | -0.97254 | -0.88633 | C | 4.49627 | 0.14561 | -3.41052 | O | -0.66128 | 5.90932 | 2.04059 |
| H | -6.08927 | 1.08232 | 1.08075 | C | 6.81279 | -0.56640 | -1.19322 | O | 3.54441 | 5.53743 | -1.82611 |
| C | -4.83688 | -1.83449 | 1.78516 | H | 2.78345 | 2.39030 | -4.10580 | N | -2.03131 | 5.05546 | 0.35142 |
| C | -3.99318 | -3.69445 | -2.08430 | H | 3.62644 | 2.76138 | -5.59904 | O | 6.04769 | -2.98388 | -2.53494 |
| O | -5.06149 | -1.97531 | 2.98493 | C | 5.55185 | 1.01618 | -2.74090 | O | 2.99945 | -6.01054 | 1.00137 |
| H | -7.15506 | -2.02051 | -0.56641 | H | 4.39502 | 4.15904 | -3.62332 | N | 5.97782 | 2.91460 | -1.50164 |
| C | -8.26224 | -0.73866 | -1.90548 | H | 5.73107 | 3.23553 | -4.33950 | N | -2.77915 | -4.53184 | 1.53205 |
| C | -4.68762 | -3.00186 | -1.60878 | C | 4.14004 | 0.82751 | -4.75221 | N | 6.07690 | 0.66426 | -1.42051 |
| H | -12.84327 | 0.59753 | -2.97793 | C | 4.78115 | 3.15098 | -3.79624 | N | 4.79620 | 4.57653 | -0.10188 |
| H | -8.65297 | 1.32041 | -1.36083 | H | 4.02093 | 2.31766 | -1.98051 | C | -0.81881 | 5.42188 | 0.92378 |
| H | -7.59302 | 1.14809 | -2.75486 | H | 4.86965 | -0.86980 | -3.57761 | N | 6.00597 | -1.63474 | -0.63101 |
| H | -5.70319 | 0.42678 | -1.72373 | C | 5.00171 | 2.41933 | -2.47726 | C | -1.76853 | 4.27834 | -0.86283 |
| S | -5.15159 | -1.66691 | -2.78509 | C | 6.4810 | | | | | | |

Optimized geometry of (+)-((*S,S,R*)(*S,S*)₇)-mixHC[8] sulfur atom oriented towards outside

| | | | | | | | | | | | |
|------------------------|----------|----------|----------|---|----------|----------|----------|---|----------|----------|----------|
| 194 | | | | H | -5.71605 | 5.43594 | -0.58504 | N | 5.07136 | 1.18196 | 1.35246 |
| E(au) = -4640.58471172 | | | | H | -5.58039 | 0.62359 | 3.71678 | O | 5.33994 | -2.44728 | 0.59156 |
| C | 3.81633 | 2.52428 | -0.15852 | H | -7.08542 | 1.24299 | 3.06268 | H | 0.05980 | -3.01834 | -1.68365 |
| C | 2.91276 | -2.55180 | 3.12161 | C | -5.86147 | 3.56493 | 1.79469 | H | 3.42437 | -3.38887 | -3.64437 |
| H | 0.03945 | 5.76947 | 2.77882 | C | -5.99908 | 1.22394 | 2.90131 | H | 2.63164 | -2.28109 | -2.53876 |
| H | -5.82566 | 4.80721 | -2.25094 | H | -6.22275 | -0.43547 | 1.49072 | H | 1.48517 | -4.88606 | -3.67184 |
| H | -5.97281 | -1.72517 | -3.67415 | C | -5.36264 | 4.66720 | -1.27338 | C | 1.35232 | -3.89116 | -3.22590 |
| H | -5.34634 | -5.15363 | 2.54419 | H | -4.64440 | 0.35723 | 1.41091 | H | -0.57278 | -4.51129 | -2.39010 |
| H | 2.75051 | 2.31507 | -0.32312 | C | -5.71918 | 0.53505 | 1.54519 | H | 0.93558 | -3.25623 | -4.01573 |
| C | 5.80625 | 1.25367 | -1.10194 | H | -3.00089 | 3.06005 | -1.96031 | C | 0.34282 | -4.00971 | -2.06007 |
| C | 8.89991 | -0.06105 | -4.23807 | H | -5.34407 | 4.52646 | 1.85011 | O | -6.92925 | -2.46742 | -0.03689 |
| H | 5.73117 | 0.31154 | 3.07221 | H | -4.39755 | 2.60475 | 0.56769 | O | 1.97244 | 5.58112 | -0.54076 |
| H | -1.20703 | 3.01924 | 2.32476 | H | -7.29446 | 1.67115 | 0.65673 | O | 1.12681 | -5.63227 | 2.43877 |
| H | -1.68645 | 5.73441 | -2.58796 | C | -6.22362 | 1.47820 | 0.46042 | O | -2.82613 | -5.80843 | -1.69579 |
| C | -3.05903 | 4.10629 | -2.30835 | C | -5.99512 | 2.31633 | -1.68701 | N | 2.53516 | -4.76352 | 0.78948 |
| H | -6.94221 | 3.75595 | 1.80554 | C | -5.45195 | 2.66680 | 2.98643 | O | -6.09257 | 2.41003 | -2.90821 |
| H | -7.56145 | -0.32851 | -0.90487 | C | -4.17985 | -0.57142 | -3.54913 | O | -3.61042 | 5.78359 | 0.72471 |
| H | -2.86601 | -0.65014 | -5.28417 | C | -6.71676 | -0.02924 | -1.53341 | N | -5.51296 | -3.41302 | -1.63785 |
| C | -4.05394 | -4.14318 | 1.13895 | H | -2.20331 | -2.64947 | -4.03085 | N | 2.22799 | 4.75699 | 1.62957 |
| C | 9.35333 | 0.93356 | -4.32369 | H | -2.89270 | -3.15531 | -5.56292 | N | -5.84425 | -1.18338 | -1.65602 |
| C | 7.06829 | 0.45191 | -0.77596 | C | -5.18948 | -1.52333 | -2.92039 | N | -4.27015 | -4.89753 | -0.09962 |
| H | 6.29050 | -0.49351 | 1.58268 | H | -3.66062 | -4.55808 | -3.59033 | C | 1.31951 | -5.19364 | 1.30748 |
| C | 4.64541 | 2.29980 | 2.04534 | H | -5.02574 | -3.80168 | -4.43527 | N | -6.06959 | 1.13419 | -0.95401 |
| H | 3.88505 | 3.01030 | -2.26115 | C | -3.65905 | -1.25746 | -4.83364 | C | 2.29481 | -4.07674 | -0.48196 |
| O | 4.80752 | 2.50783 | 3.24594 | C | -4.13189 | -3.60131 | -3.83073 | N | -1.82767 | 5.07650 | -0.60571 |
| H | 7.48402 | 0.82473 | 0.16663 | H | -3.59612 | -2.63347 | -2.00131 | C | -3.13290 | -3.80423 | 3.87631 |
| C | 8.17022 | 0.50036 | -1.84878 | H | -4.63966 | 0.39412 | -3.78305 | N | 3.84369 | -3.21674 | 2.20738 |
| C | 4.35081 | 3.35752 | -1.33230 | C | -4.52209 | -2.85252 | -2.56148 | H | 2.03077 | -3.02452 | -0.27367 |
| H | 11.71362 | -1.55914 | -4.51412 | C | -6.17506 | -2.36789 | -1.00174 | C | -2.11431 | -3.94654 | 2.72130 |
| H | 7.41151 | -1.10533 | -3.08382 | H | -7.07800 | 0.26262 | -2.52462 | N | 0.14735 | 5.04433 | 0.81607 |
| H | 6.92982 | 0.50305 | -3.62876 | H | -4.47616 | -1.28568 | -5.56717 | N | 4.38125 | -1.02192 | 2.17487 |
| H | 5.37118 | 0.87289 | -2.03477 | H | -3.35893 | -0.38424 | -2.84493 | N | -3.92724 | 4.86072 | -1.39904 |
| S | 6.14976 | 3.05047 | -1.39670 | H | -6.32365 | -4.86037 | -0.43754 | | | | |
| H | 4.04156 | 0.31482 | -0.24925 | H | -5.30730 | -5.48006 | -1.76617 | | | | |
| H | 9.02689 | -0.06821 | -1.47154 | C | -5.39895 | -4.71242 | -0.99674 | | | | |
| H | 4.12363 | 4.41905 | -1.23112 | C | -3.14172 | -2.69492 | -4.60055 | | | | |
| O | 11.07175 | -0.86931 | -4.75379 | C | -4.52583 | -3.31836 | 3.41590 | | | | |
| H | 4.59453 | -4.75863 | 1.09594 | H | -6.03656 | -3.66059 | 1.87845 | | | | |
| H | 4.11708 | 4.66021 | 2.49766 | H | -1.18551 | -4.40402 | 3.07752 | | | | |
| C | 1.56119 | -2.23236 | 5.16064 | H | -1.85950 | -2.96570 | 2.29996 | | | | |
| H | 1.21689 | 3.01573 | 2.21937 | C | -5.11381 | -4.12667 | 2.23450 | | | | |
| C | 1.32469 | 4.06480 | 2.54825 | H | -3.05702 | -5.76847 | 2.12719 | | | | |
| C | 5.44115 | -0.01917 | 2.07166 | C | -2.77633 | -4.80906 | 1.65452 | | | | |
| H | 2.54894 | 3.54480 | 4.26595 | H | -3.23891 | -4.78110 | 4.36721 | | | | |
| H | 1.68878 | 5.08430 | 4.41706 | C | -3.03899 | -5.31914 | -0.58919 | | | | |
| H | 4.04371 | 5.20492 | 0.80493 | H | -0.77765 | -6.47501 | 1.28608 | | | | |
| C | 1.60584 | 4.05502 | 4.04553 | H | -5.22097 | -3.34452 | 4.26218 | | | | |
| H | 0.53421 | 3.36184 | 5.80883 | H | -0.89497 | -6.52240 | -0.50023 | | | | |
| C | 3.02248 | -0.93346 | 6.09750 | C | -0.84943 | -5.86904 | 0.37714 | | | | |
| H | 0.46705 | 2.26128 | 4.44326 | H | -3.81835 | -3.09544 | 0.88226 | | | | |
| C | 0.42068 | 3.32368 | 4.71995 | H | -2.73908 | -3.12160 | 4.63761 | | | | |
| H | 1.91313 | -4.15712 | 4.18917 | H | -4.45457 | -2.26542 | 3.11032 | | | | |
| C | 2.20864 | -0.84434 | 5.36528 | H | 1.33943 | -5.77396 | -1.38545 | | | | |
| H | 1.47651 | -0.15813 | 5.80538 | C | 1.03340 | -4.80155 | -0.95728 | | | | |
| H | -1.75111 | 3.25679 | 4.75671 | H | 3.57886 | -5.26500 | 2.47301 | | | | |
| H | -1.08743 | 4.88028 | 4.77357 | N | -5.80293 | 3.36695 | -0.79545 | | | | |
| C | -0.96437 | 3.88534 | 4.32486 | H | 8.52465 | -0.29964 | -5.24191 | | | | |
| C | 3.64781 | 4.48898 | 1.52787 | C | 10.00039 | -1.05831 | -3.94278 | | | | |
| H | -0.25529 | 6.45410 | -0.63009 | C | 2.46380 | -3.23770 | 4.40703 | | | | |
| C | -1.17154 | 4.00945 | 2.79676 | C | 3.68088 | -4.55065 | 1.65475 | | | | |
| H | 0.40248 | 4.37451 | -2.33642 | H | 3.33081 | 0.69197 | 4.28268 | | | | |
| H | -0.58787 | 2.93614 | -2.05690 | H | 1.98058 | 0.01645 | 3.36273 | | | | |
| C | 0.01418 | 4.79671 | 2.25400 | H | 3.33951 | -3.50249 | 5.01344 | | | | |
| H | -0.59524 | 4.74174 | -4.54897 | C | 2.78545 | -0.23220 | 4.06724 | | | | |
| H | -0.02597 | 3.08366 | -4.49109 | H | 4.46667 | -1.54266 | 4.20356 | | | | |
| C | -1.71164 | 4.77775 | -2.03412 | H | 2.00659 | -2.26305 | 2.56017 | | | | |
| C | -0.77661 | 3.76639 | -4.07752 | C | 3.70118 | -1.28129 | 3.45042 | | | | |
| H | -2.29763 | 2.22356 | -4.16553 | C | 4.59649 | -2.25664 | 1.55029 | | | | |
| C | 1.50333 | 5.17073 | 0.51787 | O | 9.96447 | -1.94250 | -3.11479 | | | | |
| H | -2.30134 | 3.29793 | -0.55275 | H | 0.62867 | -2.11253 | 4.59200 | | | | |
| C | -2.19058 | 3.27577 | -4.46310 | H | 1.27509 | -2.65024 | 6.13194 | | | | |
| H | -2.11653 | 4.51541 | 2.57370 | H | 6.77113 | -0.59149 | -0.61086 | | | | |
| C | -0.81779 | 5.85234 | 0.09106 | C | 4.65647 | 1.19957 | -0.04737 | | | | |
| H | -1.34378 | 6.50980 | 0.79078 | H | 8.51201 | 1.53584 | -1.98060 | | | | |
| H | -4.30044 | 3.61329 | -4.01892 | C | 7.76257 | -0.07484 | -3.21194 | | | | |
| H | -3.36182 | 5.10863 | -4.19764 | H | 4.26299 | -3.57889 | -1.25568 | | | | |
| C | -3.33620 | 4.08323 | -3.80712 | C | 2.73254 | -3.34463 | -2.79624 | | | | |
| C | -0.56780 | 3.91534 | -2.55228 | N | 0.35111 | -5.05299 | 0.31376 | | | | |
| C | -5.48077 | 2.81430 | 0.52364 | N | -2.08084 | -5.10075 | 0.39999 | | | | |
| C | -3.17390 | 5.29082 | -0.31256 | C | 3.34885 | -4.08186 | -1.58334 | | | | |
| H | -5.77905 | 3.12791 | 3.92478 | H | 3.60697 | -5.11519 | -1.84805 | | | | |
| H | -4.35458 | 2.63133 | 3.02879 | N | 4.00576 | 3.13491 | 1.15574 | | | | |

Optimized geometry of $\text{PF}_6^-@(-)((\text{S},\text{S},\text{R})(\text{R},\text{R})_7)\text{-mixHC}[8]$ sulfur atom oriented towards outside

| | | | | | | | | | | | | |
|------------------------|----------|----------|----------|---|----------|----------|----------|--|---|-----------|----------|----------|
| 201 | | | | C | 4.52787 | -2.46510 | 1.57758 | | H | 0.78080 | 5.28760 | 3.21349 |
| E(au) = -5581.34704297 | | | | C | -0.84054 | 4.63413 | -0.85740 | | H | 2.45441 | 5.85599 | 3.29966 |
| C | 2.52159 | -2.80125 | -2.94756 | C | -0.00588 | -3.32683 | 4.44186 | | H | 4.25305 | -3.51308 | 1.73624 |
| H | -2.49125 | -1.89465 | 0.02947 | C | -2.61709 | 2.89417 | -1.21675 | | H | 3.62236 | -1.92077 | 1.28849 |
| C | 3.48809 | 4.37575 | 1.25254 | C | 1.46091 | -2.93052 | -4.06632 | | H | -0.20094 | 3.77355 | -0.60338 |
| C | -5.52243 | -1.02893 | -1.07495 | C | 3.85752 | 3.04469 | 1.89498 | | H | 0.13016 | -2.39499 | 5.00175 |
| C | 5.58855 | -2.34097 | 0.49088 | C | 3.49484 | 0.66758 | -4.66100 | | H | -0.40296 | -4.06238 | 5.15630 |
| C | -3.56310 | 0.83785 | 3.26439 | C | 0.11758 | -3.51218 | -3.57301 | | H | -3.65451 | 2.60681 | -1.01362 |
| C | 5.94712 | -0.87128 | 0.25982 | C | 1.36249 | -3.81678 | 3.91811 | | H | -1.95989 | 2.11892 | -0.81064 |
| C | 0.26932 | -4.71530 | 1.90471 | C | -1.42526 | 1.74872 | 5.00326 | | H | 1.28731 | -1.95075 | -4.52495 |
| C | -3.39989 | -4.37249 | 1.39715 | C | -2.39474 | 3.05788 | -2.73895 | | H | 1.86263 | -3.57668 | -4.86034 |
| C | 2.62403 | -4.16711 | -2.28075 | C | -1.04887 | -3.11176 | 3.31969 | | H | 4.90425 | 2.79275 | 1.69426 |
| C | 0.55192 | 6.48141 | 0.31853 | C | -1.99394 | 0.31451 | 5.09181 | | H | 3.22992 | 2.24507 | 1.48812 |
| C | -3.53707 | -2.21982 | -0.01298 | C | -0.65800 | 4.93352 | -2.34059 | | H | 3.43526 | 0.37573 | -5.71614 |
| C | 2.62310 | 5.49647 | -0.58406 | C | 5.14669 | -1.87457 | 2.86635 | | H | 2.92574 | -0.08343 | -4.09961 |
| C | -3.14221 | 2.30737 | 3.33275 | C | 6.68625 | -0.32186 | 1.47448 | | H | -0.55692 | -3.65678 | -4.42509 |
| C | -3.55833 | 4.18055 | 1.63818 | C | 3.62488 | 3.20750 | 3.41555 | | H | -0.35821 | -2.77730 | -2.91172 |
| C | 1.27595 | -4.57402 | -1.68121 | C | -1.00454 | 3.62889 | -3.09783 | | H | 2.02606 | -4.02935 | 4.76451 |
| C | -5.71852 | -0.16350 | 2.26934 | C | 2.21284 | 3.72735 | 3.76628 | | H | 1.82745 | -3.00446 | 3.34623 |
| C | -1.09959 | -4.40382 | 2.51569 | C | 5.72373 | -0.45347 | 2.67921 | | H | -1.89619 | 2.37004 | 5.77857 |
| C | -4.67667 | -2.37520 | 2.05271 | H | 3.48664 | -2.50305 | -3.37081 | | H | -0.35395 | 1.72979 | 5.23167 |
| N | -0.11269 | -5.71569 | 0.89824 | H | 2.22373 | -2.04716 | -2.21216 | | H | -3.17214 | 3.72436 | -3.13984 |
| C | -1.40321 | -5.44362 | 0.46739 | H | 4.11193 | 5.16262 | 1.71859 | | H | -2.52985 | 2.09084 | -3.23636 |
| N | -5.11315 | -1.20351 | 1.45288 | C | -6.91091 | -0.43899 | -0.81651 | | H | -2.02972 | -2.88405 | 3.75153 |
| N | -0.65185 | 5.68735 | 0.14980 | H | 6.49648 | -2.86768 | 0.84232 | | H | -0.75664 | -2.27808 | 2.67305 |
| C | -4.81513 | 2.06491 | 1.74386 | H | -2.85909 | 0.31632 | 2.59546 | | H | -1.38944 | -0.34250 | 4.45447 |
| O | 6.93084 | 2.59953 | -0.22415 | H | 5.00672 | -0.30744 | 0.14442 | | H | -1.88732 | -0.06127 | 6.11622 |
| N | 5.30861 | -2.77787 | -0.87551 | H | 0.62987 | -3.80859 | 1.39355 | | H | 0.36660 | 5.24824 | -2.56047 |
| N | -4.86187 | 0.96096 | 2.59257 | H | -3.78088 | -4.64688 | 2.38652 | | H | -1.32843 | 5.74938 | -2.64333 |
| N | 4.97508 | 3.02084 | -1.42313 | H | -3.81041 | -5.05908 | 0.65082 | | H | 4.39469 | -1.86085 | 3.66309 |
| O | 6.24570 | -2.26484 | -2.94878 | H | 2.89483 | -4.90708 | -3.05821 | | H | 5.94844 | -2.54433 | 3.20931 |
| N | 1.70079 | -5.64995 | -0.77509 | H | 0.36614 | 7.11313 | 1.18935 | | H | 6.97089 | 0.72365 | 1.32435 |
| N | -3.85928 | -0.32340 | 1.16339 | H | 0.70841 | 7.10432 | -0.56428 | | H | 7.60405 | -0.90077 | 1.64453 |
| O | 3.57872 | -5.93487 | 0.59109 | C | -3.80046 | -2.93670 | -1.34434 | | H | 3.79631 | 2.24972 | 3.91939 |
| O | 2.55526 | 6.03076 | -1.69035 | H | -3.68999 | 2.78734 | 4.16608 | | H | 4.37499 | 3.90570 | 3.81442 |
| N | 3.55419 | 4.54116 | -0.19857 | H | -3.51541 | 4.85338 | 2.50135 | | H | -0.24596 | 2.87489 | -2.85479 |
| O | -1.96876 | -5.94658 | -0.50311 | H | -4.44453 | 4.40790 | 1.03544 | | H | -0.94521 | 3.80177 | -4.17891 |
| N | 6.25882 | 1.27687 | -2.03352 | H | 0.90067 | -3.72864 | -1.08316 | | H | 2.14270 | 3.90428 | 4.84605 |
| O | -1.40955 | 5.94862 | 2.34806 | H | -6.02637 | -0.66594 | 3.18793 | | H | 1.48419 | 2.94331 | 3.52590 |
| N | -1.95946 | -4.50771 | 1.33532 | H | -6.59208 | 0.25804 | 1.77381 | | H | 4.89285 | 0.24804 | 2.53317 |
| N | 6.61806 | -0.95710 | -1.04406 | H | -1.36323 | -5.22625 | 3.20776 | | H | 6.23591 | -0.14046 | 3.59670 |
| N | 1.79213 | 5.74808 | 0.50290 | H | -3.97503 | -0.06054 | 0.10249 | | H | -5.03251 | -0.46270 | -1.87666 |
| N | -3.69351 | 2.80777 | 2.07435 | H | 5.00322 | 3.14620 | -3.50894 | | H | -3.24156 | -2.43758 | -2.14289 |
| N | -2.35268 | 4.40893 | 0.87158 | H | 5.34675 | -0.41334 | -4.24023 | | S | -5.59566 | -2.78734 | -1.66150 |
| N | 3.50915 | -4.36480 | -1.13324 | H | 5.60504 | 1.24165 | -4.82081 | | H | -3.49651 | -3.98547 | -1.32552 |
| O | -4.97125 | -2.75762 | 3.18483 | H | -0.69280 | -5.16666 | -2.39362 | | H | -6.77813 | 0.59353 | -0.47073 |
| O | -5.62652 | 2.33609 | 0.85958 | H | 0.64345 | -5.63764 | -3.45457 | | H | -7.37710 | -0.99962 | 0.00125 |
| C | -4.52463 | -1.00698 | 0.12743 | H | 1.45119 | -7.08033 | 0.65589 | | C | -7.86353 | -0.45429 | -2.02492 |
| C | 4.47609 | 2.57377 | -2.72173 | H | 0.17786 | -7.06855 | -0.59753 | | H | -8.84117 | -0.09032 | -1.68962 |
| C | 4.96707 | 0.61113 | -4.18697 | H | 7.98869 | 0.61248 | -1.17524 | | H | -8.01174 | -1.48854 | -2.36463 |
| C | 0.27101 | -4.84149 | -2.79561 | H | 7.55841 | -0.21615 | -2.69843 | | C | -7.40203 | 0.40526 | -3.20970 |
| C | 0.80622 | -6.44724 | 0.04353 | H | 2.60646 | 3.64152 | -2.99315 | | C | -8.35111 | 0.34595 | -4.41072 |
| C | -1.46228 | 5.40612 | 1.24490 | H | 2.42799 | 2.01934 | -2.30526 | | H | -6.41609 | 0.07182 | -3.55186 |
| C | 6.13919 | 2.32698 | -1.12537 | H | 1.41526 | 3.82397 | 1.26791 | | H | -7.29506 | 1.44691 | -2.88642 |
| C | 7.17296 | 0.18080 | -1.75772 | H | 5.64617 | 4.61039 | -0.31285 | | H | -7.90090 | 0.82960 | -5.28817 |
| C | 2.98588 | 2.61550 | -3.03638 | H | 4.73894 | 5.07145 | -1.78807 | | C | -9.68090 | 1.03137 | -4.18497 |
| C | 2.99244 | -5.37572 | -0.33503 | H | 5.40012 | -4.83861 | -0.49510 | | H | -8.54846 | -0.68863 | -4.71546 |
| C | 2.01854 | 4.71133 | 1.51872 | H | 5.30805 | -4.33351 | -2.21193 | | O | -10.56490 | 0.74279 | -5.17843 |
| C | 4.78292 | 4.37382 | -0.94434 | H | 4.30137 | 0.51366 | -2.15268 | | O | -9.96799 | 1.77236 | -3.27043 |
| C | 4.93705 | -4.13894 | -1.19965 | H | 2.24359 | -5.31741 | 2.59014 | | H | -11.37046 | 1.24224 | -4.96265 |
| C | 6.07282 | -2.02493 | -1.75468 | H | 0.90670 | -5.93331 | 3.57293 | | F | 2.21346 | -0.01153 | -0.23974 |
| C | 4.98770 | 1.13212 | -2.75444 | H | 1.75928 | 1.97156 | -4.71421 | | F | 0.30704 | -1.22699 | -0.79085 |
| C | 1.26390 | -5.06297 | 3.00569 | H | 3.25861 | 2.76100 | -5.17808 | | F | 1.07140 | -1.19112 | 1.39800 |
| C | 2.82370 | 2.04578 | -4.46526 | H | -1.07190 | 1.91585 | 2.84549 | | P | 0.66319 | -0.04657 | 0.29228 |
| C | -1.65160 | 2.41847 | 3.62726 | H | -1.33545 | 3.46638 | 3.65879 | | F | 0.25869 | 1.09585 | -0.81325 |
| C | -3.47123 | 0.20014 | 4.64489 | H | -3.78562 | -0.84848 | 4.62033 | | F | 1.00042 | 1.13147 | 1.38447 |
| C | -2.29426 | 4.24098 | -0.58017 | H | -4.13243 | 0.72836 | 5.34477 | | F | -0.89314 | -0.08640 | 0.82765 |
| C | 1.81780 | 5.01254 | 2.99954 | H | -2.95194 | 5.00178 | -1.04278 | | | | | |

| | | | | | | | | | | | |
|------------------------|----------|----------|----------|----------|----------|----------|----------|---------|----------|----------|----------|
| 201 | | | C | -0.63194 | 4.59765 | -1.18034 | H | 4.01418 | -3.52035 | 2.06068 | |
| E(au) = -5581.34626015 | | | C | -0.55349 | -3.26889 | 4.33410 | H | 3.46089 | -1.93714 | 1.49391 | |
| C | 2.72712 | -2.93579 | -2.76062 | C | -2.40904 | 2.85947 | -1.53807 | H | -0.02335 | 3.74763 | -0.83187 |
| H | -2.50693 | -2.02686 | -0.26612 | C | 1.77158 | -3.07379 | -3.96956 | H | -0.47343 | -2.32750 | 4.88882 |
| C | 3.53923 | 4.40188 | 1.21650 | C | 3.83225 | 3.10432 | 1.95897 | H | -1.02606 | -3.99069 | 5.01594 |
| C | -5.39921 | -0.63943 | -1.28710 | C | 3.93032 | 0.40234 | -4.52560 | H | -3.46085 | 2.59663 | -1.38265 |
| C | 5.48393 | -2.42261 | 0.90136 | C | 0.38154 | -3.63116 | -3.59225 | H | -1.79176 | 2.10349 | -1.04349 |
| C | -3.55043 | 1.08646 | 2.98131 | C | 0.85964 | -3.77064 | 3.96499 | H | 1.65298 | -2.10109 | -4.45939 |
| C | 5.89339 | -0.96986 | 0.64740 | C | -1.47983 | 2.09079 | 4.74156 | H | 2.23613 | -3.73930 | -4.71165 |
| C | -0.02697 | -4.70740 | 1.86824 | C | -2.90091 | 2.91762 | -3.05051 | H | 4.88087 | 2.81337 | 1.83688 |
| C | -3.62355 | -4.38413 | 0.95314 | C | -1.47443 | -3.07040 | 3.10663 | H | 3.20574 | 2.29699 | 1.56464 |
| C | 2.75097 | -4.28959 | -2.06193 | C | -2.02773 | 0.65157 | 4.86793 | H | 3.95748 | 0.06796 | -5.56939 |
| C | 0.71622 | 6.49798 | -0.03663 | C | -0.35242 | 4.79628 | -2.66537 | H | 3.29918 | -0.31513 | -3.98755 |
| C | -3.58310 | -2.19231 | -0.38345 | C | 4.83110 | -1.85139 | 3.20432 | H | -0.21363 | -3.78236 | -4.50041 |
| C | 2.82259 | 5.42683 | -0.73596 | C | 6.52545 | -0.38314 | 1.90424 | H | -0.14335 | -2.87873 | -2.99006 |
| C | -3.14882 | 2.56178 | 2.99561 | C | 3.51562 | 3.36882 | 3.44943 | H | 1.43151 | -3.96828 | 4.87929 |
| C | -3.49955 | 4.33077 | 1.17101 | C | -0.67274 | 3.44882 | -3.35728 | H | 1.38432 | -2.97099 | 3.42810 |
| C | 1.34756 | -4.66989 | -1.58457 | C | 2.09991 | 3.94304 | 3.67978 | H | -1.98649 | 2.73355 | 5.47591 |
| C | -5.61327 | -0.00596 | 1.93840 | C | 5.45043 | -0.44834 | 3.01570 | H | -0.41686 | 2.09919 | 5.00582 |
| C | -1.45195 | -4.37756 | 2.32394 | H | 3.73050 | -2.65755 | -3.09975 | H | -2.83154 | 3.56451 | -3.54320 |
| C | -4.71990 | -2.29886 | 1.67975 | H | 2.37470 | -2.16444 | -2.06822 | H | -2.21116 | 1.91970 | -3.48527 |
| N | -0.30517 | -5.73212 | 0.85414 | H | 4.15183 | 5.20121 | 1.67621 | H | -2.49179 | -2.83203 | 3.43420 |
| C | -1.54113 | -5.47132 | 0.28185 | C | -6.76865 | -1.31747 | -1.09820 | H | -1.10926 | -2.24953 | 2.48042 |
| N | -4.89493 | -1.01848 | 1.19081 | H | 6.34413 | -2.94979 | 1.35692 | H | -1.39721 | -0.01810 | 4.26960 |
| N | -0.48883 | 5.71216 | -0.23228 | H | -2.82624 | 0.54398 | 2.35309 | H | -1.94319 | 0.31490 | 5.90786 |
| O | -4.75618 | 2.21574 | 1.35571 | H | 4.98017 | -0.39540 | 0.42078 | H | 0.68905 | 5.08330 | -2.83947 |
| C | 7.00842 | 2.46609 | 0.11063 | H | 0.38961 | -3.81367 | 1.37678 | H | -0.98888 | 5.59912 | -3.06193 |
| N | 5.32435 | -2.91001 | -0.46746 | H | -4.11583 | -4.69980 | 1.87948 | H | 4.00795 | -1.79270 | 3.92500 |
| N | -4.83252 | 1.16504 | 2.27255 | H | -3.92161 | -5.04570 | 0.13559 | H | 5.58428 | -2.51855 | 3.64786 |
| N | 5.17446 | 2.86908 | -1.27295 | H | 3.08503 | -5.04757 | -2.79617 | H | 6.84532 | 0.65015 | 1.74072 |
| O | 6.46318 | -2.49932 | -2.46090 | H | 0.48690 | 7.18879 | 0.77707 | H | 7.41075 | -0.96997 | 2.18415 |
| N | 1.67148 | -5.73051 | -0.62102 | H | 0.94179 | 7.05835 | -0.94597 | H | 6.36025 | 2.44138 | 4.02152 |
| N | -4.08844 | -3.03871 | 0.69807 | C | -3.87904 | -2.7 | | | | | |

Optimized geometry of $\text{PF}_6^-@(+)-((\text{S},\text{S},\text{R})(\text{S},\text{S})_7)\text{-mixHC}[8]$ sulfur atom oriented towards outside

| | | | | | | | | | | | |
|------------------------|-----------|----------|----------|---|----------|----------|----------|---|----------|----------|----------|
| 201 | | | | H | 2.01523 | 2.72296 | 5.27899 | H | -7.46694 | 0.09641 | 5.48465 |
| E(au) = -5581.34569817 | | | | C | 2.01797 | 2.83981 | 4.18883 | C | -9.24803 | -0.28243 | 4.43096 |
| C | -3.25309 | 2.79815 | -0.06216 | H | 2.67467 | 4.31345 | -2.42055 | C | -2.58382 | -3.00193 | -4.32532 |
| C | -3.10893 | -2.32167 | -3.06641 | C | 1.36753 | 5.97672 | -0.17093 | C | -4.27907 | -4.25337 | -1.78918 |
| H | 0.63789 | 5.66198 | -2.95013 | H | 2.00339 | 6.55649 | -0.84846 | H | -2.97515 | 0.99036 | -4.08456 |
| H | 6.04727 | 4.25370 | 2.47226 | H | 4.18906 | 3.00644 | 3.99638 | H | -1.83974 | 0.11500 | -3.03826 |
| H | 5.17717 | -2.16590 | 3.81309 | H | 3.37659 | 4.55904 | 4.26014 | H | -3.39820 | -3.11924 | -5.05307 |
| H | 4.56724 | -5.15568 | -2.49300 | C | 3.29778 | 3.59034 | 3.74845 | C | -2.57306 | 0.00050 | -3.84439 |
| H | -2.20474 | 2.47870 | -0.03238 | C | 0.67421 | 3.86259 | 2.22867 | H | -4.37367 | -1.07155 | -4.27476 |
| C | -5.21463 | 1.65999 | 1.09185 | C | 5.47126 | 2.31415 | -0.29873 | H | -2.26231 | -2.17223 | -2.37733 |
| C | -7.94709 | 0.47691 | 4.57293 | C | 3.62159 | 5.18647 | 0.42428 | C | -3.68593 | -0.94757 | -3.41705 |
| H | -5.62417 | 0.85958 | -3.13328 | H | 5.65116 | 2.52518 | -3.71610 | C | -4.94285 | -1.88305 | -1.71059 |
| H | 1.64140 | 2.93400 | -2.00421 | H | 4.22416 | 2.20902 | -2.74198 | O | -9.50916 | -1.12157 | 3.59718 |
| H | 1.95304 | 5.53776 | 2.60099 | H | 6.09637 | 4.92626 | 0.81776 | H | -0.62200 | -2.10757 | -4.19611 |
| C | 3.18230 | 3.80839 | 2.24431 | H | 5.16971 | 0.06608 | -3.43392 | H | -1.10371 | -2.49954 | -5.84056 |
| H | 6.97713 | 3.05024 | -1.66022 | H | 6.77047 | 0.51585 | -2.86615 | H | -6.41577 | -0.06194 | 0.63900 |
| H | 7.27854 | -1.00985 | 1.17979 | C | 5.88195 | 2.99063 | -1.60184 | C | -4.21317 | 1.55500 | -0.10058 |
| H | 2.05669 | -0.60365 | 4.91743 | C | 5.69726 | 0.62777 | -2.65504 | H | -7.71066 | 2.12547 | 2.36404 |
| C | 3.25254 | -4.32793 | -0.99053 | H | 5.80183 | -1.01292 | -1.21943 | C | -7.00899 | 0.34599 | 3.36883 |
| H | -8.18559 | 1.52618 | 4.78317 | C | 5.61902 | 4.19306 | 1.47022 | H | -4.70712 | -2.98487 | 1.04117 |
| C | -6.57829 | 0.99098 | 0.90164 | H | 4.32053 | -0.05230 | -1.08741 | C | -3.12013 | -2.80368 | 2.53407 |
| H | -6.28126 | 0.15178 | -1.63353 | C | 5.39930 | 0.00397 | -1.27139 | N | -1.09815 | -5.18994 | -0.37075 |
| C | -4.35262 | 2.71702 | -2.15491 | H | 3.04994 | 2.82567 | 1.76294 | N | 1.30512 | -5.39844 | -0.36888 |
| H | -3.01172 | 3.23751 | 2.03718 | H | 5.48641 | 4.00878 | -1.66089 | C | -3.86500 | -3.57295 | 1.41729 |
| O | -4.62999 | 2.96884 | -3.32687 | H | 4.37264 | 2.22097 | -0.28974 | H | -4.26423 | -4.52222 | 1.79894 |
| H | -7.07606 | 1.46015 | 0.04576 | H | 7.14039 | 0.97190 | -0.49266 | N | -3.54541 | 3.46637 | -1.33101 |
| C | -7.51947 | 1.07228 | 2.11682 | C | 6.06498 | 0.90516 | -0.23900 | N | -4.80103 | 1.62367 | -1.43606 |
| C | -3.56690 | 3.63981 | 1.18318 | C | 6.03076 | 1.80111 | 1.89919 | O | -5.82804 | -2.02202 | -0.86752 |
| H | -10.92100 | -0.48656 | 5.24540 | C | 5.31770 | 2.12258 | -2.75235 | H | -0.44674 | -3.02295 | 1.39027 |
| H | -6.86161 | -0.71606 | 3.14172 | C | 3.61303 | -0.76363 | 3.40524 | H | -3.79366 | -2.64104 | 3.38377 |
| H | -6.03482 | 0.75045 | 3.66496 | C | 6.43774 | -0.62350 | 1.76628 | H | -2.85558 | -1.80874 | 2.15216 |
| H | -4.70296 | 1.20343 | 1.94843 | H | 1.31641 | -2.49758 | 3.55871 | H | -2.11215 | -4.41463 | 3.57629 |
| S | -5.36136 | 3.46573 | 1.48672 | H | 1.64467 | -3.07164 | 5.18938 | C | -1.83360 | -3.50830 | 3.01954 |
| H | -3.64389 | 0.62390 | -0.00404 | C | 4.55381 | -1.87079 | 2.94717 | H | -0.05030 | -4.51169 | 2.26300 |
| H | -8.48231 | 0.63614 | 1.82839 | H | 2.52241 | -6.44025 | 3.39896 | H | -1.30752 | -2.86027 | 3.72917 |
| H | -3.28355 | 4.68719 | 1.06670 | H | 3.82977 | -4.04358 | 4.43270 | C | -0.87584 | -3.90784 | 1.87208 |
| O | -10.13626 | 0.06554 | 5.40136 | C | 2.80949 | -1.33290 | 4.59790 | O | 6.53579 | -3.12120 | 0.34439 |
| H | -5.24196 | -4.33715 | -1.28197 | C | 3.07620 | -3.74351 | 3.69191 | N | -1.47939 | 6.09275 | 0.24770 |
| H | -3.57193 | 4.96334 | -2.69968 | H | 2.97332 | -2.75414 | 1.79726 | O | -1.96191 | -5.81121 | -2.44513 |
| C | -1.47021 | -2.08984 | -4.89204 | H | 4.17554 | 0.12421 | 3.71243 | O | 2.03564 | -6.27605 | 1.66508 |
| H | -0.76598 | 3.10881 | -2.06313 | C | 3.75795 | -3.09612 | 2.49178 | N | -3.21185 | -4.61452 | -0.87422 |
| C | -0.78383 | 4.09690 | -2.54861 | C | 5.67737 | -2.89395 | 1.19602 | O | 6.18502 | 1.90549 | 3.11526 |
| C | -5.37410 | 0.48883 | -2.13435 | H | 6.77213 | -0.38735 | 2.78236 | O | 4.21202 | 5.72642 | -0.51034 |
| H | -1.95006 | 3.41641 | -4.25409 | H | 3.49100 | -1.46766 | 5.45024 | N | 4.78754 | -3.81893 | 1.73377 |
| H | -0.95503 | 4.84306 | -4.57062 | H | 2.94425 | -0.47819 | 2.58616 | N | -1.68410 | 4.98297 | -1.80245 |
| H | -3.47910 | 5.55003 | -1.01957 | H | 5.52803 | -5.31239 | 0.56007 | N | 5.43546 | -1.66697 | 1.79920 |
| C | -0.98059 | 3.87995 | -4.04320 | H | 4.42068 | -5.87284 | 1.84537 | N | 3.47914 | -5.20747 | 0.16495 |
| H | 0.12461 | 2.82447 | -5.59629 | C | 4.59505 | -5.10616 | 1.08803 | C | -2.07558 | -5.26453 | -1.35139 |
| H | -2.63066 | -0.57951 | -5.92999 | C | 2.12032 | -2.67923 | 4.28284 | N | 5.95200 | 0.61202 | 1.18830 |
| H | 0.04323 | 1.97659 | -4.05355 | C | 3.71148 | -3.24830 | -3.15466 | C | -2.84260 | -3.84374 | 0.31978 |
| C | 0.17686 | 2.96441 | -4.51008 | H | 5.23618 | -3.74199 | -1.66393 | N | 2.24576 | 5.10270 | 0.57730 |
| H | -2.19031 | -3.99818 | -4.10218 | H | 0.41408 | -4.47490 | -2.98251 | C | 2.34326 | -3.73175 | -3.68487 |
| C | -1.91433 | -0.62455 | -5.09710 | H | 1.02701 | -3.09624 | -2.05285 | N | -4.23511 | -2.90380 | -3.22632 |
| H | -1.05186 | -0.02015 | -5.39840 | C | 4.31648 | -4.17298 | -2.07075 | H | -2.41397 | -2.87869 | 0.00401 |
| H | 2.33391 | 2.75504 | -4.40028 | H | 2.30278 | -5.87343 | -2.14477 | C | 1.31759 | -4.01948 | -2.56336 |
| H | 1.79456 | 4.39844 | -4.70992 | C | 1.99591 | -4.96929 | -1.58441 | N | 0.36010 | 5.25512 | -0.91650 |
| C | 1.57553 | 3.49519 | -4.12214 | H | 2.48889 | -4.64882 | -4.27416 | N | -4.49445 | -0.66615 | -2.22533 |
| C | -3.11663 | 4.79455 | -1.72198 | C | 2.24961 | -5.68869 | 0.60512 | N | 4.21439 | 4.56205 | 1.51968 |
| H | 0.83444 | 6.65335 | 0.50624 | H | -0.05792 | -6.69237 | -1.30132 | F | 1.75131 | 1.09075 | 0.04469 |
| C | 1.70855 | 3.83729 | -2.61897 | H | 4.41555 | -3.14730 | -3.98914 | F | -0.50292 | 0.75569 | 0.48062 |
| H | -0.21682 | 4.45498 | 1.99571 | H | 0.01796 | -6.74474 | 0.48816 | F | 0.25987 | 0.76391 | -1.70769 |
| H | 0.64373 | 2.95320 | 1.61913 | C | 0.03497 | -6.09064 | -0.39059 | P | 0.65293 | -0.06537 | -0.34161 |
| C | 0.55964 | 4.78023 | -2.28570 | H | 2.98411 | -3.32118 | -0.63142 | F | 1.03593 | -0.98917 | 1.01891 |
| H | 0.57078 | 4.45054 | 4.30989 | H | 1.93480 | -2.98384 | -4.37360 | F | 1.81204 | -0.88240 | -1.16853 |
| H | -0.14310 | 2.87748 | 3.98807 | H | 3.58286 | -2.24760 | -2.72477 | F | -0.44336 | -1.22281 | -0.73910 |
| C | 1.94396 | 4.65340 | 1.93540 | H | -2.14372 | -5.56796 | 1.40108 | | | | |
| C | 0.70697 | 3.52185 | 3.73730 | C | -1.70203 | -4.70374 | 0.86903 | | | | |
| H | 2.05139 | 1.82716 | 3.76794 | H | -4.22643 | -4.97469 | -2.60673 | | | | |
| C | -0.98784 | 5.50606 | -0.71628 | N | 5.91689 | 2.85287 | 0.99275 | | | | |

Optimized geometry of PF₆⁻@(+)-((S,S,R)(S,S)7)-mixHC[8] sulfur atom oriented towards inside

201

E(a.u) = -5581.34257696

| | | | |
|---|-----------|----------|----------|
| C | -3.53826 | -2.73091 | -0.28698 |
| C | -3.03011 | 2.62421 | 2.73788 |
| H | 0.01116 | -5.78228 | 2.78832 |
| H | 5.85094 | -4.60388 | -2.20770 |
| H | 5.76467 | 1.82850 | -3.50138 |
| H | 4.80105 | 4.89108 | 2.74088 |
| H | -2.44921 | -2.61361 | -0.30403 |
| C | -5.23003 | -1.14724 | -1.37374 |
| C | -8.92028 | 1.05338 | -2.90538 |
| H | -5.68357 | -0.44051 | 2.74115 |
| H | 1.22943 | -3.09036 | 2.00089 |
| H | 1.69494 | -5.54628 | -2.65346 |
| C | 3.01499 | -3.92578 | -2.14382 |
| H | 6.55523 | -3.57029 | 2.02077 |
| H | 7.44911 | 0.49429 | -0.67472 |
| H | 2.64355 | 0.60370 | -4.95549 |
| C | 3.58409 | 4.13881 | 1.12132 |
| H | -8.42236 | 0.98790 | -3.87999 |
| C | -6.67021 | -1.62349 | -1.10384 |
| H | -6.19465 | 0.23594 | 1.16728 |
| C | -4.57773 | -2.47068 | 1.81995 |
| H | -3.22147 | -4.07616 | -2.00203 |
| O | -4.90822 | -2.69120 | 2.98391 |
| H | -6.70248 | -2.71795 | -1.12056 |
| C | -7.68921 | -1.05557 | -2.10649 |
| C | -3.99855 | -3.44373 | -1.57253 |
| H | -11.79546 | 0.49797 | -4.19209 |
| H | -8.65936 | 0.42230 | -0.86638 |
| H | -7.19855 | 1.01515 | -1.62971 |
| H | -5.24012 | -0.09745 | -1.67887 |
| S | -4.43977 | -2.10188 | -2.75090 |
| H | -3.43977 | -0.54720 | -0.31539 |
| H | -8.59283 | -1.67437 | -2.09740 |
| H | -4.87579 | -4.06635 | -1.37233 |
| O | -10.90646 | 0.89099 | -4.20260 |
| H | -4.87921 | 4.63855 | 0.65850 |
| H | -4.12142 | -4.85140 | 2.33747 |
| C | -1.56638 | 2.40112 | 4.70683 |
| H | -1.19504 | -3.12876 | 1.90588 |
| C | -1.29481 | -4.12723 | 2.36168 |
| C | -5.34161 | -0.11936 | 1.75206 |
| H | -2.52110 | -3.42412 | 4.01417 |
| H | -1.62740 | -4.91425 | 4.34726 |
| H | -3.96030 | -5.43936 | 0.65788 |
| C | -1.56827 | -3.93759 | 3.84800 |
| H | -0.50385 | -2.98709 | 5.49365 |
| H | -2.88023 | 0.99554 | 5.70936 |
| H | -0.44005 | -2.09754 | 3.97407 |
| C | -0.39187 | -3.10286 | 4.40912 |
| H | -2.11495 | 4.30262 | 3.77544 |
| C | -2.09831 | 0.96855 | 4.93679 |
| H | -1.29347 | 0.33989 | 5.33333 |
| H | 1.77641 | -3.02002 | 4.43716 |
| H | 1.12361 | -4.63595 | 4.66327 |
| C | 0.99495 | -3.70551 | 4.09120 |
| C | -3.61107 | -4.70102 | 1.38424 |
| H | 0.36413 | -6.65956 | -0.69032 |
| C | 1.20174 | -4.01281 | 2.58907 |
| H | -0.42899 | -4.33443 | -2.14889 |
| H | 0.50260 | -2.91496 | -1.64631 |
| C | 0.02402 | -4.87527 | 2.15407 |
| H | 0.51177 | -4.28722 | -4.40381 |
| H | -0.11065 | -2.68118 | -4.05251 |
| C | 1.70188 | -4.68884 | -1.95337 |
| C | 0.67309 | -3.39618 | -3.77994 |
| F | 1.66748 | -1.29720 | 0.11036 |

| | | | |
|---|----------|----------|----------|
| H | 2.13385 | -1.80660 | -3.64103 |
| C | -1.46086 | -5.45782 | 0.46815 |
| H | 2.13713 | -2.63103 | -5.19317 |
| C | 2.05724 | -2.79472 | -4.11196 |
| H | 2.14847 | -4.54165 | 2.43583 |
| C | 0.89231 | -6.04821 | 0.04997 |
| H | 1.43918 | -6.69670 | 0.74290 |
| H | 4.19387 | -3.13636 | -3.79228 |
| H | 3.28694 | -6.60881 | -4.17493 |
| C | 3.24664 | -3.65805 | -3.62631 |
| C | 0.51410 | -3.79715 | -2.29455 |
| C | 5.23786 | -2.67398 | 0.56249 |
| C | 3.22963 | -5.39919 | -0.35838 |
| H | 5.11717 | -2.95937 | 3.97648 |
| H | 3.81197 | -2.49061 | 2.89767 |
| H | 5.73201 | -5.31512 | -0.57298 |
| H | 4.89685 | -0.46150 | 3.71856 |
| H | 6.48879 | -1.05361 | 3.26769 |
| C | 5.47845 | -3.40806 | 1.87684 |
| C | 5.43032 | -1.05766 | 2.96991 |
| H | 5.80295 | 0.59095 | 1.58770 |
| C | 5.36122 | -4.53051 | -1.23500 |
| H | 4.25377 | -0.22295 | 1.31828 |
| C | 5.30452 | -0.38412 | 1.58302 |
| H | 2.91975 | -2.95583 | -1.62957 |
| H | 4.98915 | -4.38647 | 1.87976 |
| H | 4.15703 | -2.47788 | 0.47093 |
| H | 7.00427 | -1.49938 | 0.91694 |
| C | 5.96295 | -1.32650 | 0.58341 |
| C | 6.01624 | -2.17929 | -1.57194 |
| C | 4.90413 | -2.51030 | 2.99918 |
| C | 4.02333 | 0.60742 | -3.27280 |
| C | 6.64240 | 0.18904 | -1.34986 |
| H | 1.96239 | 2.59059 | -3.70871 |
| H | 2.56013 | 3.10147 | -5.28002 |
| C | 5.02304 | 1.60947 | -2.70940 |
| H | 3.36502 | 4.57577 | -3.37548 |
| H | 4.71951 | 3.84182 | -4.25085 |
| C | 3.43214 | 1.24767 | -4.55065 |
| C | 3.85445 | 3.62589 | -3.60941 |
| H | 3.42358 | 2.66520 | -1.74493 |
| H | 4.51378 | -0.34131 | -3.51338 |
| C | 4.31653 | 2.91595 | -2.34151 |
| C | 6.04784 | 2.52103 | -0.84053 |
| H | 7.05719 | -0.07114 | -2.32989 |
| H | 4.21900 | 1.29197 | -5.31729 |
| H | 3.23780 | 0.40755 | -2.53513 |
| H | 6.05359 | 4.94957 | -0.19465 |
| H | 5.12724 | 5.60747 | -1.57366 |
| C | 5.16555 | 4.82227 | -0.81641 |
| C | 2.86905 | 2.66813 | -4.32152 |
| C | 3.76700 | 3.04668 | 3.32027 |
| H | 5.45221 | 3.43097 | 1.97875 |
| H | 0.58566 | 4.47580 | 2.83720 |
| H | 1.19287 | 3.05195 | 1.97550 |
| C | 4.52879 | 3.92348 | 2.29755 |
| H | 2.62357 | 5.74806 | 2.17428 |
| C | 2.31727 | 4.85834 | 1.59107 |
| H | 2.53890 | 4.53355 | 4.31539 |
| C | 2.82357 | 5.54781 | -0.56358 |
| H | 0.40786 | 6.71114 | 1.08729 |
| H | 4.38228 | 2.90586 | 4.21681 |
| H | 0.64223 | 6.70092 | -0.68886 |
| C | 0.54624 | 6.07552 | 0.20565 |
| H | 3.29005 | 3.14850 | 0.73627 |
| H | 1.87273 | 2.90784 | 4.37022 |
| H | 3.61368 | 2.05337 | 2.88133 |
| H | -1.48565 | 5.57812 | -1.76277 |

| | | | |
|---|-----------|----------|----------|
| C | -1.14106 | 4.71933 | -1.15540 |
| H | -3.96168 | 5.30068 | 2.04127 |
| N | 5.73354 | -3.22985 | -0.70356 |
| H | -9.04770 | 2.12654 | -2.70880 |
| C | -10.31275 | 0.47997 | -3.04977 |
| C | -2.57890 | 3.33908 | 4.00637 |
| C | -3.97493 | 4.53696 | 1.26148 |
| H | -3.15549 | -0.63992 | 3.90714 |
| H | -1.89644 | 0.12879 | 2.92419 |
| H | -3.44448 | 3.53126 | 4.65480 |
| C | -2.68420 | 0.31815 | 3.66126 |
| H | -4.45293 | 1.50077 | 3.89401 |
| H | -2.13744 | 2.39788 | 2.13383 |
| C | -3.70557 | 1.30011 | 3.10284 |
| C | -4.76010 | 2.20217 | 1.24494 |
| O | -10.88637 | -0.23628 | -2.25760 |
| H | -0.66318 | 2.34566 | 4.08652 |
| H | -1.26012 | 2.83780 | 5.66462 |
| H | -6.97028 | -1.33448 | -0.09034 |
| C | -4.20817 | -1.31822 | -0.20986 |
| H | -7.27227 | -1.12947 | -3.12050 |
| C | -8.08707 | 0.39764 | -1.80084 |
| H | -4.20270 | 3.13847 | -1.53038 |
| C | -2.49907 | 2.81029 | -2.86120 |
| N | -0.62826 | 5.23435 | 0.11406 |
| N | 1.77300 | 5.31602 | 0.31262 |
| C | -3.30145 | 3.66773 | -1.85356 |
| H | -3.61585 | 4.61522 | -2.31196 |
| N | -3.97284 | -3.36495 | 0.95663 |
| N | -4.76389 | -1.28902 | 1.13388 |
| O | -5.55622 | 2.33162 | 0.31489 |
| H | 0.06271 | 2.95328 | -1.48869 |
| H | -3.09985 | 2.63782 | -3.76179 |
| H | -2.31988 | 1.82370 | -2.41470 |
| H | -1.32177 | 4.32420 | -3.87312 |
| C | -1.14124 | 3.43203 | -3.25610 |
| H | 0.61754 | 4.38045 | -2.37969 |
| H | -0.58864 | 2.72715 | -0.88677 |
| C | -0.27133 | 3.83685 | -2.04242 |
| O | 6.82887 | 2.66468 | 0.09891 |
| O | -1.92723 | -5.97093 | -0.54797 |
| O | -1.64594 | 6.00702 | 2.06577 |
| O | 2.74909 | 6.14156 | -1.63868 |
| N | -2.80780 | 4.79219 | 0.43859 |
| O | 6.25819 | -2.27666 | -2.77441 |
| O | 3.71483 | -6.01462 | 0.59025 |
| N | 5.32035 | 3.53089 | -1.46490 |
| N | -2.19276 | -4.94609 | 1.53844 |
| N | 5.74889 | 1.32206 | -1.47365 |
| N | 3.97455 | 4.99876 | -0.00505 |
| C | -1.68715 | 5.40747 | 0.99220 |
| N | 5.99086 | -0.99923 | -0.84120 |
| C | -2.37130 | 3.94362 | -0.67824 |
| N | 1.87685 | -5.20919 | -0.59810 |
| C | 2.39008 | 3.62132 | 3.71934 |
| N | -4.05683 | 3.22016 | 1.87149 |
| H | -2.02564 | 2.97642 | -0.27958 |
| C | 1.49352 | 3.96082 | 2.50554 |
| N | -0.11639 | -5.29021 | 0.75772 |
| N | -4.42633 | 0.99931 | 1.86403 |
| N | 3.93847 | -4.78124 | -1.38575 |
| F | -0.31515 | 1.25681 | 0.70076 |
| F | 1.19885 | 0.70852 | -0.97157 |
| F | 1.87308 | 0.71424 | 1.24766 |
| P | 0.67500 | -0.02146 | 0.39824 |
| F | -0.52319 | -0.75750 | -0.44131 |
| F | 0.14477 | -0.74874 | 1.77596 |

6. Anion Binding Studies

Anion binding was studied in solution by ITC, and via SPE of perchlorate using silica material functionalized with mixHC[8].

6.1 Isothermal Calorimetric Titration

The titration was carried out by addition of 0.5 μL or 0.7 μL portions of guest compound solution to mixHC[8] solution in the cell with 60 s or 90 s spacing. The heat of dilution was obtained by introduction of guest solution to the solvent (CH_3OH or $\text{CH}_3\text{OH} : \text{H}_2\text{O}$ 1 :1 mixture). The first smaller addition (0.4 μL) used to compensate diffusion of guest compound from the injector during system equilibration was discarded prior to fitting procedure. Before data analysis, the heat of dilution was subtracted from the corresponding total heat of the interaction. The obtained data was processed by MicroCal PEAQ-ITC analysis software (Malvern) and fitted using one set of sites binding model.

The complexation between mixHC[8] and NaSbF_6 was studied using reversed approach: mixHC[8] solution was placed in the cell and titrated by 1 μL additions of NaSbF_6 solution with 60 s spacing.²⁴

Table S25. Summary of ITC results for binding of anions to mixHC[8] (average values). For experimental error see results of particular titrations.

| Guest | Solvent | (-)-mixHC[8] | | | (+) -mixHC[8] | | |
|----------------------|--|------------------------------|-----------------------------------|----------------------------------|------------------------------|--------------------------------|-------------------------------------|
| | | K_a (M^{-1}) | ΔH (kJ/mol) | $-T\Delta S$ (kJ/mol) | K_a (M^{-1}) | ΔH (kJ/mol) | $-T\Delta S$ (kJ/mol) |
| (TBA) ClO_4 | CH_3OH | $(4.60 \pm 0.05) \cdot 10^2$ | -30.5 ± 0.4 | 15.3 ± 0.4 | $(9.7 \pm 0.2) \cdot 10^2$ | -33.8 ± 0.7 | 16.8 ± 0.6 |
| | $\text{CH}_3\text{OH}:\text{H}_2\text{O}$ 50:50 | $(1.90 \pm 0.03) \cdot 10^2$ | -30.8 ± 0.3 | 17.8 ± 0.3 | $(4.56 \pm 0.02) \cdot 10^2$ | -40.7 ± 0.8 | 25.5 ± 0.8 |
| (TBA) PF_6 | CH_3OH | $(1.05 \pm 0.07) \cdot 10^4$ | -38.5 ± 0.6 | 15.6 ± 0.4 | $(1.59 \pm 0.04) \cdot 10^4$ | -41.7 ± 0.5 | 17.6 ± 0.6 |
| | $\text{CH}_3\text{OH}:\text{H}_2\text{O}$ 50:50 | $(0.63 \pm 0.02) \cdot 10^4$ | -44 ± 2 | 22 ± 2 | $(1.4 \pm 0.3) \cdot 10^4$ | -60.3 ± 0.5 | 37 ± 1 |
| NaSbF_6 | CH_3OH | $(2.7 \pm 0.2) \cdot 10^4$ | -41.5 ± 0.7 | 25.3 ± 0.2 | $(3.7 \pm 0.4) \cdot 10^4$ | -41 ± 1 | 26.1 ± 0.2 |
| MgSO_4 | $\text{CH}_3\text{OH}:\text{H}_2\text{O}$ 50:50 | N/A | – | – | N/A | – | – |

(TBA)ClO₄ binding to (–)-mixHC[8] in CH₃OH

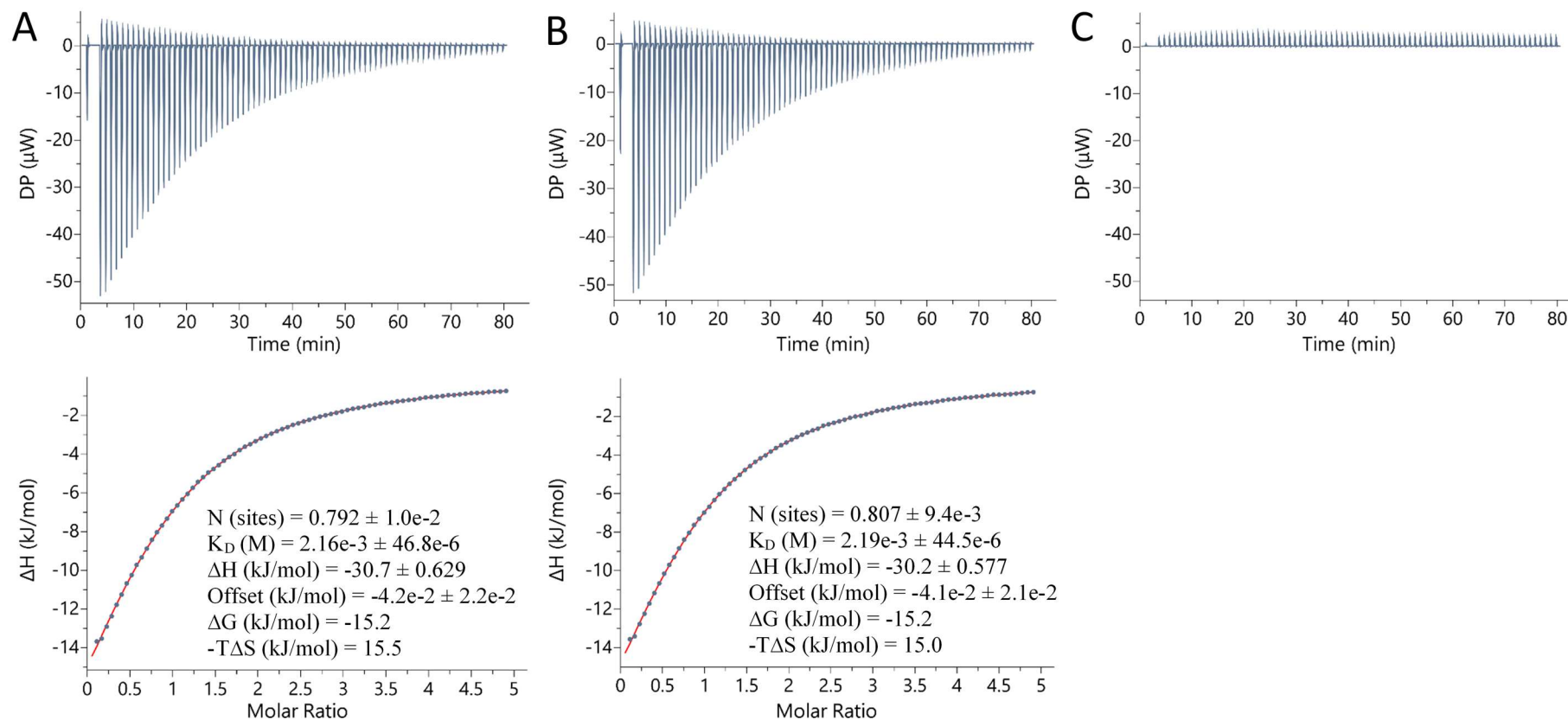


Figure S41. ITC of (TBA)ClO₄ binding to (–)-mixHC[8] in CH₃OH at 298 K (A, B) and control experiment (C). *Top:* Data obtained from the sequential injections of 0.5 μL of (TBA)ClO₄ (60.0 mM) to (–)-mixHC[8] (2.5 mM) (A,B) or to the pure solvent (C) with 60 s spacing. *Bottom:* Plot of the total heat released as a function of total guest concentration for the titration shown in the upper panel. The red solid line represents least-squares fit of the data.

(TBA)ClO₄ binding to (–)-mixHC[8] in CH₃OH:H₂O 1:1 mixture

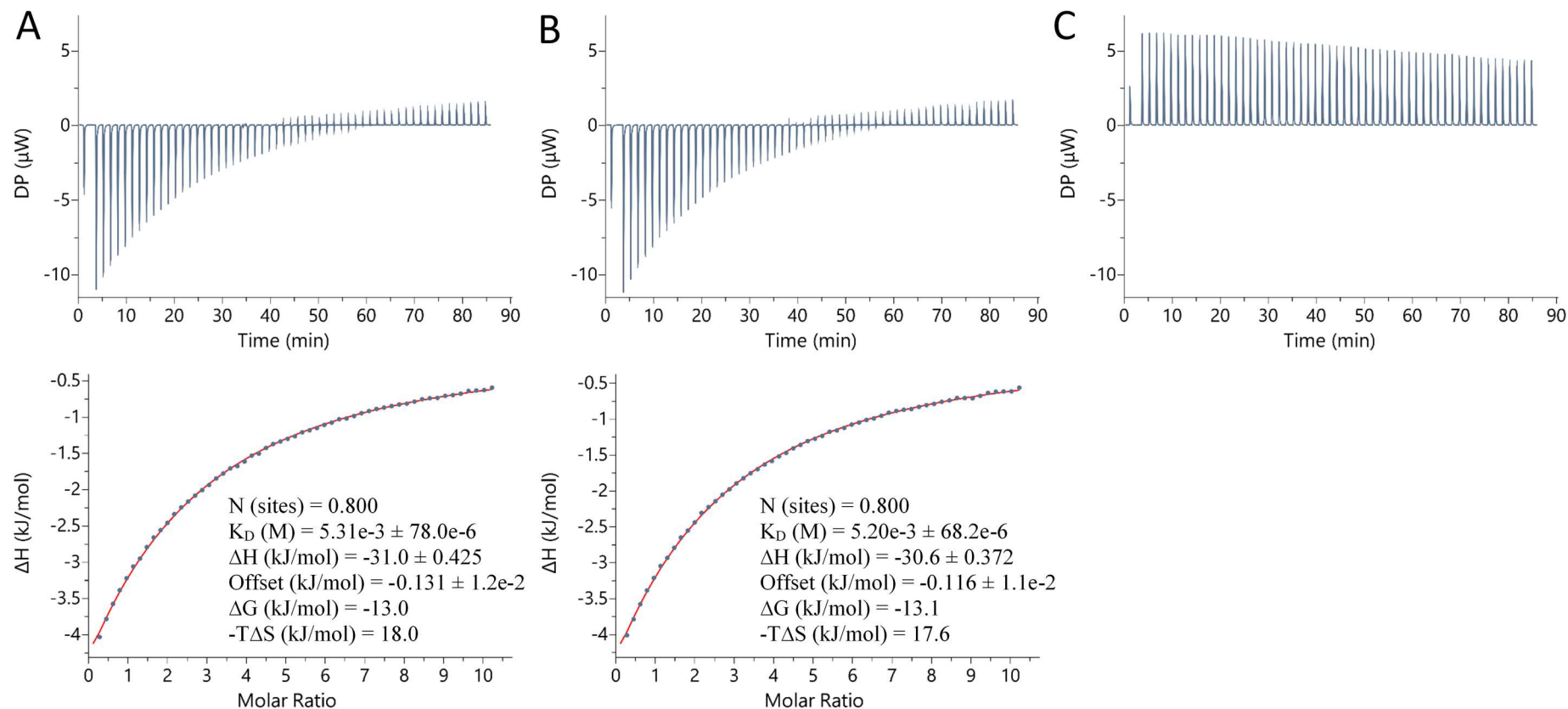


Figure S42. ITC of (TBA)ClO₄ binding to (–)-mixHC[8] in CH₃OH : H₂O 1:1 mixture at 298 K (A, B) and control experiment (C). *Top:* Data obtained from the sequential injections of 0.7 μL of (TBA)ClO₄ (50.0 mM) to (–)-mixHC[8] (1.0 mM) (A,B) or to the pure solvent mixture (C) with 90 s spacing. *Bottom:* Plot of the total heat released as a function of total guest concentration for the titration shown in the upper panel. The red solid line represents least-squares fit of the data.

(TBA)PF₆ binding to (–)-mixHC[8] in CH₃OH

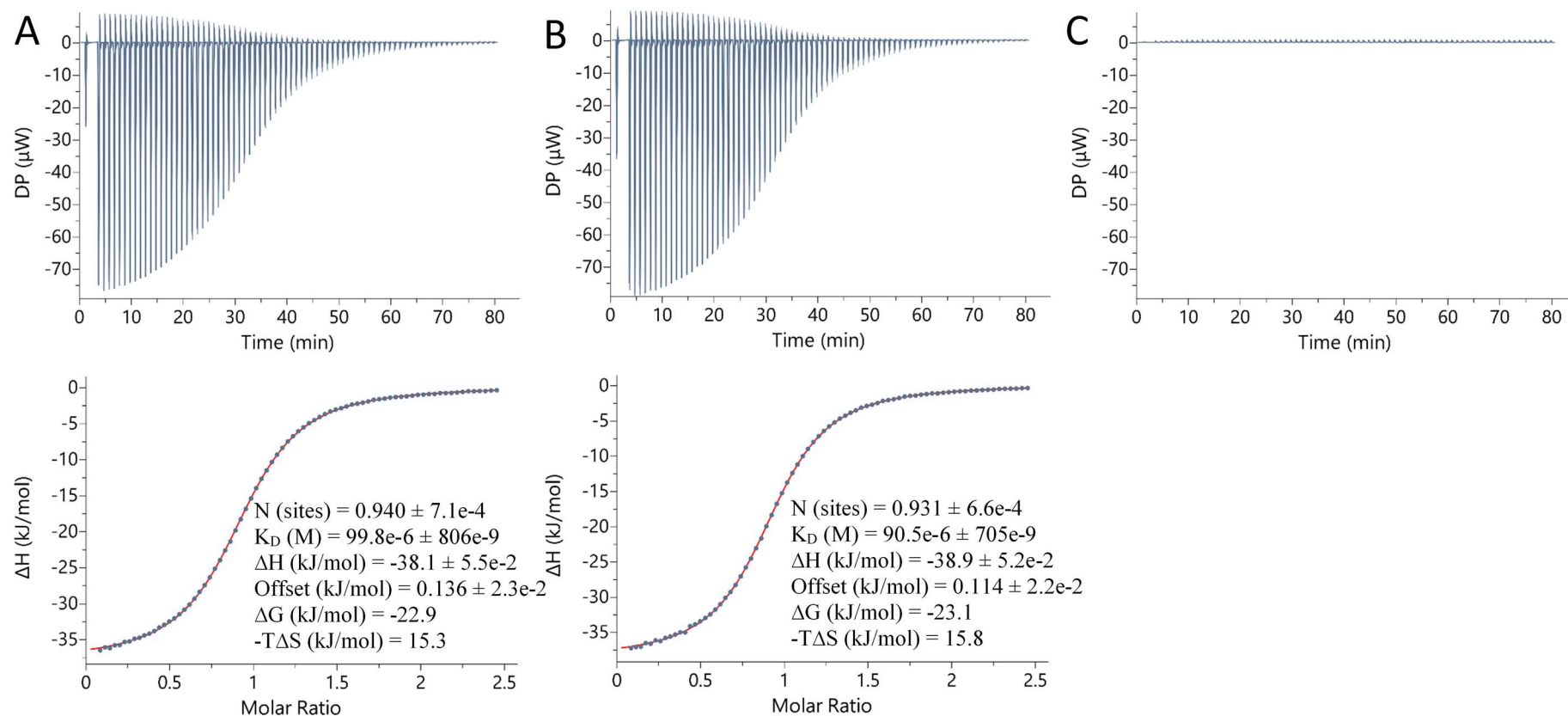


Figure S43. ITC of (TBA)PF₆ binding to (–)-mixHC[8] in CH₃OH at 298 K (A, B) and control experiment (C). *Top:* Data obtained from the sequential injections of 0.5 μL of (TBA)PF₆ (30.0 mM) to (–)-mixHC[8] (1.00 mM) (A,B) or to the pure solvent mixture (C) with 60 s spacing.

Bottom: Plot of the total heat released as a function of total guest concentration for the titration shown in the upper panel. The red solid line represents least-squares fit of the data.

(TBA)PF₆ binding to (-)-mixHC[8] in CH₃OH:H₂O 1:1 mixture

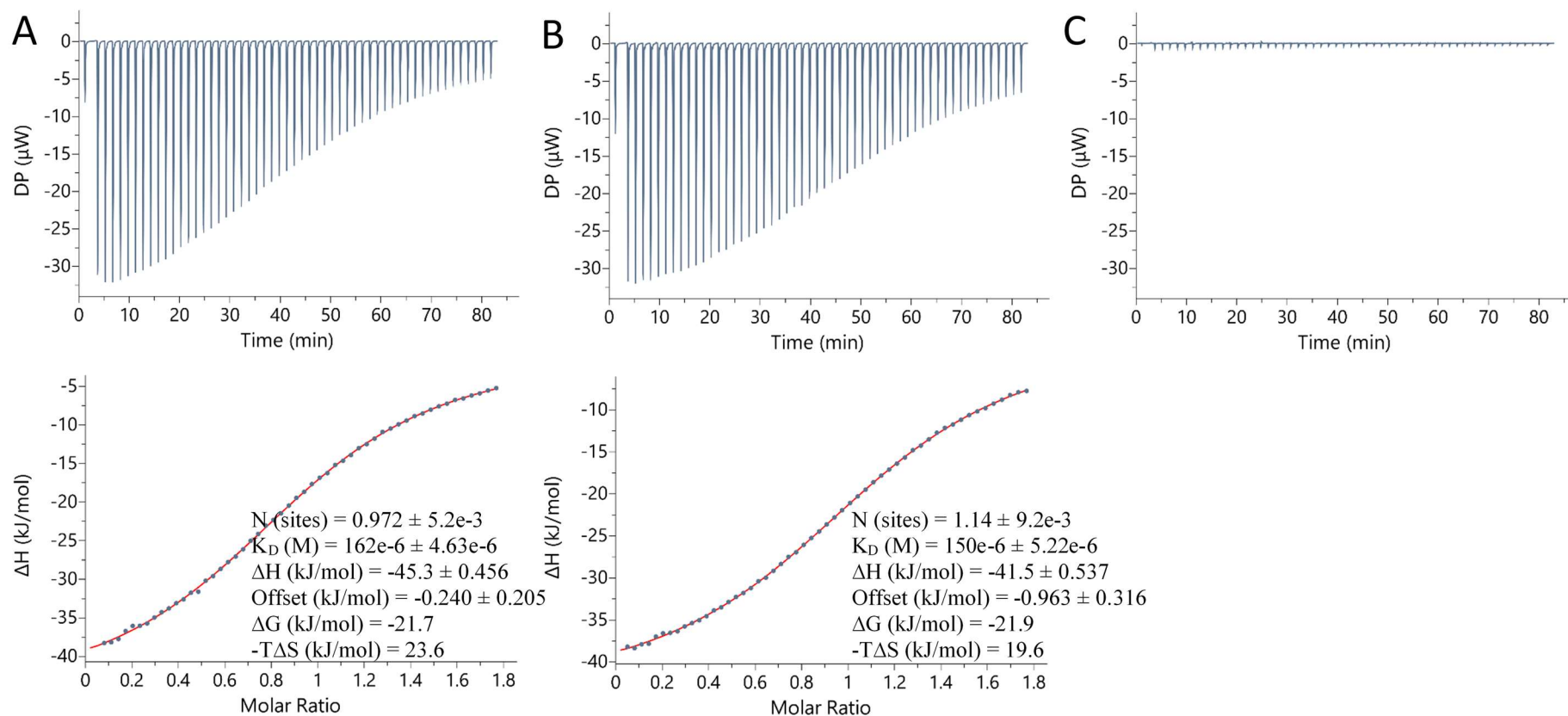


Figure S44. ITC of (TBA)PF₆ binding to (-)-mixHC[8] in CH₃OH : H₂O 1:1 mixture at 298 K (A, B) and control experiment (C). *Top:* Data obtained from the sequential injections of 0.7 μL of (TBA)PF₆ (9.0 mM) to (-)-mixHC[8] (1.0 mM) (A,B) or to the pure solvent mixture (C) with 90 s spacing. *Bottom:* Plot of the total heat released as a function of total guest concentration for the titration shown in the upper panel. The red solid line represents least-squares fit of the data. Note: subtracted dilution heat (C) is negligible in comparison to heat produced by complexation event.

(-)-mixHC[8] binding to NaSbF₆ in CH₃OH

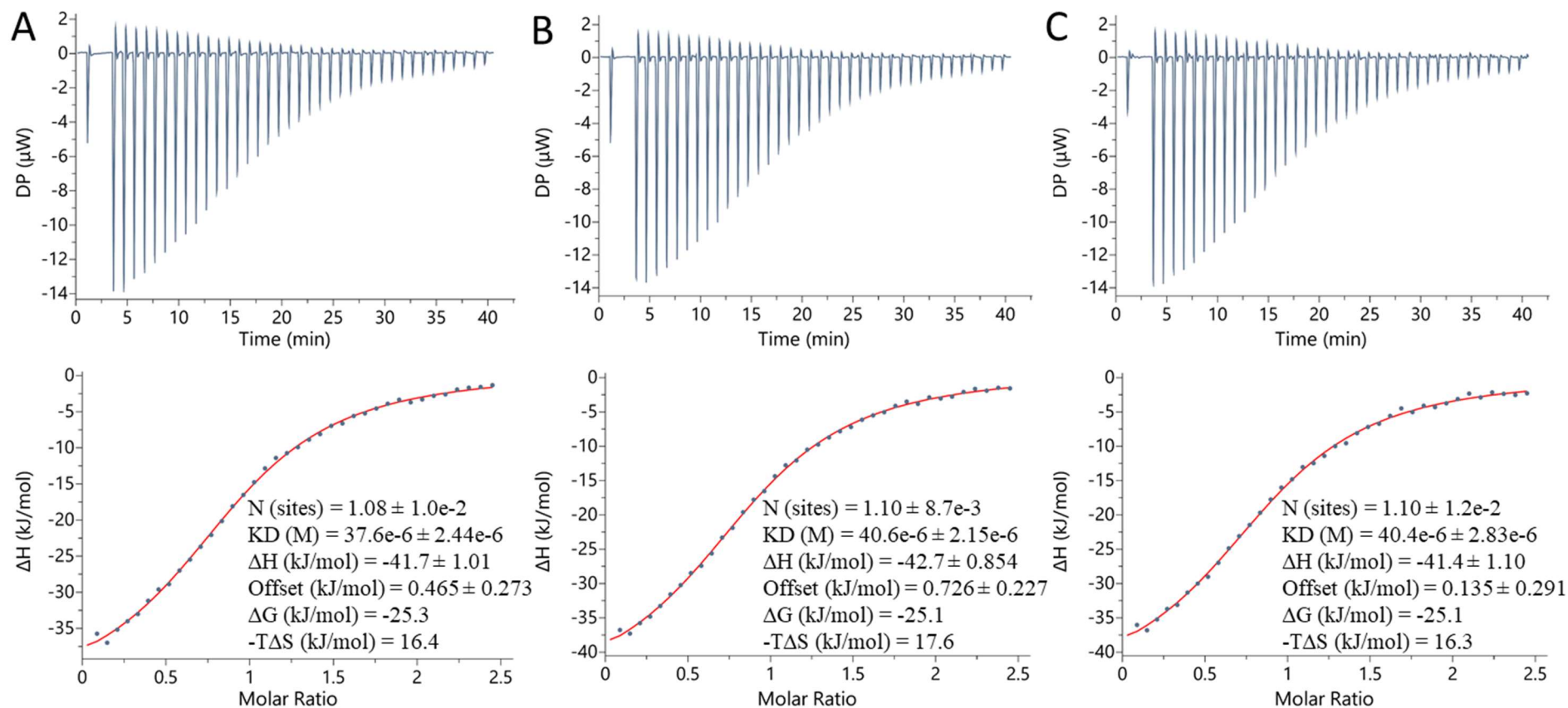


Figure S45. ITC of (-)-mixHC[8] binding to NaSbF₆ in CH₃OH at 298 K (A, B, C – parallel titrations). Top: Data obtained from the sequential injections of 1 μ L of (-)-mixHC[8] (2.5 mM) to NaSbF₆ (0.2 mM) with 60 s spacing. Bottom: Plot of the total heat released as a function of total guest concentration for the titration shown in the upper panel. The red solid line represents least-squares fit of the data.

(-)-mixHC[8] binding to NaSbF₆ in CH₃OH

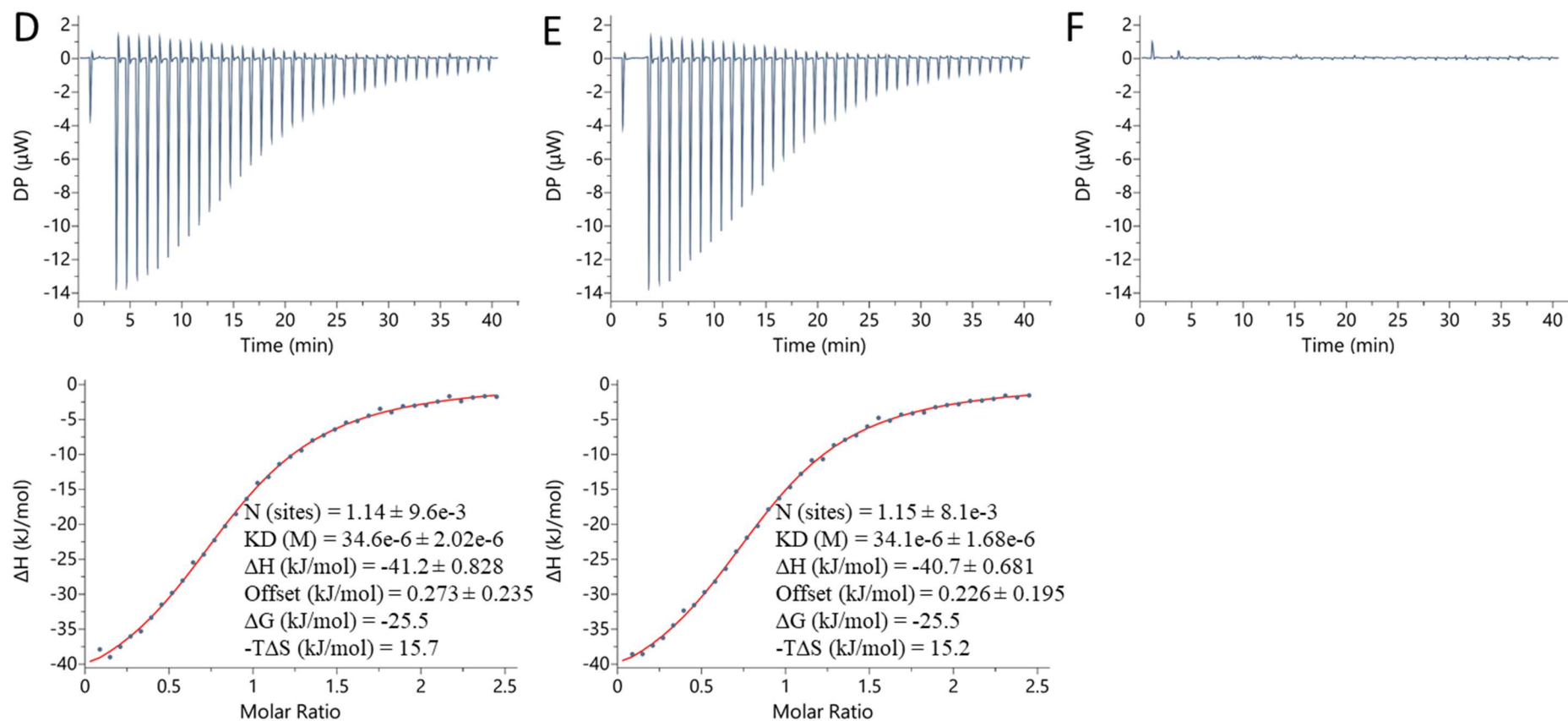


Figure S46. ITC of (-)-mixHC[8] binding to NaSbF₆ in CH₃OH at 298 K (D, E) and control experiment (F). Top: Data obtained from the sequential injections of 1 μL of (-)-mixHC[8] (2.5 mM) to NaSbF₆ (0.2 mM) (D, E) or to the pure solvent (F) with 60 s spacing. Bottom: Plot of the total heat released as a function of total guest concentration for the titration shown in the upper panel. The red solid line represents least-squares fit of the data.

MgSO₄ binding to (–)-mixHC[8] in CH₃OH:H₂O 1:1 mixture

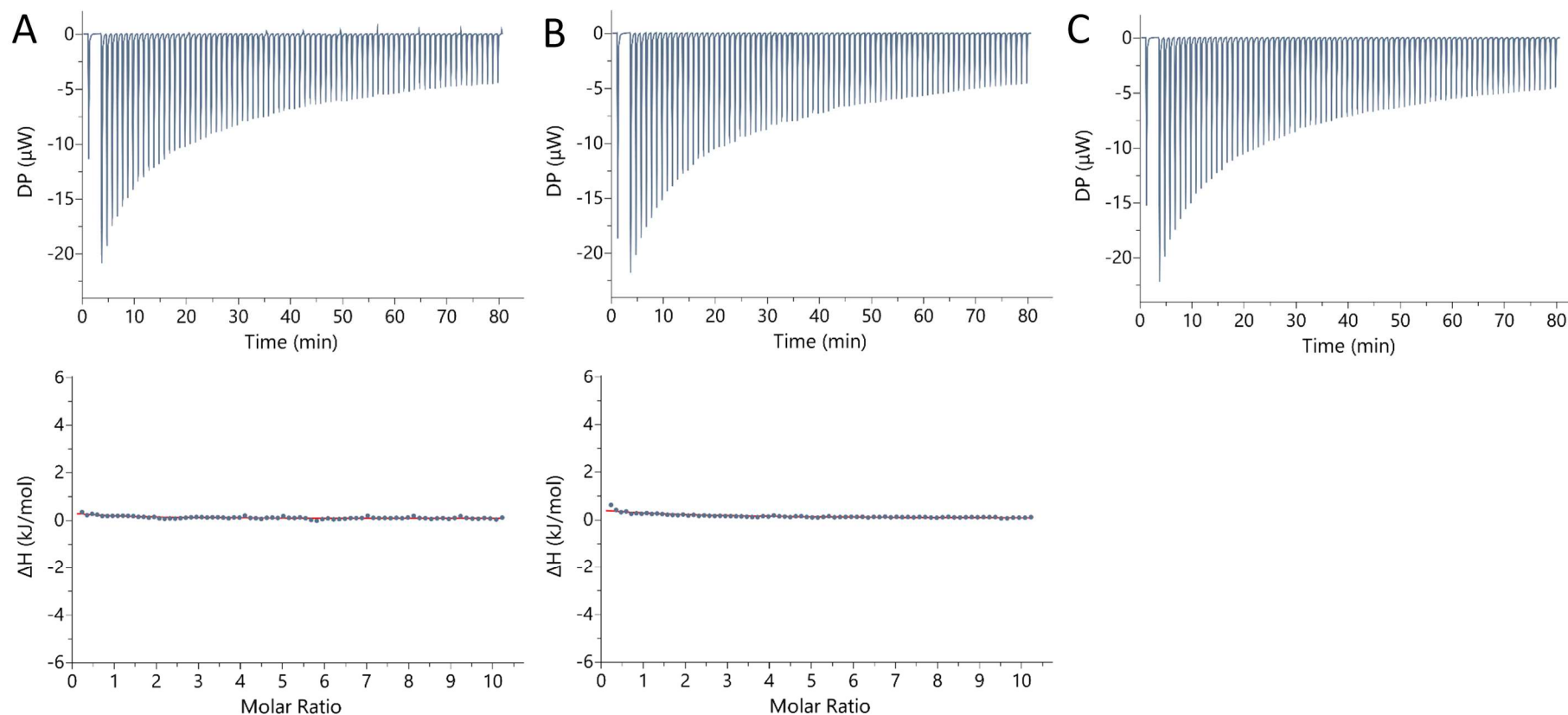


Figure S47. ITC of MgSO₄ binding to (–)-mixHC[8] in CH₃OH : H₂O 1:1 mixture at 298 K (A, B) and control experiment (C). *Top:* Data obtained from the sequential injections of 0.5 μ L of MgSO₄ (50.0 mM) to (–)-mixHC[8] (1.1 mM) (A,B) or to the pure solvent mixture (C) with 60 s spacing. *Bottom:* Plot of the total heat released as a function of total guest concentration for the titration shown in the upper panel. The red solid line represents least-squares fit of the data.

(TBA)ClO₄ binding to (+)-mixHC[8] in CH₃OH

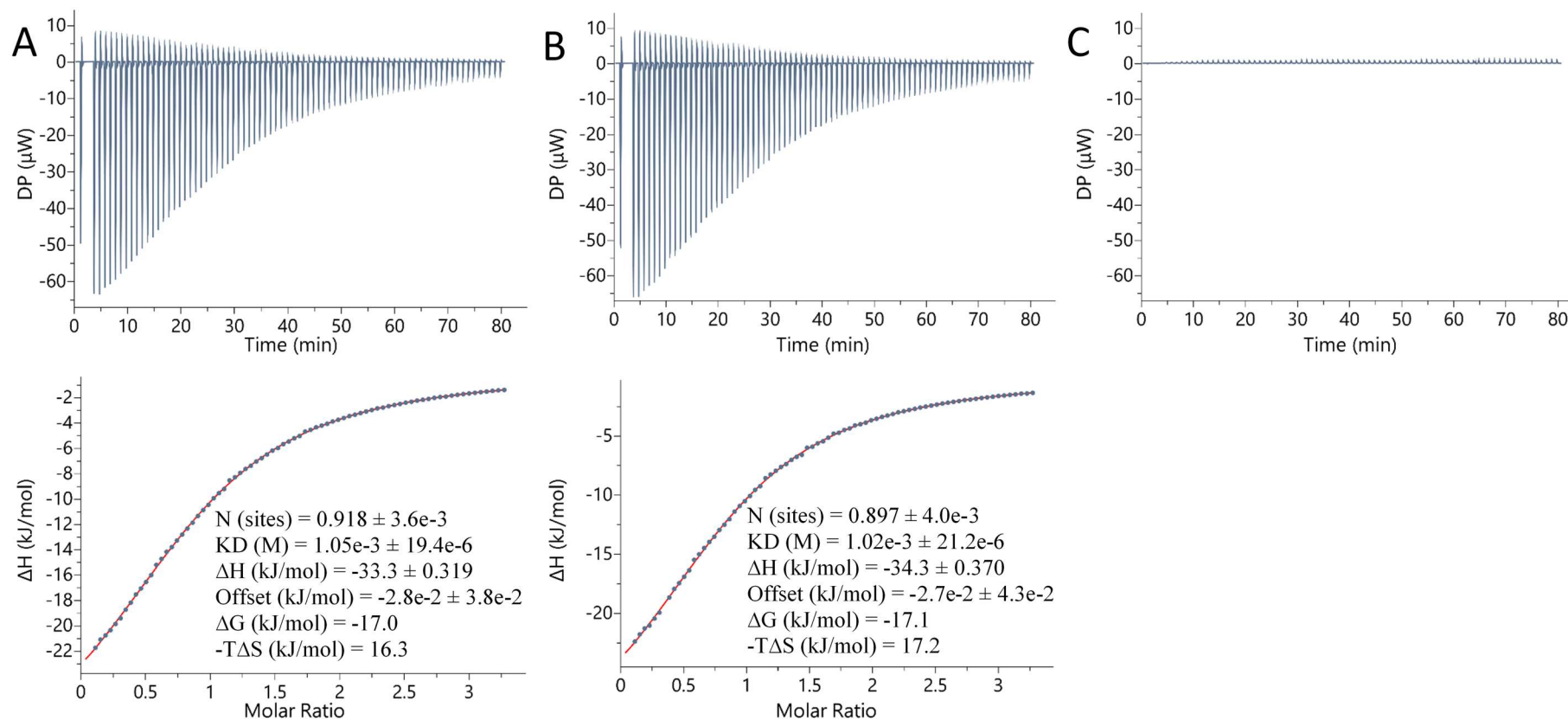


Figure S48. ITC of (TBA)ClO₄ binding to (+)-mixHC[8] in CH₃OH at 298 K (A, B) and control experiment (C). *Top:* Data obtained from the sequential injections of 0.5 μL of (TBA)ClO₄ (40.0 mM) to (+)-mixHC[8] (2.6 mM) (A,B) or to the pure solvent mixture (C) with 60 s spacing. *Bottom:* Plot of the total heat released as a function of total guest concentration for the titration shown in the upper panel. The red solid line represents least-squares fit of the data.

(TBA)ClO₄ binding to (+)-mixHC[8] in CH₃OH:H₂O 1:1 mixture

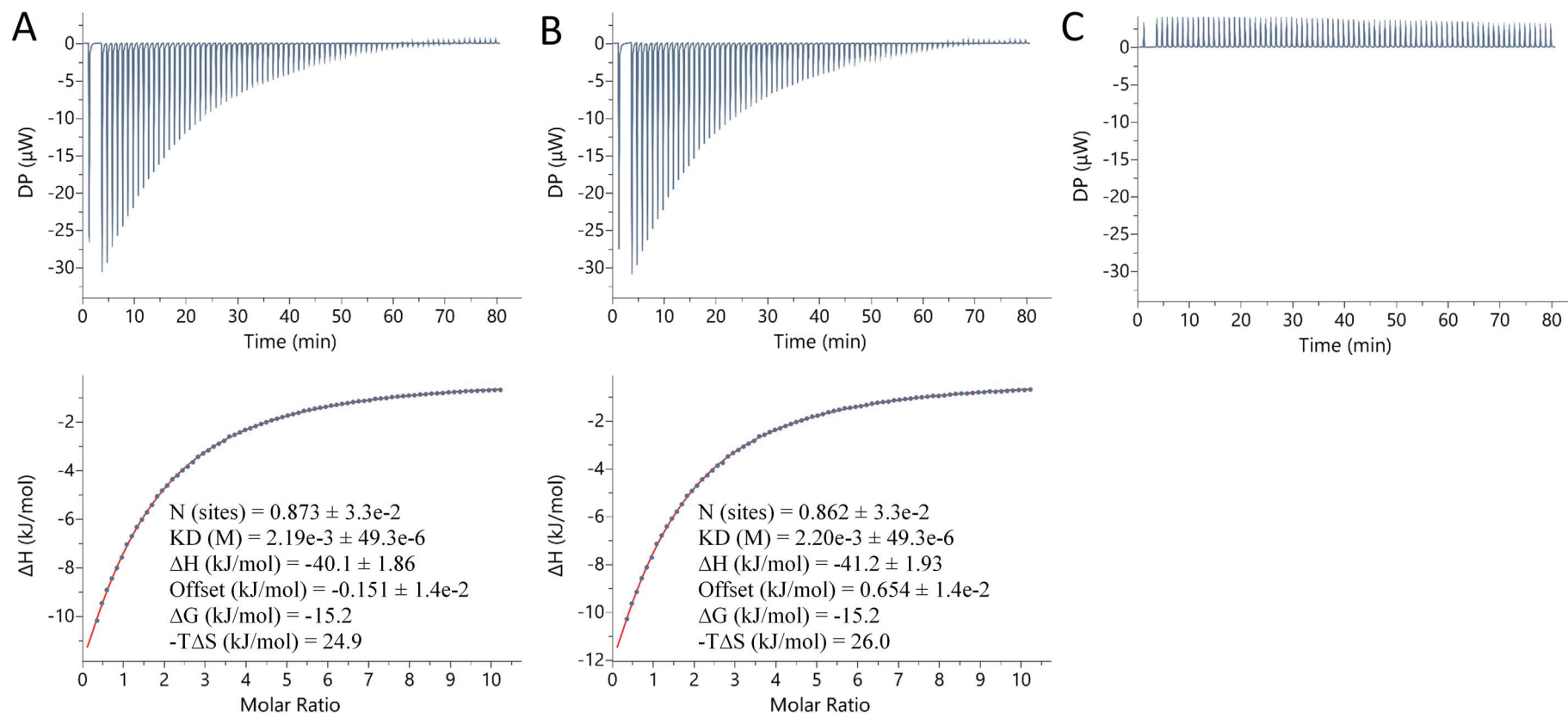


Figure S49. ITC of (TBA)ClO₄ binding to (+)-mixHC[8] in CH₃OH : H₂O 1:1 mixture at 298 K (A, B) and control experiment (C). *Top:* Data obtained from the sequential injections of 0.5 μL of TBAClO₄ (50.0 mM) to (+)-mixHC[8] (1.1 mM) (A,B) or to the pure solvent mixture (C) with 60 s spacing. *Bottom:* Plot of the total heat released as a function of total guest concentration for the titration shown in the upper panel. The red solid line represents least-squares fit of the data.

(TBA)PF₆ binding to (+)-mixHC[8] in CH₃OH

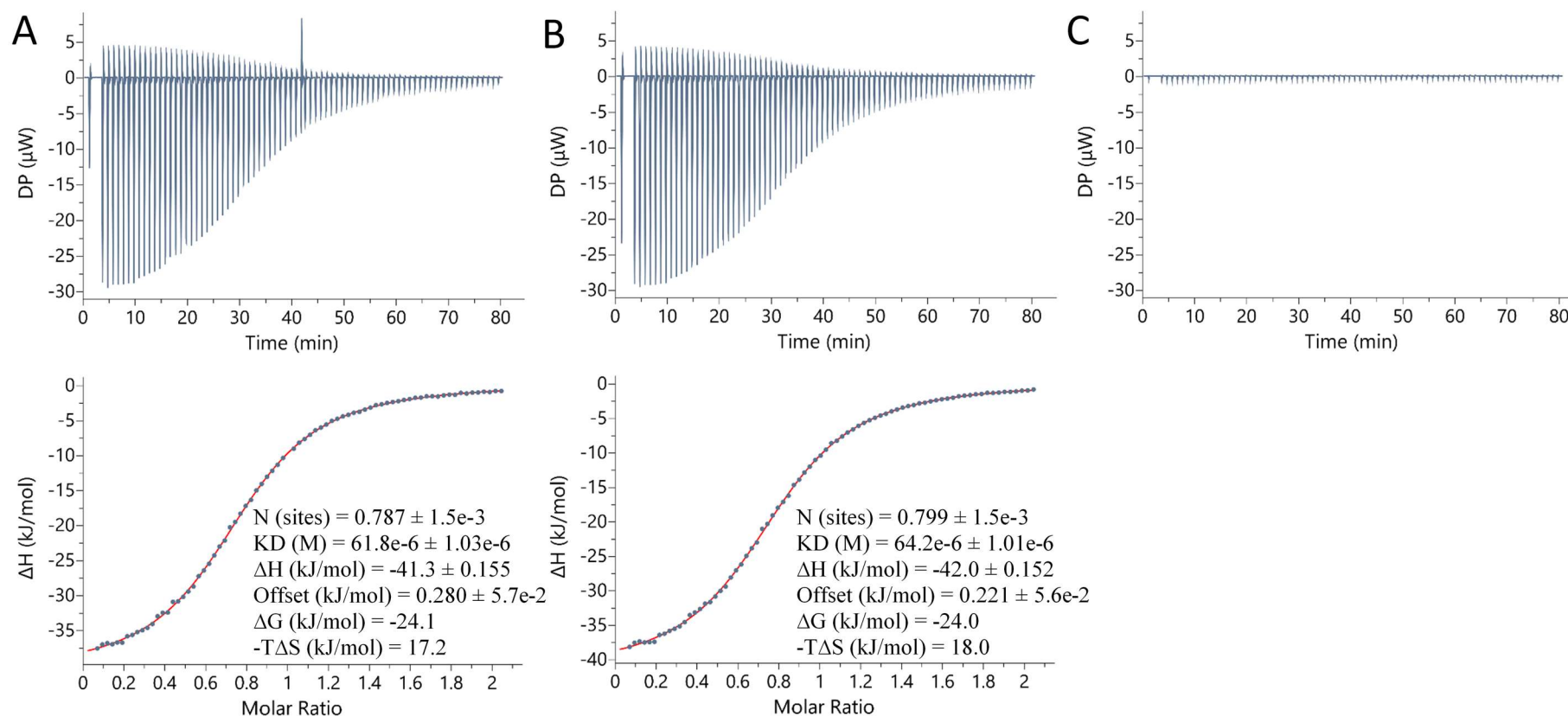


Figure S50. ITC of (TBA)PF₆ binding to (+)-mixHC[8] in CH₃OH at 298 K (A, B) and control experiment (C). *Top:* Data obtained from the sequential injections of 0.5 μL of (TBA)PF₆ (10.0 mM) to (+)-mixHC[8] (1.1 mM) (A,B) or to the pure solvent mixture (C) with 60 s spacing. *Bottom:* Plot of the total heat released as a function of total guest concentration for the titration shown in the upper panel. The red solid line represents least-squares fit of the data.

(TBA)PF₆ binding to (+)-mixHC[8] in CH₃OH:H₂O 1:1 mixture

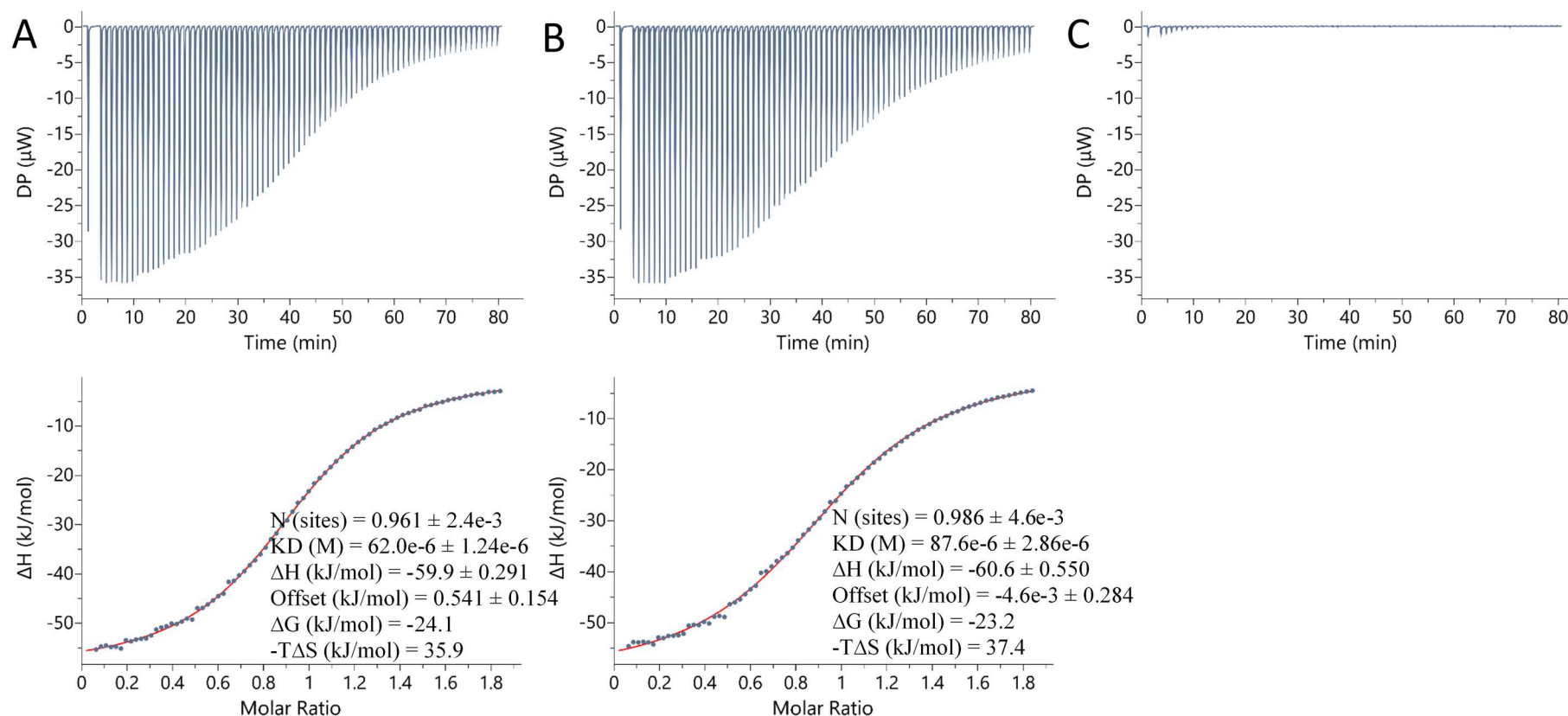


Figure S51. ITC of (TBA)PF₆ binding to (+)-mixHC[8] in CH₃OH : H₂O 1:1 mixture at 298 K (A, B) and control experiment (C). *Top:* Data obtained from the sequential injections of 0.5 μL of (TBA)PF₆ (9.0 mM) to (+)-mixHC[8] (1.1 mM) (A,B) or to the pure solvent mixture (C) with 60 s spacing. *Bottom:* Plot of the total heat released as a function of total guest concentration for the titration shown in the upper panel. The red solid line represents least-squares fit of the data.

(+)-mixHC[8] binding to NaSbF₆ in CH₃OH

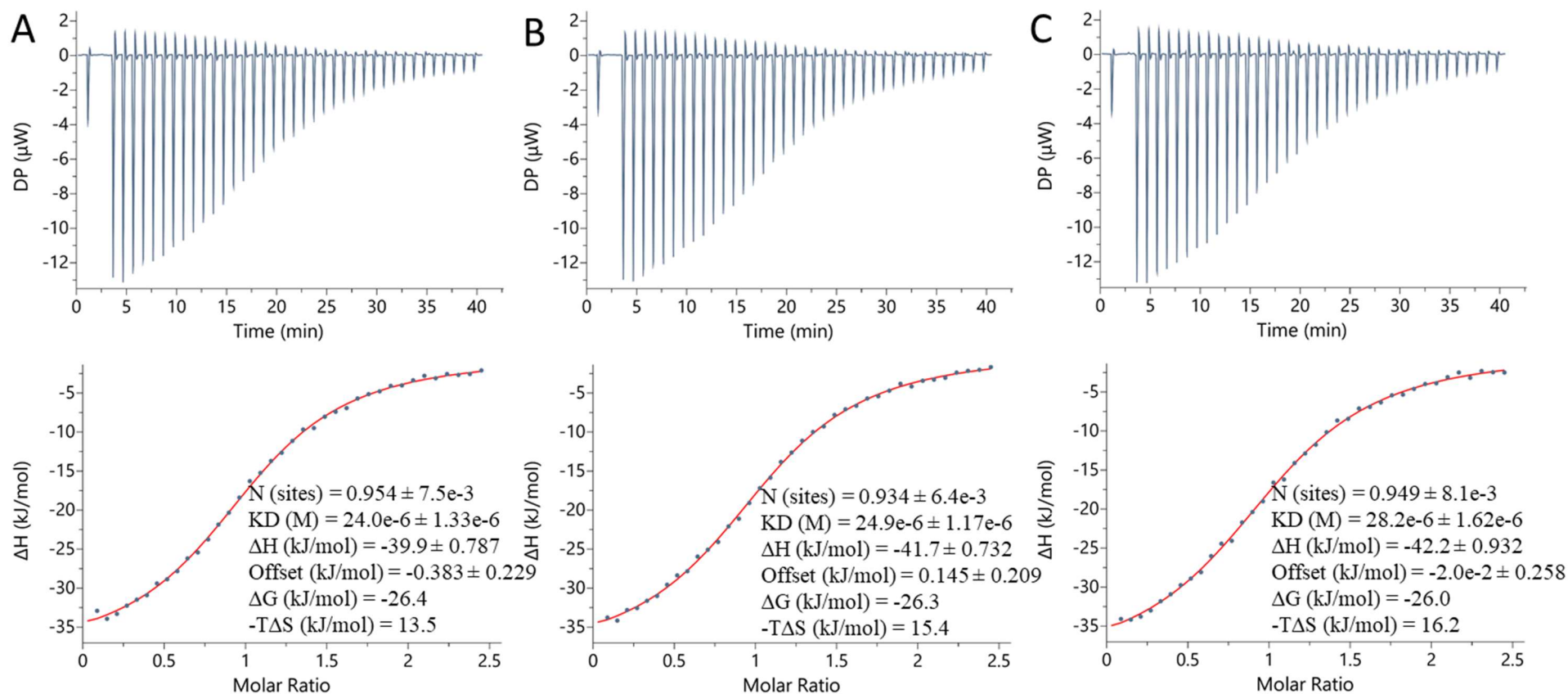


Figure S52. ITC of (+)-mixHC[8] binding to NaSbF₆ in CH₃OH at 298 K (A, B, C – parallel titrations). Top: Data obtained from the sequential injections of 1 μ L of (+)-mixHC[8] (2.5 mM) to NaSbF₆ (0.2 mM) with 60 s spacing. Bottom: Plot of the total heat released as a function of total guest concentration for the titration shown in the upper panel. The red solid line represents least-squares fit of the data.

(+)-mixHC[8] binding to NaSbF₆ in CH₃OH

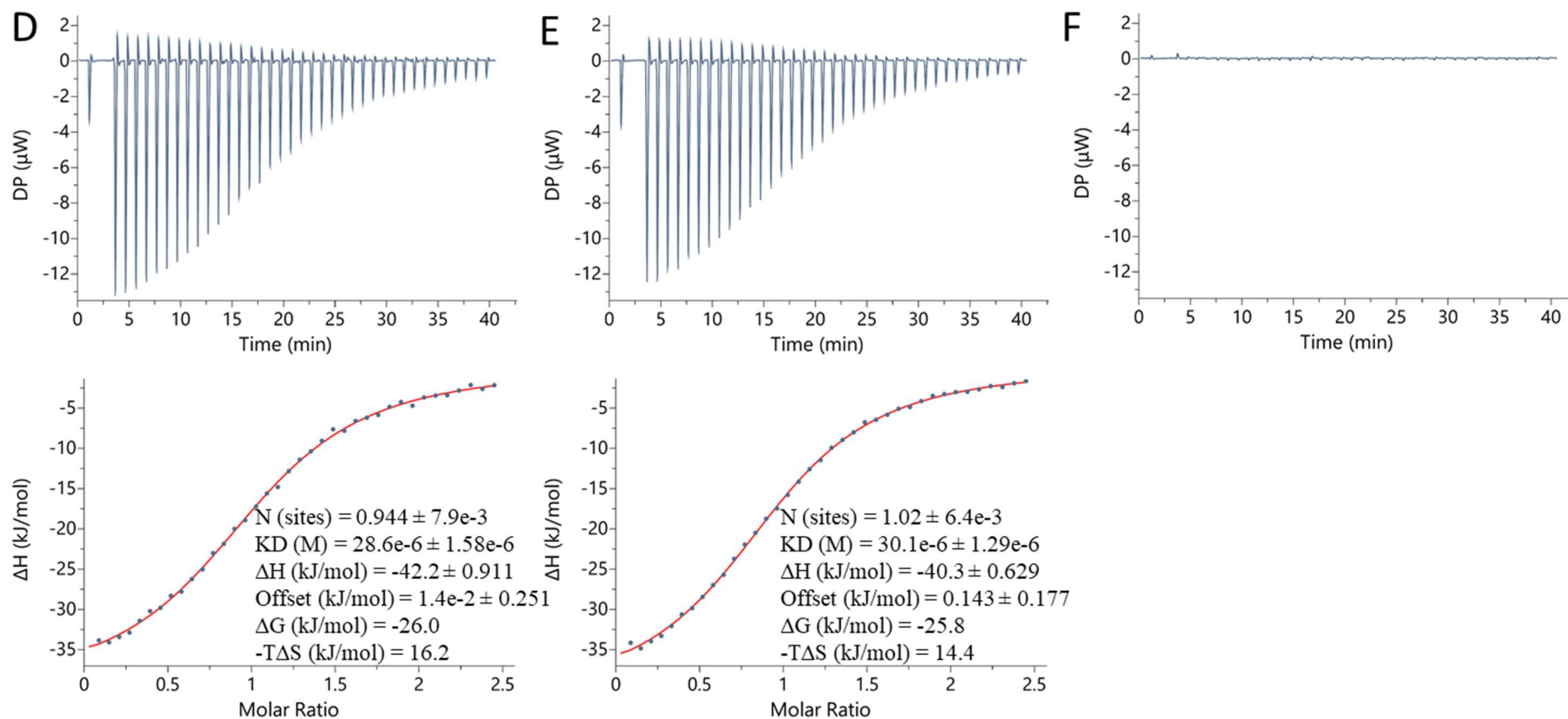


Figure S53. ITC of (+)-mixHC[8] binding to NaSbF₆ in CH₃OH at 298 K (D, E) and control experiment (F). Top: Data obtained from the sequential injections of 1 μL of (+)-mixHC[8] (2.5 mM) to NaSbF₆ (0.2 mM) (D, E) or to the pure solvent (F) with 60 s spacing. Bottom: Plot of the total heat released as a function of total guest concentration for the titration shown in the upper panel. The red solid line represents least-squares fit of the data.

MgSO₄ binding to (+)-mixHC[8] in CH₃OH:H₂O 1:1 mixture

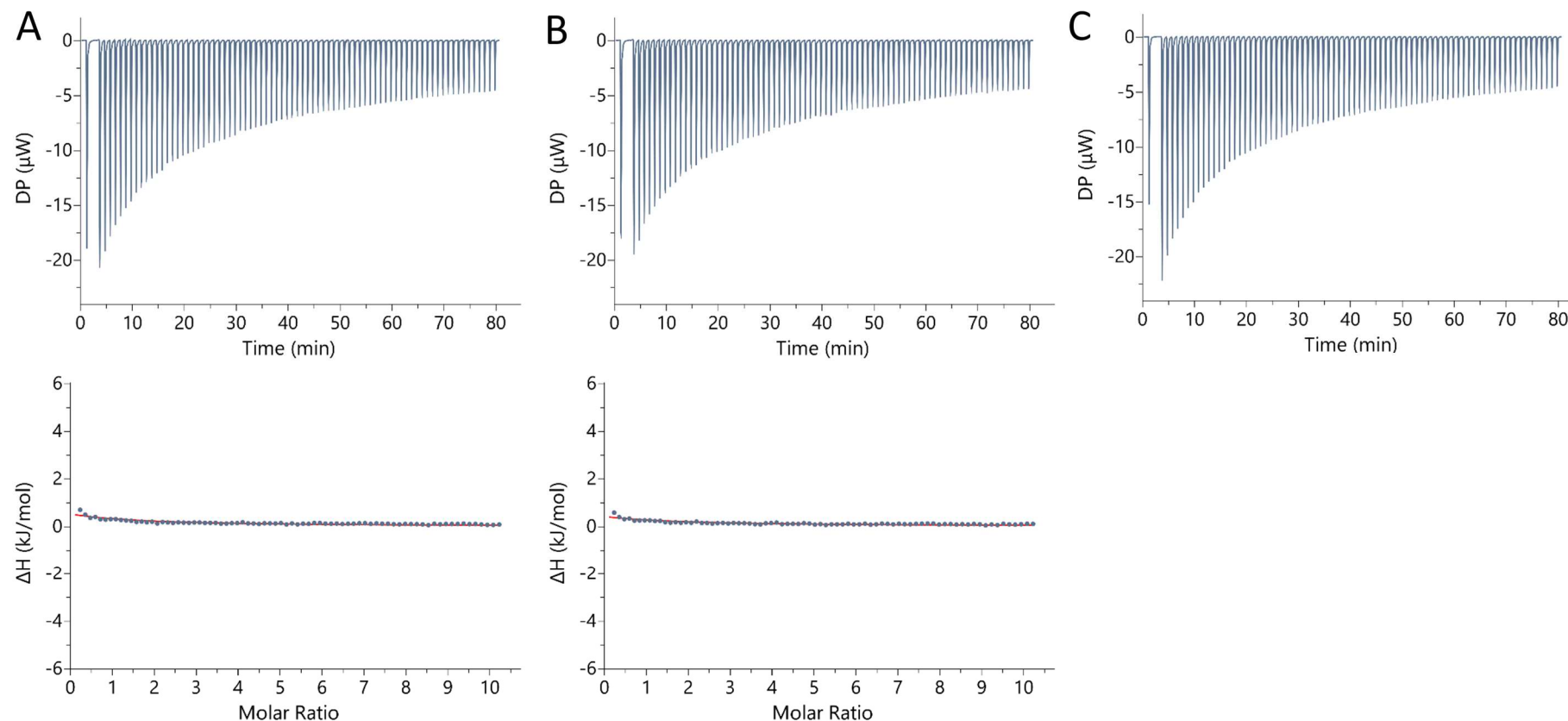


Figure S54. ITC of MgSO₄ binding to (+)-mixHC[8] in CH₃OH : H₂O 1:1 mixture at 298 K (A, B) and control experiment (C). *Top:* Data obtained from the sequential injections of 0.5 μ L of MgSO₄ (50.0 mM) to (+)-mixHC[8] (1.1 mM) (A,B) or to the pure solvent mixture (C) with 60 s spacing. *Bottom:* Plot of the total heat released as a function of total guest concentration for the titration shown in the upper panel. The red solid line represents least-squares fit of the data.

6.2 Immobilization of mixHC[8] on APS

APS (49.9 mg, corresponding to 0.050 mmol NH_2 -groups, 1 eq.), (–)-mixHC[8] (82.0 mg, 0.056 mmol, 1.1 eq.), DIC (7.9 μl [6.4 mg, P=99%], 0.050 mmol, 1 eq.) and 10 ml DCM were placed into 25 ml round bottom flask. The mixture was stirred at 700 rpm and 50 °C under argon atmosphere with reflux for 7 days. To wash the product (mixHC[8]-APS), the reaction mixture was transferred on the cotton placed into a glass Pasteur pipette. The solid was filtered out and rinsed with 5×1 ml DCM and additional 0.5 ml DCM. The last portion of DCM after rinsing was analyzed by HPLC and no peaks belonging to the macrocycle were detected. The solid product was dried with air, transferred into the vial and dried on rotovap, final weight: 43.1 mg.

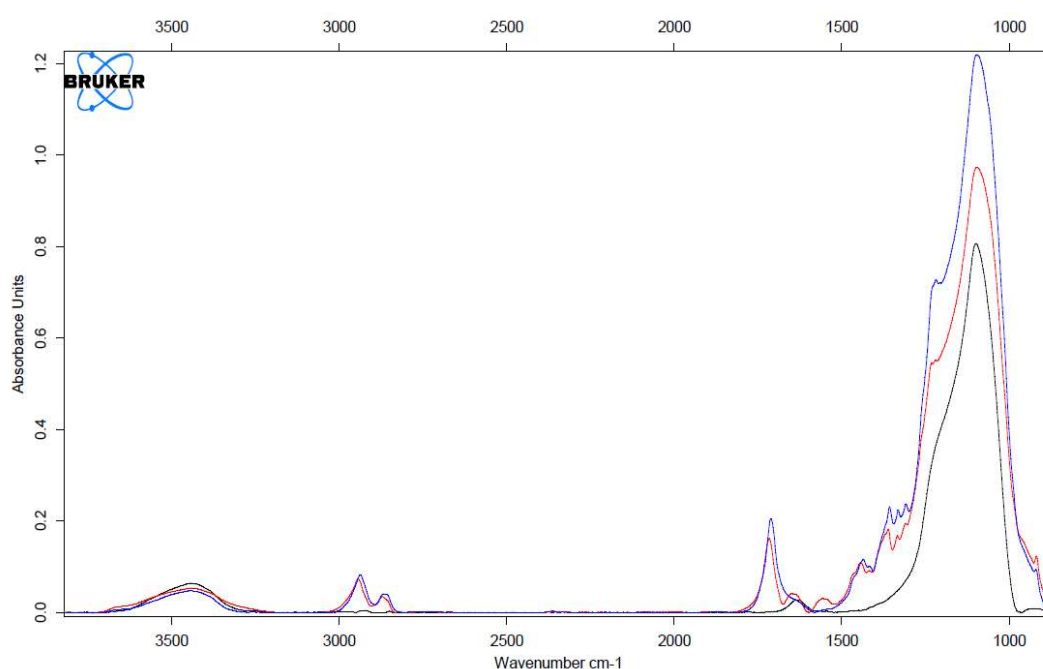


Figure S55. IR absorption spectra of APS (black), mixHC[8]-APS (red) and mixHC[8] + APS reference mixture (blue). Rough quantitation based on the carbonyl peak (1711 cm^{-1}) absorption provided mixHC[8] loading on modified APS ca. 12% by mass.

The obtained mixHC[8]-APS was tested for leaching: the solid material was stirred in methanol, which was further analyzed by HPLC-UV-MS and no macrocycle was detected.

6.3 Removal of Perchlorate from Methanol Solutions

General extraction procedure

Solid sorbent (mixHC[8]-APS or non-modified APS) was dispersed in guest methanol solution and stirred on orbital shaker for 60 min. The supernatant was filtered and clear filtrate was analysed for the guest content by IC.

Removal percentage (R , %) of the guest upon extraction was calculated using formula (3):

$$R(\%) = \frac{S_0 - S_i}{S_0} \cdot 100 \quad (3)$$

where S_0 – guest peak area in reference solution in the absence of host, $\mu\text{S}/\text{cm}$; S_i – guest peak area in experimental solution (mixed with solid host and filtered), $\mu\text{S}/\text{cm}$.

Removal experiments

The removal experiments were carried out for solid-phase extraction of ClO_4^- from its individual solution (*a*), as well as from its mixture with SO_4^{2-} (selectivity studies, *b*) and in presence of complex matrix – MGS-1 (*c*).

Table S26. Exolith Mars Global Soil Simulant (MGS-1) mineralogy^{25,26}

| Mineral | Wt. % |
|---------------------|-------|
| Anorthosite | 27.1 |
| Glass-rich basalt | 22.9 |
| Pyroxene (Bronzite) | 20.3 |
| Olivine | 13.7 |
| Mg-sulfate | 4.0 |
| Ferrihydrite | 3.5 |
| Hydrated silica | 3.0 |
| Magnetite | 1.9 |
| Anhydrite | 1.7 |
| Fe-carbonate | 1.4 |
| Hematite | 0.5 |

Stock solution of guest compound. 5 mg/L ClO_4^- in methanol (*a*); 5 mg/L ClO_4^- + 4 mg/L SO_4^{2-} in methanol (*b*); 495 mg MGS-1 + 17 mg (TBA) ClO_4 (corresponding to 5 mg ClO_4^- , or 1% by mass) was stirred in 5 ml methanol on orbital shaker for 60 min, the solution was then filtered and diluted 200 times providing ca. 4–5 mg/L ClO_4^- in methanol (*c*).

Blank suspension ($\times 1$) of host compound. 5 mg mixHC[8]-APS or non-modified APS in 2 ml methanol.

Reference solution ($\times 2$). 2 ml of stock solution.

Experimental suspension ($\times 2$). 5 mg mixHC[8]-APS or non-modified APS and 2 ml of stock solution.

Reference solution and blank and experimental suspensions were each placed into a 4 ml vial and stirred on orbital shaker at 500 rpm for 1 hr. The samples were then filtered through Minisart RC 13 mm, 0.45 μm syringe filter. The clear filtrate was analysed for the ionic content by IC.

IC analysis

IC analysis was performed on 761 Compact IC ion chromatograph with chemical suppression of eluent conductivity (Metrohm Ltd) using METROSEP A Supp 5 column (150 mm \times 4.0 mm). A mixture of 1.0 mM NaHCO_3 + 3.2 mM Na_2CO_3 was used as the mobile phase with the flow rate 0.7 ml/min; the samples were injected manually via 20 μl sampling loop.

For calibration studies, all solutions were filtered with Whatman FP 30 / 0.45 μM CA syringe filters. The samples were prepared and diluted with bi-distilled water.

Method linearity was investigated for a series of solutions of known concentrations.

ClO_4^- : 0.5 mg/L, 1 mg/L, 5 mg/L, 10 mg/L, 25 mg/L, 50 mg/L, 200 mg/L.

SO_4^{2-} : 0.01 mg/L, 0.05 mg/L, 0.1 mg/L, 0.5 mg/L, 1 mg/L, 6 mg/L, 10 mg/L, 12 mg/L, 30 mg/L, 60 mg/L, 120 mg/L.

Table S27. Analytical method characteristics.

| Analyte | Linear regression | R^2 | LoD, mg/L |
|--------------------|-------------------|--------|-----------|
| ClO_4^- | $Y=5.1068x$ | 0.9995 | 0.5 |
| SO_4^{2-} | $y = 14.588x$ | 0.9975 | 0.01 |

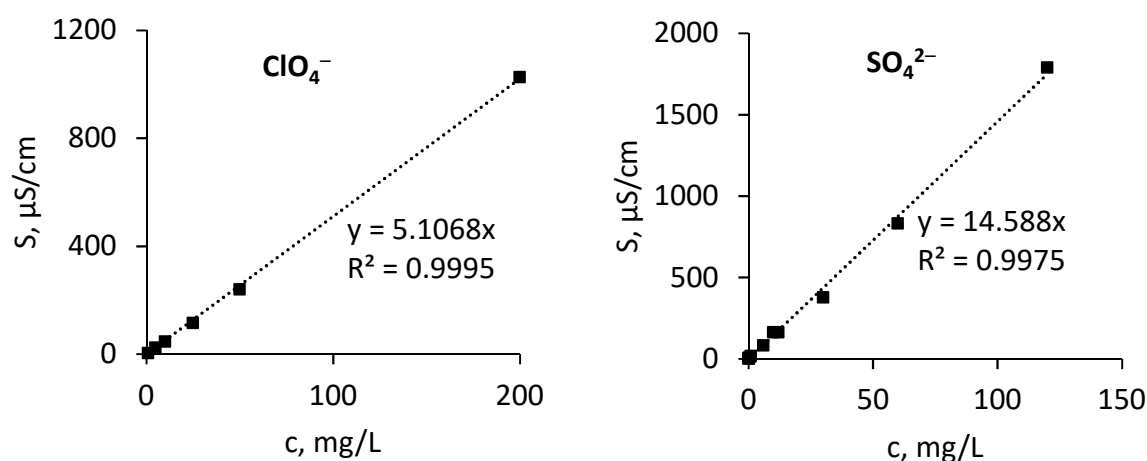


Figure S56. Calibration graph for determination of ClO_4^- and SO_4^{2-} concentration and linearity studies.

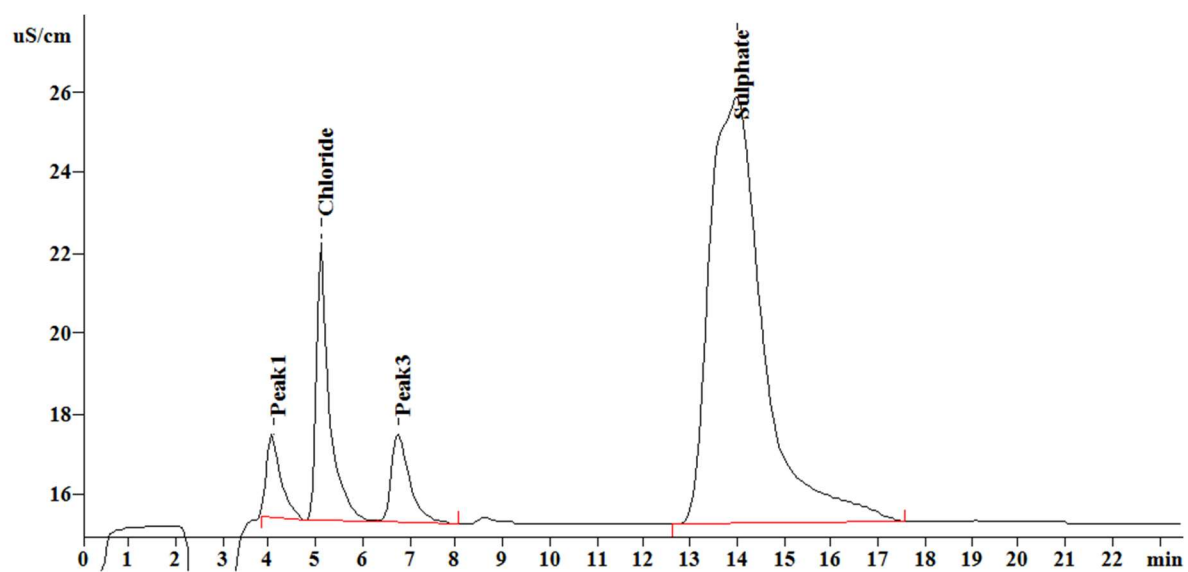


Figure S57. IC chromatogram of MGS-1 methanolic extract.

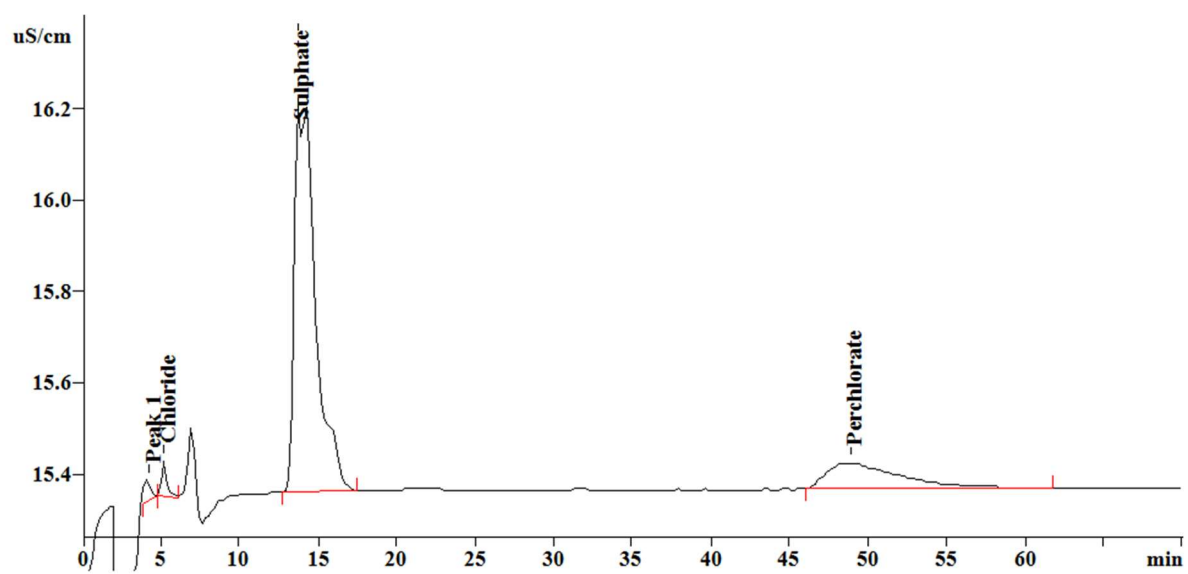


Figure S58. IC chromatogram of MGS-1 methanolic extract spiked with ClO_4^- .

Table S28. Removal of perchlorate and sulfate anions from methanol by 5 molar excess of mixHC[8], immobilized on APS, compared to non-modified APS.

| Experiment | Guest | Host | m_{host} , mg | $n_{mixHC[8]}$, μmol | c_{guest} , mg/L | n_{guest} , μmol | R , % ^a |
|--|-------------------------------|--------------|--------------------|-------------------------------------|-----------------------|----------------------------------|----------------------|
| ClO ₄ ⁻ solution | ClO ₄ ⁻ | mixHC[8]-APS | 5.0 | 0.5 | 5.0 | 0.10 | 100±0 |
| | | APS | | – | | | 22±2 |
| ClO ₄ ⁻ + SO ₄ ²⁻ solution (selectivity) | ClO ₄ ⁻ | mixHC[8]-APS | | 0.5 | 4.9 | 0.10 | 100±0 |
| | | APS | | – | | | 14±2 |
| | SO ₄ ²⁻ | mixHC[8]-APS | | 0.5 | 3.8 | 0.08 | 97.3±0.1 |
| | | APS | | – | | | 89.5±0.3 |
| MGS-1 + ClO ₄ ⁻ (spiked martian soil) | ClO ₄ ⁻ | mixHC[8]-APS | | 0.5 | 4.7 | 0.09 | 100±0 |
| | | APS | | – | | | 15±2 |
| | SO ₄ ²⁻ | mixHC[8]-APS | | 0.5 | 6.4 | 0.13 | 96.7±0.5 |
| | | APS | | – | | | 85±1 |

[a] The average R value is provided as mean result ± standard deviation between parallel experiments ($n \geq 2$)

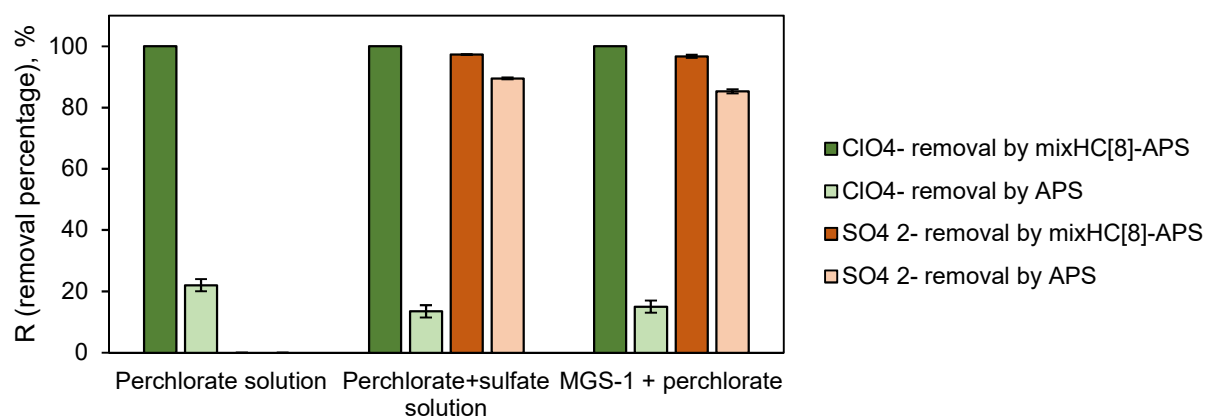


Figure 59. Removal percentage upon extraction of perchlorate and sulfate anions from methanol by mixHC[8]-APS and non-modified APS. The error bars represent standard deviation between parallel experiments ($n \geq 2$).

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