Electronic Supplementary Material (ESI) for New Journal of Chemistry.

Supporting Information: Using non-covalent interactions to direct regioselective 2+2 photocycloaddition within macrocyclic cavitand

Nga Nguyen, Aspen Rae Clements, Mahesh Pattabiraman*

1. Time dependence experiment

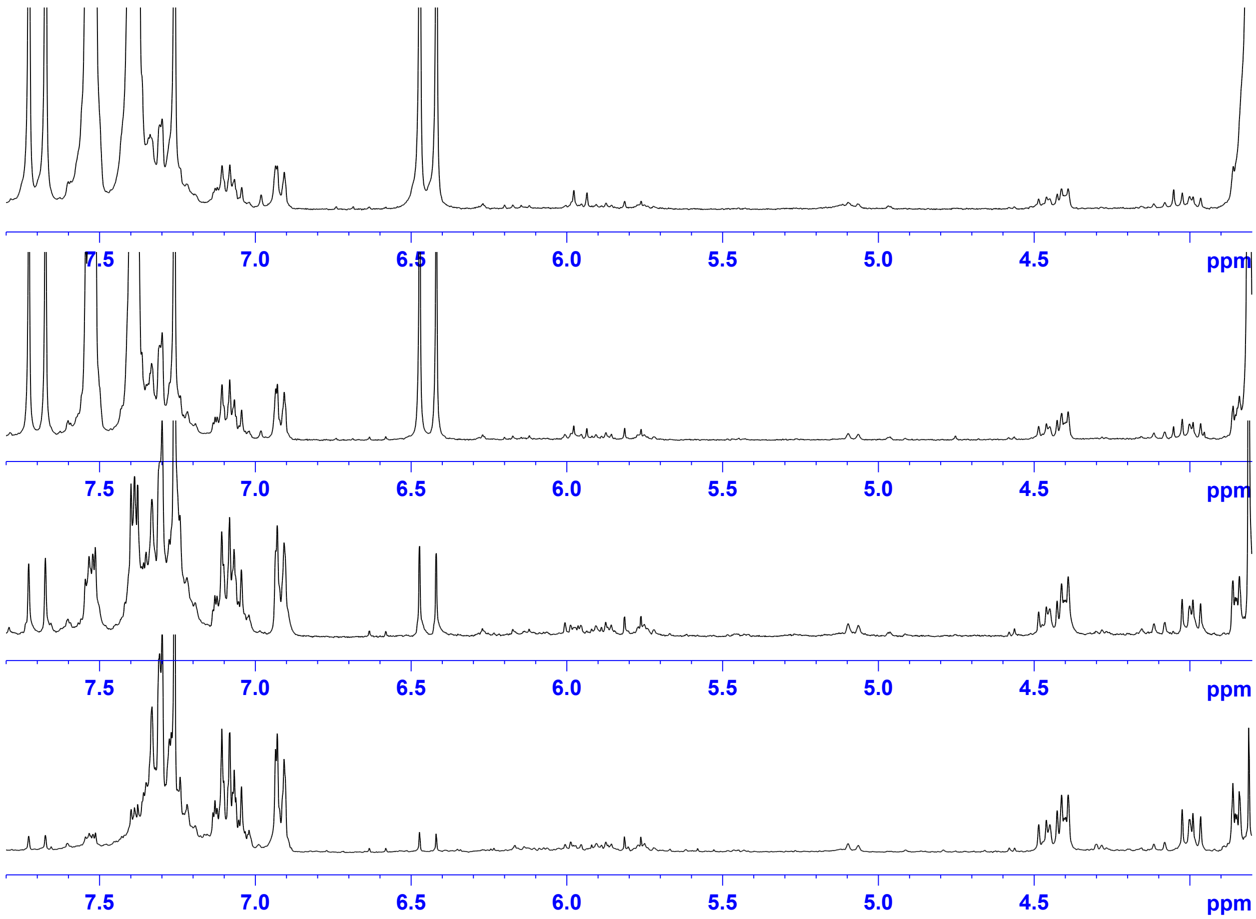


Figure 1. ^{1}H NMR spectra of reaction mixtures from irradiation of 1:2 complexes of γ-CD-methyl cinnamate for (top to bottom) 1 hr, 3 hrs, 7 hrs, and 9 hrs.

2. 2D NMR of isopropyl 2-chloro cinnamate (4d) reaction mixture

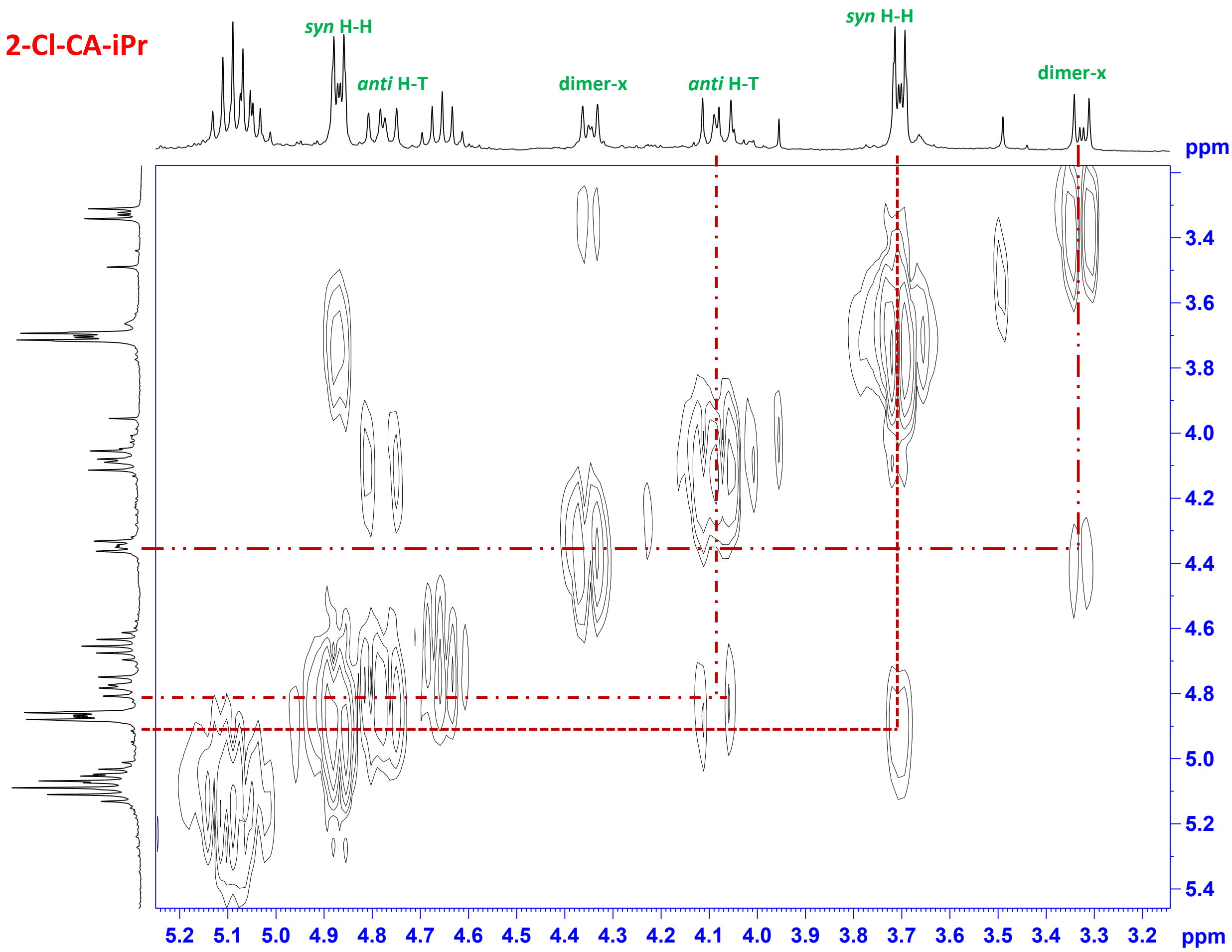
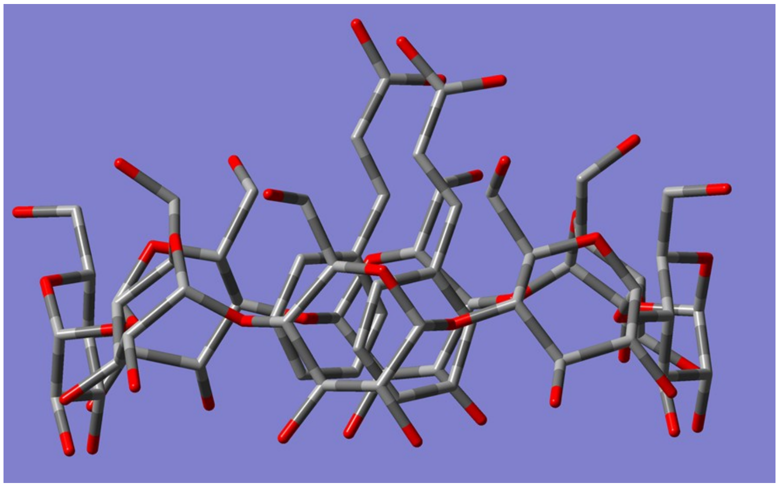


Figure 2. Partial COSY spectrum (300 MHz, $CDCl_3$) of reaction mixture showing correlations between cyclobutane signals of isopropyl 2-chloro cinnamate complex, showing presence of three different dimers.

3. Computational chemistry



$\Delta H_{primary}$ = -39.953 kcal/mol
$\Delta G_{primary}$ = -16.027 kcal/mol

$\Delta H_{primary} - \Delta H_{secondary}$ = 2.114 kcal/mol (carboxylic acid units near secondary face is more stable)

$\Delta G_{primary} - \Delta G_{secondary}$ = 1.463 kcal/mol (carboxylic acid units near secondary face more stable)

Figure 3. MM UFF energy minimized structure of two cinnamic acids (*syn* H-H arrangement) included within γ-CD in aqueous medium computed using Gaussian '09. The structure presented here is an isomeric arrangement wherein the carboxylic acid unit are near the primary side. The isomeric arrangements presented in the main paper are those of carboxylic acid (or carboxylate) units near the secondary side.

4. ^{1}H NMR chemical shifts of guests and their dimers observed in this study

Data provided below are ^{1}H NMR chemical shifts of compounds dissolved in $CDCl_3$ recorded in a 300 MHz Bruker Avance instrument.

Methyl cinnamate (1a)
δ7.72 (d, *J*=16Hz, 1H), δ7.53 (m, 2H), δ7.40 (m, 3H), δ6.45 (d, *J*=16Hz, 3H), δ3.82 (s, 3H)
***Syn* H-H dimer**
δ7.13 (m, 3H), δ 6.92 (m, 2H), δ 4.40 (m, 2H), δ 3.84 (m, 2H), δ 3.80 (s, 6H)
Anti H-T dimer
δ7.46 to δ 7.25 (m, 5H), δ 4.49 (m, 2H), δ4.03 (m, 2H), δ3.35 (s, 6H)

Ethyl cinnamate (2a)
δ7.72 (d, *J*=16Hz, 1H), δ7.54 (m, 2H), δ7.40 (m, 3H), δ6.42 (d, *J*=16Hz, 3H), δ4.27 (q, *J*=7Hz, 2H), δ1.35 (t, *J*=7Hz, 3H)
***Syn* H-H dimer**
δ7.09 (m, 3H), δ 7.92 (m, 2H), δ 4.41 (m, 2H), δ 3.83 (m, 2H), δ 3.78 (q, *J*=7Hz, 4H), δ 1.29 (t, *J*=7Hz, 6H)
***Anti* H-T dimer**
δ7.46 to δ 7.25 (m, 5H), δ 4.49 (m, 2H), δ4.03 (m, 4H), δ3.35 (s, 6H)

Isopropyl cinnamate (1c)
δ7.69 (d, *J*=16Hz, 1H), δ7.54 (m, 2H), δ7.40 (m, 3H), δ6.42 (d, *J*=16Hz, 3H), δ5.15 (sep, *J*=6.2 Hz, 1H), δ1.35 (t, *J*=6.2 Hz, 6H)

Anti H-T dimer
δ7.43 to 7.29 (m, 5H), δ 4.65 (sep, *J*=4.65 Hz, 1H), δ 4.45 (m, 2H), δ 3.92 (m, 2H), δ 1.32 (t, *J*=7Hz, 6H)

Propyl cinnamate (1d)
δ7.70 (d, *J*=16 Hz, 1H), δ7.53 (m, 2H), δ7.39 (m, 3H), δ6.46 (d, *J*=16 Hz, 3H), δ4.18 (t, *J*=7.2 Hz, 2H), δ1.76 (sex, *J*=7.2 Hz, 3H), δ1.01 (t, *J*=7.2 Hz, 3H)

Butyl cinnamate (1e)
δ7.69 (d, *J*=16Hz, 1H), δ7.52 (m, 2H), δ7.39 (m, 3H), δ6.45 (d, *J*=16Hz, 3H), δ4.21 (t, *J*=6.7 Hz, 2H), δ1.72 (m, 4H), δ1.44 (m, 4H), δ0.97 (t, *J*=6.7 Hz, 3H)

Cyclohexyl cinnamate (1f)
δ7.69 (d, *J*=16Hz, 1H), δ7.52 (m, 2H), δ7.39 (m, 3H), δ6.45 (d, *J*=16Hz, 3H), δ4.90 (m, 1H), δ1.67 (m, 10H)
Methyl 4-methyl cinnamate

Methyl ester of 4-methyl cinnamaic acid (2a)
δ7.68 (d, *J*=16Hz, 1H), δ7.44 (d, *J*=8.2 Hz, 2H), δ7.20 (d, *J*=8.2 Hz, 2H), δ6.41 (d, *J*=16Hz, 3H), δ3.81 (s, 3H), δ2.38 (s, 3H)
***Syn* H-H**
δ7.18 (d, *J*=8 Hz, 2H), δ6.80 (d, *J*=8, 2H), δ 4.33 (m, 2H), δ 3.80 (m, 2H), δ 3.75 (s, 3H), δ 2.32 (s, 3H)
***Anti* H-T**
δ7.18 (d, *J*=8 Hz, 2H), δ6.92 (d, *J*=8, 2H), δ 4.40 (m, 2H), δ 3.94 (m, 2H), δ 3.33 (s, 3H), δ 2.20 (s, 3H)

Ethyl ester of 4-methyl cinnamic acid (2b)
δ7.68 (d, *J*=16Hz, 1H), δ7.43 (d, *J*=8.2 Hz, 2H), δ7.20 (d, *J*=8.2 Hz, 2H), δ6.40 (d, *J*=16Hz, 3H), δ4.26 (q, *J*=7.2 Hz, 2H), δ1.34 (t, *J*=7.2 Hz, 3H)

Isopropyl ester of 4-methyl cinnamic acid (2c)
δ7.66 (d, *J*=16Hz, 1H), δ7.43 (d, *J*=8.2 Hz, 2H), δ7.20 (d, *J*=8.2 Hz, 2H), δ6.38 (d, *J*=16Hz, 3H), δ5.13 (sep, *J*=6.2 Hz, 1H), δ1.30 (d, *J*=6.2 Hz, 6H)

Methyl ester of 2-chloro cinnamic acid (4a)
δ8.08 (d, *J*=16Hz, 1H), δ7.63 (m, 1H), δ7.42 (m, 1H), δ7.31 (m, 2H), δ6.43 (d, *J*=16Hz, 3H), δ3.82 (s, 3H)
***Syn* H-H**
δ7.18 (m), δ7.05 (m), δ 4.91 (m, 2H), δ 3.80 (m, 2H), δ 3.77 (s, 3H)

Ethyl ester of 2-chloro cinnamic acid (4b)
δ8.10 (d, *J*=16Hz, 1H), δ7.63 (m, 1H), δ7.42 (m, 1H), δ7.31 (m, 2H), δ6.44 (d, *J*=16Hz, 3H), δ4.29 (q, *J*=7.2 Hz, 2H), δ1.36 (t, *J*=7.2 Hz, 3H)

Propyl ester of 2-chloro cinnamic acid (4c)
δ8.11 (d, *J*=16Hz, 1H), δ7.63 (m, 1H), δ7.42 (m, 1H), δ7.32 (m, 2H), δ6.44 (d, *J*=16Hz, 3H), δ4.20 (t, *J*=6.7 Hz, 2H), δ1.76 (sex, *J*=6.7 Hz, 2H), δ1.01 (t, *J*=6.7 Hz, 3H)

Isopropyl ester of 2-chloro cinnamic acid (4d)

δ8.08 (d, *J*=16Hz, 1H), δ7.63 (m, 1H), δ7.43 (m, 1H), δ7.31 (m, 2H), δ6.41 (d, *J*=16Hz, 3H), δ5.16 (sep, *J*=6.2 Hz, 1H), δ1.33 (d, *J*=6.2 Hz, 6H)

***Syn* H-H**
δ7.24 (m), δ7.04 (m), δ 4.88 (m, 2H), δ 3.71 (m, 2H), δ 5.09 (sep, *J*=6.1 Hz, 1H), δ 1.27 (s, *J*=6.1 Hz, 6H)
***Anti* H-T**
δ7.60 (m), δ7.48-7.28(m), δ 4.79 (m, 2H), δ 4.10 (m, 2H), δ 5.06 (sep, *J*=6.1 Hz, 1H), δ 1.27 (s, *J*=6.1 Hz, 6H)

Methyl ester of 3-bromo cinnamic acid (5a)
δ7.67 (m, 2H), δ7.62 (d, *J*=15.9Hz, 1H), δ7.52 (m, 1H), δ7.45 (m, 3H), δ6.44 (d, *J*=16Hz, 3H), δ3.82 (s, 3H)
***Syn* H-H**
δ7.09 (m, 2H), δ 7.21 (m, 1H), δ6.81 (m, 1H), δ 4.35 (m, 2H), δ 3.78 (m, 2H), δ 3.76 (s, 3H)
***Anti* H-T**
δ7.42 (m, 2H), δ 7.25-7.20 (m, 2H), δ 4.38 (m, 2H), δ 3.95 (m, 2H), δ 3.39 (s, 3H)

Isopropyl ester of 3-bromo cinnamic acid (5b)
δ7.68 (m, 2H), δ7.59 (d, *J*=15.9Hz, 1H), δ7.51 (m, 1H), δ7.44 (m, 3H), δ6.41 (d, *J*=16Hz, 3H), δ5.15 (sep, *J*=6.4 Hz, 1H), δ1.30 (d, *J*=6.4 Hz, 6H)
***Syn* H-H**
δ7.12 (m, 2H), δ 7.00 (m, 1H), δ6.82 (m, 1H), δ5.08 (sep, *J*=6.5 Hz, 1H), δ 4.32 (m, 2H), δ 3.72 (m, 2H), δ 1.26 (d, *J*=6.5 Hz, 6H)
***Anti* H-T**
δ7.45 (m, 2H), δ 7.38 (m, 1H), 7.23 (m, 1H), δ4.71 (sep, *J*=6.5 Hz, 1H), δ 4.38 (m, 2H), δ 3.89 (m, 2H), δ 1.05 (d, *J*=6.5 Hz, 6H)

isopropyl ester of 3-fluoro cinnamic acid (6a)
δ7.62 (d, *J*=15.9Hz, 1H), δ7.42-7.18 (m, 3H), δ7.08 (m, 1H), δ6.41 (d, *J*=16Hz, 3H), δ5.15 (sep, *J*=6.2 Hz, 1H), δ1.32 (d, *J*=6.2 Hz, 6H)
***Anti* H-T**
δ7.30 (dd, 1H), δ7.10 (d, 1H), δ7.03 (td, 1H), δ6.95 (dt, 1H), δ4.71 (sep, *J*=6.5 Hz, 1H), δ 4.42 (m, 2H), δ 3.88 (m, 2H), δ 0.73 (d, *J*=6.5 Hz, 6H)

5. Complexation studies

Even though the reactions were studied in slurry, we studied the solution phase host-guest interaction through NMR to confirm complexation.

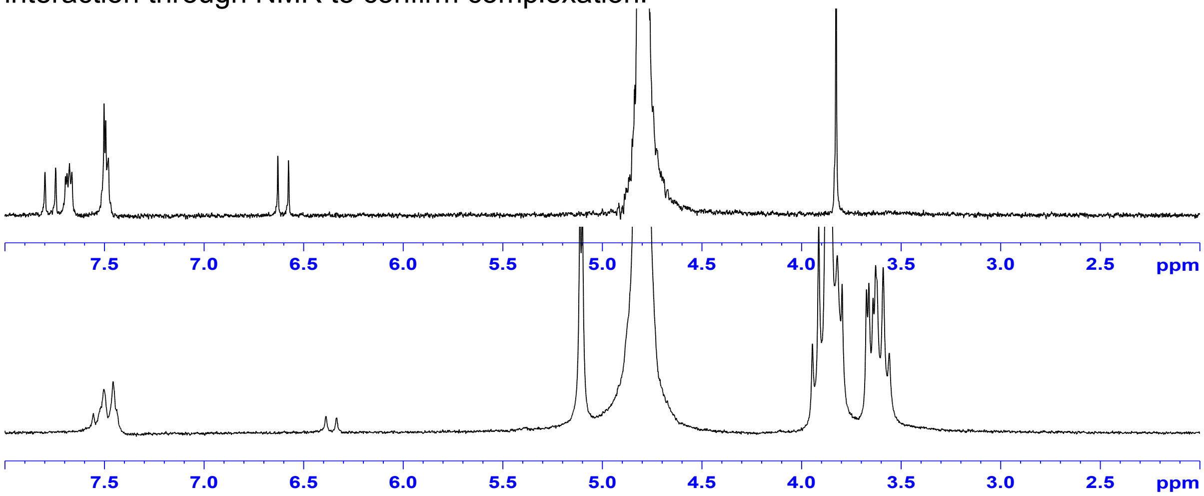


Figure 4. ${}^{1}H$ NMR in D_2O of methyl cinnamate (top), and methyl cinnamate complexed to γ-CD. Shifts in guest signals indicate complexation.

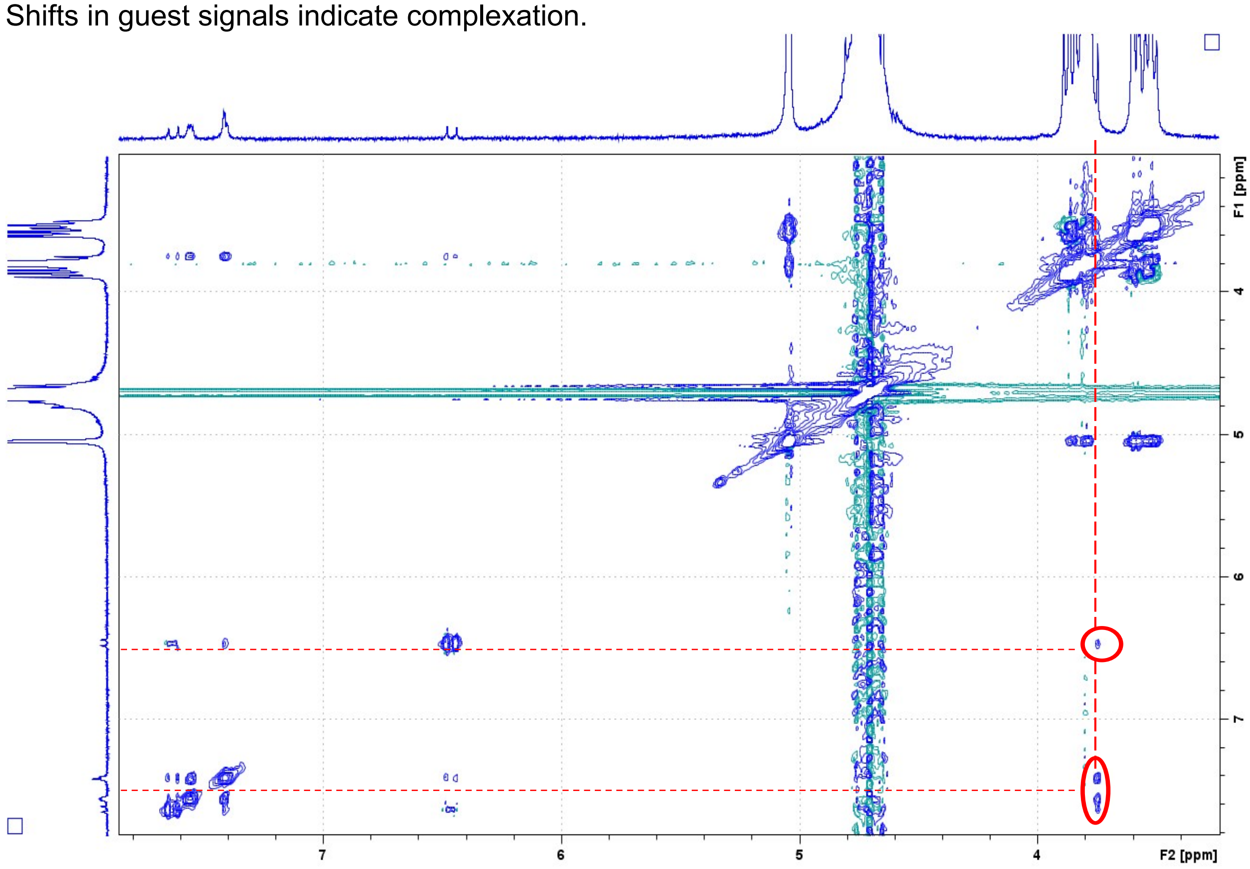


Figure 5. NOESY spectrum of the methyl cinnamate complexed to γ-CD showing crosspeaks indicating intermolecular interaction between internal hydrogens of the host and protons of the guest. Crosspeaks between guest signals are also present indicating interaction between two

guest molecules in the ternary inclusion complex. Solvent: D_2O, relaxation time: 2 s, mixing time: 500 ms.

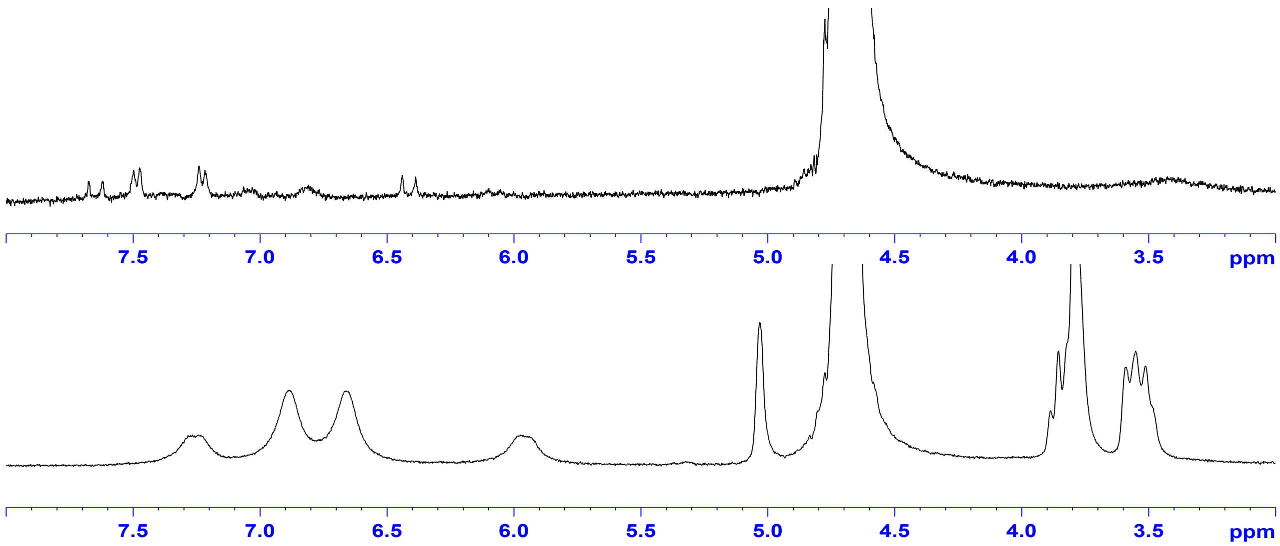


Figure 6. ^1H NMR in D_2O of isopropyl ester of 4-methyl cinnamic acid (top), and the ester complexed to γ-CD. Shifts in guest signals indicate complexation.