Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry.

Stereo- and Regioselective Photocycloaddition of Extended Alkenes Using γ-Cyclodextrin

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1. Synthesis of reactants 1a, 1b, 1c, and 1d

Chalcones **1a** to **1d** were synthesized using aldol condensation reaction. Solid sodium hydroxide (2.5g) was placed in a 125 mL Erlenmeyer flask, and water (13 mL) added to it. The mixture ws swirled until it is fully dissolved, and 13 mL of ethanol added to it. The mixture is brought to room temperature, and 1.8 mL acetone was added followed by 5.3 mL benzaldehyde. A yellow precipitate formed immediately, accumulated as the mixture was swirled for 15 minutes. The precipitate was filtered through a Büchner funnel, and transferred and washed with a small amount of cold ethanol. The crystals were air-dried. The crude, slightly wet product was spread out on a paper towel to dry for a short time, then weighed. The product was then recrystallized from ethyl acetate heated on a hot plate. Immiscible lower aqueous layer appeared in this step was decanted quickly. The resulting solution was allowed to cool during which recrystallization occurred. The final crystalline product was filtered and dried on a Büchner funnel. Final product was dried under vacuum overnight before recording NMR spectra. Typical product yield: 65-75%. Synthesis of other substrates followed same procedure involving the respective starting aldehydes.

2. Complexation and irradiation

Specific amounts of the guests (typically 20 mg) were weighed into a 20mL dram vial. Then half equivalent of γ-CD and water were added, and the mixture was sonicated for half hour followed by stirring for 12 hrs. Complexation is indicated by formation of chalky white or yellow precipitate, which forms a slurry of even consistency. The slurry was filtered using a filter funnel and dried to yield powdered complex. The precipitate was washed with cold water and methanol to remove uncomplexed host and guest.

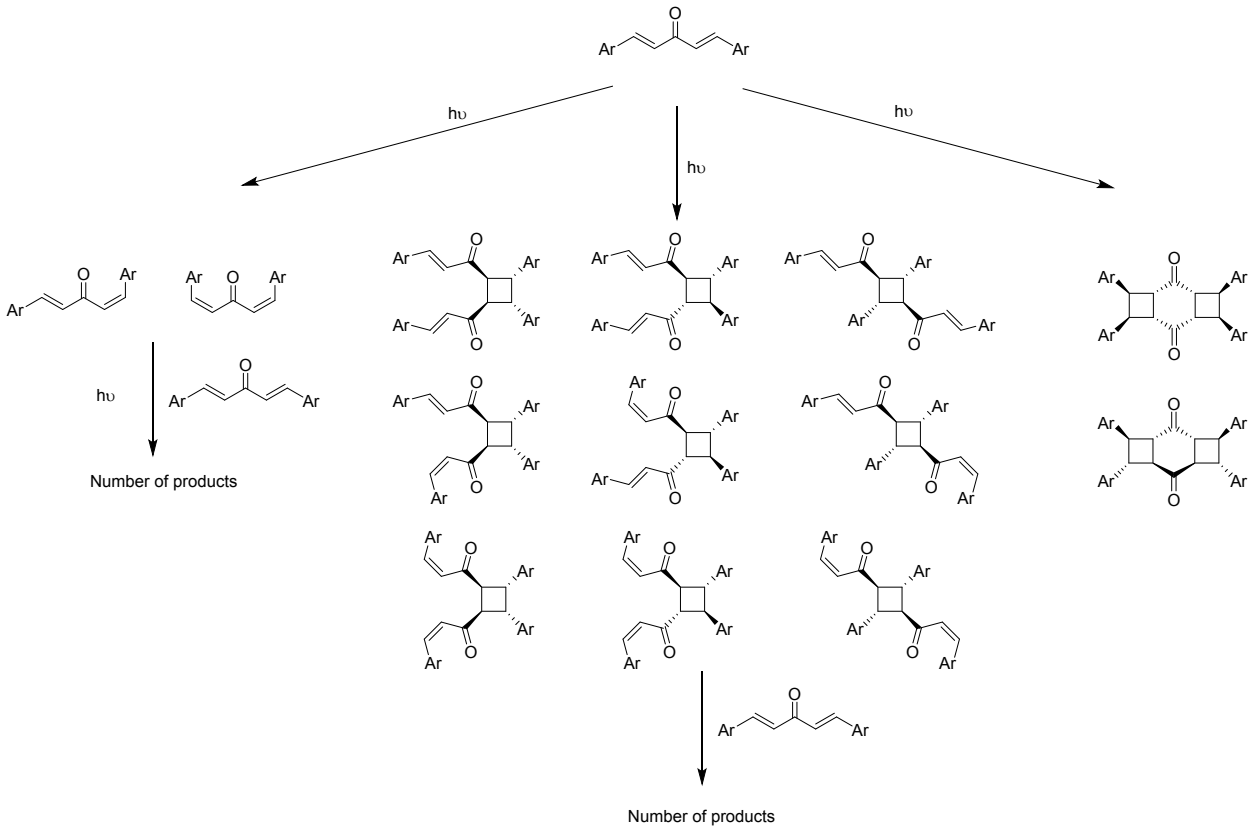
The resulting dried powder is now added to 10 mL of water and allowed to form a slurry again, and the complex is irradiated as a slurry for at least specific duration. A medium pressure photochemical lamp immersed in a water-cooled pyrex jacket was used for irradiation.

Irradiated complexes were decomplexed through biphasic extraction with 50 mL of water and 50 mL of ethyl acetate. The organic layer was separated from the aqueous layer, dried over anhydrous magnesium sulfate, and solvent removed *in vacuo*.

3. Isolation, purification of products, and characterization

Reaction mixtures with photoproducts were dissolved in 50% water/acetonitrile mixture. Compounds in the reaction mixtures were separated on a Gilson preparative HPLC. Preparative HPLC elution scheme involved initial solvent mixture of 20/80 acetonitrile/water mixture for 1 min followed by a 20 min ramp towards 80/20 acetonitrile/water mixture with the eluent flow rate maintained at 20 mL/min. Isolated products were dried in a lyophilizer to obtain pure product in solid form. Isolated compounds were characterizing primarily using ^{1}H and ^{13}C NMR spectra recorded using 400 MHz Bruker Avance spectrometer. Signals were analyzed using the *TopSpin 3.5pl7* software.

4. Scheme of possible products



Scheme S1. Possible products that could result from primary and secondary reaction of dibenzalacetones

5. ^{1}H and ^{13}C NMR spectra

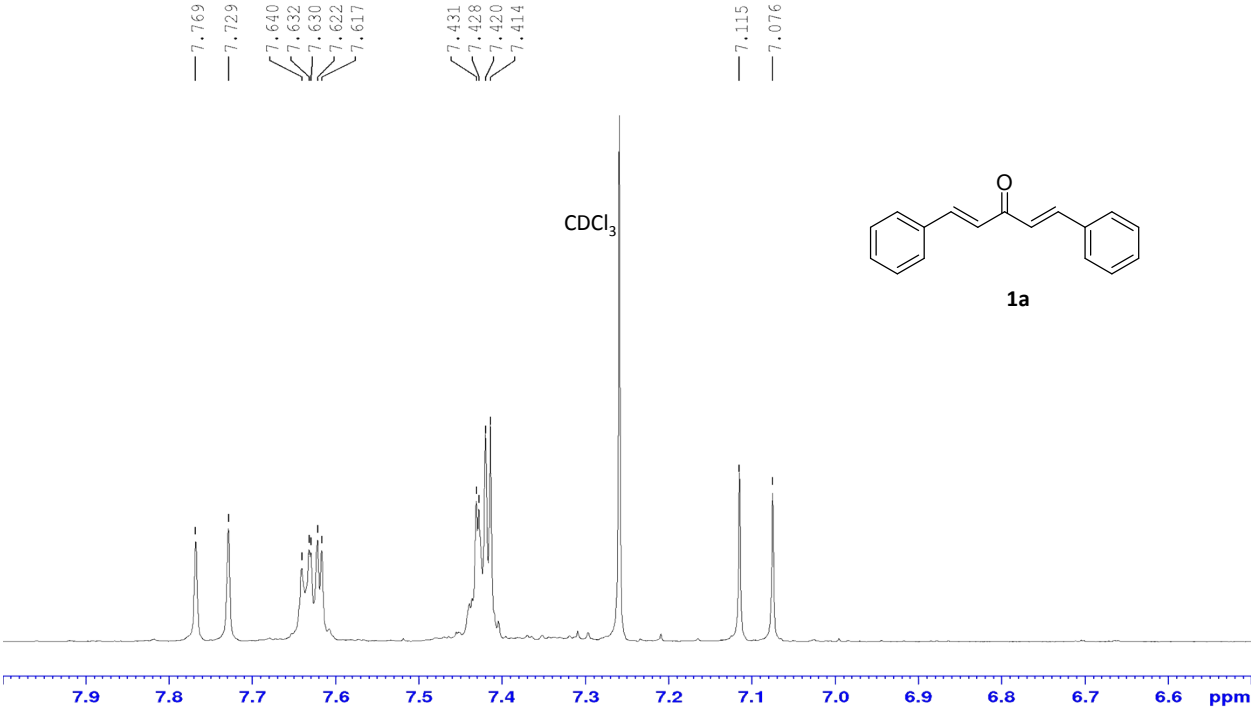


Figure S1. ^{1}H NMR spectrum of reactant **1a**

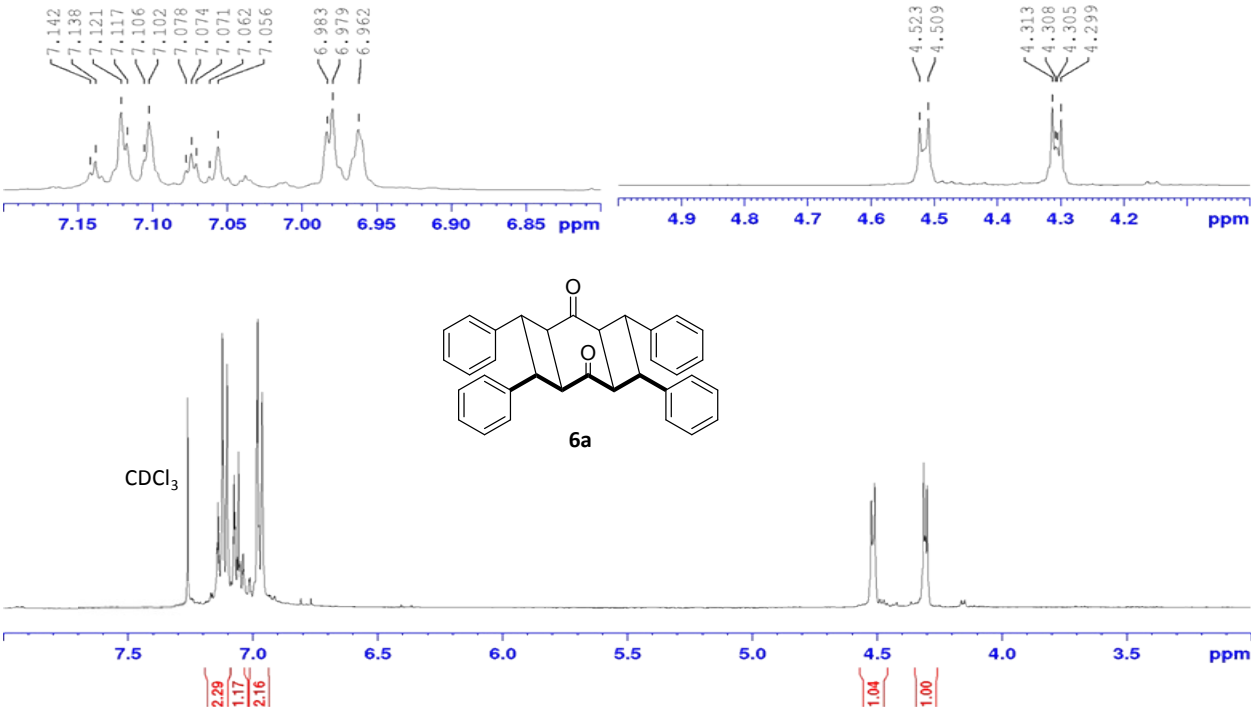


Figure S2 ^{1}H NMR spectrum of dimer **6a**

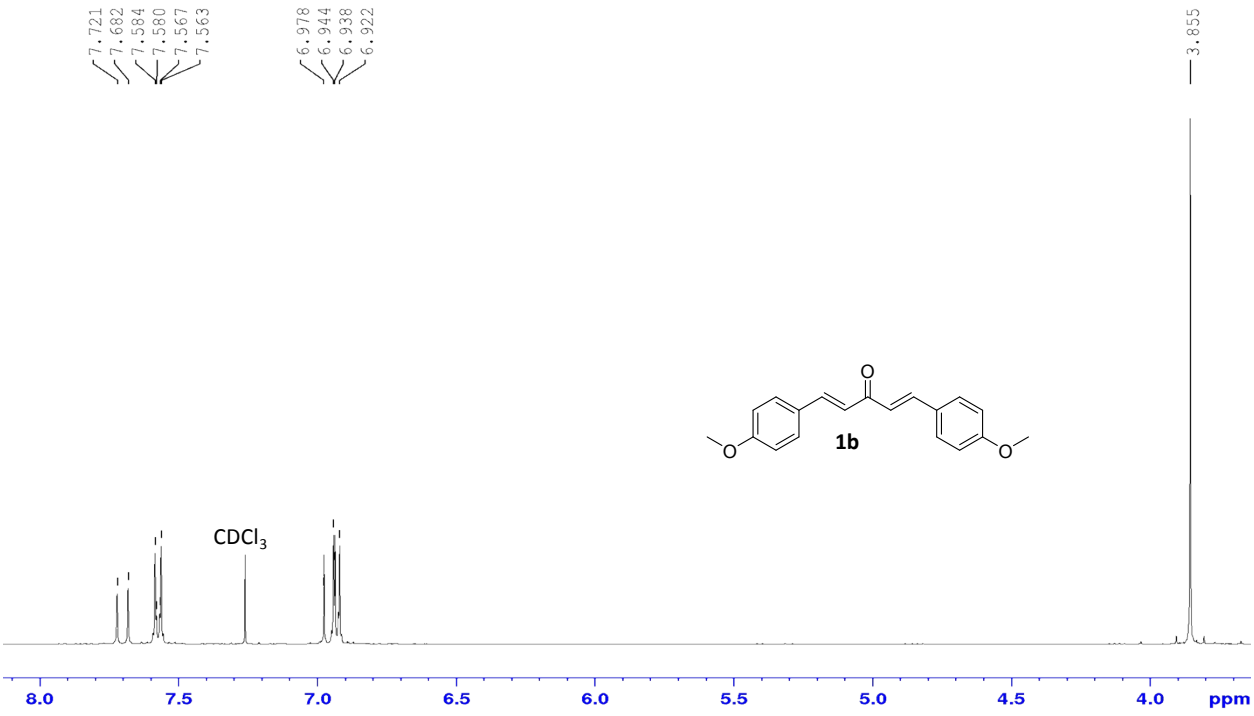


Figure S3 ^{1}H NMR spectrum of **1b**

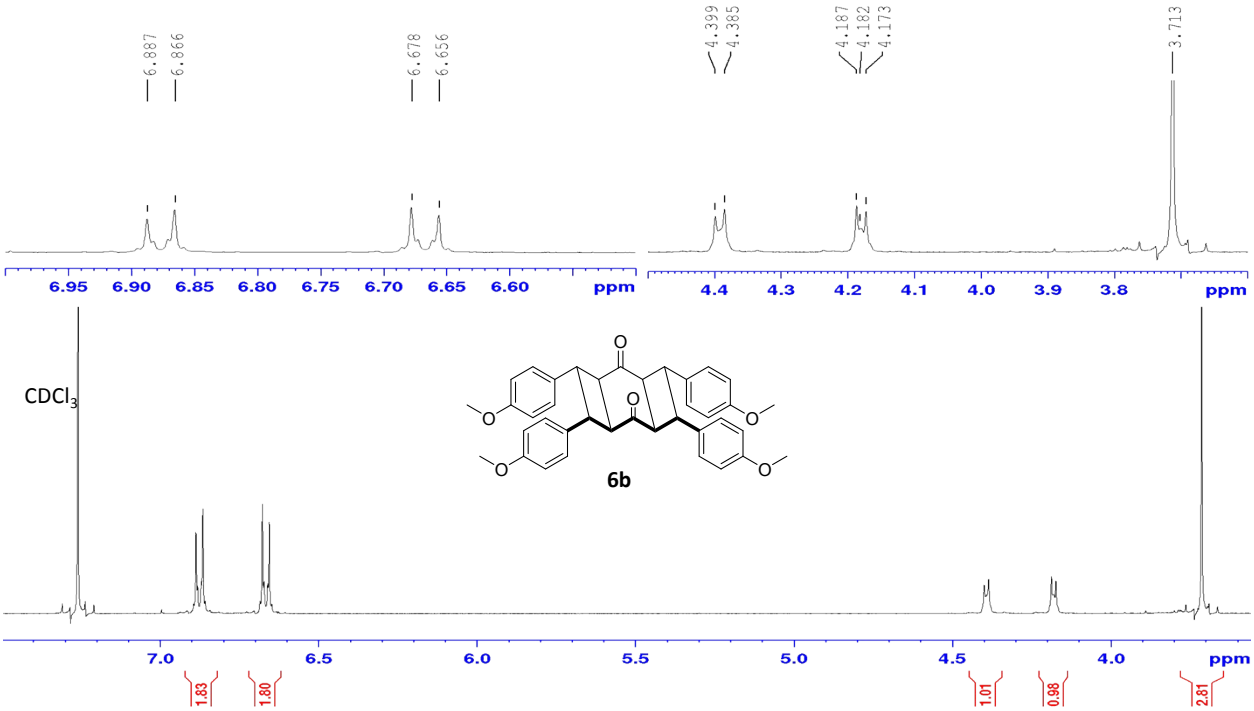


Figure S4 ^{1}H NMR spectrum of **6b**

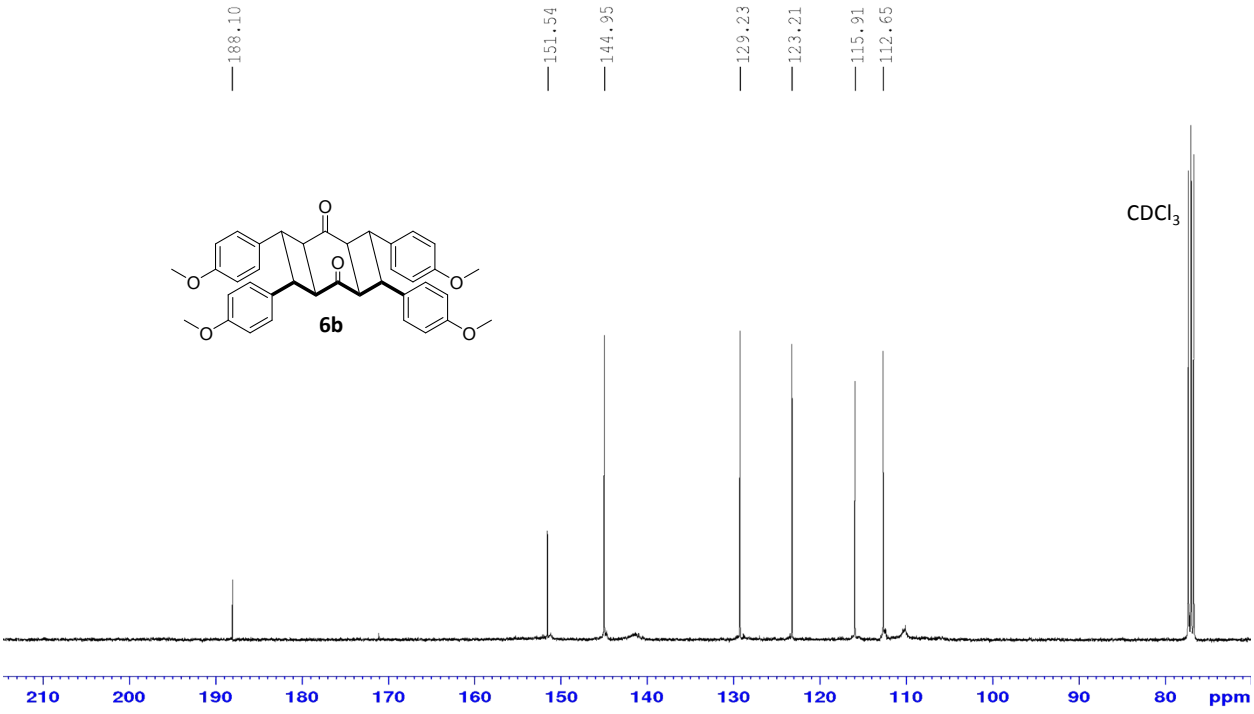


Figure S5 ^{13}C NMR spectrum of **6b**

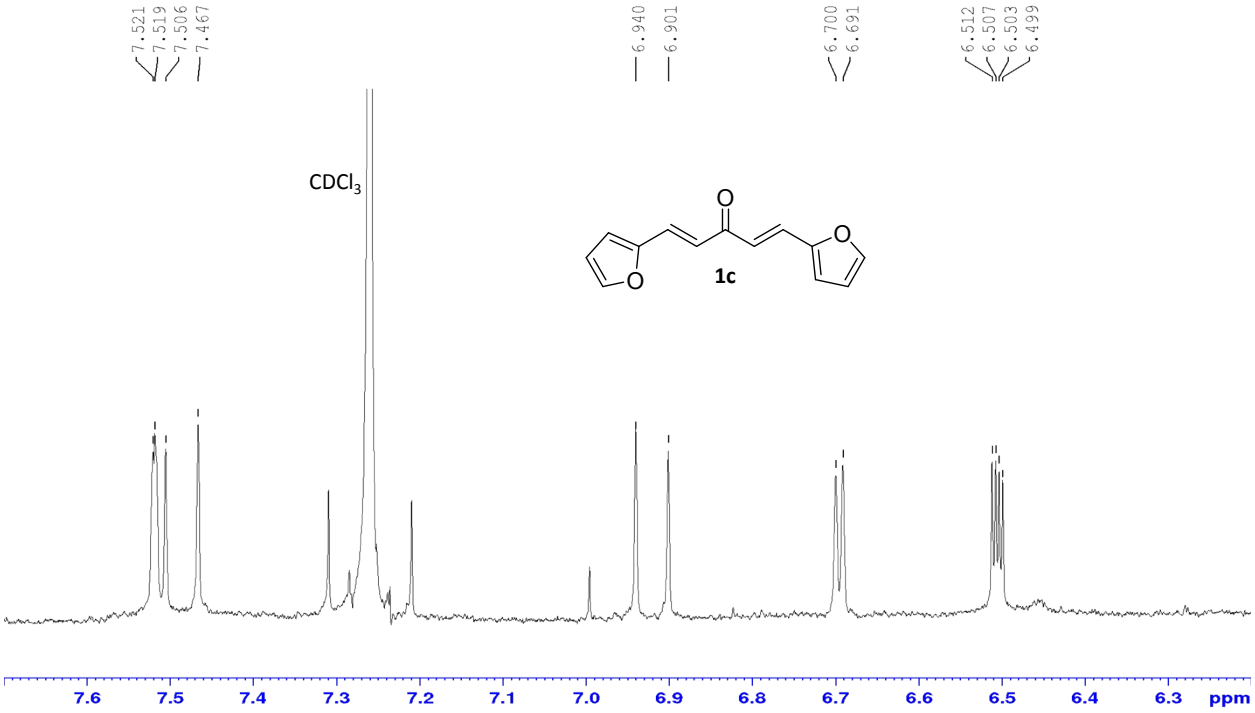


Figure S6 ^{1}H NMR spectrum of **1c**

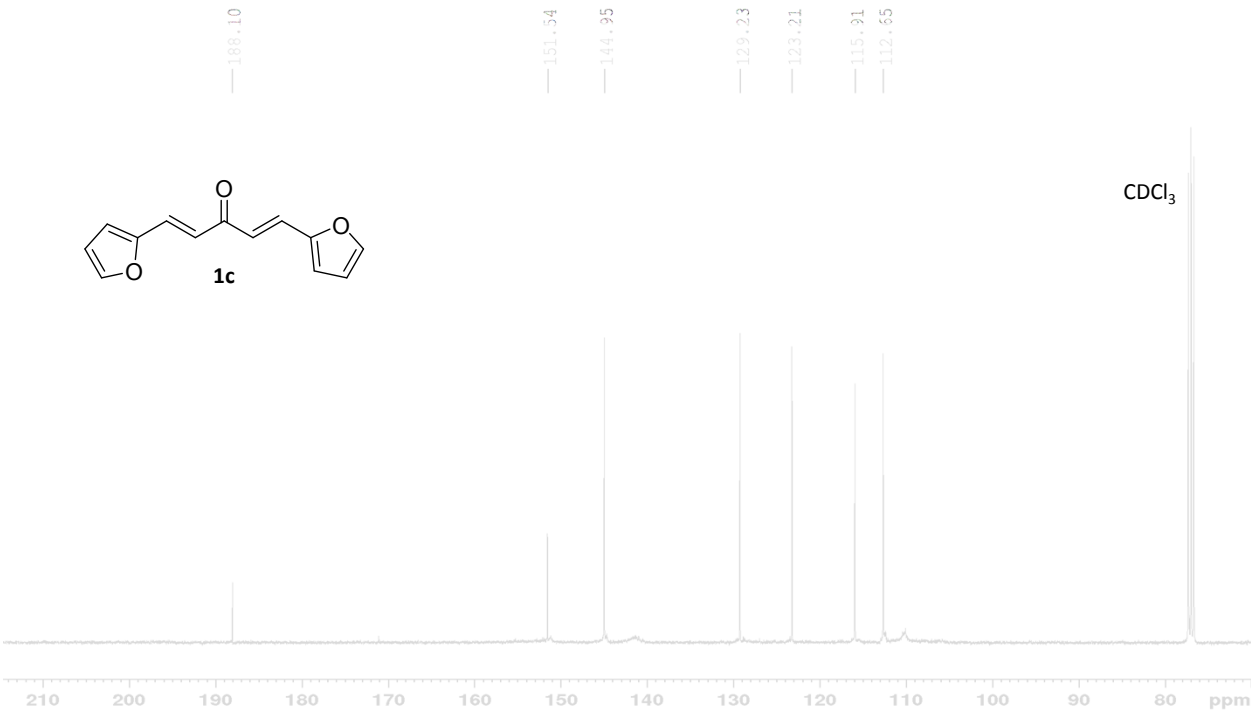


Figure S7 ^{13}C NMR spectrum of **1c**

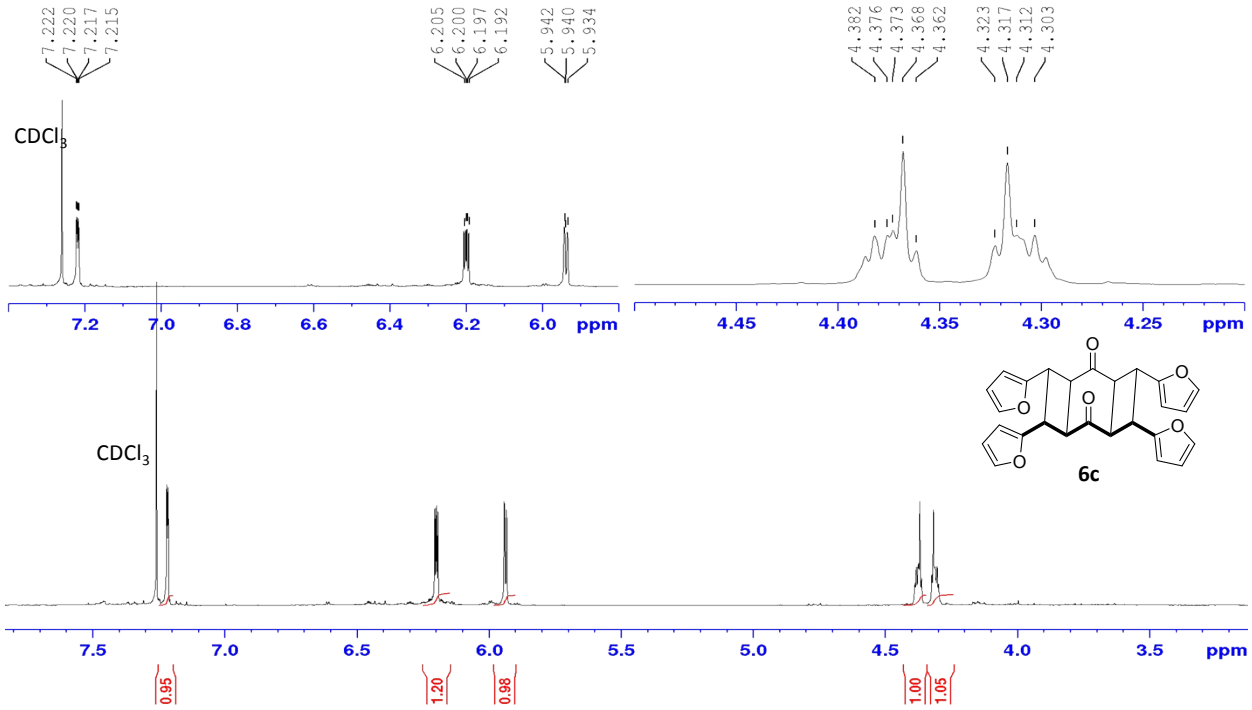


Figure S8 ^{1}H NMR spectrum of **6c**

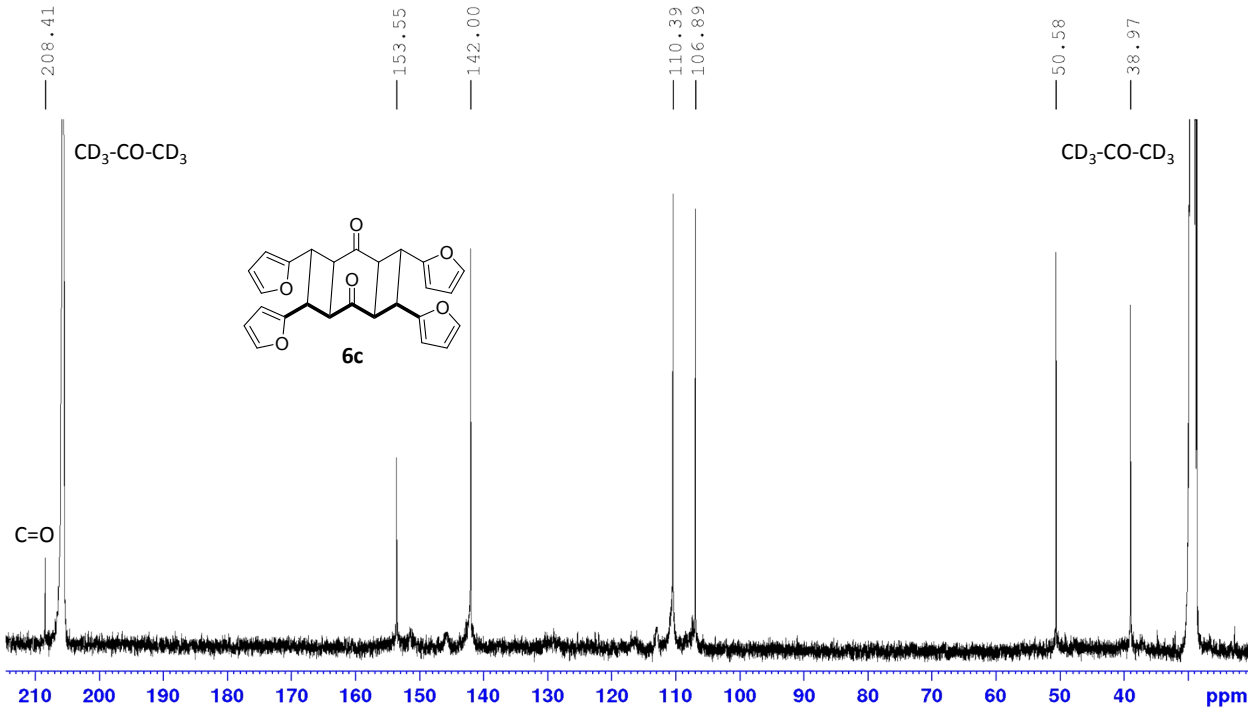


Figure S9 ^{13}C NMR spectrum of **6c**

6. Time-dependence experiment

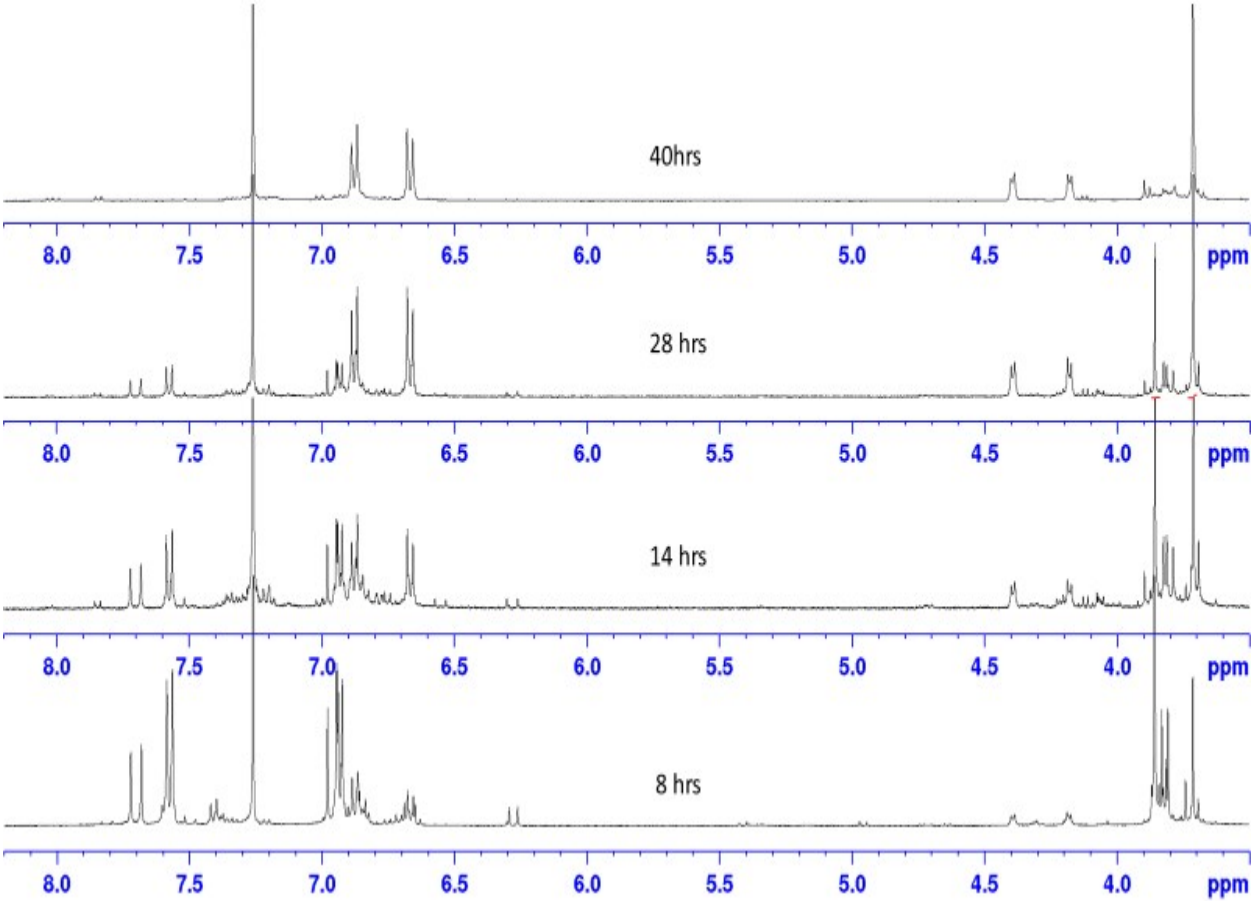


Figure S10 Time-dependent reaction of **1b**. NMR spectrum of reaction mixture of 1:2 complex irradiated for different durations as listed in the spectra.

7. NOESY spectra

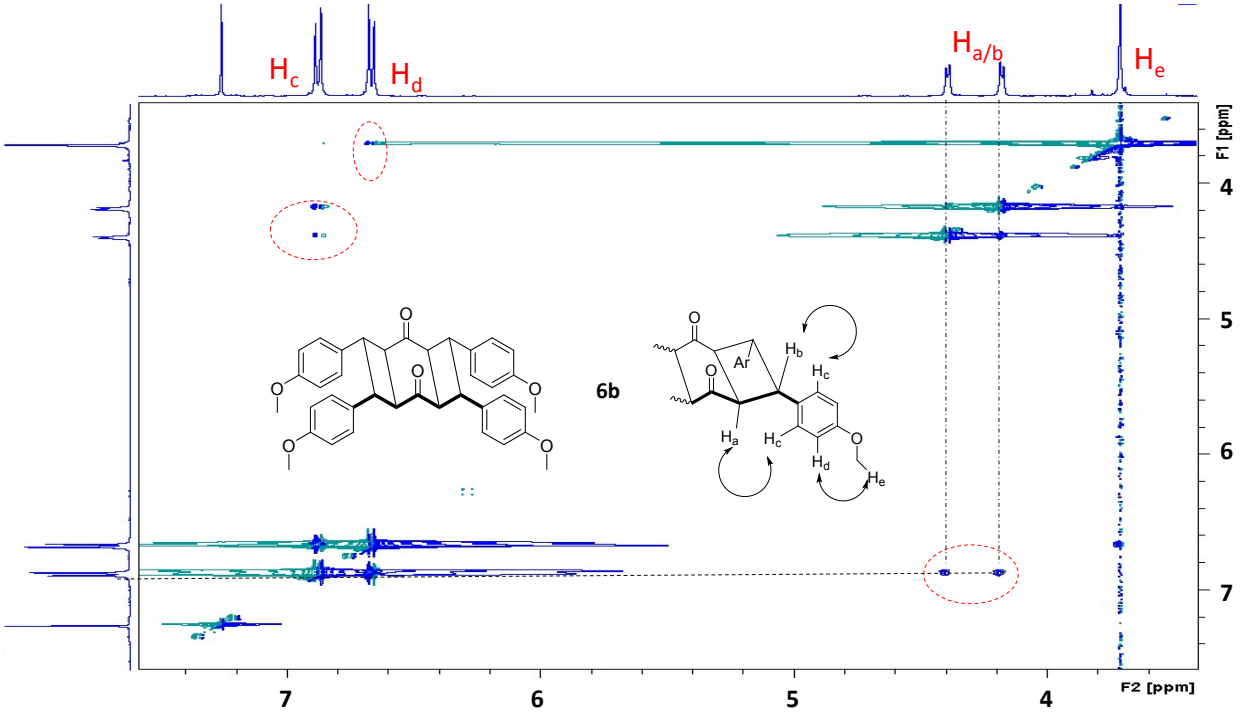


Figure S11 NOESY NMR spectrum of **6b**

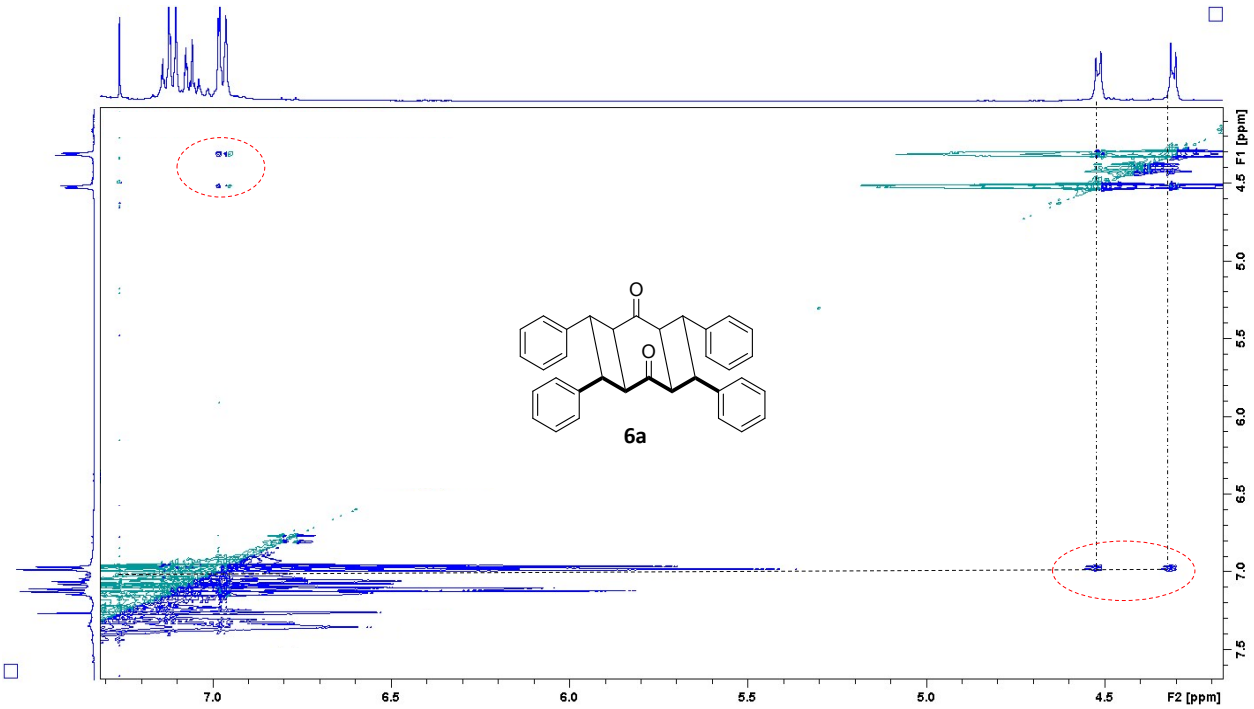


Figure S12 NOESY NMR spectrum of **6a**

8. Solution phase and irradiation of β-CD complex for compound 1b

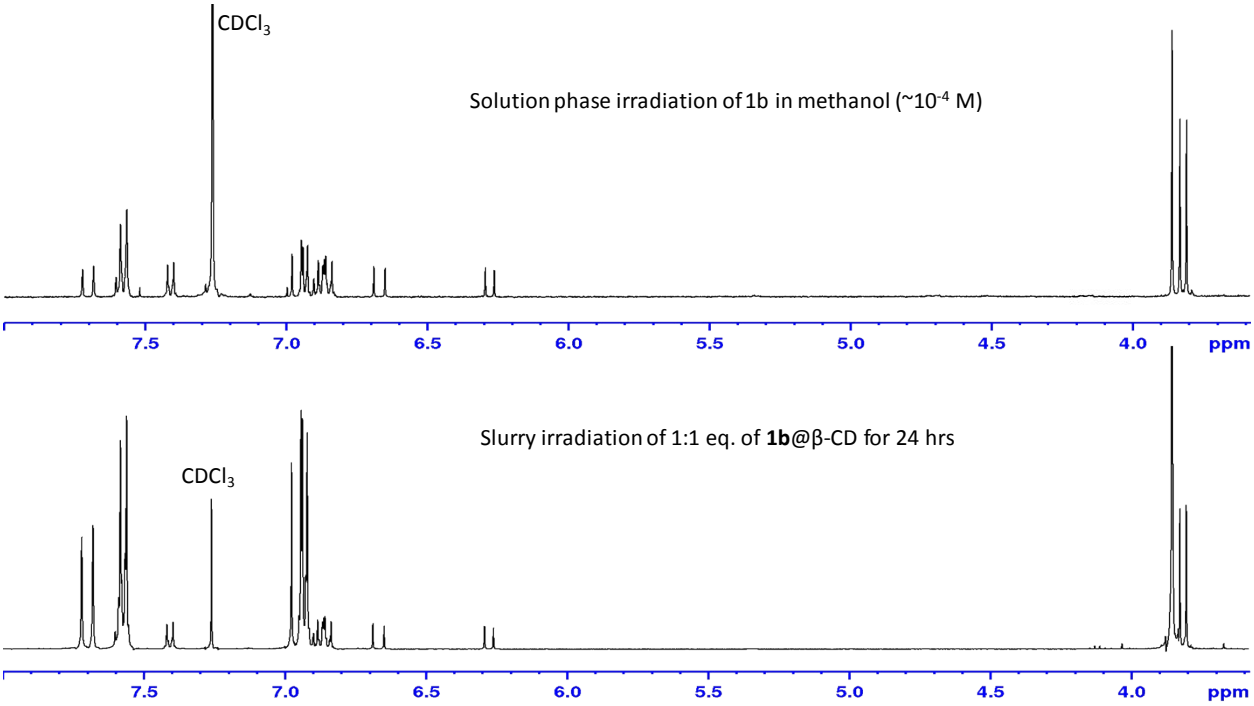


Figure S13 Product mixture obtained from irradiation of **1b** in methanol (~10-4 M, top NMR), and as a 1:1 complex with β-CD in slurry form.

9. Photoreactivity of 1d@γ-CD

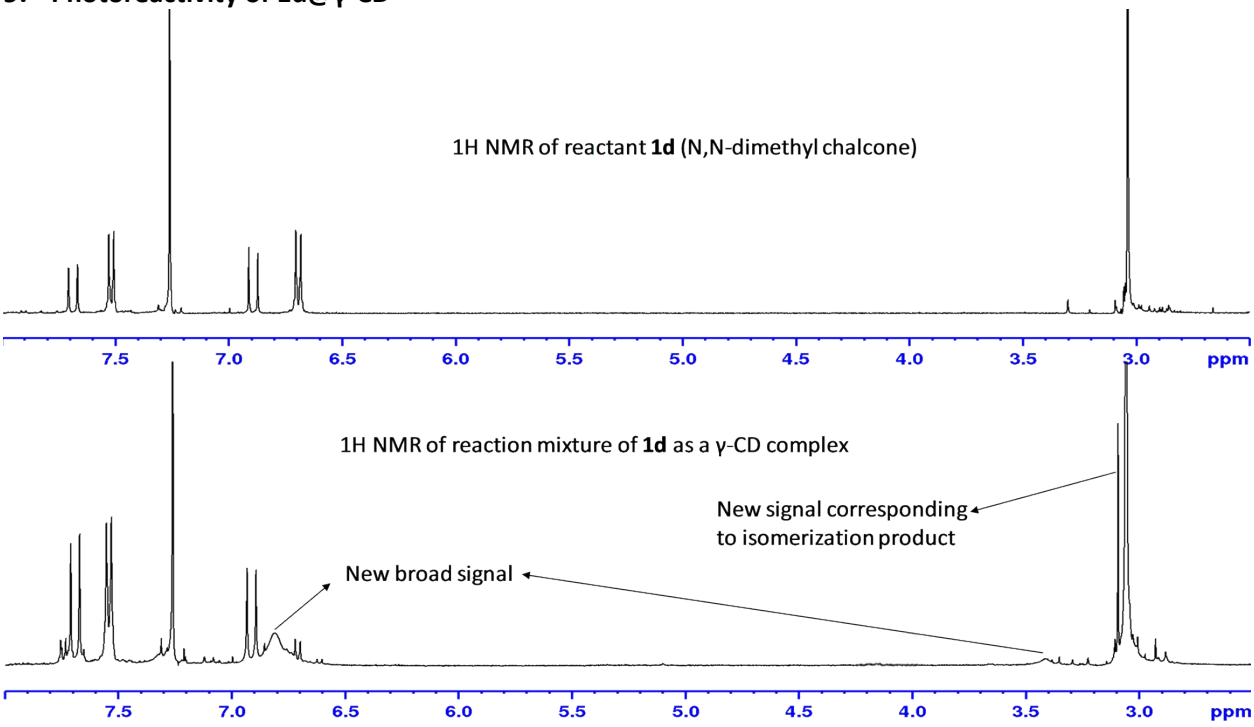


Figure S14 Product mixture obtained after irradiation of **1d**@γ-CD after 36 hrs. Appearance of new signals in the NMR spectrum suggests photoactivity. Lack of dimers suggests supramolecular influence.

10. X-Ray crystallography

Data Collection

A Leica MZ 75 microscope was used to identify a suitable colorless plate with very well defined faces with dimensions (max, intermediate, and min) 0.243 x 0.186 x 0.016 mm^3 from a representative sample of crystals of the same habit. The crystal mounted on a nylon loop was then placed in a cold nitrogen stream (Oxford) maintained at 100 K.

A BRUKER Venture X-ray (kappa geometry) diffractometer was employed for crystal screening, unit cell determination, and data collection. The goniometer was controlled using the APEX3 software suite.[1] The sample was optically centered with the aid of a video camera such that no translations were observed as the crystal was rotated through all positions. The X-ray radiation employed was generated from a Cu-Iμs X-ray tube (K_α = 1.5418Å with a potential of 50 kV and a current of 1.0mA). 45 data frames were taken at widths of 1°. These reflections were used to determine the unit cell. The unit cell was verified by examination of the *h k l* overlays on several frames of data. No super-cell or erroneous reflections were observed. After careful examination of the unit cell, an extended data collection procedure (26 sets) was initiated using omega and phi scans.

Data Reduction, Structure Solution, and Refinement

Integrated intensity information for each reflection was obtained by reduction of the data frames with the program APEX3.[1] The integration method employed a three-dimensional profiling algorithm and all data were corrected for Lorentz and polarization factors, as well as for crystal decay effects. Finally the data was merged and scaled to produce a suitable data set. The absorption correction program SADABS[2] was employed to correct the data for absorption effects.

Systematic reflection conditions and statistical tests of the data suggested the space group *P*-1. A solution was obtained readily using XT/XS in APEX3.[1,3] Hydrogen atoms were placed in idealized positions and were set riding on the respective parent atoms. All non-hydrogen atoms were refined with anisotropic thermal parameters. Absence of additional symmetry or void were confirmed using PLATON (ADDSYM).[#] The structure was refined (weighted least squares refinement on F^2) to convergence.[3,4]

Olex2 was employed for the final data presentation and structure plots.[4]

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[1] APEX3 "Program for Data Collection on Area Detectors" BRUKER AXS Inc., 5465 East Cheryl Parkway, Madison, WI 53711-5373 USA

[2] SADABS, Sheldrick, G.M. "Program for Absorption Correction of Area Detector Frames", BRUKER AXS Inc., 5465 East Cheryl Parkway, Madison, WI 53711-5373 USA.

[3] Sheldrick, G.M. (2008). Acta Cryst. A64, 112-122. Sheldrick, G. M. (2015), Acta Cryst. A71, 3-8. Sheldrick, G. M. (2015). Acta Cryst. C71, 3-8. XT, XS, BRUKER AXS Inc., 5465 East Cheryl Parkway, Madison, WI 53711-5373 USA.

[4] Dolomanov, O. V, Bourhis, L. J., Gildea, R. J., Howard, J. A. K., and Puschmann, H. "OLEX2: A Complete Structure Solution, Refinement and Analysis Program", *J. Appl. Cryst.* **2009**, *42*, 339-341.

[#] Spek, A. L., "PLATON - A Multipurpose Crystallographic Tool" *J. Appl. Cryst.* **2003**, *36,* 7-13.; Spek, A. L., Utrecht University, Utrecht, The Netherlands **2008**.

[*] Sheldrick, G. M. "Cell_Now (version **2008**/1): *Program for Obtaining Unit Cell Constants from Single Crystal Data":* University of Göttingen, Germany

§ Spek, A. L. (2015) Acta Cryst. C71, 9-18.

11. Job's continuous variation method

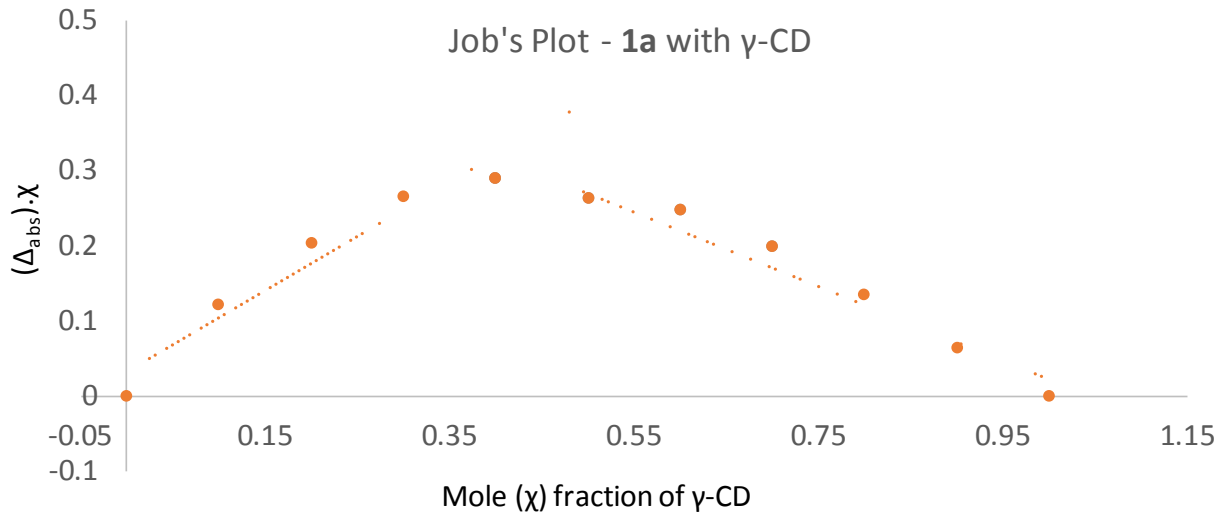

Figure S15 Job's plot for **1a** (dibenzalacetone) with γ-CD

Figure S16 Job's plot for **1d** (N,N-dimethyl chalcone) with γ-CD

12. Computational chemistry

Computational chemistry calculations were performed using Gaussian '09. Windows 10 desktop with eight dual core processors and 16 GB RAM were used for the purposes. Calculations were performed at different levels of theory to obtain complex structures for gaining insight into relative dimensions and arrangement of the components. Theory performed at molecular mechanics (MM, UFF) and semi empirical (SE PM6) using solvent effects based on IPCM were first obtained. However, the geometry-optimized structures showed the reactant chalcones in which the aromatic rings were orthogonal to the pentadienone skeleton. This was realized to be an unrealistic due to the common knowledge that the molecule is fully conjugated and should remain planar. Hence *ab initio* calculations were performed using ONIOM wB97XD/631++G(2d,2p)/Auto:PM6.

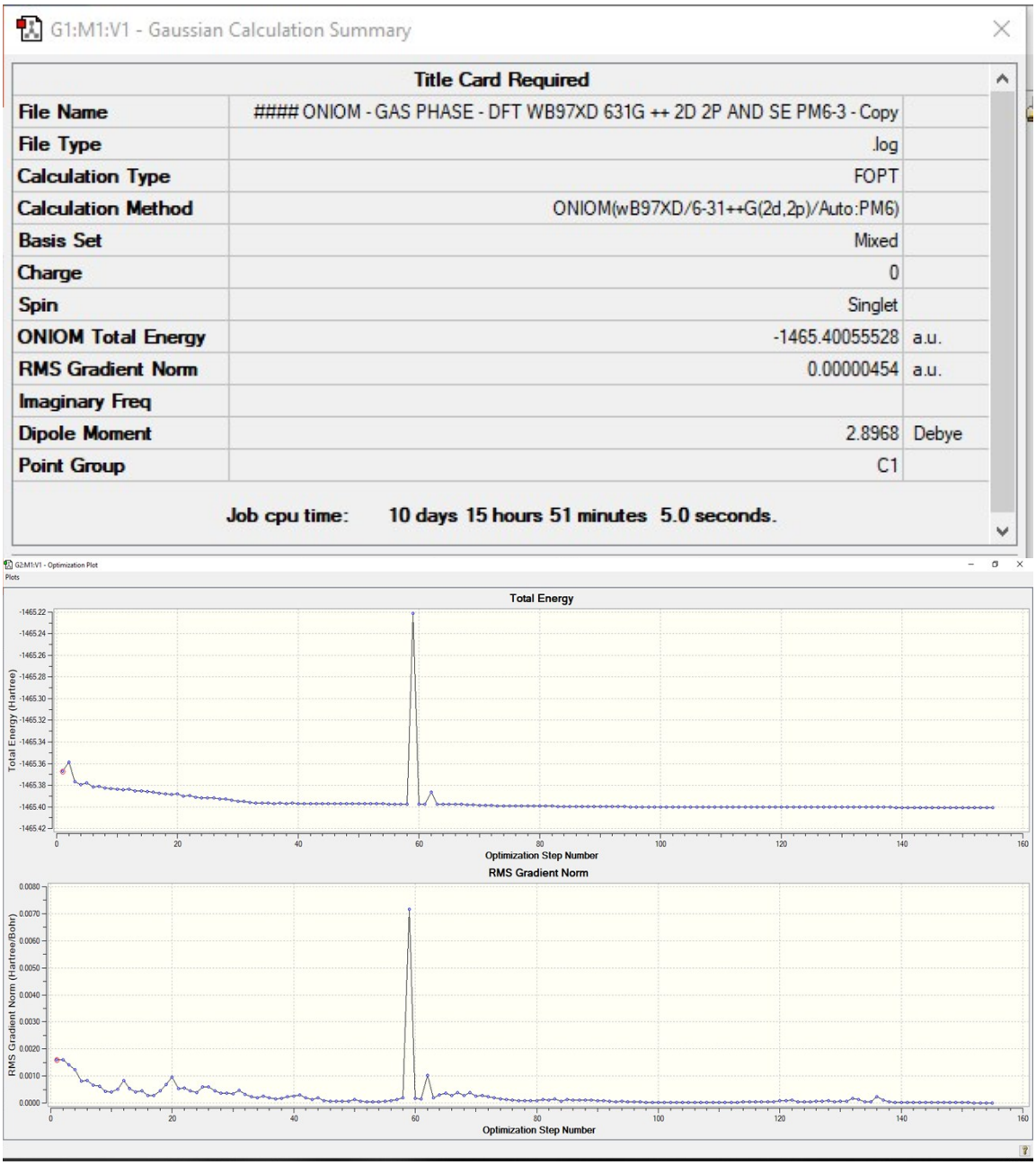

Figure S17. Output screen from calculation performed on **1a**$_2$@γ-Cd

Coordinates of final structure obtained after geometry optimization (.pdb file format)

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HETATM    1  C           0      -2.272   5.956   1.448
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H
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HETATM    4  H           0      -3.951   5.988   2.878
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HETATM  118  O           0       1.415  -4.962  -0.021
O
HETATM  119  O           0      -1.827  -6.518  -0.807
O
HETATM  120  O           0      -7.620  -3.279  -0.049
O
HETATM  121  H           0      -7.322  -2.497   0.509
H
HETATM  122  O           0      -5.811  -5.615   0.293
O
HETATM  123  H           0      -6.665  -5.552   0.784
H
HETATM  124  O           0      -2.749  -4.800   2.319
O
HETATM  125  H           0      -3.040  -4.014   1.787
H
HETATM  126  O           0       0.208  -4.972   2.534
O
HETATM  127  H           0       0.447  -5.876   2.851
H
HETATM  128  O           0      -6.616   2.022   2.179
O
HETATM  129  H           0      -5.627   2.188   2.382
H
HETATM  130  O           0      -7.154  -0.740   1.348
O
HETATM  131  H           0      -7.316  -0.428   2.272
H
HETATM  132  O           0      -4.545   3.356   3.039
O
HETATM  133  H           0      -5.137   4.020   3.462
H
HETATM  134  O           0      -2.353   5.161   3.726
O
```

```
HETATM  135  H           0      -1.552   4.563   3.560
H
HETATM  136  O           0       0.362   4.457   3.671
O
HETATM  137  H           0       0.594   5.243   4.212
H
HETATM  138  O           0       3.056   3.464   2.463
O
HETATM  139  H           0       2.840   2.911   1.656
H
HETATM  140  O           0       5.909   5.520   0.836
O
HETATM  141  H           0       6.751   5.444   1.348
H
HETATM  142  O           0       7.889   3.402   0.166
O
HETATM  143  H           0       7.697   2.468   0.497
H
HETATM  144  O           0       7.989   0.507   0.836
O
HETATM  145  H           0       8.177   0.077   1.704
H
HETATM  146  O           0       7.482  -2.414   1.155
O
HETATM  147  H           0       6.516  -2.654   1.376
H
HETATM  148  O           0       5.490  -4.099   1.645
O
HETATM  149  H           0       6.076  -4.880   1.540
H
HETATM  150  O           0       2.786  -5.389   2.086
O
HETATM  151  H           0       2.076  -4.668   2.026
H
HETATM  152  O           0      -3.102  -5.412  -3.451
O
HETATM  153  H           0      -2.600  -5.795  -2.686
H
HETATM  154  O           0      -7.139   0.094  -3.433
O
HETATM  155  H           0      -7.762   0.844  -3.291
H
HETATM  156  O           0      -5.505   4.732  -1.814
O
HETATM  157  H           0      -5.325   3.830  -2.193
H
HETATM  158  O           0      -0.029   8.307   0.560
O
HETATM  159  H           0       0.842   8.657   0.859
H
HETATM  160  O           0       1.807   3.933  -2.277
O
```

```
HETATM  161  H           0       1.814   4.310  -1.341
H
HETATM  162  O           0       5.333   3.164  -2.476
O
HETATM  163  O           0       0.594  -7.979  -1.496
O
HETATM  164  H           0      -0.171  -8.544  -1.240
H
HETATM  165  O           0       5.370  -3.931  -3.476
O
HETATM  166  H           0       5.748  -3.017  -3.344
H
HETATM  167  O           0       7.483   0.643  -3.998
O
HETATM  168  H           0       8.101  -0.122  -4.061
H
HETATM  169  C           0       2.511  -1.827   5.392
C
HETATM  170  C           0       1.615  -2.295   4.423
C
HETATM  171  C           0       0.511  -3.051   4.836
C
HETATM  172  C           0       0.303  -3.315   6.182
C
HETATM  173  C           0       1.191  -2.829   7.138
C
HETATM  174  C           0       2.296  -2.083   6.740
C
HETATM  175  H           0       3.379  -1.257   5.081
H
HETATM  176  H           0      -0.171  -3.462   4.095
H
HETATM  177  H           0      -0.554  -3.904   6.486
H
HETATM  178  H           0       1.027  -3.038   8.189
H
HETATM  179  H           0       2.997  -1.711   7.478
H
HETATM  180  C           0       1.875  -1.998   3.012
C
HETATM  181  H           0       2.900  -1.746   2.750
H
HETATM  182  C           0       0.967  -1.981   2.025
C
HETATM  183  H           0      -0.084  -2.154   2.236
H
HETATM  184  C           0       1.360  -1.691   0.632
C
HETATM  185  C           0       0.266  -1.461  -0.349
C
HETATM  186  H           0      -0.755  -1.597  -0.005
H
```

```
HETATM  187  C           0       0.557  -1.058  -1.592
C
HETATM  188  H           0       1.612  -0.911  -1.807
H
HETATM  189  C           0      -0.366  -0.773  -2.692
C
HETATM  190  C           0       0.154  -0.258  -3.884
C
HETATM  191  C           0      -1.747  -0.989  -2.611
C
HETATM  192  C           0      -0.674   0.033  -4.963
C
HETATM  193  H           0       1.220  -0.076  -3.961
H
HETATM  194  C           0      -2.573  -0.711  -3.689
C
HETATM  195  H           0      -2.185  -1.388  -1.699
H
HETATM  196  C           0      -2.041  -0.196  -4.870
C
HETATM  197  H           0      -0.253   0.447  -5.872
H
HETATM  198  H           0      -3.644  -0.900  -3.608
H
HETATM  199  H           0      -2.691   0.034  -5.706
H
HETATM  200  O           0       2.535  -1.651   0.291
O
HETATM  201  C           0      -2.786   3.571  -5.309
C
HETATM  202  C           0      -1.419   3.771  -5.145
C
HETATM  203  C           0      -0.804   3.413  -3.951
C
HETATM  204  C           0      -1.540   2.850  -2.903
C
HETATM  205  C           0      -2.916   2.665  -3.079
C
HETATM  206  C           0      -3.532   3.021  -4.269
C
HETATM  207  H           0      -3.269   3.846  -6.239
H
HETATM  208  H           0      -0.832   4.205  -5.946
H
HETATM  209  H           0       0.265   3.570  -3.814
H
HETATM  210  H           0      -3.507   2.230  -2.279
H
HETATM  211  H           0      -4.599   2.858  -4.394
H
HETATM  212  C           0      -0.834   2.474  -1.677
C
```

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HETATM  213  H           0       0.246   2.634  -1.680
H
HETATM  214  C           0      -1.360   1.955  -0.561
C
HETATM  215  H           0      -2.423   1.745  -0.467
H
HETATM  216  C           0      -0.510   1.656   0.611
C
HETATM  217  C           0      -1.187   1.009   1.751
C
HETATM  218  H           0      -2.229   0.731   1.622
H
HETATM  219  C           0      -0.551   0.804   2.915
C
HETATM  220  H           0       0.477   1.154   2.984
H
HETATM  221  C           0      -1.111   0.186   4.117
C
HETATM  222  C           0      -0.464   0.387   5.342
C
HETATM  223  C           0      -2.274  -0.595   4.095
C
HETATM  224  C           0      -0.985  -0.139   6.517
C
HETATM  225  H           0       0.451   0.969   5.369
H
HETATM  226  C           0      -2.789  -1.130   5.267
C
HETATM  227  H           0      -2.774  -0.793   3.154
H
HETATM  228  C           0      -2.151  -0.895   6.483
C
HETATM  229  H           0      -0.474   0.030   7.456
H
HETATM  230  H           0      -3.687  -1.737   5.233
H
HETATM  231  H           0      -2.555  -1.315   7.397
H
HETATM  232  O           0       0.679   1.949   0.644
O
END
CONECT    1    2    3   15   29
CONECT    2    1
CONECT    3    1    4    5  134
CONECT    4    3
CONECT    5    3    6    7  132
CONECT    6    5
CONECT    7    5    8    9   14
CONECT    8    7
CONECT    9    7   10   11   15
CONECT   10    9
CONECT   11    9   12   13  156
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CONECT   12   11
CONECT   13   11
CONECT   14    7   75
CONECT   15    1    9
CONECT   16   17   18   30   44
CONECT   17   16
CONECT   18   16   19   20  138
CONECT   19   18
CONECT   20   18   21   22  136
CONECT   21   20
CONECT   22   20   23   24   29
CONECT   23   22
CONECT   24   22   25   26   30
CONECT   25   24
CONECT   26   24   27   28  158
CONECT   27   26
CONECT   28   26
CONECT   29    1   22
CONECT   30   16   24
CONECT   31   32   33   58  162
CONECT   32   31
CONECT   33   31   34   35  142
CONECT   34   33
CONECT   35   33   36   37  140
CONECT   36   35
CONECT   37   35   38   39   44
CONECT   38   37
CONECT   39   37   40   41  162
CONECT   40   39
CONECT   41   39   42   43  160
CONECT   42   41
CONECT   43   41
CONECT   44   16   37
CONECT   45   46   47   59  103
CONECT   46   45
CONECT   47   45   48   49  146
CONECT   48   47
CONECT   49   47   50   51  144
CONECT   50   49
CONECT   51   49   52   53   58
CONECT   52   51
CONECT   53   51   54   55   59
CONECT   54   53
CONECT   55   53   56   57  167
CONECT   56   55
CONECT   57   55
CONECT   58   31   51
CONECT   59   45   53
CONECT   60   61   62   74   88
CONECT   61   60
CONECT   62   60   63   64  120
CONECT   63   62
```

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CONECT   64   62   65   66  122
CONECT   65   64
CONECT   66   64   67   68   73
CONECT   67   66
CONECT   68   66   69   70   74
CONECT   69   68
CONECT   70   68   71   72  152
CONECT   71   70
CONECT   72   70
CONECT   73   66  105
CONECT   74   60   68
CONECT   75   14   76   77   89
CONECT   76   75
CONECT   77   75   78   79  128
CONECT   78   77
CONECT   79   77   80   81  130
CONECT   80   79
CONECT   81   79   82   83   88
CONECT   82   81
CONECT   83   81   84   85   89
CONECT   84   83
CONECT   85   83   86   87  154
CONECT   86   85
CONECT   87   85
CONECT   88   60   81
CONECT   89   75   83
CONECT   90   91   92  104  118
CONECT   91   90
CONECT   92   90   93   94  150
CONECT   93   92
CONECT   94   92   95   96  148
CONECT   95   94
CONECT   96   94   97   98  103
CONECT   97   96
CONECT   98   96   99  100  104
CONECT   99   98
CONECT  100   98  101  102  165
CONECT  101  100
CONECT  102  100
CONECT  103   45   96
CONECT  104   90   98
CONECT  105   73  106  107  119
CONECT  106  105
CONECT  107  105  108  109  124
CONECT  108  107
CONECT  109  107  110  111  126
CONECT  110  109
CONECT  111  109  112  113  118
CONECT  112  111
CONECT  113  111  114  115  119
CONECT  114  113
CONECT  115  113  116  117  163
```

```
CONECT  116  115
CONECT  117  115
CONECT  118   90  111
CONECT  119  105  113
CONECT  120   62  121
CONECT  121  120
CONECT  122   64  123
CONECT  123  122
CONECT  124  107  125
CONECT  125  124
CONECT  126  109  127
CONECT  127  126
CONECT  128   77  129
CONECT  129  128
CONECT  130   79  131
CONECT  131  130
CONECT  132    5  133
CONECT  133  132
CONECT  134    3  135
CONECT  135  134
CONECT  136   20  137
CONECT  137  136
CONECT  138   18  139
CONECT  139  138
CONECT  140   35  141
CONECT  141  140
CONECT  142   33  143
CONECT  143  142
CONECT  144   49  145
CONECT  145  144
CONECT  146   47  147
CONECT  147  146
CONECT  148   94  149
CONECT  149  148
CONECT  150   92  151
CONECT  151  150
CONECT  152   70  153
CONECT  153  152
CONECT  154   85  155
CONECT  155  154
CONECT  156   11  157
CONECT  157  156
CONECT  158   26  159
CONECT  159  158
CONECT  160   41  161
CONECT  161  160
CONECT  162   31   39
CONECT  163  115  164
CONECT  164  163
CONECT  165  100  166
CONECT  166  165
CONECT  167   55  168
```

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CONECT  168  167
CONECT  169  170  174  175
CONECT  170  169  171  180
CONECT  171  170  172  176
CONECT  172  171  173  177
CONECT  173  172  174  178
CONECT  174  169  173  179
CONECT  175  169
CONECT  176  171
CONECT  177  172
CONECT  178  173
CONECT  179  174
CONECT  180  170  181  182
CONECT  181  180
CONECT  182  180  183  184
CONECT  183  182
CONECT  184  182  185  200
CONECT  185  184  186  187
CONECT  186  185
CONECT  187  185  188  189
CONECT  188  187
CONECT  189  187  190  191
CONECT  190  189  192  193
CONECT  191  189  194  195
CONECT  192  190  196  197
CONECT  193  190
CONECT  194  191  196  198
CONECT  195  191
CONECT  196  192  194  199
CONECT  197  192
CONECT  198  194
CONECT  199  196
CONECT  200  184
CONECT  201  202  206  207
CONECT  202  201  203  208
CONECT  203  202  204  209
CONECT  204  203  205  212
CONECT  205  204  206  210
CONECT  206  201  205  211
CONECT  207  201
CONECT  208  202
CONECT  209  203
CONECT  210  205
CONECT  211  206
CONECT  212  204  213  214
CONECT  213  212
CONECT  214  212  215  216
CONECT  215  214
CONECT  216  214  217  232
CONECT  217  216  218  219
CONECT  218  217
CONECT  219  217  220  221
```

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CONECT  220  219
CONECT  221  219  222  223
CONECT  222  221  224  225
CONECT  223  221  226  227
CONECT  224  222  228  229
CONECT  225  222
CONECT  226  223  228  230
CONECT  227  223
CONECT  228  224  226  231
CONECT  229  224
CONECT  230  226
CONECT  231  228
CONECT  232  216
```

Frequency calculation of optimized structure showed that there were no negative frequencies

13. **Isothermal titration calorimetry**

Isothermal titration experiments were performed on a TA nano ITC instrument with titration cell and reference cell volumes of 1000 µL, and a 100 µL syringe used to inject the titrant. Stock solutions (10^{-2}M) of γ-cyclodextrin in water and 4-methoxy chalcone **1b** in methanol were prepared, which were further diluted with water. The host concentration was diluted to 5 x 10^{-4} M, and that of guest was diluted to 5 x 10^{-5} M. The solutions were degassed for 15 mins before titration ITC experiments were performed with the cell temperature set to be maintained at 25.0 °C with each injection volume set at 4.81 µL for nineteen injections. The stirring rate during injection rate was set at 350 rpm. Blank heat from titration of 5 x 10^{-4} M host was subtracted from the host-guest complex titration before isotherm fitting algorithm. The independent binding model available in nanoAnalyze software issued along with the VP nano ITC instrument package was used to use for curve fitting.

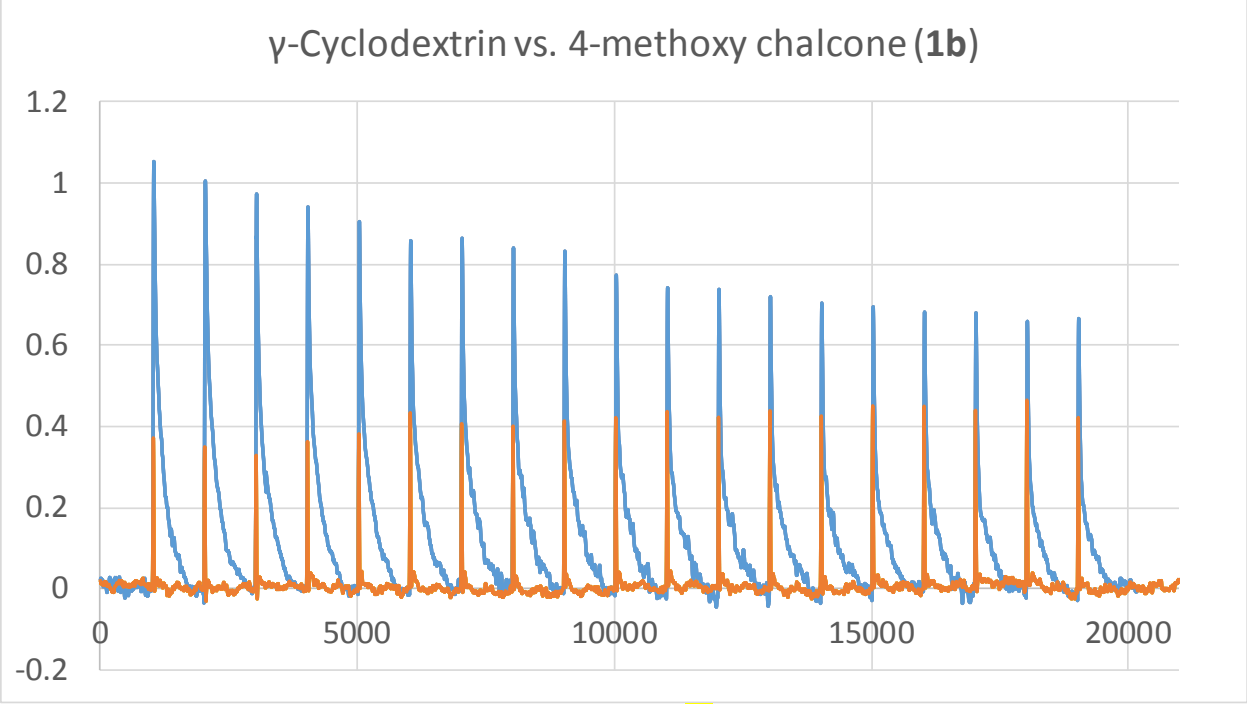

Figure S18 ITC data for titration of 5 x 10^{-4} M γ-CD to 5 x 10^{-5} M **1b** (blue), and the background titration of 5 x 10^{-4} M γ-CD to water (orange).