

## Supplementary Information

### Caveat in stereochemical outcome of organocatalytic Diels-Alder reaction in PEG-400

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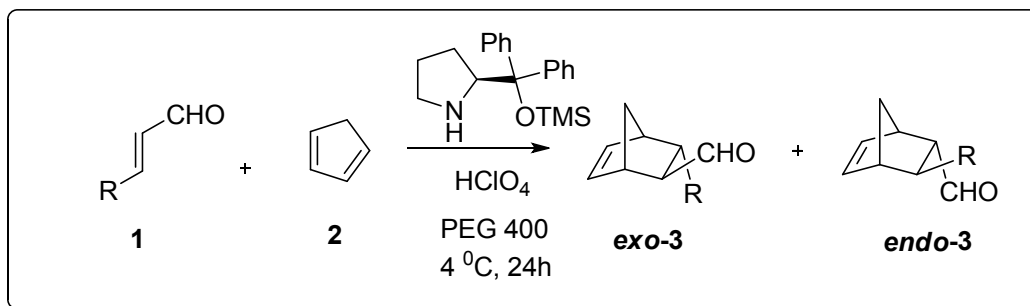
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## 1. General details

**General information:** Unless otherwise noted, all reagents and solvents were purchased from commercial suppliers and used without purification. Catalysts were obtained from Sigma-Aldrich and used without further purification. Reactions were monitored by using thin-layer chromatography (SiO<sub>2</sub>). TLC plates were visualized with UV light (254 nm), iodine treatment or using Phosphomolibdic acid stain. Column chromatography was carried out using silica gel (100-200 mesh) packed in glass columns. NMR spectra were recorded at 300, 400, 500, 600 MHz (H) and at 75, 101, 126, 151 MHz (C), respectively. Chemical shifts ( $\delta$ ) are reported in ppm, using the residual solvent peak in CDCl<sub>3</sub> (H:  $\delta$  = 7.26 and C:  $\delta$  = 77.0 ppm) as internal standard, and coupling constants ( $J$ ) are given in Hz. DSC data were recorded in DSC Q200 V24.4 Build 116. HPLC Data were recorded using OJ-H Column (250mm X 4.6mm, 5u) at 210nm by converting aldehyde into their corresponding alcohol.

## 2. Experimental procedures and analytical data

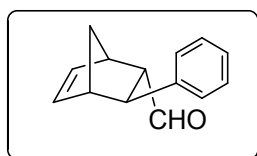
### a. General procedure for Diels-Alder reaction:



To a solution of (*S*)-2-(diphenyl((trimethylsilyl)oxy)methyl)pyrrolidine (5 mol%) in PEG-400 (1M) was added HClO<sub>4</sub> (20 mol%) followed by the addition of  $\alpha,\beta$  unsaturated aldehyde (0.5 mmol). The reaction mixture was allowed to stir for 5 min. To this freshly distilled cyclopentadiene (1.5 mmol) was slowly added and the resulting solution was stirred at 4 °C for 24h. The reaction mixture was extracted twice with ether and the combined organic extracts were washed successively with water and brine then dried over Na<sub>2</sub>SO<sub>4</sub>. The ether layer was

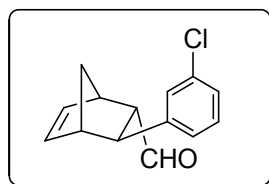
concentrated under vacuum and purified by Silica gel column chromatography (5% EA in Hexane). Ratio of *endo* and *exo* isomers were determined by  $^1\text{H-NMR}$ .

***Endo* and *exo* isomers of 3-phenylbicyclo[2.2.1]hept-5-ene-2-carbaldehyde (Table 4, entry 1).**



Prepared according to the general procedure described above with trans-cinnamaldehyde (100 mg, 0.75 mmol), cyclopentadiene (150 mg, 2.27 mmol) to afford the desired compound as a 10:90 mixture of *exo* and *endo* isomers (colorless oil, 65%). ***endo isomer*** :  $^1\text{H NMR}$  (300 MHz,  $\text{CDCl}_3$ ) 9.60 (d,  $J=2.3$  Hz, 1H), 7.13-7.34 (m, 5H), 6.42 (dd,  $J=3.3, 5.8$  Hz, 1H), 6.17 (dd,  $J=2.8, 5.8$  Hz, 1H), 3.34 (brs, 1H), 3.14 (brs, 1H), 3.09 (d,  $J=4.4$  Hz, 1H), 2.97 (dd,  $J=2.3, 3.5, 4.9$  Hz, 1H), 1.81 (d,  $J=8.7$  Hz, 1H),  $\delta$  1.64-1.60 (m, 1H);  $^{13}\text{C NMR}$  (75 MHz,  $\text{CDCl}_3$ )  $\delta$  203.5, 143.5, 139.2, 133.8, 128.6, 127.3, 126.2, 60.8, 48.4, 47.1, 45.7, 45.1. ***exo isomer*** :  $^1\text{H NMR}$  (300 MHz,  $\text{CDCl}_3$ ) 9.93 (d,  $J=2.1$  Hz, 1H), 7.13-7.34 (m, 5H), 6.34 (dd,  $J=3.4, 5.5$  Hz, 1H), 6.08 (dd,  $J=3.0, 5.5$  Hz, 1H), 3.73 (t,  $J=3.8$  Hz, 1H), 3.23 (m, 2H), 2.60 (dd,  $J=1.5, 3.4$  Hz, 1H), 1.61-1.64 (m, 2H).  $^{13}\text{C NMR}$  (126 MHz,  $\text{CDCl}_3$ )  $\delta$  202.8, 142.7, 136.3, 136.1, 128.0, 127.7, 126.1, 59.2, 48.2, 47.3, 45.3, 45.2.

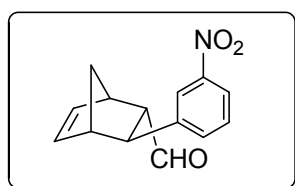
***Endo* and *exo* isomers of 3-(3-chlorophenyl)bicyclo[2.2.1]hept-5-ene-2-carbaldehyde (Table 4, entry 2).**



Prepared according to the general procedure described above from of (*E*)-3-chlorocinnamaldehyde (100 mg, 0.602 mmol) and cyclopentadiene (119 mg, 1.8 mmol) to afford the desired compound as a 12:88 mixture of *exo* and *endo* isomers (yellow oil, 62%). ***endo isomer*** :  $^1\text{H NMR}$  (500 MHz,  $\text{CDCl}_3$ )  $\delta$  9.53 (d,  $J=1.9$  Hz, 1H), 7.20 – 7.13 (m, 2H), 7.12 – 7.03 (m, 2H), 6.34 (dd,  $J=5.6, 3.3$  Hz, 1H), 6.10 (dd,  $J=5.6, 2.8$  Hz, 1H), 3.29 (brs, 1H), 3.04 (d,  $J=1.3$  Hz, 1H), 3.00 (d,  $J=4.6$  Hz, 1H), 2.87 (ddd,  $J=5.1, 3.5, 2.0$  Hz, 1H),

1.70 (d,  $J = 8.8$  Hz, 1H), 1.55-1.47(m, 1H);  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ )  $\delta$  203.8, 145.8, 139.1, 134.4, 133.9, 129.8, 127.4, 126.4, 125.7, 60.9, 48.2, 47.1, 45.3, 45.0. **exo isomer** :  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  9.83 (d,  $J = 1.8$  Hz, 1H), 7.20 – 7.13 (m, 2H), 7.12 – 7.03 (m, 2H), 6.29 (dd,  $J = 5.6, 3.2$  Hz, 1H), 5.99 (dd,  $J = 5.6, 2.8$  Hz, 1H), 3.68 – 3.63 (m, 1H), 3.15 (d,  $J = 19.0$  Hz, 2H), 2.48 (t,  $J = 6.4$  Hz, 1H), 1.50 (dd,  $J = 3.7, 1.6$  Hz, 2H);  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ )  $\delta$  202.1, 144.8, 136.6, 136.3, 134.3, 129.4, 128.0, 126.5, 126.2, 59.5, 48.4, 47.6, 45.5.

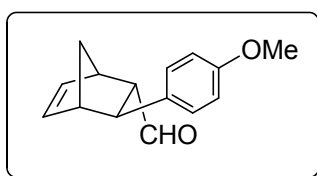
**Endo and exo isomers of 3-(3-nitrophenyl)bicyclo[2.2.1]hept-5-ene-2-carbaldehyde (Table 4, entry 3).**



Prepared according to the general procedure described above from of (*E*)-3-nitrocinnamaldehyde (100 mg, 0.564 mmol) and cyclopentadiene (112 mg, 1.69 mmol) to afford the desired compound as a 30:70 mixture of exo and endo isomers ( yellow oil, 56%).

**endo isomer** :  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ ) 9.64 (d,  $J = 1.6$  Hz, 1H), 8.10 – 7.88 (m, 2H), 7.38-7.30 (m, 2H), 6.43 (m, 1H), 6.20 (dd,  $J = 5.6, 2.7$  Hz, 1H), 3.43 (br, 1H), 3.32 – 3.14 (m, 2H), 2.96 – 2.89 (m, 1H), 1.79 – 1.69 (m, 1H), 1.69 – 1.58 (m, 1H);  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ )  $\delta$  202.2, 148.5, 145.9, 139.1, 134.2, 133.9, 129.5, 122.5, 121.4, 61.0, 48.2, 47.1, 45.3, 45.0. **exo isomer** :  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$  9.86 (d,  $J = 1.5$  Hz, 1H), 7.9 – 7.34 (m, 3H) 6.29 (dd,  $J = 5.6, 2.5$ , 1H), 5.99 (dd,  $J = 5.6, 2.8$  Hz, 1H), 3.81 (dd,  $J = 9.2, 4.6$  Hz, 1H), 3.24 – 3.04 (m, 2H), 2.57 (d,  $J = 4.7$  Hz, 1H), 1.74-1.63 (m, 2H).  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ )  $\delta$  201.5, 148.1, 144.8, 137.1, 135.9, 134.3, 129.0, 122.5, 121.5, 59.6, 48.4, 47.5, 45.5, 44.7.

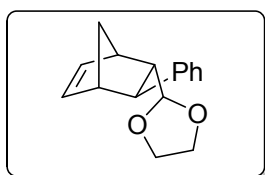
**Endo and exo isomers of 3-(4-methoxyphenyl)bicyclo[2.2.1]hept-5-ene-2-carbaldehyde (Table 4, entry 4).**



Prepared according to the general procedure described above from (*E*)-4-methoxycinnamaldehyde (100 mg, 0.162mmol) and cyclopentadiene (122 mg, 3.7mmol) to

afford the desired compound as a 14:86 mixture of *exo* and *endo* isomers ( yellow oil, 60%); ***endo isomer*** :  $^1\text{H NMR}$  (300 MHz,  $\text{CDCl}_3$ )  $\delta$  9.58 (d,  $J = 2.3$  Hz, 1H), 7.11 (d,  $J = 8.6$  Hz, 2H), 6.78 (d,  $J = 8.7$  Hz, 2H), 6.34 (dd,  $J = 5.6, 3.3$  Hz, 1H), 6.09 (dd,  $J = 5.6, 2.7$  Hz, 1H), 3.72 (s, 3H), 3.24 (br, 1H), 2.99 (br, 1H), 2.95 (d,  $J = 4.8$  Hz, 1H), 2.87 (dd,  $J = 6.5, 4.2$  Hz, 1H), 1.72 (d,  $J = 8.7$  Hz, 1H), 1.54 (dd,  $J = 8.7, 1.6$  Hz, 1H) ;  $^{13}\text{C NMR}$  (101 MHz,  $\text{CDCl}_3$ )  $\delta$  203.7, 158.0, 139.3, 135.6, 133.7, 128.3, 114.0, 60.9, 55.3, 48.7, 47.1, 45.1, 45.1 . ***exo isomer*** :  $^1\text{H NMR}$  (300 MHz,  $\text{CDCl}_3$ )  $\delta$  9.91 (d,  $J = 2.1$  Hz, 1H), 7.07 (d,  $J = 8.5$  Hz, 2H), 6.79 (d,  $J = 8.7$  Hz, 2H), 6.37 – 6.30 (m, 1H), 6.07 (dd,  $J = 2.8, 5.6$ , 1H), 3.87 (dd,  $J = 3.2, 5.2$  Hz, 1H) 3.77 (s, 3H), 3.28 (s, 1H), 3.07 (d,  $J = 1.6$  Hz, 1H), 2.31-2.36 (m, 1H), 1.67 – 1.72 (m, 1H), 1.52 – 1.57 (m, 1H).  $^{13}\text{C NMR}$  (101 MHz,  $\text{CDCl}_3$ ) 203.0 158.0, 136.6, 136.3, 134.6, 128.8, 113.6, 60.9, 55.3, 48.6, 47.1, 45.1, 44.8.

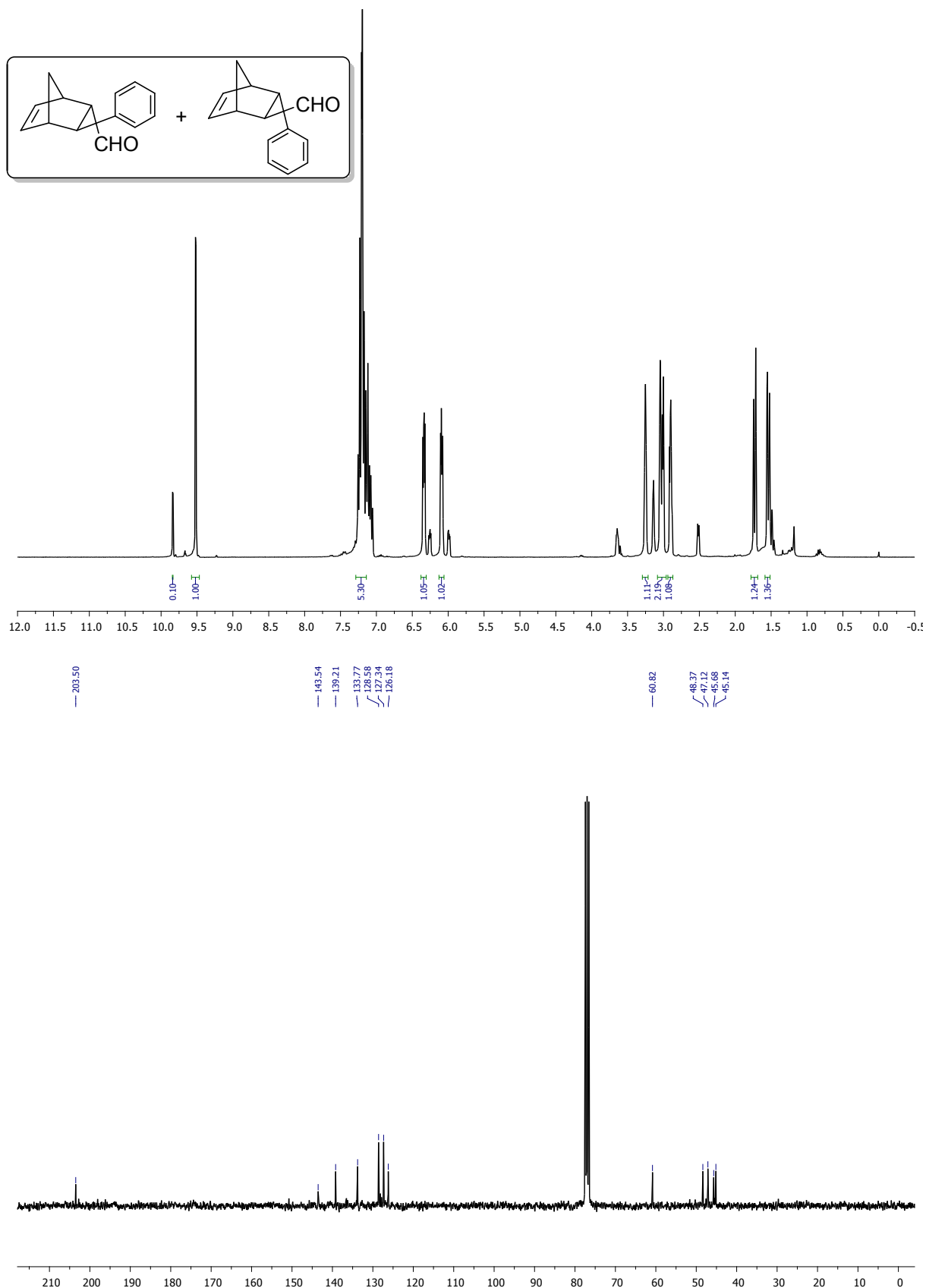
***Endo and exo isomers of 3-phenylbicyclo[2.2.1]hept-5-en-2-yl)-1,3-dioxolane (endo 4 and exo 4):***



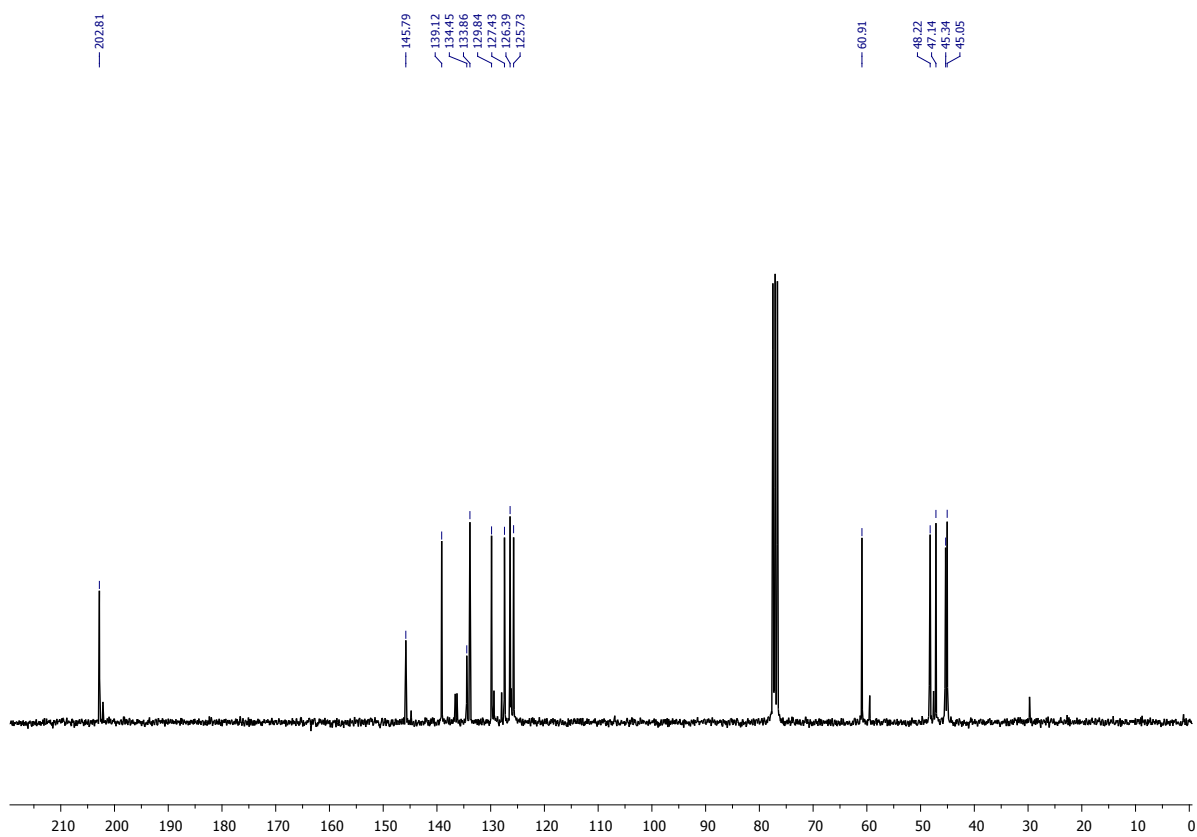
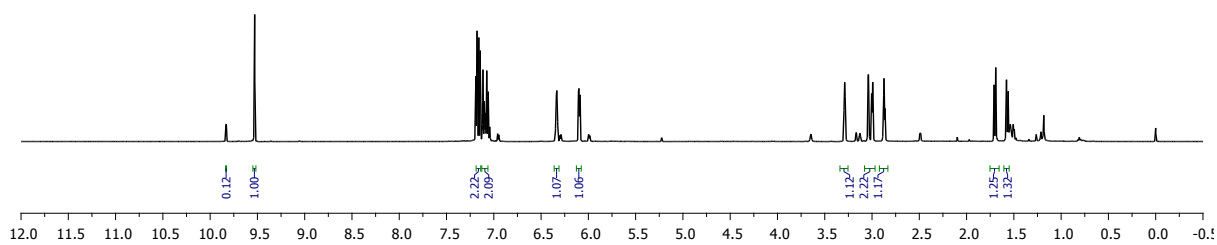
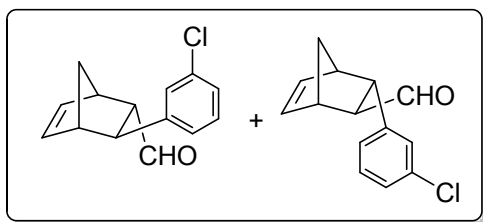
Prepared according to the general procedure described above with trans-cinnamaldehyde (100 mg, 0.75mmol), cyclopentadiene (150 mg, 2.27 mmol) in ethylene glycol(1M) to afford the glycol protected compound as a 16:84 mixture of *exo* and *endo* isomers (colorless oil, 75%). ***endo isomer*** :  $^1\text{H NMR}$  (500 MHz,  $\text{CDCl}_3$ )  $\delta$  7.33 (d,  $J = 7.6$  Hz, 2H), 7.21 (t,  $J = 7.7$  Hz, 2H), 7.09 (dd,  $J = 13.1, 5.8$  Hz, 1H), 6.27 (dd,  $J = 5.6, 3.2$  Hz, 1H), 6.11 (dd,  $J = 5.6, 2.8$  Hz, 1H), 4.38 (d,  $J = 8.1$  Hz, 1H), 3.89 – 3.82 (m, 2H), 3.76 – 3.69 (m, 2H), 2.98 (s, 1H), 2.87 (d,  $J = 0.8$  Hz, 1H), 2.48 (d,  $J = 4.4$  Hz, 1H), 2.27 – 2.19 (m, 1H), 1.65 (d,  $J = 8.6$  Hz, 1H), 1.44 (dd,  $J = 8.6, 1.6$  Hz, 1H) ;  $^{13}\text{C NMR}$  (126 MHz,  $\text{CDCl}_3$ )  $\delta$  144.9, 138.2, 134.9, 128.3, 127.8, 125.8, 108.6, 64.9, 64.8, 50.9, 49.1, 47.0, 46.6, 44.9. ***exo isomer*** :  $^1\text{H NMR}$  (500 MHz,  $\text{CDCl}_3$ )  $\delta$  7.17 – 7.14 (m, 5H), 6.24 (dd,  $J = 5.6, 3.2$  Hz, 1H), 5.87 (dd,  $J = 5.6, 2.8$  Hz, 1H), 4.86 (d,  $J = 6.1$  Hz, 1H), 3.80 – 3.76 (m, 2H), 3.71 – 3.68 (m, 2H), 3.19 (dd,  $J = 5.0, 3.5$  Hz, 1H), 3.01 (d,  $J = 9.4$  Hz, 1H), 2.98 (s, 1H), 1.88 – 1.83 (m, 1H), 1.71 (d,  $J = 8.4$  Hz, 1H), 1.40 (dd,  $J = 8.5, 1.5$  Hz, 1H).  $^{13}\text{C NMR}$  (126 MHz,  $\text{CDCl}_3$ )  $\delta$  144.0, 137.4, 135.3, 128.0, 127.9, 125.8, 107.4, 65.1, 64.9, 49.9, 48.7, 47.2, 46.8, 45.1,

### 3. $^1\text{H}$ NMR, $^{13}\text{C}$ NMR spectra:

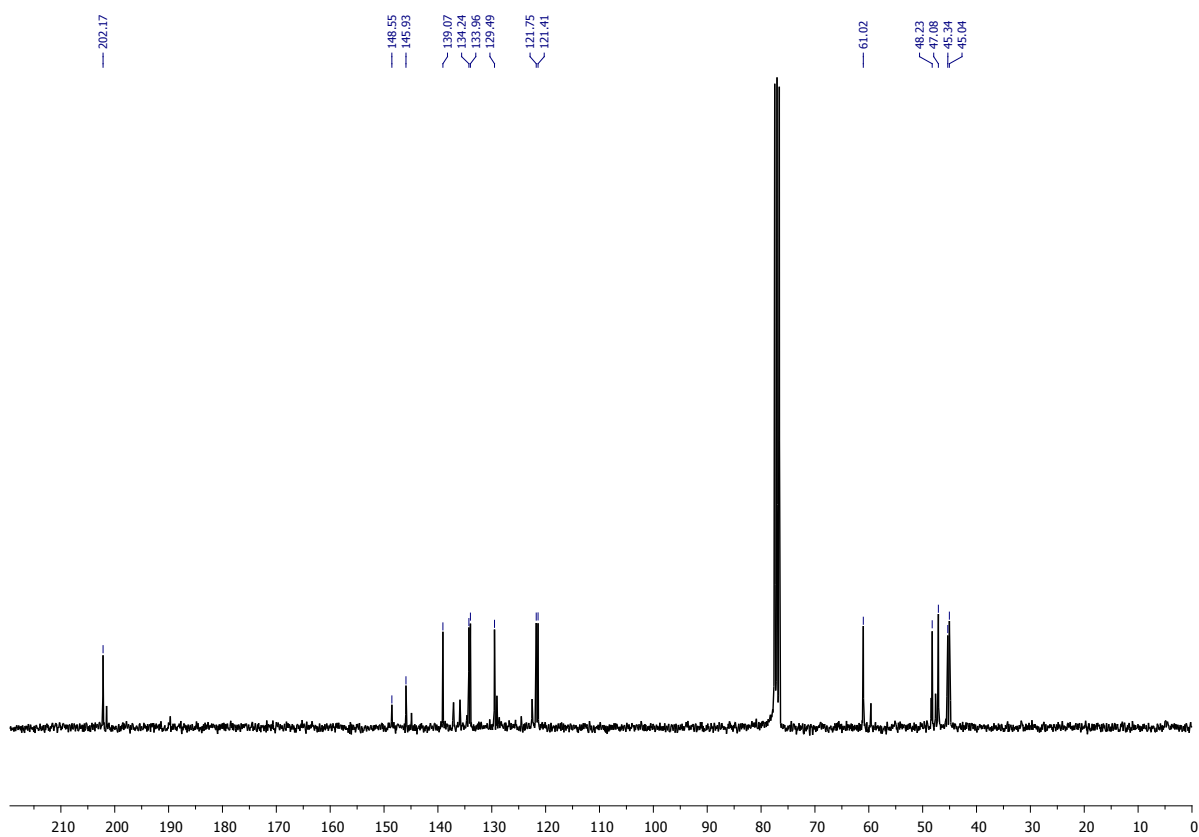
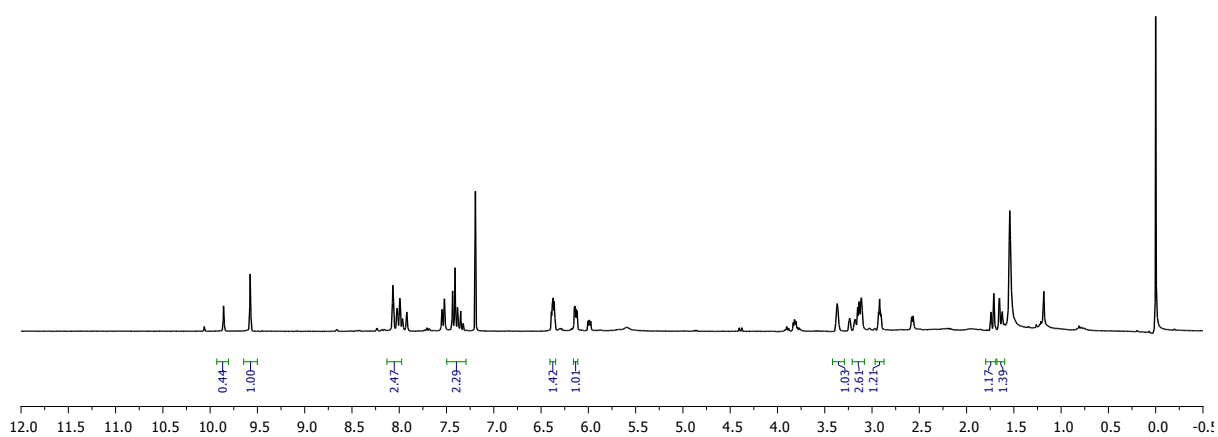
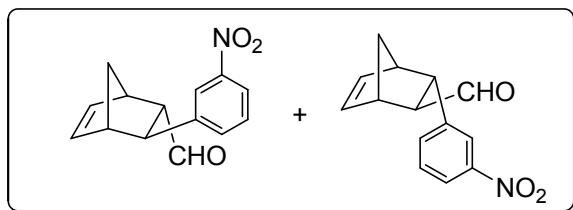
$^1\text{H}$  NMR and  $^{13}\text{C}$  NMR spectra of entry 1 Table 4:



$^1\text{H}$  NMR and  $^{13}\text{C}$  NMR spectra of entry 2 Table 4:

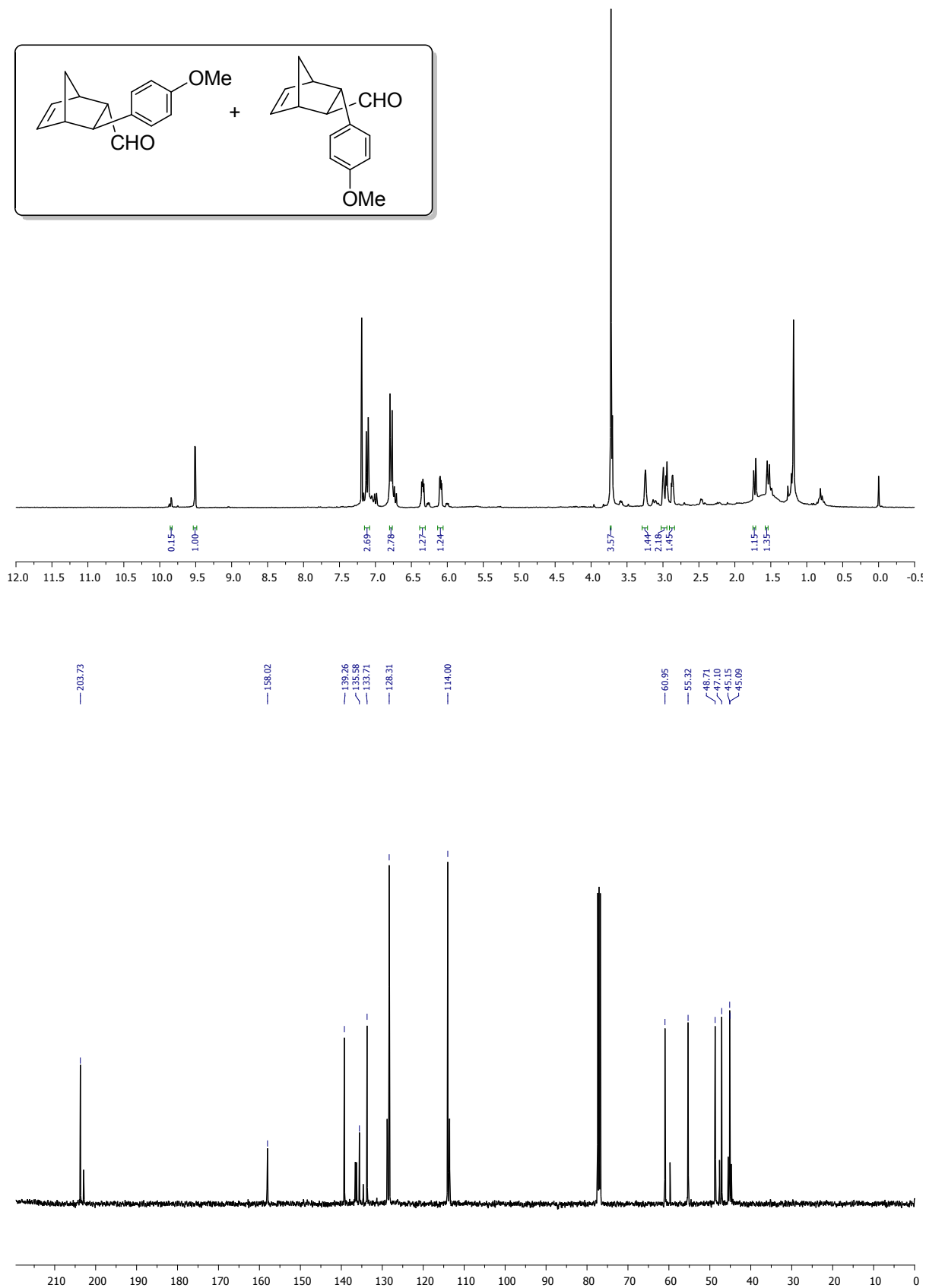


$^1\text{H}$  NMR and  $^{13}\text{C}$  NMR spectra of entry **3** Table **4**:

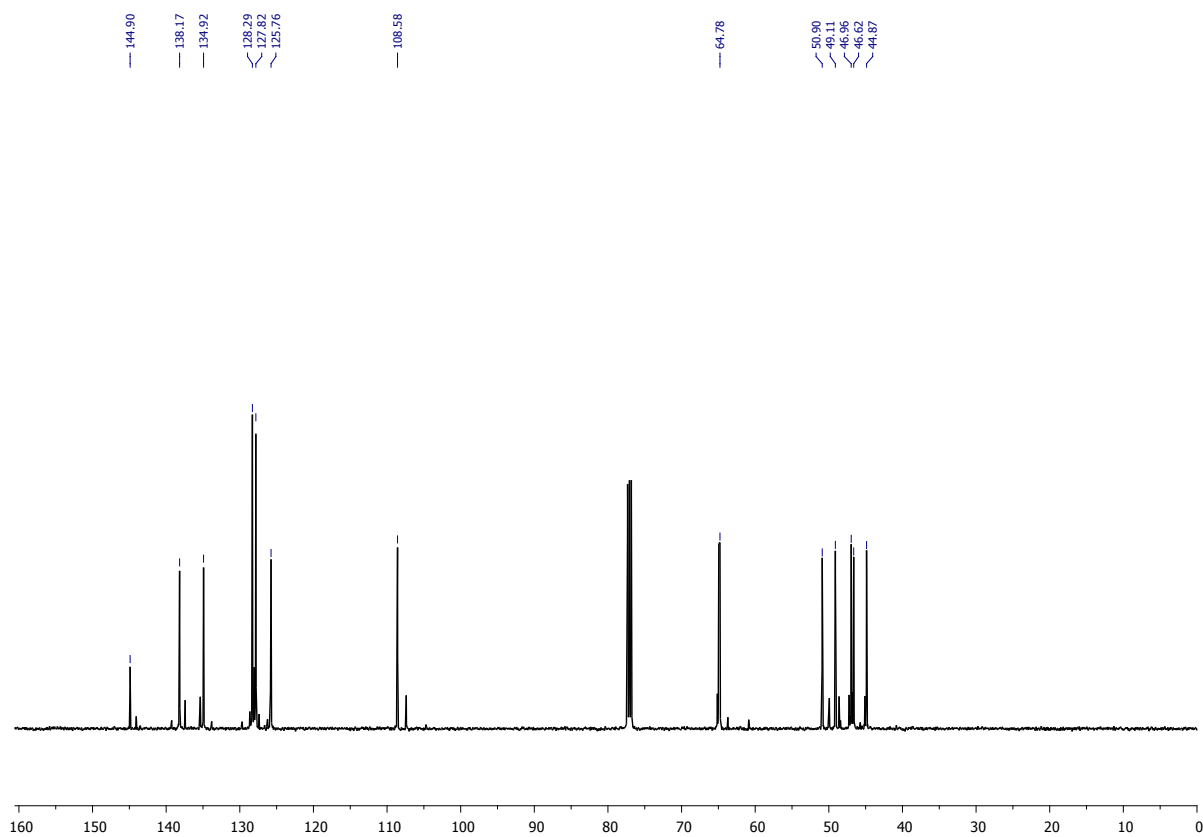
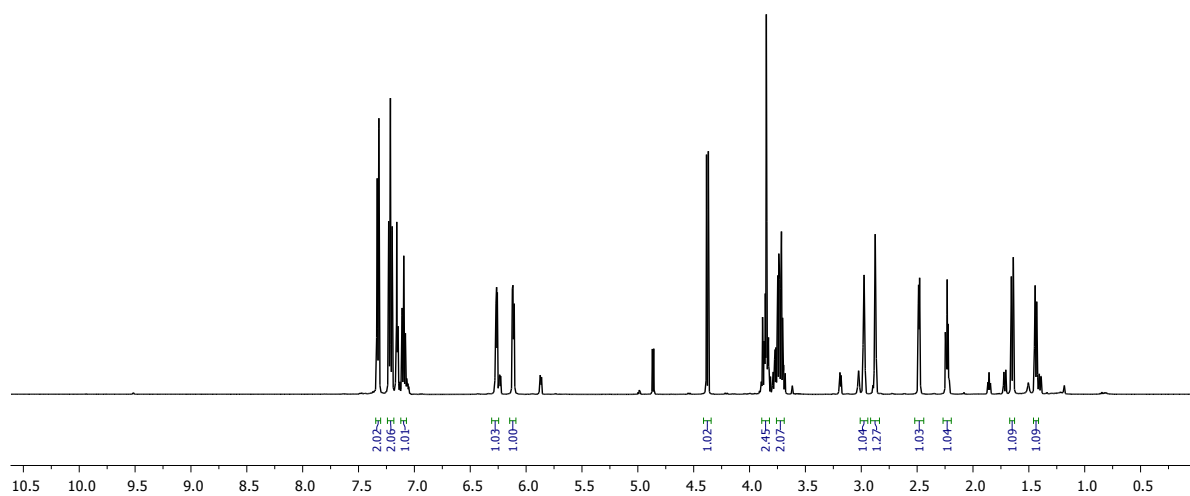
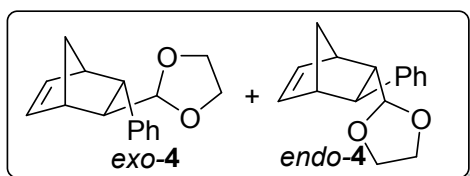




$^1\text{H}$  NMR and  $^{13}\text{C}$  NMR spectra of entry 4 Table 4:



$^1\text{H}$  NMR and  $^{13}\text{C}$  NMR spectra of entry **5** Table **3**:



#### 4. NOE spectra :

##### NOE spectra for entry 1 Table 4:

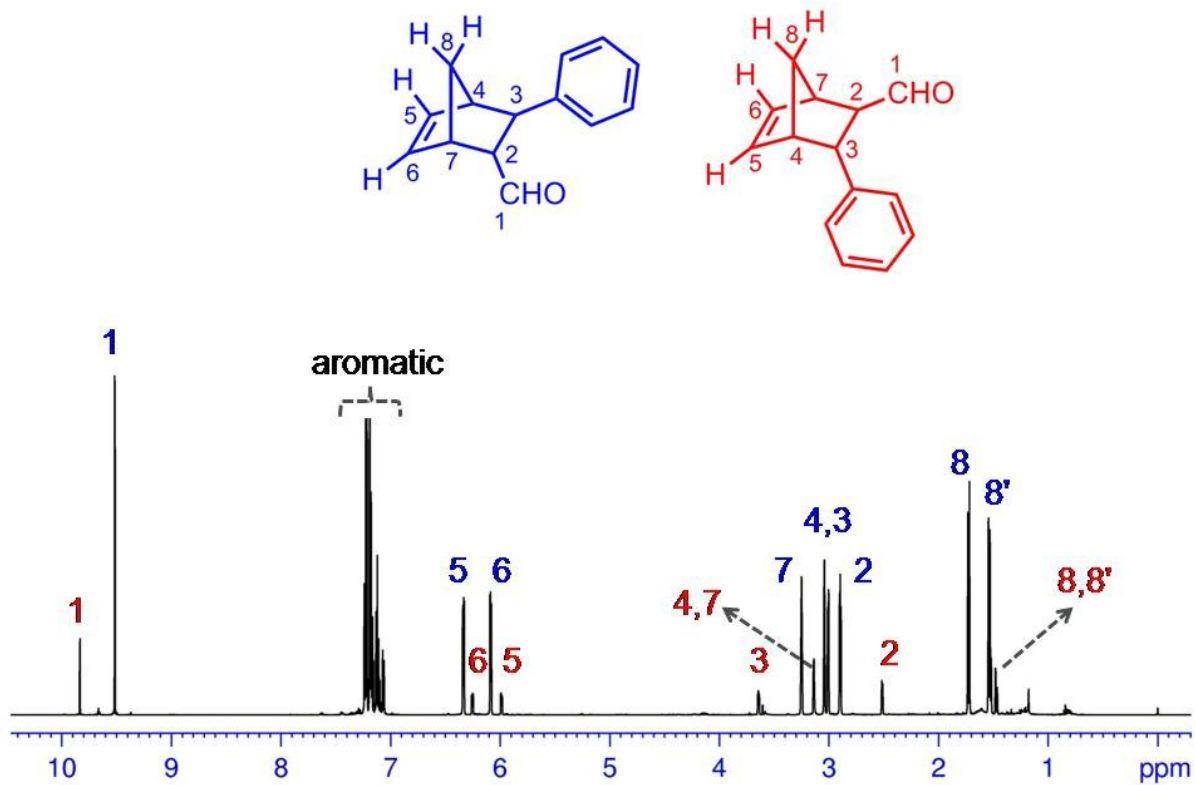
1D and 2D-NMR spectra were acquired on Bruker Avance 600 MHz (for  $^1\text{H}$ ) spectrometer and are referenced to  $\delta$  7.26 ppm and  $\delta$  77.00 ppm in  $\text{CDCl}_3$  solvent for  $^1\text{H}$  and  $^{13}\text{C}$ , respectively. The chemical shift values are presented in ppm (parts per million) units and  $J$ -coupling constants are expressed in Hz. The mixture of *endo-3* and *exo-3* isomers is characterized by using 1D ( $^1\text{H}$  and  $^{13}\text{C}$ ) and 2D- (DQFCOSY, NOESY, HSQC and HMBC) NMR experiments. The observed nOe cross peaks between 1-H(9.51 ppm)/6-H(6.09 ppm), 8-H(1.73 ppm)/Ar-H(7.18 ppm), 5-H(6.33 ppm)/3-H(3.01 ppm) and 8-H(1.73 ppm)/2-H(2.89 ppm) protons suggest that *endo-3* isomer is the major product in the adduct mixture.

Furthermore, the scalar coupling constants  $^3J_{2\text{-H}/7\text{-H}} = 3.51$  Hz and  $^3J_{3\text{-H}/4\text{-H}} = 1.68$  Hz found in *endo-3* support the conclusion that the *endo* isomer is the major product of a adduct mixture.

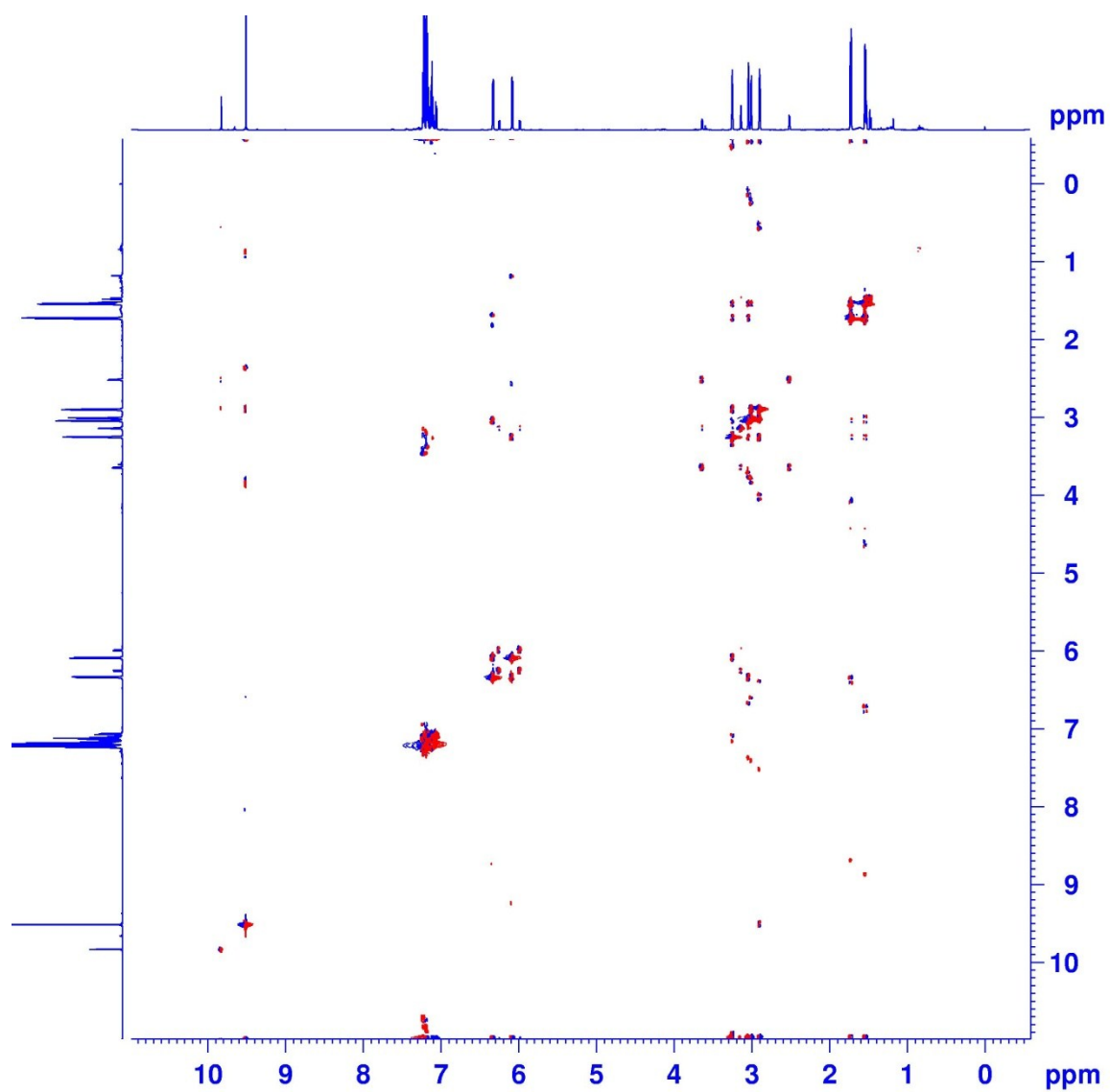
The configuration of the *exo-3* of a mixture was assigned by using the observed nOe cross peaks between 5-H(5.99 ppm)/Ar-H(7.06 ppm), 8-H(1.52 ppm)/3-H(3.64 ppm) and 2-H(2.51 ppm)/6-H(6.25 ppm) protons.

**Table 1:**  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectral data of a mixture of **endo-3** and **exo-3** in  $\text{CDCl}_3$  at 298 K (Avance 600 MHz).

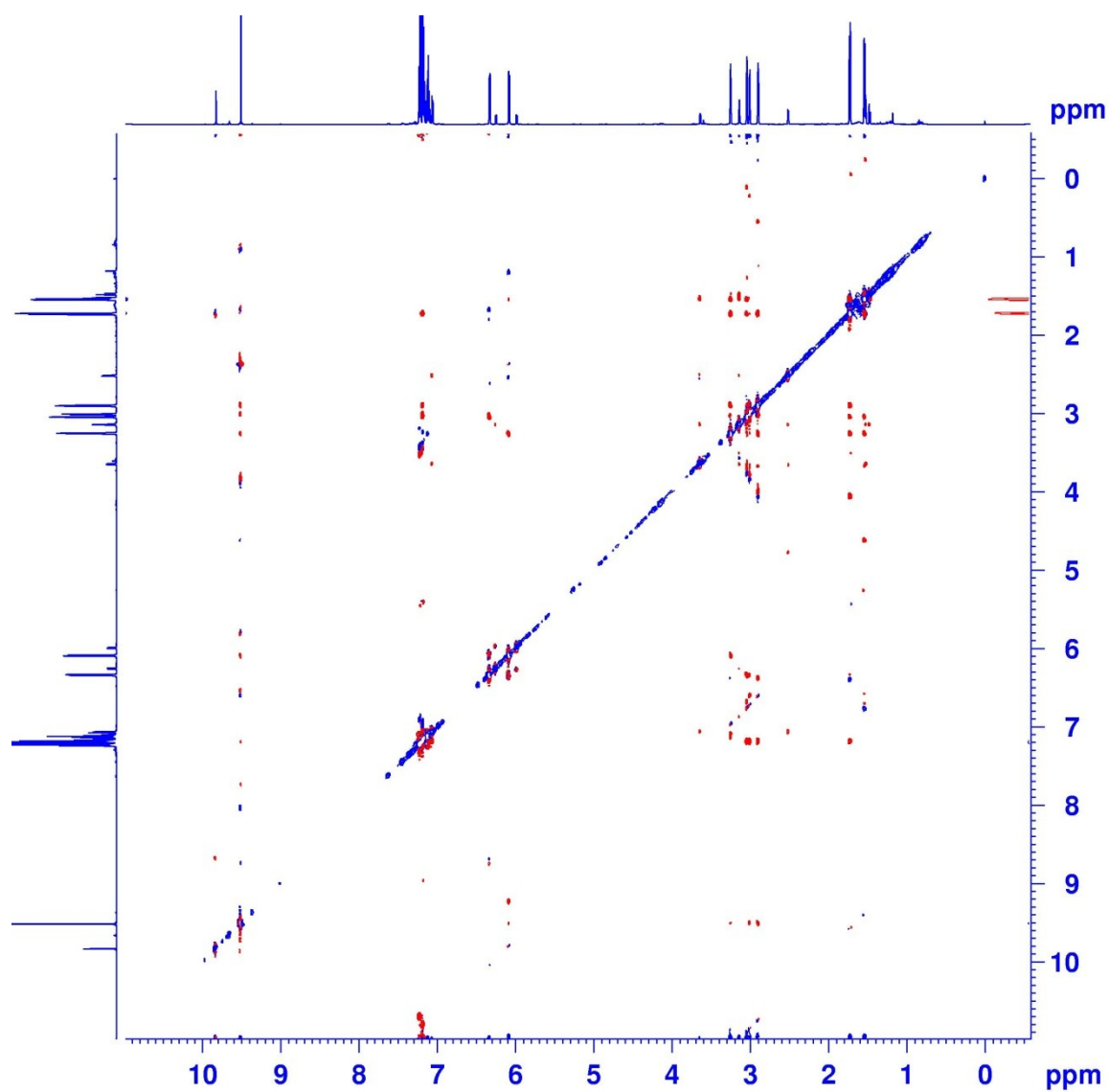
Position	<i>(endo-3)</i>		<i>(exo-3)</i>	
	$\delta_{1\text{H}}$ (ppm)	$\delta_{13\text{C}}$ (ppm)	$\delta_{1\text{H}}$ (ppm)	$\delta_{13\text{C}}$ (ppm)
<b>1</b>	9.51 (d, $J=2.23$ Hz)	203.5	9.83 (d, $J=2.0$ Hz)	202.8
<b>Aromatic</b>	7.25-7.05 (m)	-	7.25-7.05 (m)	-
<b>5</b>	6.33 (dd, $J=5.75, 3.21$ Hz)	139.1	5.99 (dd, $J=5.63, 2.86$ Hz)	136.4
<b>6</b>	6.09 (dd, $J=5.75, 2.85$ Hz)	133.7	6.25 (dd, $J=5.63, 3.2$ Hz)	136.2
<b>7</b>	3.25 (m)	45.0	3.14 (m)	45.4
<b>4</b>	3.04 (m)	48.2	3.14 (m)	45.4
<b>3</b>	3.01 (dd, $J=5.60, 1.68$ Hz)	45.5	3.64 (dd, $J=5.3, 3.4$ Hz)	45.3
<b>2</b>	2.89 (ddd, $J=5.60, 3.51, 2.23$ Hz)	60.7	2.51 (dt, $J=5.3, 1.8, 1.8$ Hz)	59.4
<b>8</b>	1.73 (m)	47.0	1.52 (m)	47.5
<b>8'</b>	1.54 (m)	47.0	1.47 (m)	47.5



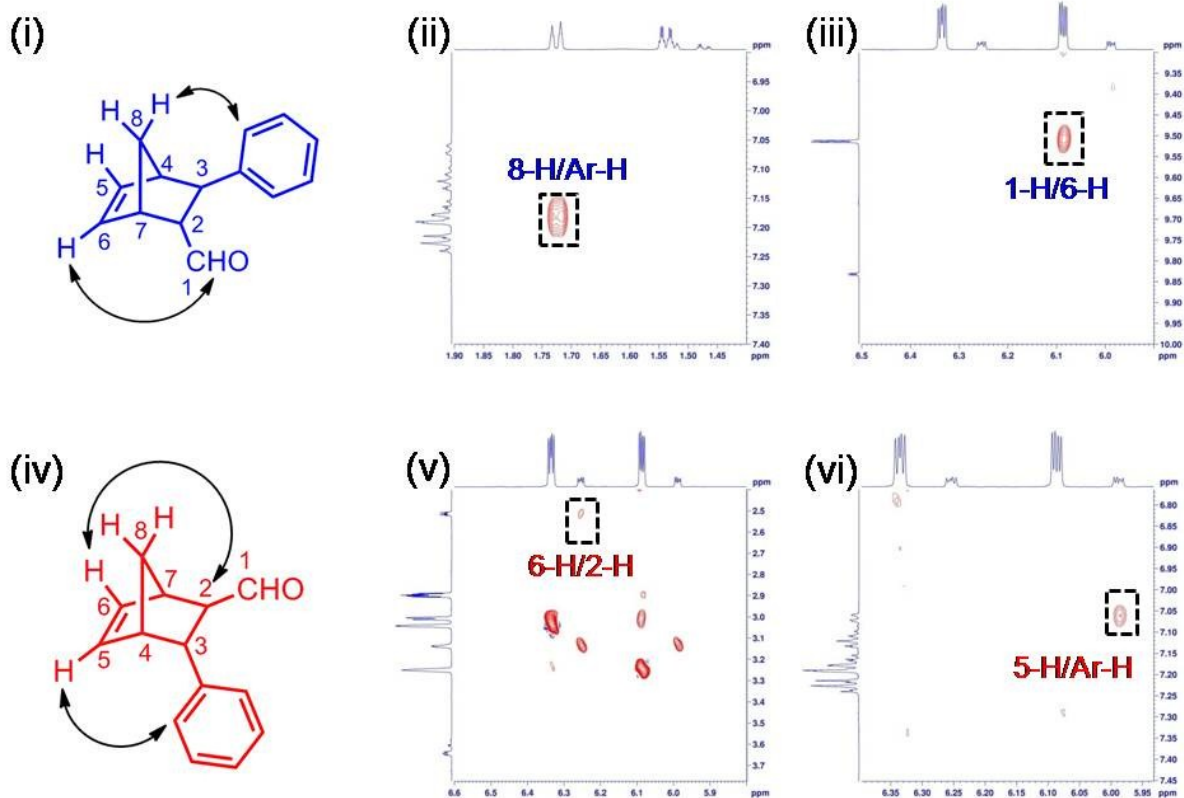
**Figure 1:**  $^1\text{H}$  NMR spectrum of a mixture of *endo*-**3** and *exo*-**3** in  $\text{CDCl}_3$  at 298 K (Avance 600 MHz).



**Figure 2:** DQFCOSY spectrum of a mixture of **endo-3** and **exo-3** in CDCl<sub>3</sub> at 298 K (Avance 600 MHz).

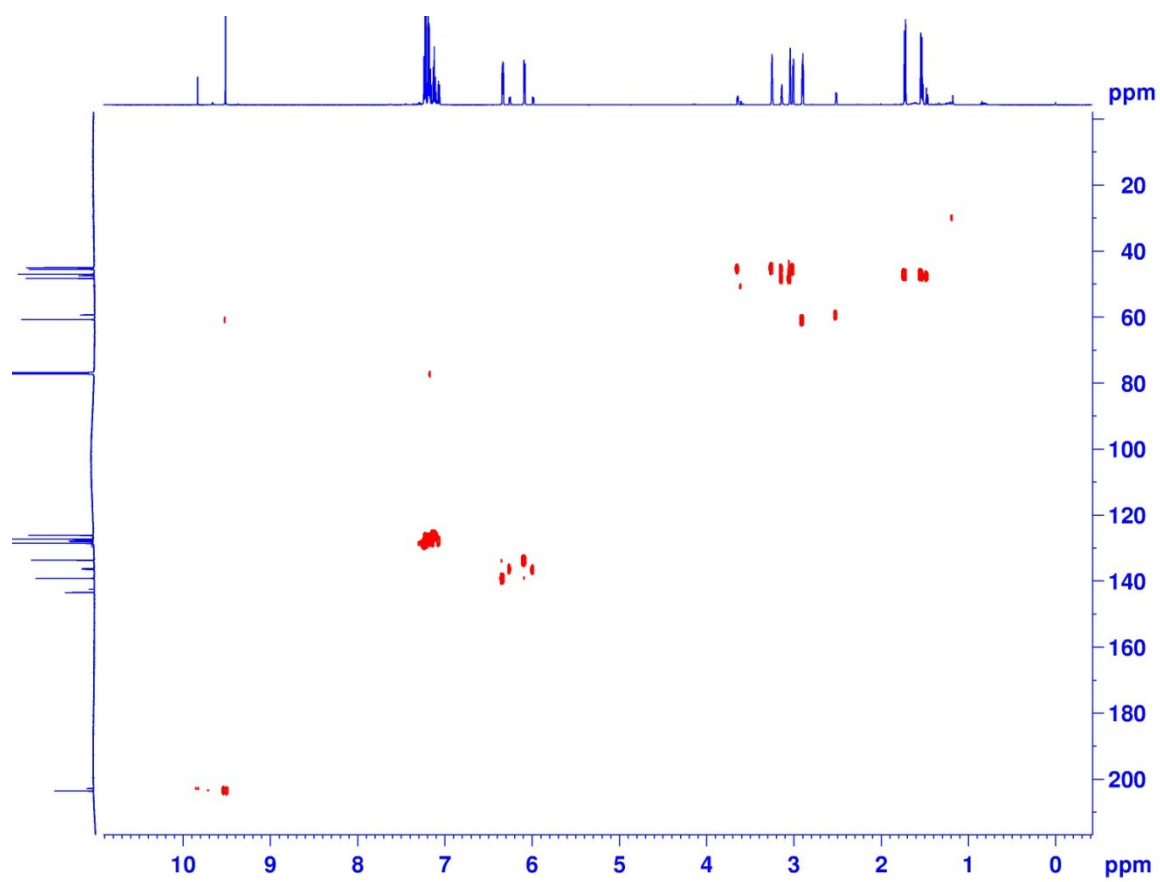


**Figure 3:** NOESY spectrum of a mixture of **endo-3** and **exo-3** in  $\text{CDCl}_3$  at 298 K (Avance 600 MHz).

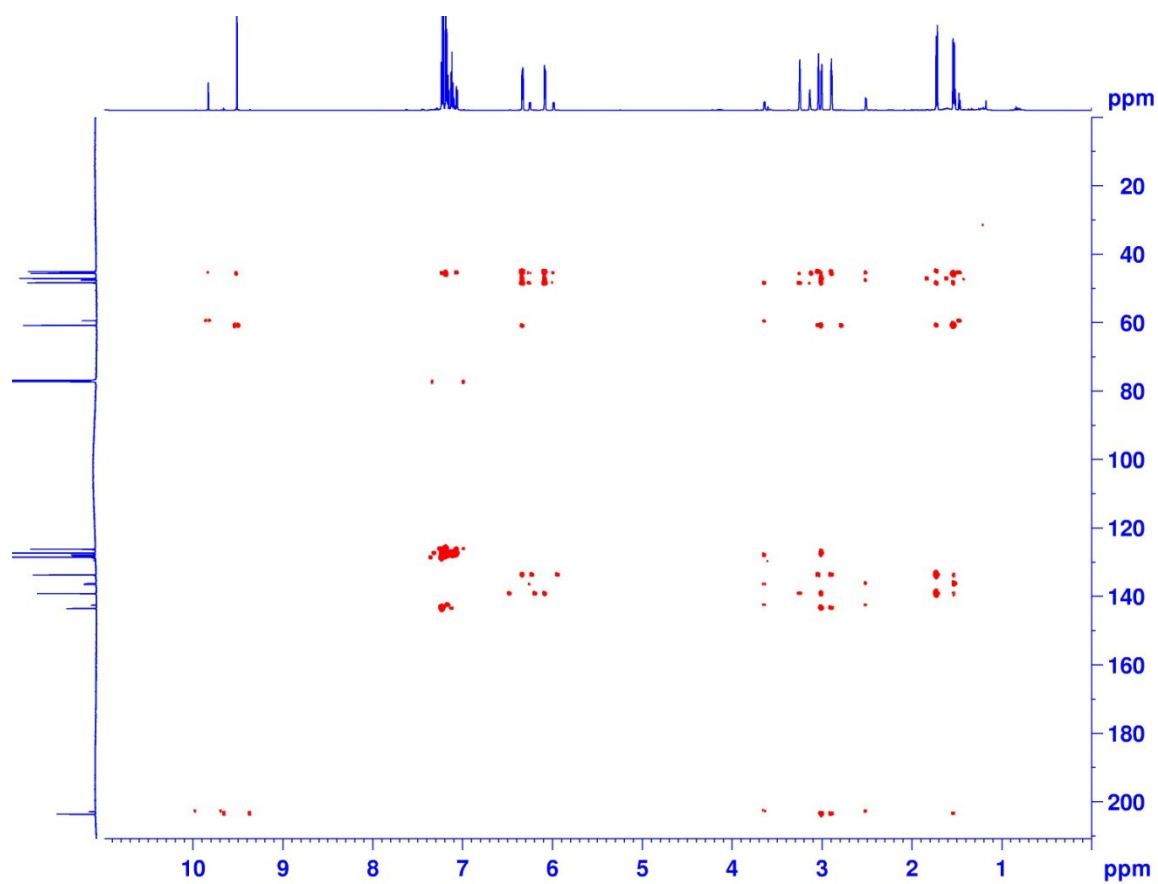


**Figure 4:** Schematic representation of the characteristic nOe correlations (shown as black arrows) in *endo*-**3** (i) and *exo*-**3** (iv). Expanded regions of NOESY spectrum of a mixture of *endo*-**3** and *exo*-**3** showing the characteristic nOe cross peaks (ii, iii, v and vi).





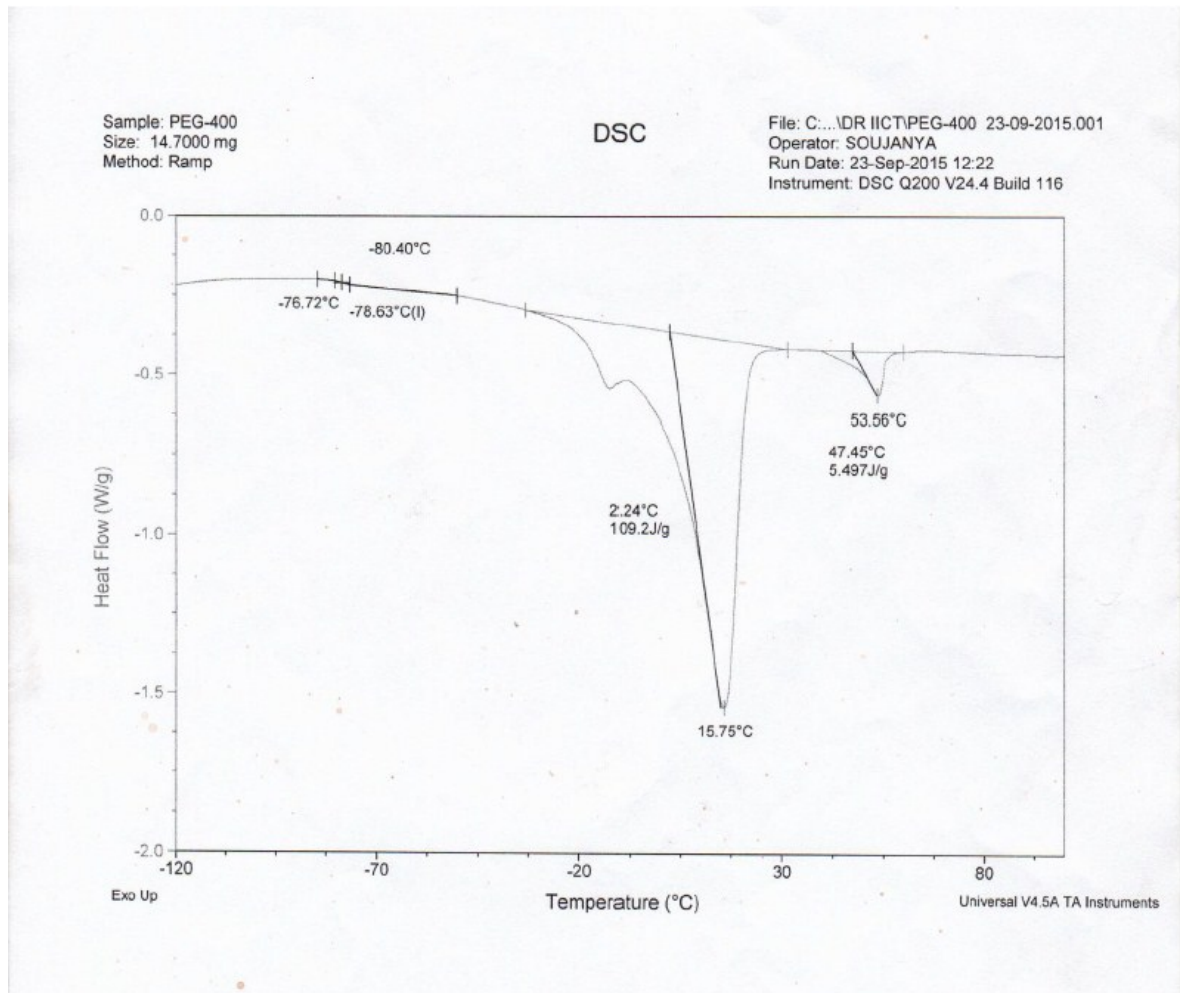
**Figure 5:** <sup>13</sup>C-<sup>1</sup>H HSQC spectrum of a mixture of **endo-3** and **exo-3** in CDCl<sub>3</sub> at 298 K (Avance 600 MHz).



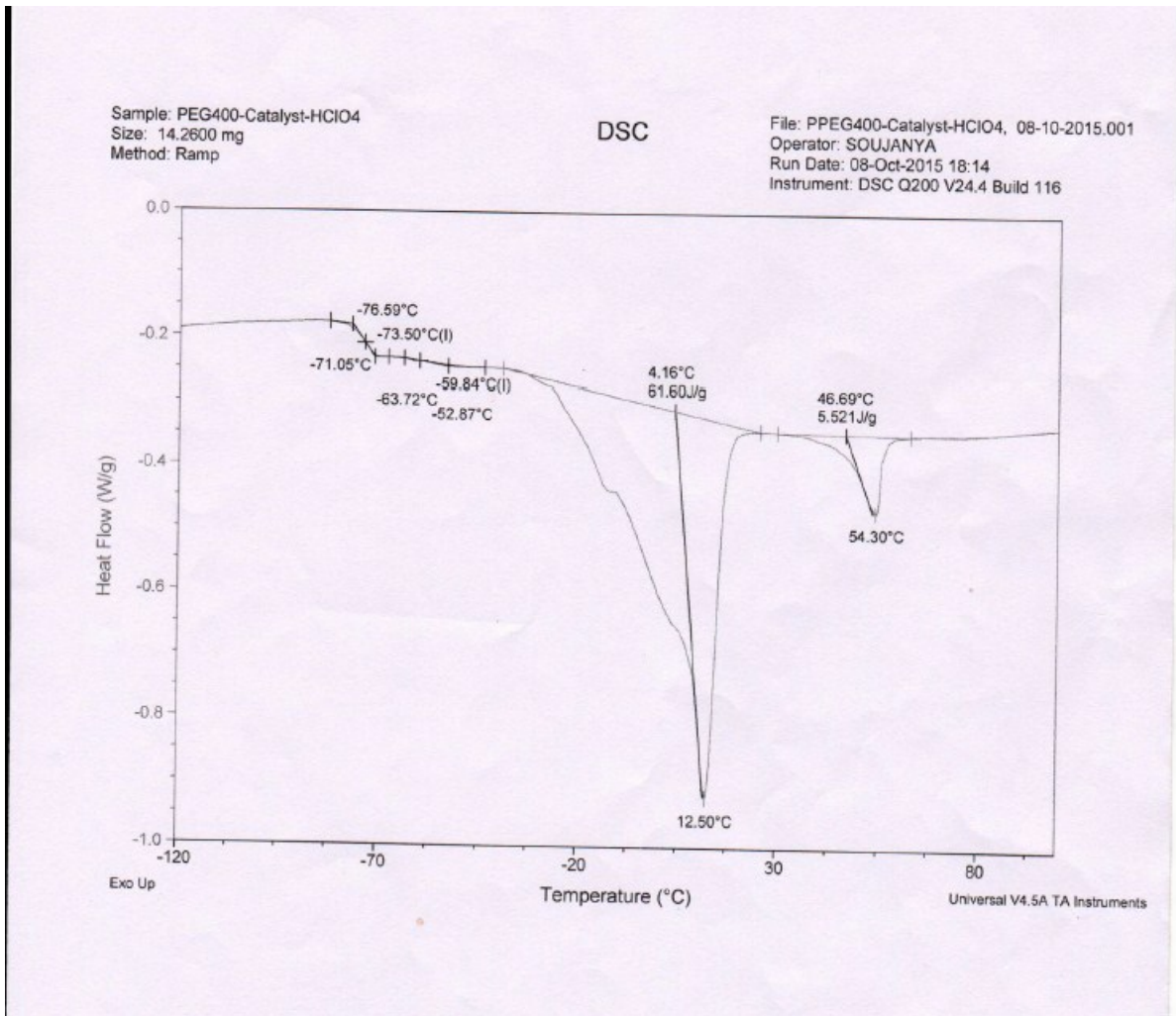
**Figure 6:**  $^{13}\text{C}$ - $^1\text{H}$  HMBC spectrum of a mixture of **endo-3** and **exo-3** in  $\text{CDCl}_3$  at 298 K (Avance 600 MHz).

## 5. DSC Data :

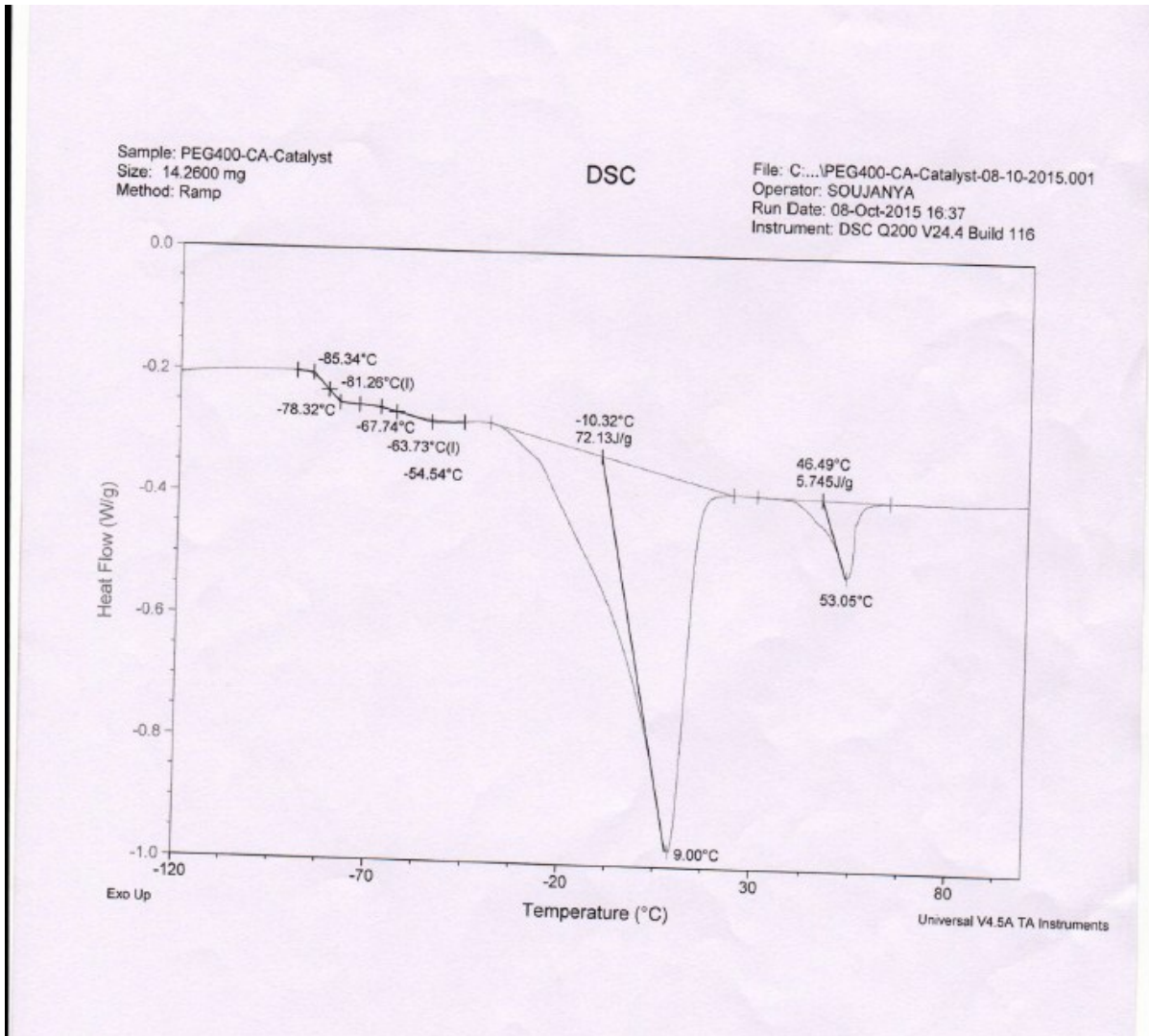
### 1. DSC data for PEG-400



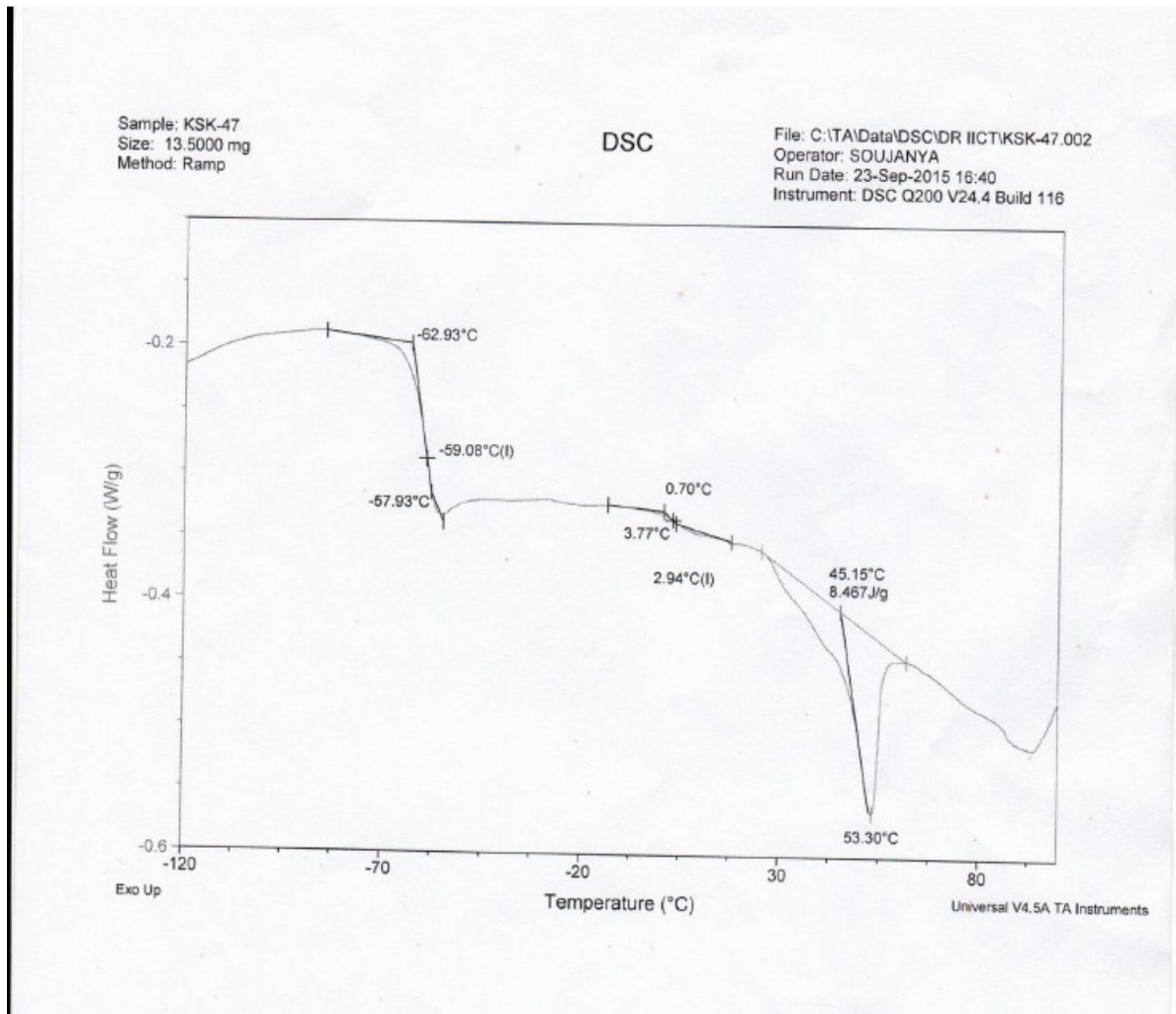
2. DSC data for PEG-400, Catalyst B, HClO<sub>4</sub>



### 3. DSC data for PEG-400, Catalyst B, Cinnamaldehyde



4. DSC data for PEG-400, Catalyst B, Cinnamaldehyde, Cyclopentadiene, HClO<sub>4</sub>





## 6. HPLC Data.

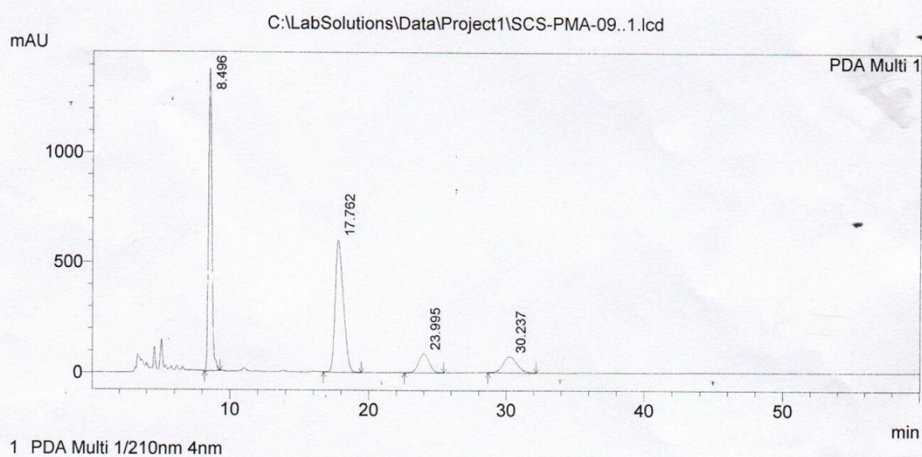
### HPLC chromatogram of *endo-3* and *exo-3* mixture of isomers

4/22/2016 15:55:51 1 / 1

#### IICT NPL

Acquired by : Admin  
 Sample Name : SCS-PMA-09  
 Sample ID : SCS-PMA-09  
 Vial # : 91  
 Injection Volume : 20 uL  
 Data File Name : SCS-PMA-09..1.lcd  
 Method File Name : ANITHA.lcm  
 Batch File Name :  
 Report File Name : Report Format.lcr  
 Data Acquired : 4/22/2016 11:19:42 AM  
 Data Processed : 4/22/2016 12:19:50 PM  
 MOBILE PHASE: 30% IPA IN HEXANE  
 COLUMN: CHIRAL PAK OJ-H 250mm X 4.6 mm, 5u  
 FLOWRATE: 1ml/min  
 DETECTION: 210nm

#### <Chromatogram>



PeakTable

Peak#	Ret. Time	Area	Height	Area %	Height %
1	8.496	23255381	1376201	40.201	64.498
2	17.762	24980389	600248	43.183	28.132
3	23.995	4538477	85372	7.846	4.001
4	30.237	5073537	71880	8.770	3.369
Total		57847784	2133701	100.000	100.000

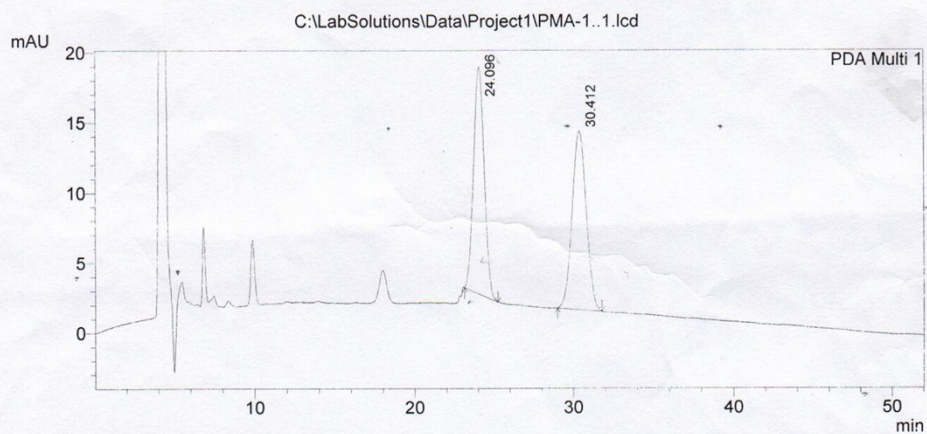
# HPLC chromatogram of *exo-3* isomer

4/5/2016 17:14:06 1 / 1

## IICT NPL

Acquired by : Admin  
Sample Name : PMA-1  
Sample ID : PMA-1  
Vial # : 1  
Injection Volume : 50 uL  
Data File Name : PMA-1..1.lcd  
Method File Name : SCS-PMA.lcm  
Batch File Name :  
Report File Name : Report Format.lcr  
Data Acquired : 4/5/2016 3:44:06 PM  
Data Processed : 4/5/2016 4:36:14 PM  
MOBILE PHASE: 30% IPA IN HEXANE  
COLUMN: CHIRAL PAK OJ-H 250mm X 4.6 mm, 5u  
FLOWRATE: 1ml/min  
DECTION: 210nm

### <Chromatogram>



1 PDA Multi 1/210nm 4nm

### PeakTable

Peak#	Ret. Time	Area	Height	Area %	Height %
1	24.096	755850	16180	49.147	56.006
2	30.412	782078	12710	50.853	43.994
Total		1537928	28890	100.000	100.000



HPLC chromatogram of *endo-3* isomer

