Supplementary information

Exploring the Synthetic Potential of g-C_3N_4.SO_3H Ionic Liquid Catalyst for One-Pot Synthesis of 1,1-Dihomoarylmethane Scaffolds via Knoevenagel-Michael Reaction

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1. Experimental

The chemicals used were commercially available and purchased from Sigma-Aldrich, Loba-Chemie, and Merck company. They were used without further purification. Melting points were determined using an electric thermal melting point apparatus and are reported without any correction. Reaction progress was monitored by thin layer chromatography, which was carried out on silica gel 60 RP-18 F254S plates using 3 NOS UV cabinets. The IR spectrum of catalyst was recorded on a Bruker FT-IR spectrometer. The SEM and TEM studies of the synthesized catalyst was carried out on Carl Zeiss EVO 18 scanning electron microscope and JEOL JEM 2100 plus transmission electron miscroscope respectively. The XRD spectrum was recorded on Rigaku Ultma IV X-Ray Diffractometer. ^{1}H and ^{13}C NMR spectrum were recorded on a JEOL 400 MHz instrument using $CDCl_3$ and DMSO-d_6 as solvents, and TMS was used as the internal standard.

1.1. General procedure for the preparation of g-C_3N_4.SO_3H (IL) catalyst

To prepare g-C_3N_4 (graphitic carbon nitride), 10 g of ground urea was placed in a silica crucible and covered with a lid. The crucible was wrapped in aluminum foil and heated in a muffle furnace at 550 °C for 2 h. After switching off the furnace, the crucible was carefully removed after 1 h to obtain yellowish-white crude g-C_3N_4 (0.531 mg). The crude material was sonicated for 30 minutes in 30 mL of dichloromethane (DCM) for dispersion. To synthesize g-C_3N_4.SO_3H, 1 mL of chlorosulfonic acid was added dropwise using a micropipette while stirring the reaction mixture in an ice bath to maintain the temperature below 5 °C. The reaction mixture was stirred for 6 h at RT and then distilled to dryness. The resulting ionic liquid was washed several times with ethanol: water (1:1) by decantation and centrifugation. It was then washed twice with distilled water. The final product (pale yellow, 0.431 mg) was collected with ethanol and dried in a hot air oven for 2 h[1] .

1.2. General procedure for the synthesis of 2,2'-(arylmethylene)bis(3-hydroxy-5,5-dimethylcyclohex-2-en-1-one)/ 2,2'-((aryl)methylene)bis(3-

hydroxy cyclohex-2-en-1-one)/ 4,4'-((3-chlorophenyl)methylene)bis(3-methyl-1-phenyl-1H-pyrazol-5-ol) (6a-h, 7a-f, 8a-f)

A mixture of dimedone/1,3-cyclohexanedione/1-phenyl-3-methyl-5-pyrazolone (2 mmol), aryl aldehydes (1 mmol), and g-C_3N_4.SO_3H (15 mg) in 2 ml of ethanol: water (1:1) solvent at RT was stirred in a round bottomed (RB) flask (25 ml) for a significant time. Reaction completion was determined by TLC and then the solvent was evaporated using a rotary evaporator. The catalyst was recovered simply by filtration aid in chloroform solvent which was further washed with ethanol and then dried in a hot air oven at 60 ^oC for about 3 h, and the pure desired product was collected after crystallization. The after-crystallization purity of the collected product was characterized by ^{1}H-NMR and ^{13}C-NMR spectral analysis.

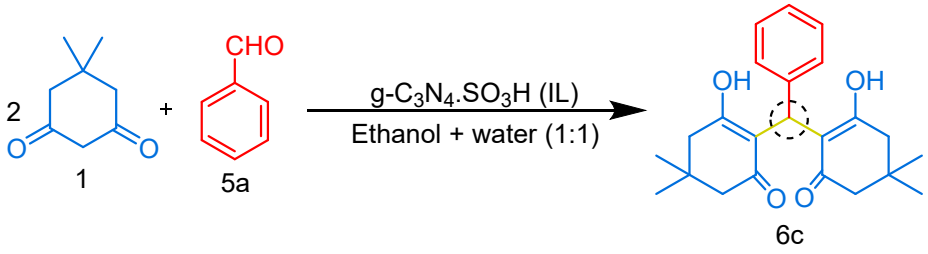
1.3. General procedure for the synthesis of 3,3'-((aryl)methylene)bis(4-hydroxy-2H-chromen-2-one) (8a-f)

In a 25 ml RB flask, a catalytic amount of g-C_3N_4.SO_3H (20 mg) was added to a stirring mixture of aryl aldehydes (1 mmol), and 4-hydroxycoumarin (2 mmol) in ethanol (2 ml) solvent at 80 ^oC and was refluxed for an appropriate time. After confirming the reaction completion by TLC, the solvent was removed by a rotary evaporator. After that, the catalyst was recovered using the same process (as above mentioned) from the crude. The expected product was then dried and recrystallized using ethanol.

2. Green chemistry matrix

2.1. Green chemistry matrix calculation for bis-dimedone

Green chemistry matrix[2-5] has been calculated for the synthesis of **6c** based on the following parameters:



Scheme S1. Model reaction for green matrix calculation

Compound Code	1	5a	6c
M.W. (g/mol)	140.17	106.12	368.47
In present work M.W. (mg)	2(140.17) = 280.34	106.12	368.47

The total mass of reactants = 386.46

Obtained product = 338 mg

EtOH (4 ml) + H_2O (4 ml) = 3.15 + 3.99 = 7.14 mg

2.1.1. Environmental factor(E-factor)

E-factor = [mass of waste]/ mass of product

Where the mass of waste = total mass of raw materials minus the total mass of product

$$\text{E-factor} \quad \frac{(280.34+106.12) - 338}{338} = \frac{386.46 - 338}{338}$$

= **0.14** (Ideal valve of E-factor is considered zero)

2.1.2. Atom-economy (AE)

The ideal valve of the AE factor is 100% means all starting material is converted into the product.

AE = MW of product ÷ Σ (MW of stoichiometric reactants) × 100

$$\text{Atom-economy} = \frac{368.47 \ X\ 100}{(280.34\ 106.12)} = \mathbf{95.34\%}$$

2.1.3. Process mass intensity (PMI)

PMI = Σ (mass of stoichiometric reactants + solvent) / mass of product

$$\text{PMI} = \frac{386.46 + 7.14}{338} = \mathbf{1.16}$$

Ideal value of PMI = E-factor + 1

PMI = 0.14 +1 = 1.14

Both results are in resemblance to each other.

2.1.4. Reaction mass efficiency (RME)

RME = mass of product /Σ (mass of stoichiometric reactants) × 100

$$RME = \frac{338}{386.46} X\ 100$$

= **87.46%** (Higher value measure the **cleanness** of reaction)

2.1.5. Eco-score (E-score)

Ideal reactions Eco-score value is 100.

Eco-scale from 0 to 100 using the following scores: > 75, excellent; > 50, acceptable; and < 50, inadequate.

E-score has been calculated for the reaction based on the following 6 parameters below.

S. No.	Parameter	Values	Penalty points
1	Yield	100-91.73/2	4.135
2	Price of the reaction component	Inexpensive	0.0
3	Safety (Reactant)	T(Toxic) = 5+5+5 = 15	15.0
4	Technical setup	Common setup	0.0
5	Temperature /time	Room temp./ <1h	0.0
6	Workup and purification	Crystallization	1.0
	Total penalty points		20.135
Based on the hazard warning symbols			

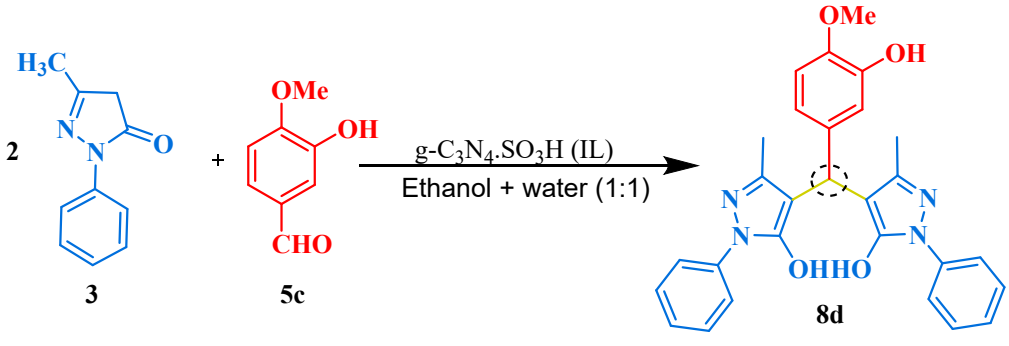
Eco-Score = 100 – the sum of individual penalties

= 100 – 20.135 = 79.865 (>75, excellent synthesis)

As per the above results, it was concluded that the reaction has a low Environment-factor (E-factor = 0.14), high atom economy (AE = 95.34%), high process mass intensity (PMI = 1.16), and high reaction mass efficiency (RME = 87.46%), with excellent eco-score (79.865%). These values clearly indicated the eco-friendliness of the present synthesis.

2.2. Green chemistry matrix calculation for bis-pyrazole

Green chemistry matrix[2-5] has been calculated for the synthesis of **8d** based on the following parameters:



Scheme S2. Model reaction for green matrix calculation

Compound Code	1	5	6
M.W. (g/mol)	174.20	152.15	482.54
In present work M.W. (mg)	2(174.20) = 348.4	152.15	482.54

The total mass of reactants = 500.55

Obtained product = 474.52 mg

EtOH (4 ml) + H_2O (4 ml) = 3.15 + 3.99 = 7.14 mg

2.2.1. Environmental factor(E-factor)

E-factor = [mass of waste]/ mass of product

Where the mass of waste = total mass of raw materials minus the total mass of the product

$$\text{E-factor} \quad \frac{(500.55) - 474.52}{474.52} = \frac{26.03}{474.52}$$

= **0.05** (Ideal valve of E-factor is considered zero)

2.2.2. Atom-economy (AE)

The ideal valve of the AE factor is 100% means all starting material is converted into the product.

AE = MW of product ÷ Σ (MW of stoichiometric reactants) × 100

$$\text{Atom-economy} = \frac{482.54 \ \text{X} \ 100}{500.55} = \mathbf{96.40\%}$$

2.2.3. Process mass intensity (PMI)

PMI = Σ (mass of stoichiometric reactants + solvent) / mass of product

$$\text{PMI} = \frac{500.55 + 7.14}{474.52} = \mathbf{1.06}$$

Ideal value of PMI = E-factor + 1

PMI = 0.05 +1 = 1.05

Both results are in resemblance to each other.

2.2.4. Reaction mass efficiency (RME)

RME = mass of product /Σ (mass of stoichiometric reactants) × 100

474.52

$$RME = \frac{\qquad}{500.55} \times 100$$

= **94.79%** (Higher value measure the **cleanness** of reaction)

2.2.5. Eco-score (E-score)

Ideal reactions Eco-score value is 100.

Eco-scale from 0 to 100 using the following scores: > 75, excellent; > 50, acceptable; and < 50, inadequate.

E-score has been calculated for the reaction on the basis of the following 6 parameters below.

S. No.	Parameter	Values	Penalty points
1	Yield	100-98.33/2	0.835
2	Price of the reaction component	Inexpensive	0.0
3	Safety (Reactant)	T(Toxic) = 5+5+5 = 15	15.0
4	Technical setup	Common setup	0.0
5	Temperature /time	Room temp./ <1h	0.0
6	Workup and purification	Crystallization	1.0
	Total penalty points		16.835
Based on the hazard warning symbols			

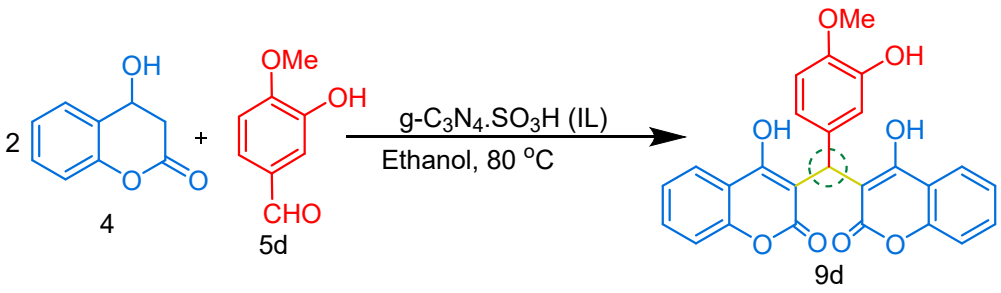
Eco-Score = 100 – the sum of individual penalties

= 100 – 16.835 = 83.165 (>75, excellent synthesis)

As per the above results, it was concluded that the reaction has a low Environment-factor (E-factor = 0.05), high atom economy (AE = 96.40%), high process mass intensity (PMI = 1.06), and high reaction mass efficiency (RME = 94.79%), with excellent eco-score (83.165%). These values clearly indicated the eco-friendliness of the present synthesis.

2.3. Green chemistry matrix calculation for bis-coumarin

Green chemistry matrix[2-5] has been calculated for the synthesis of **9d** based on the following parameters:



Scheme S3. Model reaction for green matrix calculation

Compound Code	1	5	6
M.W. (g/mol)	162.14	152.15	458.42
In present work M.W. (mg)	2(162.14) = 324.28	152.15	458.42

The total mass of reactants = 476.43

Obtained product = 441.52 mg

EtOH (5 ml) = 3.94 mg,

2.3.1. Environmental factor(E-factor)

E-factor = [mass of waste]/ mass of product

Where mass of waste = total mass of raw materials minus the total mass of product

$$\text{E-factor} \quad \frac{476.43 - 441.52}{441.52} = \frac{34.91}{441.52}$$

= **0.079** (Ideal valve of E-factor is considered zero)

2.3.2. Atom-economy (AE)

The ideal valve of the AE factor is 100% means all starting material is converted into a product.

AE = MW of product ÷ Σ (MW of stoichiometric reactants) × 100

$$\text{Atom-economy} = \frac{458.42 \ X\ 100}{476.43} = \mathbf{96.21\%}$$

2.3.3. Process mass intensity (PMI)

PMI = Σ (mass of stoichiometric reactants + solvent) / mass of product

$$\text{PMI} = \frac{476.43 + 3.94}{441.52} = \mathbf{1.08}$$

Ideal value of PMI = E-factor + 1

PMI = 0.079 +1 = 1.079

Both results are in resemblance to each other.

2.3.4. Reaction mass efficiency (RME)

RME = mass of product /Σ (mass of stoichiometric reactants) × 100

$$\text{RME} = \frac{441.52}{476.43} \ X\ 100$$

= **92.67%** (Higher value measure the **cleanness** of reaction)

2.3.5. Eco-score (E-score)

Ideal reactions Eco-score value is 100.

Eco-scale from 0 to 100 using the following scores: > 75, excellent; > 50, acceptable; and < 50, inadequate.

E-score has been calculated for the reaction based on the following 6 parameters below.

S. No.	Parameter	Values	Penalty points
1	Yield	100-96.31/2	1.845
2	Price of the reaction component	Inexpensive	0.0
3	Safety (Reactant)	T(Toxic) = 5+5+5 = 15	15.0
4	Technical setup	Common setup	0.0
5	Temperature /time	heating/ <1h	2.0
6	Workup and purification	Crystallization	1.0
	Total penalty points		19.845
Based on the hazard warning symbols			

Eco-Score = 100 – the sum of individual penalties

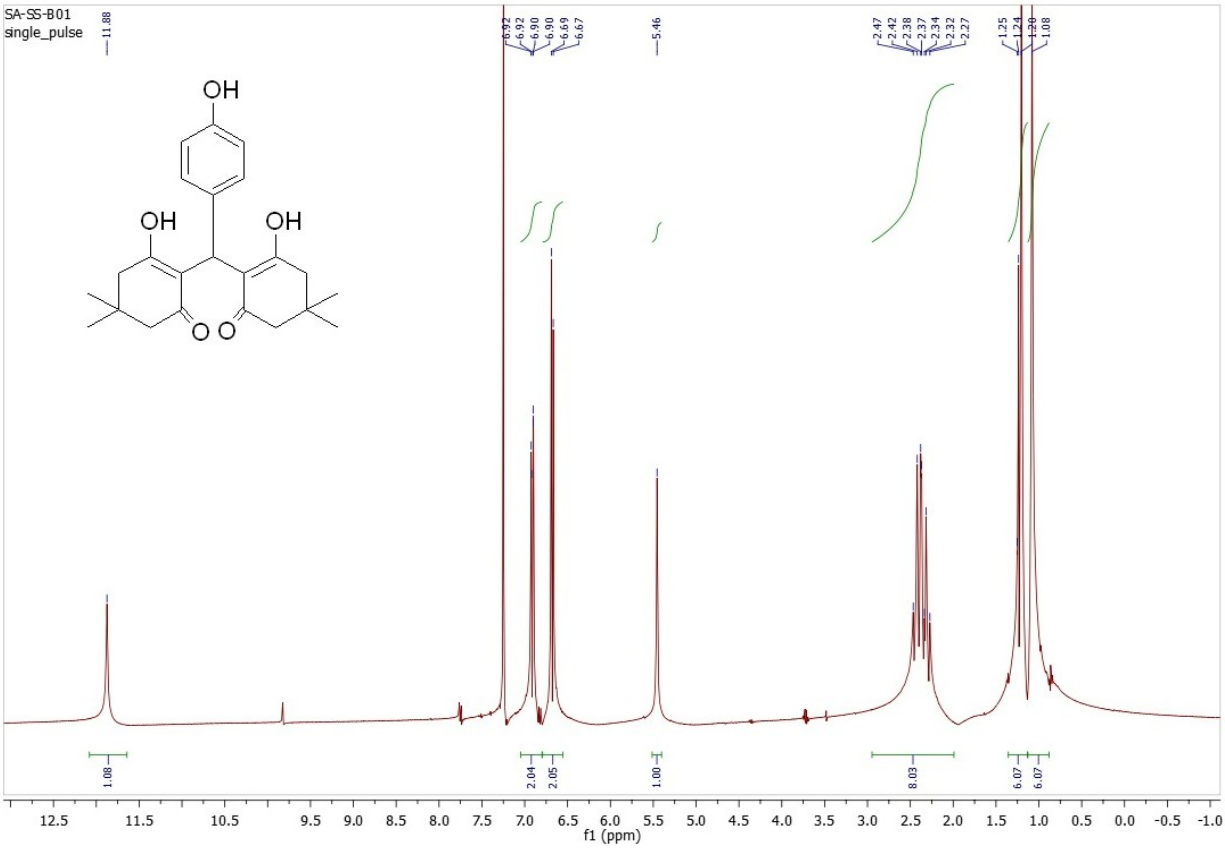
= 100 – 17.845 = 80.155 (>75, excellent synthesis)

As per the above results, it was concluded that the reaction has a low Environment-factor (E-factor = 0.07), high atom economy (AE = 96.21%), high process mass intensity (PMI = 1.08), and high reaction mass efficiency (RME = 92.67%), with excellent eco-score (80.155%). These values clearly indicated the eco-friendliness of the present synthesis.

3. Characterization of synthesized compounds:

2,2'-((4-hydroxyphenyl)methylene)bis(3-hydroxy-5,5-dimethylcyclohex-2-en-1-one) **(6a)**

Light yellow solid, yield 94%, m.p. 181-183 ^{o}C[73], ^{1}H NMR (400 MHz, $CDCl_3$): δ 11.88 (s, 1H, OH), 6.91 (dd, *J* = 9.0, 1.2 Hz, 2H, Ar-H), 6.68 (d, *J* = 8.9 Hz, 2H, Ar-H), 5.46 (s, 1H, CH), 2.47 – 2.27 (m, 8H, $4CH_2$), 1.25 – 1.20 (m, 6H, $2CH_3$), 1.08 (s, 6H, $2CH_3$). ^{13}C NMR (101 MHz, $CDCl_3$): δ 190.84, 189.70, 153.83, 129.66, 128.02, 115.88, 115.30, 47.09, 46.48, 32.09, 31.50, 31.49, 29.80, 29.76, 27.45; ESI–MS (m/z): 384.19 [M^+].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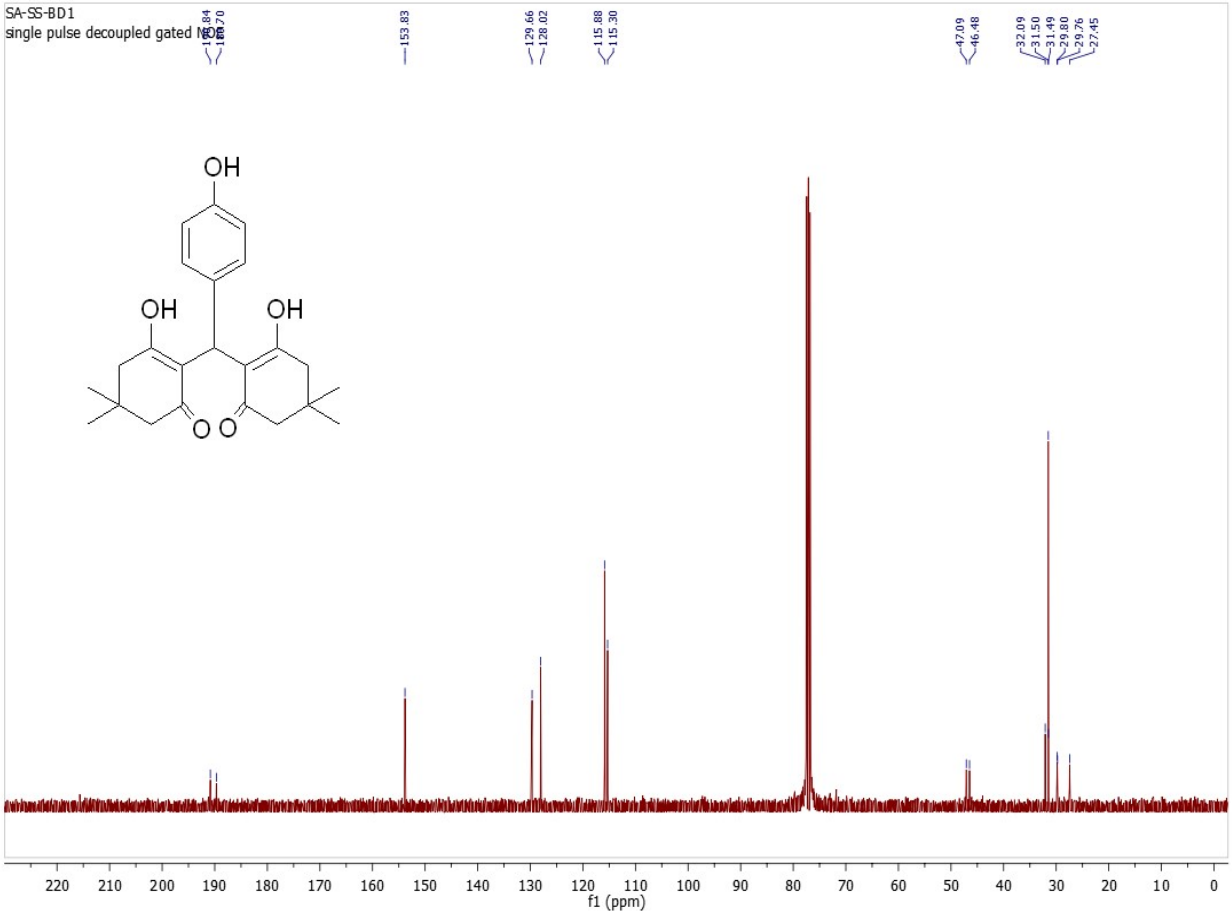
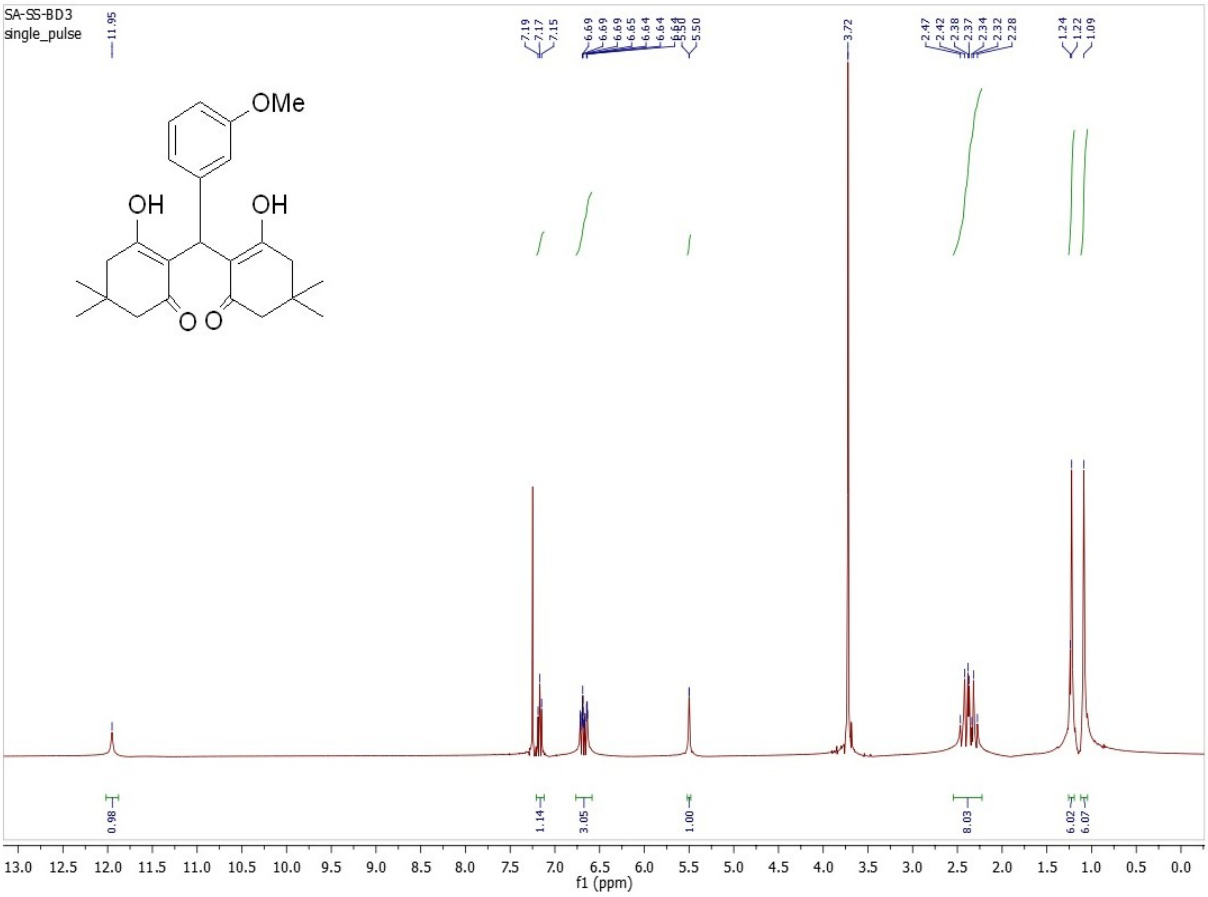
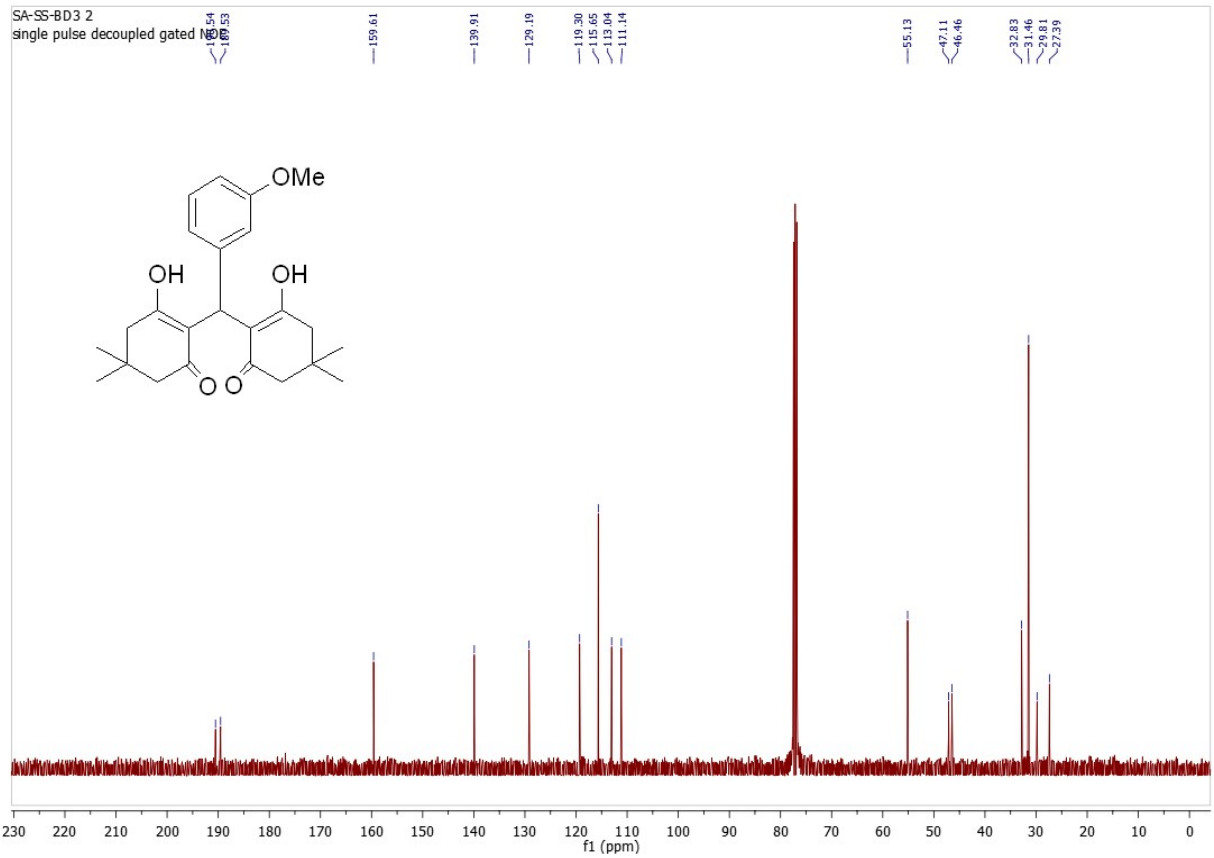
11.88
6.92
6.92
6.90
6.90
6.69
6.67
5.46
2.47
2.42
2.38
2.37
2.34
2.32
2.27
1.25
1.24
1.20
1.08
OH
OH
OH
O O
1.08
2.04
2.05
1.00
8.03
6.07
6.07
f1 (ppm)


SA-SS-BD1
single pulse decoupled gated NOE
153.83
129.66
128.02
115.88
115.30
47.09
46.48
32.09
31.50
31.49
29.80
29.76
27.45
OH
OH
OH
O O
f1 (ppm)

2,2'-((3-methoxyphenyl)methylene)bis(3-hydroxy-5,5-dimethylcyclohex-2-en-1-one) **(6b)**

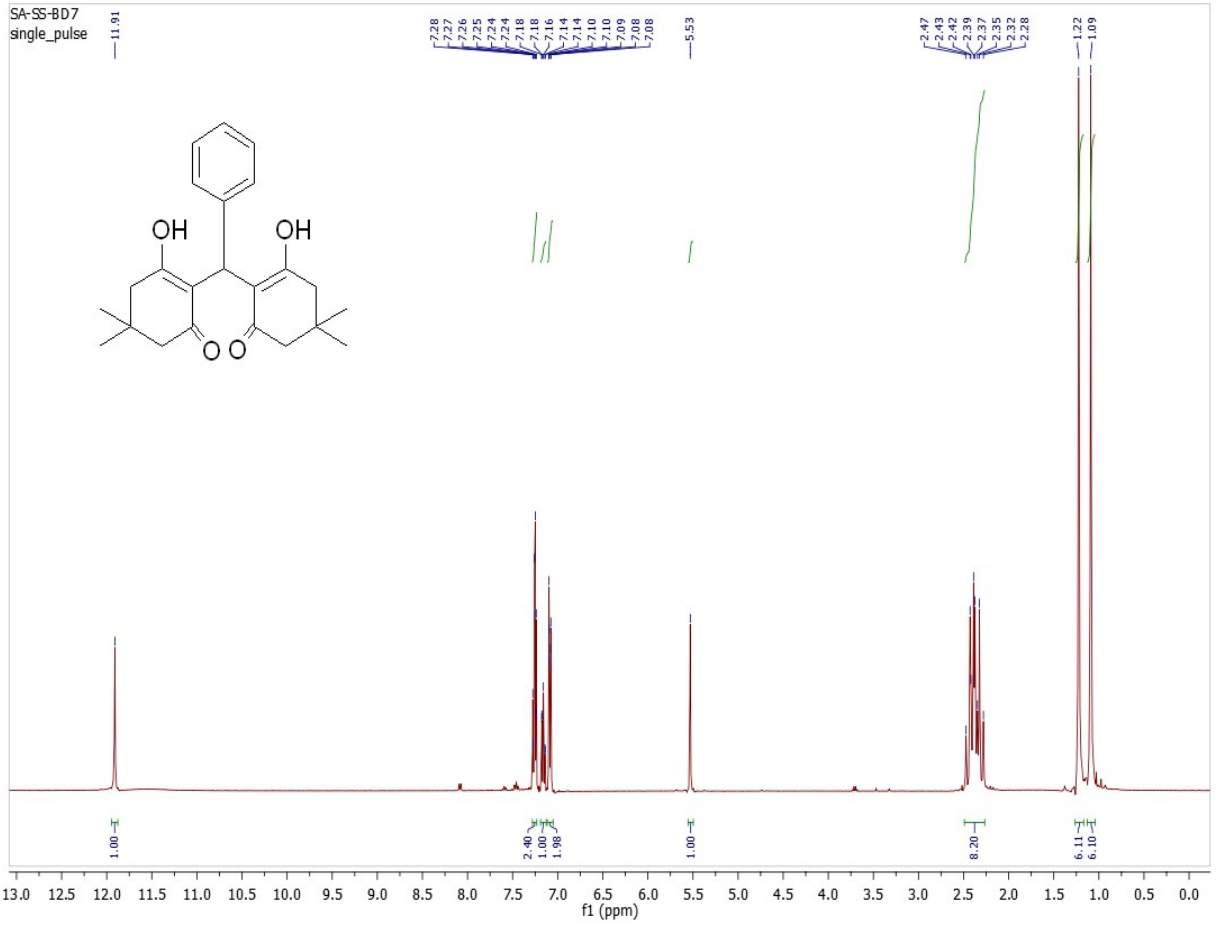
Off-white crystalline solid, yield: 78%, m.p. 194-196 ^{o}C[74], 1H NMR (400 MHz, $CDCl_3$): δ 11.95 (s, 1H, OH), 7.19-7.15 (t, *J* = 8.0 Hz, 1H, Ar-H), 6.72 – 6.63 (m, 3H, Ar-H), 5.50 (d, *J* = 1.0 Hz, IH, CH), 3.72 (s, 3H, OCH_3), 2.47 – 2.28 (m, 8H, $4CH_2$), 1.23 (d, *J* = 6.0 Hz, 6H, $2CH_3$), 1.09 (s, 6H, $2CH_3$). ^{13}C NMR (101 MHz, $CDCl_3$): δ 190.54, 189.53, 159.61, 139.91, 129.19, 119.30, 115.65, 113.04, 111.14, 55.13, 47.11, 46.46, 32.83, 31.46, 29.81, 27.39; ESI–MS (m/z): 398.21 [M^+].

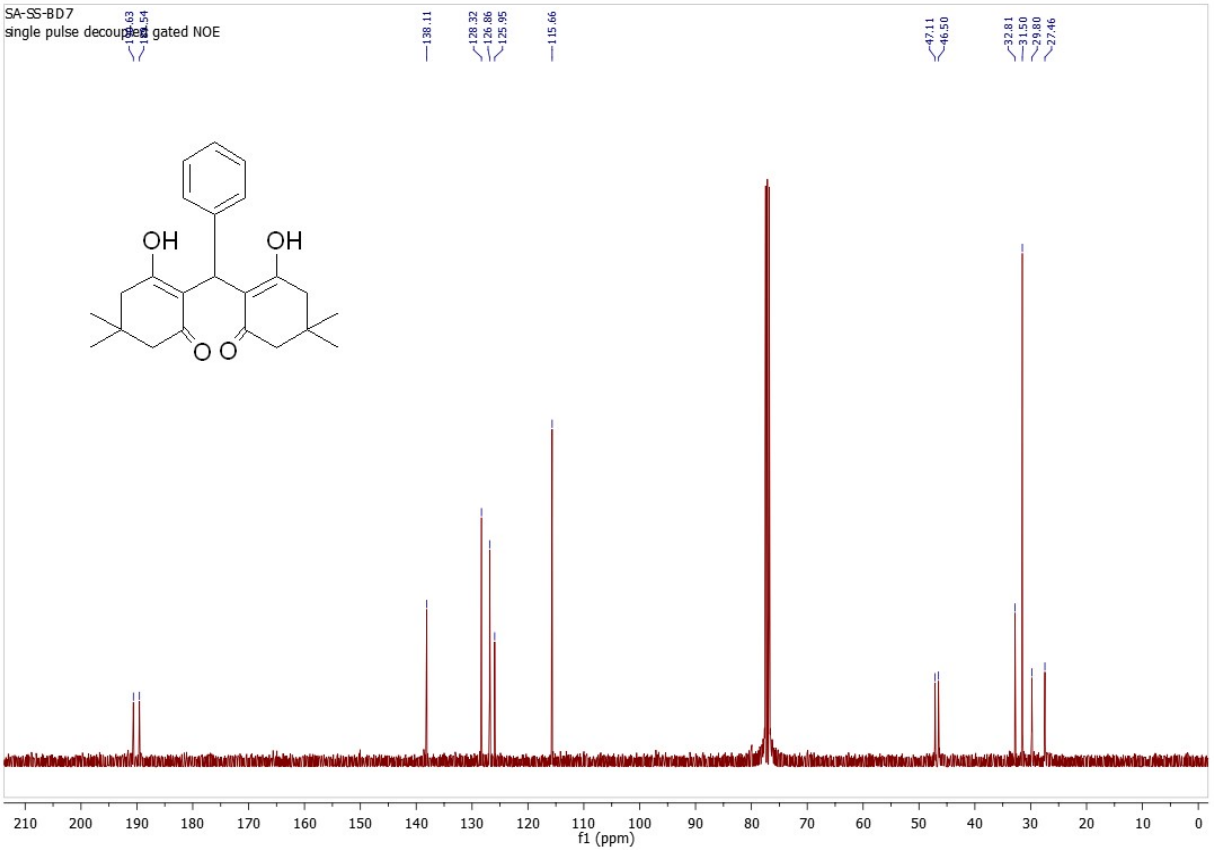




2,2'-(phenylmethylene)bis(3-hydroxy-5,5-dimethylcyclohex-2-en-1-one) **(6c)**

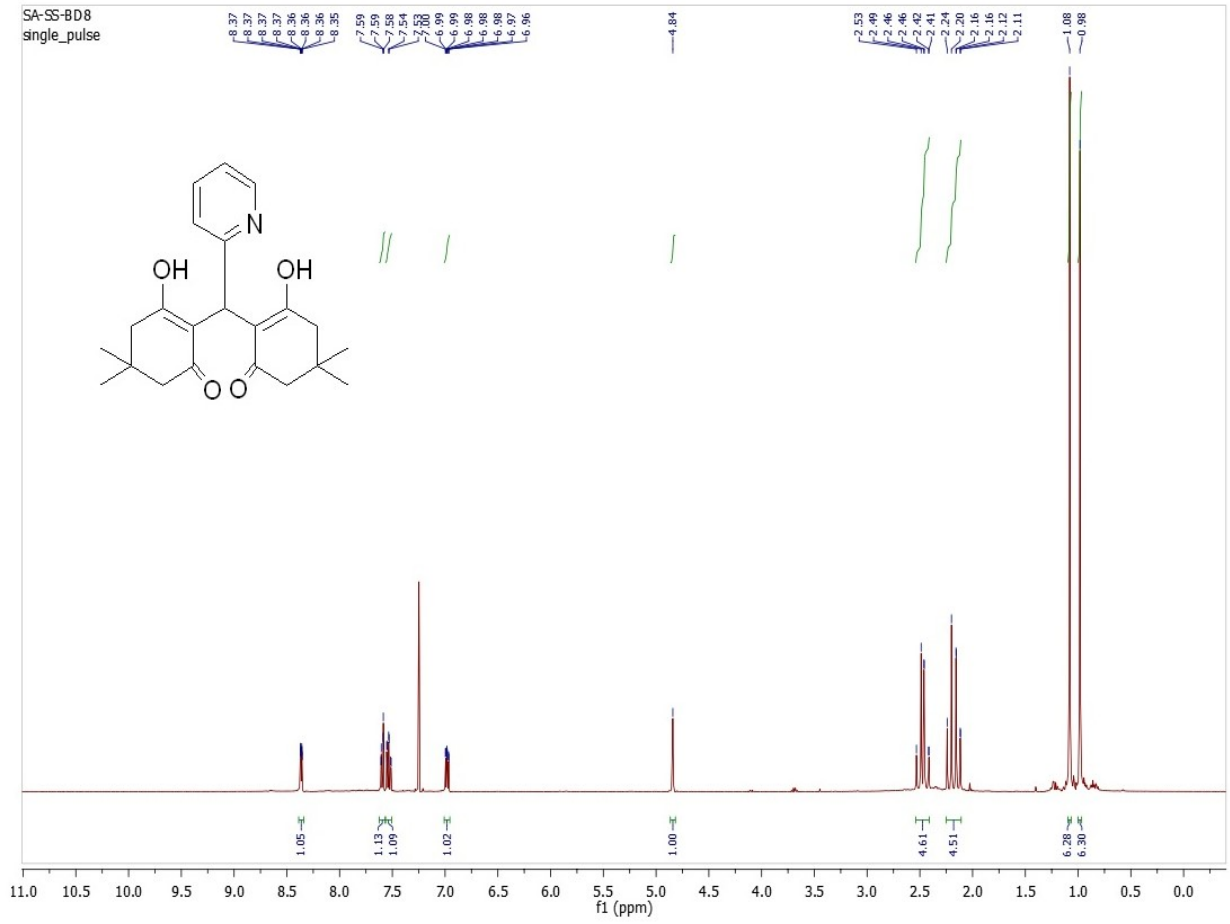
White solid, yield: 91% , m.p. 185-189 ^{o}C[73], ^{1}H NMR (400 MHz, $CDCl_3$): δ 11.91 (s, 1H, OH), 7.28 – 7.24 (m, 2H, Ar-H), 7.18 – 7.14 (m, 1H, Ar-H), 7.10 – 7.08 (m, 2H, Ar-H), 5.53 (s, 1H, CH), 2.38 (dq, J = 26.3, 17.7 Hz, 8H, $4CH_2$), 1.22 (s, 6H, $2CH_3$), 1.09 (s, 6H, $2CH_3$). ^{13}C NMR (101 MHz, $CDCl_3$): δ 190.63, 189.54, 138.11, 128.32, 126.86, 125.95, 115.66, 47.11, 46.50, 32.81, 31.50, 29.80, 27.46; ESI–MS (m/z): 368.20 [M^+].

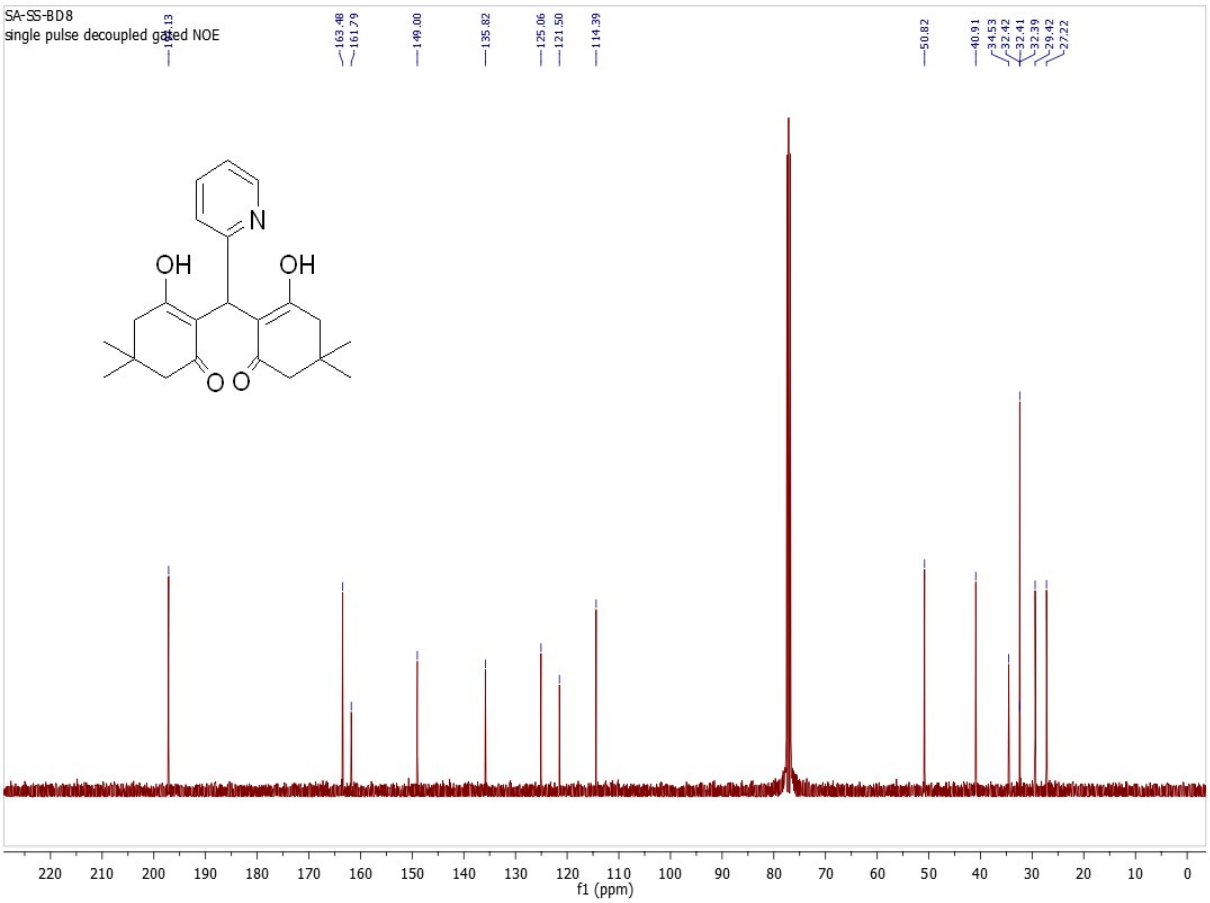

SA-SS-BD7
single_pulse
11.91
7.28
7.27
7.26
7.25
7.24
7.24
7.18
7.16
7.14
7.14
7.10
7.09
7.08
7.08
5.53
2.47
2.43
2.42
2.39
2.37
2.35
2.32
2.28
1.22
1.09
OH
OH
O O
1.00
2.40
1.00
1.98
1.00
8.20
6.11
6.10
13.0 12.5 12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


SA-SS-BD7
single pulse decoupled gated NOE
138.11
128.32
126.86
125.95
115.66
47.11
46.50
32.81
31.50
29.80
27.46
OH
OH
O O
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

2,2'-(pyridin-2-ylmethylene)bis(3-hydroxy-5,5-dimethylcyclohex-2-en-1-one) **(6d)**

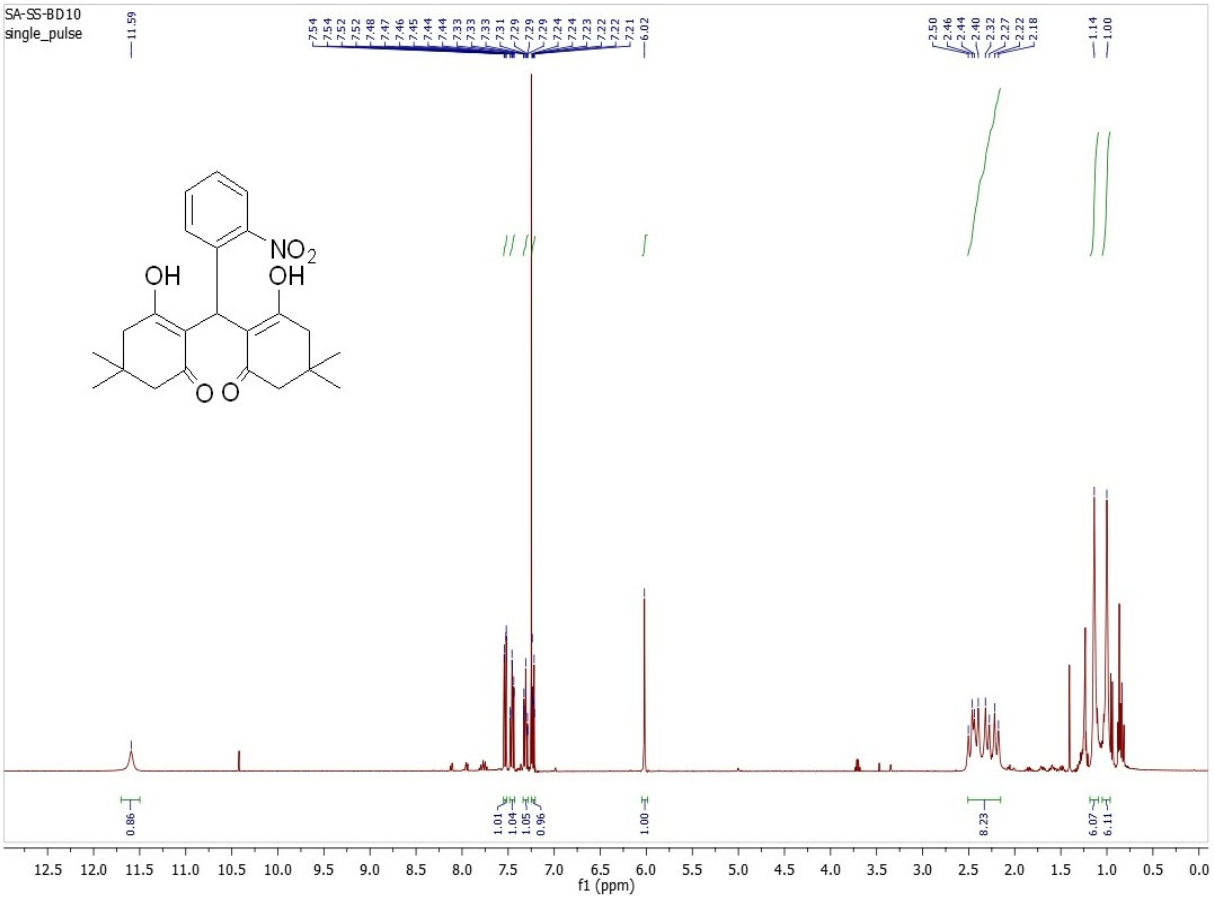
Brownish black solid, yield: 75%, m.p. 146-149 ^{o}C[75], ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.37-8.35 (ddd, *J* = 4.8, 1.7, 0.9 Hz, 1H, Ar-H), 7.59 (dt, *J* = 7.8, 1.1 Hz, 1H, Ar-H), 7.54 (td, *J* = 7.6, 1.8 Hz, 1H, Ar-H), 7.00-6.96 (ddd, *J* = 7.3, 4.9, 1.3 Hz, 1H, Ar-H), 4.84 (s, 1H, CH), 2.53 – 2.41 (m, 4H, $2CH_2$), 2.24-2.11 (dt, *J* = 16.2, 8.6 Hz, 4H, $2CH_2$), 1.08 (s, 6H, $2CH_3$), 0.98 (s, 6H, $2CH_3$). ^{13}C NMR (101 MHz, $CDCl_3$): δ 197.13, 163.48, 161.79, 149.00, 135.82, 125.06, 121.50, 114.39, 50.82, 40.91, 34.53, 32.42, 32.41, 32.39, 29.42, 27.22; ESI–MS (m/z): 369.19 [M^+].





2,2'-((2-nitrophenyl)methylene)bis(3-hydroxy-5,5-dimethylcyclohex-2-en-1-one) **(6e)**

Yellow crystalline solid, yield: 83%, m.p. 187-190 ^{o}C[73], ^{1}H NMR (400 MHz, $CDCl_3$): δ 11.59 (s, 1H, OH), 7.54-7.52 (dd, *J* = 7.9, 1.4 Hz, 1H, Ar-H), 7.48-7.44 (td, *J* = 7.7, 1.5 Hz, 1H, Ar-H), 7.33 – 7.29 (m, 1H, Ar-H), 7.24-7.21 (dt, *J* = 7.9, 1.2 Hz, 1H, Ar-H), 6.02 (s, 1H, CH), 2.50-2.18 (ddd, *J* = 56.8, 33.0, 17.1 Hz, 8H, $4CH_2$), 1.14 (s, 6H, $2CH_3$), 1.00 (s, 6H, $2CH_3$). ^{13}C NMR (101 MHz, $CDCl_3$): δ 149.76, 132.17, 131.47, 129.67, 127.27, 124.43, 114.72, 47.03, 46.91, 46.34, 46.21, 31.99, 30.11, 28.77, 28.63, 28.25, 28.16; ESI–MS (m/z): 413.18 [M^+].


SA-SS-BD10
single_pulse
11.59
7.54
7.54
7.52
7.52
7.48
7.47
7.46
7.45
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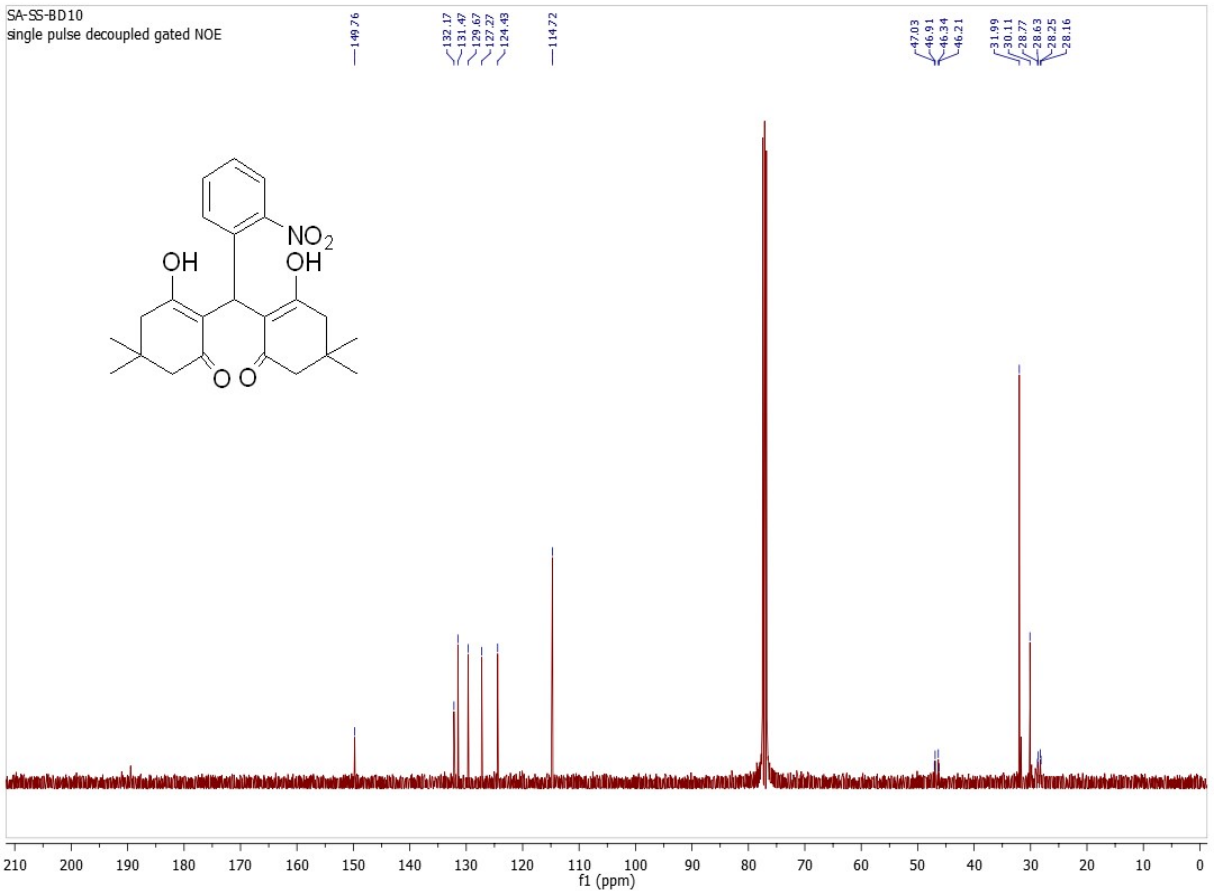
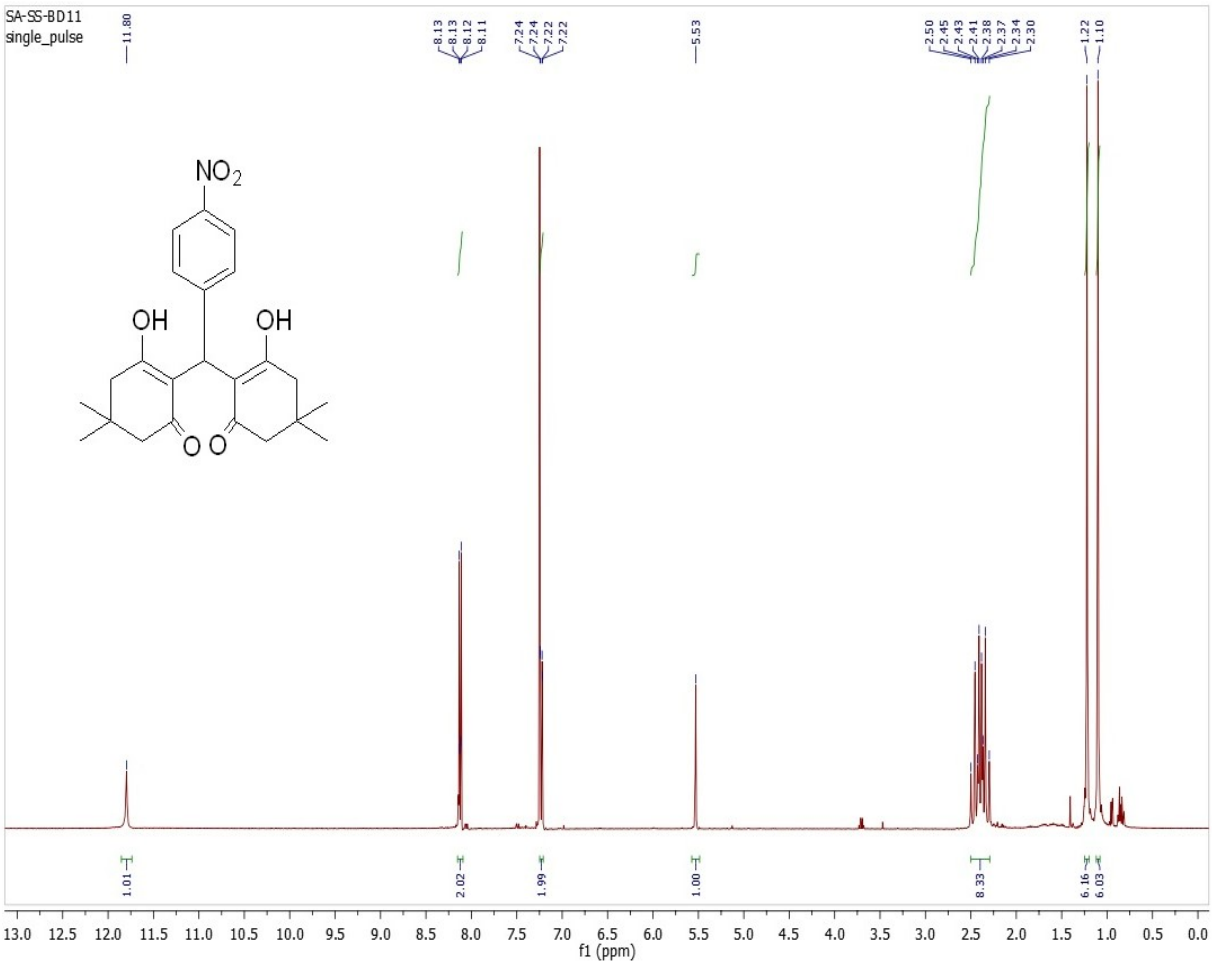
7.44
7.33
7.33
7.31
7.29
7.29
7.29
7.24
7.24
7.23
7.22
7.22
7.21
6.02
2.50
2.46
2.44
2.40
2.32
2.27
2.22
2.18
1.14
1.00
NO2
OH
OH
O O
0.86
1.01
1.04
1.05
0.96
1.00
8.23
6.07
6.11
f1 (ppm)


SA-SS-BD10
single pulse decoupled gated NOE
149.76
132.17
131.47
129.67
127.27
124.43
114.72
47.03
46.91
46.34
46.21
31.99
30.11
28.77
28.63
28.25
28.16
NO2
OH
OH
O O
f1 (ppm)

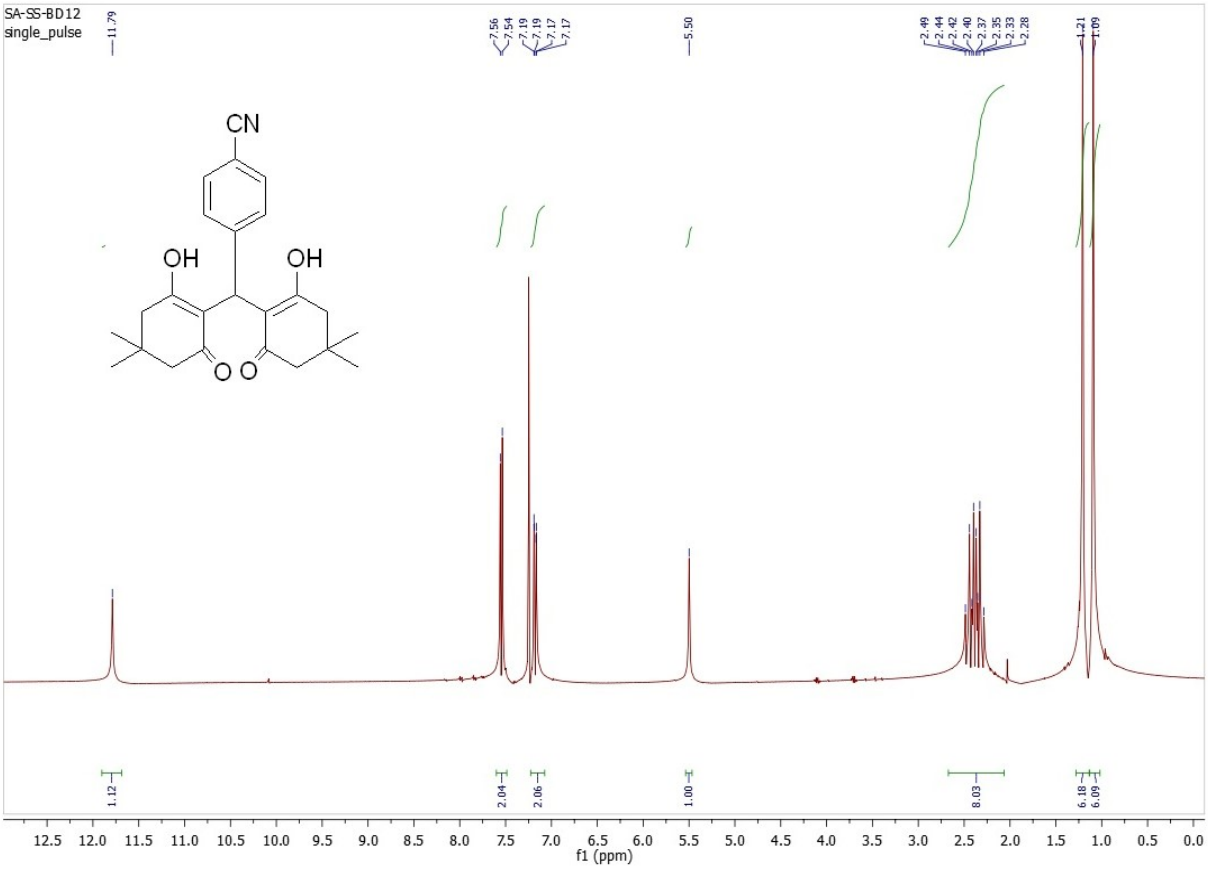
2,2'-((4-nitrophenyl)methylene)bis(3-hydroxy-5,5-dimethylcyclohex-2-en-1-one) **(6f)**

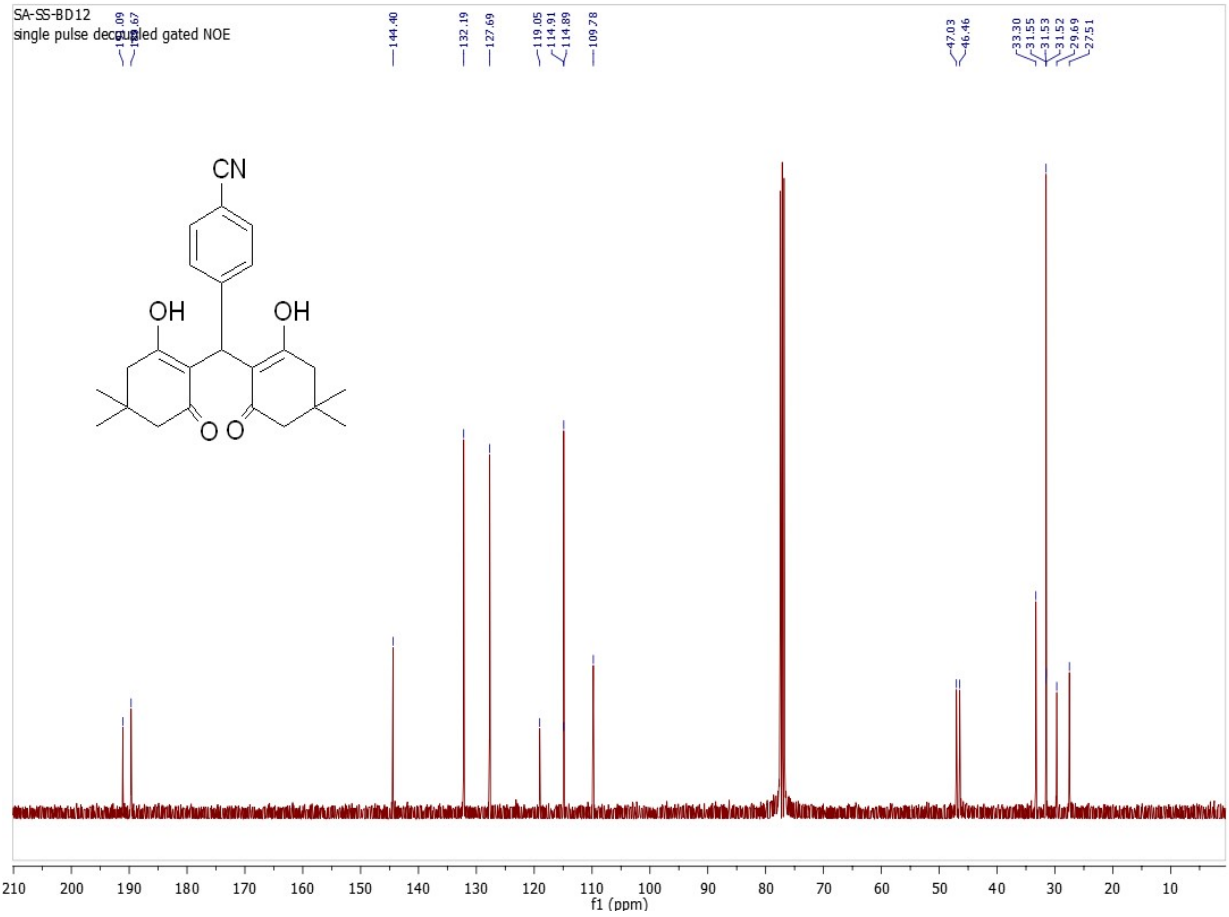
Dark yellow crystals, yield: 91%, m.p. 193-195 ^{o}C[33], ^{1}H NMR (400 MHz, $CDCl_3$): δ 11.80 (s, 1H, OH), 8.13 – 8.11 (m, 2H, Ar-H), 7.24-7.22 (dd, *J* = 9.0, 1.2 Hz, 2H, Ar-H), 5.53 (s, 1H, CH), 2.50-2.30 (dq, *J* = 27.6, 17.7 Hz, 8H, $4CH_2$), 1.22 (s, 6H, $2CH_3$), 1.10 (s, 6H, $2CH_3$); ESI–MS (m/z): 413.18 [M^+].



4-(bis(2-hydroxy-4,4-dimethyl-6-oxocyclohex-1-en-1-yl)methyl)benzonitrile **(6g)**

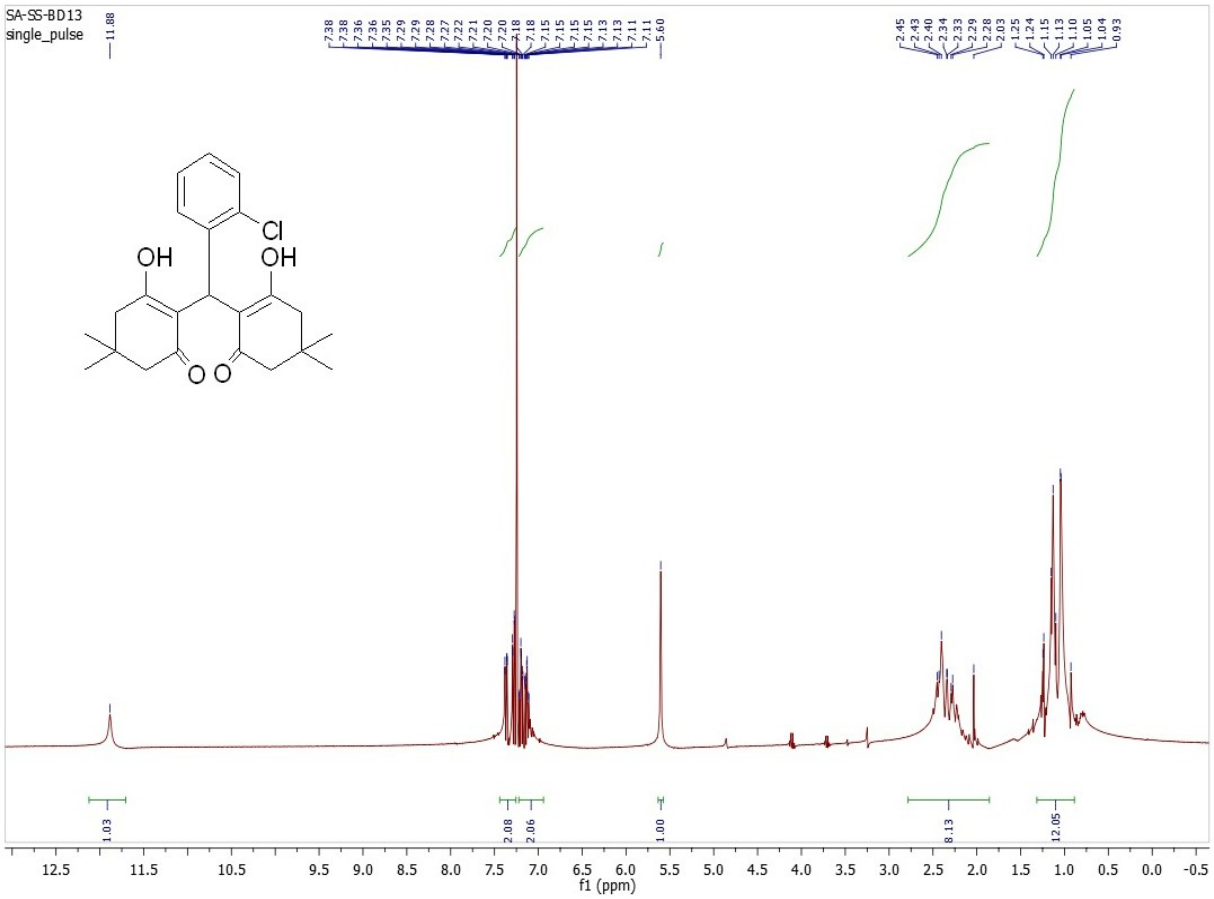
Light yellow solid, yield: 87%,m.p. 195-199 ^{o}C[33], ^{1}H NMR (400 MHz, $CDCl_3$): δ 11.79 (s, 1H, OH), 7.56-7.54 (d, *J* = 8.8 Hz, 2H, Ar-H), 7.17-7.19 (dd, *J* = 8.8, 1.3 Hz, 2H, Ar-H), 5.50 (s, 1H, CH), 2.49-2.28 (ddd, *J* = 33.7, 28.0, 17.9 Hz, 8H, $4CH_2$), 1.21 (s, 6H, $2CH_3$), 1.09 (s, 6H, $2CH_3$). ^{13}C NMR (101 MHz, $CDCl_3$) δ 191.09, 189.67, 144.40, 132.19, 127.69, 119.05, 114.91, 109.78, 47.03, 46.46, 33.30, 31.55, 31.52, 31.52, 29.69, 27.51; ESI–MS (m/z): 393.19 [M^+].

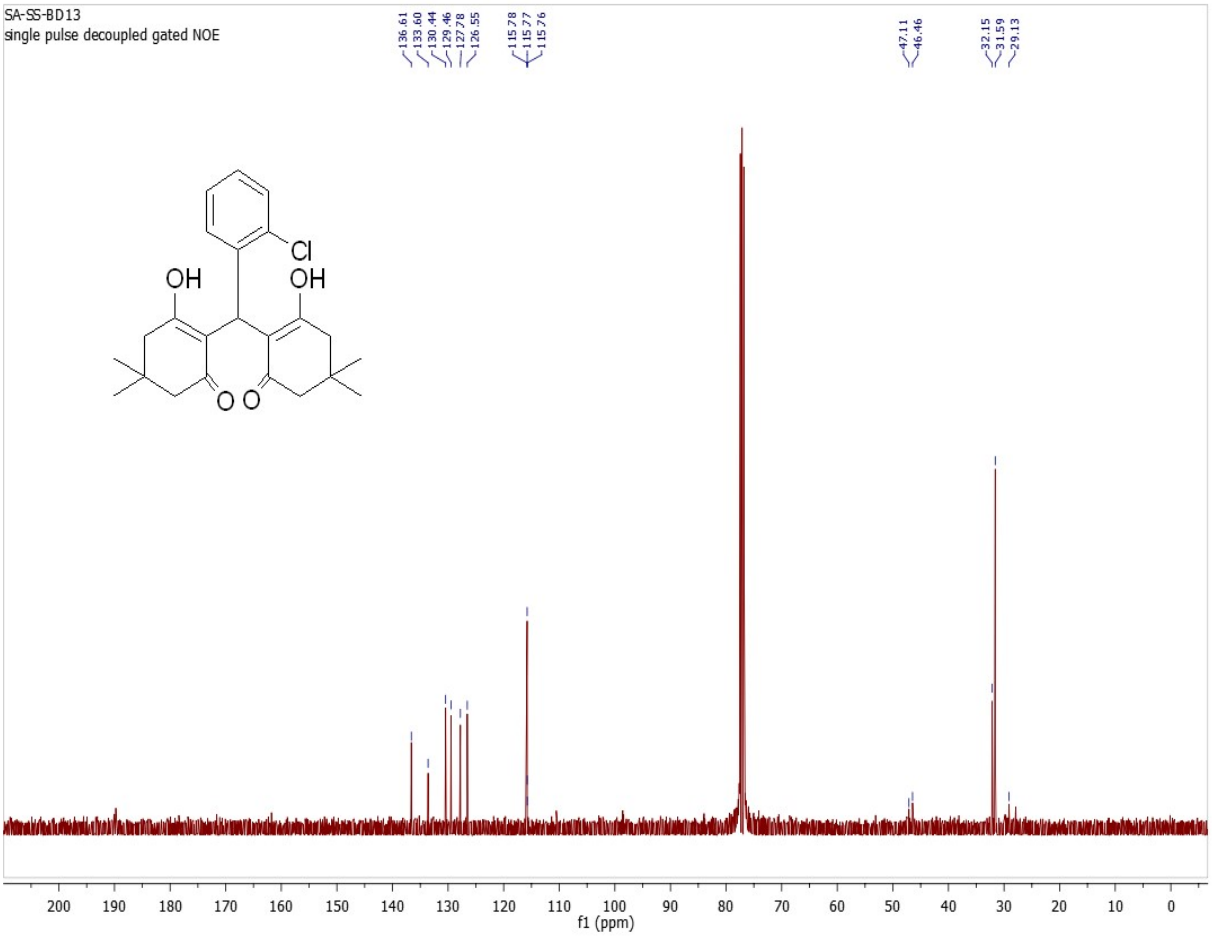

SA-SS-BD12
single_pulse
CN
OH
OH
O O
f1 (ppm)


SA-SS-BD12
single pulse decoupled gated NOE
CN
OH
OH
O O
f1 (ppm)

2,2'-((2-chlorophenyl)methylene)bis(3-hydroxy-5,5-dimethylcyclohex-2-en-1-one) **(6h)**

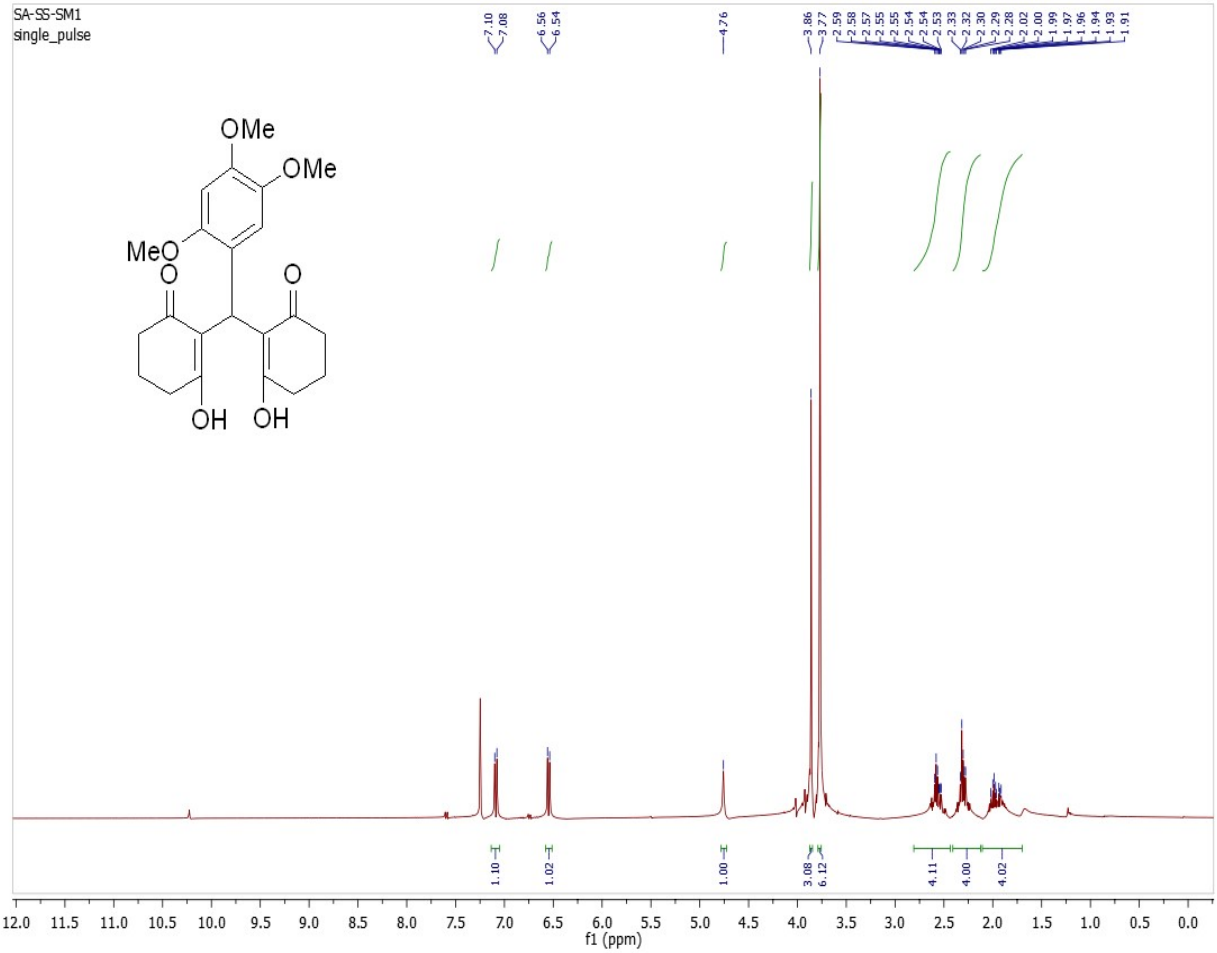
Off-white crystalline solid, yield: 78%, m.p. 205-207 ^{o}C[73], ^{1}H NMR (400 MHz, $CDCl_3$): δ 11.88 (s, 1H, OH), 7.38 – 7.27 (m, 2H, Ar-H), 7.22 – 7.11 (m, 2H, Ar-H), 5.60 (s, 1H, CH), 2.45-2.03 (ddd, *J* = 120.2, 61.5, 52.6 Hz, 8H, $4CH_2$), 1.25 – 0.93 (m, 12H, $4CH_3$). ^{13}C NMR (101 MHz, $CDCl_3$): δ 136.61, 133.60, 130.44, 129.46, 127.78, 126.55, 115.78, 115.77, 115.76, 47.11, 46.46, 32.15, 31.59, 29.13; ESI–MS (m/z): 402.16 [M^+].

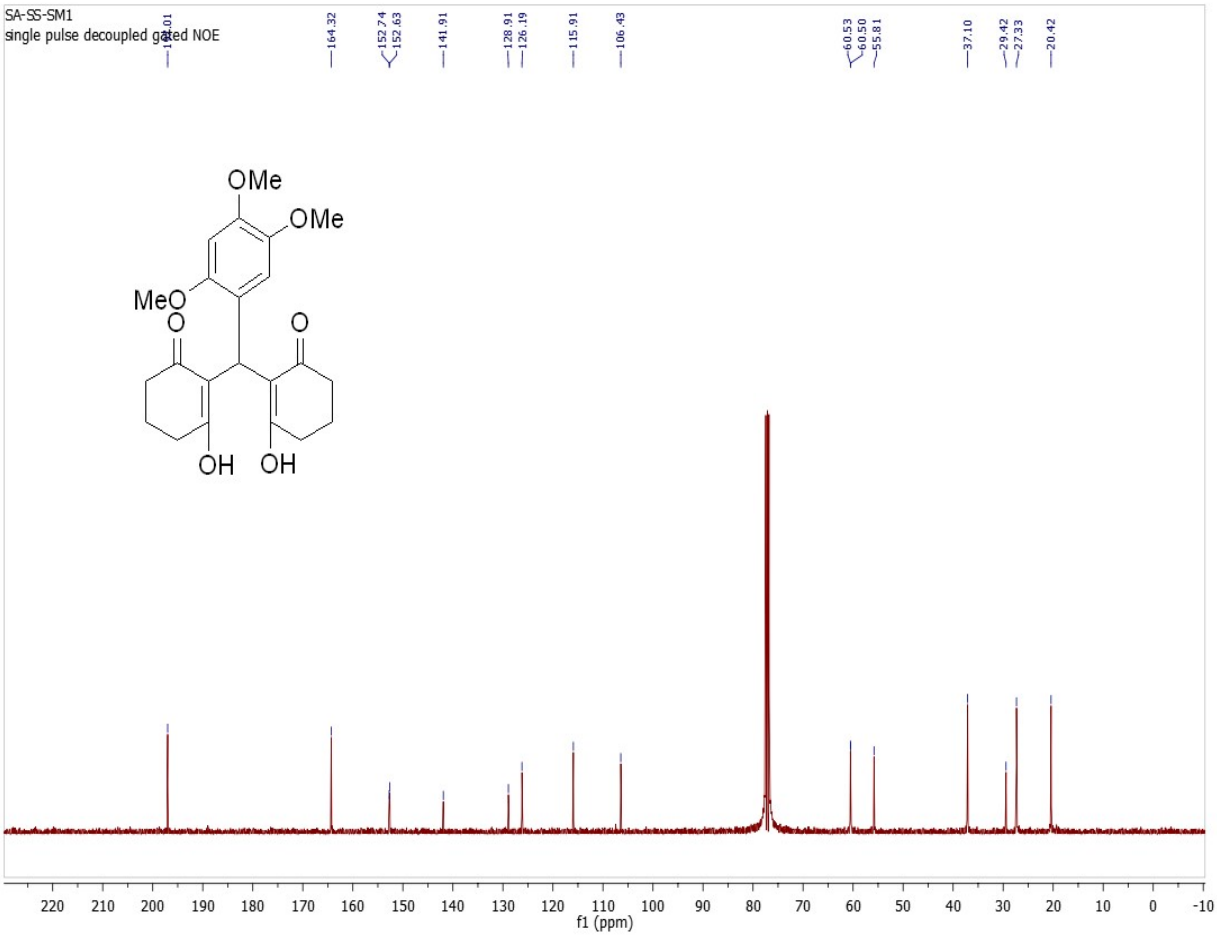




2,2'-((2,4,5-trimethoxyphenyl)methylene)bis(3-hydroxycyclohex-2-en-1-one) **(7a)**

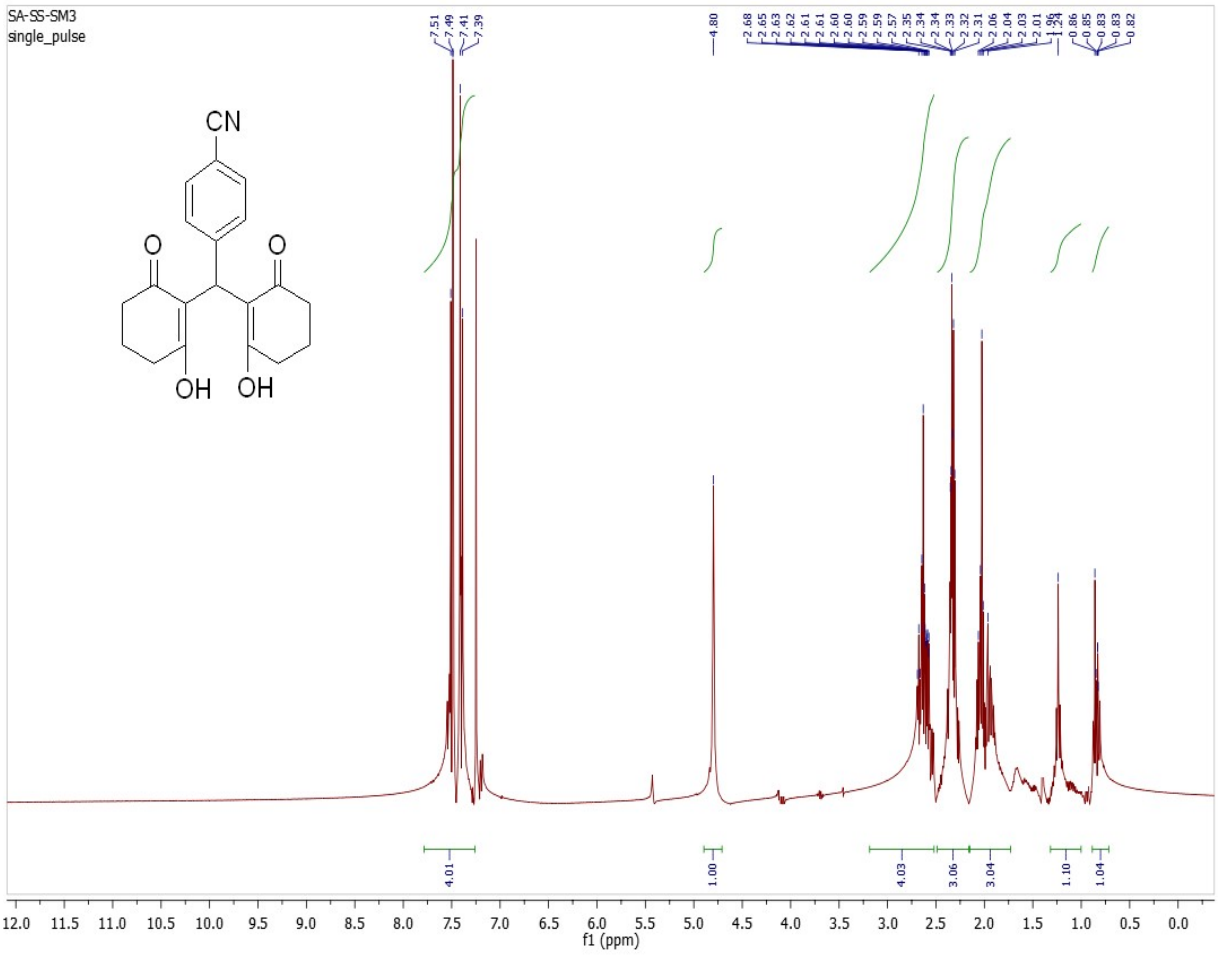
Light yellow crystals, yield: 97%, m.p. 168-171 ^{o}C, ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.10-7.08 (d, J = 8.8 Hz, 1H, Ar-H), 6.56-6.54 (d, J = 8.8 Hz, 1H, Ar-H), 4.76 (s, 1H, CH), 3.86 (s, 3H, OCH_3), 3.77 (s, 6H, $2OCH_3$), 2.59 – 2.53 (m, 4H, $2CH_2$), 2.33 – 2.28 (m, 4H, $2CH_2$), 2.02-1.91 (ddd, J = 19.0, 11.5, 7.0 Hz, 4H, $2CH_2$). ^{13}C NMR (101 MHz, $CDCl_3$): δ 197.01, 164.32, 152.74, 152.63, 141.91, 128.91, 126.19, 115.91, 106.43, 60.53, 60.50, 55.81, 37.10, 29.42, 27.33, 20.42; ESI–MS (m/z): 402.17 [M^+].

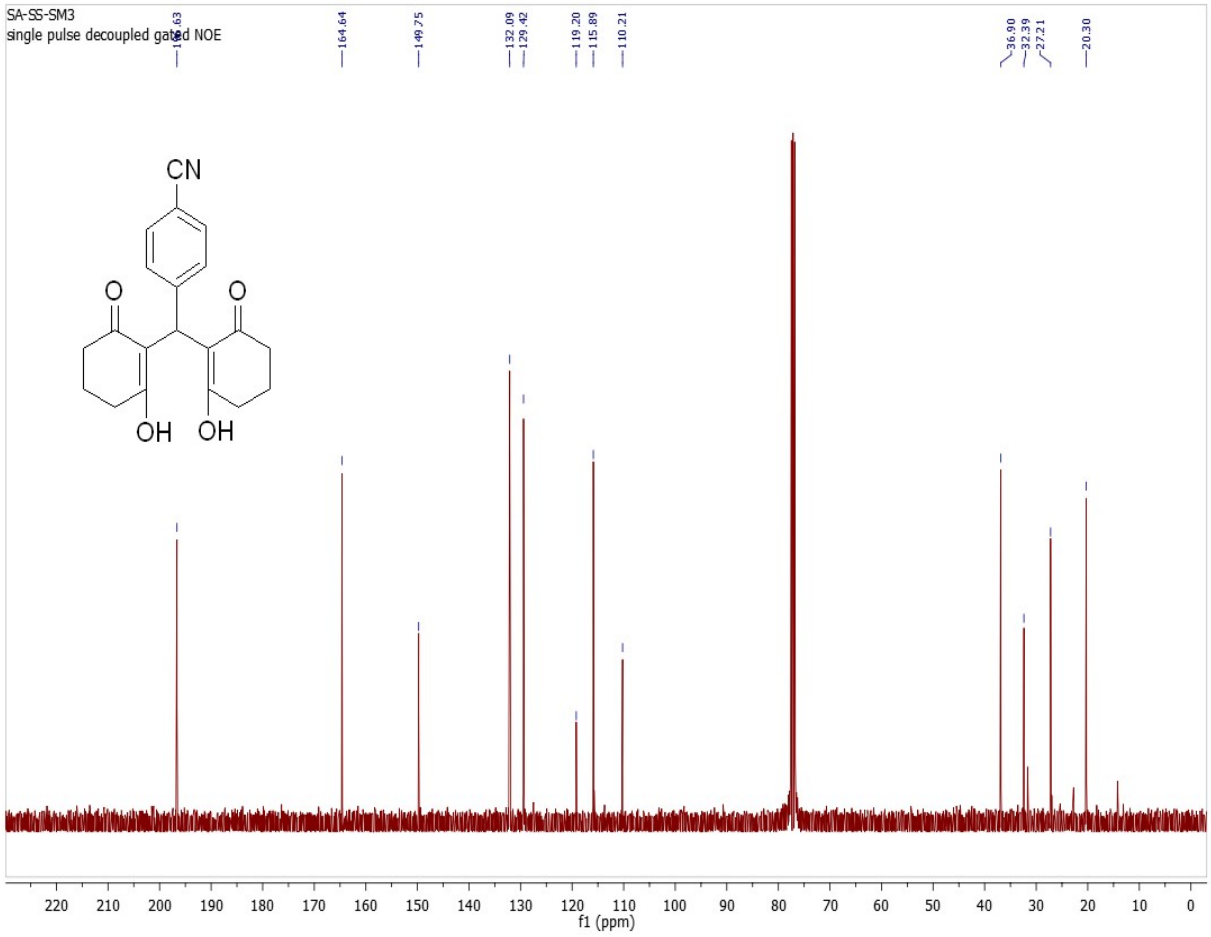

SA-SS-SM1
single_pulse
OMe
OMe
MeO
O
O
OH
OH
f1 (ppm)


SA-SS-SM1
single pulse decoupled gated NOE
OMe
OMe
MeO
O
O
OH
OH
f1 (ppm)

4-(bis(2-hydroxy-6-oxocyclohex-1-en-1-yl)methyl)benzonitrile **(7b)**

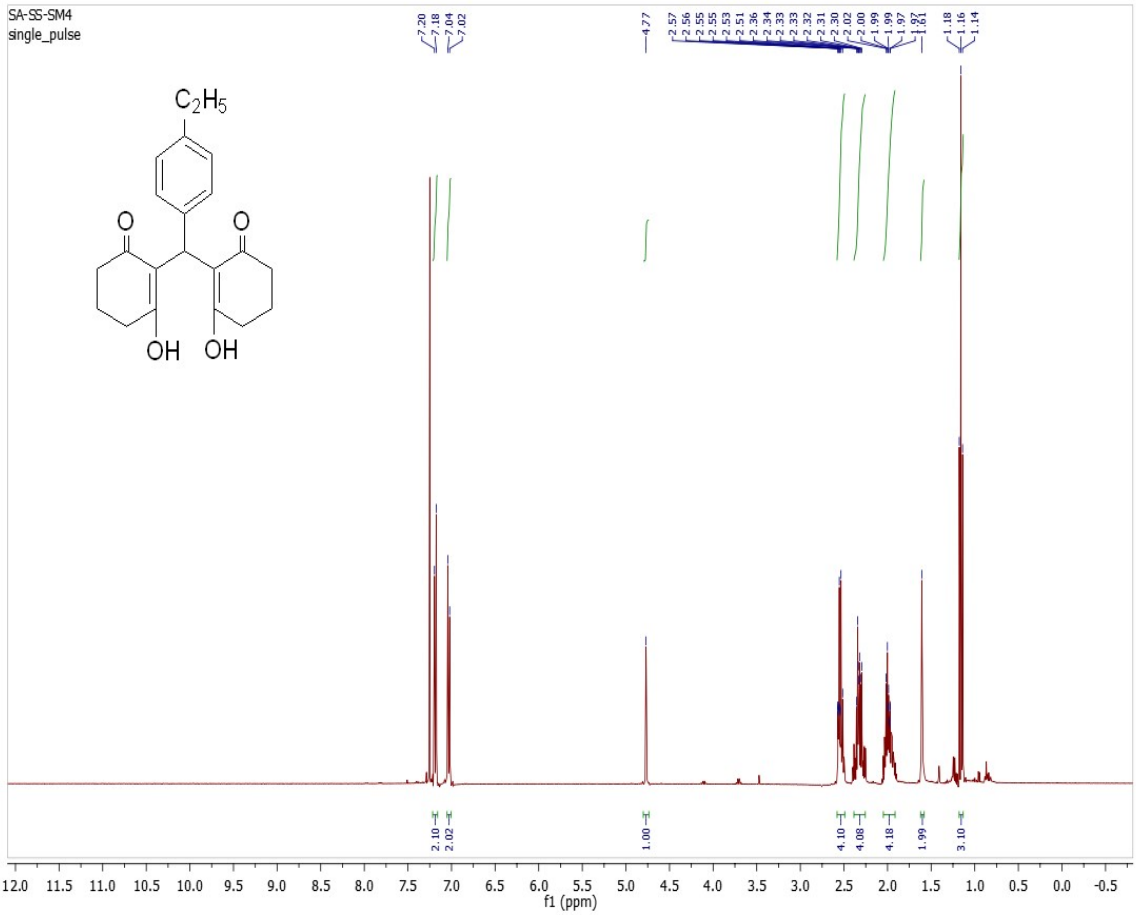
Milky white solid, yield: 82%, m.p. 256-260 ^{o}C, ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.51-7.39 (dd, *J* = 38.8, 8.7 Hz, 4H, Ar-H), 4.80 (s, 1H, CH), 2.65 – 2.62 (m, 4H, $2CH_2$), 2.35 – 2.31 (m, 3H, CH_2), 2.04 – 1.96 (m, 3H, CH_2), 1.24 (s, 1H, CH_2), 0.86 – 0.82 (m, 1H, CH_2). ^{13}C NMR (101 MHz, $CDCl_3$): δ 196.63, 164.64, 149.75, 132.09, 129.42, 119.20, 115.89, 110.21, 36.90, 32.39, 27.21, 20.30; ESI–MS (m/z): 337.13 [M^+].

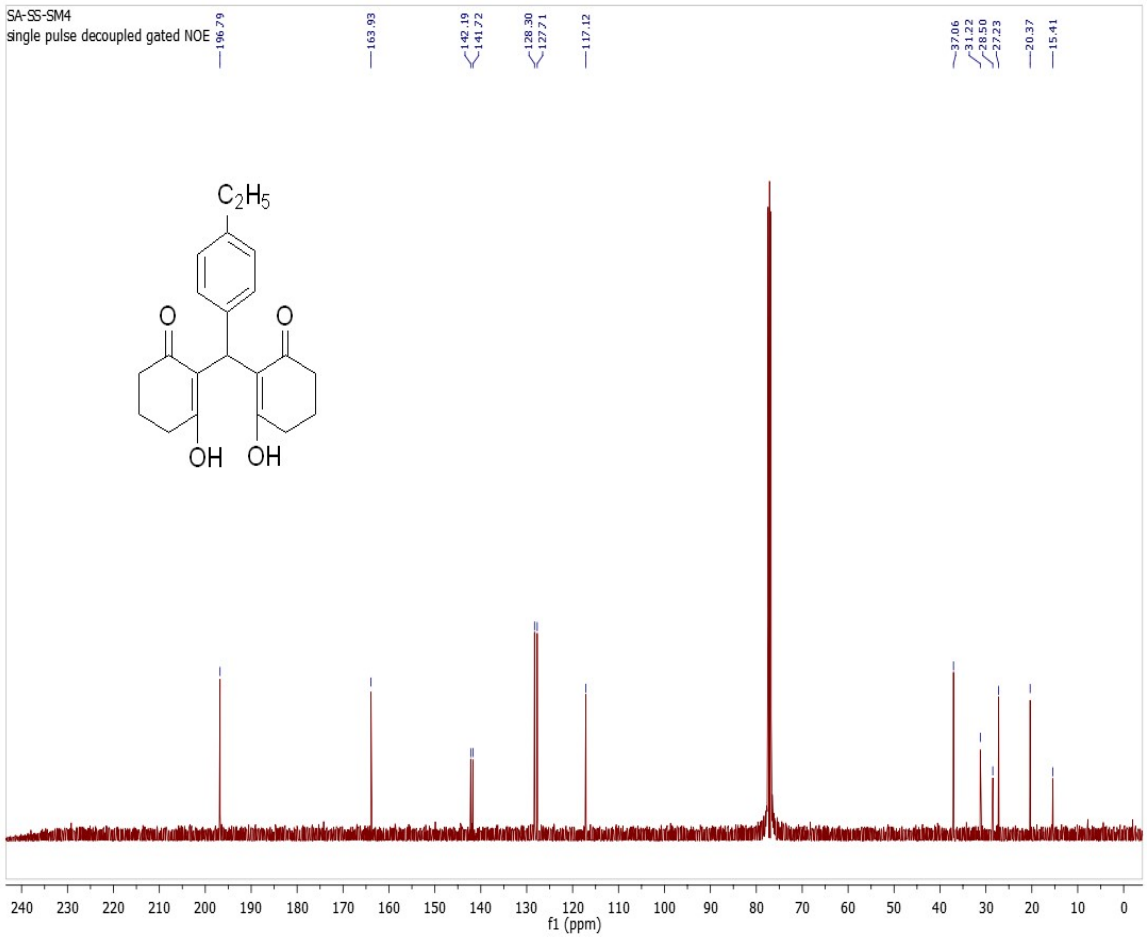




2,2'-((4-ethylphenyl)methylene)bis(3-hydroxycyclohex-2-en-1-one) **(7c)**

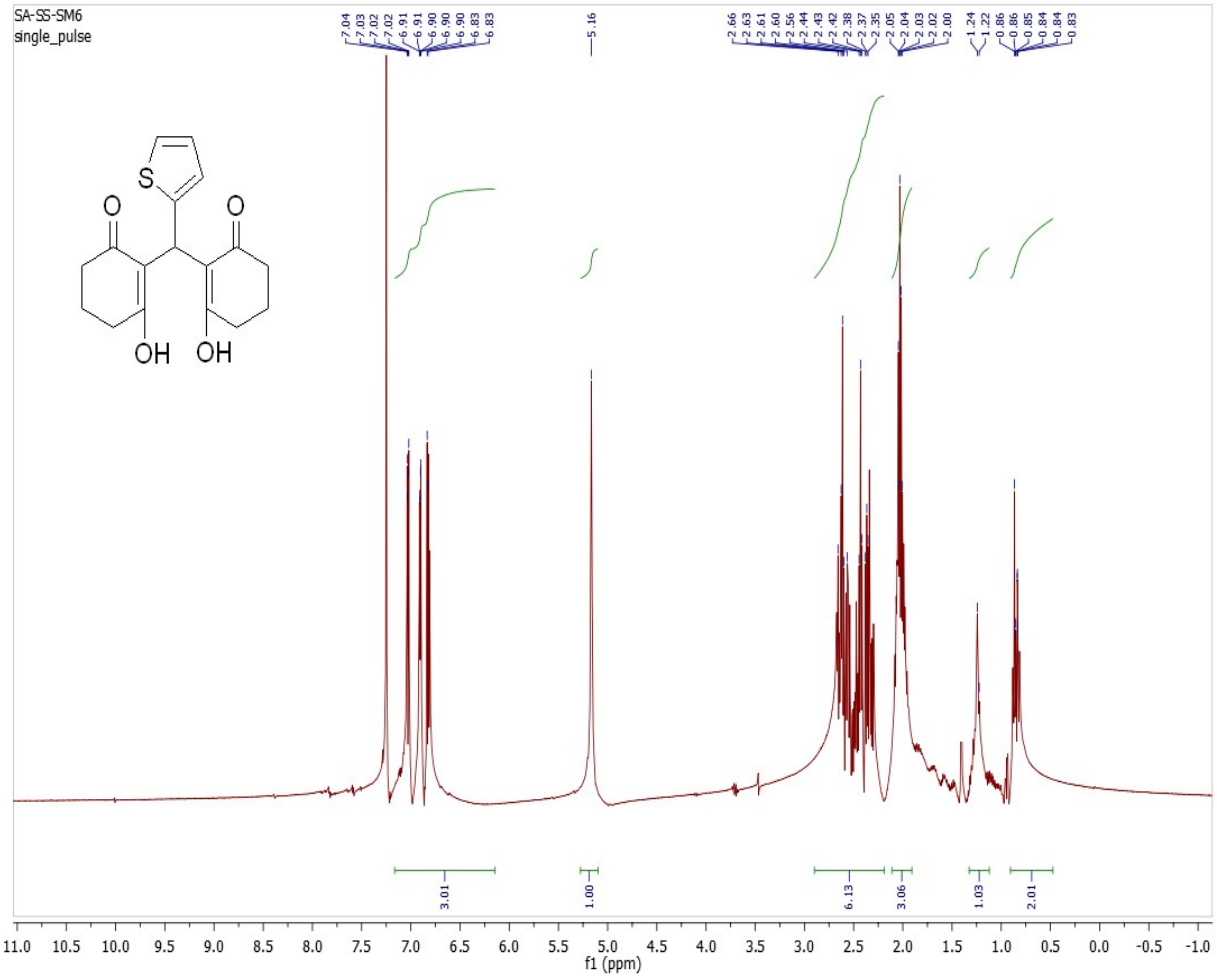
Cream solid, yield: 93%, m.p. 164-166 ^{o}C, ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.20-7.18 (d, J = 8.1 Hz, 2H, Ar-H), 7.04-7.02 (d, J = 8.2 Hz, 2H, Ar-H), 4.77 (s, 1H, CH), 2.57 – 2.51 (m, 4H, $2CH_2$), 2.36 – 2.30 (m, 4H, $2CH_2$), 2.02-1.97 (ddd, J = 7.0, 6.4, 3.2 Hz, 4H, $2CH_2$), 1.61 (s, 2H, CH_2), 1.18-1.14 (t, J = 7.6 Hz, 3H, CH_3). ^{13}C NMR (101 MHz, $CDCl_3$): δ 196.79, 163.93, 142.19, 141.72, 128.30, 127.71, 117.12, 37.06, 31.22, 28.50, 27.23, 20.37, 15.41; ESI–MS (m/z): 340.17 [M^+].

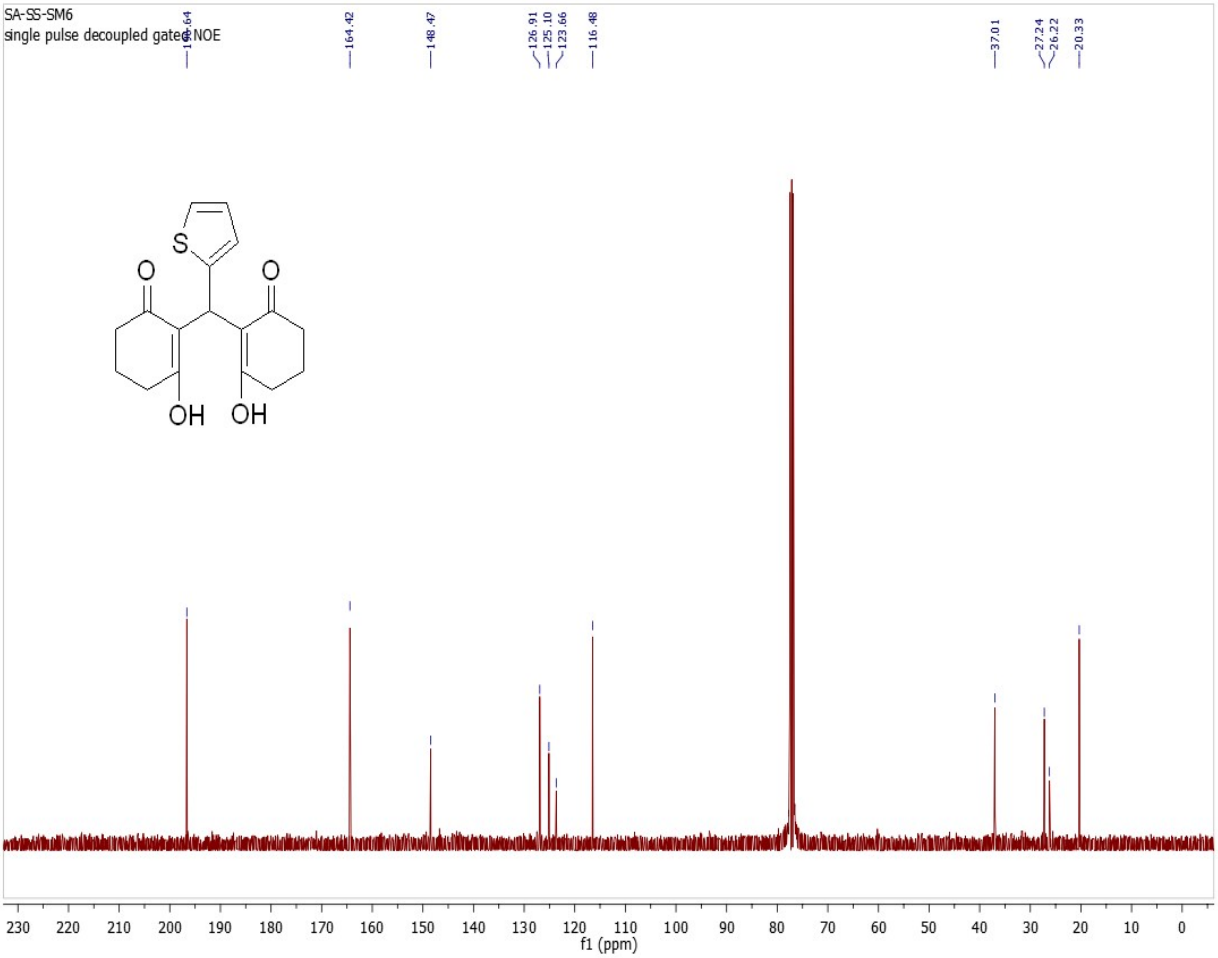

SA-SS-SM4
single_pulse
7.20
7.18
7.04
7.02
4.77
2.57
2.56
2.55
2.55
2.53
2.51
2.36
2.34
2.33
2.33
2.32
2.31
2.30
2.02
2.00
1.99
1.99
1.97
1.97
1.81
1.18
1.16
1.14
C2H5
O
O
OH
OH
2.10
2.02
1.00
4.10
4.08
4.18
1.99
3.10
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)


SA-SS-SM4
single pulse decoupled gated NOE
196.79
163.93
142.19
141.72
128.30
127.71
117.12
37.06
31.22
28.50
27.23
20.37
15.41
C2H5
O
O
OH
OH
240 230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

2,2'-(thiophen-2-ylmethylene)bis(3-hydroxycyclohex-2-en-1-one) **(7d)**

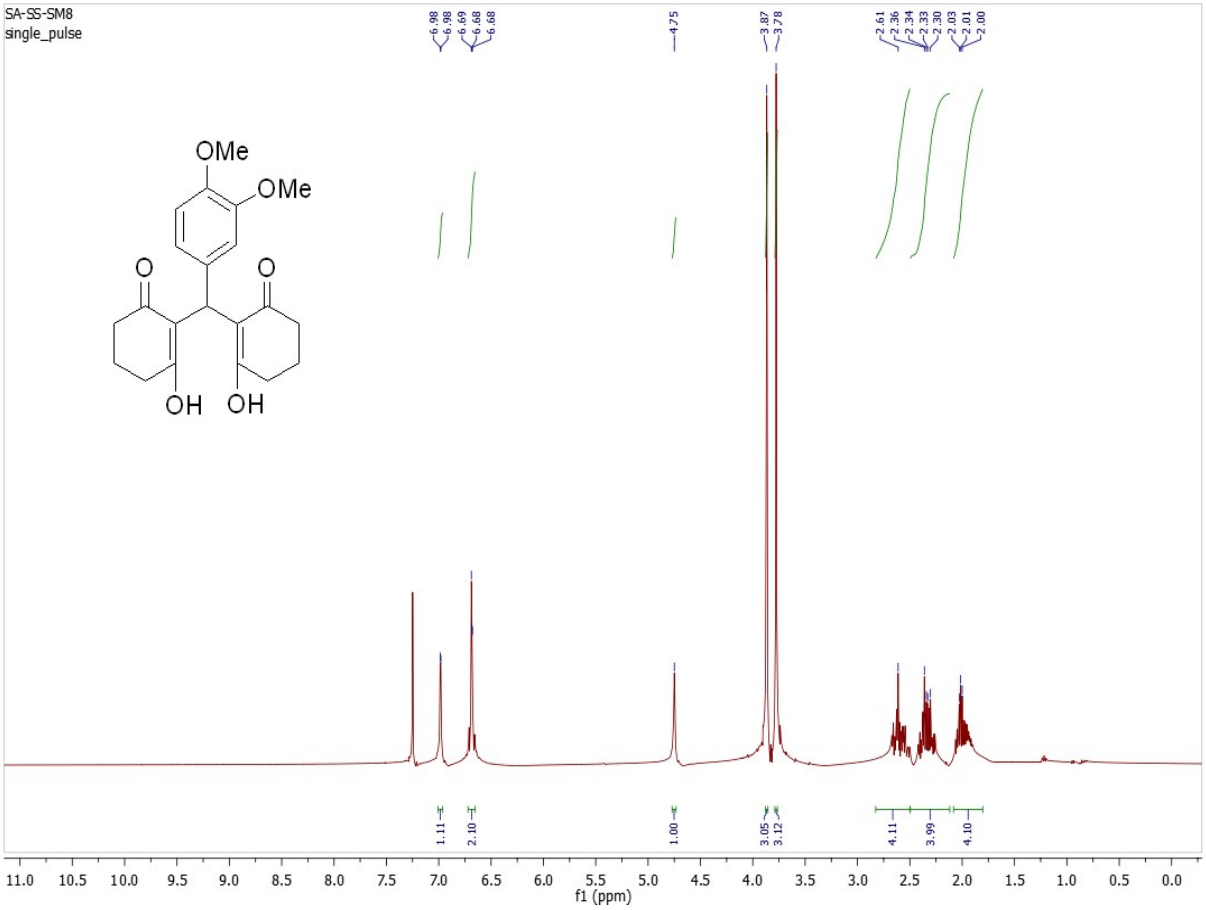
Munsell yellow, yield: 79%, m.p. 215-218 ^{o}C, ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.04 – 6.83 (m, 3H, Ar-H), 5.16 (s, 1H, CH), 2.66 – 2.35 (m, 6H, $3CH_2$), 2.05 – 2.00 (m, 3H, CH_2), 1.24-1.22 (d, J = 7.3 Hz, 1H, CH_2), 0.86 – 0.83 (m, 2H, CH_2). ^{13}C NMR (101 MHz, $CDCl_3$): δ 196.64, 164.42, 148.47, 126.91, 125.10, 123.66, 116.48, 37.01, 27.24, 26.22, 20.33; ESI–MS (m/z): 318.09 [M^+].

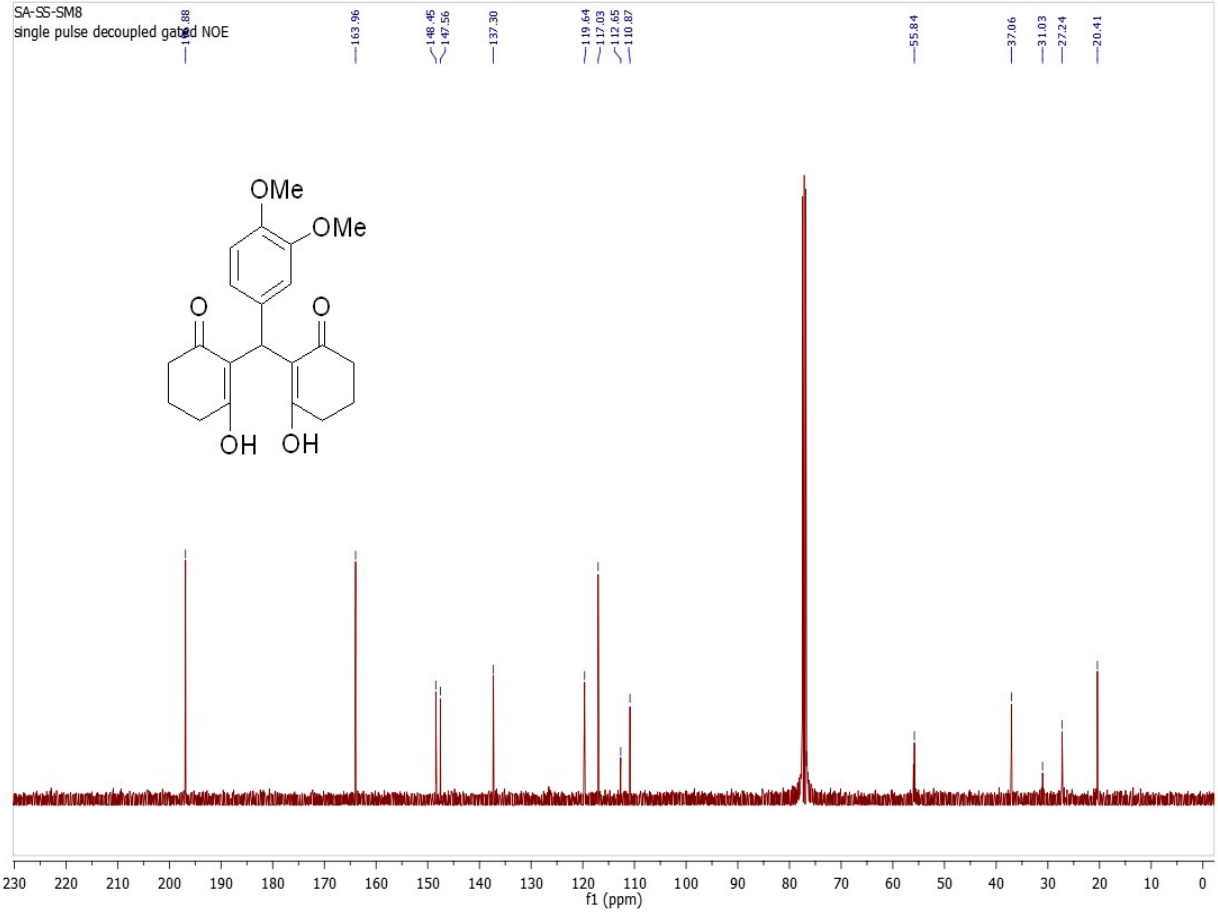




2,2'-((3,4-dimethoxyphenyl)methylene)bis(3-hydroxycyclohex-2-en-1-one) **(7e)**

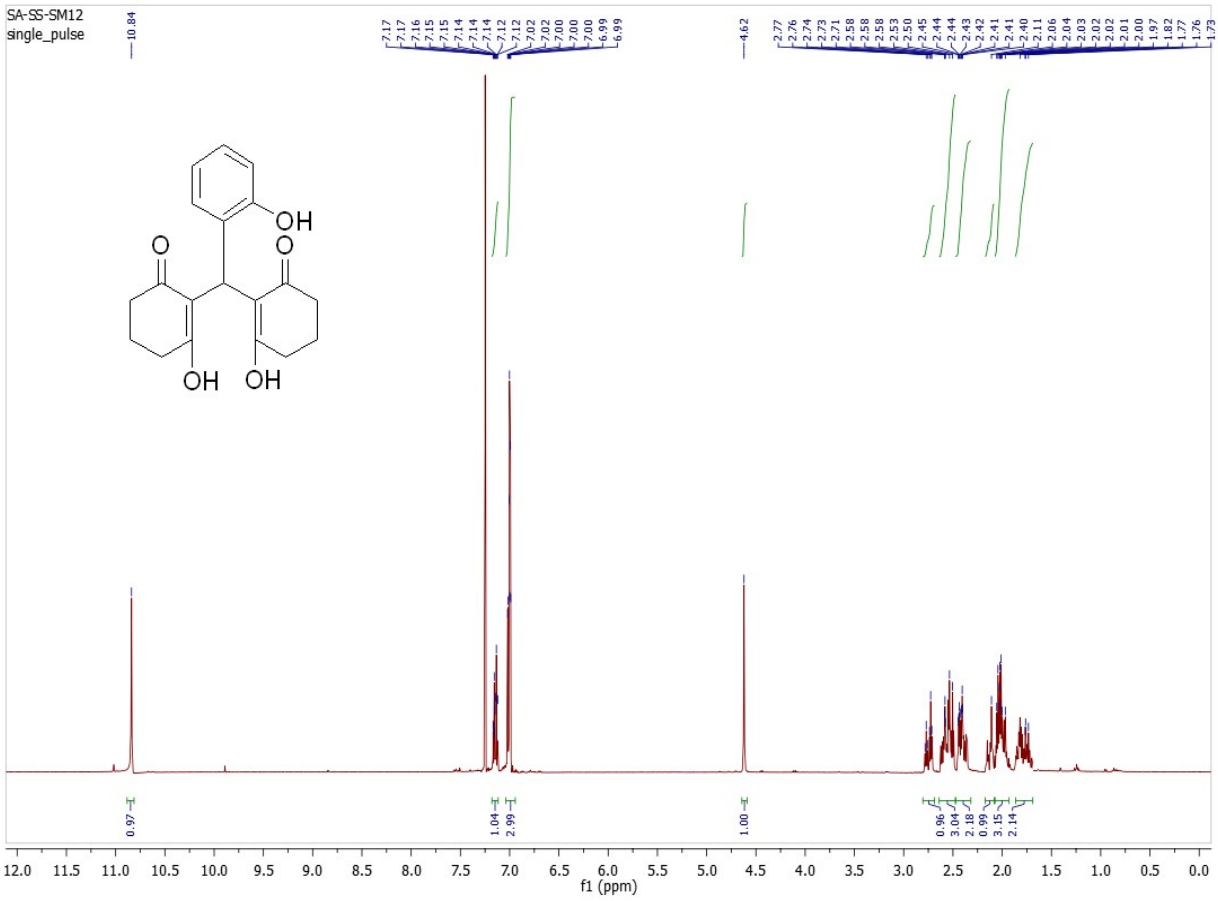
White solid, yield: 88%, m.p. 158-160 ^{o}C[76], ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.98 (d, *J* = 2.1 Hz, 1H, Ar-H), 6.69 – 6.68 (m, 2H, Ar-H), 4.75 (s, 1H, CH), 3.87 (s, 3H, OCH_3), 3.78 (s, 3H, OCH_3), 2.61 (s, 4H, $2CH_2$), 2.36-2.30 (dd, *J* = 14.2, 8.9 Hz, 4H, $2CH_2$), 2.03 – 2.00 (m, 4H, $2CH_2$). ^{13}C NMR (101 MHz, $CDCl_3$): δ 196.88, 163.96, 148.45, 147.56, 137.30, 119.64, 117.03, 112.65, 110.87, 55.84, 37.06, 31.01, 27.24, 20.41; ESI–MS (m/z): 372.16 [M^+].

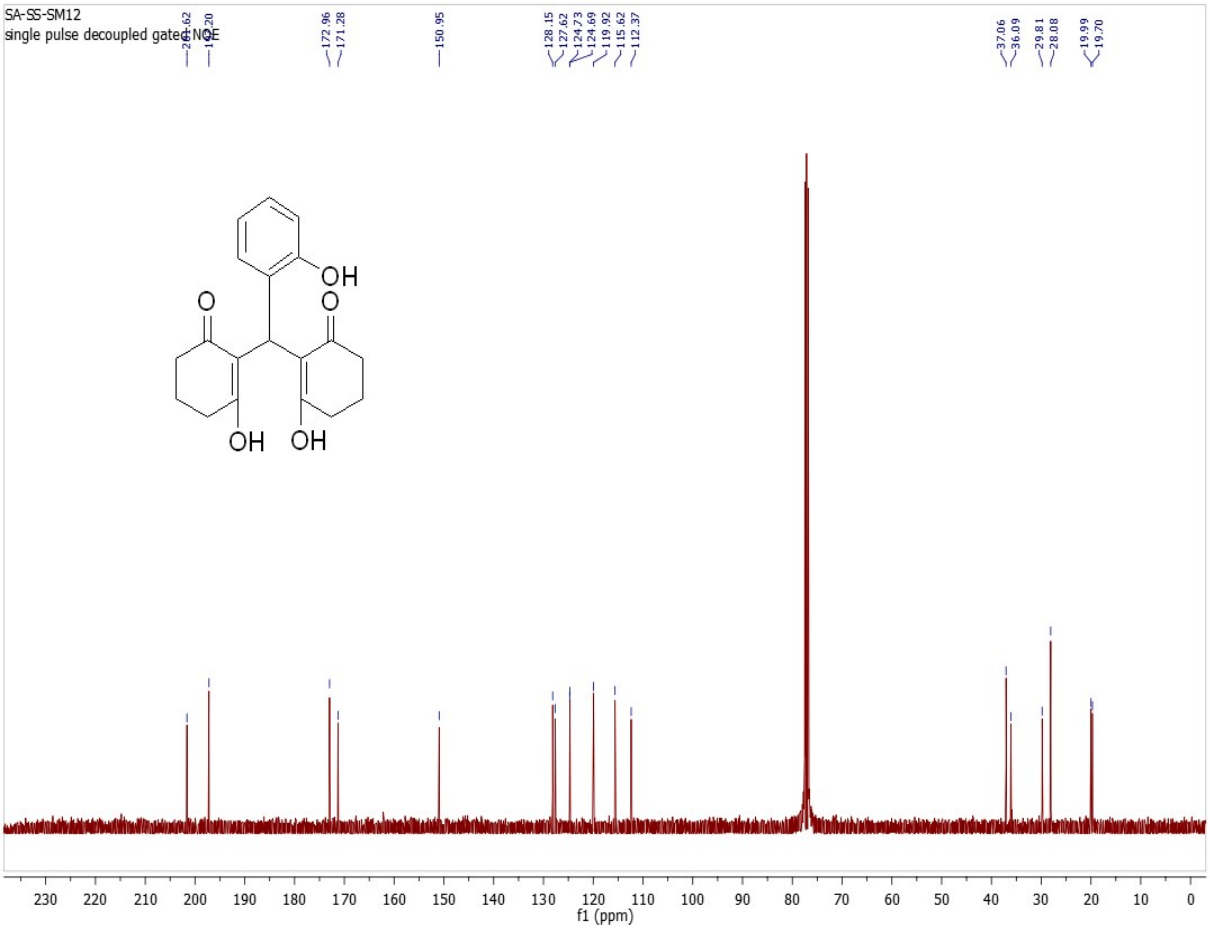

SA-SS-SM8
single_pulse
6.98
6.98
6.69
6.68
6.68
4.75
3.87
3.78
2.61
2.36
2.34
2.33
2.30
2.03
2.01
2.00
OMe
OMe
O
O
OH
OH
1.11
2.10
1.00
3.05
3.12
4.11
3.99
4.10
11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


SA-SS-SM8
single pulse decoupled gated NOE
163.96
148.45
147.56
137.30
119.64
117.03
112.65
110.87
55.84
37.06
31.03
27.24
20.41
OMe
OMe
O
O
OH
OH
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

2,2'-((2-hydroxyphenyl)methylene)bis(3-hydroxycyclohex-2-en-1-one) **(7f)**

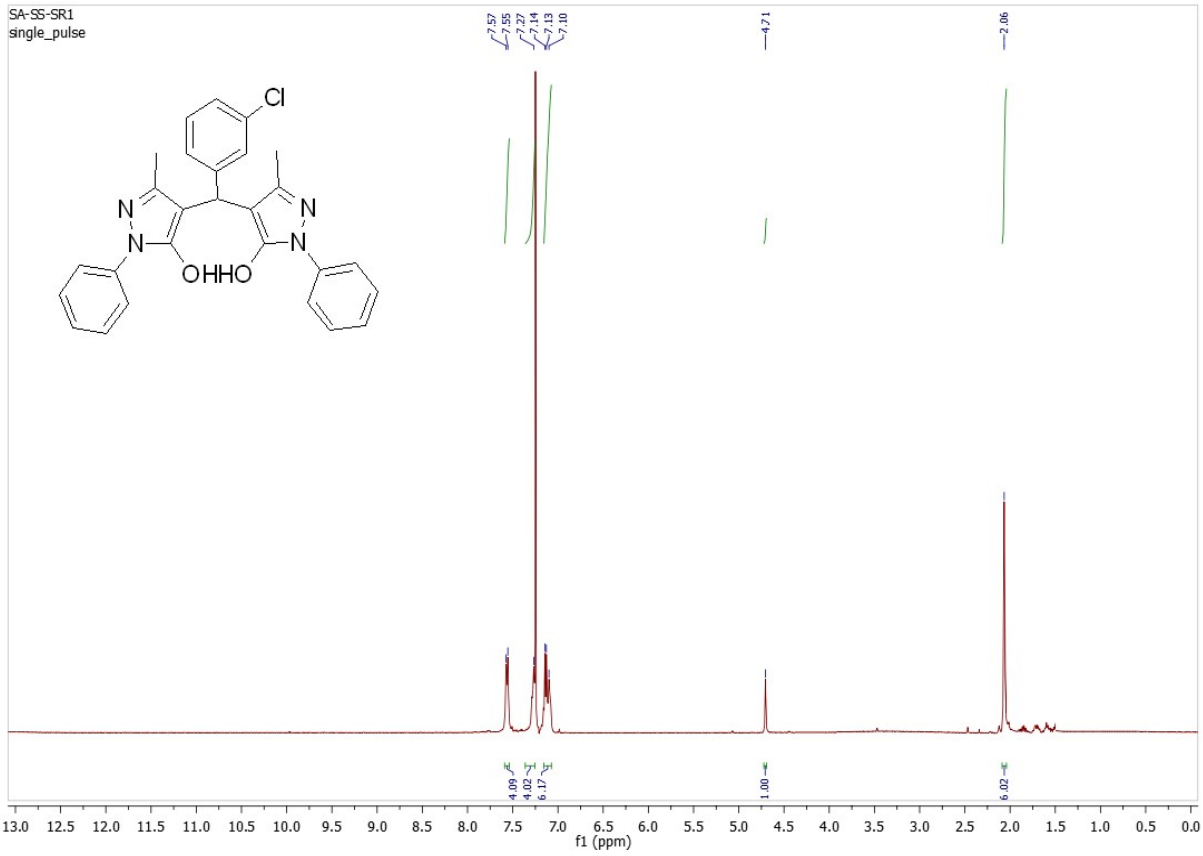
Chrome yellow, yield: 83%, m.p. 229-234 ^{o}C[55], ^{1}H NMR (400 MHz, $CDCl_3$): δ 10.84 (s, 1H, Ar-OH), 7.17 – 7.12 (m, 1H, Ar-H), 7.02 – 6.99 (m, 3H, Ar-H), 4.62 (s, 1H, CH), 2.77-2.71 (dt, *J* = 17.5, 4.5 Hz, 1H, CH_2), 2.58 – 2.50 (m, 3H, CH_2), 2.45-2.40 (ddd, *J* = 11.5, 5.2, 2.6 Hz, 2H, CH_2), 2.11 (s, 1H, CH_2), 2.06-1.97 (ddd, *J* = 19.2, 13.9, 8.7 Hz, 3H, CH_2), 1.82-1.73 (dd, *J* = 18.0, 16.3 Hz, 2H, CH_2). ^{13}C NMR (101 MHz, $CDCl_3$): δ 201.62, 197.20, 172.96, 171.28, 150.95, 128.15, 127.62, 124.73, 124.69, 119.92, 115.62, 112.37, 37.06, 36.09, 29.81, 28.08, 19.99, 19.70; ESI–MS (m/z): 328.13 [M^+].

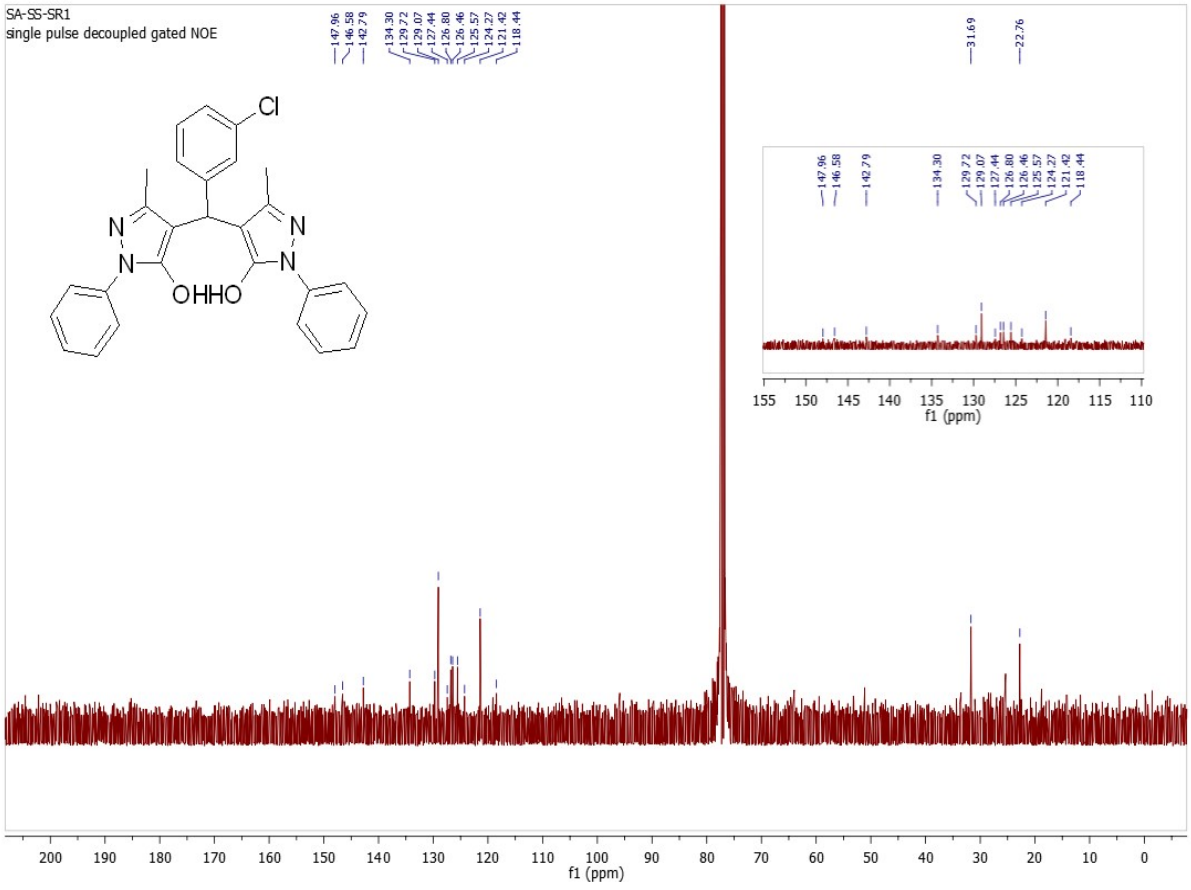




4,4'-((3-chlorophenyl)methylene)bis(3-methyl-1-phenyl-1H-pyrazol-5-ol) **(8a)**

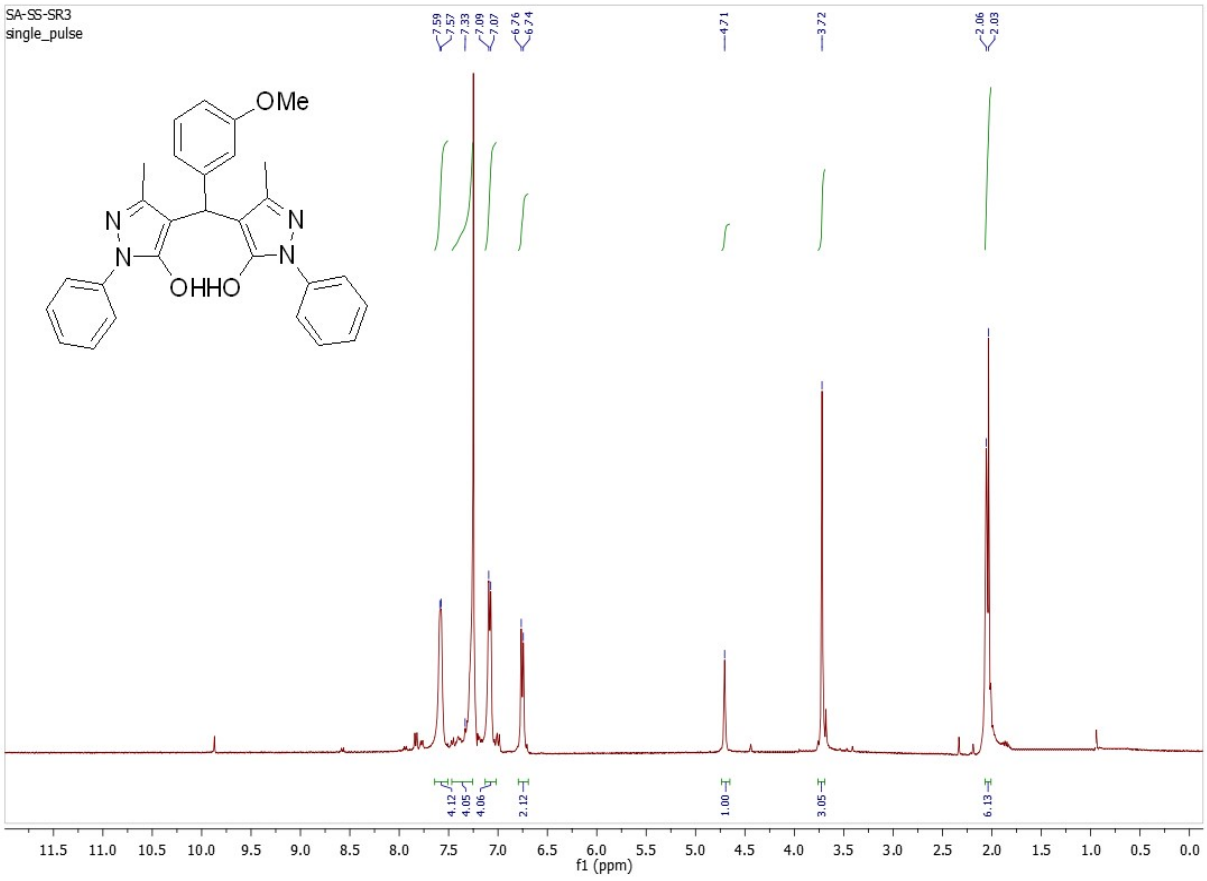
Golden yellow solid, yield: 81%, m.p. 155-159 ^{o}C[64], ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.57-7.55 (d, *J* = 7.5 Hz, 4H, Ar-H), 7.27 (s, 4H, Ar-H), 7.14 – 7.10 (m, 6H, Ar-H), 4.71 (s, 1H, CH), 2.06 (s, 6H, $2CH_3$). ^{13}C NMR (101 MHz, $CDCl_3$): δ 147.96, 146.58, 142.79, 134.30, 129.72, 129.07, 127.44, 126.80, 126.46, 125.57, 124.27, 121.42, 118.44, 31.69, 22.76; ESI–MS (m/z): 470.15[M^+].

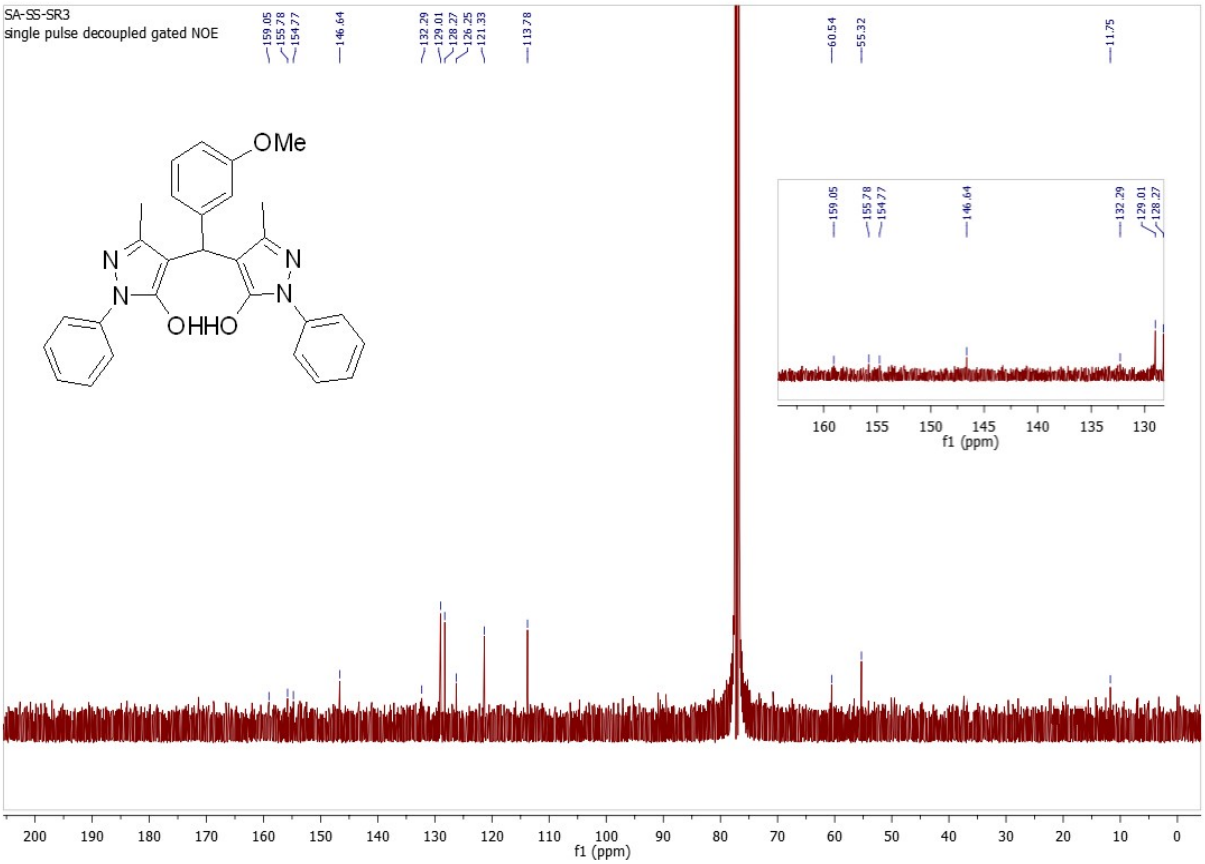

SA-SS-SR1
single_pulse
7.57
7.55
7.27
7.14
7.13
7.10
4.71
2.06
Cl
N
N
OHHO
N
N
4.09
4.02
6.17
1.00
6.02
13.0 12.5 12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


SA-SS-SR1
single pulse decoupled gated NOE
147.96
146.58
142.79
134.30
129.72
129.07
127.44
126.80
126.46
125.57
124.27
121.42
118.44
31.69
22.76
Cl
N
N
OHHO
N
N
155 150 145 140 135 130 125 120 115 110
f1 (ppm)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

4,4'-((3-methoxyphenyl)methylene)bis(3-methyl-1-phenyl-1H-pyrazol-5-ol) **(8b)**

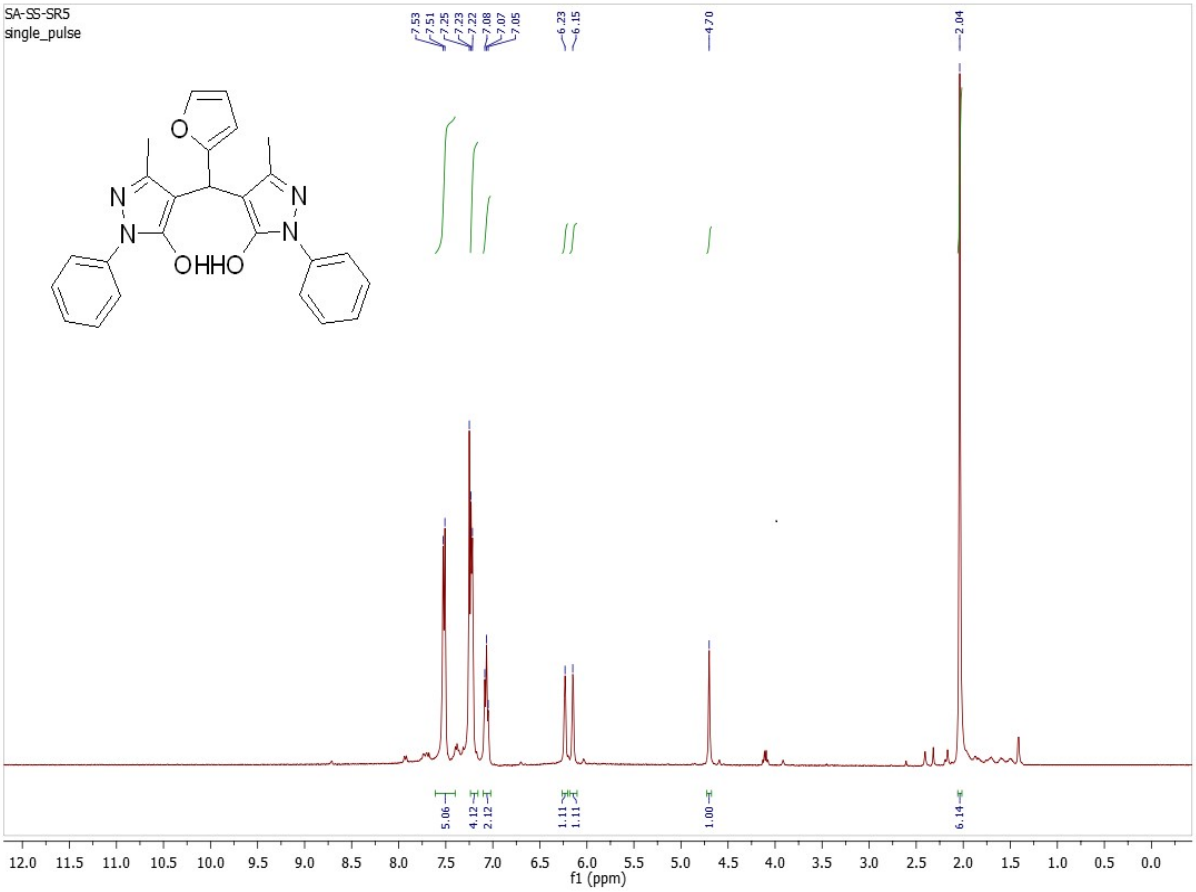
Bronze brown solid, yield: 78%, m.p. 175-178 $^{o}C^{64}$, ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59-7.57 (d, *J* = 5.5 Hz, 4H, Ar-H), 7.33 (s, 4H-Ar-H), 7.09-7.07 (d, *J* = 8.1 Hz, 4H, Ar-H), 6.76-6.74 (d, *J* = 8.3 Hz, 2H, Ar-H), 4.71 (s, 1H, CH), 3.72 (s, 3H, OCH_3), 2.06-2.03 (d, *J* = 9.5 Hz, 6H, $2CH_3$). ^{13}C NMR (101 MHz, $CDCl_3$): δ 159.05, 155.78, 154.77, 146.64, 132.29, 129.01, 128.27, 126.25, 121.33, 113.78, 60.54, 55.32, 11.75; ESI–MS (m/z): 466.20 [M^+].

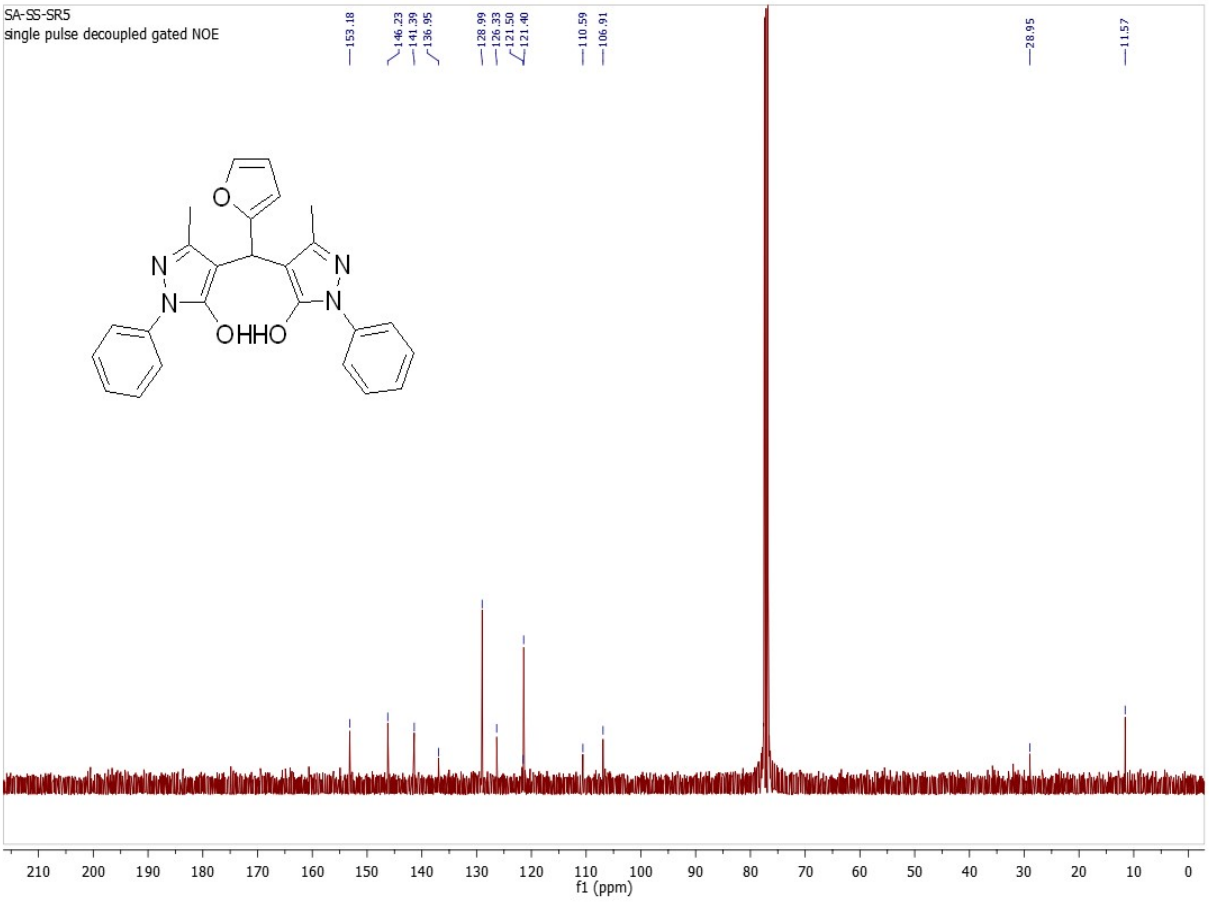




4,4'-(furan-2-ylmethylene)bis(3-methyl-1-phenyl-1H-pyrazol-5-ol) **(8c)**

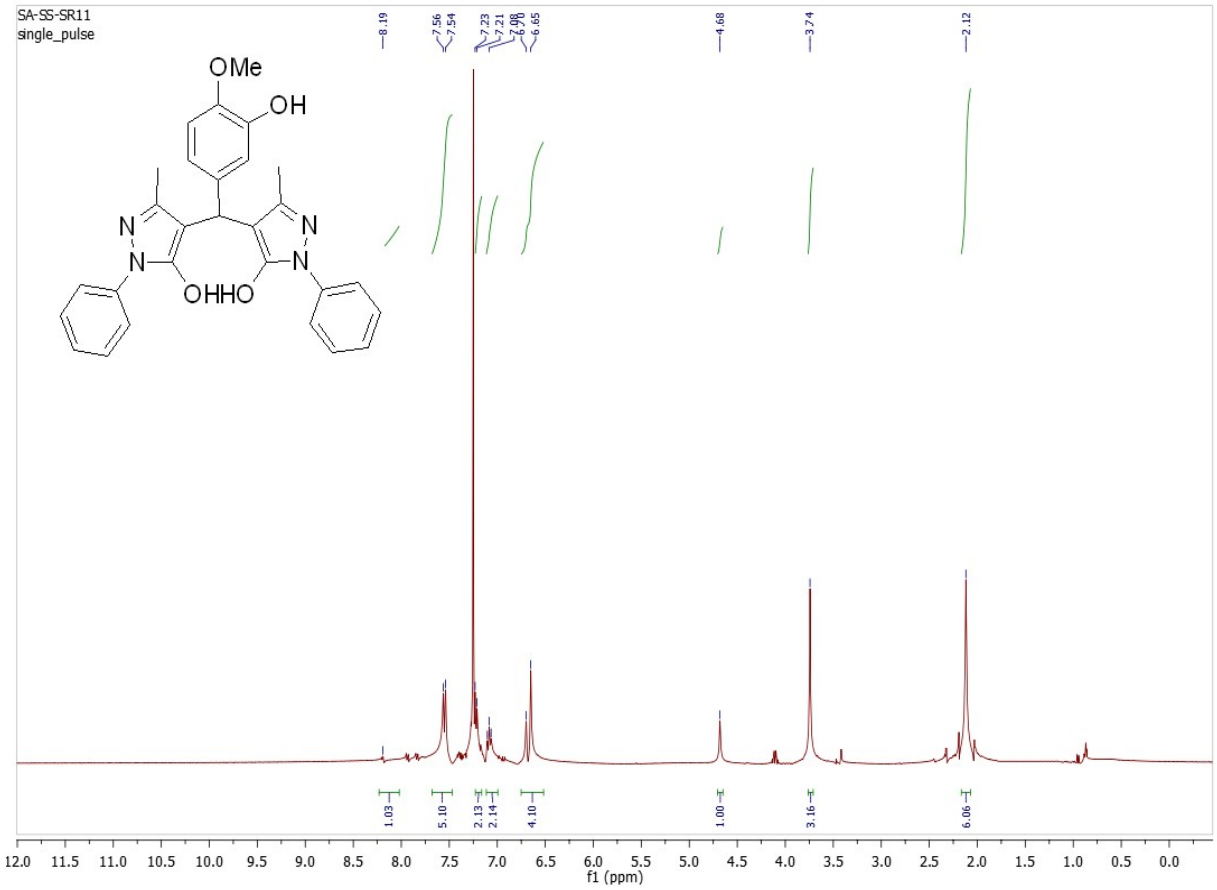
Charcoal black crystals, yield: 90%, m.p. 176-178 $^{o}C^{64}$, ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.53-7.51 (d, *J* = 7.8 Hz, 5H, Ar-H), 7.25-7.22 (d, *J* = 6.1 Hz, 4H, Ar-H), 7.08-7.05 (t, *J* = 7.3 Hz, 2H, Ar-H), 6.23 (s, 1H, Ar-H), 6.15 (s, 1H, Ar-H), 4.70 (s, 1H, CH), 2.04 (s, 6H, $2CH_3$). ^{13}C NMR (101 MHz, $CDCl_3$): δ 153.18, 146.23, 141.39, 136.95, 128.99, 126.33, 121.50, 121.40, 110.59, 106.91, 28.95, 11.57; ESI–MS (m/z): 426.17 [M^+].

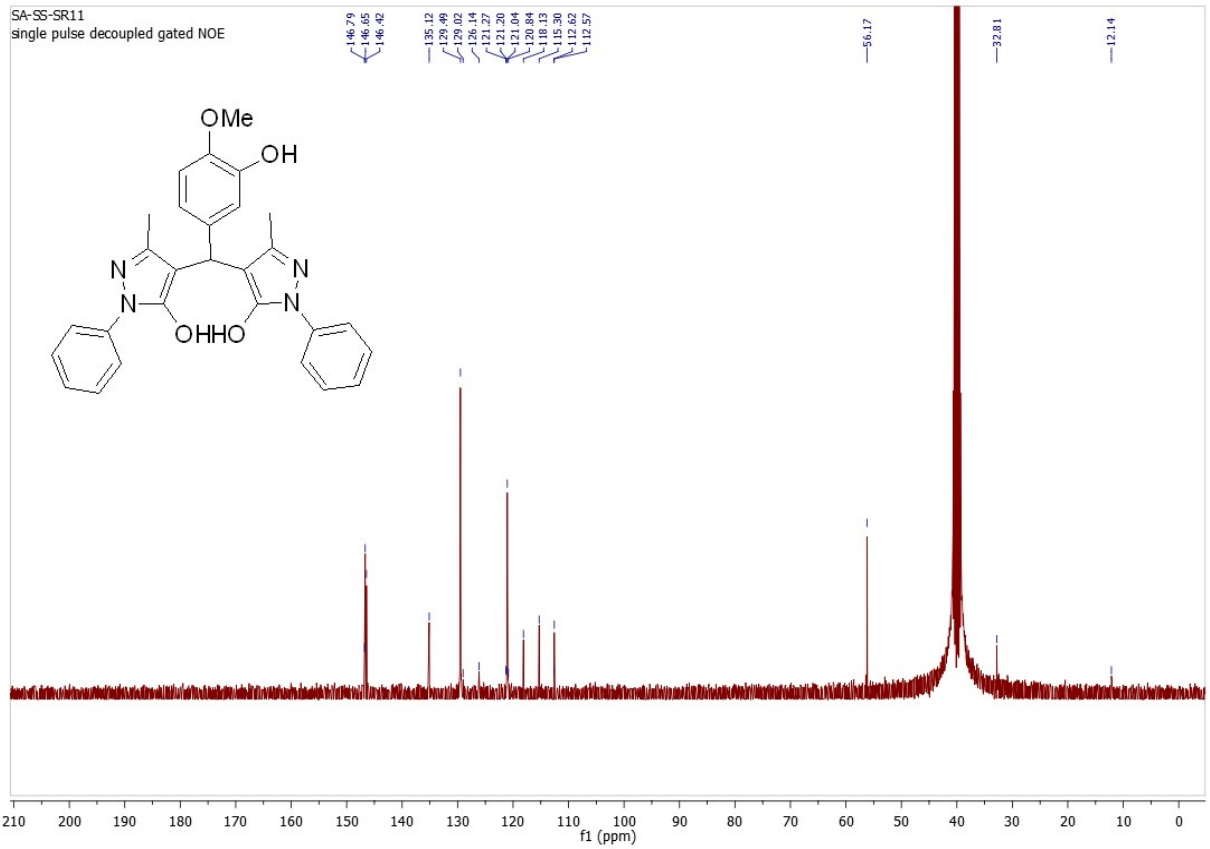

SA-SS-SR5
single_pulse
7.53
7.51
7.25
7.23
7.22
7.08
7.07
7.05
6.23
6.15
4.70
2.04
O
N
N
N
N
OHHO
5.06
4.12
2.12
1.11
1.11
1.00
6.14
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


SA-SS-SR5
single pulse decoupled gated NOE
153.18
146.23
141.39
136.95
128.99
126.33
121.50
121.40
110.59
106.91
28.95
11.57
O
N
N
N
N
OHHO
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

4,4'-((3-hydroxy-4-methoxyphenyl)methylene)bis(3-methyl-1-phenyl-1H-pyrazol-5-ol) **(8d)**

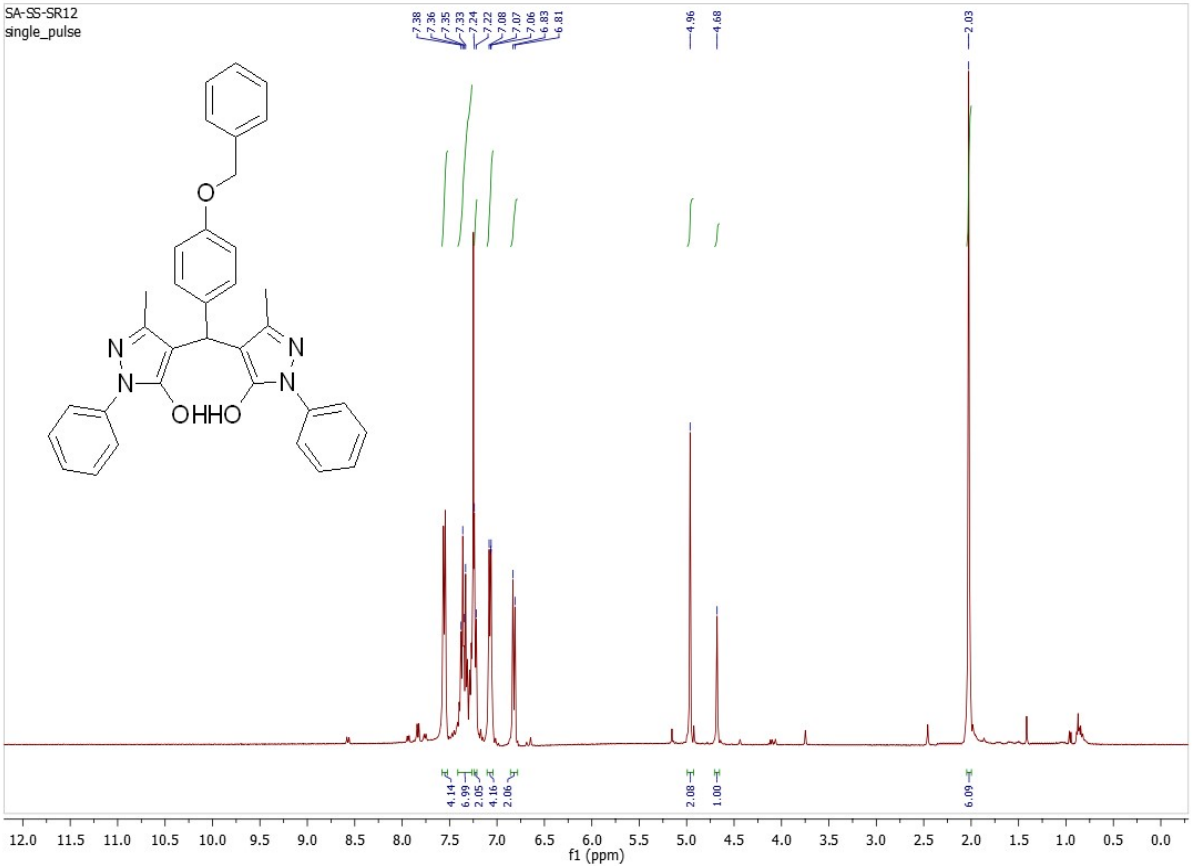
Yellow solid, yield: 98%, m.p. 189-191 $^{o}C^{26}$, ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.19 (s, 1H, OH), 7.56-7.54 (d, *J* = 9.0 Hz, 5H, Ar-H), 7.23-7.21 (s, 2H, Ar-H), 7.08 (t, *J* = 7.8 Hz, 2H, Ar-H), 6.70-6.65 (d, *J* = 19.3 Hz, 4H, Ar-H), 4.68 (s, 1H, CH), 3.74 (s, 3H, OCH_3), 2.12 (s, 6H, $2CH_3$). ^{13}C NMR (101 MHz, DMSO-d6): δ 146.79, 146.65, 146.42, 135.12, 129.49, 129.02, 126.14, 121.27, 121.20, 121.04, 120.84, 118.13, 115.30, 112.62, 112.57, 56.17, 32.81, 12.14; ESI–MS (m/z): 482.20 [M^{+}].

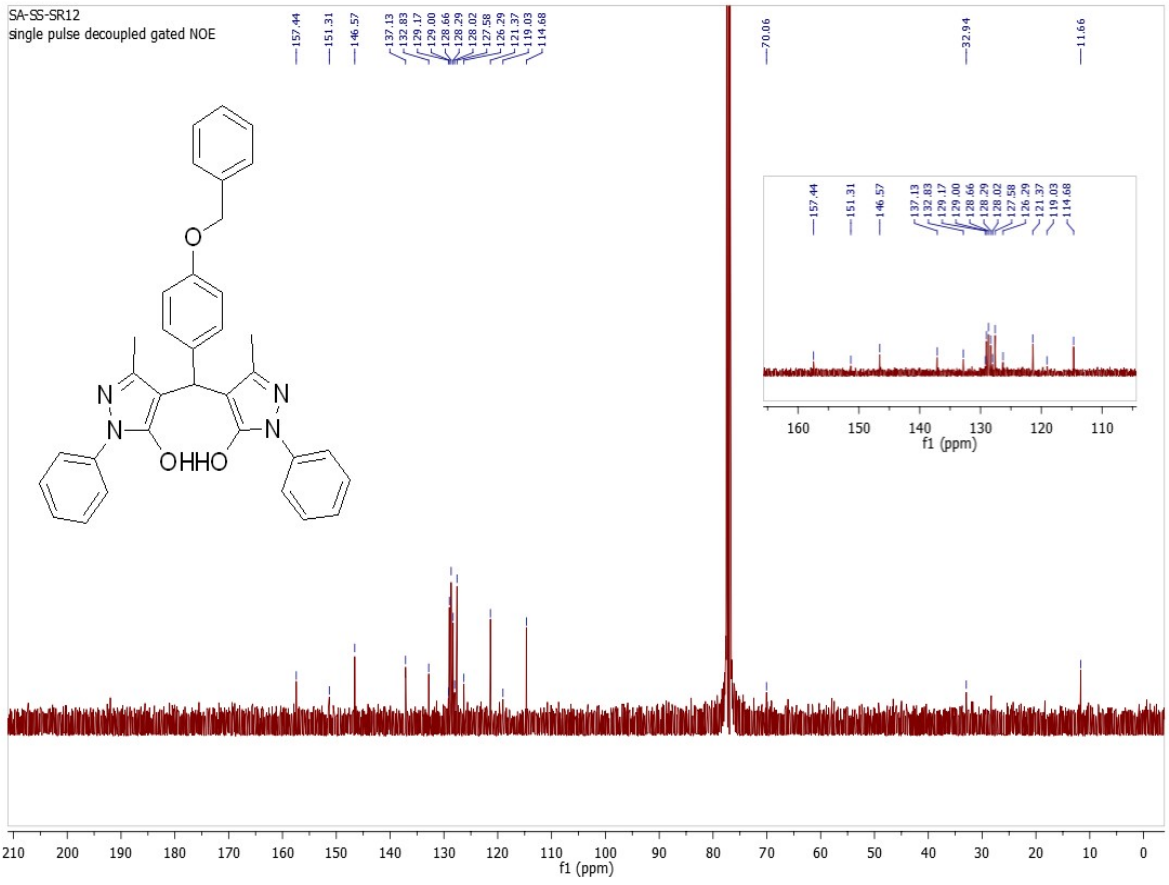




4,4'-((4-(benzyloxy)phenyl)methylene)bis(3-methyl-1-phenyl-1H-pyrazol-5-ol) **(8e)**

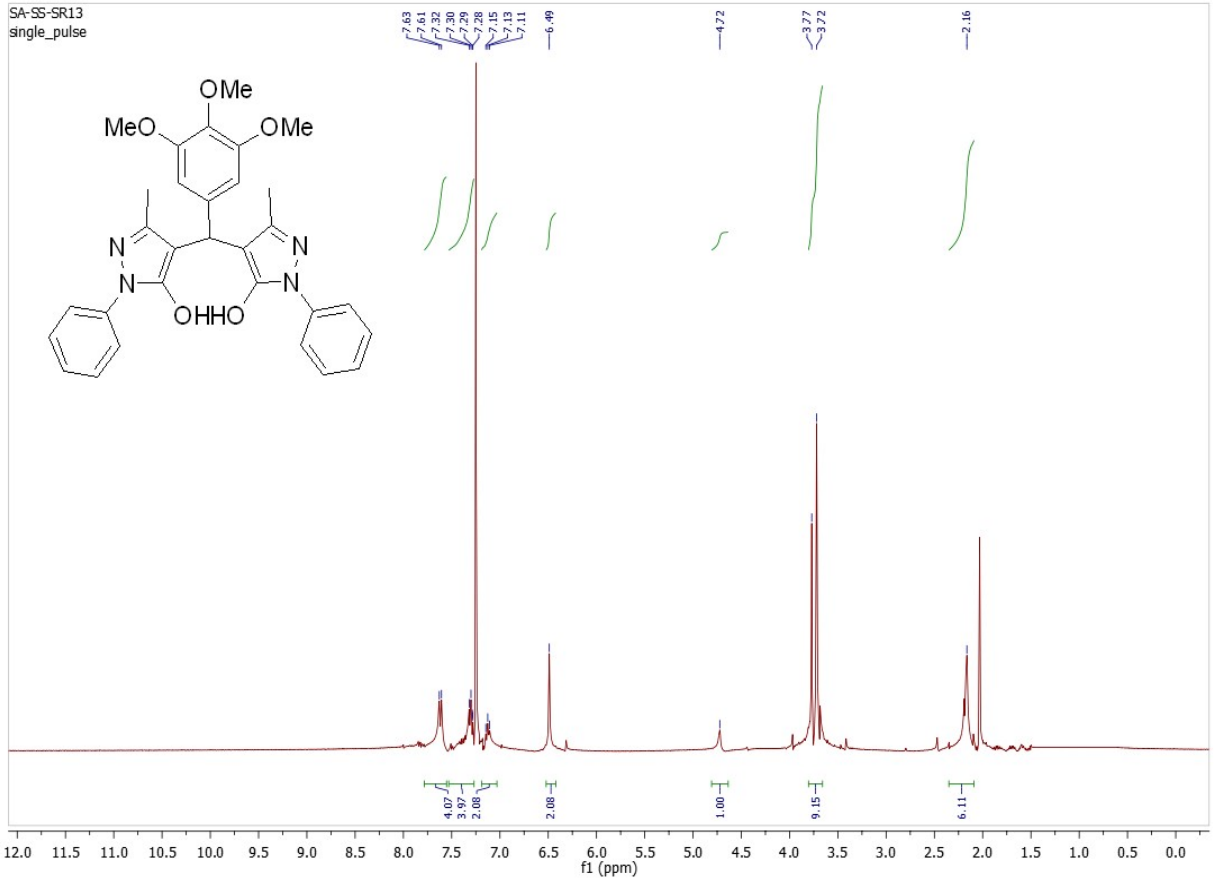
Cream solid, yield: 71%, m.p. 194-196 ^{o}C[27], ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.38-7.35 (d, *J* = 7.8 Hz, 4H, Ar-H), 7.33 (dd, *J* = 12.1, 7.2 Hz, 7H, Ar-H), 7.24-7.22 (d, *J* = 7.8 Hz, 2H, Ar-H), 7.08 – 7.06 (m, 4H, Ar-H), 6.83-6.81 (d, *J* = 8.7 Hz, 2H, Ar-H), 4.96 (s, 2H, CH_2), 4.68 (s, 1H, CH), 2.03 (s, 6H, $2CH_3$). ^{13}C NMR (101 MHz, $CDCl_3$): δ 157.44, 151.31, 146.57, 137.13, 132.83, 129.17, 129.00, 128.66, 128.29, 128.02, 127.58, 126.29, 121.37, 119.03, 114.68, 70.06, 32.94, 11.66; ESI–MS (m/z): 542.23 [M^+].

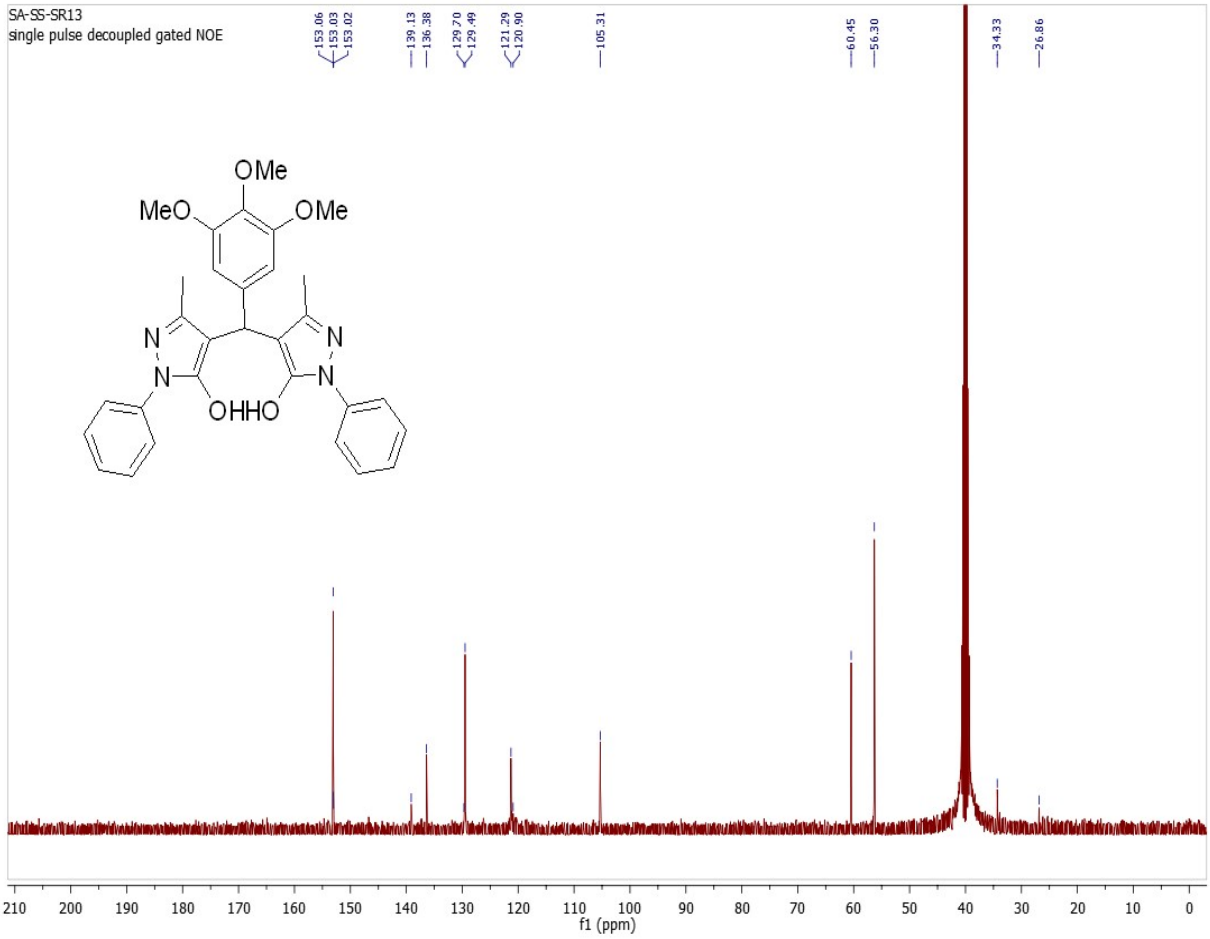

SA-SS-SR12
single_pulse
7.38
7.36
7.35
7.33
7.24
7.22
7.08
7.07
7.06
6.83
6.81
4.96
4.68
2.03
4.14
6.99
2.05
4.16
2.06
2.08
1.00
6.09
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


SA-SS-SR12
single pulse decoupled gated NOE
157.44
151.31
146.57
137.13
132.83
129.17
129.00
128.66
128.29
128.02
127.58
126.29
121.37
119.03
114.68
70.06
32.94
11.66
160 150 140 130 120 110
f1 (ppm)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

4,4'-((3,4,5-trimethoxyphenyl)methylene)bis(3-methyl-1-phenyl-1H-pyrazol-5-ol) **(8f)**

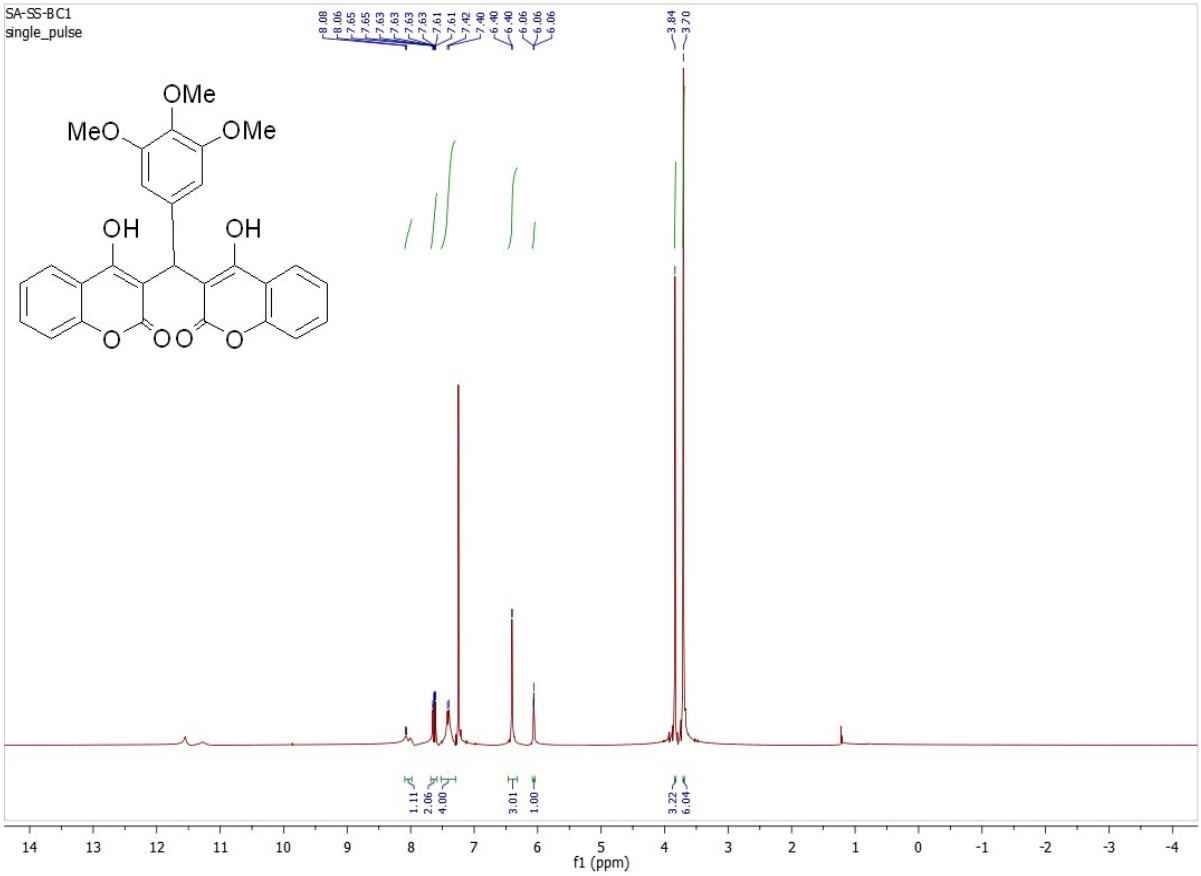
Light yellow crystals, yield: 95%, m.p. 194-199 ^{o}C[26], ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.63-7.61 (d, *J* = 9.1 Hz, 4H, Ar-H), 7.32-7.28 (dd, *J* = 10.5, 4.8 Hz, 4H, Ar-H), 7.15 – 7.11 (m, 2H, Ar-H), 6.49 (s, 2H, Ar-H), 4.72 (s, 1H, CH), 3.77-3.3.72 (d, *J* = 20.3 Hz, 9H, $3OCH_3$), 2.16 (s, 6H, $2CH_3$). ^{13}C NMR (101 MHz, DMSO-d6): δ 153.06, 153.03, 153.02, 139.13, 136.38, 129.70, 129.49, , 121.29, 120.90, 105.31, 60.45, 56.30, 34.33, 26.86; ESI–MS (m/z): 526.22 [M^+].





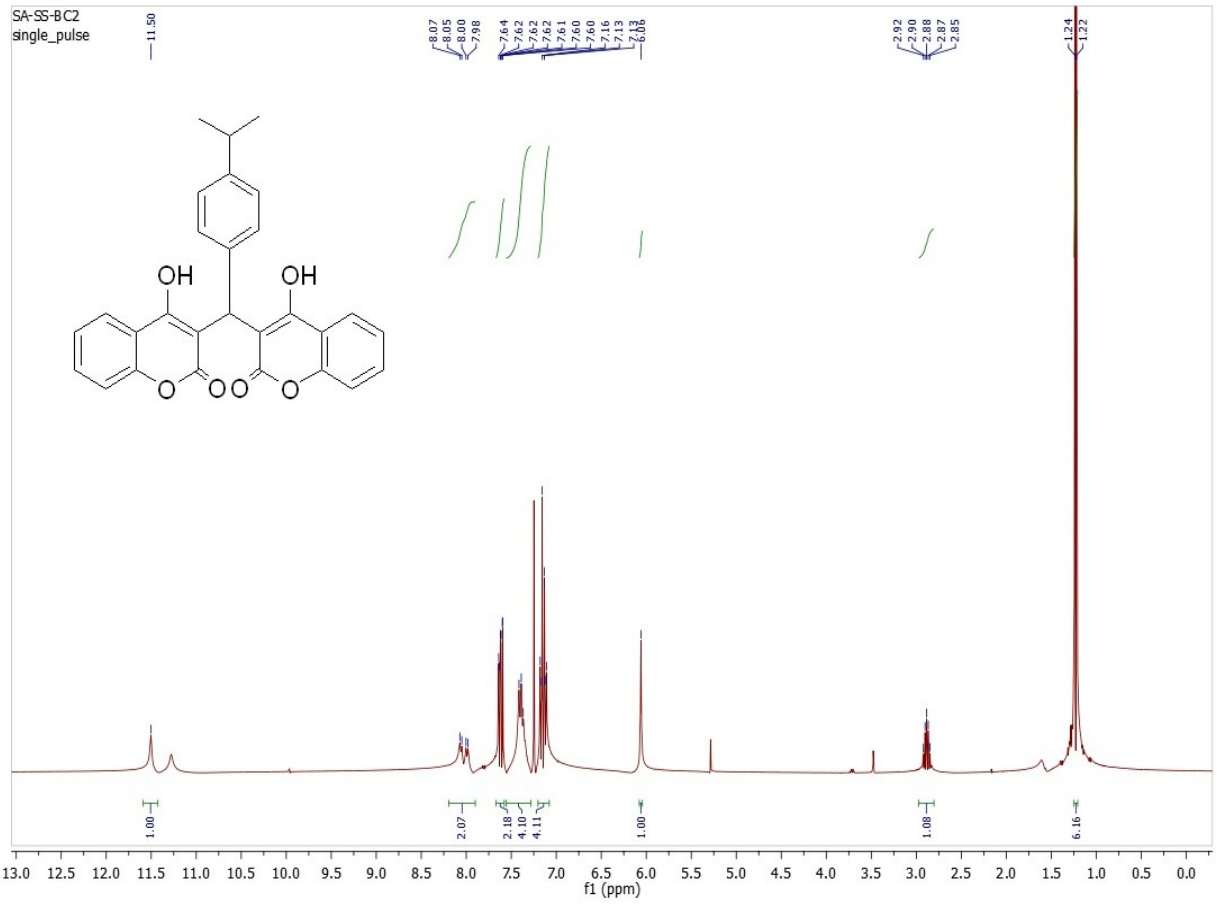
3,3'-((3,4,5-trimethoxyphenyl)methylene)bis(4-hydroxy-2H-chromen-2-one) **(9a)**

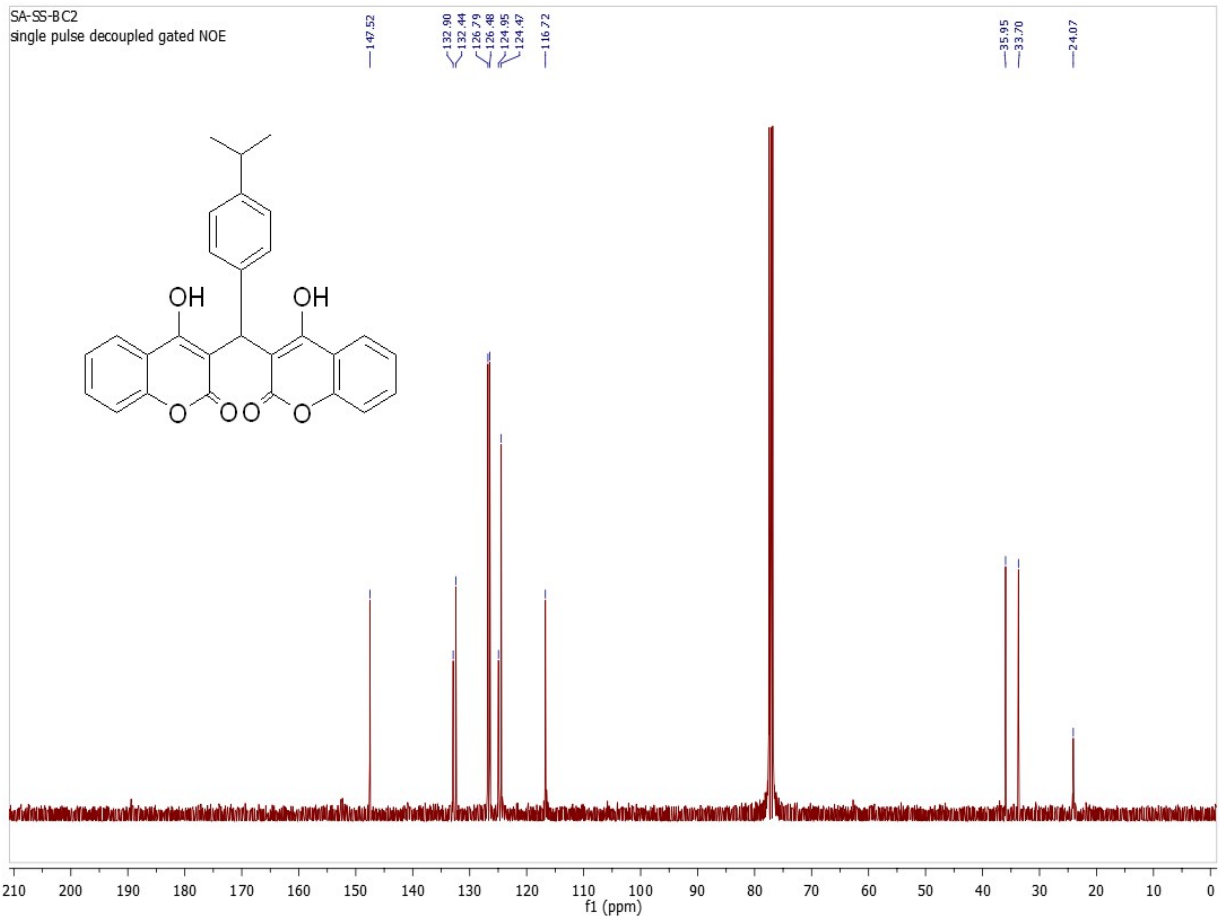
White solid, yield: 95%, m.p. 243-245 ^{o}C[77], ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.08-8.06 (d, *J* = 6.6 Hz, 1H, Ar-H), 7.65-7.61 (ddd, *J* = 8.6, 7.3, 1.7 Hz, 2H, Ar-H), 7.42-7.40 (d, *J* = 9.0 Hz, 4H, Ar-H), 6.40 (d, *J* = 1.3 Hz, 3H, Ar-H), 6.06 (m, 1H, CH), 3.84 (s, 3H, OCH_3), 3.70 (s, 6H, $2OCH_3$) ; ESI–MS (m/z): 502.13 [M^+].



3,3'-((4-isopropylphenyl)methylene)bis(4-hydroxy-2H-chromen-2-one) **(9b)**

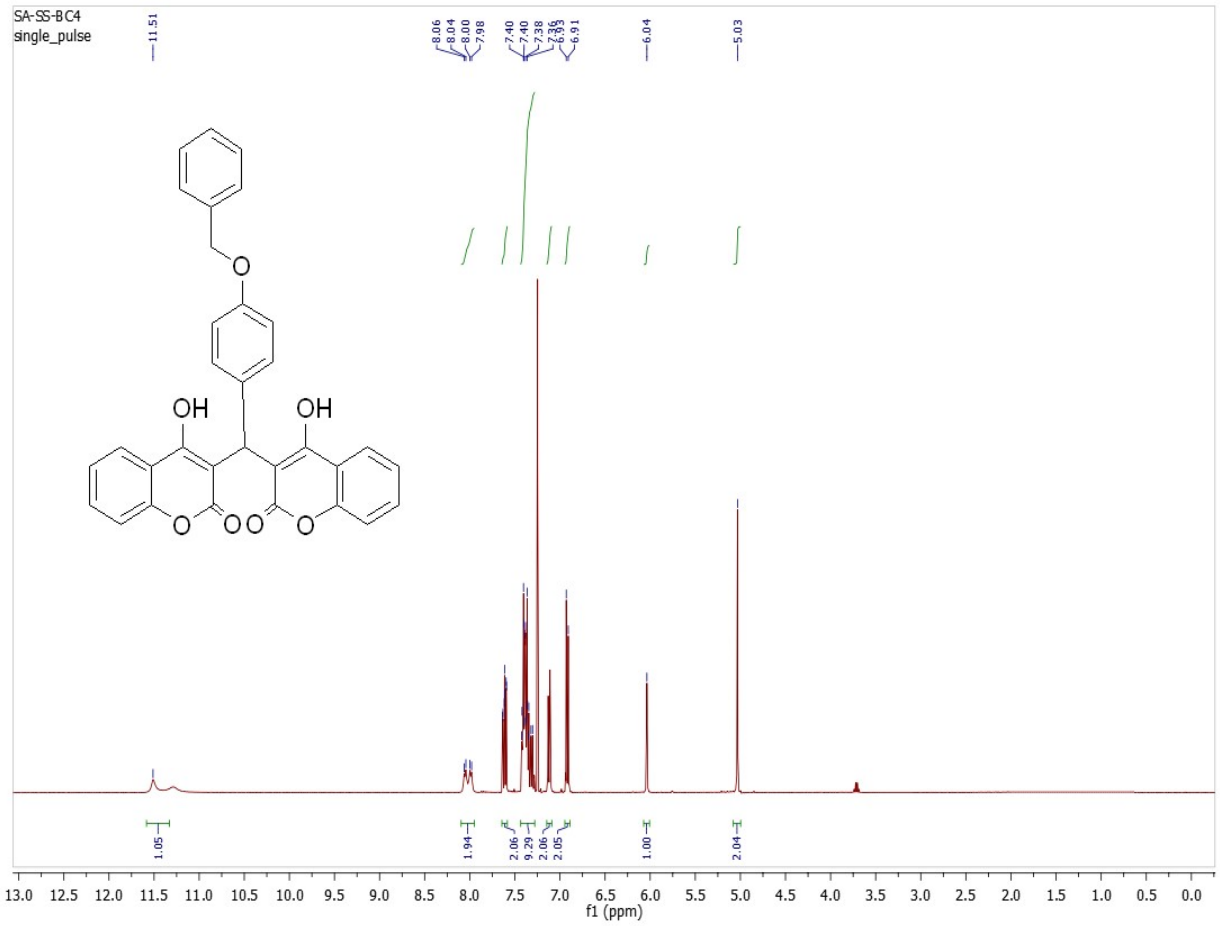
Off-white crystals, yield: 82%, m.p. 235-238 ^{o}C, ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.50 (s, 1H, OH), 8.07-8.05 (dd, *J* = 27.2, 8.7 Hz, 2H, Ar-H), 8.00-7.98 (ddd, *J* = 8.5, 7.3, 1.7 Hz, 2H, Ar-H), 7.64 – 7.60 (m, 4H, Ar-H), 7.16-7.13 (ddd, *J* = 8.7, 7.7, 3.7 Hz, 4H, Ar-H), 6.06 (s, 1H, CH), 2.92-2.85 (dt, *J* = 14.3, 7.2 Hz, 1H, CH), 1.24-1.22 (d, *J* = 7.0 Hz, 6H, CH_3). ^{13}C NMR (101 MHz, $CDCl_3$): δ 147.52, 132.90, 132.44, 126.79, 126.48, 124.95, 124.47, 116.72, 35.95, 33.70, 24.07; ESI–MS (m/z): 454.14 [M^+].


SA-SS-BC2
single_pulse
OH
OH
O
O
O
O
f1 (ppm)


SA-SS-BC2
single pulse decoupled gated NOE
OH
OH
O
O
O
O
f1 (ppm)

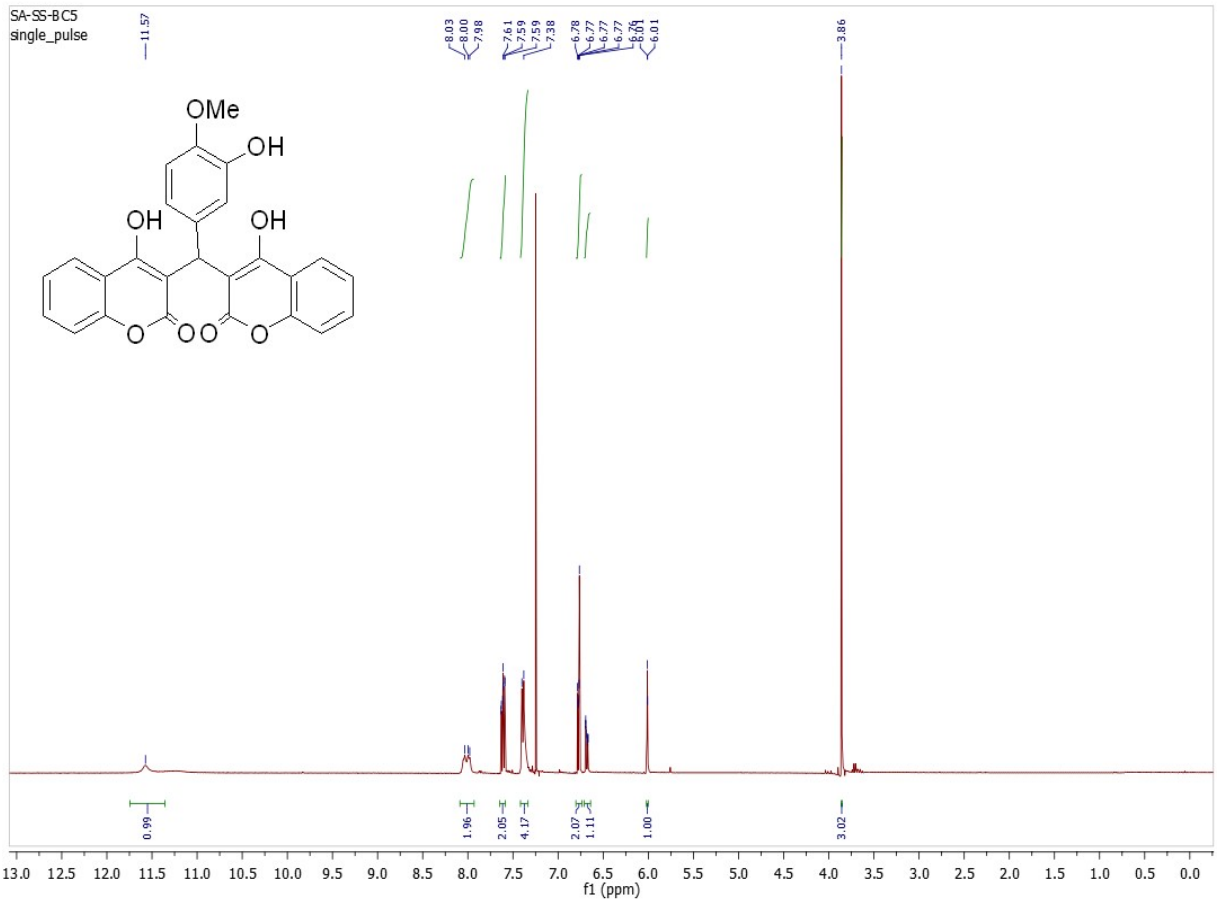
3,3'-((4-(benzyloxy)phenyl)methylene)bis(4-hydroxy-2H-chromen-2-one) **(9c)**

Light yellow solid, yield: 69%, m.p. 198-202 ^{o}C[33], ^{1}H NMR (400 MHz, $CDCl_3$): δ 11.51 (s, 1H, OH), 8.06-8.04 (dd, *J* = 25.3, 7.6 Hz, 2H, Ar-H), 8.00 – 7.98 (m, 2H, Ar-H), 7.40 (m, 9H, Ar-H), 7.38 – 7.36 (m, 2H, Ar-H), 6.93-6.91 (d, *J* = 8.9 Hz, 2H, Ar-H), 6.04 (s, 1H, CH), 5.03 (s, 2H, CH_2) ; ESI–MS (m/z): 518.14 [M^+].



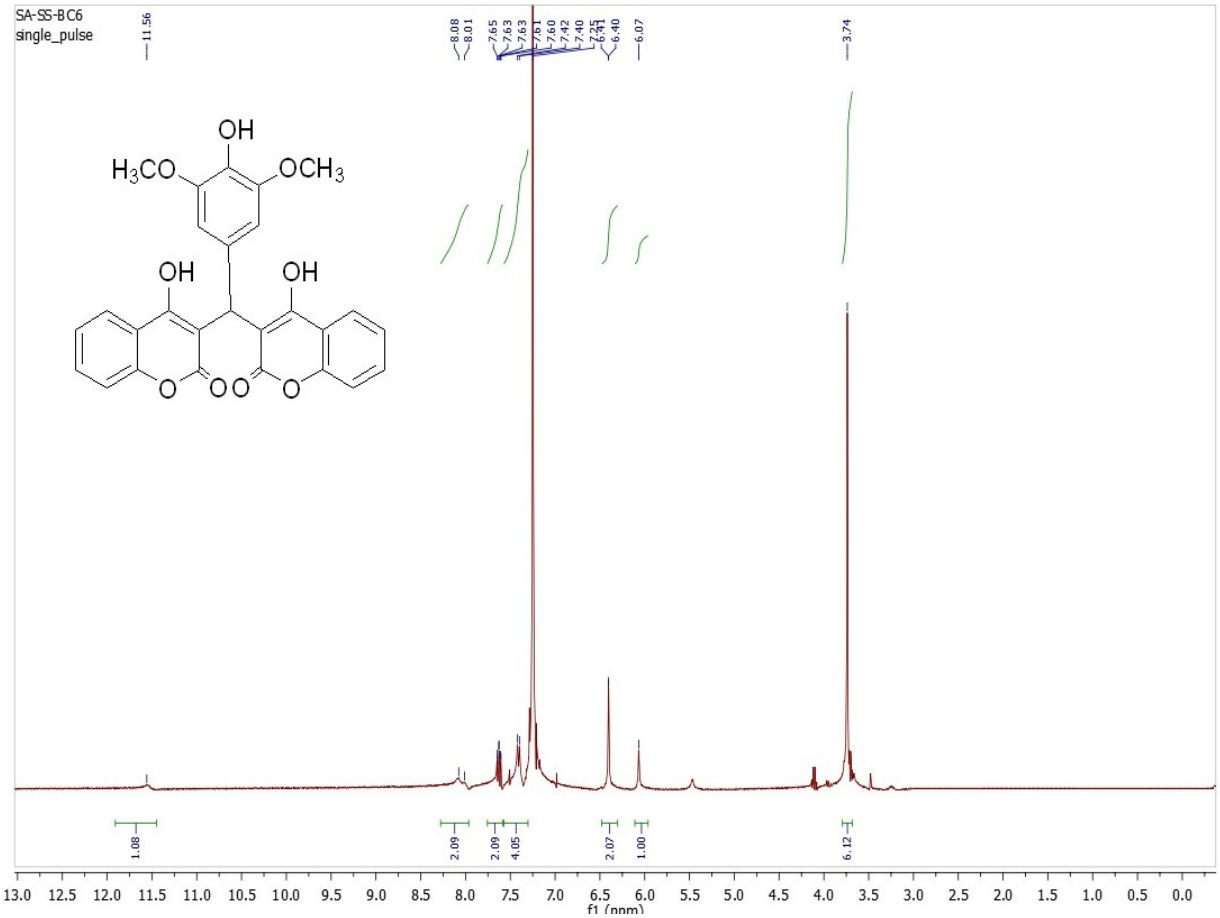
3,3'-((3-hydroxy-4-methoxyphenyl)methylene)bis(4-hydroxy-2H-chromen-2-one) **(9d)**

Off-white crystals, yield: 96%, m.p. 244-246 ^{o}C[33], ^{1}H NMR (400 MHz, $CDCl_3$): δ 11.57 (s, 1H, OH), 8.03 – 7.98 (m, 2H, Ar-H), 7.6 – 7.59 (m, 2H, Ar-H), 7.40-7.38 (d, *J* = 8.3 Hz, 4H, Ar-H), 6.78 – 6.77 (m, 2H, Ar-H), 6.76 (ddd, *J* = 8.3, 2.3, 1.3 Hz, 1H, Ar-H), 6.01 (d, *J* = 1.1 Hz, 1H, CH), 3.86 (s, 3H, OCH_3) ; ESI–MS (m/z): 458.10 [M^+].



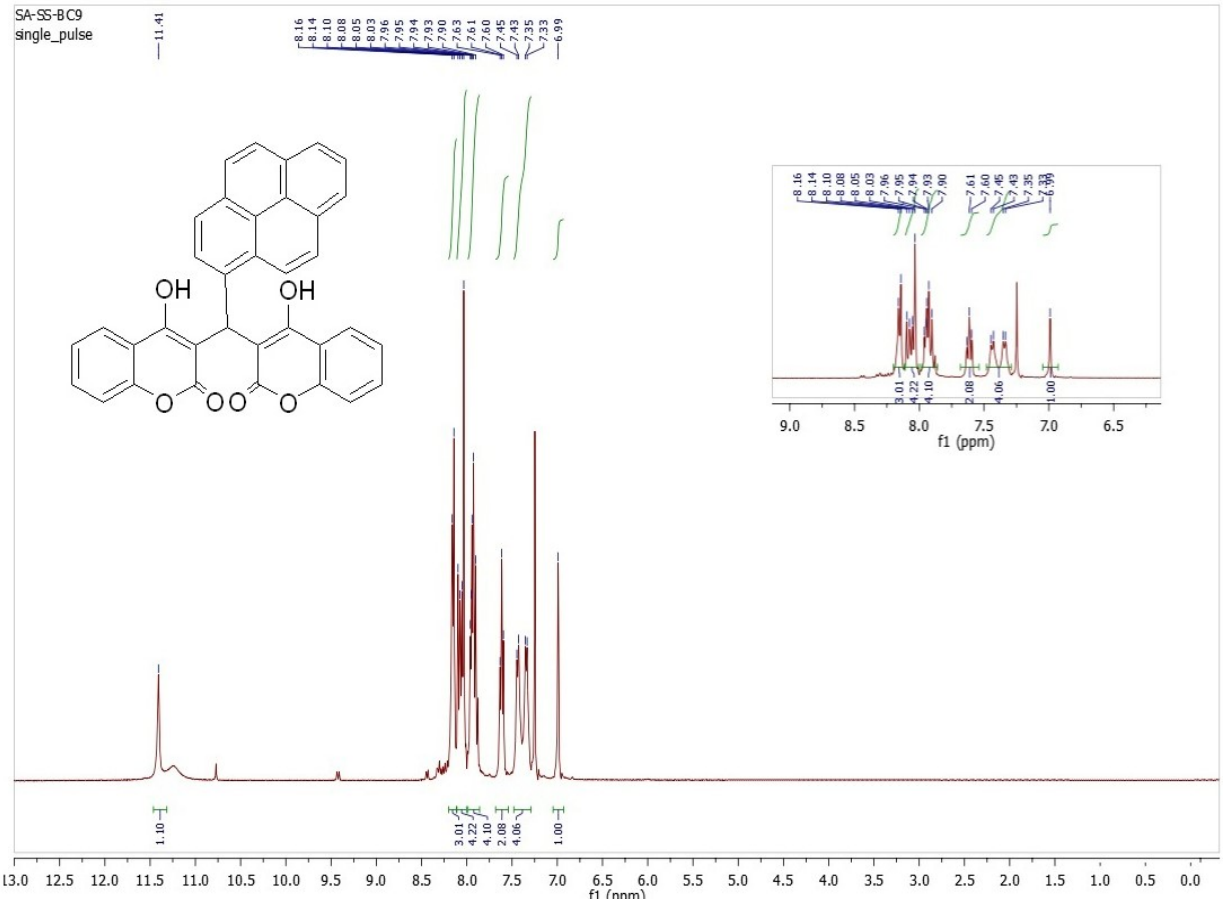
3,3'-((4-hydroxy-3,5-dimethoxyphenyl)methylene)bis(4-hydroxy-2H-chromen-2-one) **(9e)**

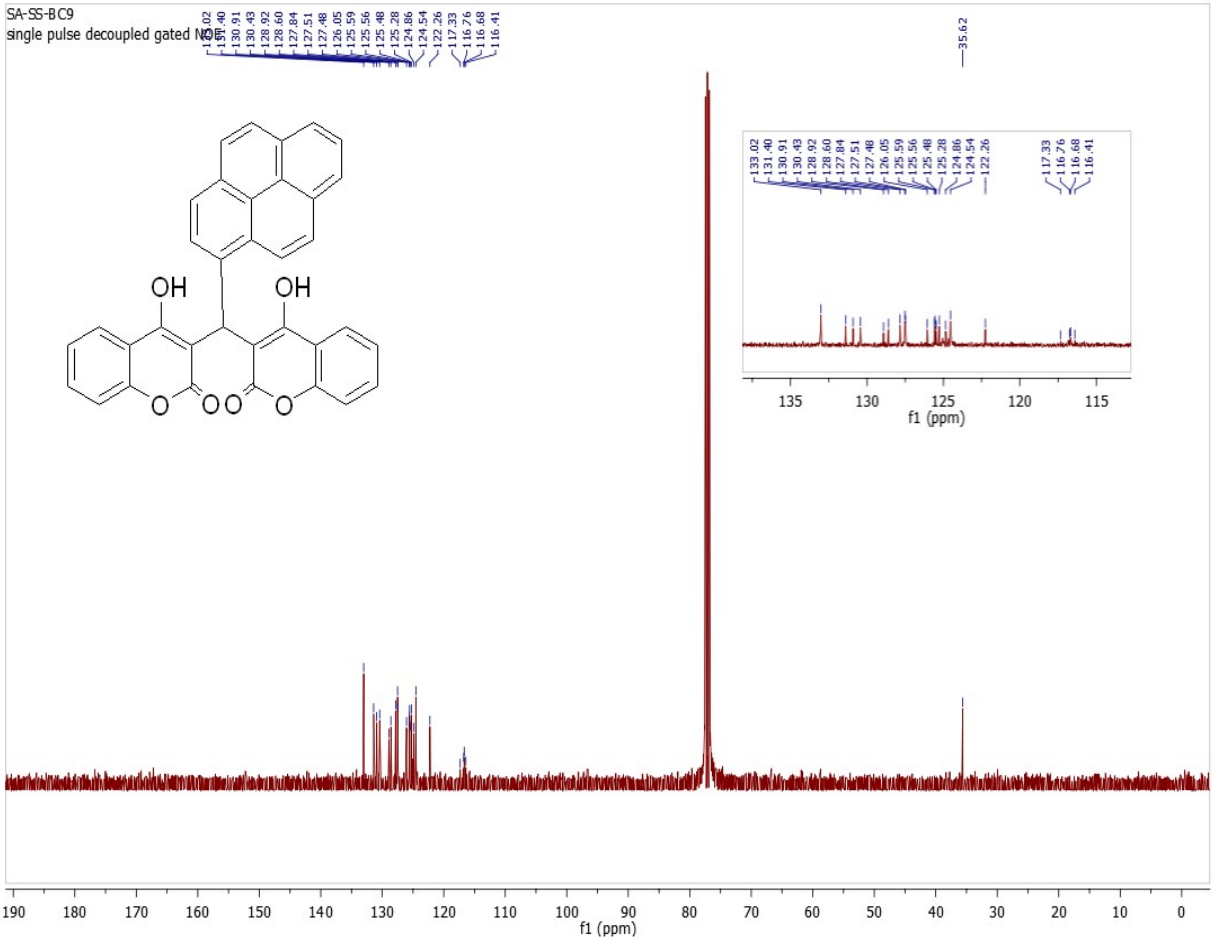
Yellow solid, yield: 79%, m.p. 192-194 ^{o}C[78], ^{1}H NMR (400 MHz, $CDCl_3$): δ 11.56 (s, 1H, OH), 8.08-8.01 (d, *J* = 25.7 Hz, 2H, Ar-H), 7.65 – 7.60 (m, 2H, Ar-H), 7.42-7.25 (d, *J* = 8.4 Hz, 4H, Ar-H), 6.41-6.40 (d, *J* = 1.3 Hz, 2H, Ar-H), 6.07 (s, 1H, CH), 3.74 (s, 6H, $2OCH_3$) ; ESI–MS (m/z): 488.11 [M^+].



3,3'-(pyren-1-ylmethylene)bis(4-hydroxy-2H-chromen-2-one) **(9f)**

Brownish-yellow solid, yield: 90%, m.p. 218-220 ^{o}C, ^{1}H NMR (400 MHz, $CDCl_3$): δ 11.41 (s, 1H, OH), 8.16-8.14 (d, *J* = 7.6 Hz, 3H, Ar-H), 8.10-8.03 (dd, *J* = 17.2, 8.4 Hz, 4H, Ar-H), 7.96 – 7.90 (m, 4H, Ar-H), 7.63-7.60 (t, *J* = 7.3 Hz, 2H, Ar-H), 7.45-7.33 (dd, *J* = 37.6, 7.4 Hz, 4H, Ar-H), 6.99 (s, 1H, CH). ^{13}C NMR (101 MHz, $CDCl_3$): δ 133.02, 131.40, 130.91, 130.43, 128.92, 128.60, 127.84, 127.51, 126.05, 125.59, 125.56, 125.48, 125.28, 124.86, 122.26, 117.33, 116.76, 116.68, 35.62; ESI–MS (m/z): 536.13 [M^+].





References:

1. Veisi, H.; Mohammadi, P.; Ozturk, T. Design, synthesis, characterization, and catalytic properties of g-C3N4-SO3H as an efficient nanosheet ionic liquid for one-pot synthesis of pyrazolo [3, 4-b] pyridines and bis (indolyl) methanes. *J. Mol. Liq.* **2020**, *303*, 112625.
2. Sheldon, R. A. (2018). Metrics of green chemistry and sustainability: past, present, and future. *ACS Sustainable Chemistry & Engineering*, *6*(1), 32-48.
3. Constable, D. J., Curzons, A. D., & Cunningham, V. L. (2002). Metrics to 'green'chemistry—which are the best?. *Green Chemistry*, *4*(6), 521-527.
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5. Sheldon, R. A. (2018). Metrics of green chemistry and sustainability: past, present, and future. *ACS Sustainable Chemistry & Engineering*, *6*(1), 32-48.