Electronic Supplementary Information

Theoretical Rationalisation of the Photophysics of TICT Excited State of Cinnamoyl-Coumarin Derivatives in Homogeneous and Biological Membrane Models

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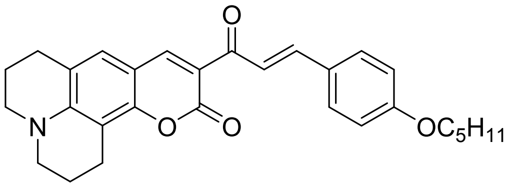
Synthesis and Characterization of the coumarin-benzylideneacetone probe (CC-OC5) by ^{1}H-NMR spectroscopy and mass spectrometry



Synthesis of CC-OC5. 200 mg (0.7 mmol) of C334 and 135 mg (0.7 mmol) of pentyloxybenzaldehyde and 3 drops of piperidine were dissolved in a mixture of solvents containing 5 mL of acetonitrile and 5 mL of ethanol. The mixture was stirred and heated to reflux for 24 hours in darkness. Once cooled, the mixture of solvents was removed under reduced pressure to afford an oily residue, which was which was purified by chromatography in column with dichloromethane to yield 165 mg (52%) of CC-OC5 as solid orange. ^{1}H-NMR δH (400 MHz, CDCl3): 8.46 (1 H, s), 8.06 (1 H, d, *J* 15.7), 7.79 (1 H, d, *J* 15.7), 7.62 (2 H, d, *J* 8.6), 7.00 (1 H, s), 6.89 (2 H, d, *J* 8.6), 3.99 (2 H, t, *J* 6.6), 3.35 (4 H, s), 2.90 (2 H, t, *J* 6.3), 2.77 (2 H, t, *J* 6.0), 2.04 – 1.92 (4 H, m), 1.80 (2 H, p, *J* 6.7), 1.42 (4 H, ddq, *J* 21.0, 14.3, 7.2, 6.8), 0.93 (3 H, t, *J* 7.0). UHPLC-MS/MS $[M+H]^+$: m/z 458.3; MS2 m/z 268.1.

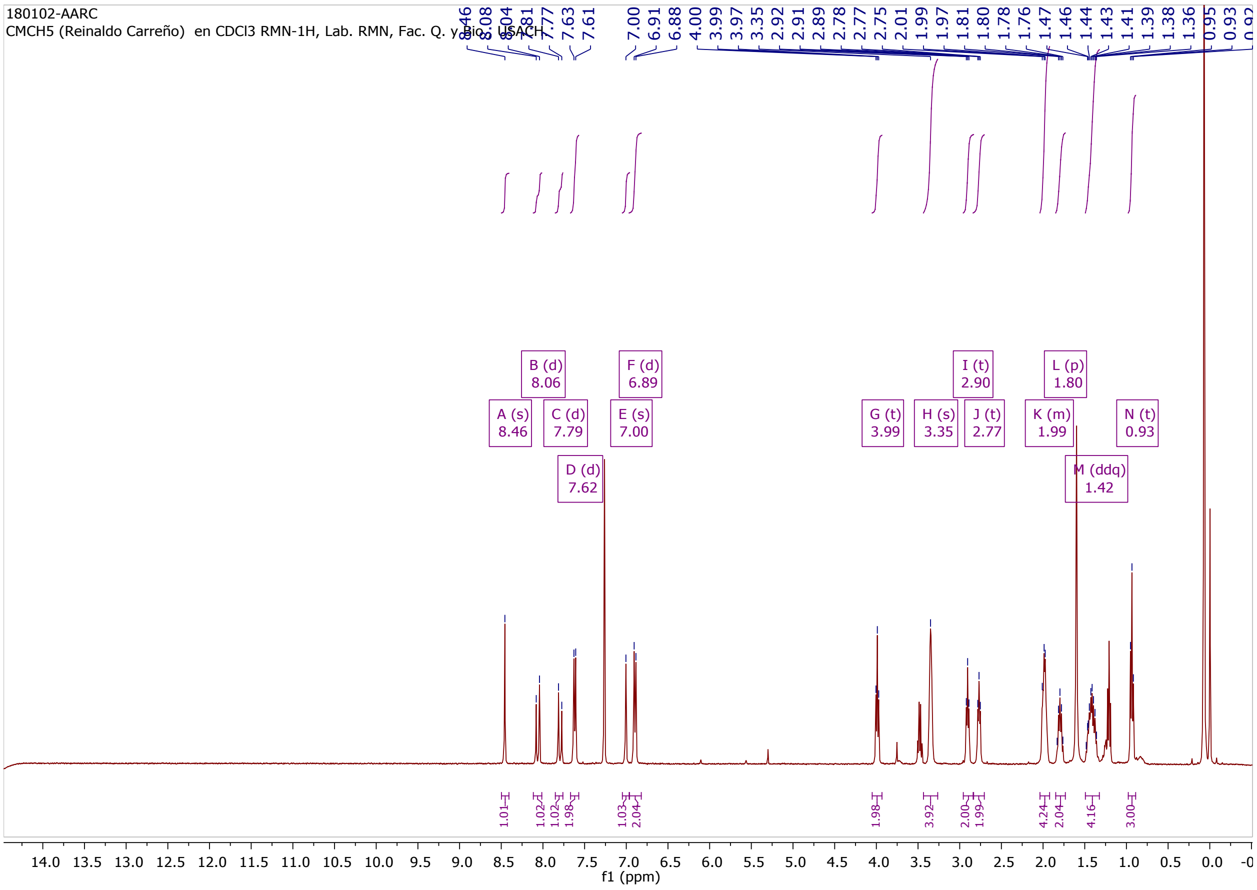


Figure S1. ^{1}H-NMR spectrum of CC-OC5 in $CDCl_3$.

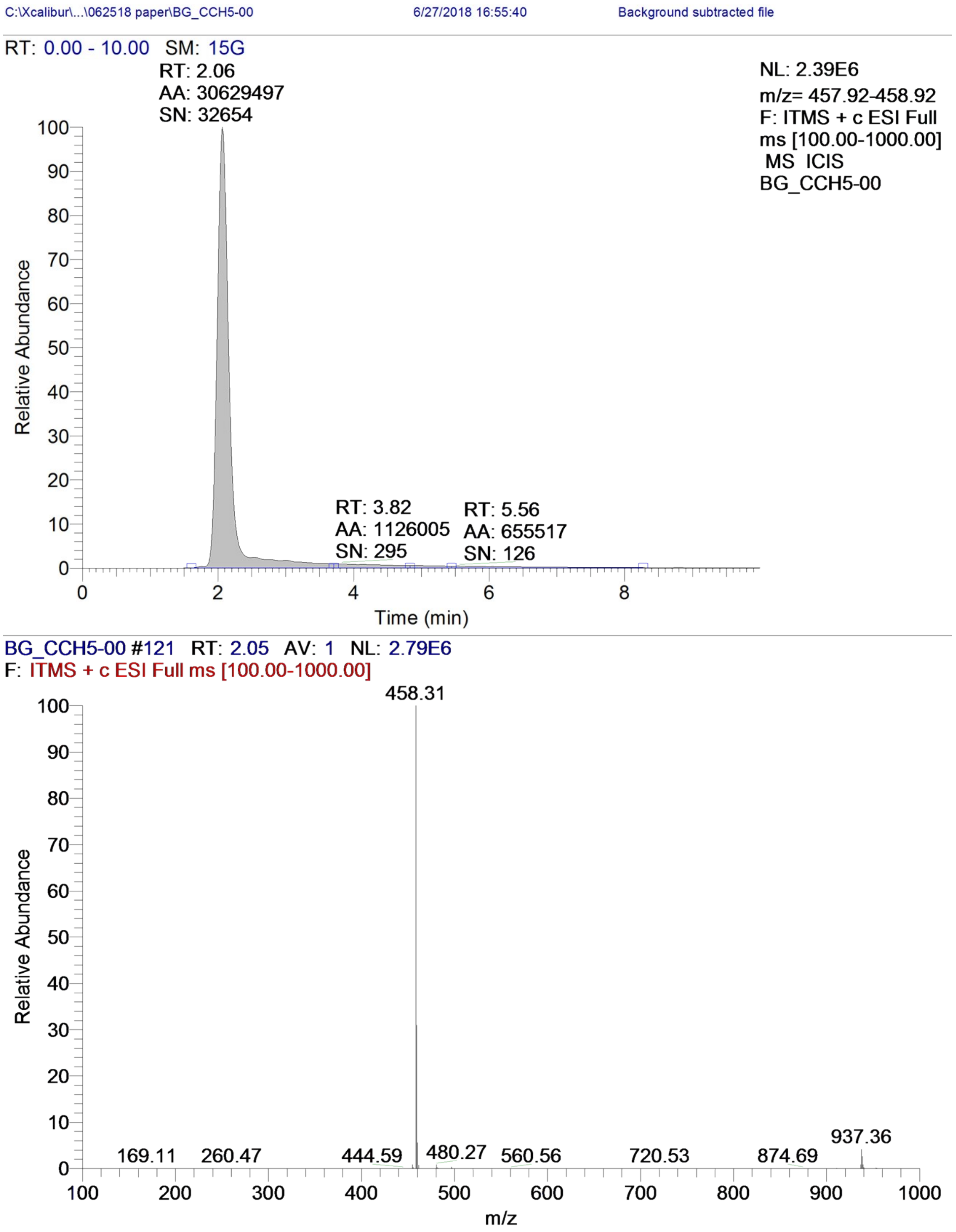


Figure S2. MS spectrum at retention time of 2.1 min corresponding to CC-OC5 recorded by UHPLC MS/MS.

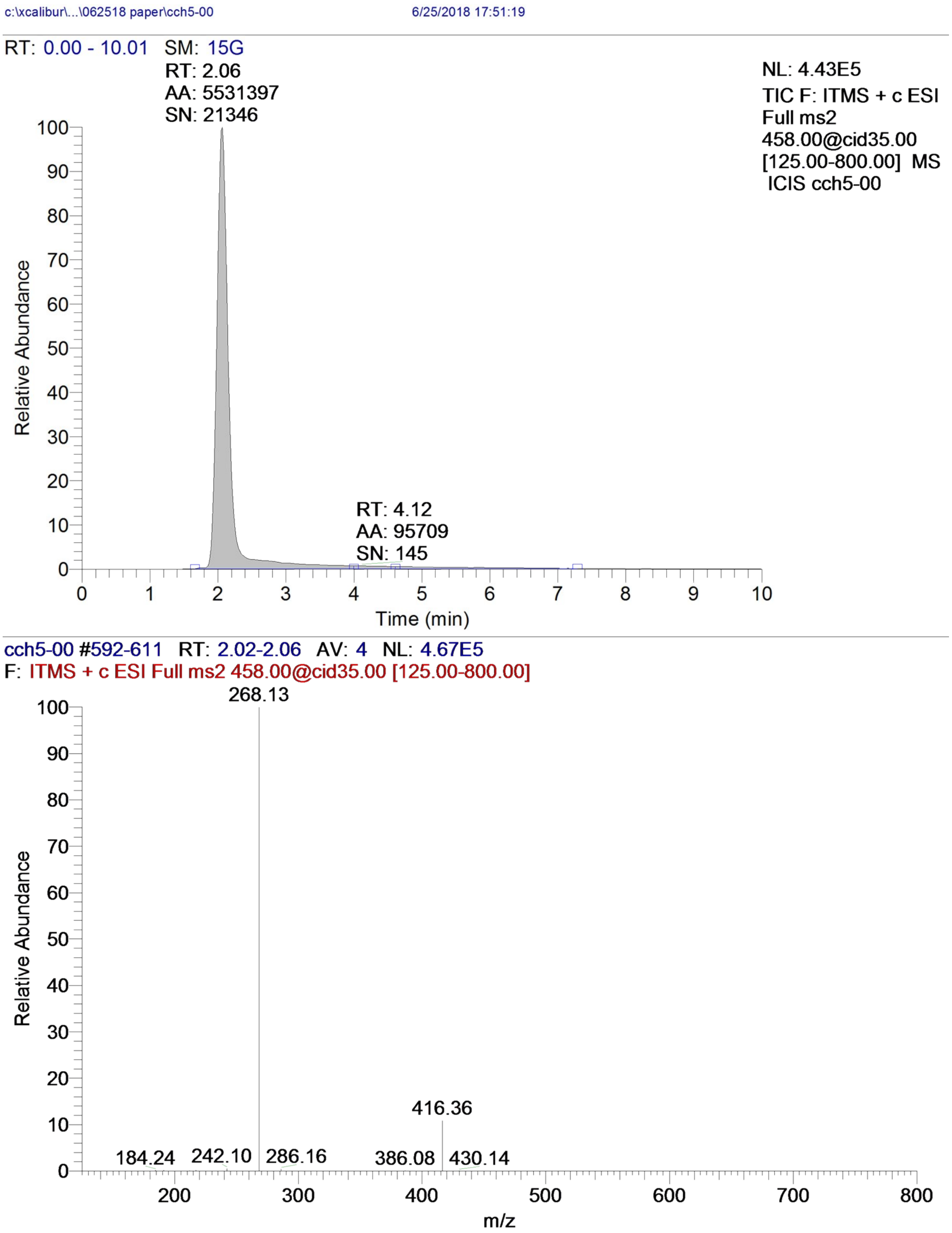
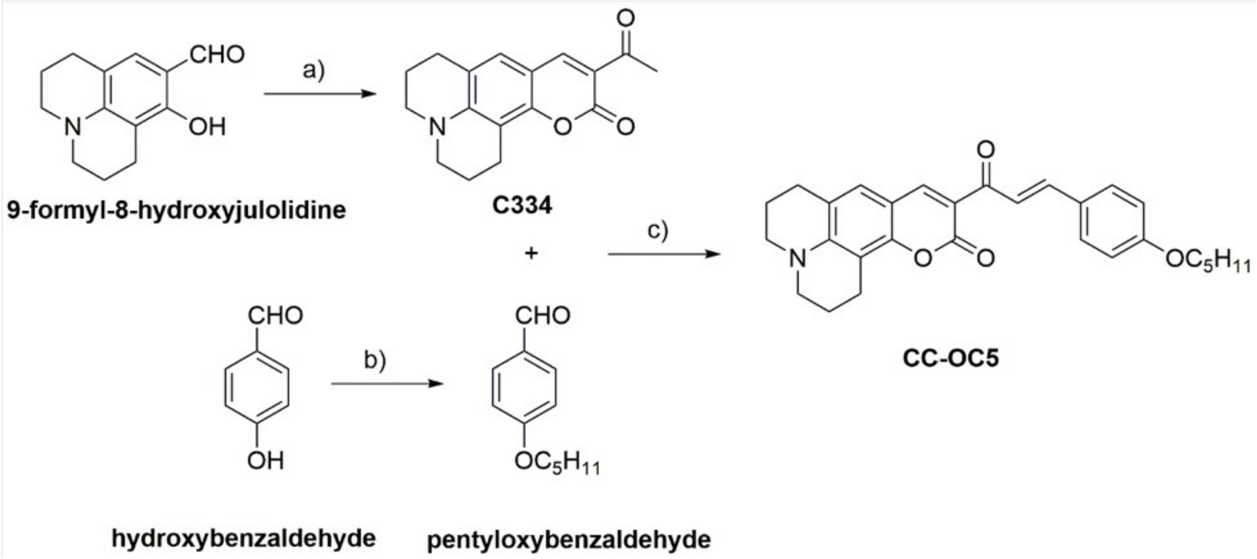
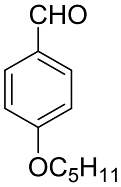


Figure S3. MS/MS spectrum of m/z 458.3 signal recorded by UHPLC MS/MS



Scheme S1. a) ethyl acetoacetate, piperidine, EtOH; b) pentylbromide, Na_2CO_3, ACN; c) piperidine, ACN/EtOH.



Synthesis of pentyloxybenzaldehyde. To a solution containing 3.05 g (25 mmol) of 4-hydroxybenzaldehyde and 30 mmol of pentylbromide dissolved in 40 ml of acetonitrile, were added 7.6 g (72 mmol) of sodium carbonate, the mixture was vigorously stirred and heated to reflux for 16 hours. Once cooled, the mixture was filtered and the solid exhaustively washed with dichloromethane. The mixture of solvents was removed under reduced pressure to afford an oily residue, which was purified by chromatography in column with gradient hexane (100%) to DCM (100%) to yield 3.8 g (79%) of product pentyloxybenzaldehyde as transparent oil. 1H-NMR δH (400 MHz, CDCl3): 9.88 (1 H, s), 7.83 (2 H, d, J 8.7), 6.99 (2 H, d, J 8.7), 4.04 (2 H, t, J 6.6), 1.82 (2 H, p, J 6.6), 1.50 – 1.35 (4 H, m), 0.94 (3 H, t, J 7.1). UHPLC-MS/MS $[M+H]^+$: m/z 193.1; MS^2 m/z 122.9

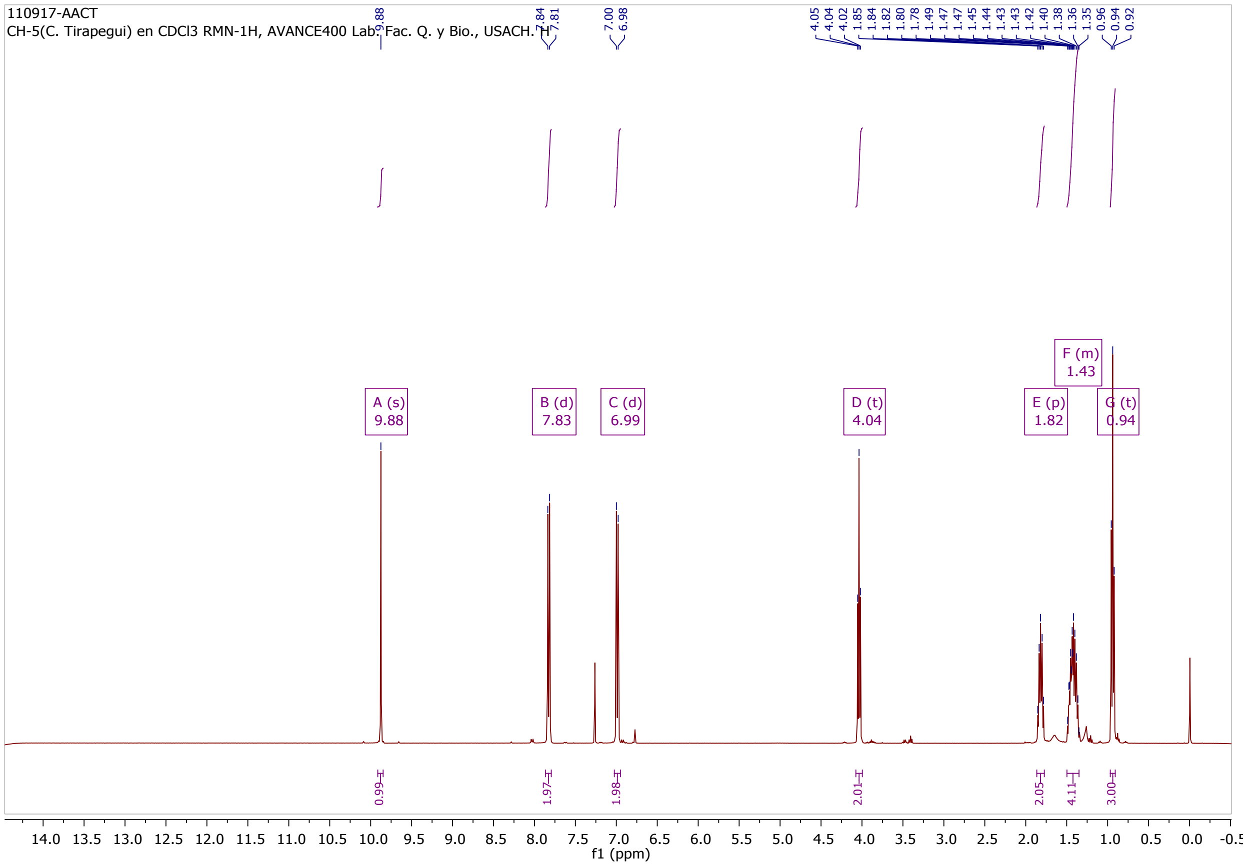


Figure S4. ^{1}H-NMR spectrum of pentyloxybenzaldehyde in CDCl$_3$

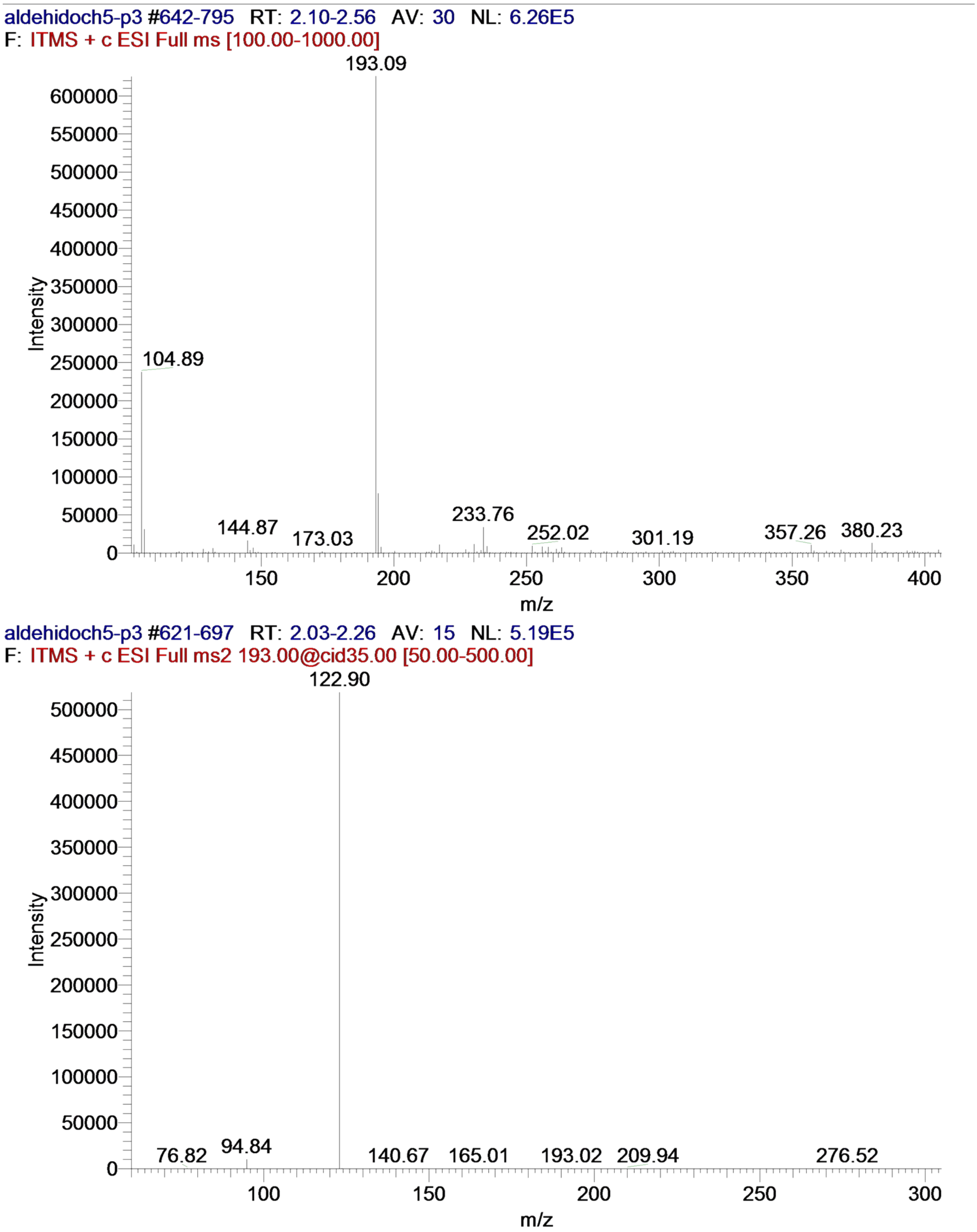
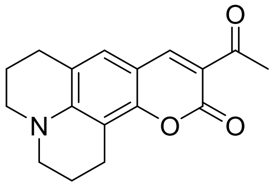


Figure S5. MS and MS^2 spectra of pentyloxybenzaldehyde obtained by UHPLC-MS/MS.



Synthesis of C_{334}. 2.17g (10 mmol) of 9-formyl-8-hydroxyjulolidine, 2.60 g (20 mmol) of ethyl acetoacetate (EAA) and 0.8 ml (8.1 mmol) of piperidine were dissolved in 50 mL of ethanol. The mixture was vigorously stirred and heated to reflux for 5 hours. After this, the solvent was reduced until precipitation of orange crystalline solid, which was filtered and washed three times with 10 mL of hexane to yield 2.7 g (95%) of C_{334} as solid yellow. ^{1}H-NMR δ_H (400 MHz, $CDCl_3$): 8.35 (1 H, s), 6.97 (1 H, s), 3.34 (4 H, q, *J* 5.3), 2.88 (2 H, t, J 6.4), 2.76 (2 H, t, *J* 6.3), 1.98 (4 H, qd, *J* 6.4, 3.0), 1.62 (3 H, s). mp 180-181°C (lit. 181-182°C)[1]. m/z (%): UHPLC-MS/MS $[M+H]^+$: m/z 284.2

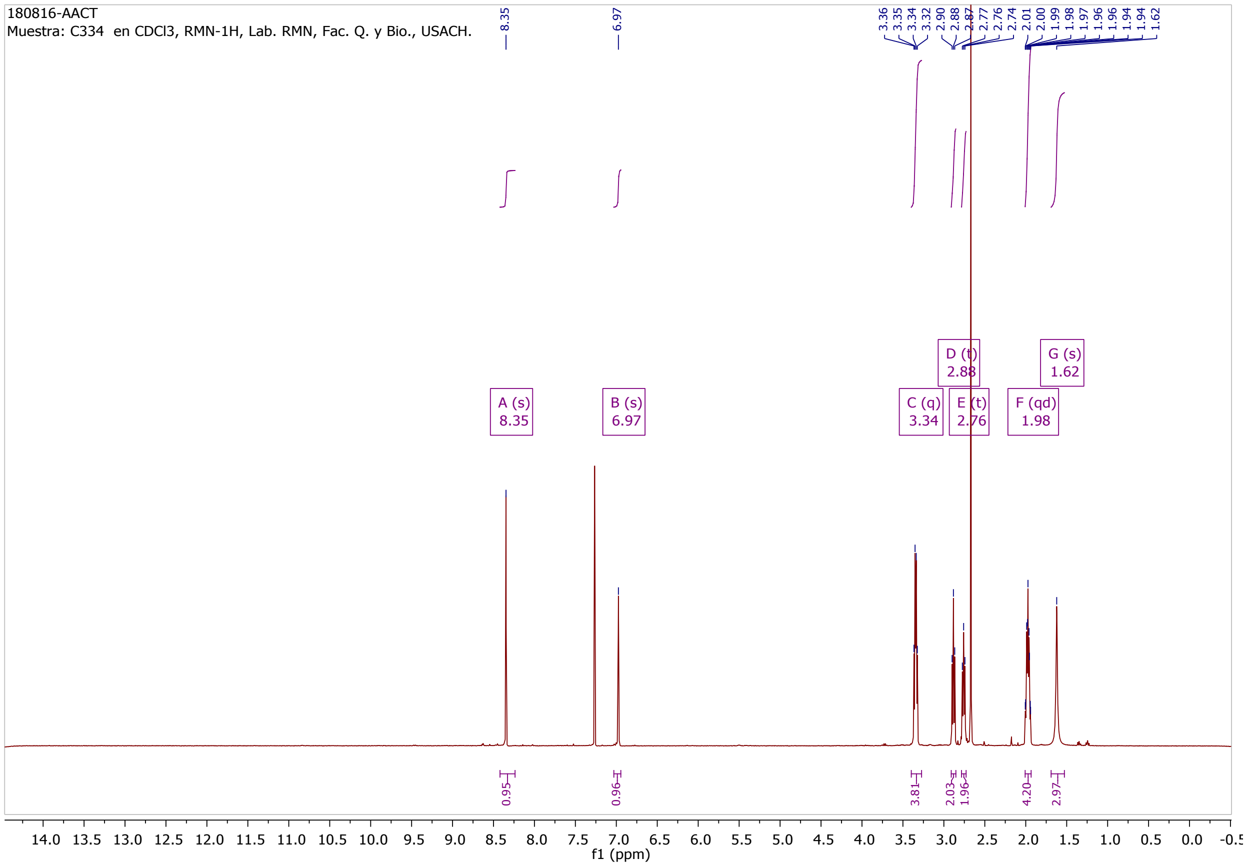


Figure S6. ^{1}H-NMR spectrum of coumarin 334 in $CDCl_3$

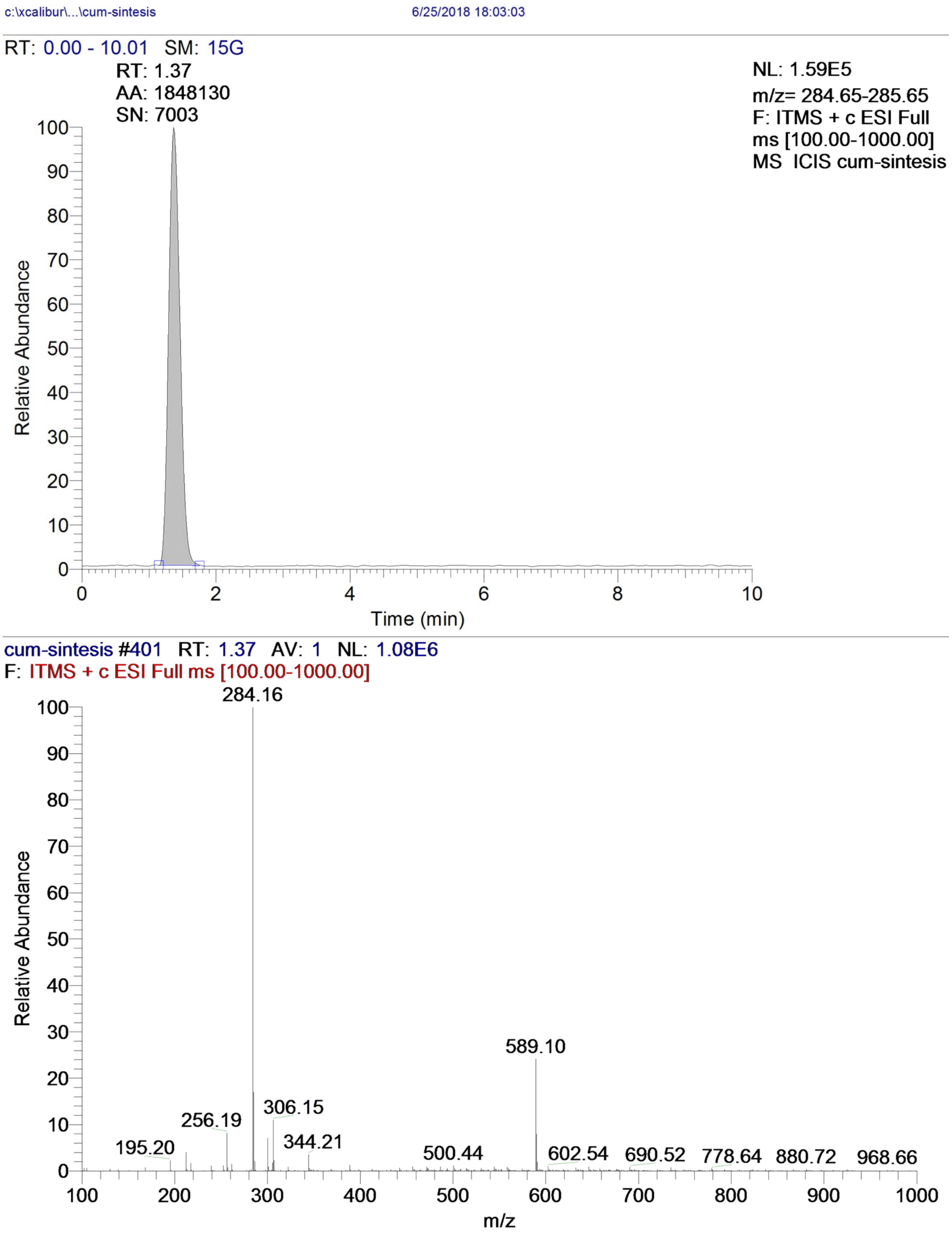


Figure S7. MS spectra of Coumarin 334 obtained by UHPLC-MS/MS.

Photophysical characteristics

Table S1. Photophysical properties of C_{334} in different solvents.

C_{334}	$\lambda_{absorption}^{max}$, **nm**	$\lambda_{emission}^{max}$, **nm**	$\Delta\bar{\nu}$, cm^{-1}	Φ_F
n-Hexane	431	439	423	0.70
Benzene	444	468	1201	0.82
Dichloromethane	451	483	1469	0.77
Acetonitrile	447	489	1922	0.64
Methanol	452	494	1881	0.61

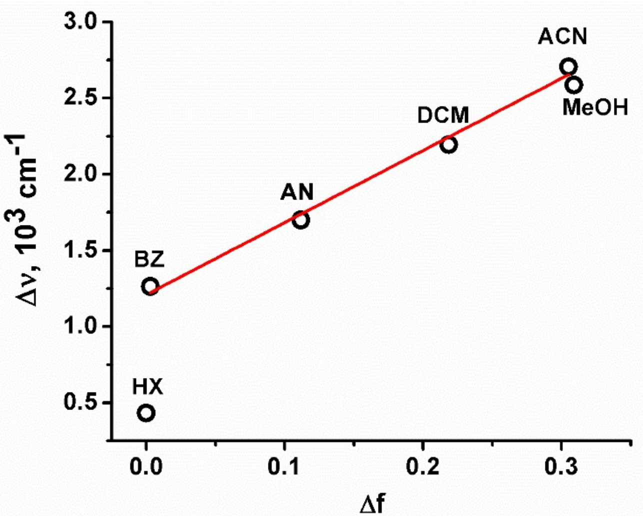


Figure S8. Representation of the stokes shift of CC-OC5 vs the polarity function of the solvent, Δf, for different solvents: hexane (HX), benzene (BZ), anisole (AN), dichloromethane (DCM), acetonitrile (ACN), methanol (MeOH).

Electronic absorption and emission spectra by TD-DFT of CC-OC5.

Table S2. Experimental and theoretical absorption wavelength (λ) and energy (E), and oscillator strength (*f*) for the calibration of functionals for CC-OC5. Theoretical values were calculated using the CPCM solvent model (methanol) and the 6-31G (d,p) basis set.

FUNCTIONAL	**Exp. λ(nm) (E/eV)**	**Theor. λ(nm) (E/eV) *f***	**Theor. Deviation (eV)**	**Functional type**
B97D	**478** (2.60)	**548** (2.26) *f*=0.807	**0.34**	**pure**
PBE1PBE	**478** (2.60)	**438** (2.83) *f*=1.260	**0.23**	**hybrid**
BKM	**478** (2.60)	**403** (3.08) *f*=1.429	**0.48**	**hybrid**
M06	**478** (2.60)	**433** (2.86) *f*=1.304	**0.26**	**hybrid**
B3LYP	**478** (2.60)	**454** (2.73) *f*=1.187	**0.13**	**hybrid**
CAM-B3LYP	**478** (2.60)	**387** (3.21) *f*=1.469	**0.61**	**range-separated hybrid**
wB97	**478** (2.60)	**358** (3.47) *f*=1.462	**0.87**	**range-separated hybrid**
wB97xD	**478** (2.60)	**381** (3.25) *f*=1.469	**0.65**	**range-separated hybrid**

Table S3. Theoretical wavelength (λ) and energy (E), and oscillator strength (*f*) for both absorption and emission of CC-OC5 in different solvents, using the B3LYP/6-31G (d, p) level of theory, and the C-PCM solvent model.

SOLVENT	**Theor. Absorption λ(nm) (E/eV) *f***	**Theor. Emission λ(nm) (E/eV) *f***
n-Hexane	**437** (2.83) *f*=1.298	**462** (2.68) *f*=1.101
Benzene	**442** (2.81) *f*=1.384	**468** (2.64) *f*=1.144
Dichloromethane	**453** (2.74) *f*=1.321	**498** (2.48) *f*=1.265
Acetonitrile	**456** (2.72) *f*=1.285	**506** (2.45) *f*=1.335
Methanol	**458** (2.74) *f*=1.292	**508** (2.44) *f*=1.335

Molecular orbital surface of CC-OC5 by twisting in δ (C14-C18-C19-C21)

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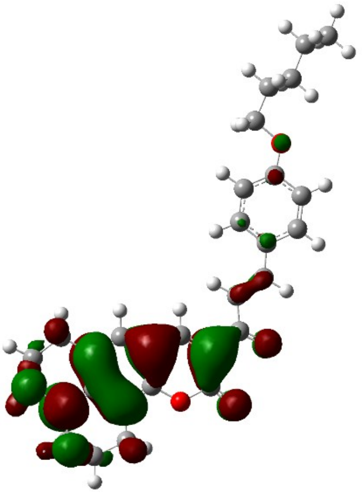	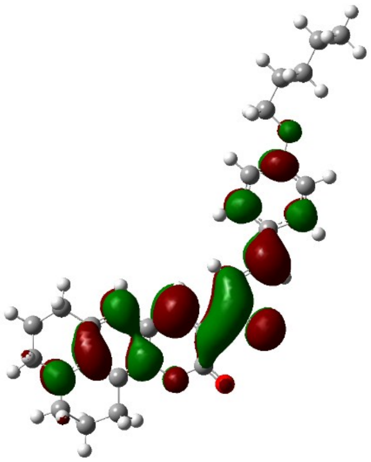
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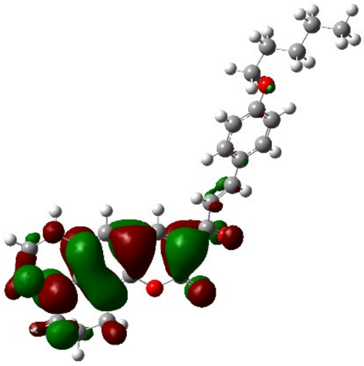	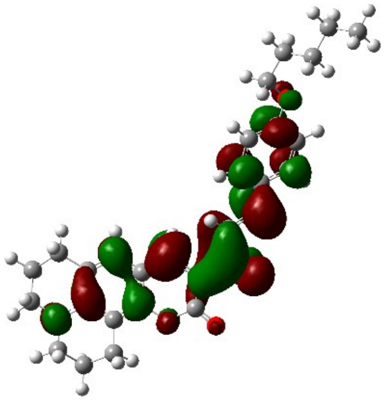
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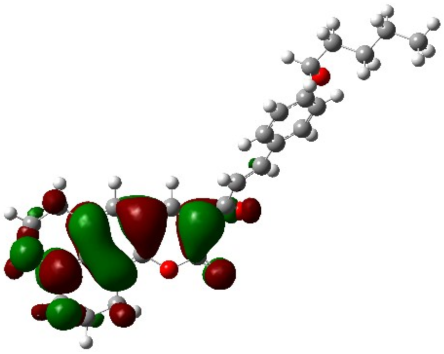	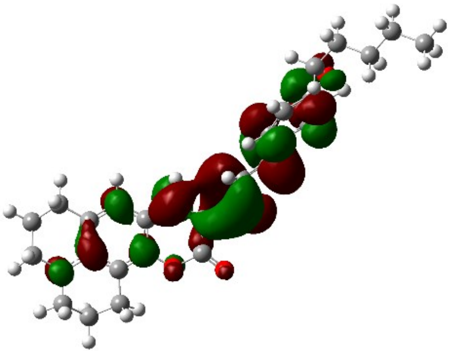
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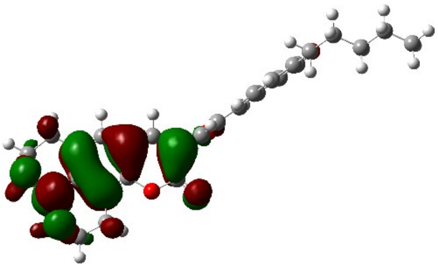	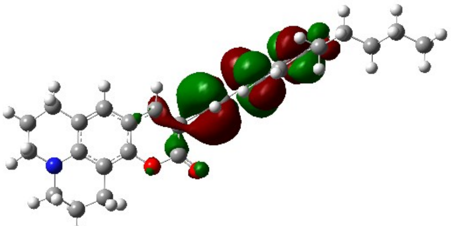

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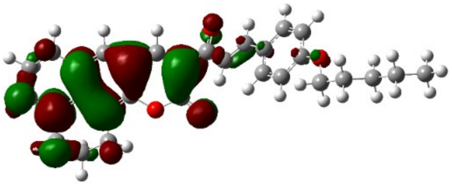	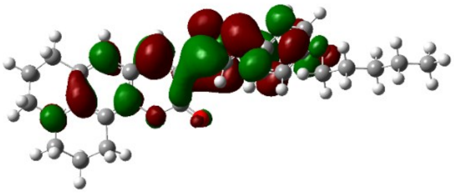
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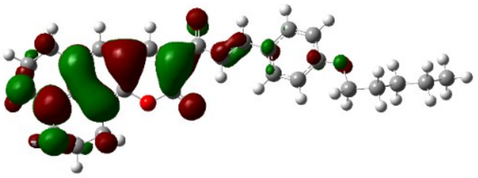	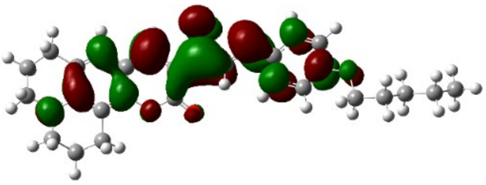
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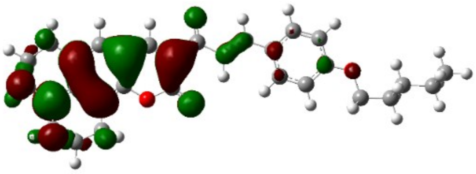	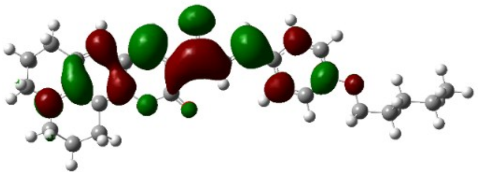
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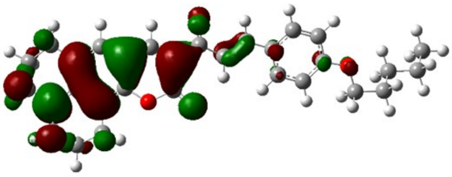	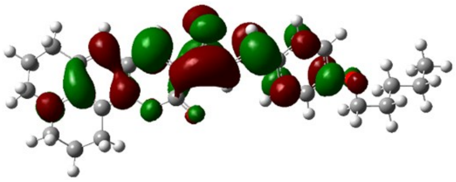
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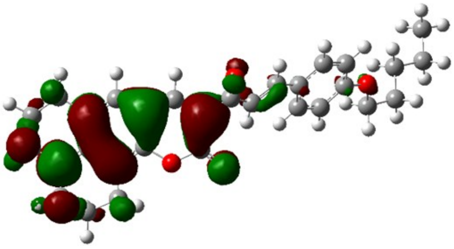	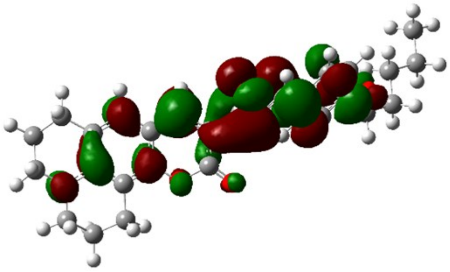
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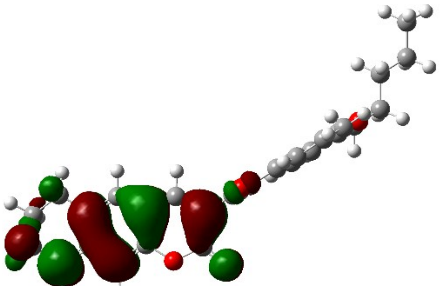	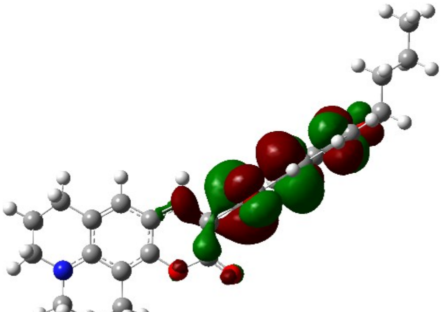

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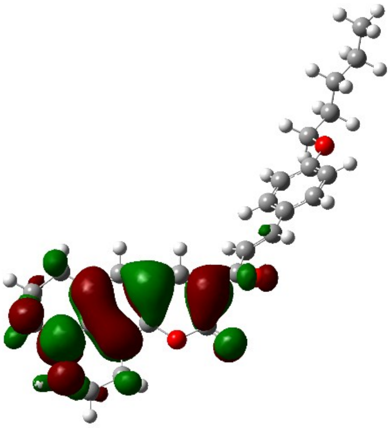	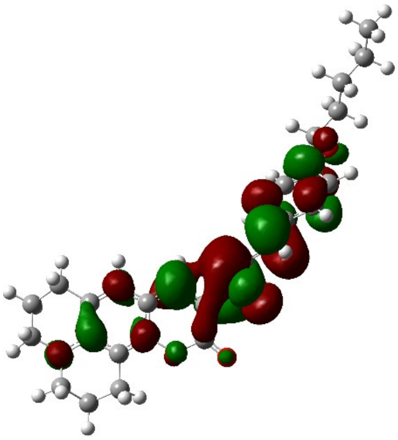
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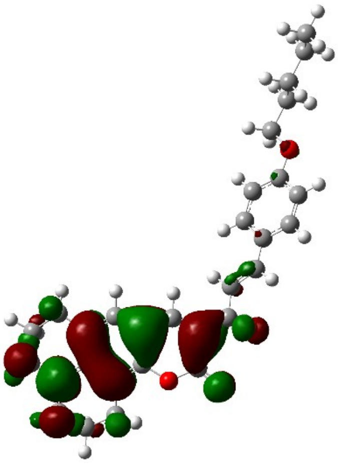	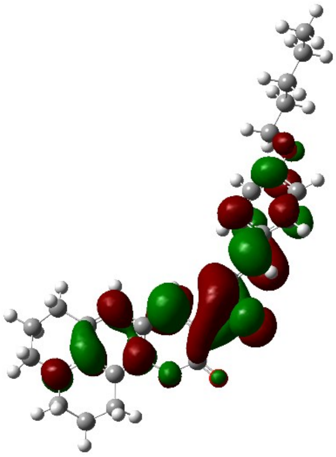
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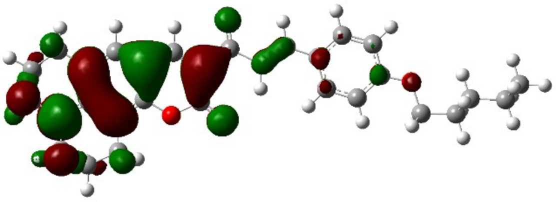	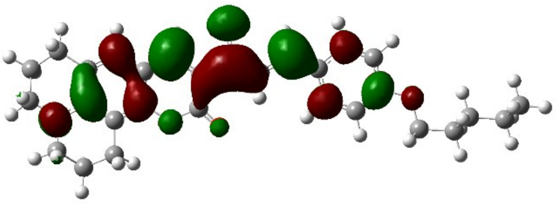

Figure S9. Molecular orbital surfaces involved in the electronic transitions of CC-OC5 by twisting in δ (C14-C18-C19-C21) calculated at the B3LYP/6-31G (d, p) level of theory in methanol.

Molecular orbital surface of CC-OC5 by twisting in δ (C21-C22-C23-C24)

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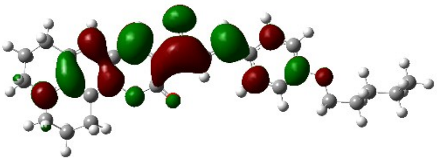	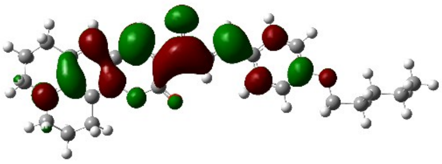
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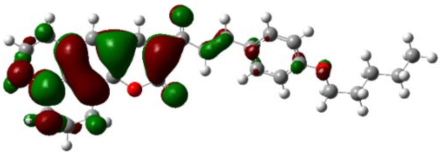	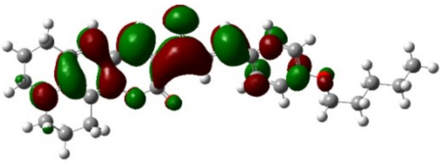
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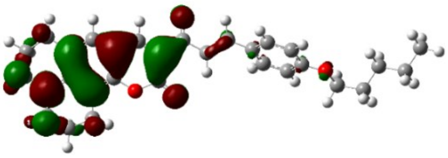	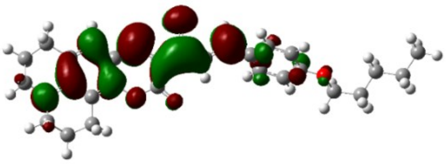
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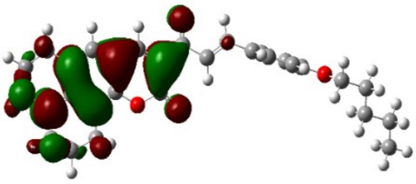	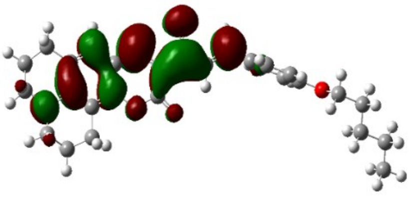

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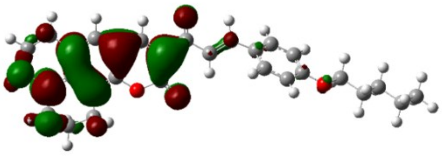	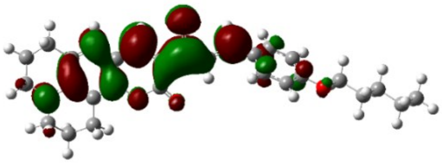
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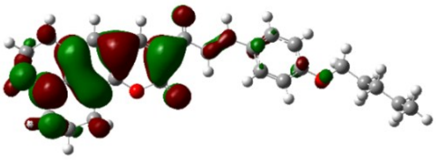	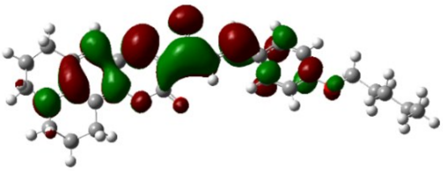
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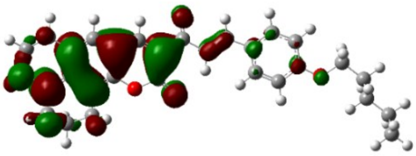	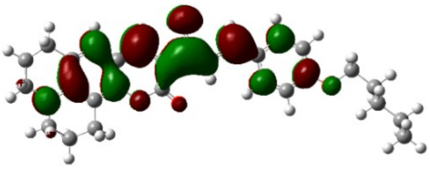
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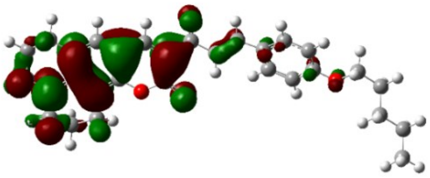	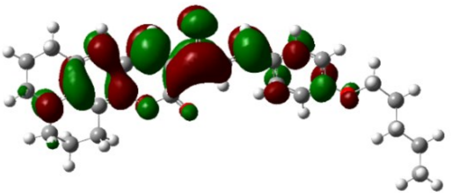
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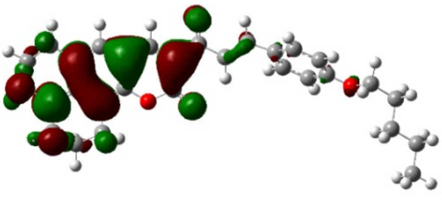	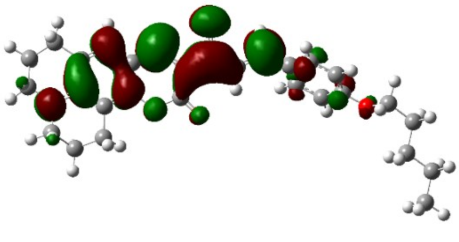
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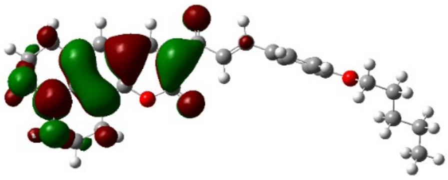	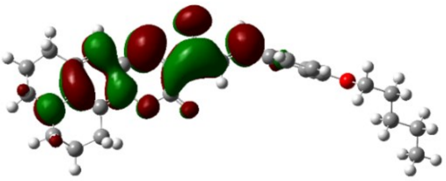

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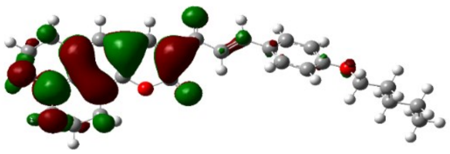	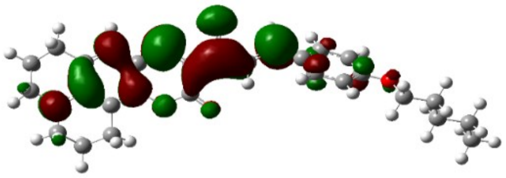
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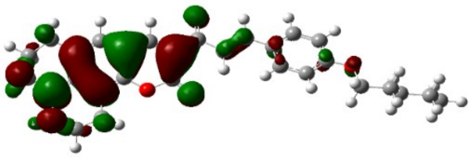	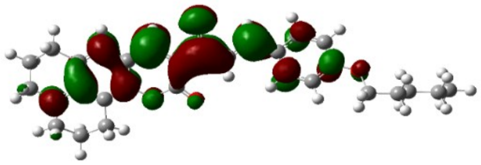
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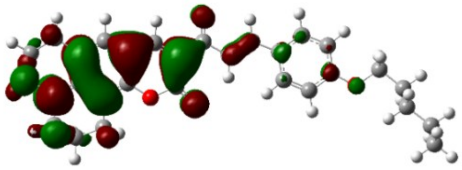	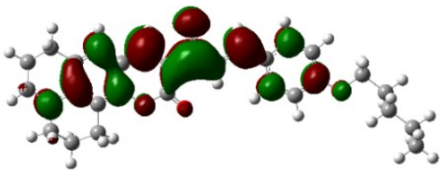

Figure S10. Molecular orbital surfaces involved in the electronic transitions of CC-OC5 by twisting in δ (C21-C22-C23-C24) calculated at the B3LYP/6-31G (d, p) level of theory in methanol.

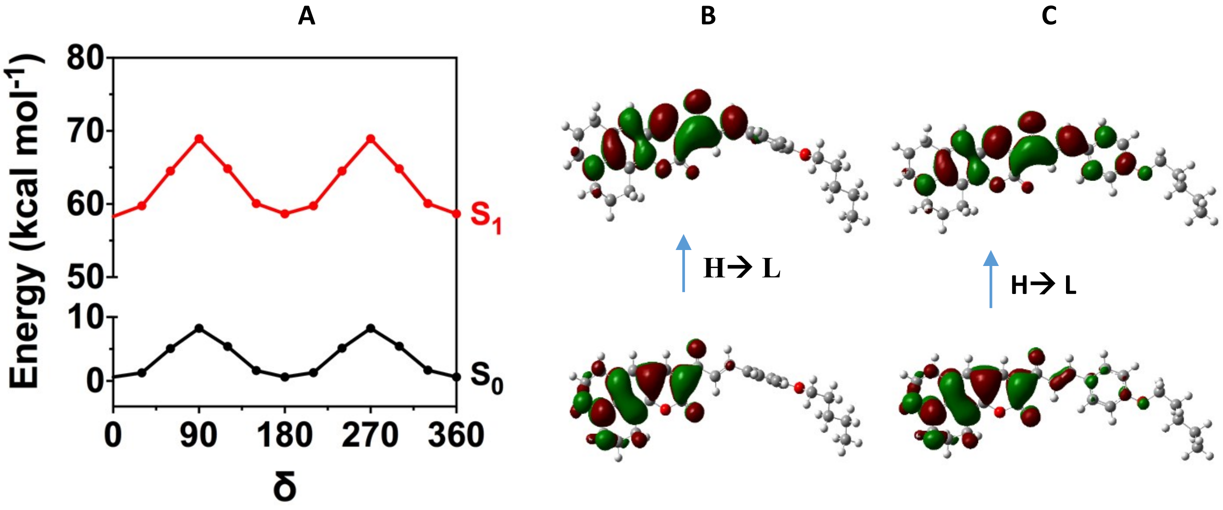

Figure S11. Potential energy profile for conformational analysis of these twisting angle φ (C21-**C22-C23**-C24) for ground state (black) and the lowest excited state (red) (A), frontier molecular orbital surfaces for conformational angle energy φ = 90º (B), and φ = 180º (C). All the calculations were performed at the B3LYP/6-31G (d,p) level of theory in the solution phase (methanol).

Molecular orbital surface by C_{334}.

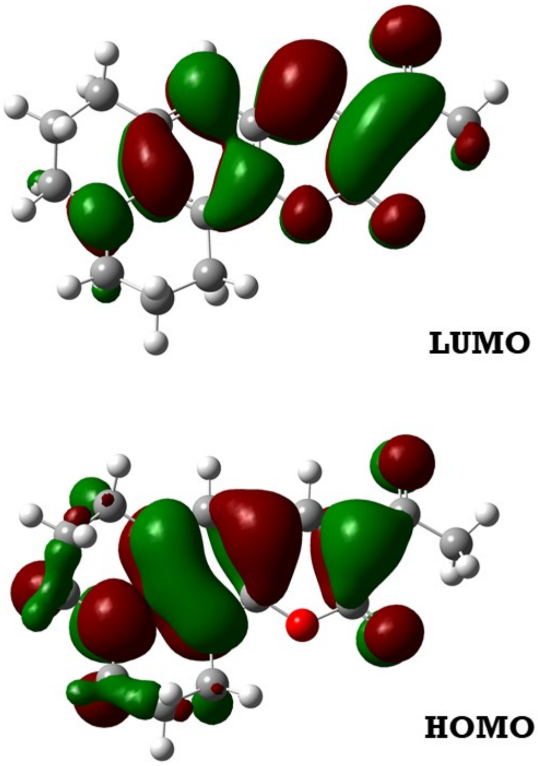

Figure S12. Molecular orbital surfaces involved in the electronic transitions of C_{334} calculated at the B3LYP/6-31G (d, p) level of theory in methanol using C-PCM solvent model.

Root mean square fluctuations calculated by molecular dynamics

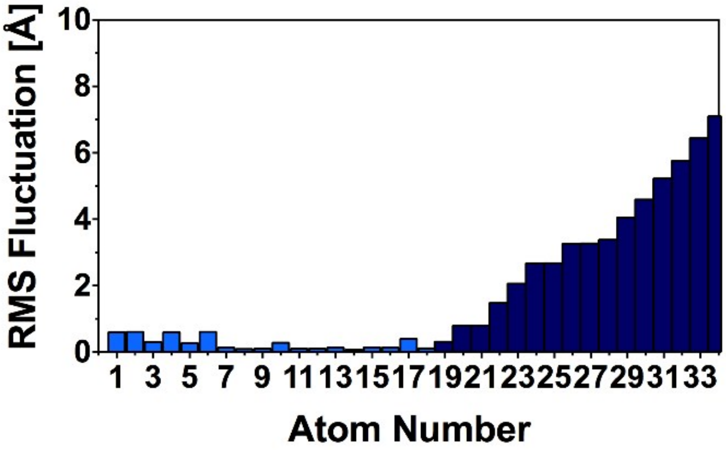

Figure S13. Fluctuations of all atoms of COH-OC5, during classic molecular dynamic simulation in water (100 ns).